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Development and application of diffusive gradients in thin films (DGT) for in situ monitoring of emerging contaminants in aquatic environments

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Abstract

There has been increasing concern about the environmental release and dispersal of emerging contaminants (ECs) and their potential risks to human and ecosystem health. The in situ passive sampling tool, diffusive gradients in thin films (DGT), has been developed as a promising alternative to traditional grab sampling in environmental research of ECs, such as pharmaceuticals, endocrine disrupting chemicals (EDCs), and some types of flame retardants. This thesis explored the role of DGT in determining ECs and understanding their sources, fate and impact in aquatic environments.

The property range of organic compounds which can be routinely sampled with the present design of DGT device (PTFE membrane filter, agarose gel diffusion layer, and HLB binding layer) was investigated. Sorption experiments and DGT deployment with 9 model chemicals [organophosphate esters (OPEs) with a wide range of log K_{OW} (0.8−9.5), molecular weight (182−435 Da)] and different functional groups showed compounds with high hydrophobicity and aromatic rings are prone to retention on membrane filters, which slows the transport of chemical to the binding resin of the sampler. The limitation of the current DGT device for some trace organics is adsorption in the diffusion layer, mainly in the membrane filter. However, it is possible to extend the DGT technique for a wider range of chemicals, for example, by replacing the current DGT membrane filter with a new type of membrane filter which does not interact with target analytes.

The potential effects of biofouling and post-deployment sample storage on DGT measurements were systematically investigated. Biofilms generated at the surface of DGT devices (8-day and 15-day) in summer and winter from a typical urban wastewater treatment plant were tested with 13 ECs; this study showed no effect on DGT measurements for most compounds. Four storage methods up to 2-month were evaluated; this study showed that intact samplers can be kept for up to 2-months at refrigerated temperature (4 °C) without significant effect on the measured concentration of the compounds, but if no refrigerators were available, keeping binding gels in elution solvent at room temperature would achieve comparable results.

DGT and grab sampling were used together to study sources and environmental fate of ECs in a dynamic river catchment, the River Thames in the United Kingdom. For chemicals that were relatively stable in the rivers, DGT and grab sampling provided

equally good representativeness. For chemicals that showed high dynamic variation in water bodies, the DGT provided a better integral of loadings and exposure than grab sampling. It took a similar time to set up and collect the DGT passive sampling system and to collect grab samples. However, for later storage and sample treatment, DGT is much more space-, cost- and time-effective.

DGT, for the first time, was combined with a water quality model (LF2000-WQX) to study sources and environmental fate of ECs, taking trimethoprim as a case study. The model needs the following key input information for the EC: per capita emission, WWTPs and in-river removal rates. DGT measurements in the River Thames network were used to assess the ability of the model to predict reasonable concentrations. This study showed that LF2000-WQX is suitable for predicting point-source ECs; predicted concentrations agreed very well with DGT measurements in winter and the model performance can be improved by improving in-river removal rate, i.e., using different in-river removal rates considering local environmental conditions such as DOC in different river reaches.

The work in this thesis is a step forward to understand the current performance of the DGT sampler and to explore its role in studying organic contaminants. It has shown that DGT is an effective tool for studying environmental issues of trace organic contaminants.

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List of papers

This thesis contains a number of papers that are published, submitted and in preparation for submission to appropriate journals, which are corresponding to Chapters 3–6 of the thesis. They are listed below, with brief description of the contribution made by the candidate and co-authors.

I. **WANG, R.**, ZOU, Y., LUO, J., JONES, K. C. & ZHANG, H. 2019. Investigating potential limitations of current diffusive gradients in thin films (DGT) samplers for measuring organic chemicals. *Analytical Chemistry*, 91, 12835-12843. (**Chapter 3**)
WANG, R. proposed the research question, did the experiments and data analysis and wrote the manuscript, with supervision from Jones, K. C. & Zhang, H. Zou, Y. and Luo, J. gave suggestions on the experiment preparation.

II. **WANG, R.**, JONES, K. C. & ZHANG, H. Monitoring organic pollutants in waters using diffusive gradients in thin films (DGT) technique: investigations into the possible effects of biofouling and degradation. *For submission to Environmental Science & Technology.* (**Chapter 4**)
WANG, R. did the experiments and data analysis and wrote the manuscript, with supervision from Jones, K. C. & Zhang, H.

III. **WANG, R.**, JUERGENS, M. D., BOWES, M. J., JONES, K. C. & ZHANG, H. Emerging contaminants in the River Thames (U.K.) using diffusive gradients in thin films (DGT) and traditional grab sampling. In preparation. (**Chapter 5**)
WANG, R. did the fieldwork, sample and data analysis and wrote the manuscript, with supervision from Jones, K. C. & Zhang, H. Juergens, M. D. and Bowes, M. J. supported the fieldwork.

IV. **WANG, R.**, RIZZO, CLARISSA., KELLER, V., JONES, K. C. & SWEETMAN, A. J. 2019 Assessing the suitability of the LF2000-WQX model in predicting environmental concentrations of antibiotics of high environmental concern. In preparation. (**Chapter 6**)
WANG, R. did data collection for the model, data analysis and wrote the manuscript, with supervision from Jones, K. C. & Sweetman, A. J. Rizzo, C. and Keller, V. ran the model.

List of Appendices

I. List of chemicals tested for DGT technique.

II. Abstract of oral presentation at DGT conference: **WANG, R.**, JONES, K. C. & ZHANG, H. Understanding potential limitations of the current DGT passive sampler for organic chemicals in aquatic systems. DGT Conference 2019. Vienna, Austria. September 18–20, 2019.

III. Co-authored paper: ZOU, Y. T., FANG, Z., LI, Y., **WANG, R.**, ZHANG, H., JONES, K. C., CUI, X. Y., SHI, X. Y., YIN, D., LI, C., LIU, Z. D., MA, L. Q. & LUO, J. 2018. Novel method for in situ monitoring of organophosphorus flame retardants in waters. Analytical Chemistry, 90, 10016-10023.

Chapter 1: Introduction

1.1 Incentive for the study

Water is at the core of sustainable development and clean water is essential for residential, commercial, industrial, agricultural and electricity water use (United Nations, 2020). However, water security can be easily threatened by pollution from human activities, such as agriculture, urban runoff and discharges of treated and untreated wastewaters (Sánchez-Avila et al., 2013). The vulnerability is also exacerbated by the rapid population increases and climate change. Under climate change effects, higher water temperature and variations in runoff are likely to produce adverse effects in water quality (O'Reilly et al., 2003, Hurd et al., 2004). Lower water levels in rivers and lakes may lead to the re-suspension of bottom sediments and releasing contaminants (Atkinson et al., 1999). Increasing intense rainfall may result in more contaminants being washed into water bodies (Xing et al., 2013, Petersen et al., 2012). Water quality monitoring and management are therefore necessary for human and ecosystem health and sustainable development of human society and economy. Water quality monitoring and assessment are required by authorities and governments (Rahman et al., 2011, WHO, 2011). Until now, water quality monitoring has still been heavily relying on traditional grab sampling, followed by laboratory-based extraction and instrumental analysis to determine contaminant concentrations (Vrana et al., 2005). However, this approach has limitations in terms of (i) high temporal and spatial resolution that may be achieved at reasonable cost, (ii) collecting, preserving, transporting and pre-treatment of samples that may be time-effective and simple to practitioners, and (iii) the information on bioavailability that may be obtained. Emerging in situ passive sampling tools such as diffusive gradients in thin films (DGT) can be a promising alternative in reducing the above limitations. Furthermore, because passive sampling technique does not need power or technical specialists, it has much broader potential of application, not only on the local scale but also on continental and global scales (Vrana et al., 2005). Some regulations such as the EU Water Framework Directive (2000) encourages their development: “Novel monitoring methods such as passive sampling and other tools show promise for future application, and their development should therefore be pursued.”

Water quality monitoring has mainly focussed on more abundant and bulk constituents—such as nutrients, biochemical oxygen demand (BOD), metals—but now we know more

and more there is also a wide array of trace organic contaminants too (Rasheed et al., 2019). For example, emerging contaminants (ECs) are a large and expanding array of relatively polar anthropogenic compounds, such as pharmaceuticals, endocrine disrupting chemicals (EDCs), some types of flame retardants, etc. (Rasheed et al., 2019). Surface water systems, such as rivers, are continually receiving ECs and affected by their breakdown products, but their impacts on human and ecosystem health are largely unknown (Johnson and Sumpter, 2015). Only in recent years have they drawn concerns from environmental authorities and scientists (Sarkar et al., 2019). Authorities, such as the U.S. Environmental Protection Agency (EPA), encourage to develop new analytical methods and tools for understanding and managing organic contaminants [e.g., EPA's Per- and Polyfluoroalkyl Substances (PFAS) Action Plan].

DGT has proved its strength in studying inorganics in different fields, including water quality monitoring, chemical speciation, dynamic processes, bioavailability and high spatial resolution measurements (Davison et al., 2016). Compared with the other passive samplers, DGT is relatively unaffected by hydrodynamic conditions when sampling analytes in waters so field calibrations are not necessary in most natural environmental conditions (Warnken et al., 2006, Challis et al., 2018b). Recently, it has emerged as a promising tool for researching trace organic contaminants. Over 150 organic compounds from different families—such as pharmaceuticals (Chen et al., 2012), pesticides (Li et al., 2019a), endocrine disrupting chemicals (Chen et al., 2018)—have been tested with DGT. These studies show promising new research areas of (i) developing DGT into a powerful monitoring tool for water quality monitoring, and (ii) using DGT as a research tool to understand the source, fate and impact of trace organic contaminants, especially ECs, in aquatic environments.

There is a major research space for the DGT technique for trace organics, but also some uncertainties and questions that need resolving (see more details in **2.8 Research gaps /needs**). A growing number of organic chemicals have been tested and validated for the DGT technique. However, re there limitations or boundaries for using the DGT sampler in the 'chemical space' (i.e., for chemicals of widely different properties)? Since DGT development and application for trace organic pollutants is a relatively new field, little work has addressed the effect of biofouling on the DGT for trace organic pollutants. In the literature, the DGT samplers were mostly treated/extracted immediately after retrieval. Little attention has been paid to analyte stability or sample storage although it may affect

the data quality (Hillebrand et al., 2013). Until now, research into DGT for organics has mainly focused on development of new configurations for various organic analytes. Applying the DGT to rivers at a catchment scale is necessary to test and demonstrate its reliability and challenges in a dynamic water system, with different environmental conditions.

1.2 Research aims

The aim of this project was to explore the role of DGT in determining trace organic contaminants, especially ECs, and understanding their sources, fate and impact in aquatic environments. Specific objectives were:

(i) to delineate potential limitations of the standard DGT samplers for organic chemicals with a wide range of physicochemical properties;
(ii) to investigate practical constrains, the effects of biofouling and within-sampler degradation, in order to propose appropriate sampling and handling protocols of DGT in the field;
(iii) to apply DGT in a dynamic water system (the River Thames catchment in the United Kingdom) to test its reliability and challenges and understand the transport, sources, and fate of ECs;
(iv) to combine DGT and water quality models to study the environmental fate of ECs, and to explore how a combination of in situ environmental monitoring with passive samplers and chemical fate models can be a powerful way to link source estimates, measurement and process understanding.

1.3 Outline of the thesis

The following literature review in **Chapter 2** comprises an introduction to emerging contaminants and a description of passive sampling techniques. It starts with the need for researching emerging contaminants in aquatic environments and the limitations of traditional sampling and measuring methods. Passive sampling techniques have shown much promise for measuring aqueous concentrations of a wide range of contaminants including emerging contaminants. Principles of passive sampling are then introduced, followed by an introduction of different types of passive samplers. A combination of measuring and modeling techniques has been suggested to represent the most robust approach to the risk assessment of organic contaminants and, therefore, different models

were introduced in order to select one suitable model to combine with DGT measurements.

A brief overview of DGT is provided: its principles and research in different fields, including water quality monitoring, chemical speciation, dynamic processes, bioavailability and high spatial resolution measurements, followed by a comprehensive overview of DGT research and applications for organics. The development and application of DGT for trace organics is still in its infancy. There are several exciting future applications, but also some continuing uncertainties and questions that need resolving. Some examples are briefly discussed.

Chapter 3 addresses the property range of compounds which can be routinely sampled with the present design of DGT device. It includes a series of laboratory-controlled sorption experiments and DGT deployment with nine model chemicals [organophosphate esters with a wide range of log K_{OW} (0.8−9.5), molecular weight (182−435 Da)] and different functional groups. A standard procedure is used to measure lag times (from minutes to days) by exposing a series of DGT samplers in waters until linear mass accumulation in samplers is achieved.

Chapter 4 describes laboratory-controlled tests of the effect of biofilms on the measurement of emerging contaminants. In addition, four sample handling and storage methods (up to 2-month) suitable for cost-effective and rapid sampling of catchments were evaluated: samplers sealed in a polyethylene bag at room temperature; binding gels stored in acetonitrile in amber vials at room temperature; samplers stored at 4 °C and binding gels stored in acetonitrile in amber vials at 4 °C. The effects of biofouling and within-sampler degradation are discussed to inform appropriate sampling and handling procedures of DGT.

Chapter 5 presents a field application of DGT in a dynamic water system, the River Thames network. DGT and the traditional grab sampling method were combined to gather two seasons' river concentration data for a range of ECs for selected established sites across the Thames catchment. DGT and grab sampling approaches were compared for their suitability to screen/monitor ECs at the catchment scale. The data generated by the DGT were used to characterize fate processes of ECs in the aquatic system and understand better the sources, transport and fate throughout the large dynamic watershed.

The significance of the concentrations detected for aquatic organisms and the implications for monitoring contaminants are also discussed.

In **Chapter 6**, DGT measurements generated in Chapter 5 were used to evaluate the suitability of the LF2000-WQX model in predicting concentrations of antibiotics (trimethoprim as a case study) in the River Thames network. Per capita emission of trimethoprim was estimated from prescription data and excretion rates of patients. Removal rates in the wastewater systems and in surface waters were estimated from the literature. DGT measured concentrations were compared with predicted concentrations to evaluate the accuracy of the model predicted concentrations and to provide a better understanding of the environmental fate of trimethoprim.

Chapter 7 provides the conclusions of the thesis and discusses the possibilities of the future work arising from this study.

Chapter 2: Literature review

2.1 Emerging contaminants in aquatic environments

Organic chemicals are essential components of our daily lives, but some can have adverse effects on ecosystem and human health. In addition to the known pollutants, large numbers of non-regulated substances with no clear immediate effects are emerging (Lamastra et al., 2016). Emerging contaminants (ECs) or micropollutants are a large and expanding array of relatively polar anthropogenic compounds, such as pharmaceuticals, endocrine disrupting chemicals (EDCs), some types of flame retardants, etc. Most of them are polar and non-volatile chemicals and they are considered to be released into surface waters mainly through treated effluents from wastewater treatment plants (WWTPs). Rivers are continually receiving ECs, but their impacts on ecosystem and human health are largely unknown (Johnson and Sumpter, 2015). Only in recent years have they drawn concerns from environmental authorities and scientists (Sarkar et al., 2019). Until now, these substances and their breakdown products are not adequately considered in legislation for several reasons, including a lack of knowledge of contaminant pathways, properties and effects of substances and reliable analytical procedures to determine their low concentrations in the environment (Lamastra et al., 2016).

2.2 Sampling and measuring emerging contaminants

Reliable and representative sampling strategies are necessary for studying the sources and environmental fate and impact of ECs. Mass spectrometers, commonly used for measuring ECs, provide instrumental detection limits at single digit μg/L (Petrie, 2015). Grab or spot sampling, such as by taking about 1 L of river water, is the most commonly used method to collect samples due to its simplicity (Vrana et al., 2005). When analytes are at only sub-ng/L or even lower concentrations, large volumes (10–100 L) of water need to be collected. The subsequent laboratory analysis of the grab sample provides a snapshot of the contaminants at the time of sampling. However, the drawbacks of this approach are significant when the concentration varies over time and flow rate, which is the case for most ECs (Coutu et al., 2013, Thomas et al., 2012). Episodic pollution events can be missed (Xing et al., 2013, Petersen et al., 2012). One solution to this issue is to increase the sampling frequency, or to use automatic sampling devices that can take time-proportional composite samples over a time period. Such systems are costly, complex for

end-users and are rarely used or not feasible in widespread monitoring campaigns (Vrana et al., 2005). In addition, collecting, preserving, transporting and pre-treatment of these samples in the laboratory is laborious and time consuming, while (large) samples in glass bottles are heavy and awkward to transport in many sampling campaigns (e.g., in remote or inaccessible areas) and may be subject to damage and contamination (Vrana et al., 2005).

2.3 Principles of passive sampling

In the last three decades, alternatives have been sought to overcome some of the sampling and analytical difficulties just discussed and passive sampling techniques have shown much promise for measuring aqueous concentrations of a wide range of contaminants (Vrana et al., 2005). Passive sampling is based on free flow of analyte molecules from an ambient fluid source (environmental phase) to an engineered sink (sampling phase), because of a difference in chemical potentials between the two phases (Górecki and Namieśnik, 2002). It has been applied to determine both inorganic and organic compounds in a variety of matrices, including air, water, soil and sediment (Vrana et al., 2005).

Mass flux between the two phases is regulated by diffusive and advective transport of the analytes to and through the sampler. Within a sampler, the net transport across it occurs mainly due to molecular diffusion. When the sampler is exposed to the environment, the uptake of the analyte proceeds pseudo-linearly with time and then decreases as the sampler comes into near thermodynamic equilibrium with the environment (Figure 2.1), which can be described by eq (2.1), a first-order one-compartment model:

$$c_S = c_W \frac{k_1}{k_2}(1 - e^{-k_2 t}) \quad (2.1)$$

Where c_S is the analyte concentration in the sampler, c_W the analyte concentration in water, k_1 and k_2 are the uptake and the elimination rate constants, respectively, and k_1/k_2 is the sampler-water partition coefficient (K).

It has been recognized that the sampler is operating in the linear uptake (kinetic) regime when $t < t_{50}$, the time at which the sampler reaches 50% of its equilibrium concentration (Roll and Halden, 2016). When $t > t_{90}$, the time at which the sampler reaches 90% of its equilibrium concentration (Mayer et al., 2003), the sampler has been assumed to be

working in the equilibrium regime. Thus, passive samplers are classified into two categories due to their working regimes: kinetic samplers and equilibrium samplers.

For kinetic samplers—DGT, Chemcatcher, polar organic chemical integrative sampler (POCIS) and semipermeable membrane device (SPMD), etc. (see 2.4 for more information about the samplers)—the analyte mass accumulated into the sampler is linearly proportional to the difference of chemical potential between the sampler and sampling water, and elimination can be negligible. Here eq (2.1) can be turned to

$$c_S = c_W k_1 t \tag{2.2}$$

or eq (2.3):

$$M_S = c_W R_S t \tag{2.3}$$

where M_S is the analyte mass accumulated in the sampler after exposure time t, R_S is the sampling rate for the analyte in the water. The water concentration c_W can be deduced based on a known sampling rate (R_S), exposure time (t) and the mass (M_S) of analyte sampled by the sampler.

For equilibrium samplers—solid phase micro extraction (SPME), polyethylene (PE), polyoxymethylene (POM), silicones rubbers (SR), etc. (see 2.4 for more information about the samplers)—the equilibrium is established between the sampler and the sampling water after a time of exposure. Eq (2.1) can be turned to eq (2.4):

$$c_S = c_W \frac{k_1}{k_2} = c_W K \tag{2.4}$$

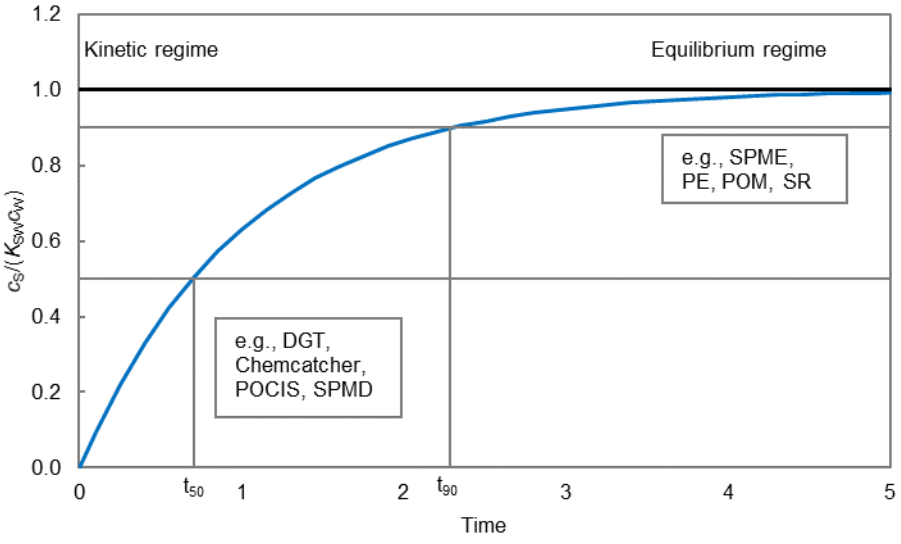

Figure 2.1. Passive samplers are classified into two categories due to their working regimes: kinetic samplers [e.g., diffusive gradients in thin films (DGT), Chemcatcher, polar organic chemical integrative sampler (POCIS), and semipermeable membrane device (SPMD)] and equilibrium samplers [e.g., solid phase micro extraction (SPME), polyethylene (PE), polyoxymethylene (POM) and silicone rubbers (SR)]. Here c_S is the analyte concentration in the sampler, c_W the analyte concentration in water, and K_{SW} (k_1/k_2) the sampler-water partition coefficient. Graphic adapted from (Roll and Halden, 2016).

Both kinetic and equilibrium samplers provide pre-concentration by acting as a preferred phase for partitioning of the analyte. The key difference between the two samplers lies in the dimension of time; equilibrium samplers (e.g., SPME) provide a time-weighted average that follows and attenuates the changes in the environmental concentration, and is biased towards the current concentration. Equilibrium samplers are typically designed for rapid equilibration. The degree of lag and attenuation is a function of the equilibration time of the sampler; SPME, which has a very short equilibration time (hours to days), will more closely approximate a discrete sample, while SPMDs, which have been investigated as proxies for aquatic animals, may require 10s of days or longer (even years) to reach equilibrium. They both capture the effect of and prevent the over- or under-representation of excursions from average concentrations of contaminants over the course of the sampling period. This is particularly attractive in situations where the number of discrete samples required to generate equivalent data would be cost-prohibitive. Kinetic samplers are frequently capable of providing lower detection limits than discrete samplers (Roll and Halden, 2016). However, they are sensitive to temperature, since temperature affects the equilibrium partitioning between the sampler and the sampling medium or surrounding environment.

2.4 Types of passive samplers for trace organics

Many passive samplers have been designed and applied for different organic analytes in aquatic systems in the last three decades (Vrana et al., 2005). The first passive sampler in water was documented in 1974, a dialysis bag (regenerated cellulose) filled with deionized water, for determination of inorganic elements (Beneš and Steinnes, 1974). The same principle, a dialysis bag (regenerated cellulose) filled with hexane, was used later as an environmental monitor of aqueous hydrophobic organics (such as DDT, PCB, etc.) (Sodergren, 1987). Overviews of the development of passive samplers for monitoring water contaminants can be found elsewhere (Vrana et al., 2005, Stuer-Lauridsen, 2005).

A number of well documented passive samplers have been introduced for sampling organics in aquatic environments since the 1990s: semipermeable membrane devices (SPMDs) (790 results when searched for TS = "semipermeable membrane device*" from Web of Science Core Collection, on Oct 6th 2019) (TS = Topic), polar organic chemical integrative samplers (POCIS) [285 results, TS = (“polar organic chemical integrative sampler" OR POCIS)], diffusive gradients in thin films (DGT) [921 results, TS = ("diffus* gradient* in thin film*")] and Chemcatcher (90 results, TS = Chemcatcher).

With the semipermeable membrane device (SPMD) approach, lay-flat low-density polyethylene tubing is filled with small amounts of neutral lipids (grass carp lipid or triolein is used). It was first used to pre-concentrate hydrophobic organics (nonpolar organochlorines) in situ in aquatic environments and to then estimate or derive an ambient concentration, based on measured uptake rates (Huckins et al., 1990). The commercially available SPMD is now composed of lay-flat low-density polyethylene tubing containing a thin film of a pure triolein (http://www.est-lab.com/spmd.php).

The polar organic chemical integrative sampler (POCIS) was developed to monitor aqueous hydrophilic organics (Alvarez et al., 2000, Alvarez et al., 2004). The commercially available POCIS is composed of two sheets of microporous (0.1 μm pore size) polyethersulfone (PES) membrane encasing a solid phase sorbent (Oasis HLB), compressed together by two stainless steel disks (http://www.est-lab.com/pocis.php).

Chemcatcher has a similar structure to POCIS; it was introduced for organics. A 47 mm C_{18} Empore disk with polysulfone membrane (0.2 μm pore size) is used for polar organics ($2<\log K_{ow}<4$) and the same sorbent with thin low-density PE membrane for non-polar organics ($\log K_{ow}>4$). They generally use polytetrafluoroethylene (PTFE) material for the housing (Kingston et al., 2000).

More single-matrix polymer samplers were developed for sampling aqueous hydrophobic organics: low-density polyethylene (LDPE) ($\log K_{ow} >6$), polyoxymethylene (POM) and silicone rubbers (SR) (Booij et al., 1998, Jonker and Koelmans, 2001, Adams et al., 2007, Mayer et al., 2014, Rusina et al., 2007).

Diffusive gradients in thin films (DGT) was first used as an in situ technique for dynamic trace metal speciation measurement in the mid-1990s (Davison and Zhang, 1994) and its research has extended from inorganic to organics since 2012 (Chen et al., 2012). Different

from dual-phase samplers (incorporating a polymeric membrane and a sorbent sampling phase: SPMD, POCIS and Chemcatcher) and single-phase samplers (a single-matrix polymer: LDPE, POM and SR), DGT is a tri-phase sampler: a sorbent binding layer, a hydrogel diffusion layer and a polymeric membrane filter, housed by a DGT piston holder (DGT Research Ltd., a base and a top cap with an exposure window made in acrylonitrile butadiene styrene plastic). Because of the large body of literature and the solid scientific foundation of DGT (Davison and Zhang, 1994, Chen et al., 2012, Guibal et al., 2019), its research into organics has attracted considerable interest and is growing rapidly. At the time of writing, DGT has also been designed and validated for approximately 150 organic compounds, including pharmaceuticals and personal care products (PPCPs), flame retardants, estrogens and pesticides, drugs, etc. (Zou et al., 2018, Guo et al., 2017a, Chen et al., 2017, Chen et al., 2018, Zhang et al., 2018). Many DGT configurations for inorganics and organics are commercially available (https://www.dgtresearch.com/).

Most aquatic passive samplers (e.g., SPMD, POCIS and Chemcatcher) are highly dependent on environmental conditions, such as water flow rates due to the effect of diffusive boundary layer (DBL) (Harman et al., 2012). The DBL at an environmental surface can be changing in response to flow, temperature, orientation etc., so measuring or predicting the DBL is complex and currently impossible as the flow near the sampler surface may vary in both time and space. Thus, in situ correction for POCIS using performance reference compounds (PRC) has been proposed in the literature. This approach corrects the target compound sampling rate relative to the in situ desorption rate of a PRC according to isotropic exchange. However, PRCs are expensive and subject to the availability of the isotope-labelled compounds, especially for ECs.

These drawbacks with other sampler designs and the inherent advantages of DGT make DGT attractive for applications to organic chemicals. Due to the fairly long diffusive path of the DGT system (≈1 mm in a standard DGT device), the DBL is negligible when water flow is above a low threshold (0.02 m/s) (Warnken et al., 2006). This has been directly proved by controlled laboratory experiment (Warnken et al., 2006, Buzier et al., 2019) and by field evaluation of DGT compared to POCIS for a total of 34 polar organic chemicals, including organophosphates and antibiotics (Challis et al., 2018b).

2.5 Combination of measuring and modeling

To carry out meaningful toxicity studies and risk assessment of substances, it is essential to know what concentrations wildlife may be exposed to. It has been suggested that a combination of measuring and modeling techniques represent the most robust approach to the risk assessment of organic contaminants from point sources in freshwater environments (Johnson et al., 2008), especially to generate large spatial and temporal data. A review of suitable models has presented elsewhere (Keller, 2006). Two groups of models are generally used for estimating environmental concentrations, multimedia and single-media models. Multimedia models—e.g., the European Union System for the Evaluation of Substances (EUSES) model—calculate the distribution of a substance in different environmental compartments such as air, water, soil, sediment and biota. These models usually treat the environmental compartments as uniformly mixed, steady state sub-systems; transport processes are described by simple equations based on measured or, more commonly, estimated parameters to describe transport rates between the different compartments (i.e., Mackay fugacity models) (Mackay et al., 1992, Mackay et al., 1996). The closed system is assumed to be at equilibrium and does not consider chemical losses. They are capable of predicting chemicals up to the global extent. Multimedia models are generally difficult to parameterize, spatially coarse, and do not allow for site-specific predictions (Grill et al., 2016).

Single-media models [e.g., the Geography-Referenced Regional Exposure Assessment Tool for European (GREAT-ER) (Feijtel et al., 1997), Low Flows 2000-Water Quality modeling eXtension (LF2000-WQX) (Williams et al., 2009)] have been developed to predict substances concentrations in river networks. They were particularly well designed for “down-the-drain” chemicals (i.e., chemicals from point sources such as WWTPs). Because they account for both spatial and temporal variability (Keller, 2006), they are suitable to be in combination with monitoring data such as those generated by passive sampling techniques. Single-media models share common assumptions and similar key mechanisms (see Figure 2.2 and detailed description in Chapter 6). LF2000-WQX has been well established in the River Thames catchment and has therefore used in this thesis; it will be described fully in Chapter 6.

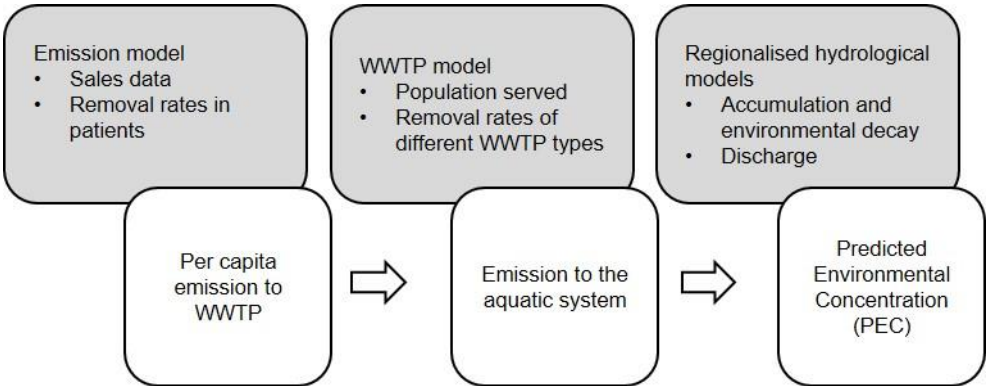

Figure 2.2. Conceptual overview of single-media chemical fate models.

2.6 DGT

2.6.1 Principles of DGT

From a physical chemistry perspective, DGT can be classed as a dynamic technique that initiates and responds to a flux of solute to the device (van Leeuwen et al., 2005). It has been widely used for in situ monitoring a range of analytes, including metal cations, oxyanions and other inorganic and organic components in waters, sediments and soils (Santner et al., 2016).

Basic principles of DGT can be found elsewhere (Davison et al., 2016). Briefly, in the DGT device, freely dissolved solutes or compounds continuously diffuse through a well-defined diffusion layer (a membrane filter and a diffusive hydrogel) and effectively accumulate on the binding layer. Figure 2.3 is a schematic diagram of a DGT sampler. When the DGT device is deployed for a known time (t), a known exposure area (the window in the device cap, A), a known diffusion coefficient (D) of the analyte through the diffusion layer well established under the deployed temperature, a known diffusion distance of the analyte (thickness of the diffusion layer, Δg, and diffusive water boundary layer, δ), by analysing mass accumulated in the binding layer, M_{DGT}, concentration in solution (c_{DGT}) can be obtained by eq (2.5):

$$c_{DGT} = \frac{M_{DGT}(\Delta g + \delta)}{DAt} \quad (2.5)$$

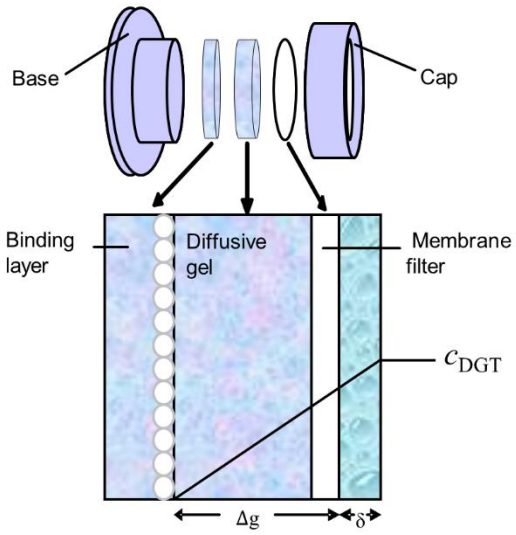

Figure 2.3. Schematic diagram of a DGT sampler, with an exploded view of the binding layer and diffusion layer (diffusive gel and membrane filter), showing the concentration gradients of the analyte. Adapted from (Chen et al., 2012).

DGT is now an established technique that is used in different fields of research, including water quality monitoring, chemical speciation, dynamic processes, bioavailability and high spatial resolution measurements.

2.6.2 Water quality monitoring

Many characteristics of DGT make it a robust sampler for in situ water quality monitoring. For simple aquatic environments where the diffusion coefficient of the analyte is known, no field calibration other than normal quality control is necessary. The fairly long diffusive path, approaching 1 mm in a standard device, ensures that the DGT measurement is insensitive to flow rate above a threshold flow of 0.02 m/s. When the environmental concentration changes with time, as might occur in a natural river, the DGT provides the time-weighted average (TWA) concentration for the deployment time. The DGT sampling system is easy to set up and retrieve. Handling, storage and transport of DGT devices need minimal personnel training. A further attractive feature for monitoring purposes is the ease of analysis. Generally, the matrices achieved from the extracts of the DGT samplers and the test solutions are clean or simple enough that there are no serious instrumental interference problems (Garmo et al., 2003).

DGT has proved to be versatile, although it was originally used for measuring trace metals. The original binding gel containing Chelex resin can be used to measure 55 metal elements (Garmo et al., 2003). Alternative binding gels have been used for sulphide (Teasdale et al., 1999), Cs (Murdock et al., 2001), Hg (Fernandez-Gomez et al., 2011),

Tc (French et al., 2005) and oxyanions (e.g., phosphate (Zhang et al., 1998) and arsenate (Bennett et al., 2011). DGT with two separate binding gels together or a mixed binding gel with a mixture of binding resins have been developed to simultaneously measure multiple elements (Motelica-Heino et al., 2003, Mason et al., 2005). A titanium dioxide gel-assembled DGT has been used to simultaneously measure arsenic, phosphorus and metals (Panther et al., 2012).

DGT has recently been extended to organic compounds (Chen et al., 2012) and until September 2019, approximately 150 organic compounds have been developed and validated using the DGT technique (see Chapter 3).

2.6.3 Chemical speciation and dynamics

It was recognized that DGT can be used as a speciation tool from the beginning of its invention (Davison and Zhang, 1994). At a simple level, it can provide a direct measure of solutes that are both mobile and labile (Leeuwen et al., 2005). The term mobile refers to the fact that species must be capable of diffusing at a reasonable rate through the diffusion layer (Davison et al., 2016). The term labile is used to denote species which can interconvert, within the timescale of their diffusional transport, to a form that can bind (Davison et al., 2016). The extent to which species contribute to a DGT measurement will depend on their size, whether they react directly with the binding layer and the rate at which they can liberate species that do interact with the binding layer (Davison and Zhang, 1994). It is possible to interpret the DGT measurement in terms of the speciation in solution coupling to modeling. Detailed interpretations of chemical speciation and dynamics are given elsewhere (Warnken et al., 2008, Zhang and Davison, 2015, Puy et al., 2016).

2.6.4 Bioavailability

Despite consensus by scientists that bioavailability is critically important to the risk assessment process, the use of the term is confounding as it has been defined differently by various disciplines (Ehlers and Luthy, 2003). A major U.S. National Research Council (NRC) report called *Bioavailability of Contaminants in Soils and Sediments: Processes, Tools and Applications* defines "bioavailability processes as the individual physical, chemical, and biological interactions that determine the exposure of organisms to chemicals associated with soils and sediments" (National Research Council, 2003). Figure 2.4 describes the bioavailability processes (A–D). Definitions of bioavailability

and bioaccessibility have been proposed by environmental scientists, linking the bioavailability processes described in the NRC report (National Research Council, 2002) (Semple et al., 2004). The bioavailable compound has been defined as that which is freely available to cross an organism's cellular membrane from the medium the organism inhabits at a given time (addresses process D in Figure 2.4) (Semple et al., 2004). The bioaccessible compound has been defined as that which is available to cross an organism's cellular membrane from the environment, if the organism has access to the chemical (encompasses processes A–D in Figure 2.4) (Semple et al., 2004). In the environment, contaminants may be either physically removed from the organism (e.g. occluded in organic matter) or occupy a different spatial range of the environment than the organism (Semple et al., 2004). These contaminants can become available quite rapidly (and hence are bioavailable), following release from labile or reversible pools; or, the organism can move into contact with the contaminant (Semple et al., 2004). Alternatively, release may occur over long timescales (e.g., years or decades) and render the chemical bioaccessible (Semple et al., 2004). To summarize, bioaccessibility includes what is actually bioavailable now plus what is potentially bioavailable (Semple et al., 2004).

In both soil and sediment, processes that determine exposure to contamination include release of a solid-bound contaminant (A) and subsequent transport (B), transport of bound contaminants (C), uptake across a physiological membrane (D), and incorporation into a living system (E). Note that A, B, and C can occur internal to an organism, such as in the lumen of the gut. The NRC report defines A, B, C, and D to be bioavailability processes, but not E, because soil and sediment no longer play a role. In contrast, we define A, B, C, and D as processes governing bioaccessibility, whereas D relates to bioavailability.

DGT mimics the way biota perturb solutes in a soil system and can provide information on the dynamic supply from the medium.

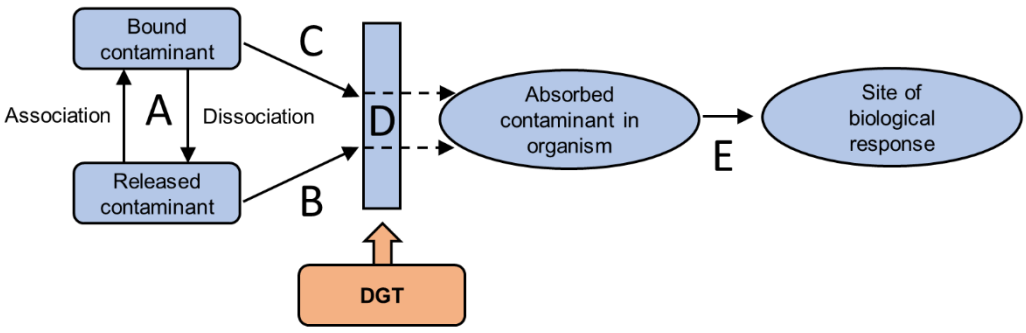

Figure 2.4. Bioavailability processes described in the NRC report. Adapted from elsewhere (Ehlers and Luthy, 2003).

The portion of a contaminant that is either bioavailable or bioaccessible in a given environment can differ substantially between organisms (Ehlers and Luthy, 2003). This

definition simply addressing supply, or potential supply across the celluar membrane of the organism, can apply to chemicals being available to microorganisms, fungi, plants, invertebrates and higher animals (Semple et al., 2004). In this context, routine chemical extraction techniques described in the literature actually estimate the bioaccessible rather than the bioavailable fraction.

DGT continually removes solute from its deployment medium to its 'zero sink' (binding gel) and it perturbs this system (Chen et al., 2014) and can provide information on the dynamic supply from the medium (Zhang and Davison, 2015). This procedure has been considered that DGT mimics the way biota perturb solutes in a soil system (process D in Figure 2.4), leading to DGT being used as a tool to predict biouptake or bioavailable fraction of a chemical, whether in waters, soils or sediments (Degryse et al., 2016).

Generally, the capabilities of DGT as an in situ perturbation and measurement tool have yet to be fully exploited (Zhang and Davison, 2015). Research that uses DGT to investigate processes relevant to bioavailability are extensively ongoing [325 results searched for TS= ("diffus* gradient* in thin film*" AND "bioavailab*") from Web of Science Core Collection, on Oct 9th 2019, with over 50% of those publications in the last five years]. DGT has been used to estimate plant uptake of soil chemicals, such as nutrients [nitrate (Cai et al., 2017), phosphorus (Yao et al., 2016)], metals [copper (Zhang et al., 2001), cadmium (Pelfrene et al., 2011), selenium (Sogn et al., 2008), etc.], arsenic (Williams et al., 2011), etc. Reviews on the progress of using DGT for bioavailability of metals are elsewhere (Batley et al., 2004, Menegario et al., 2017, Li et al., 2018a). Besides, DGT has also been used to mimic earthworm biouptake of metals in soils (Bade et al., 2012), periphyton biouptake of metals in marine coastal waters (Schintu et al., 2010). Very recently, DGT has been firstly used to assess bioavailability of pesticides by maize (Li et al., 2019b). Indeed, it is now the standard recommended method adopted for determining bioavailable P in some countries (Mason et al., 2010).

It has been recognized that DGT provides information on both solution and solid phase dynamics and supply processes in its deployment medium such as soils. Based on the availability of references on the different passive samplers, the DGT technique is the most widely used to estimate the bioavailable fraction of contaminants in the environment (Zhang et al., 2014). In addition, DGT has been listed as one of the best research tools to potentially measure processes important to biouptake (e.g., can obtain rates of release)

by the NRC report (National Research Council, 2003) and may be useful for regulators in giving information for soil and sediment criteria (Ehlers and Luthy, 2003).

2.6.5 High spatial resolution measurements

Another significant development of DGT is for one-dimensional (1D) and two-dimensional (2D) high-resolution measurements (e.g., chemical imaging), which is providing new evidence for the micro-scale (millimetre and submillimetre ranges) biogeochemical heterogeneity of soils and sediments. A comprehensive overview of DGT applications in combination with chemical imaging is given elsewhere (Santner et al., 2015). Various technologies are used: proton-induced X-ray emissions (Davison et al., 1997), computer-imaging densitometry (Teasdale et al., 1999), laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) (Warnken et al., 2004) and 2D slicing (Ding et al., 2011). So far, these or other methods have not been used for trace organic chemicals, but this is likely to be a productive area for future research.

2.7 DGT and applications for organics

DGT has proved its strength in studying inorganics in different fields, including water quality monitoring, chemical speciation, dynamic processes, bioavailability and high spatial resolution measurements. It has raised broad interest to develop it as a research tool for organic contaminants. The research of DGT into organics has been built on the extensive theory and models developed for inorganics. It is still a new area compared with the large body of literature on inorganics, but it has accelerated in the last few years, after the first publication of organics-DGT, on antibiotics (Chen et al., 2012). An overview of published research of DGT on organics is included in Chapter 3. Significant development has been made in developing new configurations for various analytes.

2.7.1 Studied chemicals

Up to February 2020, over 150 compounds from different families have been tested with DGT: pharmaceuticals, pesticides, endocrine disrupting chemicals, illicit drugs, household products, personal care products, organophosphate esters, perfluoroalkyl substances, etc. Pharmaceuticals (ca. 50% of the studied chemicals) and pesticides (ca. 20%) are the most studied chemicals so far. The list of chemicals is given in Appendix I. They cover a wide range of chemical properties: log K_{ow} (-6.5–8.5) and molecular weight (94–916 Da), and could be acids [e.g., atrazine with pKa = 3.2 (Challis et al., 2016)],

neutrals [e.g., organophosphate esters (Zou et al., 2018)] and bases [e.g., 17β-estradiol with p*K*a = 10 (Chen et al., 2018)]. Salinomycin appears to be the most hydrophobic compound tested so far (Chen et al., 2013).

The procedures for developing a DGT configuration for organic analytes have mostly followed guidelines laid out in the first publication (Chen et al., 2012). This involves a series of well-defined laboratory-based experiments and field validation: (i) sampler materials (DGT molding, diffusive gel, membrane filter) adsorption or contamination; (ii) binding layer uptake, elution and capacity; (iii) diffusion coefficient measurements in diffusion cells; (iv) linear mass accumulation over time; (v) performance in a range of environmental conditions: pH (e.g. pH 5–9), ionic strength (e.g. 0.01–0.5 M), dissolve organic matter and water flow that are typical of real-world water systems; (vi) exposure time, detection limit investigation in the field. The DGT technique for determining organic contaminants has mostly been demonstrated as a 'proof of concept' in method papers, with limited detailed validation or experimental/field applications so far.

2.7.2 DGT configurations

Table 2.1 lists the published DGT configurations and their target organic analytes. The cylindrical plastic assembly (moldings) were mostly made in traditional ABS (acrylonitrile butadiene styrene) plastic but Teflon (PTFE) has also been used as the inert material of choice (Guo et al., 2017b).

Diffusion layer

Analytes transfer solely by diffusion in the diffusion layer in a controlled manner, which can be measured by a diffusion cell in the laboratory. The material diffusion layer (commonly a membrane filter and diffusive gel) should have an open structure that allows virtually unimpeded diffusion. Ideally, chemical interactions between the diffusion layer and analytes should be negligible.

A diversity of membrane filters have been used: polyethersulfone (PES), nuclepore track-etch polycarbonate (PC), polytetrafluoroethylene (PTFE), polypropylene (GHP), polyvinylidene fluoride (PVDF), cellulose acetate, nylon, cellulose nitrate, glass fiber and aluminium screen. Most membrane filters are 25 mm of diameter and 0.45 μm of pore size, except the nylon membrane filters are 0.22 μm in these two studies (Dong et al., 2014b, Dong et al., 2014a).

Some membrane filters were found to retain some analytes and this led a few studies to propose using DGT without a membrane filter (Challis et al., 2016, Challis et al., 2018a, Stroski et al., 2018, Challis et al., 2018b, Guibal et al., 2017, Xie et al., 2018b). However, this is inadvisable because a filter is not only protecting the inner system from clogging by particles in water, the 0.45 μm (or less) pore size membranes are also stopping microorganisms entering the system. One study didn't use a membrane filter in the DGT device and observed that AG diffusive gels were grazed on and degraded by aquatic insects in the field, while APA gels were more resistant (Stroski et al., 2018).

Diffusive gels described in the literature are mainly two types of hydrogels: Agarose (AG ≈ 70% in Table 2.1) and polyacrylamide cross-linked with an agarose derivative (APA ≈ 20% in Table 2.1). AG has been dominant as the diffusive gel for organics due to its good reproducibility and low adsorption of organic compounds. However, some work has shown APA gels have less adsorption of certain groups of organics, e.g., pesticides (Guibal et al., 2017).

Binding layer

The binding layer binds the analyte rapidly and irreversibly, so that the concentration of the analyte at the surface of the binding layer and diffusion layer is effectively zero and a steady state of mass transport through the diffusion layer could be achieved. Many of the binding layers have utilized commercially available materials as the binding agent (e.g., HLB, XAD-18, Activated charcoal, XDA-1, MCX, C8, Fe-oxide, Zn-oxide, Sepra ZT, Strata-X and Titanium dioxide, Table 2.1), and laboratory-synthesized materials (activated charcoal (You et al., 2019a), porous carbon material (Ren et al., 2018) and) have also been used successfully. These binding agents were bedded in one of the three hydrogels [Agarose (AG), polyacrylamide cross-linked with an agarose derivative (APA) and polyacrylamide cross-linked with bis-acrylamide (RES)]. Other polymers were used directly as binding layers [e.g., cyclodextrin polymer (Wei et al., 2019), molecularly imprinted polymer (Li et al., 2018b) (Dong et al., 2014b, Dong et al., 2014a)]. Molecular imprinted polymer is an artificial receptor made by imprinting molecules of a template in a polymer matrix followed by removing the template molecules via thorough washing to give the permanent template grooves (Cheong et al., 2013). They show favored affinity to the template molecule compared to other molecules (Cheong et al., 2013).

Table 2.1. Configuration of DGT for organic analytes in the literature. A range of binding gels were mainly binding agents bedded in three types of hydrogels [Agarose (AG), polyacrylamide cross-linked with an agarose derivative (APA) and polyacrylamide cross-linked with bis-acrylamide (RES)]. Diffusive gels were mainly two types of hydrogels: AG and APA. Various membrane filters were described: polyethersulfone (PES), nuclepore track-etch polycarbonate (PC), polytetrafluoroethylene (PTFE), polypropylene (GHP), polyvinylidene fluoride (PVDF), cellulose acetate, nylon, cellulose nitrate, glass fiber and aluminium screen. Most membrane filters are 25 mm of diameter and 0.45 μm of pore size, except nylon membrane filters are 0.22 μm in these two studies (Dong et al., 2014b, Dong et al., 2014a)

Binding gel	Diffusive gel (thickness mm)	Membrane filter	Analyte class (No.)	Reference
HLB (AG)	AG (0.75)	PTFE	Organophosphate esters (6)	(Zou et al., 2018)
HLB (AG)	AG (0.80)	GHP	Nitrochlorobenzene compounds (4)	(Zhang et al., 2019)
HLB (AG)	AG (1.0/0.75)	Not use	Pharmaceuticals and pesticides (34)	(Challis et al., 2016, Challis et al., 2018b)
HLB (APA)	AG (1.0)	PC	Pharmaceuticals and personal care products (13); endocrine disrupting chemicals (8); Pesticides (9)	(Chen et al., 2017, Chen et al., 2018, Li et al., 2019a)
HLB (APA)	APA (0.80)	Not use	Pesticides (4)	(Guibal et al., 2017)
XAD-18 (AG)	AG (0.80)	PES	Antibiotics (40)	(Chen et al., 2012, Chen et al., 2013, Xie et al., 2018a)
XAD-18 (AG)	AG (0.80)	PES	Illicit drugs (5)	(Guo et al., 2017a, Zhang et al., 2018)
XAD-18 (AG)	AG (0.75)	PES	Perfluoroalkyl substances (2)	(Guan et al., 2018)
XAD-18 (AG)	AG (0.75)	PVDF	Endocrine disrupting chemicals (1)	(Guo et al., 2017b)
XAD-18 (AG)	AG (NA)	Nylon	Antibiotics (4)	(Sidhu et al., 2019, D'Angelo and Martin, 2018, D'Angelo and Starnes, 2016)
Activated charcoal (RES)		Nylon	Nitrophenols (3)	(You et al., 2019a)
Activated charcoal (AG)	AG (0.80)	PTFE	Biphenols (3)	(Zheng et al., 2015, Guan et al., 2017)
XDA-1 (AG)	AG (0.80)	PES	Antibiotics (20)	(Xie et al., 2018a)
XDA-1 (AG)	AG (0.80)	Not use	Endocrine disrupting chemicals (6)	(Xie et al., 2018b)
MCX (AG)	AG (0.75)	PC	Pharmaceuticals (14)	(Fang et al., 2019)
C8 (RES)[a]	AG (0.50)	Cellulose nitrate	Organotins (5)	(Cole et al., 2018)
Cyclodextrin polymer	AG (1.0)	Glass fiber	Antimicrobials and a degradation product (3)	(Wei et al., 2019)
Fe-oxide (NA)	APA (0.80)	Cellulose nitrate	Organic phosphorus (3)	(Mohr et al., 2015)
Molecularly imprinted polymer	APA (0.5)	Cellulose acetate	Antibiotics (1)	(Li et al., 2018b)
Molecularly imprinted polymer		Nylon (pretreated)	Phenols (2)	(Dong et al., 2014b, Dong et al., 2014a)
Zn-oxide (RES)		PES	Antibiotics (3)	(You et al., 2019b)

TEMED: 99% N,N,N',N'-tetramethylethylenediamine

[a]: (Cole et al., 2018) used APA gel with modification: 40% acrylamide/bisacrylamide (BPA) (Sigma-Aldrich, Poole, UK) water and with the addition of methanol at 3:1:1 (v/v/v)

However, the recent focus on molecular imprint approaches, this is unlikely to improve DGT as a sampler for organics radically. The limitations are not to do with binding gel capacity or specificity. The binding gel is 'downstream' of the key steps of compound transfer to and through the DGT device. Focus needs to be on ensuring sufficient, quantitative, predictable/understood and timely supply of compounds to the binding gel, i.e., understanding/controlling losses by sorption, retardation by the filter, possible effects on sampler performance from the biofilm formation, etc. (see below).

2.7.3 Influence of environmental factors

Environmental factors, such as water flow, pH, ionic strength and dissolved organic matter, are important, because they can influence the speciation/form and supply of target compounds to the sampler, and potentially also the diffusion and/or binding to the binding layer. When monitoring the environment, the aim is that the sampler captures the species occurring in the environment and its performance is not affected by common variables such as pH, ionic strength and DOM.

Water flow

The diffusive boundary layer (DBL) for DGT refers to a water layer close to the sampler surface where there is effectively no flow. Besides the material diffusion layer (e.g., the diffusive gel and membrane filter in the DGT device), the movement of analytes to the sampler (in the DBL) is also by diffusion. The uptake of analytes by most passive samplers (e.g., SPMD, POCIS and Chemcatcher) is dominated by the DBL, rather than by the material diffusion layer (e.g., microporous polymer membrane) (Challis et al., 2016). Water flow affects the thickness of the DBL; the layer becomes thinner with increasing flow rate (Warnken et al., 2006). Even when the deployment solution is vigorously stirred, a thin residual DBL will remain (Warnken et al., 2006). It has widely been assumed that the DBL thickness is sufficiently thin (≈0.2 mm) in a naturally flowing water system, where flow >≈0.02 m/s, compared to the diffusion distance in the sampler itself (thickness of diffusive gel + thickness of membrane filter ≈1 mm in a standard device) (Warnken et al., 2006, Challis et al., 2016, Gimpel et al., 2001). If the DBL is not significant in a certain environment, the value of DBL can be obtained by deploying different thicknesses of DGT devices and calculated (Warnken et al., 2006) (Chapter 5).

Ionic strength and pH

Ionic strength and pH are two critical chemical parameters that can vary significantly in and between natural systems and that can affect the speciation and accurate performance of the sampler. Ionic strength may affect sampling by the 'salting-out effect' reducing the solubility of organic chemical (Endo et al., 2012) and can reduce the electrostatic repulsions due to the screening effect of the surface charge of the diffusive gel (Fontecha-Cámara et al., 2007). The effect of a wide range of ionic strength (0.0001 to 1 M, imposed with NaCl or $NaNO_3$) should always be tested when a new compound is being considered for sampling/study by DGT. Sampling by DGT has been found to be independent of ionic strength (usually from 0.001 to 0.5 M) for the following compounds/classes: pharmaceuticals (including antibiotics) (Li et al., 2018b, Ren et al., 2018, You et al., 2019b, Fang et al., 2019), endocrine disrupting chemicals (EDCs) (Chen et al., 2018), bisphenols (Zheng et al., 2015), estrogens (Guo et al., 2017b), drugs (Zhang et al., 2018), flame retardants (Zou et al., 2018), nitrophenols (You et al., 2019a) and nitrochlorobenzene compounds (Zhang et al., 2019).

Solution pH may affect the properties of analytes and therefore affect their sampling. A wide range of pH (3–11) has been tested in the literature and DGT has been demonstrated no influence by pH on sampling organics for most studied compounds, which have been listed elsewhere (Guibal et al., 2019). However, sampling of some compounds was found to vary with pH, depending on p*K*a of compounds. The pH may alter the binding strength between the analyte and the binding agent (Dong et al., 2014a, Guibal et al., 2017) and diffusion through the diffusion layer (Xie et al., 2018a). Some future focussed applications of DGT would be to investigate speciation/form of compounds in the environment, either in the field or under carefully controlled laboratory conditions. This type of research has been widely conducted for inorganics, but is in its infancy for organics.

Dissolved organic matter

Dissolved organic matter (DOM) present in natural waters may affect the uptake of analytes by passive samplers through two pathways: (1) DOM competing with analyte for sorption to the binding layer and (2) reactions between DOM and analytes alter analyte diffusion (Davison et al., 2015). Up to 20 mg/L DOM was found no impact on DGT sampling of some pharmaceuticals (You et al., 2019b), perfluoroalkyl substances (Guan et al., 2018), endocrine disrupting chemicals (Chen et al., 2018), organophosphate esters (Zou et al., 2018) and household and personal care chemicals (Chen et al., 2017).

Temperature

Temperature affects mainly the water viscosity and molecular thermic agitation (Brownian motion) and consequently affects diffusion coefficient (*D*) of the analyte. The temperature dependency of *D* can be measured in the controlled laboratory and needs to be done for each compound for which DGT is used. With field deployments, DGT measurement can be calculated based on the average temperature recorded. Commercial devices such as temperature data loggers, can easily record temperature for relevant time frequencies, e.g., one reading every 2 hour (Fang et al., 2019), two readings per hour with ±0.2 °C accuracy (Challis et al., 2018b).

Biofouling

Biofilms composed of algae, bacteria, fungi, and products from cell metabolism form and grow on solid surfaces in natural waters. They will form, to a greater or lesser extent, on the sampler surface during deployments. This could potentially also affect the DGT measurement, due to physicochemical interactions with analytes and/or thickness of the biofilm (Uher et al., 2017). Studies have previously investigated the potential influence of biofouling on the uptake of inorganic species (Díez and Giaggio, 2018, Uher et al., 2012a, Uher et al., 2012b, Chlot et al., 2013, Zhang et al., 1998). However, since the DGT development and application for trace organic pollutants is a relatively new field, little work has addressed the effect of biofouling on the DGT for trace organic pollutants.

In the literature, short deployment times and biofouling resistant membrane filters were recommended and applied to minimize biofouling interference (Chen et al., 2012). Less than one month (Chen et al., 2012) and 2–4 weeks (Challis et al., 2016) deployment times in rivers were suggested and 7-day deployment in raw wastewater was recommended (Chen et al., 2013), because of concerns over the potential influence of the biofilm. Biofouling on the surface of the DGT sampler was not observed when deployed for 8 hours in seawater (Dalian coast, China) (Xie et al., 2018a), 14 days in seawater (Belgian Oostende Harbour, Belgium) (Guo et al., 2017b), and up to 33 days in a city lake and river (Nanjing, China) (Guan et al., 2018). Tested chemicals in household and personal care products (HPCPs) and endocrine disrupting chemicals (EDCs) sampled by DGT were found to have plateaued or declined after 18 days in samplers deployed in the influent of a wastewater treatment plant (WWTP) (China). The authors suggested biofouling could have an influence, although this would not explain the apparent declines in compound mass retained by the DGTs (Chen et al., 2017).

Several studies have used DGT without an outside membrane filter (Challis et al., 2016, Challis et al., 2018a, Stroski et al., 2018, Challis et al., 2018b, Guibal et al., 2017, Xie et al., 2018b) but only three studies mentioned the issue of biofouling. No biofouling was observed on the diffusive gel after 3-day deployment in seawater (Dalian coast, China) (Xie et al., 2018b). Even with extensive biofilm formation on the surface of the retrieved samplers (polyacrylamide gels as outer diffusive gels), the DGT measurement of pesticides and pharmaceuticals agreed well with grab sampling measurements (Challis et al., 2018b). One study showed no detectable analytes existed on the biofilm formed on the outer diffusive gel but failed to demonstrate if biofilms have any influence on analyte uptake (Challis et al., 2016). However, a comprehensive characterization of biofouling on DGT measurement for organics is lacking.

2.7.4 Applications and field deployment

Until now, research into DGT for organics has mainly focused on development of new configurations for various organic analytes (Table 2.1) and they were validated or used in a few environmental matrices: (1) surface freshwaters (Chen et al., 2012, Fauvelle et al., 2015, Mohr et al., 2015, Zheng et al., 2015, Guibal et al., 2017, Guan et al., 2018, Zhang et al., 2018, Zou et al., 2018, Fang et al., 2019, Li et al., 2019a, Wei et al., 2019, Zhang et al., 2019), (2) raw and/or municipal wastewaters (Chen et al., 2013, Challis et al., 2016, Chen et al., 2017, Guo et al., 2017a, Guo et al., 2017b, Chen et al., 2018, Ren et al., 2018), (3) industrial wastewaters (Dong et al., 2014a, Meng et al., 2019, You et al., 2019a) and (4) sea waters (Cole et al., 2018, Ren et al., 2018, Xie et al., 2018a, Xie et al., 2018b). Some of the DGT configurations were validated in multiple aquatic systems: surface freshwaters, wastewaters and seawaters (Belles et al., 2017, Guo et al., 2019). One study validated the DGT configuration for sampling antibiotics in pig breeding wastewater (You et al., 2019b). DGT has shown its strength in different environmental matrices.

DGT was evaluated over POCIS across a wide suite of polar pharmaceuticals and pesticides in surface freshwaters in Canada (Challis et al., 2018b). DGT provided sufficient sensitivity and capacity to measure a suite of analytes over a wide concentration range (nearing 4 orders of magnitude) and was less affected by the DBL than POCIS (Challis et al., 2018b).

DGT has been applied to study desorption kinetics of antibiotics (Chen et al., 2014) and bisphenols (Guan et al., 2017) in soils, and antibiotics in municipal biosolids (D'Angelo and Starnes, 2016, D'Angelo and Martin, 2018, Sidhu et al., 2019). A dynamic model of the DGT-soil system (DIFS, DGT induced fluxes in soils) that describes the diffusional transport and dynamic exchange of solute between solid phase and solution, when a soil is perturbed by a DGT device (Ernstberger et al., 2002, Ernstberger et al., 2005), was adopted in these studies to obtain kinetic and pool size parameters of the soil from the DGT measurements. DGT has great scope as a research tool to improve our understanding of the mobility and availability of organics in soils and sediments.

Different deployment systems of DGT devices have been used in the field. Generally, the deployment system consists of a holder system and a floating/non-floating system. As illustrated in Figure 2.5, many holders for multi-DGT devices [3 (a), 6 (b), 12 (g, h), 24 (c), and more (d)] have been used. An automatic sampler using DGT devices (Figure 2.5-h, https://www.ael-environnement.nc/thoe/) is programmable and can provide time series monitoring over several months. It can be immersed up to 1000 m depth in water systems. These holders with DGT devices are either floating with buoys or fixed with steel rods or other methods (see Chapter 5) in the water system. Floating deployment systems can be used in deep waters such as a sea and non-floating deployment systems are commonly used in rivers and lakes (Fang et al., 2019).

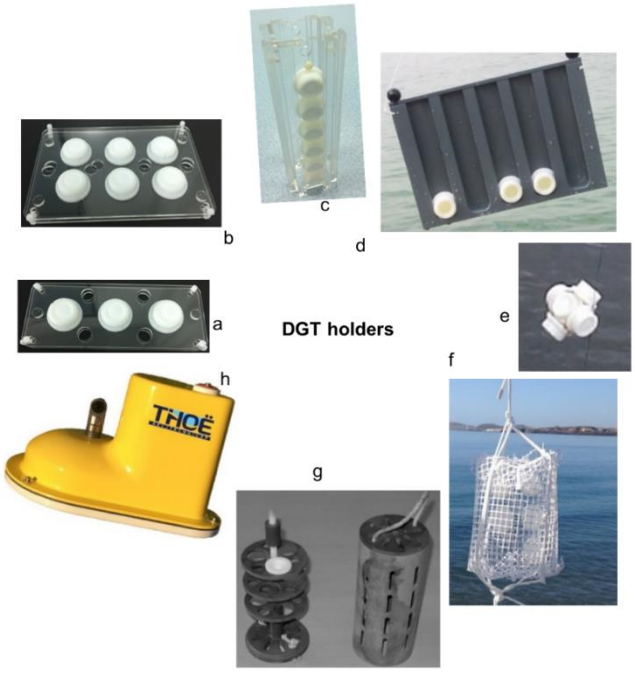

Figure 2.5. DGT holders used in the deployment system of DGT.

2.8 Research gaps/needs

As highlighted by this brief review, the development and application of DGT for trace organics is still in its infancy. There are several exciting future applications, but also some continuing uncertainties and questions that need resolving. Some examples, not an exhaustive list, are briefly discussed here.

Chemicals of relatively hydrophobic nature can sorb onto the membrane filter and exhibit substantial lag-times (i.e., delays of mass increase in binding gels in the early time of sampling). Indeed, various chemicals have been detected in the membrane filter in substantial amounts, sometimes even more than in the binding gels (Challis et al., 2016). Like other passive samplers, the sorption to the membrane filter can also cause slow responses to fluctuating aqueous phase concentrations (Vermeirssen et al., 2012). Although many types of membranes have been tested and most studies mentioned they found different extents of chemical sorption on the membranes, very few studies have focused on how sorption influence the performance of the sampler. Chapter 3 is designed to address this issue, to explore the limitations or boundaries of using DGT in a 'chemical space', i.e., for chemicals of widely different properties.

As discussed above, studies have previously investigated the potential influence of biofouling on the uptake of inorganic species (Díez and Giaggio, 2018, Uher et al., 2012a, Uher et al., 2012b, Chlot et al., 2013, Zhang et al., 1998). However, since the DGT development and application for trace organic pollutants is a relatively new field, little work has addressed the effect of biofouling on the DGT for trace organic pollutants. In the literature, the DGT samplers were mostly treated/extracted immediately after retrieval. Little attention has been paid to chemicals stability or sample storage although it may affect the data quality (Hillebrand et al., 2013). It is important to understand the chemical's stability during common sampler storage scenarios and to provide a uniform procedure for the preservation of the DGT samplers. Chapter 4 has focused on these issues.

Until now, research into DGT for organics has mainly focused on development of new configurations for various organic analytes. Applying the DGT to rivers at a catchment scale is necessary to test and demonstrate its reliability and challenges in a dynamic water system, with different environmental conditions. Exploring sources and environmental fates of ECs using DGT provides a 'real world' field-testing of the use of DGT for

environmental monitoring of trace organics (Chapter 5). Finally, one of the powerful applications of DGT is to be able to deploy many samplers across a catchment quickly and concurrently, to build up a picture of source types and strengths, and to couple such time-integrated and spatially resolved data with appropriate catchment-specific/parameterized models (Chapter 6).

These studies focus on a range of ECs: some flame retardants (organophosphate esters), pharmaceuticals and endocrine disrupting chemicals. They are raising concerns in public and environmental science. In addition, they possess varied properties for testing/use of DGT and are often from diffusive sources so ideal for time-integrated sampling.

Chapter 3: Investigating potential limitations of current diffusive gradients in thin films (DGT) samplers for measuring organic chemicals

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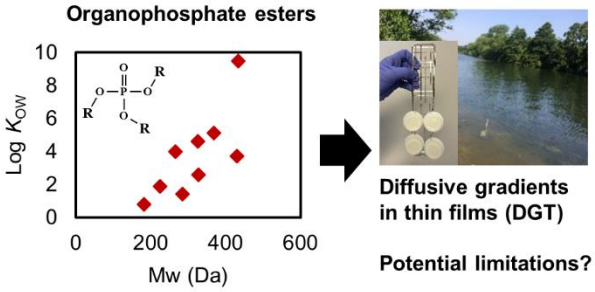

Abstract: The diffusive gradients in thin films (DGT) passive sampler has emerged as a powerful tool for measuring in situ concentrations of organic contaminants in waters with appropriate spatial and temporal resolution at low cost. This study addresses the property range of compounds which can be routinely sampled with the present design of DGT device. Sorption experiments and DGT deployment with 9 model chemicals [organophosphate esters with a wide range of log K_{OW} (0.8–9.5), molecular weight (182–435 Da)] and different functional groups showed compounds with high hydrophobicity and aromatic rings are prone to retention on membrane filters, which slows the supply of chemical to the binding resin of the sampler. The current DGT sampler (PTFE membrane filter, agarose gel diffusion layer and HLB binding layer) is potentially reliable for measuring hydrophilic [log K_{OW} (0.8–2.6)] and non-aromatic-ring chemicals. For

compounds of higher values of K_{OW} or with aromatic rings, knowledge of the lag phase is necessary to optimize sampling times to avoid biasing subsequent laboratory analyses. A standard procedure is used to measure lag times (from minutes to days), by exposing a series of DGT samplers in waters until linear mass accumulation in samplers is achieved. We discuss how monitoring of a wide array of organic contaminants across classes should be possible in future, with a range of validated new DGT devices, optimized for the choice of membrane filter, diffusive material and binding resin.

3.1 Introduction

The organic chemical status of water bodies is crucial to water supply, human health, natural ecosystems and biodiversity. However, organic pollutants are ubiquitous and have often been poorly controlled (Mailler et al., 2014). Many of them are continuously discharged into aquatic systems, as waste water treatment plants (WWTPs) are normally not designed to remove them from the dissolved phase. Regulation is still limited, especially in developing countries; for example, there are no specific organic compounds on the compulsory control list of the current discharge standard of pollutants for municipal WWTPs in China (GB 18918–2002). Water management authorities need surface water monitoring networks to properly monitor contaminants and report long-term trends. Surveillance, operational monitoring and investigative monitoring programmes need different monitoring designs, taking account of the spatial and temporal variability within a water body. Sufficient samples need to be taken to identify sources and to give a coherent, comprehensive overview of the chemical status of the water body. When monitoring trace level organic pollutants, the balance between costs and sufficient coverage of samples in time and space is challenging. Preservation, storage and transport of water samples and sufficient education and training for field personnel are all essential to the quality of sampling activities, but also increase the challenge. Spot sampling is used for most monitoring in water bodies. However, at places where contaminant concentrations are heavily influenced by flow conditions and temporal variation, flow-proportional or time-proportional samples may be needed for more representative sampling (Roll and Halden, 2016). State-of-the-art passive water sampling techniques, such as diffusive gradients in thin films (DGT), the polar organic chemical integrative sampler (POCIS) and Chemcatcher, give ecotoxicologically relevant, time-weighted average (TWA) concentrations and enable cost-effective multiple site sampling (Roll and Halden, 2016). Hence they have attracted increasing attention over the past

decades as water authorities seek to balance their financial resources against a tendency to monitor using traditional grab or spot sampling. Considerable research now supports: using passive water sampling with accuracy and reliability; increasing the range of chemicals and sampling environments; and procedures to improve real-world applications, with varying water flow rates, biofouling and physicochemical conditions (Table S3.1). Yet our understanding of sampling mechanisms of organic chemicals should be further explored for a broader use of passive samplers.

A significant advantage of the DGT technique over other passive sampling techniques is that contaminant uptake by DGT is independent of hydrodynamic conditions above a low flow threshold, so no extra calibration is needed for in situ monitoring (Davison and Zhang, 1994). It was invented and first applied to inorganics over 20 years ago and is built on a solid scientific foundation (Davison and Zhang, 2012). There are now over 800 peer reviewed papers on developments and applications of the DGT technique for metals and nutrients in waters, soils and sediments since the 1990s. In contrast, research and development of DGT for organic chemicals only started in 2012, but it has already attracted considerable interest and is developing rapidly (Chen et al., 2012). To date, sampler development and testing of 136 organic compounds has been reported in the literature (a few from personal communication), with more being conducted (Li et al., 2018, Chen et al., 2012, Chen et al., 2013, Chen et al., 2014, Chen et al., 2015a, Chen et al., 2015b, Chen et al., 2017, Chen et al., 2018, Cole et al., 2018, Dong et al., 2014b, Dong et al., 2014a, Fauvelle et al., 2015, Mohr et al., 2015, Zheng et al., 2015, Guan et al., 2017, Zou et al., 2018, Wei et al., 2019, Guan et al., 2018, Challis et al., 2016, Challis et al., 2018a, Stroski et al., 2018, Challis et al., 2018b, Guibal et al., 2017, Belles et al., 2017, Guo et al., 2017a, Zhang et al., 2018, Guo et al., 2017b, Xie et al., 2018a, Xie et al., 2018b, Ren et al., 2018, You et al., 2019, Sidhu et al., 2019, D'Angelo and Martin, 2018, D'Angelo and Starnes, 2016). Compound classes include pharmaceuticals and personal care products, illicit drugs, endocrine disrupting chemicals and pesticides etc. Table S3.1 summarizes these publications. Different sampler configurations have been optimized for different groups of chemicals. Seventeen types of binding layers with 15 different binding agents, 5 types of diffusion layers and 9 types of membrane filters have been described in the literature. Apart from those membranes recommended so far, a few others have also been tested. Some membrane filters give problems of retention of some compounds. This led a few studies to propose using DGT without a membrane filter

(Challis et al., 2016, Challis et al., 2018a, Stroski et al., 2018, Challis et al., 2018b, Guibal et al., 2017, Xie et al., 2018b), but this is inadvisable because a filter is not only protecting the inner system from clogging by particles in water, the 0.45 μm pore size membranes are also stopping microorganisms entering the system.

As we seek to extend the use of DGT to organic chemicals, it is critical to understand any limitations of the standard sampler design and any constraints to the range of possible analytes. This can inform future developments and applications. The objectives of this study were therefore to: i). characterize sorption of target chemicals on the standard DGT device and investigate the effects of physicochemical properties of those compounds on sorption; ii). delineate limitations of the standard DGT configuration for measuring organic chemicals; and iii) recommend practical criteria for using DGT in monitoring organics in waters.

3.2 Experimental section

3.2.1 Choice of compounds for study

Five hydrophilic organophosphate esters (OPEs: TCEP, TCPP, TDCPP, TPrP and TBP) were tested for in situ monitoring in aquatic systems using the DGT technique in a previous study (Zou et al., 2018). In this study, a group of 9 OPEs was chosen to expand the range of functional group diversity and range of physicochemical properties (Figure 3.1). Details of the compounds are given in Supporting Information (SI, Table S3.2 and Figure S1). The 9 chemicals can be sub-divided into three groups: four with alkyl moieties of different lengths (TEP, TPrP, TBP and TEHP); three with chlorinated alkyl moieties (TCEP, TCPP and TDCPP) and two with phenyl moieties (TPP and ToCP). Their log K_{OW} (a parameter describing hydrophobicity) and molecular weight vary from 0.8 to 9.5 and from 182 to 435 Da. These ranges cover ~75% of the organic chemicals for which the DGT technique has been developed (Table S3.1). Whilst log K_{OW} is clearly not the only physicochemical property controlling compound behavior, it is a primary marker of compound behavior, routinely measured for chemicals of commerce and environmental pollutants and an excellent surrogate to represent aqueous solubility and partitioning behavior (Keiluweit and Kleber, 2009).

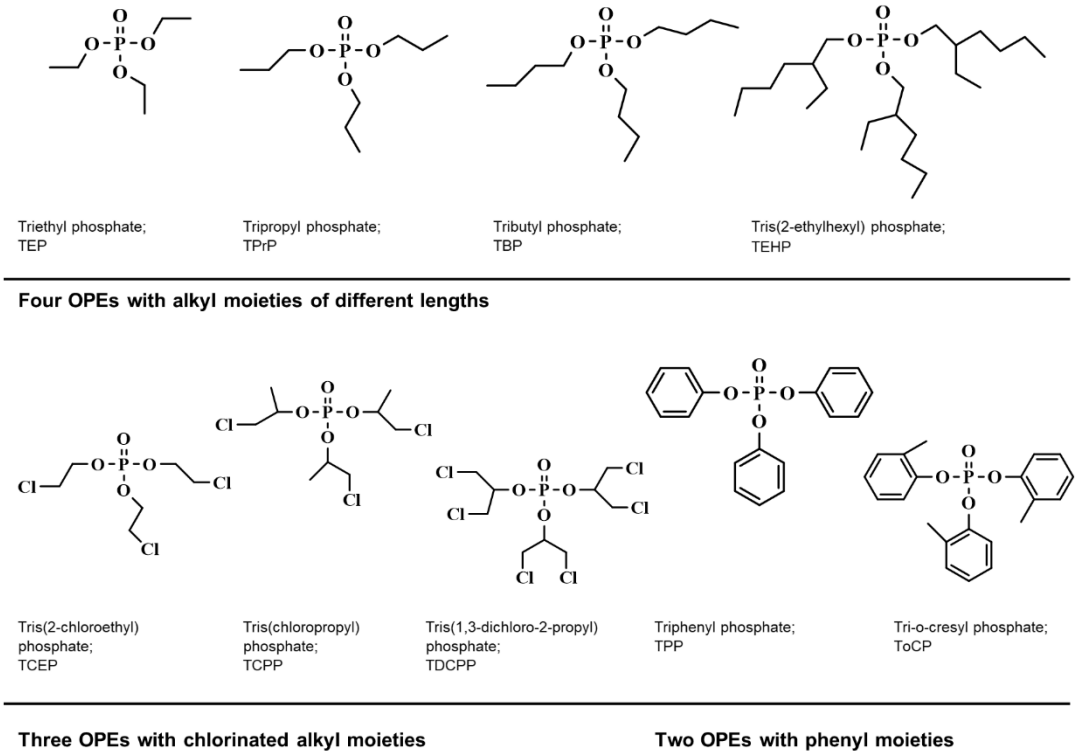

Figure 3.1. Chemical structures of nine organophosphate esters (OPEs) selected for this study.

3.2.2 Chemicals and reagents

Stock solutions of all 9 chemicals and a mixture of 7 chemicals (all except for ToCP and TEHP) were prepared in acetonitrile at 100 mg/L. A surrogate internal standard (SIS) mixture was prepared in acetonitrile at 500 μg/L. Further details of these and other reagents are provided in the SI.

3.2.3 Sampler details

The DGT configuration in this study comprised a 0.4 mm thickness of hydrophilic-lipophilic-balanced (HLB) resin gel as the binding layer (7 mg HLB per disc, nominal), a 0.8 mm thickness of agarose gel (AG gel) as the diffusion layer and a polytetrafluoroethylene (PTFE) membrane (0.45 μm pore size, 150 μm thickness) as the standard filter. More details about the DGT sampler and the technique were first described previously (Zhang and Davison, 1995).

3.2.4 Instrumental analysis

An ultra-high-performance liquid chromatography-tandem mass spectrometer (UHPLC-MS/MS) was used to determine the target compounds. Separations were achieved by a Shimadzu Nexera UHPLC (Kyoto, Japan) equipped with two binary pumps, an

autosampler, a degasser and a column oven connected to a Phenomenex Kinetex Biphenyl column (50×2.1 mm, 2.6 μm). Detections were conducted by a triple quadrupole mass spectrometer (Shimadzu LCMS-8040, Kyoto, Japan), with an electrospray ionisation source operated in positive ion mode. Details about the instrument, the LC gradient method, MS source parameters, an illustrative chromatogram (Figure S3.2), MRM parameters (Table S3.3), calibration curves (Table S3.4), instrumental limits of detection (LOD), limits of quantitation (LOQ) and method detection limits (MDL) (Table S3.5) are given in the SI.

3.2.5 Sorption experiments

Before laboratory experiments, all containers including tubes, vials, beakers, DGT holders, pipette tips used in the study were tested for possible contamination. Since OPEs are widely used compounds, e.g. they could be found in new vials from plastic packing procedures, all glassware used in this study was ultrasonically cleaned for 30 min in a 5% (w/v) non-ionic surfactant solution, then extensively rinsed with tap water followed by MQ water, and then followed by methanol. Plastic materials were replaced with metal or glassware as much as possible for the experiment to avoid chemical losses by adsorption. HLB resins from the cartridges were thoroughly washed with acetonitrile. All solvents are carefully checked to be OPE-free.

For any DGT testing experiments using standard solutions, the concentrations of the targeted chemicals should be approximately constant. There should not be significant losses in mass during experiments due to adsorption on the container walls. In order for the DGT technique to work optimally, all the materials for the sampler, except the binding gel, should have no significant affinity for adsorbing the targeted chemicals.

Different standard solutions (2.5, 20, 200, 1000 μg/L) of OPEs prepared in 0.01 M NaCl were used in the following experiments. They were placed in appropriate containers (5 L glass beakers, 15 mL and 50 mL glass vials and the diffusion cells) and were shaken on a horizontal shaker for suitable times in an air-conditioned room (25 °C) at a speed of 150 rpm. Solution concentrations were measured frequently to check for any changes compared to the initial concentrations. Samples of 0.2 mL solution were collected and spiked with 0.1 mL acetonitrile and 0.1 mL SIS solution and then filtered through a 0.2 μm PTFE syringe filter into LC amber vials before analysis by LC-MS/MS.

DGT sampler materials such as moldings, diffusive gels and membrane filters were tested for possible sorption losses separately. They were immersed in a 25 mL solution containing ca. 200 μg/L OPEs and 0.01 M NaCl for 6 hours. After spiking of 50 ng SIS, DGT moldings, diffusive gels and membrane filters were separately eluted with 3 × 2 mL aliquots of acetonitrile and sonicated for 5 minutes between each elution. The elution solution was evaporated to dryness by gentle nitrogen and reconstituted in 1 mL of acetonitrile and water (v:v = 50:50) and then filtered through a 0.2 μm PTFE syringe filter into LC amber vials. Samples were stored at 4 °C before analysis by LC-MS/MS. Solution concentrations were measured to calculate the mass losses from mass balance. The detailed sample treatment procedure is given in Extraction efficiency in SI.

The sorption and permeation properties of polymeric membranes are governed by their molecular characteristics and membrane structures (pore size, distribution and density, surface roughness, thickness, etc.) (Vermeirssen et al., 2012). Although there is great potential for materials science and industry to improve membrane properties for passive samplers (Endo and Matsuura, 2018), one aim of this study is to characterize the present available membrane filters to find the most suitable one for DGT devices for measuring organic contaminants and to investigate their influences on the DGT sampler. Three types of membrane filters were tested for possible sorption of model compounds. They were hydrophilic polyethersulfone (PES) membranes (thickness: 140 μm, diameter: 25 mm, pore size: 0.45 μm, PALL), which is a well-studied membrane filter (Challis et al., 2016, Endo and Matsuura, 2018); hydrophilic polytetrafluoroethylene (PTFE) membranes (thickness: 150 μm, diameter: 25 mm, pore size: 0.45 μm, ANPEL); and hydrophilic polypropylene (GHP) membranes (thickness: 114 μm, diameter: 25 mm, pore size: 0.45 μm, PALL)—two of the most commonly used membrane filters for organic DGT samplers (Table S3.1). Sorption to PTFE membrane filters was also investigated in *DGT deployment* for 7 days. Solutions in DGT deployment were renewed every 12 hours to ensure stable concentrations. Further details are in the SI.

3.2.6 Diffusion coefficient measurements

One of the advantages of the DGT technique (compared to other passive sampling techniques) is that temperature specific diffusion coefficients (*D*) through the diffusion layer are well established in the laboratory, generating more reliable field measurements without the need for further field calibration. The *D* values of targeted compounds were

measured with a cast glass two-compartments diffusion cell (source and receptor) connected by a circular window (1.6 cm diameter) with a 0.8 mm thick diffusive gel (AG gel without filter). Both compartments were filled with 50 mL of 0.01 M NaCl solution. A 0.5 mL volume of stock solution containing 7 OPEs (100 mg/L) was spiked into the source compartment and the same volume of acetonitrile without OPEs was spiked into the receptor compartment. The solutions in both compartments were well stirred with mini glass-coated stirrer bars during the experiment. Solutions of 0.2 mL from both compartments were collected for analysis, after 5 minutes and then at intervals of 15 minutes for 3 hours.

The masses of analyte in the receptor compartment were plotted as a function of time to obtain a linear line with a slope that equals the first-order diffusion rate constant, k (mass, M, over time t). Eq (3.1) below was then used to calculate D (cm^2/s), where Δg is the diffusive gel thickness, c_s is the initial analyte concentration in the source compartment, and A_s is the area of the connecting window:

$$D = \frac{k\Delta g}{c_s A_s} \tag{3.1}$$

It is assumed that the thickness of the diffusive boundary layer (DBL) (δ) in the diffusion cell is negligible under the vigorously mixed conditions used in the experimental set-up (Garmo et al., 2006).

3.2.7 Uptake kinetics

The binding agent (Oasis HLB, 60 μm particle size, 80 Å pore size, 830 m^2/g surface area) used in the DGT devices is a water-wettable polymer, with high capacity for a wide range of compounds and is stable at pH 0–14. Uptake kinetics of the binding layer were investigated by immersing binding gel discs in 40 mL solutions containing ca. 200 μg/L OPEs and 0.01 M NaCl at 21 ± 2 °C (in triplicate), and shaken horizontally for 24 hours. Solution samples (0.2 mL) were collected at different times up to 24 hours, for further instrumental analysis, and the mass taken up by the binding gels was derived from the mass balance calculation.

3.2.8 DGT deployment

To test the DGT principle for measuring OPEs, DGT devices were deployed in 2.5 L solution containing ca. 20 μg/L OPEs and 0.01 M NaCl for various deployment times up to 45 hours at 19 ± 1 °C. According to the DGT eq (3.2), the mass of OPEs accumulated in the devices (M_{DGT}) should be increased linearly with deployment time (t).

$$c_{\mathrm{DGT}} = \frac{M_{\mathrm{DGT}}\Delta g}{tAD} \quad (3.2)$$

Further test was conducted for longer deployment time up to 7 days in solution with lower OPEs concentration. Devices were exposed in 2.5 L solution containing approximately 2.5 μg/L OPEs and 0.01 M NaCl and the solution was renewed every 12 hours to keep the concentrations approximately constant. The solution temperature ranged from 19 to 22 °C over the course of the experiment. To minimize the diffusive boundary layer, samplers were fixed on a steel frame in the solution and the solution was well stirred at 300 rpm by a glass-coated stirrer bar. Solution samples were collected before, during and after renewing the solution and samplers were retrieved at different times from 3 hours to 7 days. Binding gels, diffusive gels and membrane filters from every DGT device were extracted by acetonitrile immediately after deployment to obtain the mass of chemicals on them.

3.2.9 Quality assurance and quality control

Quality control standards (50 μg/L) were prepared using independent weighing and they were run every 10 samples (concentration to be within 20% of target). Linearity (R^2) of calibration standards was >0.99 over all analyses and all compounds. Matrix matched calibrators made by blank DGT extracts and 0.01 M NaCl solution were compared with calibrators made by pure acetonitrile and water. As a result, the matrix effects were negligible. The instrumental limit of detection (LOD) was from 0.01 (TEP) to 0.62 (TDCPP) μg/L (more details in SI). Where concentrations were below the detection limit, in statistical analyses, these values were substituted with LOD divided by the square root of 2.

3.3 Results and discussion

3.3.1 Sorption

Sorption on glassware walls

There was negligible sorption of 7 OPEs [TEP, TCEP, TPrP, TCPP, TDCPP, TBP, TPP, log K_{OW} (0.8–4.6), water solubility (1.9–5.0×10^5 mg/L)] in all glass containers and diffusion cells as their concentrations were stable at all 4 levels (2.5, 20, 200, 1000 μg/L). The concentrations of the 2 most hydrophobic OPEs [ToCP and TEHP, log K_{OW} (5.11, 9.49)] with much lower water solubility (360 and 600 μg/L) were stable at low

concentrations such as 2.5 and 20 μg/L but decreased sharply at high concentration 200 μg/L (Figure S3.5).

Sorption on DGT materials

i) DGT moldings and gels: Seven OPEs (except ToCP and TEHP) reached sorption equilibrium quickly (<3 hours), on the DGT plastic moldings and diffusive agarose gels, with negligible sorption (<1% of total mass in the solution) observed, as the concentrations in test solution hardly decreased. When extracting OPEs from DGT plastic moldings and diffusive agarose gels by acetonitrile, very small amounts (<1% of total mass in the solution) of chemicals, including ToCP and TEHP, were detected. This is consistent with studies on other organic chemicals (Chen et al., 2012, Zheng et al., 2015, Xie et al., 2018a) and it is encouraging, as the application of the current DGT moulding units and diffusive agarose gels are becoming widespread for the environmental sampling of trace organic chemicals.

ii) Membrane filters: Sorption varied considerably between membrane filters and compounds, but one finding was consistent: more hydrophobic compounds (TDCPP, TBP, TPP, ToCP and TEHP, log K_{OW} from 3.7 to 9.5) were always more prone to sorption onto the 3 types of membrane filters than more hydrophilic compounds (TEP, TCEP, TPrP and TCPP, log K_{OW} is from 0.8 to 2.6). However, less sorption occurred with PTFE than with the other two membrane filter types (Figure 3.2). In detail, there was little adsorption of TEP (0.28% ± 0.02% of total mass 5 μg), TCEP (0.38% ± 0.01%), TPrP (0.42% ± 0.04%) and TCPP (0.78% ± 0.03%) onto the PTFE membrane filter; slightly higher adsorption of TDCPP (6.8% ± 2.7%) and TBP (1.5% ± 0.11%) onto PTFE membrane filters was found; TPP (14.2% ± 5.1%) and ToCP (41.9% ± 11.2%) were significantly absorbed by PTFE membrane (see later for the detailed sorption profiles). PTFE was therefore chosen to be the filter for further study.

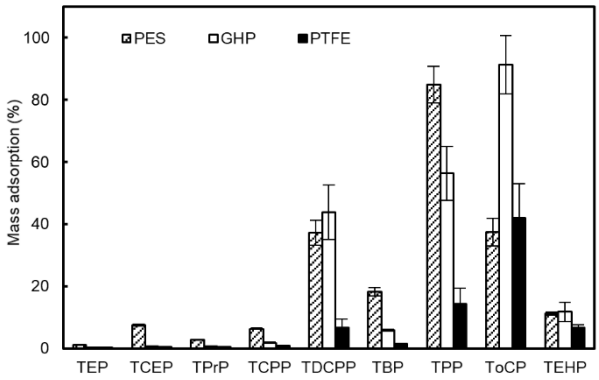

Figure 3.2. Adsorption of tested OPEs by 3 types of membrane filters in 25 mL solutions containing ca. 200 μg/L OPEs and 0.01 M NaCl for 6 hours. Error bars were calculated from the standard deviation of triplicates. Note, TPP, ToCP and TEHP appeared to have not reached sorption equilibrium after 6 hours, the time of this experiment.

For three chemicals (TPP, ToCP and TEHP) sorption equilibrium to membrane filters had not reached equilibrium after 6 hours, as the solution concentrations of those chemicals continued to decrease in the test solution. Experiments over much longer time were carried out and the results showed that TPP did not reach equilibrium until about 4 days, while ToCP and TEHP needed >6 days (Figure 3.3 for sorption profiles of OPEs on PTFE membrane filters). Endo and Matsuura did a sorption experiment which also showed that 6 out of 14 chemicals did not reach apparent equilibrium on PES polymer over 7 days (Endo and Matsuura, 2018).

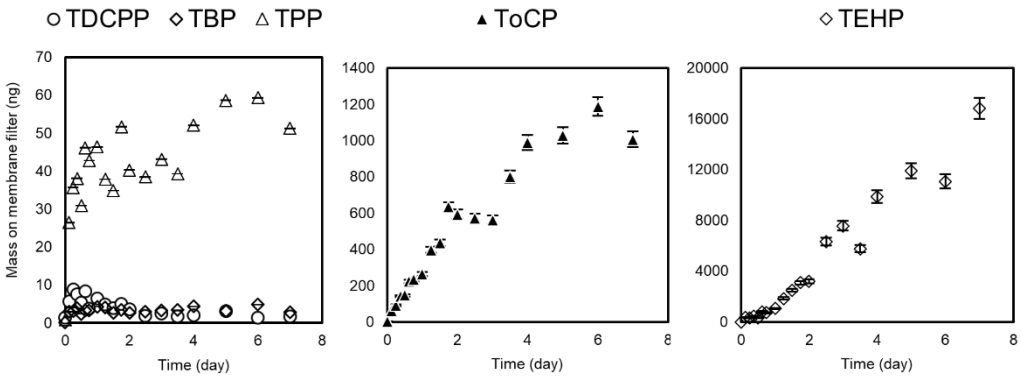

Figure 3.3. Sorption profiles of 5 OPEs on PTFE membrane filters from DGT samplers exposed in solution with a few micrograms per liter OPEs (Figure S3.8) and 0.01 M NaCl from 3 hours to 7 days (note that the solution was renewed every 12 hours to keep the concentrations approximately constant), error bars were calculated from the standard deviation of triplicates. The other 4 compounds (TEP, TCEP, TPrP and TCPP) showed negligible sorption on PTFE membrane filters and are not present here.

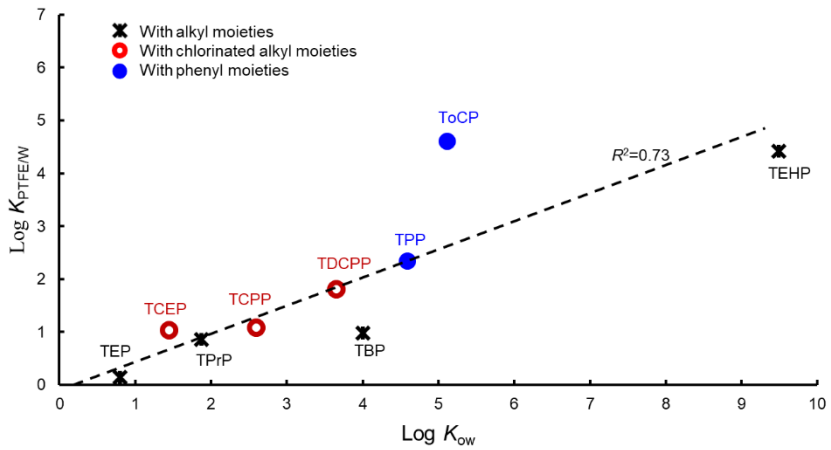

Figure 3.4. Log $K_{PTFE/W}$ vs log K_{OW} (note that $K_{PTFE/W}$ of TEHP were estimated based on membrane filters sorption study the sorption capacity of PTFE membrane filter for TEHP was higher than 16 µg). The dashed line indicates the linear regression for studied chemicals (log $K_{PTFE/W}$ = 0.52 log K_{OW} – 0.02, R^2 = 0.73, p < 0.05).

$K_{PTFE/W}$ values (the ratio of the concentration of a studied chemical in PTFE membrane filter and water at equilibrium at the temperature in this study) were plotted against K_{OW} to compare the sorption strength of the PTFE membrane filter across studied chemicals (Figure 3.4). Log $K_{PTFE/W}$ was significantly correlated with log K_{OW} (log $K_{PTFE/W}$ = 0.52 log K_{OW} – 0.02, R^2 = 0.73, p < 0.05). Note that for TEHP, which didn't reach equilibrium after 7 days, a sorption mass of 16.8 µg on the 7th day was used (R^2 = 0.76 if estimated sorption mass was 2 times of 16.8 µg, R^2 = 0.82 if estimated sorption mass was 10 times of 16.8 µg). Although sorption by PTFE in comparison to K_{OW} has been conducted before with, e.g., carcinogens, industry additives, solvents and pharmauceticals (Endo and Matsuura, 2018, Leggett and Parker, 1994), no significant correlations between log $K_{PTFE/W}$ and log K_{OW} were found. We consider the chemical property ranges were not wide enough to see a correlation. Log $K_{PTFE/W}$ was <1.78 for all studied chemicals in the study by Leggett and Parker (Leggett and Parker, 1994), log $K_{PTFE/W}$ was <1.65 for all studied chemicals in study by Endo and Matsuura (Endo and Matsuura, 2018), while this study substantially pushed the boundary to 4.61 (log $K_{PTFE/W}$ of ToCP). Thus, hydrophobicity (as reflected by log K_{OW}) seems one factor influencing chemicals sorption on PTFE polymer and this slow equilibration (Figure 3.4). Diffusion through the filter pores is strongly retarded by sorption to the polymeric matrix. However, this cannot explain that relatively hydrophilic chemicals, like caffeine (log K_{OW} = –0.07, 194.2 Da) showed slow sorption equilibration (>7 d) on the PES matrix (Endo and Matsuura, 2018). ToCP stands out of the regression line in Figure 3.4, which seems also to suggest hydrophobicity is not the only factor influencing this slow equilibration. We speculate

that aromatic rings in caffeine (imidazole ring) cause slow equilibration, by increasing electrostatic interactions between electron-rich π systems and the polymeric matrix (Keiluweit and Kleber, 2009), the same as ToCP (benzene ring) in this study.

3.3.2 Diffusion coefficients

Diffusion coefficients of seven OPEs in diffusive gel measured using the diffusion cell are presented in Table S3.7. Good linear relationships (R^2 from 0.97 to 0.99) of diffused masses versus time were obtained (Figure S3.3). The two least water soluble compounds ToCP and TEHP (360 and 600 μg/L, respectively) showed significant sorption to the diffusion cell wall, which made it impossible to keep the concentrations in source compartment stable with the normal diffusion cell system used here. The difficulties of working with very low aqueous solubility compounds in laboratory experiments is well known (Di and Kerns, 2006, Su et al., 2016); different approaches, such as the use of a generator column or a loaded stirrer bar, may be useful in future studies on these types of chemicals.

The diffusion coefficients (D) at 25 °C were 6.77×10^{-6}, 6.19×10^{-6}, 5.47×10^{-6}, 6.17×10^{-6}, 5.26×10^{-6}, 4.46×10^{-6} and 5.61×10^{-6} cm^2/s for TEP, TCEP, TPrP, TCPP, TDCPP, TBP and TPP, respectively, which agreed well with D of 5 OPEs (TCEP, TCPP, TDCPP, TPrP and TBP) published before (Zou et al., 2018). The ratios of D in this study to those published by Zou et al were in the range of 0.9–1.1.

3.3.2 Uptake kinetics

When the DGT binding layer rapidly and irreversibly binds target chemicals, this ensures the concentration of the analyte at the interface between the binding layer and diffusion layer is effectively zero. Then the mass transport of the analyte through the diffusion layer can achieve a steady state and the DGT eq (3.2) can be used to accurately determine the DGT concentration (c_{DGT}) of the analyte in the solution.

The OPEs were taken up rapidly (ca. 40% uptake in 1 hour) by the binding gels, followed by more gradual uptake (Figure S3.4) for all the compounds except ToCP and TEHP. The concentration of ToCP and TEHP decreased sharply, due to rapid sorption to the glassware (Figure S3.5). Further procedures mentioned earlier are needed to keep ToCP and TEHP water concentrations relatively constant, in order to assess uptake kinetics.

As the DGT principle only works within the linear accumulation range of the resin gel, it is important to verify the DGT performance by deploying devices in a solution at constant concentration for different times. For all 9 OPEs tested, 7 of them (except ToCP and TEHP) showed linear increase in accumulated mass with deployment time. The linear relationship was compared with a theoretical line of mass versus time predicted using DGT eq (3.2). At initial stages of the deployment, analytes have to diffuse through the membrane filter and then the diffusive gel layer. For chemicals with high affinity to the membrane filter, the resulting lag times cause the actual mass accumulation line to deviate from the theoretical line as shown in Figure 3.5 except ToCP. The greater the sorption onto the membrane filter, the greater the deviation from the theoretical linear line. This point is demonstrated by the results of TPP, ToCP and TEHP (Figures 3.5, S6).

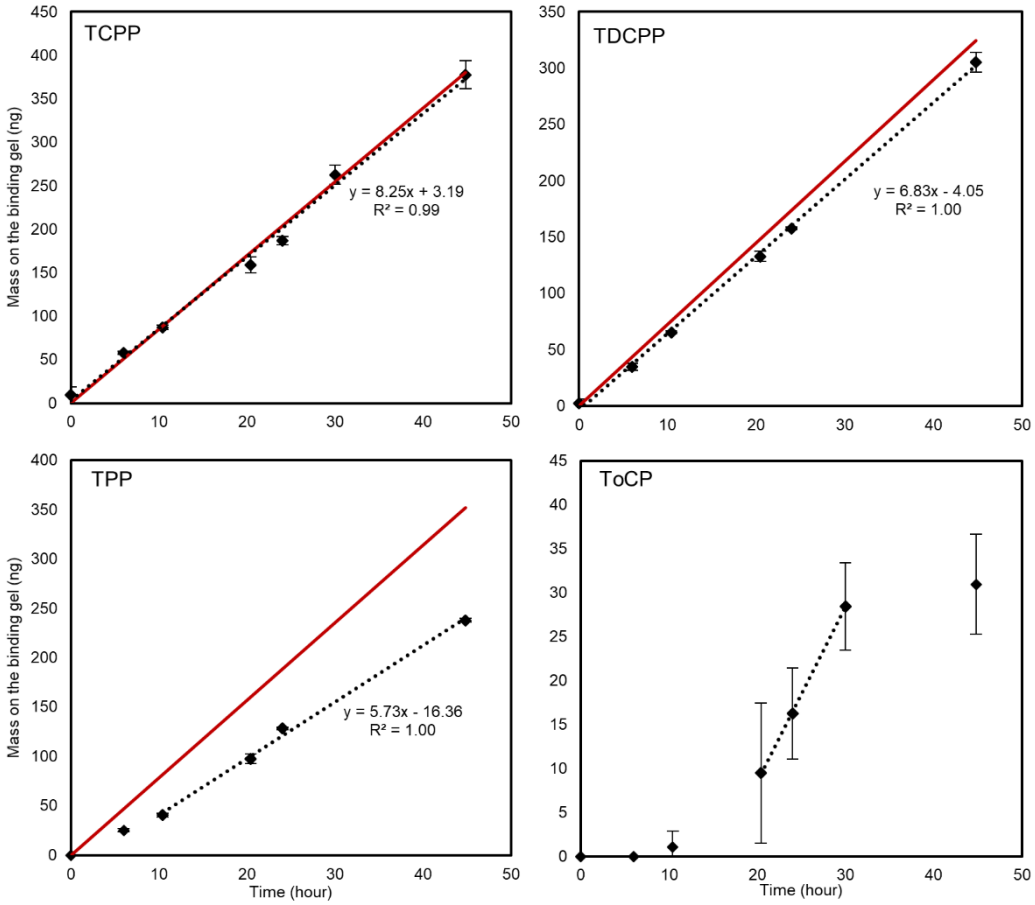

Figure 3.5. Linear mass accumulation of 4 selected OPEs over time by DGT samplers exposed in 2.5 L solution containing ca. 20 µg/L OPEs and 0.01 M NaCl for various deployment times up to 45 hours. The red solid line is the theoretical mass accumulation line, assuming δ = 0.3 mm. Error bars were calculated from the standard deviation (SI) of triplicates. (Figure S3.6 presents all the compounds).

3.3.2 Establishing steady state

The time to achieve linear mass accumulation (steady state), t_{ss}, can be estimated using eq (3) (Davison and Zhang, 2016). Here Δg represents the diffusion layer thickness, with the diffusion coefficient being an aggregated value for the diffusive gel and membrane filter.

$$t_{ss} = \frac{\Delta g^2}{2D} \quad (3)$$

If the overlaid membrane filter had negligible adsorption effect, the transient times for OPEs (except ToCP and TEHP) were about 16 minutes, which would be consistent with previous works (Zhang et al., 1995, Garmo et al., 2008b, Garmo et al., 2008a). However, the interactions of analytes with the membrane filter substantially extend the time needed to reach steady state. This study provides a standard procedure to measure it by exposing a series of DGT samplers at environmental concentration levels (nanograms to micrograms per liter) (Wang et al., 2015, Xu et al., 2019) of a testing solution until linear mass accumulation is achieved.

Figure 3.6 illustrates the masses accumulated in binding gels for the longer deployment time of 7 days. Black dotted lines show the establishment of steady state in the binding gels and intercepts of the time-axis are the lag times required for establishing it. For DGT device with a 0.8 mm thick diffusive gel and a 0.14 mm thick PTFE membrane filter under the testing solution conditions (a few micrograms per liter OPEs, Figure S3.8), steady state was effectively reached within 18 minutes for TEP and 42 minutes for TCEP. The errors caused by lag time are <3% for deployments of 24 h or greater for shorter sampling windows. Longer deployment times of >24 h for TPrP and more than a week for TCPP are necessary to ensure <10% error. For TDCPP, TBP, TPP, ToCP and TEHP, the recommended minimum deployment time would be 2 weeks to 2 months due their long lag times (Table S3.8). As shown in Figure 3.7, DGT measured concentrations of TEP, TCEP, TPrP and TCPP agreed well with the bulk solution concentrations, with cDGT/csoln ranging from 0.95–0.99, whereas the deviation of DGT measurement from the solution concentration increased for TDCPP, TBP and TPP. The theoretical method quantitation limits (MQLs) of the DGT technique can be converted from MDLs [1.05 ng/L (TEP), 0.49 ng/L (TCEP) and 0.43 ng/L (TPrP), refer Table S3.5, MDGT equals 1.05, 0.49 and 0.43 ng, respectively] to a concentration by eq (3.2), depending on the deployment time. For 24 hour deployment, using D = 6.77E-06 cm^2/s (TEP), 6.19E-06

cm^2/s (TCEP), 5.47E-06 cm^2/s (TPrP), Δg = 0.125 cm, A_s = 3.14 cm2, the MQLs are 71 ng/L (TEP), 36 ng/L (TCEP) and 36 ng/L (TPrP) and for 1 week deployment, the MQLs are 10 ng/L (TEP), 5 ng/L (TCEP) and 5 ng/L (TPrP). The single-digit ng/L sensitivity agrees well with this field study (Challis et al., 2018b). It is worth mentioning that the lag time was tested at a general environmental concentration level (a few micrograms per liter). In the case where the adsorption of the chemicals on the membrane filter is significant, the lag time is dependent on not only the D value, but also the concentration of the chemicals in the environment due to the adsorption capacity of the membrane filter. If the testing solution is at very high concentrations or the environmental concentrations are extraordinary high (>10s μg/L or even >100s μg/L), the lag time could be negligible.

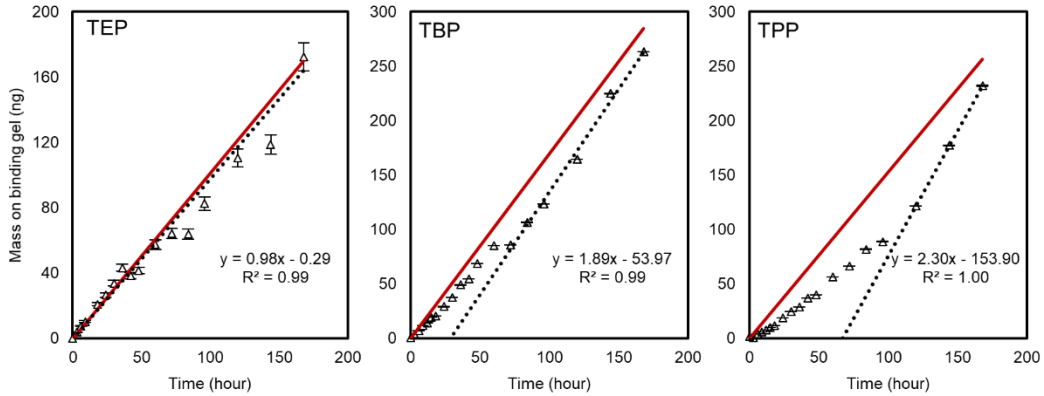

Figure 3.6. Mass accumulation of 3 selected OPEs over time by DGT samplers exposed in 2.5 L solution containing a few micrograms per liter OPEs (Figure S3.8) and 0.01 M NaCl from 3 hours up to 7 days. The red solid line is a theoretical mass accumulation line, δ = 0.3 mm. Error bars were calculated from the standard deviation (SI) of triplicates (Figure S3.7 for all the compounds).

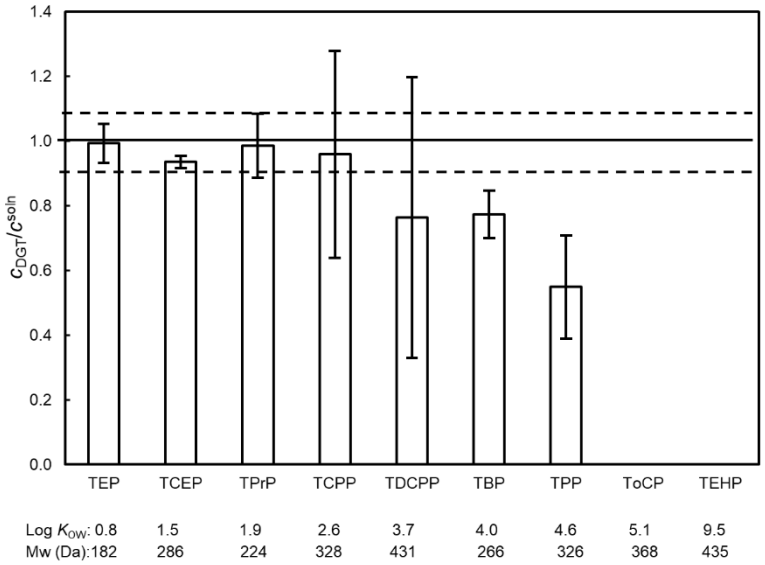

Figure 3.7. Ratios of DGT-measured OPEs concentrations, c_{DGT}, to their concentrations in the bulk solution, c^{soln}, during *DGT deployment* in which DGT samplers were exposed

in 2.5 L solution containing a few micrograms per liter OPEs (Figure S3.8) and 0.01 M NaCl from 3 hours up to 7 days. The solid line represents the target value of 1.0. Values were expressed as mean ± standard deviation of 18 DGT samplers.

3.4 Conclusions

DGT integrated with UHPLC-MS/MS can be used to monitor trace organic pollutants in aquatic systems. This study used 9 OPEs as model chemicals, which covered ~75% of the organic chemicals (in terms of log K_{OW} and molecular weight) for which the DGT technique has been developed, to investigate limitations of the standard DGT configuration for measuring organic chemicals. We have demonstrated that DGT is potentially reliable for measuring hydrophilic [log K_{OW} (0.8–2.6)] and non-aromatic-ring chemicals at short and long deployment times. Organic chemicals with high hydrophobicity or aromatic rings are prone to retention on membrane filters, which delays their diffusion, causing a lag time before linear mass accumulation in the DGT sampler. For those compounds, a standard procedure to determine lag times is presented, by deploying a series of DGT devices in waters until linear mass accumulation with time in the devices is achieved and the time-axis intercepts are treated as lag times. In practice, a deployment time of 24 hours in an experiment or field monitoring situation would have a sampling time error of <3% for compounds TEP and TCEP; when the deployment time is 2 weeks, the sampling time error is <10% for most compounds (TEP, TCEP, TPrP, TCPP, TDCPP and TBP) but is higher for TPP (~20%), ToCP (~40%) and TEHP (>40%). Although a membrane filter could cause retention from minutes to days, it is necessary to protect the diffusive gel from clogging by particles and to prevent organisms going into the DGT device. This study focuses on the limitation of the current DGT sampler for measuring organic chemicals and we have identified the absolute limitation to use the current DGT device for organics is adsorption in the diffusion layer, mainly in membrane filters. However, it is possible to extend the DGT technique for a wider range of chemicals, for example, by replacing the current DGT membrane filter with a new type of membrane filter which does not interact with compounds such as ToCP and TEHP. New configurations of DGT devices using different materials for housing the binding and diffusion layers, new types of diffusion layer and membrane filters should be developed for both fields of research and monitoring. Studies are being undertaken to address concerns over effects of biofouling and compound degradation/loss during sample handling/storage on the sampler performance and will be the subject of a separate article.

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Notes

The authors declare no competing financial interest.

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Supporting information

Detailed list of studies on the DGT technique, further details of chemicals and reagents, detailed information on tested chemicals, analytical methods, experimental details, statistical analysis, supplementary results and discussion (PDF)

SUPPLEMENTARY INFORMATION

Investigating potential limitations of current diffusive gradients in thin films (DGT) samplers for measuring organic chemicals

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3.2 Results and discussion

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Table S3.2. Physicochemical properties of the 9 chemicals

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Figure S3.2. Example chromatograms of OPEs

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Figure S3.4. Uptake kinetics of OPEs by binding gels in 40 mL solutions containing ca. 200 μg/L OPEs and 0.01 M NaCl at 21 ± 2 °C. Error bars were calculated from the standard deviation (SD) of triplicates.

Figure S3.5. Concentrations of ToCP and TEHP in 0.5 L 0.01 M NaCl solution (1 L glass beaker) after spiking 1 mL of 100 μg/mL stock solution.

Figure S3.6. Linear mass accumulation of OPEs over time by DGT samplers exposed in 2.5 L solution containing ca. 20 μg/L OPEs and 0.01 M NaCl for various deployment times up to 45 hours (19–22 °C). The red line is the theoretical mass accumulation line, assuming δ = 0.3 mm (average concentrations were used when calculating theoretical accumulation of mass). Error bars were calculated from the standard deviation (SD) of triplicates.

Figure S3.7. Mass accumulation of OPEs over time by DGT samplers exposed in 2.5 L solution containing a few micrograms per liter(see Figure S3.8) OPEs and 0.01 M NaCl from 3 hours up to 7 days (19–22 °C). The red line is a theoretical mass accumulation line, δ = 0.3 mm (average concentrations were used when calculating theoretical accumulation of mass). Error bars were calculated from the standard deviation (SD) of triplicates.

Figure S3.8. Solution concentration (μg/L) of all 9 compounds over the 7 d test experiment. Solution was renewed every 12 hours and the solution samples were collected every time before, middle and after renewing the solution. Black square data points represent mean and standard deviation of 34 sampling points over 7 d. The minimum (orange triangles) and maximum (blue circles) over 34 sampling points are also shown.

Table S3.1. Studies on DGT technique for organic compounds from 16 research groups

Research group	Analyte	DGT configuration	Validated pH and ionic strength	Comments	Reference
Lancaster University, U.K.	Sulfamethoxazole	0.5 mm XAD18 agarose binding gel+0.8 mm agarose diffusive gel+ poly(ether sulfone) membrane (PES)	pH 6.0–9.0 0.001–0.1 M NaCl	DGT was for the first time developed for in situ sampling of organics taking one antibiotic as a model compound.	(Chen et al., 2012)
	40 antibiotics			DGT was validated in the influent and effluent of a typical UK wastewater treatment plant (WWTP) for 40 antibiotics.	(Chen et al., 2013)
	Sulphonamide and trimethoprim antibiotics			DGT was used to study the sorption/desorption of antibiotics in soils.	(Chen et al., 2014)
	Sulphonamide and trimethoprim antibiotics			Reported the first use of DGT for organics in soil systems to gain insight into the mobility and lability of organics.	(Chen et al., 2015a)
	16 antibiotics			DGT was employed to assess the occurrence and removal of antibiotics in waste water treatment plants (WWTPs).	(Chen et al., 2015b)
	HPCPs including seven preservatives and one of their metabolites, two antioxidant and three disinfectants	Oasis HLB polyacrylamide binding gel+ agarose diffusive gel+ Nuclepore track-etch membrane	pH 3.5–9 .5 0.001–0.1 M NaCl	DGT was developed for HPCPs by evaluating the performance of different binding agents.	(Chen et al., 2017)
	8 endocrine disrupting chemicals	0.4 mm HLB and XAD18 polyacrylamide binding gel+1mm agarose diffusive gel+ Nuclepore track-etch membrane	pH 3.5–9.5 0.001–0.5 M NaCl DOM 0–20 mg/L	Three different binding agents were investigated for their suitability as the binding phase for DGT devices.	(Chen et al., 2018)
University of Portsmouth, UK	Organotins (monobutlytin (MBT), dibutyltin (DBT), tributyltin (TBT), diphenyltin (DPhT), triphenyltin (TPhT))	C8 and C18 silica binding gel+ agarose diffusive gel+ cellulose nitrate	pH 4–9 0.01–1.0 M NaCl	Devices were used to investigate DGT fluxes and pore water concentrations of organotins in coastal sediment collected from a contaminated site.	(Cole et al., 2018)
Northeastern University, Shenyang University of Chemical Technology, China	Phenol	molecularly imprinted polymer binding gel+ pretreated nylon membrane	pH 3–7 0.0001–0.1 M	DGT was developed for the sampling of phenol in water.	(Dong et al., 2014b)
	4-chlorophenol		pH 3–7 0.0001–0.1 M	DGT was developed for the sampling of 4-chlorophenol in water.	(Dong et al., 2014a)
University of the French West Indies, France	Glyphosate (2.57) and aminomethyl phosphonic acid	Titanium Dioxide binding gel+ polyacrylamide cross-linked with an	pH 5–8.5 UPW	DGT was validated for estimating concentration of a herbicide and its	(Fauvelle et al., 2015)

		agarose derivative + PES membrane		major degradation products in surface water.	
University of Oslo, Norway	Adenosine monophosphate (AMP) and myo-inositol hexakisphosphate (IP6)	Fe-oxide binding gel+ 0.8 mm agarose polyacrylamide diffusive gel+ 0.12 mm cellulose nitrate membrane		DGT was validated for low molecular weight organic phosphorus (LMWOP) compounds.	(Mohr et al., 2015)
Nanjing University, China	Biphenols: BPA, BPB and BPF	Activated charcoal agarose binding gel+0.8 mm agarose diffusive gel + Hydrophilic PTFE	pH 4.98–7.73 0.001–0.5 M	DGT was developed for 3 BPs (BPA, BPB, and BPF).	(Zheng et al., 2015)
				Assessment of bisphenols desorption from soils by DGT technique.	(Guan et al., 2017)
	6 organophosphorus flame retardants (OPFRs)	0.5 mm HLB agarose gel+0.75 mm agarose diffusive gel+ Hydrophilic PTFE	pH 3.1–9.5 0.0001–0.5 M DOM 0–20mg/L	DGT was developed for 6 relatively hydrophilic with lower log K_{OW} OPFRs (TCEP, TCPP, TDCPP, TPrP, TBP and TBEP).	(Zou et al., 2018)
	Triclocarban, triclosan and methyl triclosan	cyclodextrin polymer membrane binding phase+ 1 mm agarose diffusive gel+glass fiber filter	pH, ionic strength and DOM have little influence.	A cyclodextrin polymer membrane-based passive sampler for measuring triclocarban, triclosan and methyl triclosan in rivers.	(Wei et al., 2019)
	Perfluorooctanoic acid (PFOA) and Perfluorooctane sulfonate (PFOS)	XAD18 binding gel+ 0.75 mm agarose diffusive gel+hydrophilic PES filter membrane	pH 4.3–7.8, ionic strength 1–500 mmol/ L NaCl, and DOM concentrations 0–20 mg/L	DGT was developed for in situ measurement of perfluoroalkyl substances in aquatic systems.	(Guan et al., 2018)
University of Manitoba, Canada	34 pharmaceuticals and pesticides	0.75 mm, 25 mg Oasis agarose HLB binding gel+1.0 mm agarose diffusive gel		DGT without membrane was developed for pharmaceuticals and pesticides.	(Challis et al., 2016)
	30 pharmaceuticals and pesticides			Reported the freezer storage stability of pharmaceuticals and pesticides for DGT and POCIS.	(Challis et al., 2018a)
	31 pharmaceuticals and pesticides	Sepra™ ZT binding gel+polyacrylamide diffusive gel		A new configuration was developed.	(Stroski et al., 2018)
	34 pharmaceuticals and pesticides	0.75 mm Oasis agarose HLB binding gel+0.75 mm agarose diffusive gel	agricultural and wastewater-influenced freshwater systems	Field evaluation of the DGT in natural surface waters.	(Challis et al., 2018b)
University of Limoges, France	Bentazon, chlorsulfuron, ioxynil and mecoprop	0.8 mm Oasis HLB polyacrylamide binding gel+ polyacrylamide diffusive gel (15% acrylamide, 0.3% DGT Research patented crosslinker) (more suitable)		DGT without membrane was optimized for anionic pesticides.	(Guibal et al., 2017)

PSL Research University, France	16 emerging pollutants and pesticides	0.7 mm StrataX reversed phase sorbent agarose gel+1.2 mm agarose diffusive layer+Aluminium screen		Evaluated DGT is suitable for sampling contamination pulses as short as 5 min without deviation from the actual average concentrations of pollutants.	(Belles et al., 2017)
Chinese Research Academy of Environmental Sciences, China	Ketamine, methamphetamine, and amphetamine	0.5 mm XAD 18 agarose binding gel+0.8 mm agarose diffusive gel+ 0.14 mm PES membrane	pH 4–9 0.001 –0.1 M	Validated DGT method for three illicit drugs.	(Guo et al., 2017a)
	Methcathinone and ephedrine		pH 4–11 0.001–0.5 M	DGT was developed for two drugs.	(Zhang et al., 2018)
Vrije Universiteit Brussel, Belgium	17β-estradiol (E2)	0.5 mm XAD 18 agarose gel + agarose diffusive gel +hydrophilic PVDF	pH 5–8 0.001–0.5 M	Validated DGT method for 17β-estradiol (E2) as the model steroid hormone.	(Guo et al., 2017b)
Dalian University of Technology, China	20 antibiotics	0.5 mm XDA 1 agarose gel+ 0.8 mm agarose diffusive gel + polyethersulfone filter membrane	pH 7.3–8.9, 0.5–0.8 M	Validated DGT method for 20 antibiotics (Four were not included by (Chen et al., 2013): Azithromycin, Florfenicol, Thiamphenicol, Chloramphenicol) in seawater.	(Xie et al., 2018a)
	6 endocrine disrupting chemicals (edcs)	0.5 mm XDA 1 agarose gel+ 0.8 mm agarose diffusive gel	pH 7.0–9.0, 0.4–0.8 M	DGT without membrane was optimized for endocrine disrupting chemicals in seawarter.	(Xie et al., 2018b)
	20 antibiotics	porous carbon material (PCM) binding gel+agarose diffusive ge+PES membrane	pH 4.2–8.4 ionic strength 1–500mM	A new configuration for in situ measurement of antibiotics in water.	(Ren et al., 2018)
Liaoning University of Petroleum & Chemical Technology, Shenyang University of Chemical Technology, Northeastern University(2nd study), China	Nitrophenols : o-nitrophenol (ONP), p-nitrophenol (PNP), and 2,4-dinitrophenol (DNP)	lignocellulose hazelnut shell-derived activated carbons binding gel+ nylon membrane	pH 3–6 0.7–3 M	DGT was developed for measurement of nitrophenols in acidic aqueous solutions.	(You et al., 2019a)
	Tetracyclines (tetracycline, oxytetracycline and chlortetracycline)	nanosized ZnO particles binding agent + PES membrane	pH 5–9 0.001–0.1 pNaCl 0.155–3	DGT was developed for in situ sampling of TCs in pig breeding wastewater.	(You et al., 2019b)
University of Florida, USA	Ciprofloxacin (CIP) and azithromycin (AZ)	XAD18 agarose binding gel+ agarose diffusive gel+ Nylon filter		Desorption kinetics of CIP from biosolids were also evaluated by DGT.	(Sidhu et al., 2019)
University of Kentucky, USA	Tetracycline (TET)	XAD18 agarose binding gel+ agarose diffusive gel+ Nylon filter		Tetracycline desorption kinetics in municipal biosolids and poultry litter amendments determined by DGT.	(D'Angelo and Martin, 2018)
	Ciprofloxacin (CIP)			Desorption kinetics of ciprofloxacin in municipal biosolids	(D'Angelo and

				determined by DGT.	Starnes, 2016)
Bohai University, China	Ciprofloxacin (CIP)	ciprofloxacin-molecularly imprinted polymer binding agent+ 0.5mm agarose polyacrylamide diffusive gel+ cellulose acetate membrane	pH 2–11 0.0001–0.5 M	DGT was developed for sampling and measurement of ciprofloxacin in water.	(Li et al., 2018)

3.1 Materials and methods

3.1.1 Further details of chemicals and reagents

The nine organophosphate esters (OPEs) belong to three different chemical structural groups: four non-halogenated alkyl phosphates: triethyl phosphate (TEP), tripropyl phosphate (TPrP), tributyl phosphate (TBP) and tris(2-ethylhexyl) phosphate (TEHP); three halogenated (chlorinated) alkyl phosphates, tris(2-chloroethyl) phosphate (TCEP), tris(chloropropyl) phosphate (TCPP), and tris(1,3-dichloro-2-propyl) phosphate (TDCPP); and two aryl phosphates, triphenyl phosphate (TPP) and tri-o-cresyl phosphate (ToCP). OPE standards were purchased from Qmx (UK). HPLC grade acetonitrile (ACN) was supplied by Fisher Scientific UK limited. Deionised water used in all experiments was obtained from a Milli-Q water purification system (>18.2 MΩ cm^{-1}, Millipore, UK). Three types of membranes were tested: hydrophilic polytetrafluoroethylene (PTFE) membrane (thickness: 0.15 mm, diameter: 25 mm, pore size: 0.45 μm, ANPEL), hydrophilic polyethersulfone (PES) membrane (thickness: 0.14 mm, diameter: 25 mm, pore size: 0.45 μm, PALL) and hydrophilic polypropylene (GHP) membrane (thickness: 0.11 mm, diameter: 25 mm, pore size: 0.45 μm, PALL). The shiny side of the membranes were put towards the solution. HLB resins were extracted from Oasis-HLB solid-phase extraction (SPE) cartridges purchased from Waters Corporation (UK). Gel solution for making binding gels and DGT holders were provided by DGT Research Ltd (Lancaster, UK). Sodium chloride (NaCl), ammonium persulfate (APS) and N, N, N′, N′-tetramethylethylenediamine (TEMED) were purchased from Sigma-Aldrich (UK) and agarose was obtained from Bio-Rad Laboratories (UK). Samples were filtered through 0.2 μm PTFE syringe filters (diameter: 13 mm, GE Healthcare Life Sciences, Whatman) before analysis by LC-MS/MS.

Table S3.2. Physicochemical properties of the 9 chemicals

Abbreviation	Molecular weight (Da)	Log K_{OW}	Water solubility at 25 °C (mg/L)
TEP	182.16	0.8	5.00E+05
TCEP	285.49	1.4	7.00E+03
TPrP	224.24	1.9	6.45E+03
TCPP	327.57	2.6	1.20E+03
TDCPP	430.91	3.7	7.00E+00
TBP	266.32	4.0	2.80E+02
TPP	326.29	4.6	1.90E+00
ToCP	368.37	5.1	3.60E-01
TEHP	434.65	9.5	6.00E-01

Note: Blue colour figures indicate experimental database information, others are estimated (EPISUITE v4.00).

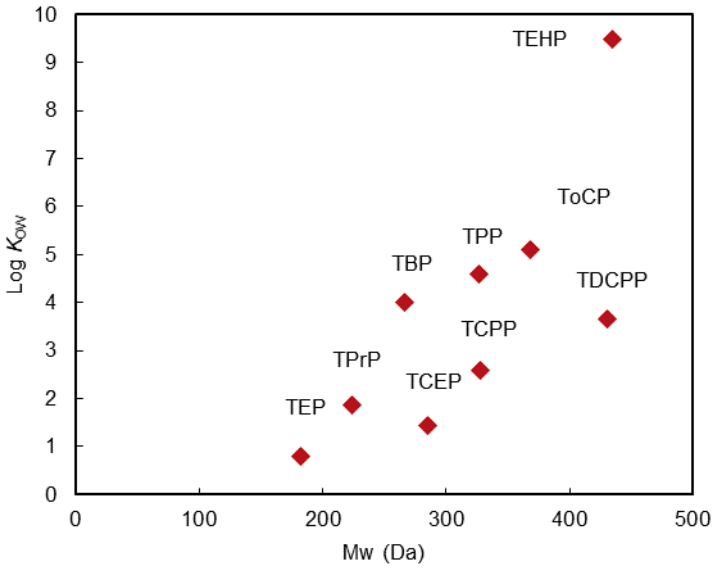

Figure S3.1. Molecular weight and log K_{OW} for the nine model chemicals

3.1.2 Instrumental analysis details

The chromatographic instrument was a Shimadzu Nexera UHPLC (Kyoto, Japan) equipped with LC-30AD pumps, a CTO-20AC column oven, a DGU-30A5 degasser, and an SIL-30AC autosampler. The autosampler was cooled at 20 ºC and the column temperature was at 45 ºC. The mobile phase consisted of (A) deionized water and (B) acetonitrile using a gradient elution of 40% B (1.0 min)–50% B (3.0 min)–60% B (7.0 min)–80% B (7.5 min)–100% B (8.0 min) –100% B (11.0 min)–40% B (11.5 min)–40% B (17.0 min). The flow rate was 0.2 mL/min. The injection volume was 10 µL. A triple quadrupole mass spectrometer (Shimadzu LCMS-8040, Kyoto, Japan) was connected to the LC instrument via an electrospray ionization (ESI) interface. The mass spectra were acquired in positive ion mode. The DL temperature was set at 250 ºC, heat block

temperature at 400 ºC, nebulizing gas at 2.0 L/min and drying gas at 15.0 L/min. The MRM parameters and dwell time are shown in Table S3.2. OPEs gradient standards were prepared by diluting stock solution with deionized water and acetonitrile (v:v = 1:1). TBP and TPP were calibrated using matched isotope labelled standards as surrogate internal standards and the other target compounds were calibrated using the external standard method. All the target compounds were separated in 10.5 minutes and the RSD% of retention time of all the target compounds in all the samples were between 0.11 and 1.8. The calibration curves of eight OPEs gave correlation coefficients (r) >0.999; TEHP was 0.998, as shown in Table S3.3.

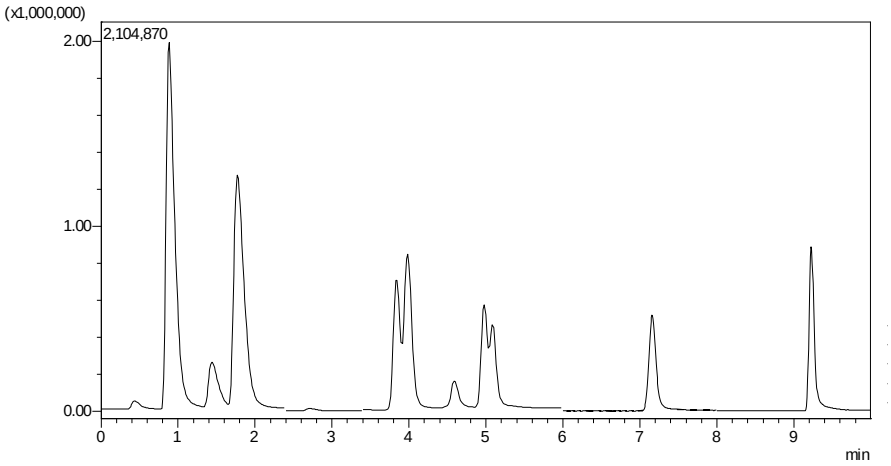

Figure S3.2. Example chromatograms of OPEs

Table S3.3. MRM parameters of OPEs and isotope labelled OPEs

Compound	Precursor ion (*m/z*)	Product ion *(m/z)*	Dwell time (msec)	Q1 pre bias (V)	CE (V)	Q3 pre bias (V)
TEP	182.80	99.05*	100	-12.0	-21.0	-16.0
		127.00	100	-12.0	-14.0	-21.0
TCEP	265.40	203.85*	150	-17.0	-8.0	-12.0
		183.35	150	-18.0	-7.0	-18.0
TPrP	266.05	99.20	100	-18.0	-24.0	-14.0
		225.2*	100	-15.0	-7.0	-15.0
TCPP	326.90	99.35*	300	-22.0	-26.0	-17.0
		251.20	300	-22.0	-10.0	-24.0
TDCPP	337.15	255.35*	100	-22.0	-11.0	-27.0
		276.05	100	-23.0	-9.0	-11.0
TBP-d27 (SIS)	294.35	102.2*	100	-19.0	-20.0	-18.0
		166.15	100	-19.0	-13.0	-30.0
TBP	308.10	99.25	100	-20.0	-22.0	-19.0
		267.3*	100	-20.0	-7.0	-11.0
TPP	344.00	327.15*	100	-16.0	-11.0	-21.0
		152.20	100	-23.0	-46.0	-27.0
TPP-d15 (SIS)	359.10	342.3*	100	-24.0	-11.0	-22.0
		82.30	100	-24.0	-45.0	-30.0
ToCP	385.80	369.25*	200	-26.0	-12.0	-24.0
		165.35	200	-26.0	-47.0	-28.0
TEHP	498.25	457.45*	250	-23.0	-12.0	-21.0
		345.40	250	-17.0	-24.0	-15.0

*: Quantitative transition; SIS: surrogate internal standard

Table S3.4. The calibration curves of the 9 OPEs

Compound	Calibration curve	r	Calibration range (μg/L)
TEP	Y = – 197.139X^2 + 245,983X – 8,443.41	0.9999	0.03–500
TCEP	Y = – 30.7575X^2 + 32,230.0X + 5,303.00	0.9998	1.07–500
TPrP	Y = – 113.091X^2 + 137,298X + 10,787.8	0.9998	0.31–500
TCPP	Y = – 0.842095X^2 + 1,603.31X + 395.449	0.9999	1.15–500
TDCPP	Y = – 23.4851X^2 + 13,264.4X + 5,029.62	0.9999	1.89–200
TBP	Y = – 0.021743^2 + 0.819491X + 0.038736	0.9997	0.31–500
TPP	Y = – 0.004587X^2 + 0.740110X + 0.001444	0.9999	0.87–500
ToCP	Y = – 34.6646X^2 + 67,008.4X – 10,932.4	0.9999	0.06–500
TEHP	Y = – 445.094X^2 + 174,051X + 396,866	0.9981	0.11–100

The instrumental limit of detection (LOD) and limit of quantitation (LOQ) were defined as the lowest concentration of analyte for which the observed signal/noise ratio (S/N) = 3 and 8. The method detection limit (MDL) was defined as mean blank DGT concentration plus three times the standard deviation (3σ).

Table S3.5. LOD, LOQ and MDL for all nine model chemicals

Compound	TEP	TCEP	TPrP	TCPP	TDCPP	TBP	TPP	ToCP	TEHP
LOD (µg/L)	0.01	0.35	0.10	0.38	0.62	0.10	0.29	0.02	0.04
LOQ (µg/L)	0.03	1.07	0.31	1.15	1.89	0.31	0.87	0.06	0.11
MDL (ng/L)	1.05	0.49	0.43	2.45	0.88	0.14	1.08	0.84	1.39

3.1.3 Experimental details

Sorption experiments

A plastic diffusion cell and PTFE-coated stirrer bars are typically used to measure the diffusion coefficients of metals and other polar organics. However, we found appreciable mass losses on the surface of the plastic diffusion cell and PTFE-coated stirrer bars, especially for the relatively more hydrophobic OPEs (e.g. TDCPP, TBP, TPP, ToCP and TEHP). Thus, a cast glass injection-molded diffusion cell and glass-coated stirrer bars were used in this study. In this study, we assume nine OPEs are stable and with no significant degradation at neutral pH over a period of seven days at room temperature.(Su et al., 2016)

Extraction efficiency

DGT samples (binding gels) were processed by ultrasound-assisted extraction. Therefore, an accurate and precise determination of the extraction efficiency of the analytes from the binding gel is needed. Six binding gels were exposed in 0.5 L of ca. 20 µg/L OPEs solution for 6 hours (shaken at 300 rpm). The binding gels were retrieved and placed in a 15 mL glass vial separately, spiked with 50 ng of surrogates directly onto the gel and left for 15 minutes, to allow the surrogates to soak into the binding gel. Separate 3 × 2 mL aliquots of acetonitrile were added with sonication for 5 min between each addition. The aliquots were combined in a separate vial and evaporated to dryness by gentle nitrogen blowdown. Dried samples were reconstituted in 1 mL of acetonitrile and water (v:v = 50:50) and filtered through a 0.2 µm PTFE syringe filter into LC amber vials. Samples were stored at 4 °C before analysis by LC-MS/MS. The mass of analyte on the binding gel and the mass decrease in the solution was used to determine recoveries.

Solution samples that were collected from the synthetic solutions were analyzed by LC-MS/MS after being spiked with ACN and SIS and filtered through a 0.2 µm PTFE syringe filter. DGT binding gels, diffusive gels and membranes were processed in the above described method and corrected with the achieved extraction efficiencies (Table S3.6).

Table S3.6. Extraction recoveries for the nine target analytes

Compound	Recovery (%)	Compound	Recovery (%)	Compound	Recovery (%)
TEP	31.4 ± 4.3	TCPP	55.3 ± 7.3	TPP	99.4 ± 0.2
TCEP	67.5 ± 4.1	TDCPP	33.1 ± 2.4	ToCP	19.7 ± 4.3
TPrP	30.7 ± 2.5	TBP	99.9 ± 0.1	TEHP	5.4 ± 0.4

Diffusion measurements

A diffusion cell containing two compartments (source and receptor) connected by a circular window (1.6 cm diameter) with a 0.8 mm diffusive gel (AG gel without filter) was used. Both compartments were filled with 50 mL of synthetic solution. The stock solution of 7 compounds was spiked into the source compartment and the same volume of acetonitrile was spiked into the receptor compartment. The solutions in both compartments were well stirred with mini glass-coated stirrer bars during the experiment. Solutions from both compartments were collected and analyzed at intervals of 30 min for four hours.

3.1.4 Statistical analysis

SPSS23 rel1 was used for statistical analysis. A one-way ANOVA with a Tukey posthoc test was used to compare measured analyte concentrations by DGT and solution concentration directly measured by LC-MS/MS. Significant differences were defined as $p < 0.05$. Errors were presented as standard deviations of the mean.

3.2 Results and discussion

Table S3.7. Diffusion coefficients of OPEs measured in the two-compartment diffusion cell

D (cm^2/s)	TEP	TCEP	TPrP	TCPP	TDCPP	TBP	TPP
D (23 °C)	6.41E-06	5.86E-06	5.18E-06	5.84E-06	4.98E-06	4.23E-06	5.31E-06
D (25 °C)	6.77E-06	6.19E-06	5.47E-06	6.17E-06	5.26E-06	4.46E-06	5.61E-06

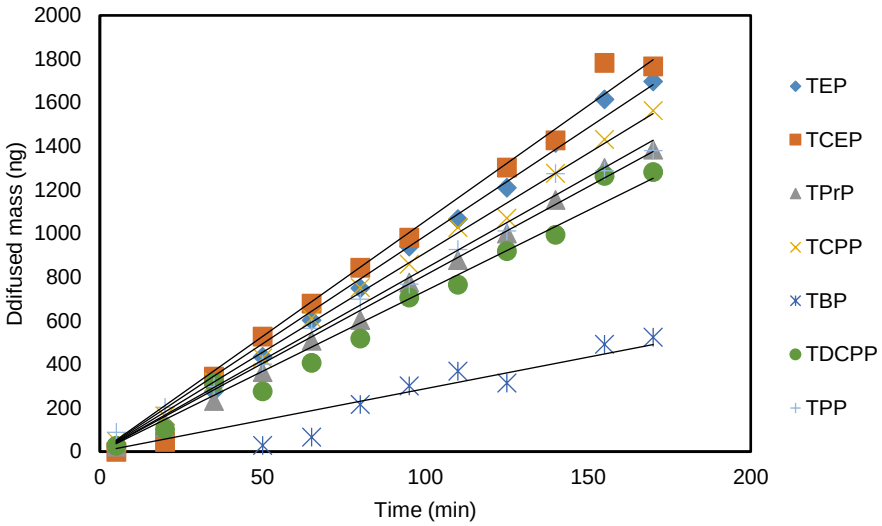

Figure S3.3. Diffused masses of TEP, TCEP, TPrP, TCPP, TDCPP, TBP and TPP in the acceptor compartment through 0.8 mm thick AG gel at different times in a cast glass diffusion cell with ca. 1 mg/L analytes in the source compartment at the beginning. Conditions: temperature was 23 ± 0.2 °C, ionic strength was 0.01 M NaCl.

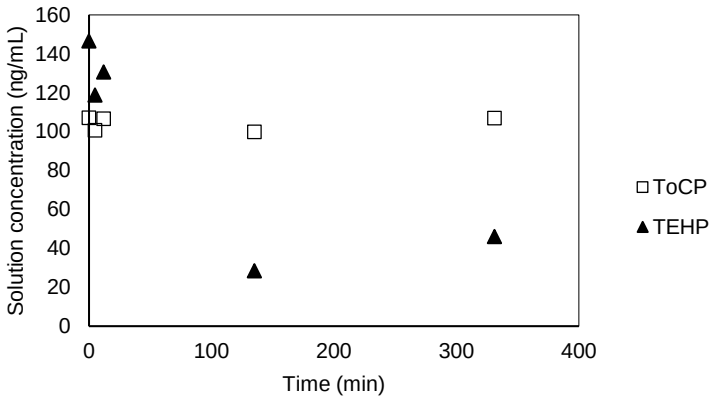

Figure S3.5. Concentrations of ToCP and TEHP in 0.5 L 0.01 M NaCl solution (1 L glass beaker) after spiking 1 mL of 100 µg/mL stock solution.

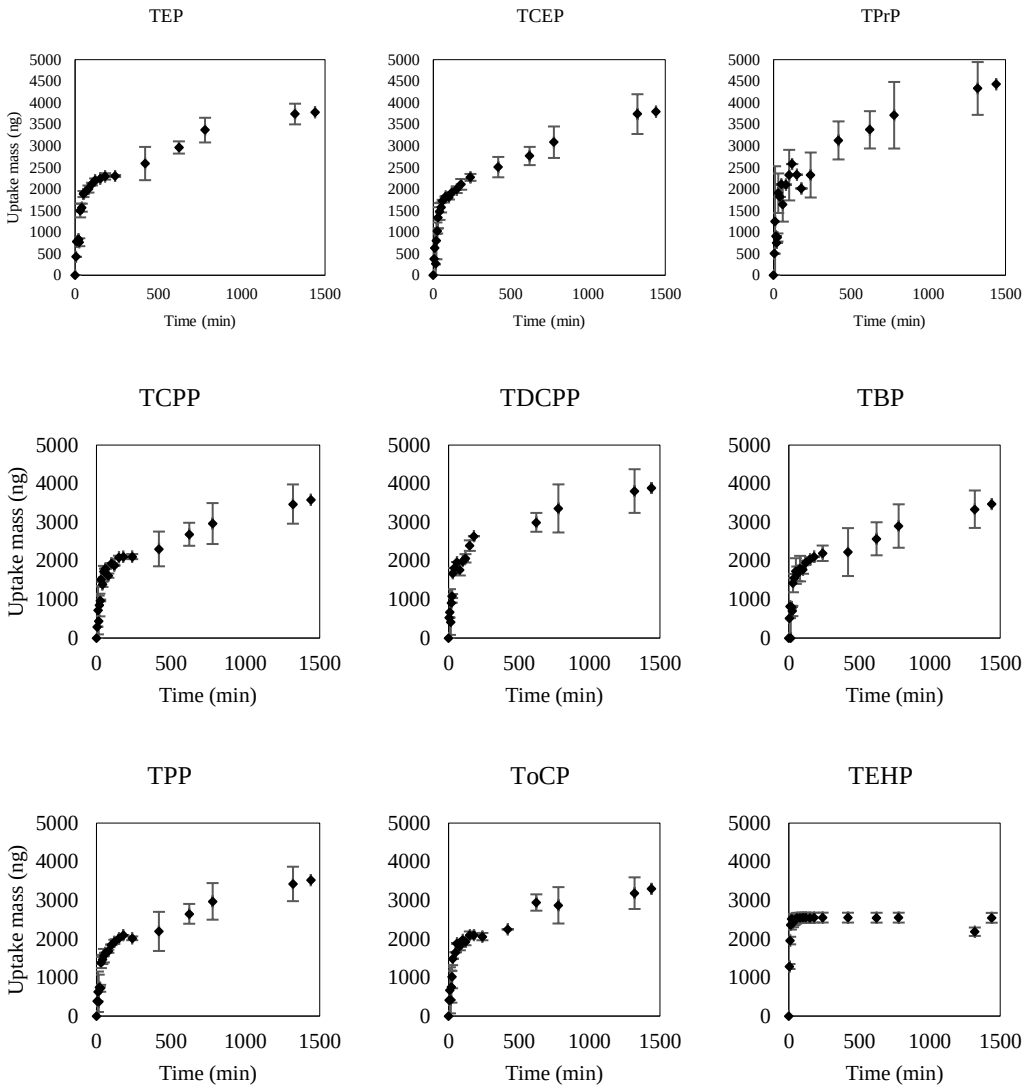

Figure S3.4. Uptake kinetics of OPEs by binding gels in 40 mL solutions containing ca. 200 μg/L OPEs and 0.01 M NaCl at 21 ± 2 °C. Error bars were calculated from the standard deviation (SD) of triplicates.

Table S3.8. Lag times required for establishing steady state in present study

Compound	TEP	TCEP	TPrP	TCPP	TDCPP	TBP	TPP	ToCP	TEHP
lag-phase time (hour)	0.3	0.7	2	14.3	28.2	28.6	67	132.5	>132.5

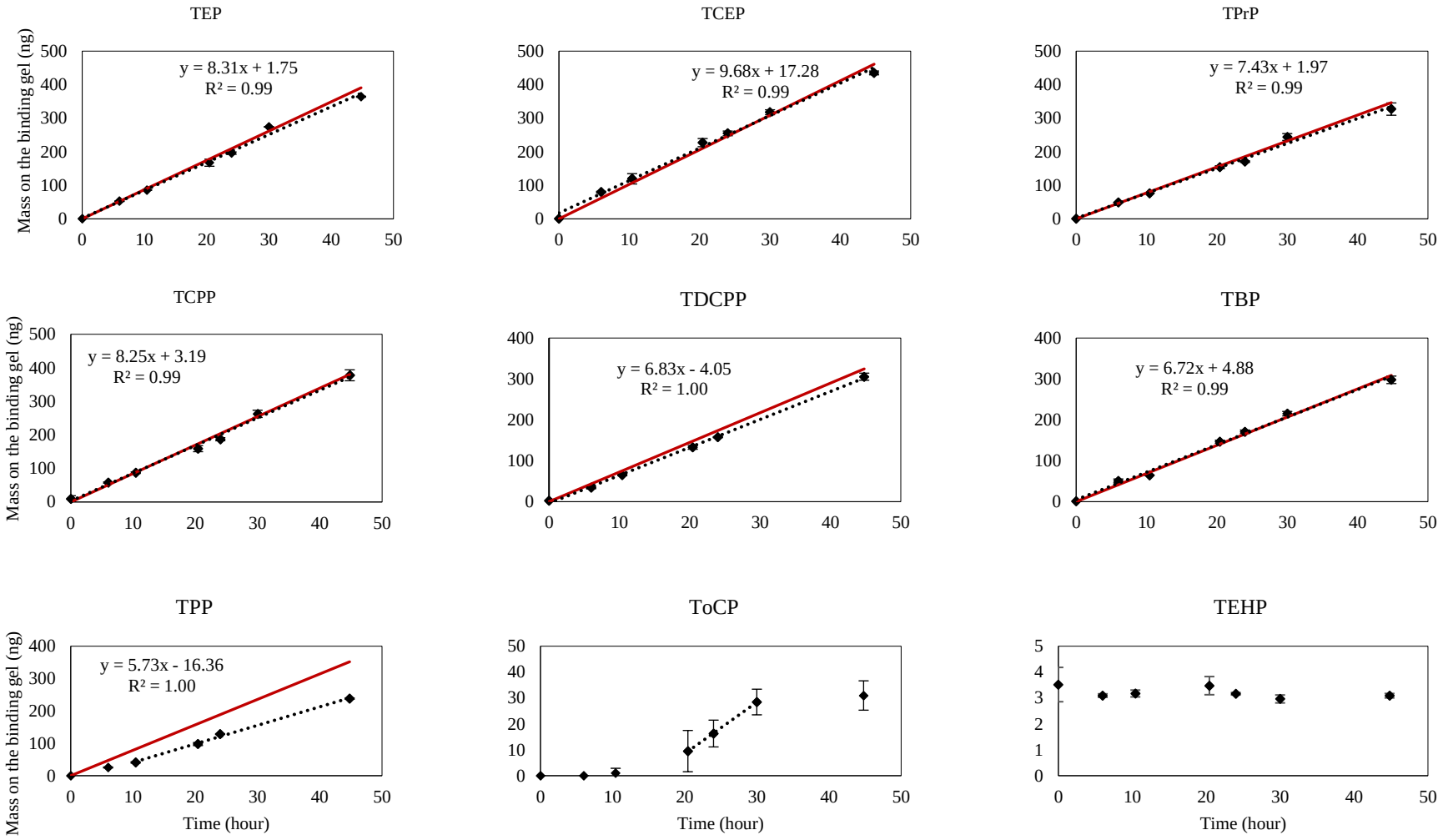

Figure S3.6. Linear mass accumulation of OPEs over time by DGT samplers exposed in 2.5 L solution containing ca. 20 μg/L OPEs and 0.01 M NaCl for various deployment times up to 45 hours (19–22 °C). The red line is the theoretical mass accumulation line, assuming δ = 0.3 mm (average concentrations were used when calculating theoretical accumulation of mass). Error bars calculated from the SD of triplicates.

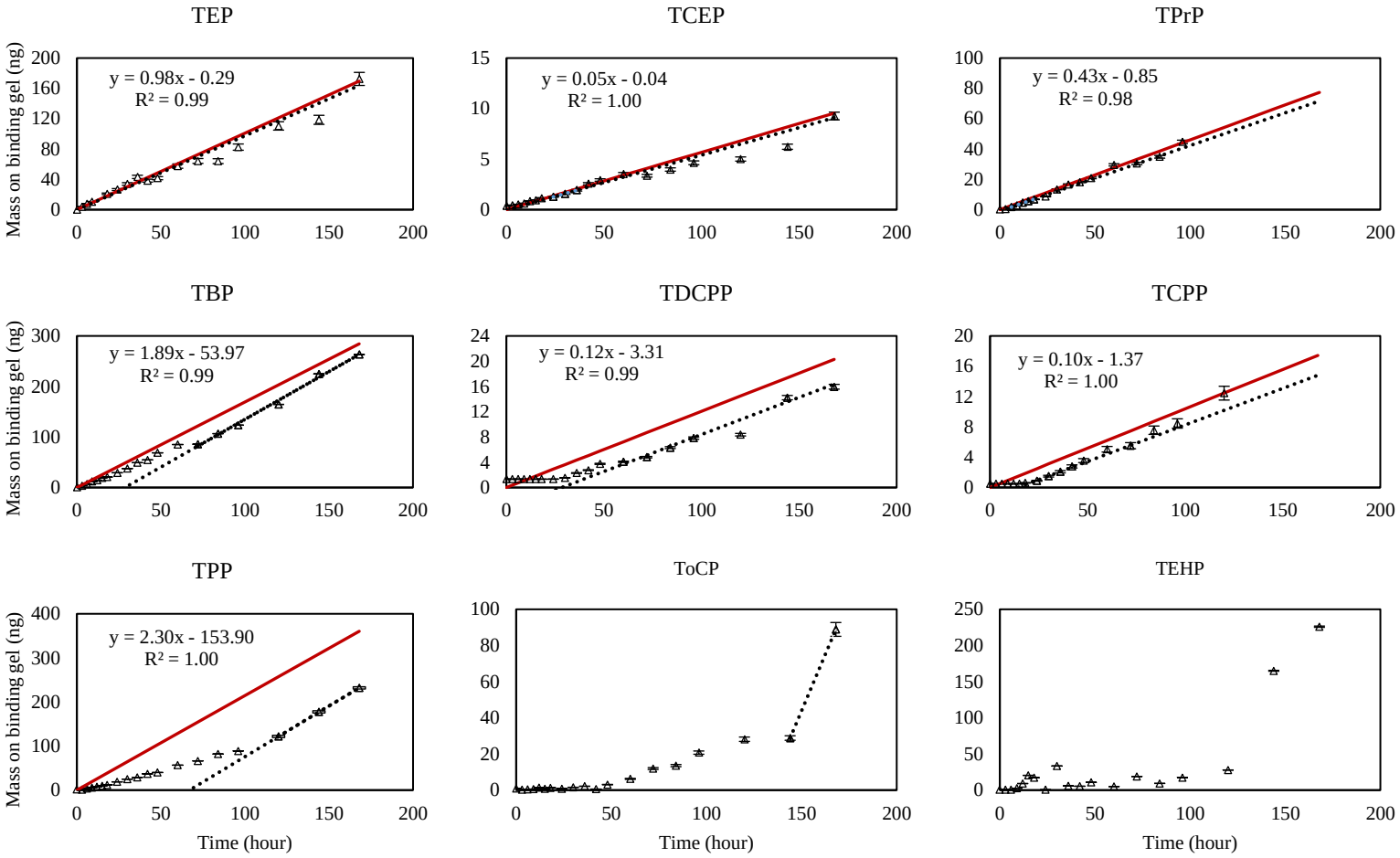

Figure S3.7. Mass accumulation of OPEs over time by DGT samplers exposed in 2.5 L solution containing a few micrograms per liter(see Figure S3.8) OPEs and 0.01 M NaCl from 3 hours up to 7 days (19–22 °C). The red line is a theoretical mass accumulation line, δ = 0.3 mm (average concentrations were used when calculating theoretical accumulation of mass). Error bars were calculated from the standard deviation (SD) of triplicates.

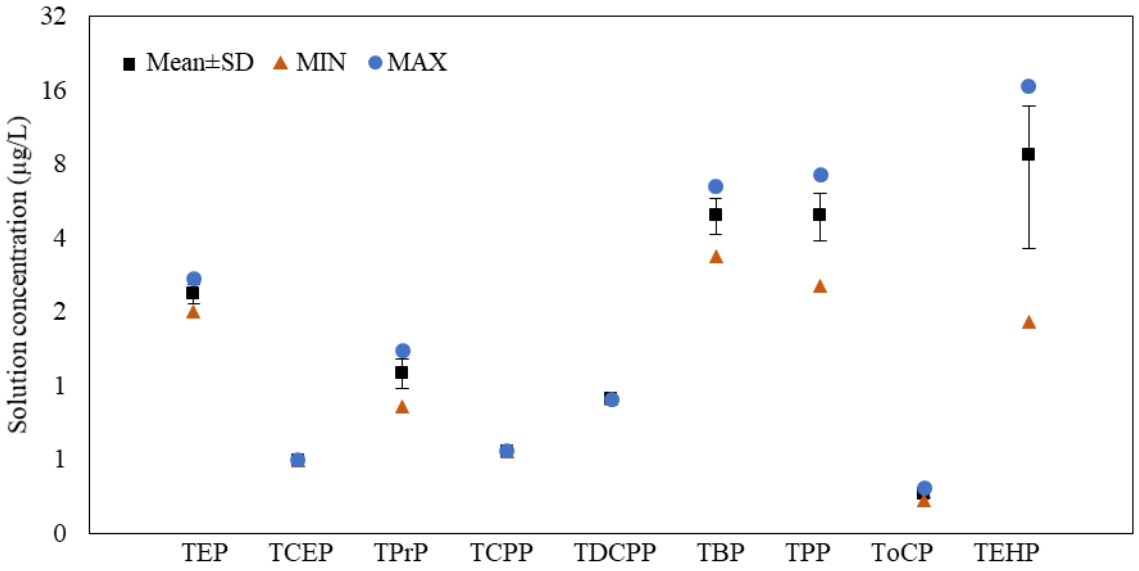

Figure S3.8. Solution concentration (µg/L) of all 9 compounds over the 7 d test experiment. Solution was renewed every 12 hours and the solution samples were collected every time before, middle and after renewing the solution. Back square data points represent mean and standard deviation of 34 sampling points over 7 d. The minimum (orange triangles) and maximum (blue circles) over 34 sampling points are also shown.

Chapter 4: Monitoring organic pollutants in waters using the diffusive gradients in thin films (DGT) technique: investigations into the possible effects of biofouling and degradation

4.1 Introduction

Passive sampling is increasingly accepted and used to sample trace organic compounds from diverse water environments (Kaserzon et al., 2019, Hale et al., 2019, Galle et al., 2019, Martinez Bueno et al., 2009). In contrast to traditional grab sampling and automatic sampling methods, passive sampling provides cost-effective time integrated in situ continuous monitoring of the labile biologically relevant fraction of compounds (Chen et al., 2013, Amato et al., 2016, Degryse et al., 2016, Zhang and Davison, 2015). The diffusive gradients in thin films (DGT) sampler was originally invented in the 1990s for inorganic sampling (Davison and Zhang, 1994, Zhang and Davison, 1995); there are now over 940 peer-reviewed publications describing the development, testing and application of DGT for environmental monitoring and research in waters, sediments and soils. Most of these papers address heavy metals and nutrients, but at the time of writing, DGT has also been tested for over 150 different organic compounds, including pharmaceuticals and personal care products (PPCPs), flame retardants, pesticides and drugs (Zou et al., 2018, Guo et al., 2017a, Chen et al., 2017, Chen et al., 2018, Zhang et al., 2018).

A major driver behind the development and application of DGT and other passive samplers is for screening, surveillance and monitoring many classes of organic chemicals in wastewaters and surface waters, such as those listed under the EU Water Framework Directive 2000/60/EC (WFD) (European Commission, 2000). However, there is a need to better understand some of the practical constraints and potential limitations and to make recommendations on deployment, sampling handling, analysis and data interpretation.

One issue is ‘biofouling’—biofilms composed of algae, bacteria, fungi, and products from cell metabolism form and grow on passive samplers and other surfaces in water bodies over time. Studies have previously investigated the potential influence of biofouling on the uptake of inorganic species (Díez and Giaggio, 2018, Uher et al., 2012a, Uher et al., 2012b, Chlot et al., 2013, Zhang et al., 1998). The impact of biofouling on DGT measurements for monitoring purposes is difficult to predict and to quantify (Österlund et al., 2016). The biofilm may have biological, physical and chemical

interactions with the analytes (Österlund et al., 2016). The presence of the biofilm may affect the overall thickness of the DGT diffusion layer and/or the diffusion coefficient of the target compound. It may be seen as an additional inert diffusion layer on the surface of the DGT membrane filter (Chlot et al., 2013, Zhang et al., 1998) or might actively interact with a compound (Uher et al., 2012b). If the presence of a biofilm is shown to interfere with sampling, shorter DGT deployment times would prevent/reduce biofouling, but this reduces the scope for time-integrated sampling. It has been suggested that samplers should be checked for fouling upon retrieval and data obtained from DGT devices displaying any signs of biofouling should be interpreted with caution (Österlund et al., 2016). Obviously environmental organic chemicals possess a wide range of properties and may be prone to compound-specific bio-sorption, biotransformation and degradation. However, further work is needed on organics to assess whether biofilm formation is a real or perceived problem. We therefore selected a range of emerging contaminants (ECs) for study here, which possess a range of physicochemical properties and with reported degradation in the environment. These include antibiotics, chemicals in household and personal care products, a hormone and another endocrine disrupting compound. We considered a 'worst case' with wastewaters in this study. Pre-exposed membrane filters with biofouling built up in influent and effluent of a WWTP up to 15 days were compared with new clean membrane filters.

The possibility of degradation/loss of analytes within the passive sampler during deployment and storage is another issue. This could happen mainly due to hydrolysis, biodegradation, photolysis and evaporation, as happens in water samples (Barceló and Alpendurada, 1996, Lin et al., 2019). As DGT samplers are non-transparent, photolysis is likely to be minimal. However, the remaining water in the binding gels of the DGT sampler may lead to chemical hydrolysis (Challis et al., 2018a). Any such within-sampler degradation would lead to erroneous reports of water concentrations, especially for analytes with high levels of degradability and with longer sampling and sampler storage times. Nevertheless, very little attention has been paid so far to chemical degradation/loss within the DGT sampler during the sampling procedure, sample shipment and preservation. Challis et al. found changes of a range of compounds in DGT stored at –20 °C after approximately 18 months were minor (9 ± 9%) across 30 pharmaceuticals and pesticides (Challis et al., 2018a). To avoid chemical losses after a freezing/thawing cycle (Fedorova et al., 2014), we examined how well the samplers could be stored at

room and chilled temperatures, as may happen during transport of samplers and their storage before analysis. We also conducted experiments to compare different sample handling procedures, to test whether degradation/loss of compounds may occur post-deployment and pre-analysis. To date, there is no uniform procedure for the preservation of DGT samplers. Most studies treat DGT samplers immediately after retrieval and transport to the laboratory (Chen et al., 2012, Chen et al., 2017, Stroski et al., 2018), while in projects covering large monitoring areas this becomes less practical and on some occasions samples have to be kept for a while before they are analyzed, so an evidence-based sampler storage protocol is needed. Thus, investigating the effects of biofouling and within-sampler degradation is critical to the use of passive samplers, appropriate sampling and handling protocols and the quality of data obtained when monitoring water quality. We therefore tested for worst-case biofouling effects on DGT measurements of ECs using biofilms collected at a typical UK urban WWTP, and investigated the impact of within-sampler degradation/loss with four different storage methods for up to two months.

4.2 Materials and methods

4.2.1 Chemicals and Reagents

Target compounds were selected ECs, which are of increasing environmental concerns and for which a validated DGT sampling and analysis technique has already been developed. They were a range of antibiotics [sulfapyridine (SPD), sulfamerazine (SMR), sulfadoxine (SDX), trimethoprim (TMP), norfloxacin (NFX), ofloxacin (OFX)], chemicals in household and personal care products [methylparaben (MEP), ethylparaben (ETP), propylparaben (PRP), butylparaben (BUP), o-phenylphenol (OPP)], and endocrine disrupting chemicals [estriol (E3) and bisphenol A (BPA)]. High purity chemical standards were purchased from Sigma-Aldrich (U.K.). Corresponding stable isotope-labelled compounds used as surrogate internal standards (SISs) were purchased from Sigma-Aldrich (U.K.) and QMX Laboratories (U.K.). The structures of the studied ECs are shown in Figure S4.1. Their selected chemical properties are listed in Table S4.1. Details of chemicals, SISs and other reagents are provided in the Supporting Information (SI).

4.2.2 Sampler details

The standard DGT configuration in this study comprised a 0.4 mm thickness of hydrophilic-lipophilic-balanced (HLB) resin gel as the binding layer (50 mg wet weight HLB per disc), a 0.8 mm thickness of agarose gel (1.5% agarose) as the diffusion layer and a hydrophilic polypropylene (GHP) membrane (thickness: 0.11 mm, diameter: 25 mm, pore size: 0.45 μm, PALL) as the membrane filter (see Figure 2.3 for schematic of the DGT sampler configuration). More details about the DGT sampler and the technique were first described in Zhang and Davison (Zhang and Davison, 1995).

4.2.3 Instrumental analysis

An ultra-high-performance liquid chromatography-tandem mass spectrometer (UHPLC-MS/MS) was used to determine the target compounds. Separations were achieved by a Shimadzu Nexera UHPLC (Kyoto, Japan) equipped with two LC-30AD pumps, a CTO-20AC column oven, a DGU-30A5 degasser, an SIL-30AC auto-sampler and a column oven connected to a Waters Xbridge C18 column (2.5 μm, 2.1 × 100mm). The auto-sampler was cooled at 20 ºC and the column temperature was at 25 ºC. The mobile phases for six antibiotics (SPD, SMR, SDX, TMP, NFX and OFX) and seven other chemicals (MEP, ETP, PRP, BUP, OPP, E3 and BPA) were different. The mobile phase for 6 antibiotics consisted of (A) deionized water with 0.1% formic acid (v/v) and (B) acetonitrile with 0.1% formic acid (v/v) using a gradient elution of 20% B (5.0 min)-60% B (9.0 min)-100% B (10.0 min)-100% B (12.0 min)-20% B (13.0 min)-20% B (17.0 min). The mobile phase for 7 other PPCPs consisted of (A) deionized water with 5 mM NH_4OH and (B) acetonitrile with 5 mM NH_4OH using a gradient elution of 15% B (4.0 min)-80% B (13.0 min)-100% B (18.0 min)-100% B (22.5 min)-15% B (23.0 min)-15% B (30.0 min). The flow rate was 0.2 mL/min. The injection volume was 10 μL. A triple quadrupole mass spectrometer (Shimadzu LCMS-8040, Kyoto, Japan) was connected to the LC instrument via an electrospray ionization (ESI) interface. The mass spectra for six antibiotics were acquired in positive ion mode and for seven other chemicals were acquired in negative ion mode. The DL temperature was set at 250 ºC, heat block temperature at 400 ºC, nebulizing gas at 2.0 L/min and drying gas at 15.0 L/min. Details about MRM parameters, calibration curves, instrumental limits of detection (LOD), limits of quantitation (LOQ) and method detection limits (MDL) are given in the SI.

4.2.4 Biofouling study

Biofilm collection and assessment

Wastewater treatment plants are considered microorganism-rich (Wagner et al., 2002, McLellan et al., 2010) and were, therefore, chosen to be ideal places to collect biofilms in this study. DGT samplers were deployed in the influent and effluent of an urban wastewater treatment plant at Lancaster (U.K.) for different periods, to let biofilms build up on the DGT outer membrane filter surface. Details about the Lancaster WWTP are given in the SI (Figure S4.3). Two batches of DGT samplers were fixed at 50 cm beneath the water surface in a metal frame box: (1) Six DGTs were placed in the influent and three DGTs in the effluent for 7-days in September 2017 (Figure S4.5); (2) Six DGTs in the influent and six DGTs in the effluent for 8-days, six DGTs in the influent and six DGTs in effluent for 15-days in May and June 2018 (Figure S4.6).

After their retrieval, DGT samplers were assessed using a camera and a microscope (0.02 mm resolution at 40x magnification). The cross-section of the fouled membrane filters from the third batch samplers were measured for the thickness of the fouled membrane filters. Target compounds accumulated on the fouled membrane filters were analyzed.

The membrane filters with biofilms, which had been 'harvested' from the WWTP, were then assembled into clean DGT devices and used in experiments to compare with standard samplers (using clean DGT materials without biofilm).

Laboratory tests of fouled DGTs

Test I: exposed diffusive gel versus clean diffusive gel. Before testing the effect of biofouling on membrane surfaces, diffusive gels exposed to wastewaters were used to reassemble DGT samplers, to test whether the diffusion properties of the gel were affected by the biofouling. Diffusive gels from DGTs deployed in the influent in September 2017 were used in Test I. Reassembled DGT samplers with clean diffusive gels or exposed diffusive gels were deployed in a glass tank containing 4 L water with 10 mM NaCl spiked with a mixture of target compounds (ca. 20 µg/L) and the solution was renewed every 12 hours, to maintain the chemical concentrations constant during deployment (see Figure S4.7). Two treatments were included: (i) DGT sampler with clean membrane filter + clean diffusive gel + clean binding gel; (ii) DGT sampler with clean membrane filters + exposed diffusive gel from the field + clean binding gel. Solution pH

(6.8 ± 0.2) and the temperature (25 ± 2 °C) was relatively stable over the course of the test. Samplers were suspended in the solution stirred at 200 rpm by a PTFE-coated stirrer bar. Solution samples of 1 mL were collected every 24 hours (duplicates), spiked with SISs (50 ng of each SIS), evaporated to dryness under gentle nitrogen and reconstituted in 1 mL of acetonitrile and water (v:v = 20:80). DGT samplers were retrieved after ca. 48 hours and were washed with deionized water before disassembling. All the membrane filters, diffusive gels and binding gels were separately spiked with SISs and eluted by two 30 min ultrasonic extractions in acetonitrile (two 5 mL acetonitrile plus extra 1 mL acetonitrile of rinsing glassware walls) following a method published elsewhere (Chen et al., 2018). The elution solution was evaporated to dryness under a gentle stream of nitrogen and reconstituted in 1 mL of acetonitrile and water (v:v = 20:80). All the samples were filtered through a 0.2 μm PTFE syringe filter into LC amber vials and stored at 4 °C before analysis by LC-MS/MS within a week.

Test II: Effect of membrane filter biofouling of different times on DGT performance. Fouled membrane filters from DGTs deployed in the influent and effluent in May and June 2018 for 8 days and 15 days were used to reassemble samplers, to investigate the impact of biofilm formation time on sampler performance. Five treatments of membrane filters were used to reassemble DGT samplers: (A) clean membrane filter; (B) fouled membrane filter from the DGT deployed in the influent for 8 days; (C) fouled membrane filter from the DGT deployed in the influent for 15 days; (D) fouled membrane filter from the DGT deployed in the effluent for 8 days; (E) fouled membrane filter from the DGT deployed in the effluent for 15 days. Reassembled DGT samplers with those 5 treatments of membrane filters, clean binding gels and clean diffusive gels were exposed (in triplicate) in a 12-hour renewed synthetic solution containing ca. 20 μg/L target compounds and 10 mM NaCl for 24 hours (Figure S4.8). Solution pH (6.8 ± 0.2) and temperature were relatively stable (21 ± 2 °C) during the experiments. Solution concentrations were checked and all the membranes and binding gels were separately spiked with SISs and eluted immediately after retrieval (see sample treatment method above).

4.2.5 Degradation study

Appropriate preservation of samplers is a key part of the processing and analytical steps after sampling. Samplers might not be analyzed immediately in routine and large scale

monitoring projects. Consequently, different storage times and storage strategies could potentially result in degradation or loss of analytes, leading to underestimation of water concentrations. Four storage methods were therefore designed to mimic: i. samplers just being sealed in a polyethylene (PE) bag at room temperature after sampling; ii. binding gels stored in elution solvent in amber vials at room temperature after samplers were disassembled; iii. samplers stored at 4 °C in the refrigerator; and iv. binding gels stored in elution solvent in amber vials at 4 °C in the refrigerator after the samplers dismantled. Acetonitrile was chosen as the keeper solvent due to simplicity, since it is used both for extraction and the organic mobile phase.

Samplers were loaded with target compounds by deploying them in a synthetic solution containing ca. 20 μg/L target compounds and 10 mM NaCl for ca. 38 hours. Solution pH (6.8 ± 0.2) and temperature were relatively stable (18 ± 2 °C) during the deployment. Four of them were analyzed immediately after deployment, to determine the initial compound loading quantities. Others were prepared and stored in triplicate in the four different ways mentioned above. Group 1 were kept directly in a sealed PE bag at room temperature (18–26 °C) and were analyzed after 7, 15, 30 and 60 days (as were all treatments). Group 2 were disassembled and the binding gels were stored in 5 mL elution solvent (acetonitrile) in amber vials at room temperature (18–26 °C) and were analyzed (in triplicate) over the same time intervals. Group 3 were samplers stored at 4 °C in the refrigerator and then extracted and analyzed over the same time intervals. Group 4 were disassembled and the binding gels were stored in 5 mL elution solvent (acetonitrile) in amber vials at 4 °C in the refrigerator over the same time intervals. All the samples were treated as the method described in test I and stored at 4 °C before analysis by LC-MS/MS.

4.2.6 Quality assurance and quality control

Quality control standards (50 μg/L) were prepared using independent weighing and they were analyzed with every 10 samples. Instrumental limits of detection (LOD) were between 0.01 (TMP) and 0.75 (NFX) μg/L (see SI for more details). Where concentrations were below the detection limit, in statistical analyses, these values were substituted with LOD divided by the square root of 2. IBM SPSS Statistics (version 24) was used for statistical analysis below.

4.3 Results and discussion

4.3.1 Effects of biofouling on DGT measurements

Test I: fouled diffusive gel versus clean diffusive gel

MEP, ETP, PRP, BUP, E3, BPA and OPP were used to test whether the matrix of wastewaters altered the diffusion properties of the diffusive layer. The difference of mass for each compound between the two groups [reassembled DGT samplers with exposed diffusive gels and clean DGT samplers (with clean diffusive gels)] were evaluated by an independent-sample t test (n = 3). The results (Figure 4.1) showed that the DGT samplers accumulated comparable amounts of all the test compounds, with one exception. DGT samplers with exposed diffusive gels accumulated more estriol (239 ± 14 ng) than samplers with clean diffusive gels (198 ± 16 ng) ($p < 0.05$). Although the outer membrane filters were severely fouled, the diffusive gels were still clean and transparent (see Figure S4.9). Hardly any target chemicals were detected in the diffusive gels from the fouled samples. Thus, wastewater matrix generally did not alter diffusion properties of the diffusive gel in DGT samplers for the tested compounds. This study also demonstrated that the 0.45 μm pore size membrane filter is important for protecting the diffusive layer of the DGT sampler from fouling. The delicate diffusive gel which is 98.5% water, could become fouled, clogged, corroded and damaged without protection from the membrane filter. Because the membrane filter may slow the initial mass transfer rate of some chemicals, some DGT users have advocated removing the membrane filter completely from the DGT sampler (Challis et al., 2018b, Challis et al., 2018a). However, we believe this is inadvisable, because the filter protects the diffusive gel and the inner system (i.e., binding gel properties may change due to biofouling). We have therefore devised a method to know and correct (as a function of K_{ow}) for the lag-time in uptake/transfer through the membrane filter, as reported recently (Chapter 3) (Wang et al., 2019).

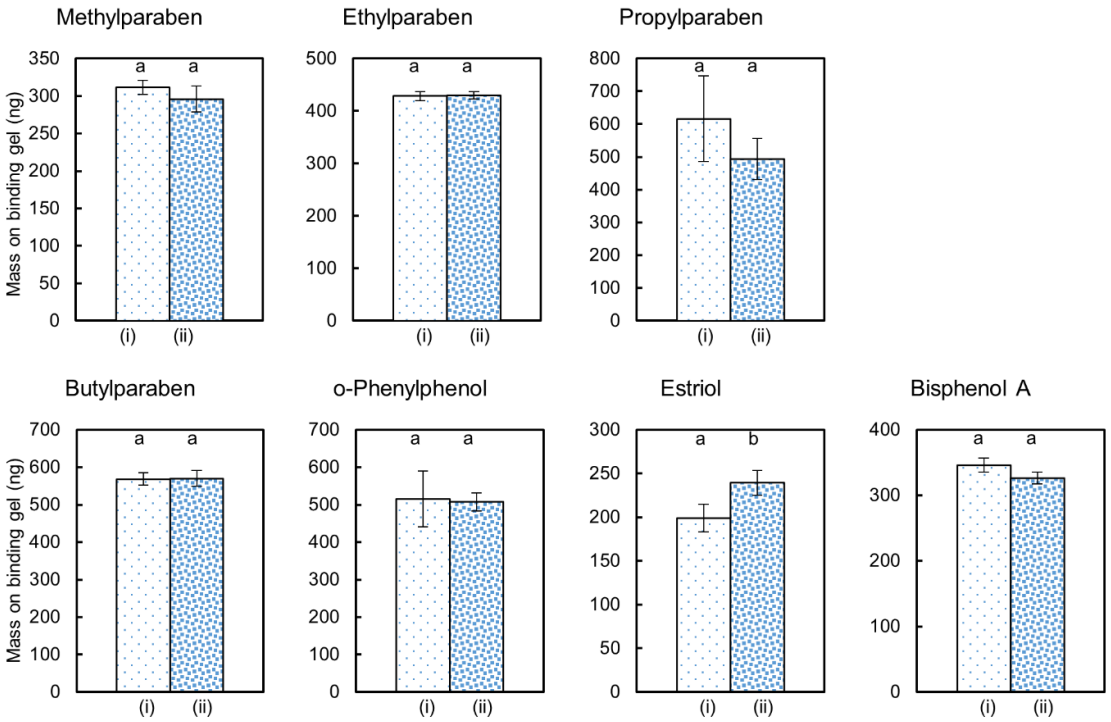

Figure 4.1. Masses of target compounds on the binding gels of diffusive gradient in thin films (DGT) samplers with clean (i) and (ii) pre-exposed diffusive gels deployed for 48 hours in a 4 L 10 mM NaCl solution spiked with a mixture of target compounds (ca. 10 µg/L) (pH 6.8 ± 0.2, 25 ± 2 °C) and renewed every 12-hours. Bars with the same letter are not statistically different; $p > 0.05$ level using an independent-sample t test.

Test II: Effect of membrane filter biofouling of different times on the DGT performance

All 13 compounds were used to investigate the impacts of membrane filter surface biofouling and its formation time on sampler performance. Chemical accumulation differences on the binding gels of five groups of exposed samplers (A: DGT samplers with clean membrane filters, B: reassembled DGT samplers with 8-day influent fouled membrane filters, C: reassembled DGT samplers with 15-day influent fouled membrane filters, D: reassembled DGT samplers with 8-day effluent fouled membrane filters, E: reassembled DGT samplers with 15-day effluent fouled membrane filters) were evaluated by the one-way ANOVA with Tukey post hoc test. When data violated the assumption of homogeneity of variances (Table S4.4), an alternative Welch's ANOVA with Games-Howell test was carried out (see Table S4.5. for *p*-values).

For 8-day fouled membrane filters (influent and effluent), none of the chemicals showed any statistically significant difference in accumulation (Table S4.5). The thickness of 8-day influent and effluent fouled membrane filters were 0.28 ± 0.05 mm (n = 4) and 0.14 ± 0.03 mm (n = 5), equivalent to approximately 20% and 10% of the diffusive distance

(0.8 mm diffusive gel + 0.11 mm membrane filter + 0.3 mm assumed DBL) (Figure S4.4). Studies on metals have also reported no effect on uptake caused by biofilms of <10 days growth (Díez and Giaggio, 2018, Uher et al., 2012b). You et al. noted no effect of DGT biofouling on tetracyclines after 5 days (You et al., 2019).

The thickness of the 15-day influent fouled membrane filters slightly increased from that after 8 days (0.34 ± 0.30 mm, n = 5). The thickness of the effluent fouled membrane filters stabilized after 8-day deployment (0.14 ± 0.03 mm, n = 5; 0.14 ± 0.02 mm after 15 days, n = 3). In total, 10 out of 13 chemicals showed no statistically significant difference in mass accumulated between the five treatments (Figure 4.2). The results suggested that biofilms (from the influent or effluent) and biofilms with different formation times (one or two weeks) did not affect uptake of the compounds tested here. However, there were a couple of exceptions. BPA of group C (reassembled DGT samplers with 15-day influent fouled membrane filters) showed a statistically significant difference from the other groups, but this was due to the smaller SD of group C. The mass accumulations in five groups were similar [from 181 ± 14 ng (group A) to 264 ± 52 ng (group B)]. Ethylparaben and propylparaben accumulated less in group E (reassembled DGT samplers with 15-day effluent fouled membrane filters) than in the other groups. We hypothesize that the two parabens were degraded by specific microorganisms since the biofilm thickness was the same between 8 days and 13 days fouled membrane filters.

This test suggested that up to two weeks developed biofilms didn't influence DGT sampler performance, due to their thickness but some chemical-specific effects caused by microorganisms on the biofilms may interfere the chemical mass transfer.

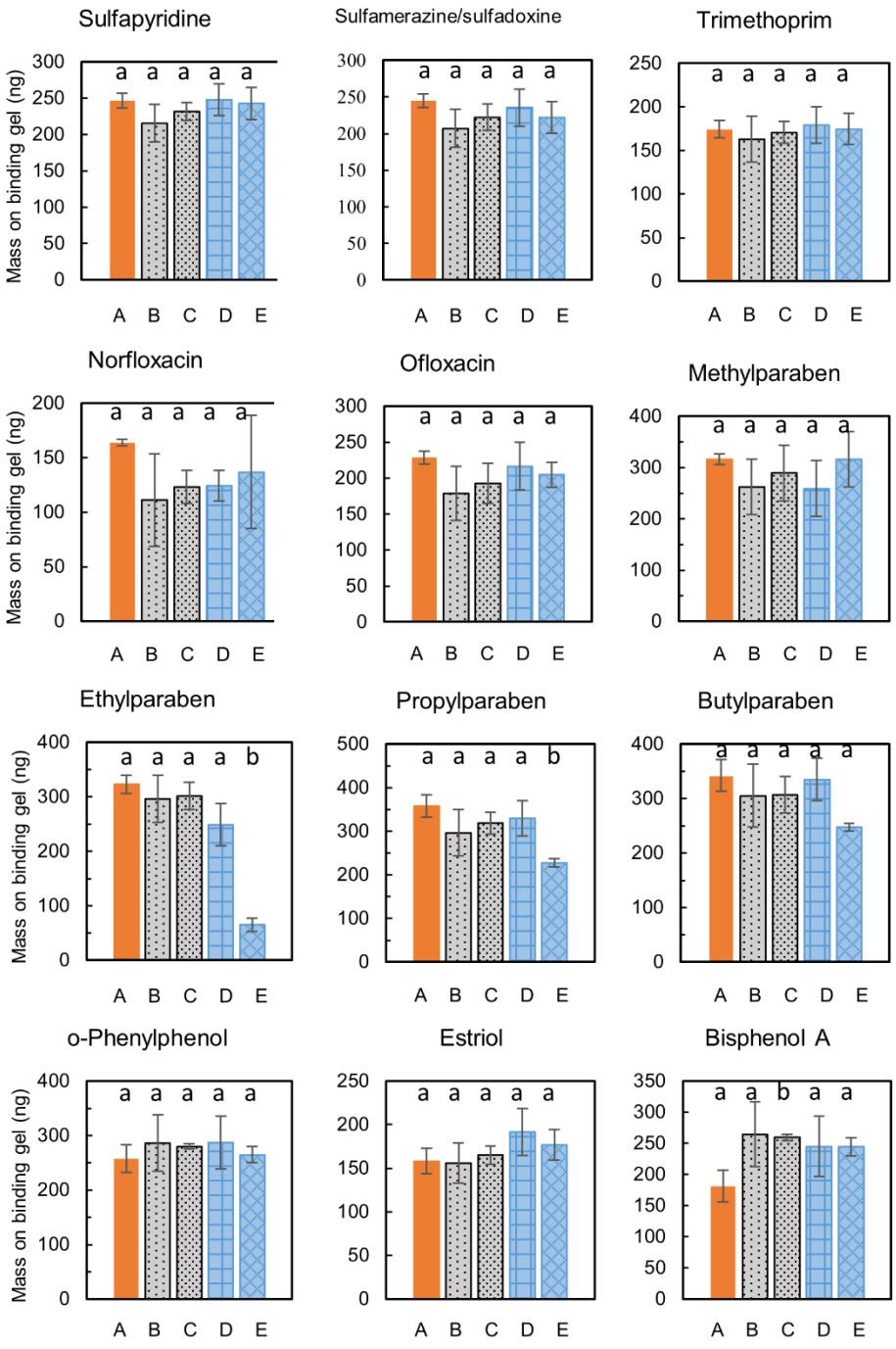

Figure 4.2. Mass of target compounds accumulated on the binding gels of diffusive gradient in thin films (DGT) samplers in five groups in test II (A: clean samplers, B (C): reassembled samplers with 8-day (15-day) influent fouled membrane filters, D (E): reassembled samplers with 8-day (15-day) effluent fouled membrane filters,). DGT samplers were exposed in a synthetic solution containing 10 mM NaCl and ca. 20 µg/L target compounds for 24 hours (pH 6.8 ± 0.2, 21 ± 2 °C) and the solution was renewed every 12-hours. The error bar lengths represent the relative standard deviations on mean (triplicates). Bars with the same letter are not statistically different; $p > 0.05$ level evaluated by the one-way ANOVA with Tukey post hoc test.

4.3.2 Effect of chemical degradation on DGT measurements

Generally, freezing water samples without any pre-treatment is the most common method of storage because it doesn't involve complications during fieldwork (e.g., acidification or filtering of samples). However, organic pollutants may be lost during a freezing/thawing cycle and stability of target compounds in the samples should be checked to obtain reliable data (Fedorova et al., 2014). Passive sampling approaches pre-concentrate analytes in situ, which avoids collecting, preserving and shipping large volumes of water samples. It also reduces the risks of sample damage/loss (e.g., glass bottles may break during shipping) and contamination. Thus, passive sampling approaches have potentially greatest benefit with large scale field monitoring and surveillance campaigns, particularly in developing countries. Currently, there is no uniform procedure for the storage of DGT samplers before analysis. It has been shown that DGT samplers can be kept in freezers for at least one year without statistically significant mass losses of organic analytes (Challis, et al., 2018). In the field, there may be no access to refrigeration and unsuitable conditions for handling the key 'fragile' component of the samplers (i.e., the binding gel layer). The tests performed here were, therefore, designed to consider alternative scenarios, ranging from: i. a worst-case where the samplers cannot be treated for weeks to an ideal case where the samplers can be treated immediately and kept in an appropriate condition (a potentially realistic scenario where a volunteer is given simple instructions for sample recovery from remote field locations, and then transfer them as the intact sampler back to a central laboratory, where they would be handled possibly weeks after exposure), to: ii. an 'ideal' scenario where samplers are processed quickly by a trained and accomplished operator, with transfer of the binding gel to organic solvent and/or rapid chilled storage of the intact sampler. Hence, samplers evenly loaded with target compounds were stored in two different ways, as intact DGT samplers sealed in PE bags or as just the binding gels soaked in 5 mL elution solvent. Two temperature ranges (18–26 °C room temperature or 4 °C in the refrigerator) were compared for storage intervals of one week up to two months.

The remaining mass of a compound on the binding gel at each condition was compared with its initial compound loading quantity ($mass_t$ versus $mass_i$) by the one-way ANOVA with Tukey post hoc test or the Welch's ANOVA with Games-Howell test when data violated the assumption of homogeneity of variances. The stability of all tested chemicals during the four storage scenarios is presented in Table 4.1 (see Table S4.6 for *p*-values

or mass loss percentages of chemical remaining compared with its initial mass loading quantity at the four storage scenarios). When there was no statistically significant difference from the initial mass loading, the compound/handling procedure is marked 'NS' in Table 4.1. Other results are marked as either '<20%' or '>20%' [($mass_i$-$mass_t$)/$mass_i$ × 100%] when there was a statistically significant difference from the initial mass loading (Hillebrand et al., 2013). There were several chemicals which showed non-significant mass changes in each scenario (4 chemicals in scenarios 1 and 2, and 9 in scenarios 3 and 4) throughout the test time (60 days), which was a result of the storage but also a reflection of the good quality control in the loading, extraction and analysis of DGT samplers.

Scenario 1: intact samplers stored at room temperature 18–26 °C When DGT samplers were sealed in PE bags at room temperature (18–26 °C), percentages of chemicals that exhibited non-significant mass changes or <20% mass loss were: 92% (7-day), 85% (15-day), 77% (30-day) and 54% (60-day). Only one chemical (NFX) and two chemicals (NFX and OFX) showed >20% mass loss in 7-day and 15-day storage times, respectively. For a large majority of studied chemicals, DGT samplers were stored for up to 30-day without significant mass loss or with <20% mass loss. More than half of the studied chemicals showed non-significant mass loss or <20% mass loss after 60-day storage.

Scenario 2: intact samplers kept under refrigeration When DGT samplers sealed in PE bags were stored in the refrigerator at 4 °C, percentages of chemicals that exhibited non-significant mass changes or <20% mass loss were: 92% (7-day), 92% (15-day), 92% (30-day) and 85% (60-day). A single chemical (NFX) showed >20% mass loss after 7-day, 15-day and 30-day storage times. Only two chemicals (NFX and OFX) showed >20% mass loss after 60-day storage time.

Scenario 3: storage of binding gels in the solvent at room temperature 18–26 °C When binding gels were kept in the solvent, percentages of chemicals that exhibited non-significant mass changes or <20% mass loss were: 92% (7-day), 92% (15-day), 85% (30-day) and 85% (60-day). Again, a single chemical (NFX) showed >20% mass loss after 7-day and 15-day storage times; two chemicals (NFX and OFX) showed >20% mass loss after 30-day and 60-day storage times.

Scenario 4: storage of binding gel in the solvent and rapid refrigeration When binding gels were kept in the solvent and stored in the refrigerator, percentages of chemicals that

exhibited non-significant mass changes or <20% mass loss were: 92% (7-day), 92% (15-day), 92% (30-day) and 92% (60-day). A single chemical (NFX again) showed >20% mass loss in the four storage times.

The target chemicals have been tested for DGT sampling and showed little adsorption on DGT materials (membrane filters, diffusive gels and moldings) (Chen et al., 2013, Chen et al., 2017, Chen et al., 2018). Because of the non-transparent design of DGT samplers and amber glass vials used for keeping binding gels and sample analysis, photolysis should be minimal in the four storage regimes. Biodegradation is not considered in the study since the laboratory loading, extraction and analysis procedures were relatively bacteria-free. Hydrolysis and volatilization are the most likely loss processes that could happen in the four storage regimes. The stabilities of target chemicals increased as follows: scenario 1 (>90% chemicals stable up to 7-days) < 3 (>90% chemicals stable up 15-days) < 2 (>90% chemicals stable up to 30-days) < 4 (>90% chemicals stable at least 60-days). It appears that low temperature, which decreased volatilization, was important to keep the chemicals stable, such as in scenarios 2 and 4. Hydrolysis could potentially occur in scenarios 1 and 2 due to the residual water in the binding gels of DGT samplers. The fluoroquinolones (NFX and OFX) were more subject to loss than the other target chemicals across all four storage regimes. NFX showed declining mass with increasing storage time (R^2 = 0.55–0.74), with mass losses of 25–81%. OFX also showed a decline under the first three storage regimes (R^2 = 0.61–0.90), except that it showed non-significant mass loss when intact samplers were stored at room temperature and in the refrigerator for up to one week. Its mass loss was within 20% up to 60 days when binding gels were kept in the solvent and stored at 4 °C. An explanation is that the fluoroquinolones are prone to degradation (hydrolysis) under basic conditions due to the carboxyl group. Therefore, adding acid (e.g., acetic acid) into the keeping solvent may stabilize them (Maštovská et al., 2004). This family of compounds is known to be unstable from previous studies. NFX concentrations decreased with time from spiked wastewater stored at –18 °C (Fedorova et al., 2014). NFX and OFX were both lost rapidly from spiked deionized water at −20 °C, and when loaded onto Oasis HLB SPE cartridges stored at −20 °C (Llorca et al., 2014). They represent a challenge for any environmental sampling and analysis project. For these compounds, it is advisable to do pre-treatment (i.e., acidification) during fieldwork or to keep DGT samplers cold during transportation and to analyze them as soon as possible to avoid significant loss.

Overall, most compounds were stable or with small mass loss (<20%) over one week, when DGT samplers were simply stored at room temperature 18–26 °C. This may give the DGT technique an advantage over conventional water sampling when projects cover large catchments or/and remote areas. This also illustrated that in a one-week sampling window, within-sampler degradation/loss during sampling seemed negligible in most environments.

Keeping binding gels in the solvent stored in the refrigerator gave the best preservation, with most chemicals stable up to two months. Keeping intact DGT samplers in the refrigerator is an easy way (without organic solvents involved) to achieve good sample preservation, with the majority of chemicals kept stable for up to one month. This is in agreement with a recent study (Challis et al., 3018). If refrigeration is not possible, keeping binding gels in the solvent at room temperature gives comparable stability of the target compounds, with most chemicals kept stable for up to half a month.

Table 4.1. Stability of 13 tested chemicals during four storage scenarios of diffusive gradients in thin films (DGT) samplers. NS indicates no statistically significant difference between the mass recovered after sample storage and initial mass loading; other results are marked as either '<20%' or '>20%' [$(mass_i\text{-}mass_t)/mass_i \times 100\%$] when there was a statistically significant difference from the initial mass loading.

	① Intact samplers at 18–26 °C				② Intact samplers at 4 °C			
	7-day	15-day	30-day	60-day	7-day	15-day	30-day	60-day
SPD	<20%	<20%	<20%	>20%	NS	NS	NS	<20%
SMR	<20%	<20%	<20%	>20%	NS	NS	<20%	<20%
SDX	NS	NS	<20%	<20%	NS	NS	<20%	<20%
TMP	NS	<20%	<20%	>20%	NS	NS	NS	<20%
NFX	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%
OFX	NS	>20%	>20%	>20%	NS	<20%	<20%	>20%
MEP	NS	NS	>20%	>20%	NS	NS	<20%	<20%
ETP	NS	NS	NS	NS	NS	NS	NS	NS
PRP	NS	NS	NS	NS	NS	NS	NS	NS
BUP	NS	NS	NS	NS	NS	NS	NS	NS
OPP	NS	NS	NS	NS	NS	NS	NS	NS
E3	NS	NS	NS	<20%	NS	NS	NS	<20%
BPA	NS	NS	NS	NS	NS	NS	NS	NS
	③ Binding gels in solvent at 18–26 °C				④ Binding gels in solvent at 4 °C			
	7-day	15-day	30-day	60-day	7-day	15-day	30-day	60-day
SPD	NS	NS	NS	NS	NS	NS	NS	NS
SMR	NS	NS	NS	NS	NS	NS	NS	NS
SDX	NS	NS	NS	NS	NS	NS	NS	NS
TMP	NS	NS	NS	NS	NS	NS	NS	NS
NFX	>20%	>20%	>20%	>20%	>20%	>20%	>20%	>20%
OFX	<20%	<20%	>20%	>20%	<20%	<20%	<20%	<20%
MEP	NS	NS	NS	NS	NS	NS	NS	NS
ETP	NS	NS	NS	NS	NS	NS	NS	NS
PRP	NS	NS	NS	NS	NS	NS	NS	NS
BUP	NS	NS	<20%	<20%	NS	NS	<20%	<20%
OPP	NS	NS	NS	NS	NS	NS	NS	NS
E3	NS	NS	NS	NS	NS	NS	NS	NS
BPA	NS	NS	<20%	<20%	NS	NS	NS	NS

4.4 Conclusion and implications

The DGT sampler is an ideal passive sampling tool which is being used for surveillance and monitoring, because it is cheap, easy to deploy at many sites simultaneously and provides a time-integrated concentration of the dissolved/bioavailable fraction in waters. Applications include wastewater and effluent screening and catchment/regional scale sampling campaigns of rivers in different regions of the world. Worst-case sampling in wastewaters showed that despite rapid biofilm formation after 1–2 weeks, biofilm formation did not significantly affect uptake of the compounds tested. The results of the storage trials indicate that the safest procedure is to store samplers or only binding gels in appropriate keeper solvent at 4 °C until analysis. Some compounds are prone to loss, which may need acidification of the keeper solvent, while the other compounds studied here were well preserved over the 2-month trial period. Campaigns for measuring other compounds using DGT or other passive samplers should ideally perform similar checks as a precaution. Clear protocols for DGT deployment, transport and storage can be designed to ensure good quality robust data is obtained. DGT samplers can be deployed in different environmental conditions including wastewaters and effluents up to two weeks without biofouling affecting DGT measurement. If intact samplers were simply stored in polythene bags at ambient temperatures, most compounds were stable over a week, although this practice should be minimized if possible. Keeping DGT samplers in the refrigerator was the best way (without organic solvents involved) to preserve samples after collection from the field. If refrigeration is not possible (e.g. during remote sampling campaigns), keeping binding gels in the elution solvent at room temperature gives comparable stability of the target compounds. With good protocols for deployment and sample treatment/storage, the DGT technique is a powerful tool for surveillance and monitoring organic pollutants in all types of environments.

Supporting information

Information including chemicals, reagents, experiment details, supplementary tables and figures, and some additional discussion is given in the supplementary information.

SUPPLEMENTARY INFORMATION

Monitoring organic pollutants in waters using the diffusive gradients in thin films (DGT) technique: investigations into the possible effects of biofouling and degradation

Number of pages: 22

Number of Tables: 6

Number of Figures: 11

Contents of Supporting Information:

4.1 Materials and methods

4.1.1 Chemicals and reagents

4.1.2 Instrumental analysis

4.1.3 Experimental details

4.2 Results and discussion

4.2.1 Biofouling formation on membrane filters

4.2.2 Laboratory tests of fouled DGTs

Table S4.1. Selected chemical properties of the studies compounds

Table S4.2. MRM parameters of 6 antibiotics and their isotope labelled standards

Table S4.3. MRM parameters of 7 other target chemicals and their isotope labelled standards

Table S4.4. Test of homogeneity of variances of mass accumulations between the five groups for each compound of Test II

Table S4.5. *P*-values from one-way ANOVA or Welch's ANOVA test mass accumulation mean difference between five groups (A: DGT samplers with clean membrane filters, B: reassembled DGT samplers with 8-day influent fouled membrane filters, C: reassembled DGT samplers with 15-day influent fouled membrane filters fouled membrane filters, D: reassembled DGT samplers with 8-day effluent fouled membrane filters, E: reassembled DGT samplers with 15-day effluent fouled membrane filters). It is grey shaded when $p < 0.05$

Table S4.6. *P*-values or mass loss percentages (when $p < 0.05$) of chemicals' remaining mass compared with its initial mass loading quantity at four storage scenarios by the one-way ANOVA with Tukey post hoc test or the Welch's ANOVA with Games-Howell test

Figure S4.1. Structures of the studied compounds.

Figure S4.2. Example chromatograms of 6 antibiotics (up) and 7 other chemicals (down) and their isotope labelled standards.

Figure S4.3. Lancaster Wastewater Treatment Plant (WWTP) diagram.

Figure S4.4. Images of fouled membrane filters under a microscope (0.02 mm resolution at 40x magnification) from influent and effluent at 8 days deployment in an urban WWTP. Red rectangle indicates biofilm on the membrane filter.

Figure S4.5. Images of fouled membrane filters from influent (left) and effluent (right) deployed from 19th to 26th September 2017 for 7 days at Lancaster WWTP, U.K.

Figure S4.6. Images of fouled membrane filters from influent (left) and effluent (right) deployed for 8 days and 15 days in May and June 2018 at Lancaster WWTP, U.K.

Figure S4.7. Test I: reassembled DGTs [(a) DGT with clean membrane filter + clean diffusive gel + clean binding gel; (b) DGT with clean membrane filters + fouled diffusive gel from the field + clean binding gel. In triplicate] exposed in the synthetic solution with target compounds (ca. 20 µg/L) and 10 mM NaCl.

Figure S4.8. Test II: reassembled DGTs with 5 treatments of membrane filters [(A) clean membrane filter; (B) fouled membrane filter from the DGT deployed in the influent for 8 days; (C) fouled membrane filter from the DGT deployed in the influent for 15 days; (D) fouled membrane filter from the DGT deployed in the effluent for 8 days; (E) fouled membrane filter from the DGT deployed in the effluent for 15 days. In triplicate] exposed in the synthetic solution with ca. 20 µg/L target compounds and 10 mM NaCl.

Figure S4.9. Photos of membrane filters (left) and diffusive gels (right) from the DGT samplers at Lancaster WWTP.

4.1 Materials and methods

4.1.1 Chemicals and reagents

The structures of the studied emerging contaminants are shown in Figure S4.1. Details of chemicals, SISs and other reagents are provided below.

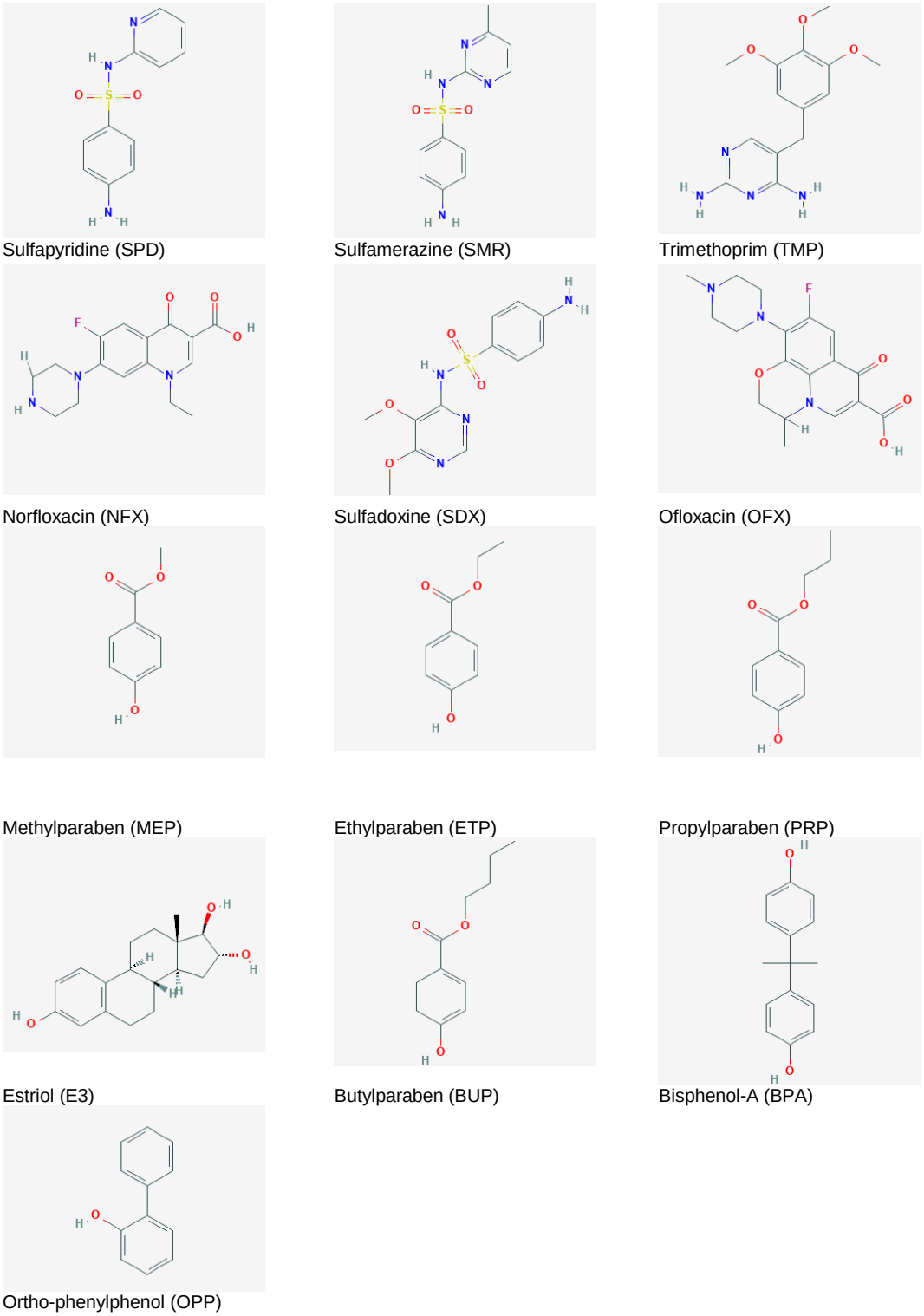

Figure S4.1. Structures of the studied compounds.

Table S4.1. Selected chemical properties of the studies compounds

Compound	Mw (Da)	logK_{ow}		Sw 25°C (g/L)		Vapor pressure mm Hg at 25 °C	pKa	Catalogue	Measured D (E−6 cm^2/s) 25°C	Molecular formular	STP removal			
											Total Removal (%)	Total Biodegradation (%)	Total Sludge Adsorption (%)	Total to air
Sulfapyridine	249.29	0.35	α	0.268	*	4.14E-08	2.58;8.43;8.4	antibiotic	4.75	C11H11N3O2S1	1.86	0.09	1.76	0.00
Sulfamerazine	264.30	0.14	α	0.212	*	4.71E-09		antibiotic	3.79	C11H12N4O2S1	1.85	0.09	1.76	0.00
Sulfadoxine	310.33	0.70	β	2.697	#	2.15E-09		antibiotic	3.85	C12H14N4O4S1	1.87	0.09	1.77	0.00
Trimethoprim	290.32	0.91	α	0.400	*	7.52E-09	3.23;6.76	antibiotic	3.79	C14H18N4O3	1.88	0.09	1.79	0.00
Norfloxacin	319.34	1.03	α	0.200	*i	8.13E-12		antibiotic	2.46	C16H18F1N3O3	1.85	0.09	1.75	0.00
Ofloxacin	361.38	0.39	α	28.260	#	9.84E-13		antibiotic	2.24	C18H20F1N3O4	1.85	0.09	1.76	0.00
Methylparaben	152.15	1.96	α	2.500	*	8.55E-04	8.31	preservative	6.85	C8H8O3	2.21	0.10	2.12	0.00
Ethylparaben	166.18	2.47	α	0.885	*	9.29E-05	8.5	preservative	6.45	C9H10O3	3.01	0.10	2.91	0.00
Propylparaben	180.20	3.04	α	0.500	*	3.07E-04	8.23	preservative	5.92	C10H12O3	6.04	0.13	5.92	0.00
Butylparaben	194.23	3.57	α	0.207	*	2.51E-04	8.5	preservative	5.61	C11H14O3	14.72	0.20	14.53	0.00
Ortho-phenylphenol	170.21	3.09	α	0.700	*	7.06E-04	9.65	disinfectant	5.18	C12H10O1	6.59	0.13	6.40	0.06
Estriol	288.39	2.45	α	0.003	*	9.37E-12	10.33;13.62	hormone	4.59	C18H24O3	2.96	0.10	2.86	0.00
Bisphenol A	228.29	3.32	α	0.120	*	2.27E-07	9.65;10.45	bisphenol	5.03	C15H16O2	9.54	0.16	9.39	0.00

α: Exper. Database match from Hansch C, Leo, A. and Hoekman, D. (1995). Exploring QSAR: Hydrophobic, electronic, and steric constants. Am Chem Soc, Washington.
β: Octanol-Water Partition Coefficients: Fundamentals and Physical Chemistry. Sangster J 1994 Wiley, New York. Pomona College Medicinal Chemistry Project, Claremont, CA 91711, Log P Database, (C. Hansch and A. Leo), July 1987 edition.
*: Exper. Database match from Handbook of Aqueous Solubility Data
#: water solubility estimate from LogKow (WSKOW V1.42)
i: Sw is at pH 7.4 phosphate buffer

All reagents were at least analytical grade with ≥98% purity. Organic solvents were HPLC grade. Formic acid and ammonia solution (NH_4OH, 4.97 M) were purchased from Sigma-Aldrich (U.K.). Sodium chloride (NaCl), methanol (MeOH), and acetonitrile (ACN) were obtained from Fisher Scientific (U.K.). Deionised water used in all experiments was obtained from a Milli-Q water purification system (> 18.2 MΩ cm-1, Millipore, U.K.). HLB resins were extracted from Oasis-HLB solid-phase extraction (SPE) cartridges purchased from Waters Corporation (U.K.). The HLB was washed with MQ water to remove salts and then conditioned with methanol followed by a MQ water wash before use. Gel solution for making binding gels and DGT holders were provided by DGT Research Ltd (Lancaster, U.K.). Ammonium persulfate (APS) and N, N, N′, N′-tetramethylethylenediamine (TEMED) were purchased from Sigma-Aldrich (U.K.) and agarose was obtained from Bio-Rad Laboratories (U.K.). Samples were filtered through 0.2 µm PTFE syringe filters (diameter: 13 mm, GE Healthcare Life Sciences, Whatman) before analysis by LC-MS/MS.

4.1.2 Instrumental analysis

Details about MRM parameters, calibration curves, instrumental limits of detection (LOD), limits of quantitation (LOQ) and method detection limits (MDL) are given below.

Table S4.2. MRM parameters of 6 antibiotics and their isotope labelled standards

Name	Type	ISTD	Precursor m/z	Product m/z	Dwell Time (msec)	Q1 Pre Bias (V)	CE	Q3 Pre Bias (V)
SPD	Target	1	250	156.15	50	-16	-17	-27
			250	108.25	50	-26	-25	-18
SMR	Target	1	265	156.1	50	-12	-17	-27
			265	108.3	50	-17	-26	-18
TMP	Target	2	291.1	261.15	50	-13	-26	-26
			291.1	230.2	50	-19	-24	-22
NFX	Target	3	319.8	302.1	50	-21	-20	-30
			319.8	279.3	50	-21	-15	-29
OFX	Target	3	362.1	344.35	50	-24	-23	-11
			362.1	318.4	50	-12	-21	-14
SDX	Target	1	311	156.25	150	-20	-19	-30
			311	92.4	150	-20	-32	-16
SMX-d4	ISTD	1	257.75	96.3	150	-17	-31	-17
			257.75	160.05	150	-17	-17	-29
CAF-13C3	ISTD	2	198.15	140.05	50	-21	-20	-24
			198.15	43.2	50	-21	-37	-15
d3-OFX	ISTD	3	364.85	321.3	50	-24	-20	-20
			364.85	261.2	50	-24	-30	-26

Table S4.3. MRM parameters of 7 other target chemicals and their isotope labelled standards

Name	Type	ISTD	Precursor m/z	Product m/z	Dwell Time (msec)	Q1 Pre Bias (V)	CE	Q3 Pre Bias (V)
MEP	Target	1	151	92.05	100	15	22	17
			151	135.95	100	15	17	24
ETP	Target	2	165	92.1	100	17	25	17
			165	137	100	17	21	18
d6-MEP	ISTD	1	157.2	98.1	50	16	21	18
			157.2	142.05	50	10	18	26
d6-ETP	ISTD	2	171.15	98.05	50	17	22	20
			171.15	143.05	50	17	16	26
d6-PRP	ISTD	3	185.2	98.1	150	12	24	19
			185.2	142.1	150	19	17	29
PRP	Target	3	179	92.1	150	18	23	17
			179	135.95	150	18	15	24
d6-BUP	ISTD	4	199.2	98.1	50	13	26	18
			199.2	142.05	50	20	16	26
E3	Target	5	287	171.1	100	30	37	30
			287	145.15	100	30	45	26
BUP	Target	4	193	92.1	80	20	24	17
			193	137.05	80	19	15	14
d2-E3	ISTD	5	289.1	173.2	50	19	38	30
			289.1	146.95	50	13	45	27
BPA	Target	6	227	211.95	50	24	18	23
			227	133	50	23	24	25
OPP	Target	7	169	115.1	50	30	31	24
			169	141.05	50	11	16	25
d16-BPA	ISTD	6	241.2	223.05	50	16	19	24
			241.2	142.1	50	11	24	25
13C-OPP	ISTD	7	175.2	121.1	25	17	33	23
			175.2	147.1	25	17	25	27

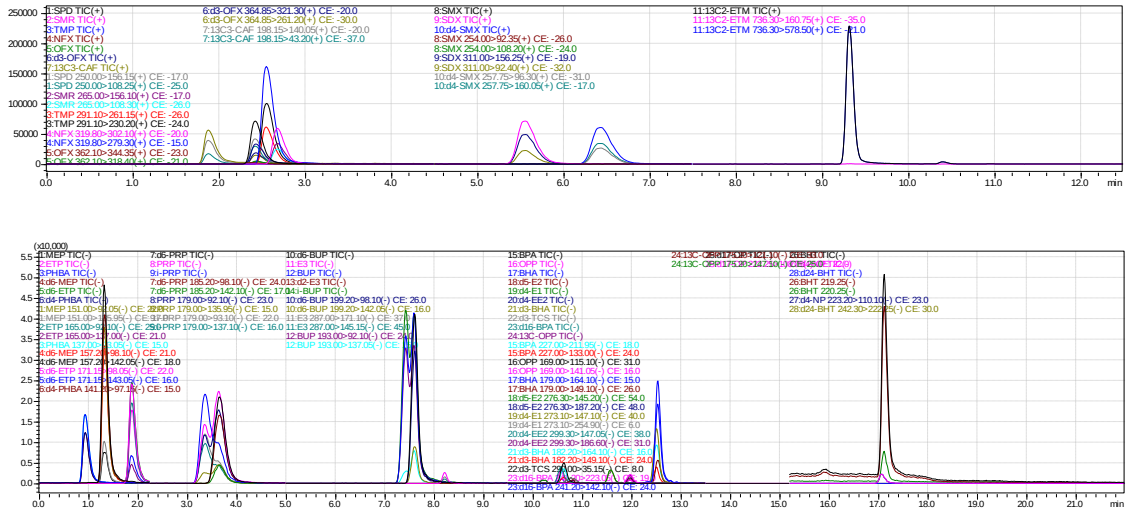

Figure S4.2. Example chromatograms of 6 antibiotics (up) and 7 other chemicals (down) and their isotope labelled standards.

4.1.3 Experimental details

Biofilm collection and assessment

The first batch of DGTs was deployed in the influent and effluent of Lancaster WWTP from 19th to 26th September 2017 for 7 days; the second batch of DGTs was deployed from 21st to 28th November 2017 for 7 days; and the third batch was deployed on 22nd and 29th of May 2018 separately and all collected on 6th June 2018 so that the DGT deployment times were 8 and 15 days.

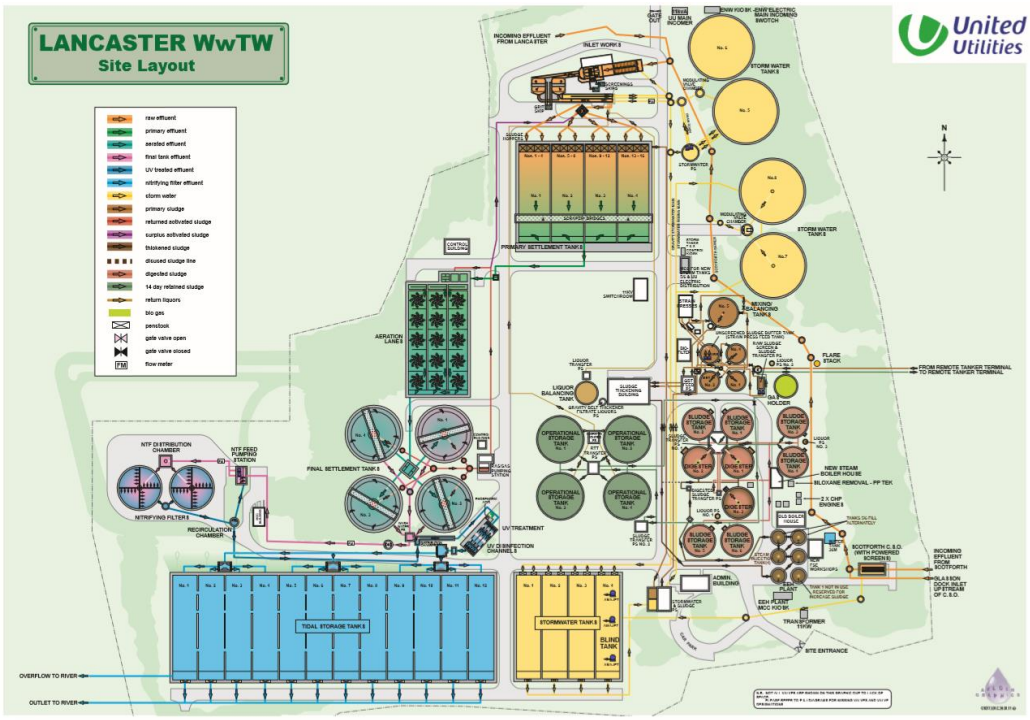

Figure S4.3. Lancaster Wastewater Treatment Plant (WWTP) diagram.

4.2 Results and discussion

4.2.1 Biofouling formation on membrane filters

Under the microscope, biofouling was generally heterogeneously dispersed on the membrane filters and therefore the largest thickness was recorded when measuring (refer Figure S4.3). Thickness of 8-day influent fouled membrane filters were 0.28 ± 0.05 mm (n = 4) and slightly increased at 15-day deployment time (0.34 ± 0.30 mm, n = 5), but with a bigger deviation. Thickness of fouled membrane filters from the effluent stabilised after 8-day deployment time (0.14 ± 0.03 mm, n = 5) and remained at this thickness after 15-day deployment (0.14 ± 0.02 mm, n = 3).

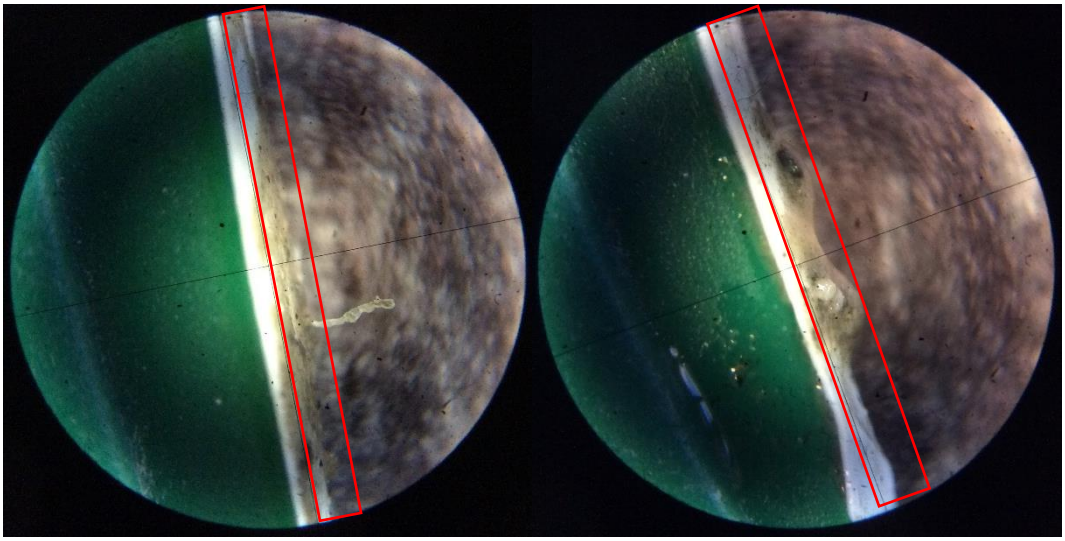

Figure S4.4. Images of fouled membrane filters under a microscope (0.02 mm resolution at 40x magnification) from influent and effluent at 8 days deployment in an urban WWTP. Red rectangle indicates biofilm on the membrane filter.

Figure S4.5. Images of fouled membrane filters from influent (left) and effluent (right) deployed from 19th to 26th September 2017 for 7 days at Lancaster WWTP, U.K.

Figure S4.6. Images of fouled membrane filters from influent (left) and effluent (right) deployed for 8 days and 15 days in May and June 2018 at Lancaster WWTP, U.K.

4.2.2 Laboratory tests of fouled DGTs

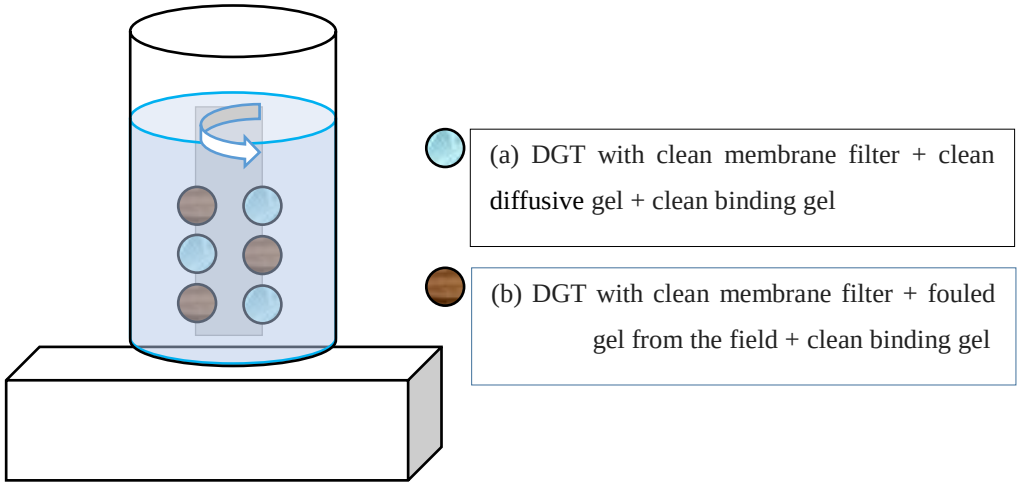

Figure S4.7. Test I: reassembled DGTs [(a) DGT with clean membrane filter + clean diffusive gel + clean binding gel; (b) DGT with clean membrane filters + fouled diffusive gel from the field + clean binding gel. In triplicate] exposed in the synthetic solution with target compounds (ca. 20 µg/L) and 10 mM NaCl.

Figure S4.8. Test II: reassembled DGTs with 5 treatments of membrane filters [(A) clean membrane filter; (B) fouled membrane filter from the DGT deployed in the influent for 8 days; (C) fouled membrane filter from the DGT deployed in the influent for 15 days; (D) fouled membrane filter from the DGT deployed in the effluent for 8 days; (E) fouled membrane filter from the DGT deployed in the effluent for 15 days. In triplicate] exposed in the synthetic solution with ca. 20 µg/L target compounds and 10 mM NaCl.

Figure S4.9. Photos of membrane filters (left) and diffusive gels (right) from the DGT samplers at Lancaster WWTP.

Table S4.4. Test of homogeneity of variances of mass accumulations between the five groups for each compound of Test II

Compound	*P*-value	Homogeneity of Variances
sulfapyridine	0.438	Equal
sulfamerazine	0.47	Equal
trimethoprim	0.502	Equal
norfloxacin	0.032	Unequal
sulfadoxine	0.536	Equal
ofloxacin	0.189	Equal
methylparaben	0.054	Marginally significant equal
ethylparaben	0.1	equal
propylparaben	0.074	Marginally significant equal
butylparaben	0.074	Marginally significant equal
o-phenylphenol	0.677	Equal
estriol	0.246	Equal
bisphenol A	0.03	Unequal

Table S4.5. *P*-values from one-way ANOVA or Welch's ANOVA test mass accumulation mean difference between five groups (A: DGT samplers with clean membrane filters, B: reassembled DGT samplers with 8-day influent fouled membrane filters, C: reassembled DGT samplers with 15-day influent fouled membrane filters fouled membrane filters, D: reassembled DGT samplers with 8-day effluent fouled membrane filters, E: reassembled DGT samplers with 15-day effluent fouled membrane filters). It is grey shaded when $p < 0.05$

		P-values from one-way ANOVA or Welch's ANOVA test of mean difference between columns i and ii												
i	ii	SPD	SMR	SDX	TMP	NFX	OFX	MEP	ETP	PRP	BUP	OPP	E3	BPA
A	B	0.35	0.25	0.27	0.94	0.43	0.23	0.34	0.79	0.25	0.73	0.72	1.00	0.30
	C	0.87	0.69	0.81	1.00	0.12	0.51	0.85	0.90	0.63	0.77	0.86	0.99	0.01
	D	1.00	0.98	0.63	1.00	0.11	0.98	0.29	0.07	0.84	1.00	0.70	0.29	0.17
	E	1.00	0.68	0.61	1.00	0.88	0.81	1.00	0.00	0.01	0.06	1.00	0.77	0.14
B	A	0.35	0.25	0.27	0.94	0.43	0.23	0.34	0.79	0.25	0.73	0.72	1.00	0.30
	C	0.84	0.90	0.81	0.99	0.98	0.97	0.85	1.00	0.93	1.00	1.00	0.97	1.00
	D	0.31	0.50	0.94	0.82	0.98	0.47	1.00	0.36	0.76	0.85	1.00	0.23	0.97
	E	0.47	0.90	0.95	0.94	0.95	0.77	0.33	0.00	0.17	0.38	0.88	0.68	0.97
C	A	0.87	0.69	0.81	1.00	0.12	0.51	0.85	0.90	0.63	0.77	0.86	0.99	0.01
	B	0.84	0.90	0.81	0.99	0.98	0.97	0.85	1.00	0.93	1.00	1.00	0.97	1.00
	D	0.83	0.94	1.00	0.98	1.00	0.81	0.79	0.26	0.99	0.88	1.00	0.50	0.91
	E	0.95	1.00	1.00	1.00	0.99	0.98	0.85	0.00	0.05	0.34	0.96	0.95	0.87
D	A	1.00	0.98	0.63	1.00	0.11	0.98	0.29	0.07	0.84	1.00	0.70	0.29	0.17
	B	0.31	0.50	0.94	0.82	0.98	0.47	1.00	0.36	0.76	0.85	1.00	0.23	0.97
	C	0.83	0.94	1.00	0.98	1.00	0.81	0.79	0.26	0.99	0.88	1.00	0.50	0.91
	E	1.00	0.93	1.00	1.00	0.99	0.98	0.29	0.00	0.03	0.09	0.87	0.88	1.00
E	A	1.00	0.68	0.61	1.00	0.88	0.81	1.00	0.00	0.01	0.06	1.00	0.77	0.14
	B	0.47	0.90	0.95	0.94	0.95	0.77	0.33	0.00	0.17	0.38	0.88	0.68	0.97
	C	0.95	1.00	1.00	1.00	0.99	0.98	0.85	0.00	0.05	0.34	0.96	0.95	0.87
	D	1.00	0.93	1.00	1.00	0.99	0.98	0.29	0.00	0.03	0.09	0.87	0.88	1.00

Table S4.6. *P*-values or mass loss percentages (when $p < 0.05$) of chemicals' remaining mass compared with its initial mass loading quantity at four storage scenarios by the one-way ANOVA with Tukey post hoc test or the Welch's ANOVA with Games-Howell test

	Intact samplers at 18–26 °C				Intact samplers at 4 °C			
	7-day	15-day	30-day	60-day	7-day	15-day	30-day	60-day
SPD	15%	13%	15%	<80%	0.50	0.14	12%	12%
SMR	12%	15%	17%	<80%	0.17	11%	15%	14%
SDX	0.99	0.08	13%	19%	0.09	0.07	12%	12%
TMP	1.00	17%	20%	<80%	0.50	0.73	0.93	20%
NFX	<80%	<80%	<80%	<80%	<80%	<80%	<80%	<80%
OFX	0.41	<80%	<80%	<80%	1.00	18%	18%	<80%
MEP	0.95	1.00	<80%	<80%	0.08	0.50	18%	20%
ETP	0.69	0.78	1.00	0.31	1.00	0.86	0.44	0.31
PRP	0.65	1.00	0.25	0.18	0.58	1.00	0.24	0.21
BUP	0.51	0.95	0.61	0.14	0.43	1.00	0.06	0.16
OPP	1.00	1.00	0.68	0.73	0.74	1.00	0.71	0.99
E3	0.50	1.00	0.13	20%	0.78	1.00	0.24	12%
BPA	0.23	0.55	0.85	0.12	0.45	0.05	0.08	0.22
	Binding gels in solvent at 18–26 °C				Binding gels in solvent at 4 °C			
	7-day	15-day	30-day	60-day	7-day	15-day	30-day	60-day
SPD	0.16	1.00	1.00	1.00	0.14	0.14	1.00	0.98
SMR	0.49	0.90	0.95	0.06	0.31	0.51	1.00	0.18
SDX	0.27	0.99	1.00	0.30	0.07	0.13	0.54	0.30
TMP	1.00	1.00	0.62	1.00	0.32	0.39	1.00	0.64
NFX	<80%	<80%	<80%	<80%	<80%	<80%	<80%	<80%
OFX	20%	18%	<80%	<80%	19%	19%	12%	20%
MEP	0.71	1.00	1.00	1.00	0.22	1.00	1.00	0.50
ETP	0.25	0.35	0.17	0.16	0.14	0.16	0.13	0.12
PRP	0.69	1.00	0.25	0.16	0.55	0.85	0.31	0.18
BUP	0.58	0.38	17%	20%	0.33	0.35	16%	20%
OPP	0.78	1.00	0.97	0.82	0.51	0.95	0.72	0.10
E3	0.79	0.68	1.00	0.98	0.76	1.00	0.42	0.06
BPA	0.34	0.69	17%	20%	0.51	0.39	0.30	0.15

Chapter 5: Emerging contaminants in the River Thames (U.K.) using diffusive gradients in thin films (DGT) and traditional grab sampling

5.1 Introduction

River water pollution by anthropogenic activities is a threat to human and ecosystem health and its protection is a key objective of environmental authorities and governments (Lamastra et al., 2016). In addition to the known and well-characterized pollutants, new substances with no clear immediate effects are emerging (Lamastra et al., 2016). Emerging contaminants (ECs) or micropollutants are a large and expanding array of relatively polar compounds that are commonly present in water, but they have only been identified as significant water pollutants in recent years (Sarkar et al., 2019). Until now, these substances are not adequately considered in legislation for several reasons, including a lack of knowledge of contaminant sources and pathways, properties and effects of substances and analytical detection techniques (Lamastra et al., 2016). Collecting samples with good representativeness of ECs is challenging. The concentrations of ECs, such as pharmaceuticals, chemicals in household and personal care products (HPCPs), endocrine disrupting chemicals (EDCs) organophosphate esters (OPEs), etc., in water bodies range widely, from pg/L to mg/L (Petrie et al., 2015). Current mass spectrometry instruments can provide sub- to single-digit μg/L instrumental detection limits, so a pre-concentration approach is needed for ECs at trace levels (pg/L to ng/L). Furthermore, intra-day and inter-day concentrations of ECs in water bodies could vary markedly (Coutu et al., 2013, Thomas et al., 2012). When these contaminants pass through drinking water and wastewater treatment systems, breakdown products are generated but their chemical properties are as yet undetermined (Rosenfeld and Feng, 2011). Thus, reliable and representative samples are necessary for studying the sources and environmental fate and impact of ECs.

Grab or spot sampling is the most commonly used method to collect samples, due to its simplicity (Vrana et al., 2005). Over 50 ECs, including pharmaceuticals and potential EDCs, were screened from 2 L samples of U.S. drinking waters (Benotti et al., 2009). Grab samples of 1 L water were collected from 40 rivers around the Bohai Sea to understand the occurrence and spatial distribution of OPEs (Wang et al., 2015). Samples of 1 L can be concentrated to 1 mL, so when pollutants are at sub-ng/L or even lower levels, large volumes (10–100 L) of water need to be collected. The subsequent laboratory analysis of the grab sample only provides a snapshot of the pollutants at the time of

sampling. The drawbacks of this approach are obvious when the contaminant concentrations vary over time and flow rate, which is the case for most ECs (Coutu et al., 2013, Thomas et al., 2012). Episodic pollution events can be missed. Field studies with high temporal resolution showed that, during rain events, concentrations of agricultural pesticides in small streams could increase by a factor of 10–100 or more within hours (Xing et al., 2013, Petersen et al., 2012). One solution to this issue is to increase the sampling frequency, such as high frequency sampling, or to use automatic sampling devices that can take time-proportional composite samples over a period. Some regulations, such as the current discharge standard of pollutants for municipal wastewater treatment plants (WWTPs) in China (GB 18918–2002), require 24-hour time-proportional (2 h×12) samples for monitoring regulated pollutants (COD, BOD_5, total nitrogen, etc.). Half-day time-proportional composite site samples (45 min×16) were taken for studying 213 pesticides in small streams with an automatic sampling device (Spycher et al., 2018). Such systems are costly, complex for end-users and are rarely used in widespread monitoring campaigns (Vrana et al., 2005). In addition, collecting, preserving, transporting and pre-treatment of these samples in the laboratory is laborious and time consuming and samples in glass bottles are also subject to damage and contamination.

Passive sampling has emerged as a representative and practical sampling approach for target analysis and non-target screening. It pre-concentrates analytes in situ and provides in situ related concentrations (Roll and Halden, 2016). The most common aquatic passive sampler for polar organic chemicals—the polar organic chemical integrative sampler (POCIS)—is highly dependent on environmental conditions, such as water flow rates, because of the effect of the diffusive boundary layer (DBL) (Harman et al., 2012). However, measuring or predicting DBL is complex, so in situ correction for POCIS using performance reference compounds (PRC) has been proposed in the literature. This approach corrects the target compound sampling rate relative to the in situ desorption rate of a PRC according to isotropic exchange. Nevertheless, this is not only expensive but also subject to the availability of the isotope-labelled compounds, especially for ECs.

These drawbacks make the diffusive gradients in thin films (DGT) technique promising for determining organic chemicals. Due to the fairly long diffusive path of the DGT system (≈1 mm in a standard DGT device), DBL is negligible when water flow is above a low threshold (0.02 m/s) (Warnken et al., 2006). This has been directly proved by

controlled laboratory experiments (Warnken et al., 2006, Buzier et al., 2019) and field evaluation of POCIS and DGT for a total of 34 polar organic chemicals, including organophosphates and antibiotics (Challis et al., 2018). Because of the large body of literature and the solid foundation of DGT (Davison and Zhang, 1994, Chen et al., 2012, Guibal et al., 2019), research into the use of DGT for organics is attracting considerable interest and is growing rapidly. At the time of writing, DGT has been designed and validated for over 150 organic compounds, including pharmaceuticals and personal care products (PPCPs), flame retardants, estrogens and pesticides, drugs, etc. (Zou et al., 2018, Guo et al., 2017, Chen et al., 2017, Chen et al., 2018, Zhang et al., 2018). Until now, research into DGT for organics has mainly focused on laboratory development and calibration (Chen et al., 2012, Zheng et al., 2015, Challis et al., 2016, Zhang et al., 2019), with a few field evaluations conducted mostly in raw or treated wastewaters (Chen et al., 2013, Chen et al., 2017, You et al., 2019). Applying DGT to rivers at a catchment scale is necessary to test and demonstrate its reliability and challenges in a dynamic water system, with different environmental conditions. Exploring sources and environmental fates of ECs using DGT provides a 'real world' field-testing of the use of DGT for environmental monitoring of trace organics.

The River Thames and its tributaries play an important role in the Thames catchment supporting approximately 13 million inhabitants, including London, the capital of the United Kingdom. London (Greater London) was estimated to sustain a population of nine million in mid-2018 by the Office for National Statistics (2019). This makes London the most populous city in the European Union and accounting for 13% of the U.K. population (Wikipedia). The river system is the main source of drinking water in this area. It is also actively influenced by anthropogenic activities, with 352 WWTPs discharging into it (Williams et al., 2009). The rivers are also extensively used for recreational activities, such as fishing, swimming and boating.

The River Thames is one of the most monitored and studied rivers in the United Kingdom. Due to its importance as a drinking water source, some water quality parameters, such as phosphorus and nitrogen, have been continuously monitored (Bowes et al., 2018). It therefore offers a unique study area with high-quality data support, such as river flow, catchment area, land cover, wastewater treatment systems, and population density. From a practical perspective, there are intensive ongoing monitoring programs to build on (Bowes et al., 2014, Williams et al., 2009) and field campaigns in this study were built

on the Centre for Ecology and Hydrology's (CEH) Thames Initiative research platform (see later for details).

Large numbers of unregulated ECs, such as pharmaceuticals and drugs have been found in rivers, groundwater and drinking water across the United Kingdom (Peng et al., 2019, Kasprzyk-Hordern et al., 2009, Kasprzyk-Hordern et al., 2008a, Kasprzyk-Hordern et al., 2008b, Kasprzyk-Hordern et al., 2007, Roberts and Thomas, 2006, Ashton et al., 2004), while their occurrence in the River Thames catchment is largely unknown. A limited number of pharmaceuticals were investigated in the River Thames and its tributaries by grab sampling (500 mL water sample) (Nakada et al., 2017, White et al., 2019) and automatic sampling (500 mL 24-hour composite sample) (Hanamoto et al., 2018). Organophosphate esters (OPEs) are listed on the High Production Volume Chemicals (HPVC) and have raised concerns over their ubiquitous contamination and potential hazards (Wang et al., 2015). However, no information is available about OPEs in the Thames catchment.

The objectives of this study were therefore to: (i) compare DGT and grab sampling approaches for their suitability to screen and monitor ECs at the catchment scale, (ii) use the data generated by DGT to characterize fate processes of ECs in the aquatic system and understand better the transport, sources, and fate throughout the large dynamic watershed, (iii) to investigate seasonal changes of ECs in selected established sites across the Thames catchment, and (iv) discuss the significance of the concentrations detected for aquatic organisms and the implications for monitoring contaminants.

5.2 Materials and methods

5.2.1 Study area and sampling sites

The River Thames in south England extends 354 km from its source in the Cotswold Hills to its tidal limit at Teddington, covering a catchment area of 9948 km^2, with a population density ca. 960 people km^{-2} (Bowes et al., 2014). The mean annual runoff is 245 mm. A total of 345 WWTPs are located in this region (before the tidal limit). A more detailed catchment description can be found elsewhere (Bowes et al., 2014).

This study was built on the Centre for Ecology and Hydrology's (CEH) Thames Initiative research platform. The Thames Initiative is a major integrated monitoring program that brings together water quality and ecological research across the River Thames catchment.

This chemical and biological monitoring program provides a research platform to support a wide range of cross-disciplinary science both within CEH and externally. It currently supports collaborative external projects, ranging from nutrient pollution modelling, assessment of novel in situ analyzer technologies, pharmaceutical pollutants, microbial metagenomics studies and nanoparticles (https://www.ceh.ac.uk/our-science/projects/river-thames-initiative).

This study focused on the River Thames from Swinford to Runnymede, above the tidal reach (Figure 5.1). Three sampling sites are on the main stream of the River Thames—upstream (Swinford, TS), midstream (Wallingford, TW), downstream (Runnymede, TR)—and the others selected are on six tributaries—Cherwell (Ch), Ray (Ra), Ock (Oc), Thame (Th), Pang (Pa) and the Cut (Cu). The catchment areas, distance to source, land cover and WWTPs population equivalent (PE) upstream of each sampling site and the corresponding WWTPs population equivalent density are listed in Table 5.1. The study area has a big variety of sub-catchments, from the predominantly rural River Pang (with WWTPs population equivalent densities of <30 km^2 and <5% urban and semi-urban land cover) to rivers that are predominantly urban and receiving high WWTPs effluent loadings, such as the Cut (with WWTPs PE density of over 1500 PE/km^2, which is five-fold of the average WWTPs PE density in the study area). With this sampling site design, each field campaign (DGT sampler setup and collection one week after, grab sample collection on the first and third day of the DGT deployment time) could be effectively done within one day.

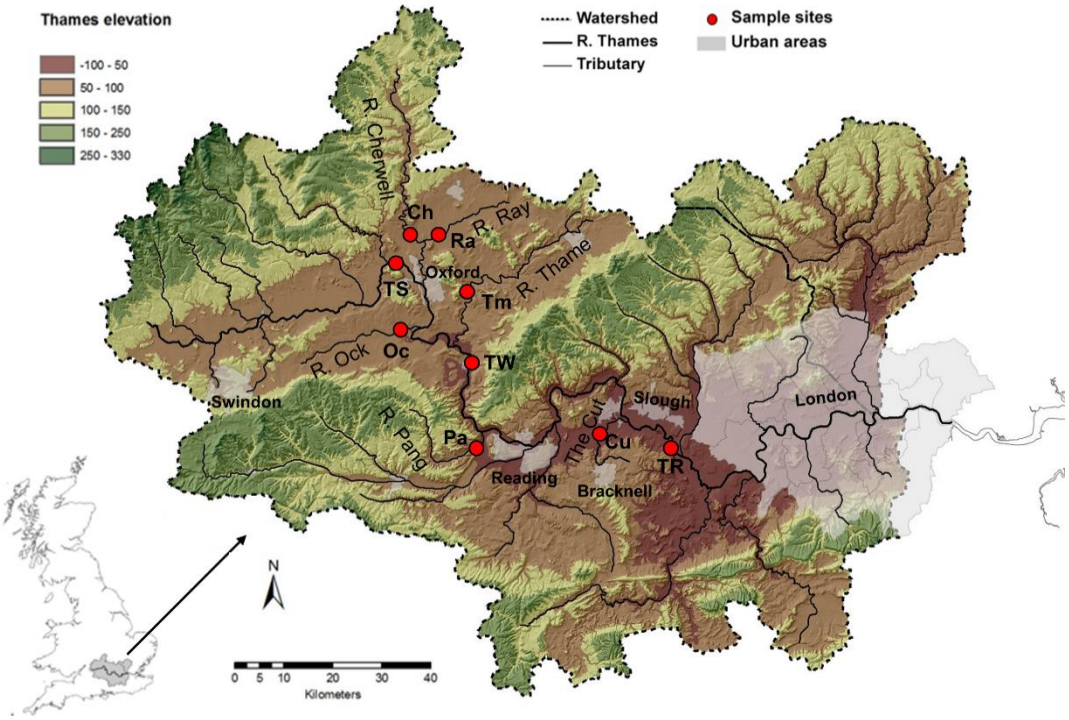

Figure 5.1. Map of Thames catchment, showing location of monitoring sites.

Two seasons of field campaigns were carried out, one in summer (June 25–July 02, 2018) and one in winter (Feb 11–Feb18, 2019). River flow at the sampling site or the nearest gauging station was obtained from the National River Flow Archive (https://nrfa.ceh.ac.uk/data). Table 5.2 shows the mean flow, 95% (low flow), 50% and 5% (high flow) exceedance flows in the record period. Figure 5.2 shows the gauged daily flow during the sampling times. The river flow of the Cut is updated to September 2018, while the rest are all updated to August 2019. The river flow over the whole study duration was slightly lower but close to the long-term average.

Table 5.1. Monitoring site location and catchment characterization

Site code	River	Sampling site	Grid reference	Catchment area (km^2)	Distance to source (km)	% Land cover				WWTPs population equivalent	WWTPs population equivalent density (PE/km^2)
						Woodland	Grassland	Arable	Urban and semi-urban		
TS	Thames	Swinford	SP442085	1623	89	10.8	35.1	45.5	6.7	338,300	209
TW	Thames	Wallingford	SU609902	4213	134	10.3	35.6	45.1	7.3	1,027,910	244
TR	Thames	Runnymede	TQ006723	7192	222	13.2	34.0	40.4	10.5	2,661,370	370
Ch	Cherwell	Hampton Poyle	SP499152	566	69	9.1	33.3	50.4	6.4	112,270	198
Ra	Ray	Islip	SP527139	290	32	11.3	40.1	42.6	5.3	46,020	159
Oc	Ock	Abingdon	SU495967	255	33	8.0	33.0	51.0	7.3	36,780	144
Tm	Thame	Wheatley	SP612050	532	53	9.7	32.4	35.7	8.3	153,710	289
Pa	Pang	Tidmarsh	SU636747	175	28	17.6	27.6	46.0	4.1	4990	29
Cu	The Cut	Paley Street	SU869762	63	20	20.8	32.7	9.8	35.3	103,600	1644

Table 5.2. River flows at the sampling site or the nearest gauging station were obtained from National River Flow Archive. Mean flow, 95%, 50% and 5% exceedance flow in the record period are shown in the table

Site code	River	Sampling site	Gauging station	Mean flow (m^3/s)	Q95 (m^3/s)	Q50 (m^3/s)	Q5 (m^3/s)	Period of record
TS	Thames	Swinford	Farmoor	14.91	0.96	9.22	52.10	1992–2018
TW	Thames	Wallingford	Sutton Courtenay	27.50	2.50	16.00	95.69	1973–2018
TR	Thames	Runnymede	Royal Windsor Park	59.19	14.79	40.74	173.00	1979–2018
Ch	Cherwell	Hampton Poyle	Banbury	1.14	0.02	0.42	4.70	1966–2018
Ra	Ray	Islip	Islip	2.09	0.13	0.73	9.54	1995–2018
Oc	Ock	Abingdon	Abingdon	1.58	0.34	0.91	5.32	1962–2018
Tm	Thame	Wheatley	Wheatley	3.77	0.73	1.78	14.12	1998–2018
Pa	Pang	Tidmarsh	Pangbourne	0.66	0.20	0.54	1.19	1968–2018
Cu	The Cut	Paley Street	Binfield	0.40	0.07	0.24	1.30	1957–2018

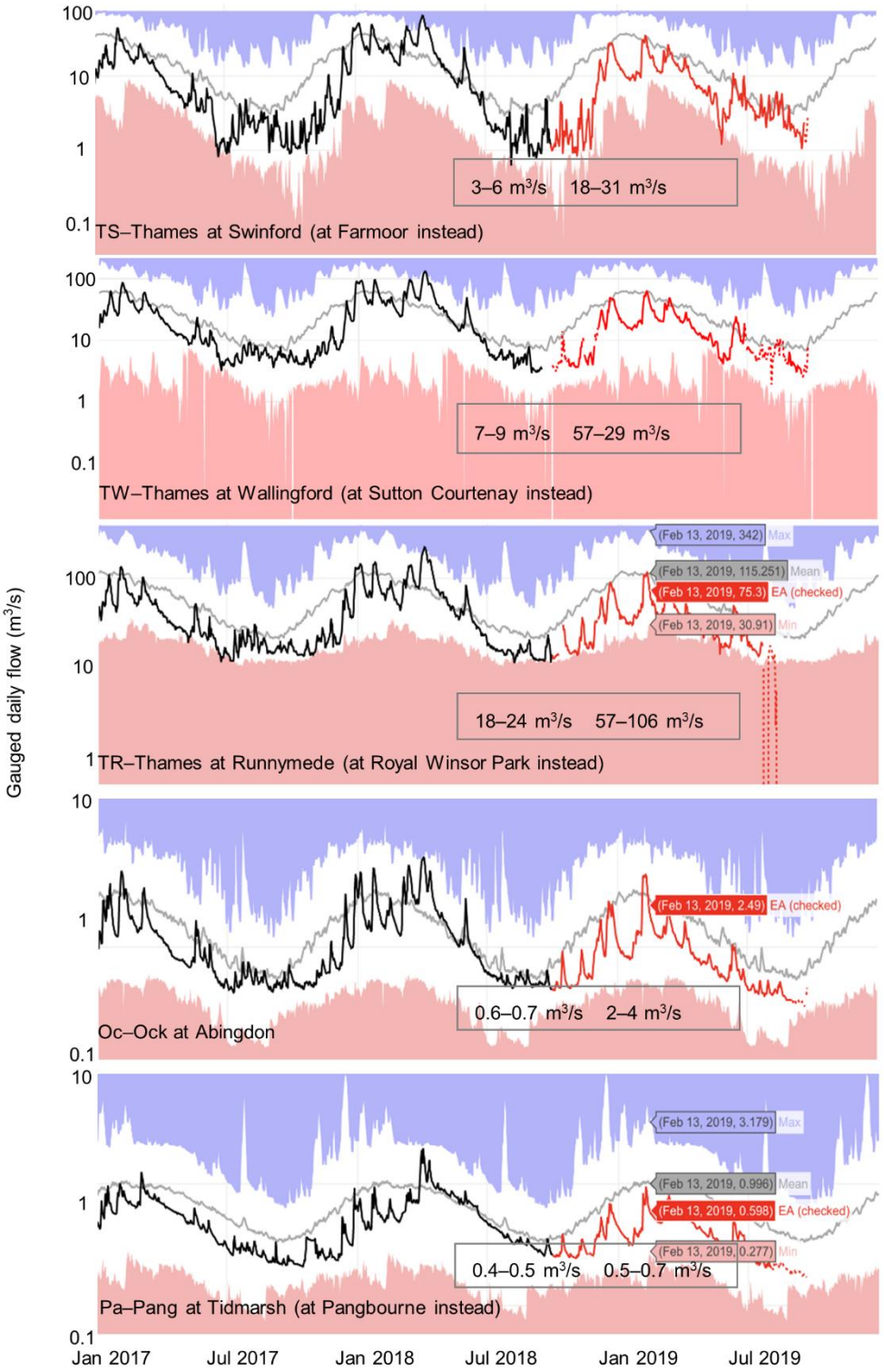

Figure 5.2. Daily flow ranges of 5 sampling sites at two sampling periods (June 25–July 02, 2018 and Feb 11–Feb18, 2019) are shown on the graph, which are used in Results and discussion 3.4. Red and blue envelopes represent the lowest and highest flows on each day over the period of record. The grey line represents the mean flow. The black line represents NRFA data. Red solid and red dotted lines represent Environment Agency checked and unchecked data. Adapted from NRFA.

5.2.2 Analytes of interest and reagents

An essential issue faced by scientists and regulators is which compounds to investigate. More than 200 pharmaceuticals alone have been reported in river waters globally in 2015 (Petrie et al., 2015), while approximately 2000 pharmaceuticals are registered in the United Kingdom and more than 3000 are approved for prescription in the United States (Benotti et al., 2009). Selection of the 13 target chemicals (Table 5.3) in this study was based on several criteria (Benotti et al., 2009): (a) prescription drug status, (b) volume of use, (c) toxicity, (d) occurrence and public concerns, (e) chemical classes, and (f) availability of the DGT and analytical methods. Isotope-labelled chemicals were used as surrogate internal standards (SIS): SMX-d_4, CAF-$^{13}C_3$, MEP-$^{13}C_6$, PRP-$^{13}C_6$, BUP-$^{13}C_6$, PHBA-d_4 and E3-d_2.

High purity chemical standards were purchased from Sigma-Aldrich (U.K.). Corresponding stable isotope-labelled compounds were purchased from Sigma-Aldrich (U.K.) and QMX Laboratories (U.K.). The structures of the studied ECs are shown in Figure 5.3.

The studied pharmaceuticals and an endocrine disrupting chemical are ionic organic chemicals, which contain at least one polar functional group, such as amino, hydroxyl and carboxyl. These chemicals can be neutral, cationic, anionic or zwitterionic under different pH conditions. It has been shown that the DGT uptake is unaffected by pH 6.2–9 for SPD, SMR, SDX and TMP (Chen et al., 2012, Xie et al., 2018), by pH 3.5–9.5 for MEP, PRP, BUP, PHBA and E3 (Chen et al., 2017, Chen et al., 2018). OPEs with alkyl groups (TEP in this study, Figure 5.3) and with chlorinated groups (TCEP and TCPP in this study, Figure 5.3) exhibit great hydrolytic stability and are stable at neutral and basic conditions (pH 7–11) for up to 35 days (Su et al., 2016). The DGT measurement of the studied OPEs is independent of pH 3.1–9.7 (Zou et al., 2018, Wang et al., 2019). The above literature also showed the DGT measurement of these target chemicals is independent of ionic strength (0.001–0.1 M) and dissolved organic matter (0−20 mg/L). Overall, DGT measurement of these target chemicals in rivers in the Thames catchment is not expected to be affected by pH (pH = 7.9±0.2 in sampling periods), ionic strength (average 0.01 M) and dissolved organic matter (DOM = 7.2±2.6 mg/L in sampling periods) (pH and DOM measured and provided by CEH).

Table 5.3. Target chemicals, their selected physicochemical properties and descriptions

Compound (Abbr.)	CAS No.	Mw (Da)	Log K_{OW}	Sw 25°C (mg/L)	pK_a	Vapor pressure mm Hg at 25 °C	Description
Pharmaceuticals							
Sulfapyridine (SPD)	144-83-2	249.3	0.35 [a]	268*	8.43	4.14E-08	Veterinary antibiotic
Sulfamerazine (SMR)	127-79-7	264.3	0.14 [a]	212*	NA	4.71E-09	Human and veterinary antibiotic
Sulfadoxine (SDX)	2447-57-6	310.3	0.70 [b]	2697[#]	NA	2.15E-09	Human and veterinary antibiotic
Trimethoprim (TMP)	738-70-5	290.3	0.91 [a]	400*	7.12	7.52E-09	Human and veterinary antibiotic
Methylparaben (MEP)	99-76-3	152.2	2.00 [a]	2500*	8.40	8.55E-04	An anti-fungal agent often used in a variety of cosmetics and personal care products
Propylparaben (PRP)	94-13-3	180.2	2.98 [a]	500*	8.50	3.07E-04	A preservative in many water-based cosmetics, such as creams, lotions, shampoos and bath products, and in food
Butylparaben (BUP)	94-26-8	194.2	3.47 [a]	207*	8.47	2.51E-04	A preservative in food, pharmaceutical, and personal care products
4-Hydroxybenzoic acid (PHBA)	99-96-7	138.1	1.58 [a]	5000*	4.54	1.44E-05	A preservative, a main hydrolysis metabolite of parabens
Endocrine disrupting chemicals (EDCs)							
Estriol (E3)	50-27-1	288.4	2.81 [a]	3*	10.54	9.37E-12	One of the three major human estrogens, used as a medication
Organophosphate esters (OPEs)							
Triethyl phosphate (TEP)	78-40-0	182.2	0.80 [a]	500000[#]	NA	3.93E-01	Mostly applied as plasticizers, antifoaming agents and additives
Tris(2-chloroethyl) phosphate (TCEP)	115-96-8	285.5	1.44 [c]	7000[#]	NA	6.13E-02	Predominantly used as flame-retardants in furniture, textiles, mattresses, electronics
Tripropyl phosphate (TPrP)	513-08-6	224.2	1.87 [a]	6450[#]	NA	2.40E-02	Mostly applied as plasticizers, antifoaming agents and additives
Tris(chloropropyl) phosphate (TCPP)	13674-84-5	327.6	2.59 [c]	1200[#]	NA	5.64E-05	Predominantly used as flame-retardants in furniture, textiles, mattresses, electronics

[a]: Exper. Database match from Hansch C, Leo, A. and Hoekman, D. (1995). Exploring QSAR: Hydrophobic, electronic, and steric constants. Am Chem Soc, Washington.
[b]: Octanol-Water Partition Coefficients: Fundamentals and Physical Chemistry. Sangster J 1994 Wiley, New York. Pomona College Medicinal Chemistry Project, Claremont, CA 91711, Log P Database, (C. Hansch and A. Leo), July 1987 edition.
[c]: Exper. Database from Chemicals inspection and testing institu (1992) from EPI Suite
*: Exper. Database match from Handbook of Aqueous Solubility Data
[#]: water solubility estimate from log K_{ow} (WSKOW V1.42)
The data of pKa collected from U.S. national Library of Medicine

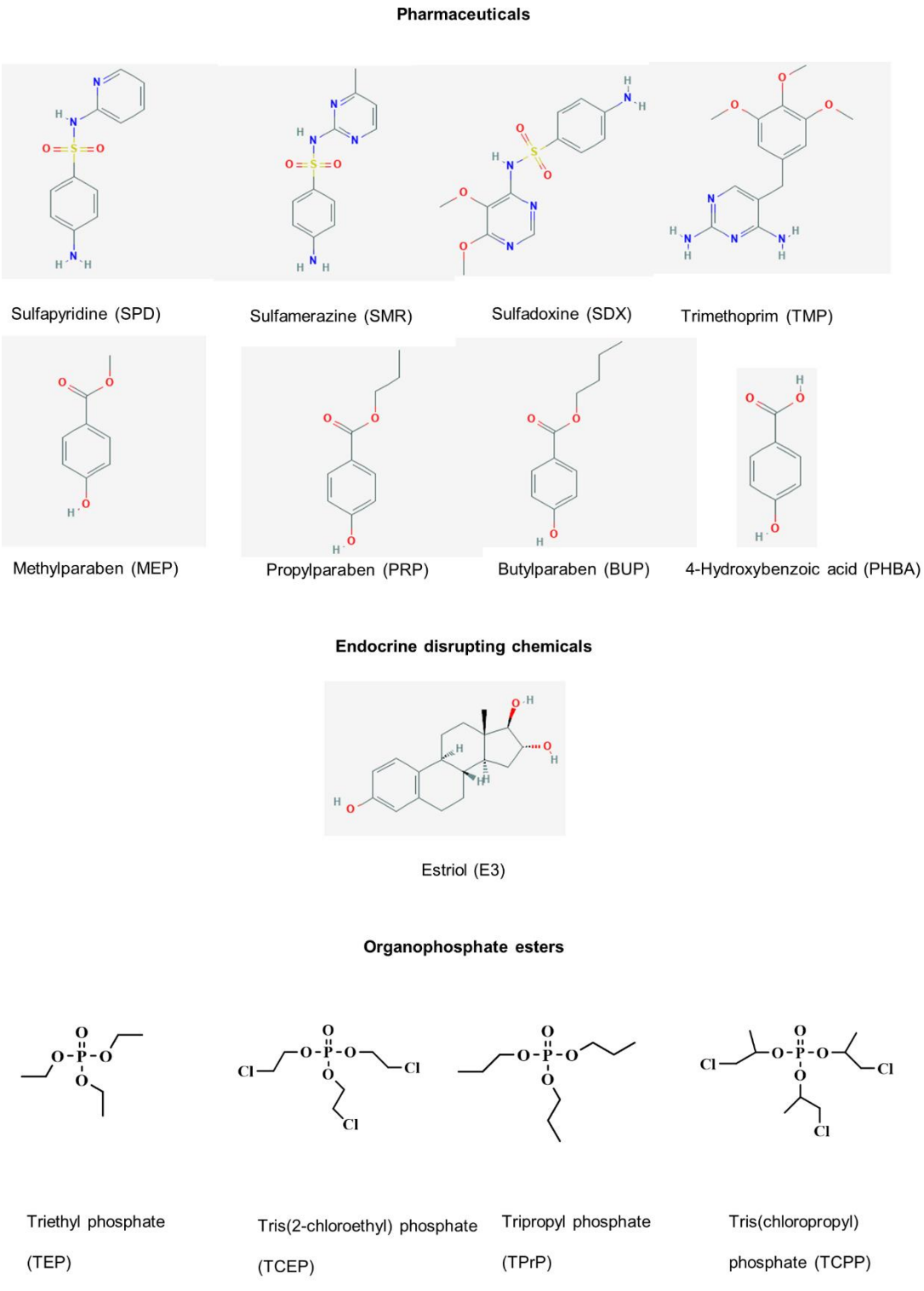

Figure 5.3. Structures of the target compounds.

5.2.3 DGT preparation

DGT moldings were provided by DGT Research Ltd. (Lancaster, U.K.) and the binding gels and diffusive gels were made in the laboratory in one batch before the fieldwork. The DGT device in this study comprises a 0.4 mm thickness of hydrophilic-lipophilic-

balanced (HLB) resin gel as the binding layer (50 mg wet weight HLB per disc), a 0.8 mm thickness of agarose gel (1.5% agarose) as the diffusion layer and a hydrophilic polypropylene (GHP) membrane (thickness: 0.11 mm, diameter: 25 mm, pore size: 0.45 μm, PALL) as the membrane filter. The other two thicknesses agarose gels (0.35 mm and 1.15 mm) were made for DBL measurement. More details about the DGT sampler and the technique were first described in Zhang and Davison (Zhang and Davison, 1995).

5.2.4 Field campaigns

Grab water sampling

Grab samples were collected at the beginning and third day of DGT deployment time. Water samples (1.2 L) from the main river flow were collected in solvent cleaned amber glass bottles rinsed with the water from the sampling site prior to the sample collection. Where the sampling site could not be reached by wading in (the Cut at Paley Street, Ray at Islip, Ock at Abingdon), a bucket was used to collect water from the bridge or the bank and then transferred into an amber glass bottle. Following collection, samples were placed in the dark, in cool-boxes containing frozen icepacks and transported back to a sample store walk-in refrigerator (4 °C) within 12 hours. Three amber glass bottles with deionized water from the laboratory were taken to the field sites and used as field blanks for each field campaign. Replicate samples at two random sites (the River Thames at Wallingford and Swinford) were taken to check the repeatability of the sampling and analytical methods.

DGT sampling

At most sites DGT samplers were fitted on a holder fixed onto a steel rod, which was vertically inserted into the riverbed (Figure 5.4-a; b). However, at three sampling sites (the Cut at Paley Street, Ray at Islip, Ock at Abingdon) an alternative approach was needed. The riverbed at the Cut at Paley Street consists of boulders and rocks and the water depth was 0.3–0.5 m. Here the steel rod was therefore placed lying on the riverbed with DGT samplers facing upwards (Figure 5.4-c). At the sampling sites for the Ray at Islip and Ock at Abingdon, the steel rod was suspended from a tree on the riverbank (Figure 5.4-d). Generally, the DGT samplers were at least 0.3 m below water surface.

The DGT samplers were deployed in flowing water, but in positions which would avoid high turbulence which would generate bubbles. Three standard DGT samplers (HLB

resin + 0.8 mm Agarose gel + GHP membrane filter) were deployed simultaneously at each site. Three new DGT samplers were used for field blanks. The DGT samplers' exposure time was approximately one week. After retrieval, the sampler surface was examined carefully and no obvious biofouling was spotted across all the DGT samplers (Figure 5.5). After rinsing the DGT sampler with deionized water and shaking off obvious surface water, it was disassembled with a screwdriver. The resin gels were carefully put in amber glass vials separately and then placed in the dark cool-boxes containing frozen icepacks. After transporting back to the CEH laboratory, three surrogate standard mixtures (50 µL of each, containing 50 ng of each isotopically labelled chemicals) were spiked onto the resin gel in each vial and 5 mL of acetonitrile was put in each vial on the sampling day and they were stored in a refrigerator (4 °C) before sonication extraction at Lancaster laboratory within one week.

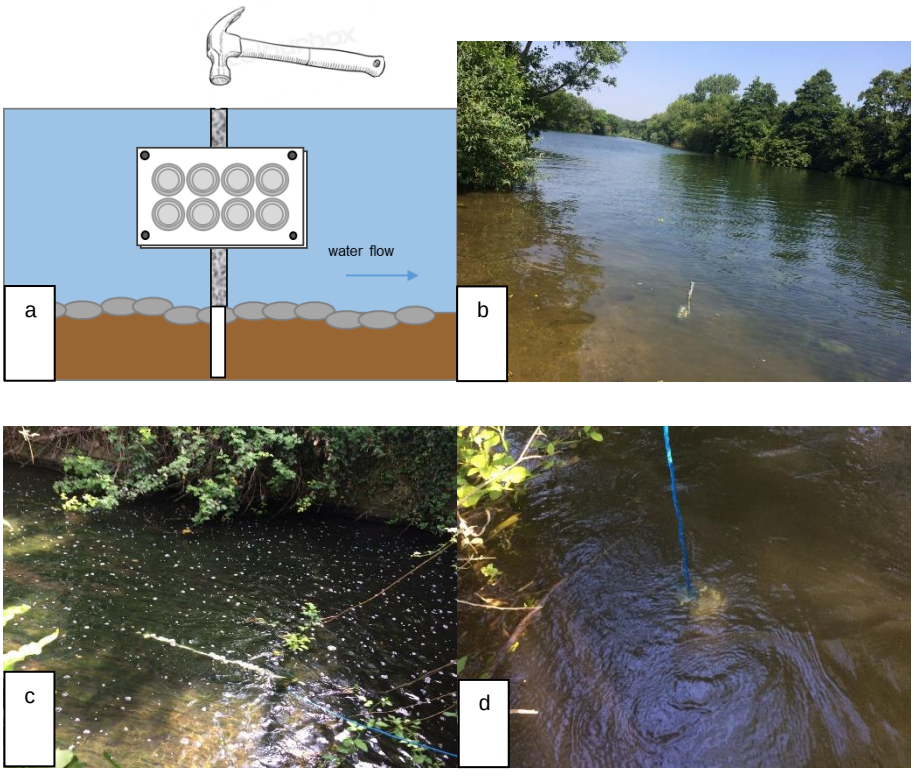

Figure 5.4. Deployment design of the DGT samplers and the three scenarios in the field: (a, b) the DGT samplers on a holder fixed onto a steel rod, which was vertically inserted into the riverbed and this was the most cases, (c) the steel rod was lying on the riverbed at the Cut at Paley Street and (d) the steel rod was hanging from a tree on the riverbank at sampling sites of Ray at Islip and Ock at Abington.

Figure 5.5. Photographs showing DGT retrieved after deployment; no obvious biofouling was observed on any of the DGT samplers.

DBL measurement

The DGT samplers with different thicknesses of diffusive layers (Δg) could be deployed in situ to estimate the environmental related DBL thickness (δ) by using the eq (5.1). The reciprocal of accumulated masses of test chemicals ($1/M$) was plotted against the thickness of the diffusive layer (Δg); δ can then be calculated using the ratio of the intercept and the slope of the regression line (Warnken et al., 2006).

$$\frac{1}{M} = \frac{\Delta g}{c_{DGT} DAt} + \frac{\delta}{c_{DGT} DAt} \quad (5.1)$$

Therefore, the DGT samplers with four different values of Δg [0.11 (membrane filter only), 0.46, 0.91 and 1.26 mm] were deployed at three of the sites, selected to have low, median and fast flow rates (Ock at Abingdon, Thames at Wallingford and the cut at Paley Street).

Summary of samples

In total, 25 grab samples and 66 DGT samplers were collected (Table 5.4).

Table 5.4. No. of obtained samples and average temperature during DGT deployment

Site code	River	Sampling site	2018 (June 25–July 02) Spot sample (June 25)	Spot sample (June 28)	2018 (June 25–July 02) No. of DGTs [thickness of Δg (mm)] [Average temp (°C)]	2019 (Feb 11–Feb 18) No. of DGTs [thickness of Δg (mm)] [Average temp (°C)]
TS	Thames	Swinford	1	2	3 (0.91), 1 (0.11) (22)	3 (0.91), 1 (0.11) (7)
TW	Thames	Wallingford	2	1	3 (0.91), 1 (0.11), 2 (0.46), 2 (1.26) (22)	3 (0.91), 1 (0.11) (7)
TR	Thames	Runnymede	1	1	3 (0.91), 1 (0.11) (22)	3 (0.91), 1 (0.11) (7)
Ch	Cherwell	Hampton Poyle	1	1	NA	NA
Ra	Ray	Islip	1	NA	NA	NA
Oc	Ock	Abingdon	1	1	3 (0.91), 1 (0.11), 2 (0.46), 2 (1.26) (18)	3 (0.91), 1 (0.11) (7)
Tm	Thame	Wheatley	1	1	3 (0.91), 1 (0.11) (21)	NA
Pa	Pang	Tidmarsh	1	1	3 (0.91), 1 (0.11) (15)	3 (0.91), 1 (0.11) (8)
Cu	The Cut	Paley Street	1	1	3 (0.91), 1 (0.11), 2 (0.46), 2 (1.26) (20)	NA
Field blank			3	3	3 (0.91)	3 (0.91)

NA: No samples obtained due to sample loss, interference by people or no accessibility to the sampling site

5.2.5 Sample preparation

Grab sample preparation

Grab samples were filtered and extracted on the second day of the sampling. Water samples were filtered through glass fiber filters (GF/F, 0.45 μm, Whatman, U.K.), and spiked with 3 surrogate standard mixtures (50 μL of each, containing 50 ng of each isotopically labelled pharmaceuticals, antibiotics and organophosphate flame retardants). The Oasis HLB cartridges (200 mg, 6cc, Waters, U.K.), which were used for concentrating water samples, were conditioned with 10 mL acetonitrile, followed by 10 mL of deionized water at a flow rate of 1 mL/min. After conditioning, the water samples (1000 mL) were passed through the SPE cartridges at a flowrate of 10 mL/min and allowed to run dry for a minimum period of 30 min. The dried cartridges were labelled, sealed in the original cartridge plastic bag and were kept frozen for up to a few weeks. Glass fiber filters were sealed in aluminum foil, labelled, and kept frozen. After transporting back to the Lancaster laboratory in a cool-box with frozen icepacks, the cartridges were eluted with 5 mL methanol twice and 5 mL acetonitrile. The combined elution solution was evaporated to dryness by gentle nitrogen and reconstituted in 1 mL of acetonitrile and water (v:v = 20:80) and then filtered through a 0.2 μm PTFE syringe filter into LC amber vials. Samples were stored at 4 °C before analysis by an ultra-high-performance liquid chromatography-tandem mass spectrometer (UHPLC-MS/MS). A

Waters Xbridge C18 column (2.5 μm, 2.1 × 100mm) was used for separation. Measured concentrations were quantified by the surrogate method.

DGT sample preparation

The resin gel was eluted with 2 × 5 mL aliquots of acetonitrile and sonicated for 30 minutes between each elution and rinsed by another 2 mL acetonitrile. The elution solution was evaporated to dryness by gentle nitrogen and reconstituted in 1 mL of acetonitrile and water (v:v = 20:80) and then filtered through a 0.2 μm PTFE syringe filter into LC amber vials. Samples were stored at 4 °C before analysis by LC-MS/MS.

5.2.6 Instrumental analysis

An ultra-high-performance liquid chromatography-tandem mass spectrometer (UHPLC-MS/MS) was used to determine the target compounds. Separations were achieved by a Shimadzu Nexera UHPLC (Kyoto, Japan) equipped with two LC-30AD pumps, a CTO-20AC column oven, a DGU-30A5 degasser, an SIL-30AC auto-sampler and a column oven connected to a Waters Xbridge C18 column (2.5 μm, 2.1 × 100mm). The auto-sampler was cooled at 20 ºC and the column temperature was at 25 ºC. The mobile phases for SPD, SMR, SDX and TMP consisted of (A) deionized water with 0.1% formic acid (v/v) and (B) acetonitrile with 0.1% formic acid (v/v) using a gradient elution of 20% B (5.0 min)–60% B (9.0 min)–100% B (10.0 min)–100% B (12.0 min)–20% B (13.0 min)–20% B (17.0 min). The mobile phases for MEP, PRP, BUP, PHBA and E3 consisted of (A) deionized water with 5 mM NH4OH and (B) acetonitrile with 5 mM NH4OH using a gradient elution of 15% B (4.0 min)–80% B (13.0 min)–100% B (18.0 min)–100% B (22.5 min)–15% B (23.0 min)–15% B (30.0 min). The flow rate was 0.2 mL/min. The injection volume was 10 μL. A triple quadrupole mass spectrometer (Shimadzu LCMS-8040, Kyoto, Japan) was connected to the LC instrument via an electrospray ionization (ESI) interface. The mass spectra for SPD, SMR, SDX and TMP was acquired in positive ion mode and for MEP, PRP, BUP, PHBA and E3 was acquired in negative ion mode. The DL temperature was set at 250 ºC, heat block temperature at 400 ºC, nebulizing gas at 2.0 L/min and drying gas at 15.0 L/min. A Phenomenex Kinetex Biphenyl column (50×2.1 mm, 2.6 μm) was used for separating TEP, TCEP, TPrP and TCPP and other details are elsewhere (Chapter 3).

5.2.7 Quality assurance and quality control

Field blanks were collected to ensure no contamination during fieldwork, sample transport and storage. SIS was used in both grab samples and the DGT samples to recover chemical loss during sample processing (filter, transfer, extraction, nitrogen blowing, and instrumental fluctuation). DGT samplers were deployed in triplicate at all the sampling sites and grab samples were taken in duplicate at two sampling sites, to check the reproducibility of the sampling method. Quality control standards (10 and 50 µg/L) were prepared using independent weighing and they were analyzed with every 10 samples. Instrumental limits of detection (LOD) were between 0.01 (TEP) and 0.50 (PHBA) µg/L. Detailed information about the instrumental limit of detection (LOD) and method quantification limit (MQL) of the SPE method (grab samples) and the DGT method is given in Table 5.5.

Table 5.5. The instrumental limit of detection (LOD) and method quantification limit (MQL) of the SPE method (grab samples) and the DGT sampler, diffusion coefficients (D) of studied compounds and minimum mass (M_{DGT}) for DGT quantification is also given.

Compound	LOD (µg/L)[a]	MQL of SPE (ng/L)	Calculation of DGT MQL (7-day deployment at 25 °C)		
			D (E-6) cm²/s at 25 °C[b]	Minimum M_{DGT} for DGT quantification (ng)	MQL of DGT[c] (ng/L)
SPD	0.16	0.49	4.75	0.49	6.0
SMR	0.16	0.48	3.79	0.48	7.5
SDX	0.33	1.02	3.85	1.02	15
TMP	0.07	0.20	3.79	0.20	3.1
MEP	0.18	0.55	6.85	1.44	12
PRP	0.25	0.75	5.92	1.13	11
BUP	0.13	0.40	5.61	0.40	4.2
PHBA	0.50	1.53	7.30	2.04	16
E3	0.37	1.14	4.59	1.14	15
TEP	0.01	0.03	6.77	1.05	9.1
TCEP	0.35	1.07	6.19	1.07	10
TPrP	0.10	0.31	5.47	0.43	4.6
TCPP	0.38	1.15	6.17	2.45	23

[a]: The instrumental limit of detection (LOD) was defined as the lowest concentration of analyte for which the observed signal/noise ratio (S/N) = 3. The method quantification limit (MQL) was defined as mean blank sample concentration plus three times the standard deviation (3σ).

[b]: Diffusion coefficients (D) of studied compounds are obtained from studies (Chen et al., 2017, Chen et al., 2018, Chen et al., 2013)

[c]: Used equation $c_{DGT} = \frac{M_{DGT}(\Delta g+\delta)}{tAD}$ to calculate MQL of DGT at 25 °C, assuming that δ = 0.2 mm.

5.2.8 Calculation of DGT measurement

When the concentration of the analyte in surrounding solution changes, as may occur in a river, DGT provides the time-weighted average concentration (c_{TWA}) of the fully dissolved analytes during the deployment time (t). The diffusion coefficient (D) through the diffusion layer is well established in the laboratory. The exposure area of a standard DGT device is 3.14 cm^2. By determining the mass of the analyte accumulated in the binding gel by mass spectrometry, the c_{DGT} is derived (eq 5.2):

$$c_{DGT} = \frac{M_{DGT}(\Delta g + \delta)}{tAD} \quad (5.2)$$

Diffusion coefficients (Table 5.6) of the target chemicals at 25 °C (D_{25}) are obtained elsewhere (Chen et al., 2013, Chen et al., 2017, Chen et al., 2018) and at other temperatures are calculated using eq 3 (Chen et al., 2013):

$$\log D_{t_2} = \frac{1.37023(t_2-25) + 8.36 \times 10^{-4}(t_2-25)^2}{109 + t_2} + \log\frac{D_{25}(273 + t_2)}{298} \quad (5.3)$$

Average temperature during DGT deployment was used for calculation (see Table 5.4 for temperature). When using the DGT, it has widely been assumed that the DBL thickness is sufficiently thin compared to the diffusion distance in the sampler itself (thickness of diffusive gel + thickness of membrane filter). In this study, the measured DBL was derived and was different for different chemicals; this was also the case for another field application (Challis et al., 2018). It ranged from 0.2–0.9 mm for SPD and 0.2–0.8 mm for TMP. Measuring DBL is challenging in the field, especially when the target analytes are at trace levels (ng/L or even lower) and, in addition, the flow near the sampler surface may vary in both time and space. The thickness of the DBL has been derived at $\approx$0.2 mm in moderate to well-stirred solutions (Warnken et al., 2006). Field applications have used δ = 0.3 mm (Challis et al., 2018) and δ = 0.2 mm (Challis et al., 2016) for DGT measuring organics. It is suggested that δ = 0.2 mm is applied when DGT used in naturally flowing streams and rivers (flow rate $\geq \approx$ 2cm/s) (Challis et al., 2016, Gimpel et al., 2001). Thus, δ = 0.2 mm is applied in the calculation.

Table 5.6. Diffusion coefficients of studied chemicals at 1–35 °C

T (°C)	SPD	SMR	SDX	TMP	MEP	PRP	BUP	PHBA	E3	TEP	TCEP	TPrP	TCPP
1	2.22	1.77	1.80	1.77	3.20	2.76	2.62	3.41	2.14	3.16	2.89	2.55	2.88
2	2.30	1.84	1.86	1.84	3.32	2.87	2.72	3.54	2.22	3.28	3.00	2.65	2.99
3	2.39	1.90	1.93	1.90	3.44	2.97	2.82	3.67	2.31	3.40	3.11	2.75	3.10
4	2.48	1.97	2.01	1.97	3.57	3.08	2.92	3.80	2.39	3.53	3.23	2.85	3.21
5	2.56	2.05	2.08	2.05	3.70	3.20	3.03	3.94	2.48	3.66	3.34	2.95	3.33
6	2.66	2.12	2.15	2.12	3.83	3.31	3.14	4.08	2.57	3.79	3.46	3.06	3.45
7	2.75	2.19	2.23	2.19	3.97	3.43	3.25	4.23	2.66	3.92	3.58	3.17	3.57
8	2.85	2.27	2.31	2.27	4.10	3.55	3.36	4.37	2.75	4.06	3.71	3.28	3.70
9	2.94	2.35	2.39	2.35	4.24	3.67	3.48	4.52	2.84	4.19	3.83	3.39	3.82
10	3.04	2.43	2.47	2.43	4.39	3.79	3.59	4.67	2.94	4.34	3.96	3.50	3.95
11	3.14	2.51	2.55	2.51	4.53	3.92	3.71	4.83	3.04	4.48	4.10	3.62	4.08
12	3.25	2.59	2.63	2.59	4.68	4.04	3.83	4.99	3.14	4.63	4.23	3.74	4.22
13	3.35	2.67	2.72	2.67	4.83	4.18	3.96	5.15	3.24	4.77	4.37	3.86	4.35
14	3.46	2.76	2.80	2.76	4.98	4.31	4.08	5.31	3.34	4.93	4.50	3.98	4.49
15	3.56	2.84	2.89	2.84	5.14	4.44	4.21	5.48	3.44	5.08	4.65	4.11	4.63
16	3.68	2.93	2.98	2.93	5.30	4.58	4.34	5.65	3.55	5.24	4.79	4.23	4.77
17	3.79	3.02	3.07	3.02	5.46	4.72	4.47	5.82	3.66	5.40	4.94	4.36	4.92
18	3.90	3.11	3.16	3.11	5.63	4.86	4.61	6.00	3.77	5.56	5.08	4.49	5.07
19	4.02	3.20	3.26	3.20	5.79	5.01	4.74	6.17	3.88	5.72	5.23	4.63	5.22
20	4.13	3.30	3.35	3.30	5.96	5.15	4.88	6.35	3.99	5.89	5.39	4.76	5.37
21	4.25	3.39	3.45	3.39	6.13	5.30	5.02	6.54	4.11	6.06	5.54	4.90	5.53
22	4.37	3.49	3.55	3.49	6.31	5.45	5.17	6.72	4.23	6.24	5.70	5.04	5.68
23	4.50	3.59	3.65	3.59	6.49	5.61	5.31	6.91	4.35	6.41	5.86	5.18	5.84
24	4.62	3.69	3.75	3.69	6.67	5.76	5.46	7.11	4.47	6.59	6.02	5.32	6.01
25[a]	**4.75**	**3.79**	**3.85**	**3.79**	**6.85**	**5.92**	**5.61**	**7.30**	**4.59**	**6.77**	**6.19**	**5.47**	**6.17**
26	4.88	3.89	3.95	3.89	7.04	6.08	5.76	7.50	4.71	6.95	6.36	5.62	6.34
27	5.01	4.00	4.06	4.00	7.22	6.24	5.92	7.70	4.84	7.14	6.53	5.77	6.51
28	5.14	4.10	4.17	4.10	7.41	6.41	6.07	7.90	4.97	7.33	6.70	5.92	6.68
29	5.28	4.21	4.28	4.21	7.61	6.58	6.23	8.11	5.10	7.52	6.88	6.08	6.85
30	5.41	4.32	4.39	4.32	7.80	6.75	6.39	8.32	5.23	7.71	7.05	6.23	7.03
31	5.55	4.43	4.50	4.43	8.00	6.92	6.55	8.53	5.36	7.91	7.23	6.39	7.21
32	5.69	4.54	4.61	4.54	8.21	7.09	6.72	8.74	5.50	8.11	7.41	6.55	7.39
33	5.83	4.65	4.73	4.65	8.41	7.27	6.89	8.96	5.63	8.31	7.60	6.72	7.57
34	5.97	4.77	4.84	4.77	8.62	7.45	7.06	9.18	5.77	8.52	7.79	6.88	7.76
35	6.12	4.88	4.96	4.88	8.83	7.63	7.23	9.41	5.91	8.72	7.98	7.05	7.95

5.3 Results and discussion

5.3.1 Detection by grab and DGT sampling

The compound-specific method quantification limits (MQLs) of the grab sampling procedure were in the range 0.03–1.5 ng/L (with 1 L water samples), while those for DGT were in the range 3–23 ng/L, based on a 1-week deployment of standard devices of 3.14 cm^2 surface area (see Table 5.5). These were sufficient to detect most of the analytes at most of the locations. The MQLs for grab samples can be lowered (i.e. improved) by

taking bigger sample volumes, greater pre-concentration and injecting larger sample volumes on-column. The MQLs of the DGT procedure can be lowered by longer deployment times, bulking of individual samplers together, use of a sampler with a larger surface area, greater concentration of the sampler, and injection of a larger sample volume on-column. In other words, sampling campaigns can be designed and adapted with either approach, to optimize detection conditions.

Most of the target analytes were detected at least once in the grab samples, although SDX and BUP were lower than detection limits in all the retrieved grab samples. Table 5.7 shows the detection frequencies of target analytes in the main stream of the River Thames and tributaries. The detection frequencies of all the target ECs, pharmaceuticals, EDCs and OPEs were consistent, with the highest values in the three tributaries (Cherwell, Thame and the Cut), the lowest values in one tributary (Pang) and median values in the main stream of the River Thames and the other two tributaries (Ray and Ock).

Table 5.7. Detection frequencies of target analytes in the main stream of the River Thames and tributaries

Detection freq. of target analytes	Thames			Ch	Ra	Oc	Th	Pa	Cu
	TS	TW	WR						
All target ECs (%)	69	69	65	81	62	65	77	50	77
Pharmaceuticals (%)	56	56	56	75	50	50	69	38	63
EDCs (%)	50	50	0	50	0	50	50	0	100
OPEs (%)	100	100	100	100	100	100	100	88	100

Given the types of compounds and their primary uses, sources to the river are most likely to be linked to human-related effluents (i.e. to WWTPs). In the small streams (tributaries) where dilution effect is weak (e.g. mean flow < 4 m^3/s), the WWTPs population equivalent density appeared to be more relevant than the size of the catchment area. For example, the Cut with the smallest catchment (63 km^2) had high values of detection frequencies. However, the dilution effect seemed strong in the main stream of the River Thames where mean flow ≥15 m^3/s, as the value of detection frequency didn't increase from upstream to downstream with the increasing population density. This suggests that smaller streams may have generally higher concentrations of certain groups of chemicals, due to specific discharges and less dilution. Although they make up the majority of the river network length (e.g., an estimated 80% in Europe) only a small percentage of studies have been conducted in small streams (Spycher et al., 2018). Routine monitoring coverage should pay more attention to small water bodies. As expected, there was no

evidence to link sub-catchments with high agricultural activity (e.g., Ock) to higher occurrences of the test ECs.

A model developed and parameterized for the Thames catchment will be used later in the thesis to fully explore the link between measured concentrations, mass loadings in the river, and the potential role of discharges from WWTPs.

100% of target OPEs were detected across the studied sites (except Pang which was 88%) with high concentration levels (see later). This is the first report of OPEs in the River Thames catchment.

5.3.2 Grab and DGT sampling at the catchment scale

The DGT as an in situ sampling sampler, is sampling a period of time, from hours (Guo et al., 2019) to weeks (Challis et al., 2018) while grab sampling only gives a specific time of sampling. Figure 5.6 shows the water concentrations measured by the DGT (c_{DGT}, dark grey) and grab sampling (discrete water concentration, c_1 and c_2, grey and white) at each sampling site in the River Thames catchment. The two grab samples at each site were collected at different times of the day. For example, grab samples at Thame (Th) were collected at 16:35 on June 25 and 13:28 on June 28, 2019. Variations in levels of pharmaceuticals (SPD, TMP and PHBA) between c_1 and c_2 were generally quite low across the seven sampling sites (c_1/c_2 = 0.4–2.4). As effluents of WWTPs are considered the main source of pharmaceuticals in streams, the two comparable values of grab samples suggested that pharmaceuticals (SPD, TMP and PHBA) from the effluents varied little, resulting in little variations of the chemicals in the studied rivers. For the case of these pharmaceuticals (SPD, TMP and PHBA), the c_{DGT} was comparable with c_1 and c_2, with ratios of c_1 and c_2 to c_{DGT} ranging from ~0.5 to 2.3 (mean: 1.2). Thus, for chemicals which were relatively stable in the river, grab sampling and the DGT sampling provide good representativeness.

The OPEs (TEP, TCEP, TPrP and TCPP) showed a different picture. The c_1 and c_2 of OPEs varied more than for pharmaceuticals (c_1/c_2 = 0.2–7.9). For OPEs, greater variations between c_{DGT} and discrete water concentrations (c_1 and c_2) were also evident, with ratios of c_1 and c_2 to c_{DGT} ranging from <0.1 to 3.7 (mean: 0.8). This was most noticeable for all the OPEs at the sampling site on the Cut (Cu) and for TCPP at all seven sampling sites (see Figure 5.6). At the Cut, c_1 (c_2) of OPEs (TEP, TCEP, TPrP and TCPP)

were 0.04 (0.04), 0.2 (0.2), 0.1 (0.1) and 0.5 (0.1) of c_{DGT}. The c_{DGT} of TCPP at the seven sites was 100s to 1000s ng/L, while for discrete water concentrations only c_2 for the Thames at Wallingford (TW) (320 ng/L, 60% of c_{TWA}) and c_1 at the Cut (Cu) (1910 ng/L, 50% of c_{TWA}) were close to c_{DGT}. The differences between the two grab samples suggests that the inputs of OPEs were not as stable as the pharmaceuticals. It appeared that the input patterns of OPEs were different from pharmaceuticals. For chemicals which showed high dynamic variations in water bodies, the DGT with one-week sampling window integrates varying OPE levels while grab sampling cannot fully capture it.

It is interesting that OPEs should vary more than pharmaceuticals, since it might have been assumed that WWTPs are the main sources for both these classes of chemicals.

Overall, the DGT with a longer sampling window can integrate fluctuating pollutant concentrations and better represent the general water quality status, especially for those chemicals with fluctuating concentrations in highly dynamic water bodies.

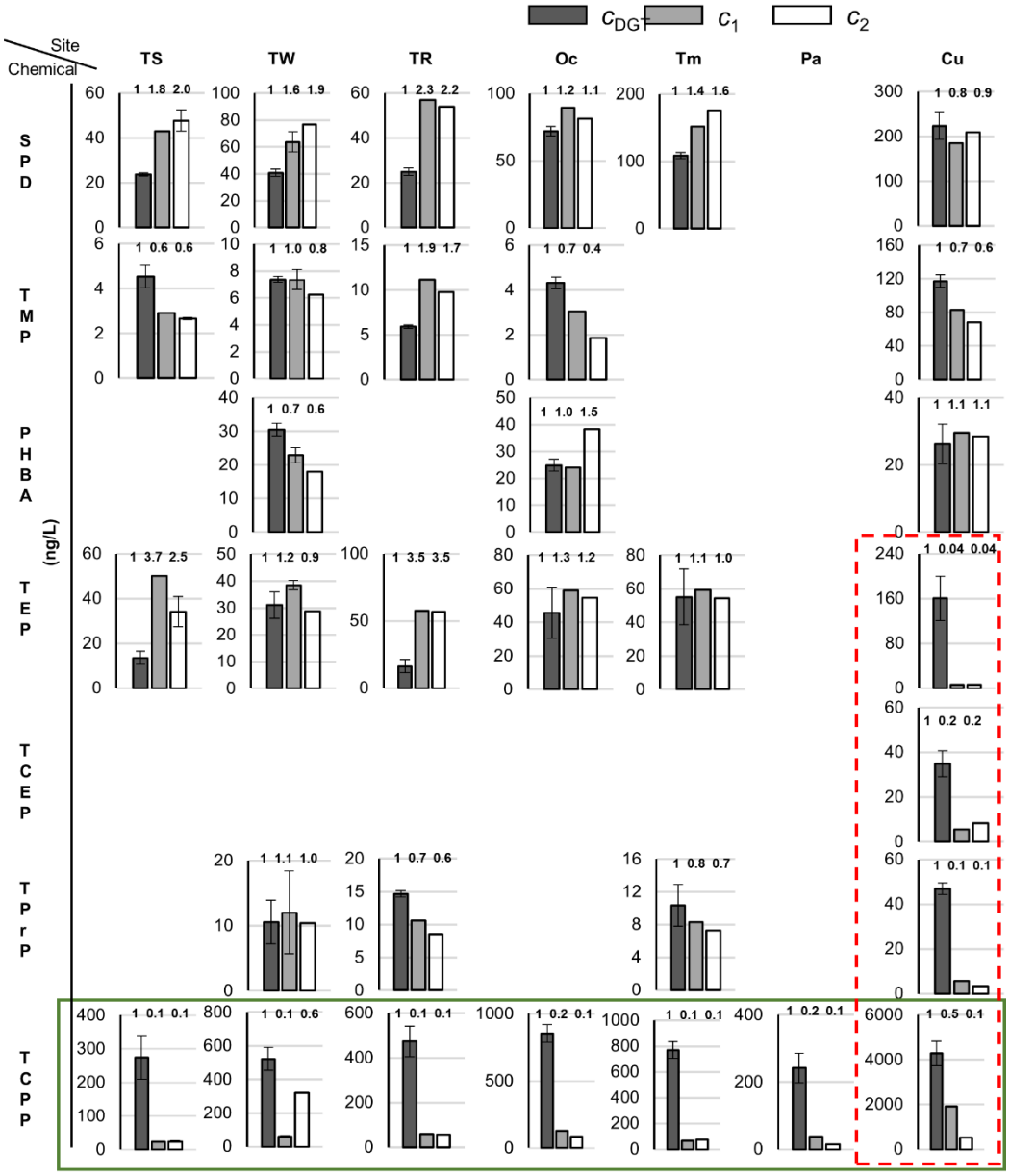

Figure 5.6. Concentrations in water measured by the DGT ($c_{DGT,}$ dark grey) and grab sampling (discrete water concentration, c_1 and c_2, grey and white) at the obtained sampling sites in the River Thames catchment. Numbers above the columns are ratios of c_1 and c_2 to c_{DGT}. DGT samplers were exposed for approximately one week and grab samples were collected at the beginning (c_1) and third day (c_2) of deploying the DGTs. When <MQL of DGT, it was regarded as not detectable and is not shown in the figure. Error bars of c_{DGT} are standard deviation of triplicate DGT measurements and error bars of c_1 at TW (Thames at Wallingford) and c_2 at TS (Thames at Swinford) are standard deviation of duplicate measurements.

5.3.3 Detection limits, sensitivity and other comparators of grab and DGT sampling

Diffusion coefficients (D) of the target analytes at 25 °C range from 3.79×10^{-6} (TMP) to 7.30×10^{-6} (PHBA) cm^2/s. According to eq (5.4), the corresponding sampling rate Rs at 25 °C can be derived through D, sampling area (A = 3.14 cm^2) and diffusion distance

($\Delta g + \delta = 0.91 + 0.2 = 1.11$ mm). DGT sampling rates for the target analytes at 25 °C are therefore 9.3 mL/d (TMP) to 17.8 mL/d (PHBA).

$$R_s = \frac{DA}{(\Delta g + \delta)} \tag{5.4}$$

Sensitivity of the DGT sampler does not only relate to the instrument detection limit but also to the deployment time. The DGT is able to provide greater sensitivity with longer deployment time and gave single-digit ng/L sensitivity for most compounds when deployed for 2–3 weeks (Challis et al., 2018). MQLs of the DGT (7-day deployment at 25 °C) were single-digit to double-digit ng/L (Table 5.5), which is at the same order of magnitude with this study (Challis et al., 2018).

Detection frequencies of the target analytes from the DGT samplers were comparable or slightly lower than these from grab samples for most compounds (Table 5.8) while for compounds—such as SMR, MEP, PRP, PHBA, E3, and TCEP—a longer deployment time will improve the detection frequency.

Table 5.8. Detection frequencies of the target analytes from grab samples and the DGT samplers

Year	Sample type	No. (Sampling site)	Detection rate (%)												
			SPD	SMR	SDX	TMP	MEP	PRP	BUP	PHBA	E3	TEP	TCEP	TPrP	TCPP
2018	Grab sample (June 25)	9	100	22	0	89	100	56	0	100	44	100	89	100	100
	Grab sample (June 28)	8	100	25	0	88	100	38	0	100	38	100	88	100	100
	DGT sample (June 25–July 02)	7	86	0	0	71	0	0	0	43	0	86	14	57	100
2019	DGT sample (Feb 11–Feb 18)	5	100	100	0	80	0	0	0	40	0	100	80	100	100

In situ passive samplers are affected by hydrodynamic conditions, membrane filter, biofouling and within-sampler degradation, while for grab sampling these are lesser concerns. At a solid surface in a flowing solution, there will be a layer close to the surface where there is effectively no flow. It is recognized as the DBL, where the mass transfer of solutes is restricted to molecular diffusion. The thickness of DBL (δ) decreases with increasing flow rate and stabilizes at approximate 0.2 mm when the flow rate is above 2 cm/s (Warnken et al., 2006). However, it should be realized that in many situations the flow near the sampler surface may vary in both time and space. That makes both predicting and measuring DBL challenging. As the diffusion distance (0.91 mm here) in

the DGT sampler is much larger than the DBL (0.2 mm), the sampling of the DGT is diffusive layer controlled. By applying δ=0.2 mm in the naturally flowing rivers in this study, the error caused by DBL is acceptable (Warnken et al., 2006). The outside membrane filter can cause a lag time before the target analyte reaching steady-state in the sampler if the membrane filter accumulates the analyte (Chapter 3). The target analytes covered here have been shown to have little interaction with the membrane filter and thus no further calibration is necessary. Eight-day old biofouling in the-worst-scenario (in influent and effluent of WWTPs) showed no interference with the DGT sampler performance (Chapter 4). The target analytes were also shown to have little degradation/loss at room temperature within one week (Chapter 4). The passive sampling system here therefore was shown to have good quality control.

An accessible and secure site to deploy the passive sampling system is fundamental to the DGT sampling. Otherwise, the samplers may be subject to damage or loss. In this study, no DGT samplers were recovered at two sampling sites in the summer campaign and four in the winter campaign, due to either sample loss, interference by the public or lack of accessibility to the sampling site (Table 5.4). It took 10 minutes per site to set up and collect the DGT passive sampling system and 5 minutes to collect grab samples. However, for later storage and sample pretreatment, the DGT method is much more space-effective and time-effective. The space for a 1 L glass bottle could contain at least 10 DGT samplers with bagging. It took two working days to pretreat 12 grab samples while it only needed one day to pretreat 40 DGT samplers.

DGT allows repeated measurements without greatly increasing the overall cost and laboratory workload. Triplicate DGT samplers were deployed at each of the sampling sites and showed good repeatability across the obtained analytes, with coefficients of variation (CV, or relative standard deviation) ranging from 1% to 33% (mean: 10%).

5.3.4 Profile of chemicals detected in the Thames

Parabens (MEP, PRP and BUP) are widely used in cosmetics and personal care products, such as creams, lotions, shampoos and bath products. Their common metabolite (PHBA) is used as a preservative in food, pharmaceuticals, and personal care products. These substances mimic estrogen and can act as potential hormone (endocrine) system disruptors. They belong to category 1 (at least one in vivo study providing clear evidence for endocrine disruption in an intact organism) of the European Endocrine Disrupter

Priority List for wildlife and human health. These substances should not be found from drinking water.

Three parabens (MEP, PRP and BUP) were not detected by the DGT sampler, due to their 7-day average concentration being lower than their MQLs (12, 11 and 4 ng/L). MEP and PRP were detected in 100% and 38% of grab samples, respectively, while BUP was not detected in grab samples. The highest MEP concentrations were found in the Cut (31 ng/L), with other sampling sites in the range 2–12 ng/L. Three high points of PRP were found in the Cherwell (148 ng/L), the Thames at Swinford (77 ng/L) and the Cut (70 ng/L), with other sampling sites lower than 32 ng/L. Their metabolite (PHBA) was detected at all the sampling sites, in the range14–46 ng/L (mean: 26 ng/L). These substances are ubiquitous in the Thames river system, which is the main source of drinking water for a large population living in and around London.

OPEs are on list of High Production Volume Chemicals (HPVC) (>1000 tons/year in Europe); they are used as flame retardants and plasticizers in plastics, textiles, furniture and many other materials (Wang et al., 2015). However, they tend to be released from their host materials (Reemtsma et al., 2008). They have now been found to be ubiquitous in water, especially wastewater, and air, particularly associated with airborne particulate matter. Four OPEs (0.016–26 μg/L) were found in the River Aire (U.K.), with TCPP ranged from 2900–6700 ng/L (Cristale et al., 2013). However, before this study, no data are available for OPEs in the Thames catchment. TEP (13–160 ng/L in summer, 18–46 ng/L in winter) and TCPP (242–4282 ng/L in summer, 215–854 ng/L in winter) were the main OPEs, according to the 7-day time-weighted average concentrations obtained by the DGT. The comparison between data generated by grab sampling and the DGT sampling indicated that the input patterns of OPEs were different from pharmaceuticals. High concentrations of OPEs (only c_{DGT}, Figure 5.6) were found at the Cut, which receives the highest WWTPs effluent loadings, indicating effluents from WWTPs are important source of OPEs. The generally high c_{DGT} of TCPP found across the sampling sites in both summer and winter imply higher levels occurred in the time period not covered by grab sampling. The photodegradation or phototransformation of most OPEs (except TCEP, which is recalcitrant) occurs mainly by indirect mechanisms and the presence of inorganic constituents (nitrite, nitrate, carbonate and some iron species) in river water increases the photodegradation rates (Cristale et al., 2017). One possible

explanation of the lower levels of OPEs measured by grab sampling could be the active indirect photodegradation pathways of OPEs in the day, especially for TCPP.

There were 5 analytes (SDX, MEP, PRP, BUP and E3) not detected by the 7-day DGT sampling, due to their low concentrations. The other 8 ECs were detected at least once at all the sampling sites. Figure 5.7 shows the composition and mean concentration of TCPP and the mean sum concentration of ECs from the obtained sampling sites in the Thames catchment. The mean sum of 8 ECs concentrations ranged from 242 ng/L (Pang) to 4890 ng/L (the Cut) in summer and from 372 ng/L (Pang) to 1001 ng/L (Thames at Swinford) in winter, indicating large variability between the sampling sites. Tributaries (242–4890 ng/L in summer) showed larger variability than the main stream (316–643 ng/L in summer, 482–1001 ng/L in winter), showing that tributaries were affected more by local discharges, while the main stream had greater dilution and 'smoothed' concentrations. Within the five sampling sites where both summer and winter data obtained, two sites (Thames at Wallingford, Ock) summer ECs were higher than winter ECs (by factors of 1.3 and 2.0) and for the other three sites (Thames at Swinford and Runnymede, Pang) winter ECs were higher than summer ECs (by a factor of 1.5). River flow peaks happened in the winter sampling period (Feb 11–Feb 18, 2019) with flow increased to approximately 5-fold of the flow in the summer sampling period (June 25–July 02, 2018) in the main River Thames (Figure 5.2). Strong seasonal differences were not evident, probably because the inputs of ECs can also change (e.g. more discharges from WWTPs in flood) (Castro-Jimenez et al., 2014, Salamova et al., 2014). However, the composition of ECs was more diverse in winter than in summer, with TCPP dominant in summer (81%–100%) and lower in winter (45%–85%).

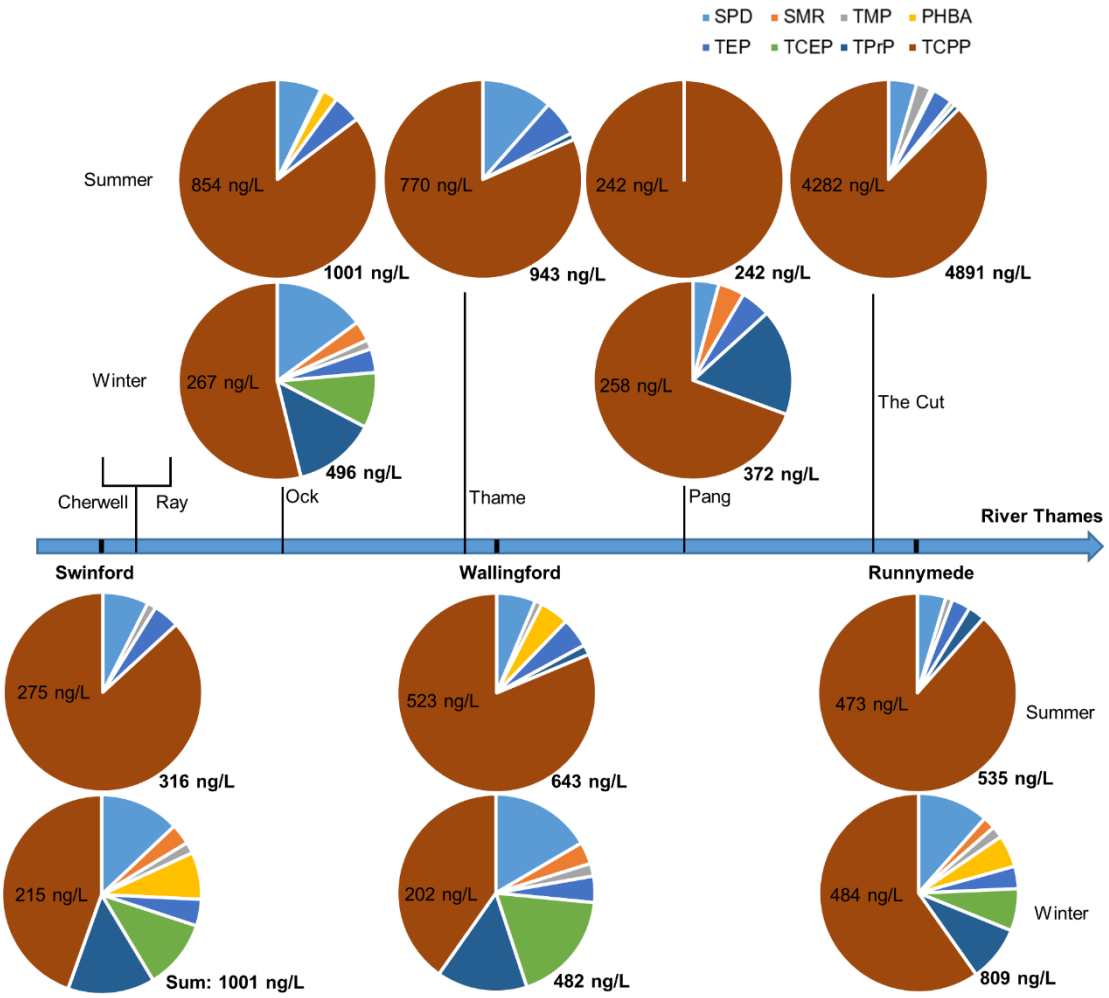

Figure 5.7. Composition, mean concentration of the main constituent TCPP (on the pie) and mean sum concentration of ECs (on the right corner) by the DGT sampling from the obtained sampling sites in the Thames catchment.

5.3.5 Preliminary risk assessment for aquatic organisms

Following the EU's technical guidance document on risk assessment (European Comission, 2003), standardized chemical risk assessments are carried out by comparing environmental concentrations with the associated environmental quality standards (EQS). If the environmental concentration exceeds the EQS, a risk for aquatic organisms can be assumed (European Comission, 2003). A comparison of the environmental concentration and the acute quality standard (AQS) may be helpful for assessing the likelihood of possible damage to the organisms within the next 24 to 96 hours (European Comission, 2003). Chronic quality standards (CQS) are recommended for water quality monitoring and they are used for assessing pollution over an extended time-period (European Comission, 2003). For the continuous input of micro-pollutants from treated effluents, the chronic quality standard is particularly relevant and helps to protect the organisms against the consequences of long-term pollution (European Comission, 2003). However,

in practice, especially for the unregulated ECs, very limited EQS is available. The only available EQS of the target ECs is for TMP from Switzerland. Thus, a predicted no effect concentration (PNEC) was derived by dividing the lowest short-term L(E)C50 value or no observed effect concentration (NOEC) value by an assessment factor (AF) (European Comission, 2003). Since the toxicity data are also very limited for the target ECs (Table 5.9), most ECs do not yet have toxicity data for all three trophic levels (algae, invertebrate, fish). As a result, the highest AF = 1000 was used for all the ECs. In this study, the grab water samples were filtered and only the totally dissolved phase was sampled by the DGT and therefore the concentrations measured in this study were considered fully bioavailable to aquatic organisms. The highest water concentrations of target ECs at the sampling site measured by grab sampling and the DGT sampling was used as the measured environmental concentration (MEC). The risk quotient was calculated by eq (5.5):

$$RQ = \frac{MEC}{PNEC} \tag{5.5}$$

RQs were <1 for most target EC and the exposure point concentrations were less than the risk screening benchmarks, indicating no significant risk. RQs of TCPP were ≥1 at 5 out of 7 sampling sites where c_{DGT} were available and the highest RQ = 7 at the Cut, indicating a small potential risk of TCPP across the Thames catchment.

This risk assessment is highly restricted by the lack of toxicity data of the target ECs. It is recommended that the availability of short-term toxicity data for fish, daphnia and algae is a minimum for calculating PNEC (European Comission, 2003), while this is only the case for two ECs (TCEP and TCPP) here. For target ECs that are believed to have continuous inputs from effluents of WWTPs, a long-term risk assessment is necessary. Lower assessment factors (AF) can also be used when increasing the confidence with which a PNEC can be derived from the available toxicity data. Adverse effects of the breakdown products should also be taken into account. For substances with a log K_{ow} >3, such as BUP (log K_{ow} = 3.5) here, they are expected to have a bioaccumulation effect. These require a long-term risk assessment to be carried out, even if they show no toxicity in the short-term. The endocrine disrupting effects of E3 should be taken into account. However, existing knowledge does not allow a more standardized approach for risk assessment of such substances at present (European Comission, 2003).

Table 5.9. PNEC determination and estimated RQs for the target ECs

Compound (Abbr.)	Taxonomic group	Species	Exposure time and criterion	L(E)C50 mg/L	Reference	PNEC (ng/L)	MEC_{max} (ng/L)	RQ
Sulfapyridine (SPD)	Fish		LC_{50}	246	ECOSAR[a]			
	Daphnia	*Daphnia magna*	EC_{50}	6.2	ECOSAR[a]			
	Algae	*Scenedesmus vacuolatus*	24-h EC_{50} (growth-inhibition)	5.3	(Białk-Bielińska et al., 2011)	5.0E+02	223	<1
	Plant	*Lemna minor (duckweed)*	24-h EC_{50} (growth-inhibition)	0.5	(Białk-Bielińska et al., 2011)			
Sulfamerazine (SMR)	Fish		LC_{50}	101	https://cfpub.epa.gov/ecotox/			
	Daphnia	*Hyalella azteca*	4-week EC_{50} (mortality)	1.03	(Bartlett et al., 2013)	1.0E+03	18	<1
	Daphnia	*Daphnia magna*	48-h EC_{50} (immobility)	277	(De Liguoro et al., 2009)			
	Algae		EC_{50}	11.90	https://cfpub.epa.gov/ecotox/			
Trimethoprim (TMP)				Chronic quality standard of Switzerland adopted		1.2E+05	117	<1
Methylparaben (MEP)	Fish	*Pimephales promelas*	48-h LC_{50} (mortality)	160	(Dobbins et al., 2009)	5.7E+03	31	<1
	Fish	*Oreochromis niloticus*	EC_{50}	67.11	(Silva et al., 2018)			
	Daphnia	*Daphnia magna*	48-h LC_{50} (mortality)	24.6	(Dobbins et al., 2009)			
	Daphnia	*Daphnia magna*	48-h EC_{50} (immobility)	41.08	(Kamaya et al., 2005)			
	Daphnia	*Daphnia magna*	EC_{50} (immobility)	5.7	(Lee et al., 2017)			
	Algae	*Pseudopediastrum boryanum*	Chlorophyll	81.18	(Puerta et al., 2020)			
Propylparaben (PRP)	Fish	*Pimephales promelas*	48-h LC_{50} (mortality)	9.7	(Dobbins et al., 2009)	160	148	<1
	Zebrafish	*Danio rerio*	NOEC	1	(Torres et al., 2016)			
	Sea Urchin	*Paracentrotus lividus*	NOEC	0.16	(Torres et al., 2016)			
	Daphnia	*Daphnia magna*	48-h LC_{50} (mortality)	12.3	(Dobbins et al., 2009)			
Butylparaben (BUP)	Fish	*Pimephales promelas*	48-h LC_{50} (mortality)	4.2	(Dobbins et al., 2009)	4.2E+03	<MQL	
	Daphnia	*Daphnia magna*	48-h LC_{50} (mortality)	5.3	(Dobbins et al., 2009)			
4-Hydroxybenzoic acid (PHBA)	Daphnia	*Daphnia magna*	48-h EC_{50} (immobility)	1690	(Kamaya et al., 2005)	1.7E+06	46	<1
Estriol (E3)				The PNEC estimated in literature is adopted (Caldwell et al., 2012)		6.0E+01	5	<1
Triethyl phosphate (TEP)	Daphnia	*Daphnia magna*	96-h LC_{50} (mortality)	350	(Lai et al., 2019)	3.5E+05	160	<1
Tris(2-chloroethyl) phosphate (TCEP)	Fish	*na*	96-h LC_{50} (mortality)	6.3	(Lai et al., 2019)	2.0E+02	92	<1
	Daphnia	*Daphnia magna*	24-h EC_{50} (immobility)	7.1	(Lai et al., 2019)			
	Algae	*Scenedesmus subspicatus*	72-h EC_{10} (biomass)	0.2	(Lai et al., 2019)			
Tris(chloropropyl) phosphate (TCPP)	Fish	*Lepomis macrochirus*	96-h NOEC (mortality)	6.3	(Lai et al., 2019)	6.0E+02	4282	7
	Daphnia	*Daphnia magna*	48-h NOEC (mobility)	33.5	(Lai et al., 2019)			
	Algae	*Pseudokirchneriella subcapitata*	96-h NOEC (growth)	6	(Lai et al., 2019)			

a: ECOSAR: toxicity data was determined using the US EPA Ecological Structure Activity Relationships model (ECOSAR v2.0). NOEC stands for No Observed Effect Concentration.

5.4 Conclusion and implications

A monitoring survey was designed and conducted for ECs in the River Thames catchment (U.K.) using DGT, a well-characterized passive sampler, and traditional grab sampling. Results showed that routine monitoring should pay more attention to small water bodies, because smaller streams appeared to have higher concentrations of the target analytes than main streams, because they are closer to point/discharge source and have less dilution. The ubiquitous presence of endocrine disrupting chemicals, parabens (MEP, PRP, BUP) and their metabolite (PHBA), in the Thames river system (the main source of drinking water in this area), is of concern. This study is also the first to report OPEs in the Thames catchment. TEP (13–160 ng/L in summer, 18–46 ng/L in winter) and TCPP (242–4282 ng/L in summer, 215–854 ng/L in winter) were the main OPEs, according to the 7-day time-weighted average concentrations obtained with the DGT sampler. TCPP was determined a small potential risk across the Thames catchment, especially at the Cut, which receives the highest loadings of WWTPs effluent. A comparison of 7-day time-weighted average concentration measured by the DGT and discrete concentrations by grab sampling showed the treated effluents input of pharmaceuticals (SPD, TMP and PHBA) was relatively stable while input of OPEs was more dynamic and with different input patterns and/or fate processes. For chemicals, which were relatively stable in the rivers, grab sampling and the DGT, sampling provides equally good representativeness. For chemicals, which show high dynamic variation in water bodies, the DGT provides a better integral of loadings and exposure than grab sampling. However, 1 L grab samples provided greater sensitivity than the one-week DGT sampling method with the field and lab procedures used in this study. For chemicals where greater sensitivity (sub- or low-single digit ng/L) is needed, options include: longer sampler deployment; combination of multiple samplers; use of a sampler with a higher surface area; greater sampler concentration or injection volumes.

The in situ DGT passive sampling system could be affected by hydrodynamic conditions, biofouling of the membrane filter, and within-sampler degradation/loss. Good quality control is therefore required. An accessible and secure site to deploy the passive sampling system is fundamental to the DGT sampling. The DGT allows repeated measurements without greatly increasing the overall cost and laboratory workload. It took relatively the

same time to set up and collect the DGT passive sampling system and to collect grab samples. However, for later storage and sample pre-treatment, the DGT method is much more space-, cost- and time-effective. The DGT is proved a powerful tool to characterize fate processes of ECs throughout a large dynamic watershed.

Chapter 6: A combination of diffusive gradients in thin film (DGT) sampling and water quality modelling to study sources and environmental fate of emerging contaminants: a case study with trimethoprim

6.1 Introduction

6.1.1 Presence of antibiotics in surface waters and associated issues

Emerging contaminants (ECs), or chemicals of emerging concerns, include pharmaceuticals (antibiotics, stimulants, analgesics, antihistamines and hormones), chemicals from household and personal care products, flame retardants and others (Petrie et al., 2015). Their widespread use and ubiquitous presence in surface waters has raised concern over the last 10–20 years (Petrie et al., 2015). Major sources of ECs to surface waters are generally considered to be effluents from small- and large-scale wastewater treatment plants (WWTPs) from municipal and industrial sources, as well as hospitals (Santos et al., 2013). Many ECs are not completely removed by wastewater treatment processes (Coutu et al., 2013). Other sources could include landfill leachates, surface runoff, atmospheric deposition, and application of biosolids and manure to agricultural land (Rasheed et al., 2019). Antibiotics, a particular class of ECs, are being increasingly examined for their presence in surface waters and WWTPs, due to concerns over the potential selection and dissemination of antimicrobial resistance at environmentally relevant concentrations (ng/L to μg/L) of such compounds (Gullberg et al., 2011). The selection pressure from antibiotics in the environment may accelerate the evolution of antibiotic-resistant pathogens (Bengtsson-Palme and Larsson, 2016). Ecotoxicological effects have also been reported with aquatic microorganisms, especially cyanobacteria and ammonium oxidizing bacteria to antibiotics (Valitalo et al., 2017). Because of the concerns outlined above, a number of antibiotics (erythromycin, clarithromycin, azithromycin, amoxicillin and ciprofloxacin) have been added to the European Water Framework Directive watch list (European Commission, 2018). The watch list requires member states to gather monitoring data to assess risks to the environment (Comber et al., 2018). More antibiotics have been noted to be of high concern because of their high consumption, frequent occurrence in surface waters and adverse environmental effects at environmentally relevant concentrations (e.g., trimethoprim) (Boxall et al., 2002). There is now growing concern about trimethoprim resistance, which has led the UK's National

Health Service (NHS) to reduce the use of trimethoprim prescribed from April 2017 (Croker et al., 2018).

6.1.2 Determination of antibiotic residues in surface water compartments

It is challenging to produce adequate measured environmental concentrations (MECs) of antibiotics in surface waters to fully represent seasonal variation, spatiotemporal differences and hydrological conditions (Coutu et al., 2013, Thomas et al., 2012, Burns et al., 2017). This is often due to commonly used grab sampling methods only representing a snapshot of the pollutants at the time of sampling and episodic pollution events can be missed. Moreover, the field campaign and subsequent laboratory analysis can be costly and laborious for a large catchment. The use of modelling to derive predicted environmental concentrations (PECs) has therefore been suggested as a possible alternative approach, or—ideally—an approach to be used in combination with measurement campaigns and estimates of sources/discharges. Generally, therefore, the model(s) used should incorporate information on human consumption and excretion rates in the patient (to help derive a per capita estimate of discharges to untreated waters), removal in the wastewater system (following treatment of the effluents) and in surface waters (i.e. with dilution and losses via reactions/removal to sediments etc.) (Boxall et al., 2014).

A range of in-stream water quality models have been developed to characterize the fate of point-source "down-the-drain" contaminants (including some antibiotics) in a specific river catchment. For example: Geo-referenced Regional environmental Exposure Assessment Tool for European Rivers (GREAT-ER) (Feijtel et al., 1997), Pharmaceutical Assessment and Transport Evaluation Model (PhATE) (Anderson et al., 2004) and Low Flows 2000-Water Quality eXtension (LF2000-WQX) model (Keller and Young, 2004). These models often incorporate treatment plant specific wastewater flows and/or catchment specific river flows, in order to provide more refined PEC estimates. Such estimates account for spatiotemporal differences in contaminant concentrations and are often output as annual mean PECs across river stretches (Johnson et al., 2008).

6.1.3 Study aims

Model input data are often highly variable and difficult to obtain, so model estimates often do not agree with measurements made in the field. In practice, there should therefore be an iterative process, with measurement, modelling and source estimates, to

refine and improve understanding. DGT, as an in situ monitoring tool, can provide weekly average concentrations with good representation of seasonal variation, spatiotemporal differences and hydrological conditions. The objective of this study was to use DGT measurements in combination with the LF2000-WQX model for one reasonably well characterized and understood antibiotic (trimethoprim as model compound) in the River Thames catchment. The study focused on human antibiotic emissions to the environment, given that this is believed to be the dominant route (Straub, 2013). Further discussion of why the study area and antibiotic were selected is given in section 6.2.2. The specific aims of the study were to: (i) estimate per capita emission (PCE) of trimethoprim from prescription data, excretion rates and England population data and analyse its uncertainty, (ii) estimate removal rates in the wastewater system and in surface waters from the literature and analyse their uncertainties, (iii) compare the DGT MECs of trimethoprim (from Chapter 5) with PECs to evaluate the accuracy of the model estimates and to provide a better understanding of the environmental fate and behaviour of trimethoprim, (vi) compare PECs of trimethoprim with previously published data to evaluate if the NHS reduction actions of trimethoprim prescription has resulted in decreases of the surface water concentrations, and (v) compare PECs against environmental risk thresholds for ecotoxicity and antimicrobial resistance of trimethoprim.

6.2 Materials and methods

6.2.1 LF2000-WQX model description

Low Flows 2000-Water Quality modelling eXtension (LF2000-WQX) (Keller and Young, 2004) is a combination of the Low Flows 2000 (LF2000) software system (Young et al., 2003) and a range of catchment scale water quality models. It has been developed to predict environmental concentrations of point-source “down-the-drain” chemicals in river stretches downstream of major WWTPs in the U.K. (Rowney et al., 2009, Johnson et al., 2007). LF2000 is a Geographical Information System (GIS) based software, including a series of regionalised hydrological models (Holmes et al., 2002a, Holmes et al., 2002b), designed to characterise river flows (derived from flow duration curves) at gauged and ungauged sites for any UK river reach mapped at a 1:50,000 scale (Johnson et al., 2007).

The water quality modelling extension is essentially based on the GREAT-ER model (Geography-Referenced Regional Exposure Assessment for European Rivers) (Feijtel et al., 1997). The GREAT-ER model is a deterministic approach coupled with stochastic techniques (Monte Carlo simulation) which calculates distributions of PECs at a river reach level for conservative and degradable chemicals (Johnson et al., 2007). The GREAT-ER model has been applied to a number of rivers across Europe and has been shown to give reasonable evidence of measured concentrations of "down-the-drain" chemicals such as pharmaceuticals (Schowanek and Webb, 2002) and chemicals from personal care products (Wind et al., 2004, Price et al., 2010a).

Generally, estimates of per capita loads from the population served by the WWTP are combined with estimates of chemical removal efficiencies in WWTPs to give effluent loads to the river (Rowney et al., 2009). This information combined with the population served and the dry weather flow from each WWTP allows calculation of the concentrations in the WWTP effluents (Rowney et al., 2009, Price et al., 2010b). Within the model, a distinction is made between Primary Removal, Secondary Biological (SB) Removal, Secondary Activated Sludge (SAS) Removal and Tertiary Removal on a WWTP specific basis (Williams et al., 2009). Modelled pollutants (from upstream reaches and WWTP inputs via effluent discharges) are 'immediately mixed' through combination with river reach specific flow data via mass balance equations which determine gains and dilution via flow (Price et al., 2010b). In-river removal is then applied via a non-process specific first order removal rate, which integrates all removal processes including biodegradation, photolysis, sorption and volatilization (Price et al., 2010b). Inputs can be applied as a statistical distribution through a Monte Carlo simulation at all stages from chemical emission, wastewater removal and in-river removal. Starting at the head of a river/lower order streams, flows are modelled sequentially and combined with estimated point-source "down-the-drain" chemical emissions via WWTP discharges along the modelled river stretch to predict statistical distributions of environmental concentrations (Kugathas et al., 2012). The predictions are made across a series of pre-defined river reaches to the outlet of the river basin or to a pre-defined downstream node (Lambert et al., 2013). Model outputs include mean predicted environmental concentrations (PECmean), 90th percentile predicted environmental concentration (PEC90) and 95th percentile predicted environmental concentrations (PEC95) in river concentrations for each river reach (Price et al., 2010a). The model has

been applied to assess the concentrations of a range of point-source contaminants to U.K. surface waters including pharmaceuticals (Johnson et al., 2007, Boxall et al., 2014), cytotoxic drugs (Rowney et al., 2009), glucocorticoids (Kugathas et al., 2012), microscopic polymer particles (Lambert et al., 2013), steroid estrogens (Williams et al., 2009) and triclosan (Price et al., 2010a).

The model requires some basic datasets, including data describing all WWTPs within each region (the location, the type of primary and secondary treatment, the dry weather flow (DWF) from the plants, and the population served by the plant) and data describing the reaches within a river network within the catchment. These data are taken from elsewhere (Williams et al., 2009).

6.2.2 Study area and antibiotic selections

The River Thames catchment was selected as the study area because: (i) it is one of the U.K.'s most monitored and studied rivers and therefore it offers a unique study area with high-quality data support - such as river flow, catchment area, land cover, wastewater treatment systems, and population density, (ii) it is also actively influenced by anthropogenic activities, with 352 WWTPs discharging into it (Williams et al., 2009), (iii) it has a wide variety of sub-catchments, from the predominantly rural River Pang (with WWTPs population equivalent densities of <30 km^2 and <5% urban and semi-urban land cover) to rivers that are predominantly urban and receiving high WWTPs effluent loadings, such as the Cut (with WWTPs PE density of over 1500 PE/km^2, which is five-fold of the average WWTPs PE density in the study area) and (iv) the LF2000-WQX model has been well established in this catchment (Price et al., 2010a). A map of the Thames catchment is shown in Chapter 5.

Trimethoprim was selected as the model compound. It is on the EC list in Chapter 5 and showed relatively high concentrations in the catchment. An initial literature search for model inputs, including human consumption and excretion rates, WWTP removal rates and in-river removal rates was carried out. It was clear that for some of the candidate ECs there is a lack of such data, especially for the human consumption and removal rates.

6.2.3 Per capita emission

Urinary tract infection (UTI), a common type of human bacterial infection (Nicolle, 2002), is a frequent presentation in primary care, accounting for 1–3% of all GP

consultations in the United Kingdom (Croker et al., 2018). Until recently, trimethoprim was the most commonly prescribed antibiotic used for empirical treatment of uncomplicated UTI (Croker et al., 2018). National consumption of trimethoprim in England for the year 2018 (201803–201902) was calculated using NHS prescription data. This includes prescription data at the practice level (NHS Digital) and hospital level (NHS Business Services Authority). The prescription database is a list of all medicines, dressings and appliances that are prescribed by all practices/hospitals in England each month. Five types of trimethoprim have been prescribed (tablets 100 mg, tablets 200 mg, oral suspension 50 mg/5 mL, liquid special 20 mg/5 mL and liquid special 200 mg/5 mL). Thus, the total mass of each type was calculated by multiplying the standard quantity unit by the total quantity. The total annual quantity of trimethoprim was the sum of each type prescribed in each month. The population of England was estimated to be 55,977,178 in mid-2018 (Office for National Statistics). The excretion rate of trimethoprim was derived from a review of the literature (Dollery, 1991, Huschek et al., 2004, Straub, 2013, Carballa et al., 2008, ter Laak et al., 2010). An estimated PCE rate (μg capita^{-1} day^{-1}) of trimethoprim was therefore determined by multiplying the annual total amount of drug prescribed by its excretion rate (*Exc*) and subsequently dividing by the total England population (*P*) and the number of days in a year (eq 1) (Price et al., 2010a).

$$PCE = \frac{Total\ annual\ of\ antibiotic\ prescribed \times Exc}{365 \times P} \quad (6.1)$$

It is important to note that this approach assumes that losses between prescription and consumption (through not finishing course/disposal of antibiotics within refuse) of trimethoprim are zero. Similarly, no direct inputs to the WWTP system through direct disposal of antibiotic down drains (thereby foregoing metabolism and excretion) was also assumed.

6.2.4 Wastewater treatment plant removal rates

WWTPs in England have been classified into seven types: Primary only, secondary treatment by biological filter or activated sludge, and secondary biological filter or activated sludge types with two different sorts of additional tertiary treatment (Williams et al., 2009). A total of 347 WWTPs, serving a total population of 6,060,000, discharge within the Thames catchment (Williams et al., 2009). Of these, 136 large WWTPs serving 90% of the population and constituted 95% of the total discharged DWF to the River Thames network were selected. They were: secondary biological filter (30); secondary

activated sludge (24); tertiary activated sludge of type 1 (4); tertiary activated sludge of type 2 (28); tertiary biological filter of type 1 (22); tertiary biological filter of type 2 (28) (Williams et al., 2009).

Briefly, primary treatment involves the physical removal of the suspended and heavy solid content of wastewater (oils, sand, grit and particulate settleable solids) by mechanical methods (sedimentation and filtration) (Michael et al., 2013). In most UK WWTPs, this is often followed by a secondary treatment involving a biological filter process (biofiltration through a granular media containing a fixed film process) or a secondary activated sludge process (suspended-growth biological in oxygenated sludge tanks) (Gardner et al., 2013). In general, antibiotic removal from wastewater predominantly occurs through physical sorption to the solid phase and also through biodegradation (Michael et al., 2013). Chemical degradation via hydrolysis and/or photolysis also takes place to a lesser extent (Michael et al., 2013). Hydrophobic antibiotics appear to partition to sludge most effectively. However, some antibiotics are sufficiently hydrophilic in nature (log K_{ow} < 3) for sorption to be discounted as a significant removal process (Gardner et al., 2013).

Trimethoprim is an organic base with no hydrolysable bonds (Figure 6.1). Hydrolysis in fresh water is not significant for trimethoprim. With a reasonably high water solubility of 400 mg/L at 25 °C and a log K_{ow} between 0.6 and 1.1 (Table 6.1), trimethoprim is expected to remain predominantly in the aqueous phase and thus sorption is not significant. Vapour pressure is low at 1.3×10^{-6} Pa, hence the Henry's Law Constant is low and the substance is not expected to volatilize from water. With a base pK_a around neutral pH (6.6–7.6) (Table 6.1), trimethoprim is at least partly dissociated in most environmental waters and it will be more hydrophilic and will volatilize even less. Moreover, antibiotics are also designed to be resistant to biodegradation, as is demonstrated by the recalcitrant nature of trimethoprim within AS batch reactors (Le-Minh et al., 2010).

Trimethoprim removal rates by WWTPs were collated from literature sources taken from studies conducted across the globe (Schaar et al., 2010, Roberts and Thomas, 2006, Golovko et al., 2014, Gracia-Lor et al., 2012, Guerra et al., 2014, Segura et al., 2007, Watkinson et al., 2007, Karthikeyan and Meyer, 2006, Miège et al., 2009, Göbel et al., 2004, Göbel et al., 2007, Wahlberg et al., 2011, Bendz et al., 2005, Lindberg et al., 2005,

Straub, 2013, Batt et al., 2006, Ternes et al., 2007, Verlicchi et al., 2014, Senta et al., 2013, Nakada et al., 2017).

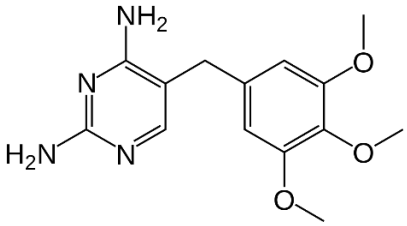

Figure 6.1. Structure of trimethoprim.

Table 6.1. Properties of trimethoprim

Property	Method	Value	Reference
CAS number		738-70-5	
Molecular mass (g/mol)		290.3	ChemSpider
Boiling point (°C, at 760 mmHg)		405.2 ± 55.0	ChemSpider
Melting point (°C)	experimental	199–203	ChemSpider
Water solubility (mg/L, 25 °C)	experimental	400	ChemSpider
Octanol/water partition coefficient (log K_{ow})	experimental	0.6–1.1	(Straub, 2013)
Vapour pressure (Pa)	experimental	1.3E-06	Gros et al. 2006
Dissociation constant (pK_a)	experimental	6.6–7.6	(Straub, 2013)
Henry's law constant (atm m^3/mol)	estimated	2.4E-14	National Library of Medicine HSDB Database

6.2.5 In-river removal rates

In-river or in-stream removal rates for individual removal processes (e.g., adsorption, photolysis, hydrolysis, biodegradation and volatilization) were discounted as the model requires an overall degradation rate (K) which encompasses all removal processes (Williams et al., 2009). The model required K needs to be independent of flow or dilution. However, the K values measured in situ can be a combination of hydrological and geomorphologic properties of the river system under study (Osorio et al., 2012). Where removal rates were expressed as degradation half-lives ($t_{1/2}$), they were converted to a first order degradation constant (K, day^{-1}) using eq (6.2) (Li et al., 2018). Trimethoprim in-river removal rates were collated from the literature sources taken from studies conducted in the field and from laboratory measurements (Luo et al., 2011, Acuña et al., 2015, Lam et al., 2004).

$$K = \frac{Ln2}{t_{1/2}} \tag{6.2}$$

6.2.6 Comparison of PECs versus MECs

PECs and MECs were compared at the six sampling sites in summer and five sampling sites in winter in the River Thames catchment. Detailed information about MECs is contained in Chapter 5. Briefly, three sampling sites were on the main stream of the River Thames—upstream (Swinford, TS), midstream (Wallingford, TW), downstream (Runnymede, TR)—and the others selected were on three tributaries—Ock (Oc), Pang (Pa) and the Cut (Cu) (see Figure 6.3). DGT samplers were not obtained (lost) at the Cut site in winter. Comparisons between PECs and MECs were also made at the catchment scale to provide indicative information on the dominant process responsible for the removal of trimethoprim in the River Thames (e.g., degradation or dilution).

6.2.7 Risk assessment

A risk assessment of trimethoprim for aquatic organisms was carried out in Chapter 5, which indicated no significant risk when a chronic water quality standard by the Swiss Water Protection Ordinance was used. Here a risk assessment for antimicrobial resistance was carried out. The Swiss Water Protection Ordinance has suggested a chronic water quality standard for trimethoprim of 120 μg/L, which is far higher than the MECs in Chapter 5. However, it doesn't account for antimicrobial resistance and neither does the current regulatory systems on antibiotic pollution (Ashbolt et al., 2013). This is because the role of antibiotic pollution in the natural environment in the selection of antimicrobial resistance is still unclear (Boxall et al., 2012). If the environmental occurrence of antibiotic residues is demonstrated to be an important driver for resistance selection, it may be necessary to develop approaches to consider antimicrobial resistance in the natural environment as an end point in the risk assessment of antibiotic substances (Boxall et al., 2012). Limits for environmental regulation considering antimicrobial resistance have been proposed recently (Bengtsson-Palme and Larsson, 2016). The resulting PNECs for resistance selection ranged from 8 ng/L (itraconazole) to 64 μg/L (clavulanic acid), which are generally much lower than PNECs for ecotoxicity (see Chapter 5) (Bengtsson-Palme and Larsson, 2016). Modelled PECs and MECs (from Chapter 5) were compared against risk threshold for resistance selection (500 ng/L) proposed by this work (Bengtsson-Palme and Larsson, 2016) to indicate any risk for antimicrobial resistance of trimethoprim in the Thames catchment. Maximum PEC95 values were divided by PNECs to provide a risk quotient (RQ). RQs were derived across different environmental compartments (influent, effluent and river waters).

6.3 Results and discussion

6.3.1 Model input parameters and their uncertainties

Model input parameters (per capita emission, WWTP and in-river removal rates) are listed in Table 6.2. The raw data used to derive all model inputs are presented below.

Table 6.2. Model input parameters for trimethoprim

Parameter description	Trimethoprim
Per capita emission (μg capita^{-1}day^{-1})	88
Removal rates in WWTPs	
Secondary biological filter (%)	46 ± 37
Secondary activated sludge and all tertiary (%)	45 ± 27
In-river removal rate (day^{-1})	0.12 ± 0.03E-01

Per capita emission

Per capita emission of trimethoprim was estimated from prescription data, excretion rates and the population of England. In theory, these data should be a reasonable guide, since in the United Kingdom antibiotics are only obtained by prescription from a medical practice or a hospital. In total, 191,030 and 7680 prescriptions were recorded in England in the year 2018 (201803-201902) at practice level (NHS Digital) and hospital level (NHS Business Services Authority), respectively. National consumption of trimethoprim in England was 3892 kg over the study period. The average consumption was 190 μg capita^{-1} day^{-1} when considering the population of England, which was estimated to be 55,977,178 in mid-2018 by the Office for National Statistics. However, the amount of trimethoprim prescribed varied between months, ranging from 28 to 436 kg (Figure 6.2) which corresponds to the consumption of 16 to 260 μg capita^{-1} day^{-1}. There was no clear reason why the amount of trimethoprim prescribed in February 2019 was substantially lower than the other months. Except for February 2019, the consumption of trimethoprim varied from 138 to 260 μg capita^{-1} day^{-1}, i.e., a variation of less than a factor of 2. The model assumes a constant input from patient excretion, which introduces a degree of uncertainty. Different ranges of excretion rates were obtained from the literature (Table 6.3) and a weighted mean, taking into account the number of patients was used to calculate per capita emission.

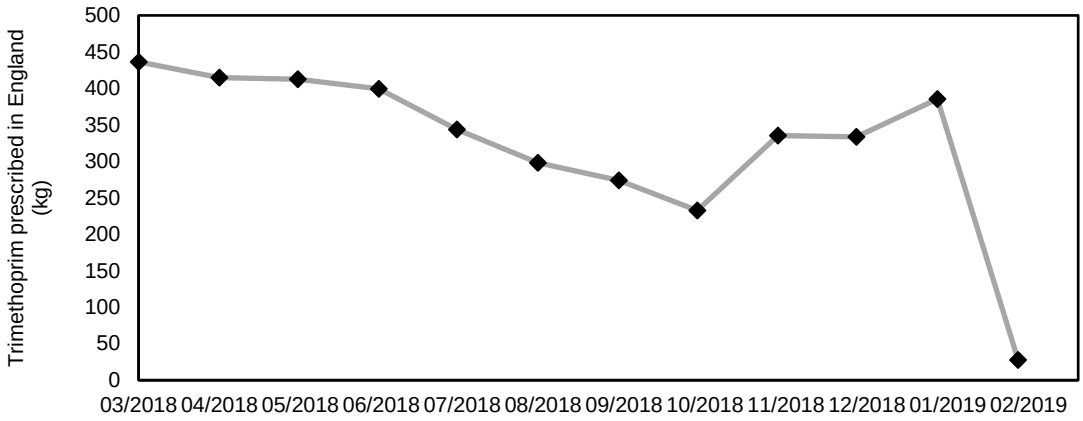

Figure 6.2. Monthly trimethoprim prescribed in England in 2018 (201803–201902)

Table 6.3. Proportion of trimethoprim excreted by patients

Reference	Trimethoprim excretion (%)
(Dollery 1991)*	44-48
(Huschek, Hansen et al. 2004)	40-60
(Straub 2013)	Up to 60
(Carballa, Omil et al. 2008)	43
(ter Laak, van der Aa et al. 2010)	45
Expected excretion[#]	46
Highest excretion	60
Lowest excretion	43

[#] Calculated as a weighted mean taking into account the number of patients

Wastewater treatment plant removal rates

Removal rates of trimethoprim were investigated in WWTPs from different regions across the United Kingdom (Roberts and Thomas, 2006, Kasprzyk-Hordern et al., 2009) and different countries (Schaar et al., 2010, Bendz et al., 2005, Golovko et al., 2014), and were found to range from 0 to 80% (Segura et al., 2007, Watkinson et al., 2007). Results from two studies investigating WWTPs in Southern England (Table 6.4**)** were adopted as they are considered to be close to the studied catchment specific conditions including loading rate, solids retention time, sludge growth rate, and temperature. Moreover, the removal efficiency of ECs such as antibiotics during wastewater treatment may also be affected by temperature (Sui et al., 2011) and flow conditions (Kasprzyk-Hordern et al., 2009), which can bring uncertainties to the model estimation. For example, trimethoprim removal performance improved from 30 to 80% in the Beijing summer, which might have been temperature related (Sui et al., 2011). The efficiency of the antibiotic removal was found to be affected by variable flow conditions at a WWTP in Wales, although more research is needed to draw explicit conclusions (Kasprzyk-Hordern et al., 2009).

Table 6.4. Removal rates of trimethoprim in WWTPs

Reference	Location of TP	Activated sludge WWTP		Biological filter WWTP	
		No. of TP	Mean % (SD %)	No. of TP	Mean % (SD %)
(Nakada et al., 2017)	Southern England	3	44 (23)	2	47 (27)
(Johnson et al., 2017)	Southern England	2	47 (15)	2	44 (25)
Expected removal*		45 (27)		46 (37)	

* Calculated as a weighted mean taking into account the number of TP studied

In-river removal rates

Studies on natural attenuation of trimethoprim in river systems are limited and no specific data are available for the River Thames catchment. The overall in-river degradation rates (K= 0.13 ± 0.02 h^{-1} and 0.25 ± 0.02 h^{-1}) achieved elsewhere (Luo et al., 2011) cannot be used for the model, since they accounted for flow but can be used as reference values. A flow-corrected in-river degradation rate of 0.07 ± 0.12 h^{-1} for trimethoprim has been reported in four river reaches within the Ebro basin (Iberian Peninsula, reported as half-life time 9.5 ± 14.4 h) (Acuña et al., 2015). A laboratory experiment derived an overall degradation rate for trimethoprim of 5.2E-03 ± 1.3E-04 h^{-1} (reported as half-life time 5.7 ± 0.1 d) in pond water (Lam et al., 2004). A degradation rate of 5.2E-03 ± 1.3E-04 h^{-1} (0.12 ± 0.003 day^{-1}) for trimethoprim was selected for the model input, which is in line with the above study (Luo et al., 2011) and was also close to in situ measured first-order degradation rates of other pharmaceuticals (ibuprofen, naproxen and metoprolol) (Fono et al., 2006).

Transport and attenuation of trimethoprim in aquatic systems can be influenced by hydrological factors such as flow (dilution) and environmental chemistry factors such as pH, dissolved organic matter (DOM), sediment total organic matter (TOM) and cation exchange capacity (CEC) (Luo et al., 2011). A Chinese field study in Haihe River showed that—apart from river flow rate—water dissolved organic carbon (DOC) exerted the most significant effect on trimethoprim degradation in rivers (Luo et al., 2011). It has been shown that hydrolysis and biodegradation were not significant loss processes for trimethoprim in aquatic systems while indirect photolysis could be contributing to the overall fate (Lam et al., 2004). DOC is a known producer of hydroxyl radicals (•OH) required for indirect photolysis reactions (Cristale et al., 2017). This supports the suggestion that DOC is important for trimethoprim degradation in rivers. Thus, local environmental conditions such as DOC in different river reaches could affect the

degradation rate of trimethoprim. Additionally, removal rates of trimethoprim may vary within the water column, depending upon water depth, suspended solid concentration, light penetration and weather (Ciffroy et al., 2017).

6.3.2 Comparison of PECs versus MECs

The model is able to predict river water concentrations of trimethoprim at high temporal and spatial resolution, which makes it possible to compare the PECs and MECs in terms of time and space. In total, concentrations (monthly PECmean, PEC90 and PEC95) for 457 individual river reaches (total length of 1398 km) of the whole River Thames network were predicted. The river flow observed was close to or in the range of modelled mean flow during the two sampling periods (June 2018 and February 2019, see Table 6.5) and, therefore, PECmean values were compared with DGT measured concentrations (DGT-MECs) to assess the accuracy of the model prediction. Figure 6.3 illustrates the PECmean values in June and February across the whole River Thames network and at the DGT sampling sites. Table 6.5 collates DGT-MECs and PECmean values (ng/L) of trimethoprim at the DGT sampling sites for the two sampling months. Overall, PECmean values of trimethoprim were in good agreement with DGT-MECs across the sampling sites but they were better in winter than in summer. In February, all the five DGT-MECs fell in the PECmean ranges. For example, DGT-MEC of the main stream at Swinford (8.1–9.3 ng/L) fell in the PECmean range (2.3–14.3 ng/L). In June, DGT-MECs of Ock and the Cut fell in the PECmean ranges while DGT-MECs of the other four sites were slightly lower than the PECmean values. A possible explanation is a seasonal factor reducing the environmental concentration (e.g., indirect photolysis) at some of the river reaches. As discussed in 6.2.5, DOC is important for indirect photolysis of trimethoprim in rivers and local environmental conditions such as DOC in different river reaches could affect the degradation rate of trimethoprim (Luo et al., 2011, Lam et al., 2004). If this is important, then in-river removal rate used in the model cannot represent the whole catchment.

Annual average prescription data (190 μg capita^{-1} day^{-1}) was used for per capita emission in the model and although the monthly prescription data showed a sharp drop in February 2019 (16 μg capita^{-1} day^{-1}) the model prediction accuracy was not affected. There is likely to be a time delay from the prescription to actual emission. For example, patients are taking the antibiotics over a period of time.

Although model basic datasets (e.g., population, river flow, and flow from the WWTPs) and model input parameters (per capita emission, WWTP and in-river removal rates) all have some degree of uncertainty, when assessed by DGT measurements the model overall provides predicted concentrations which are in reasonable agreement with measured values for trimethoprim.

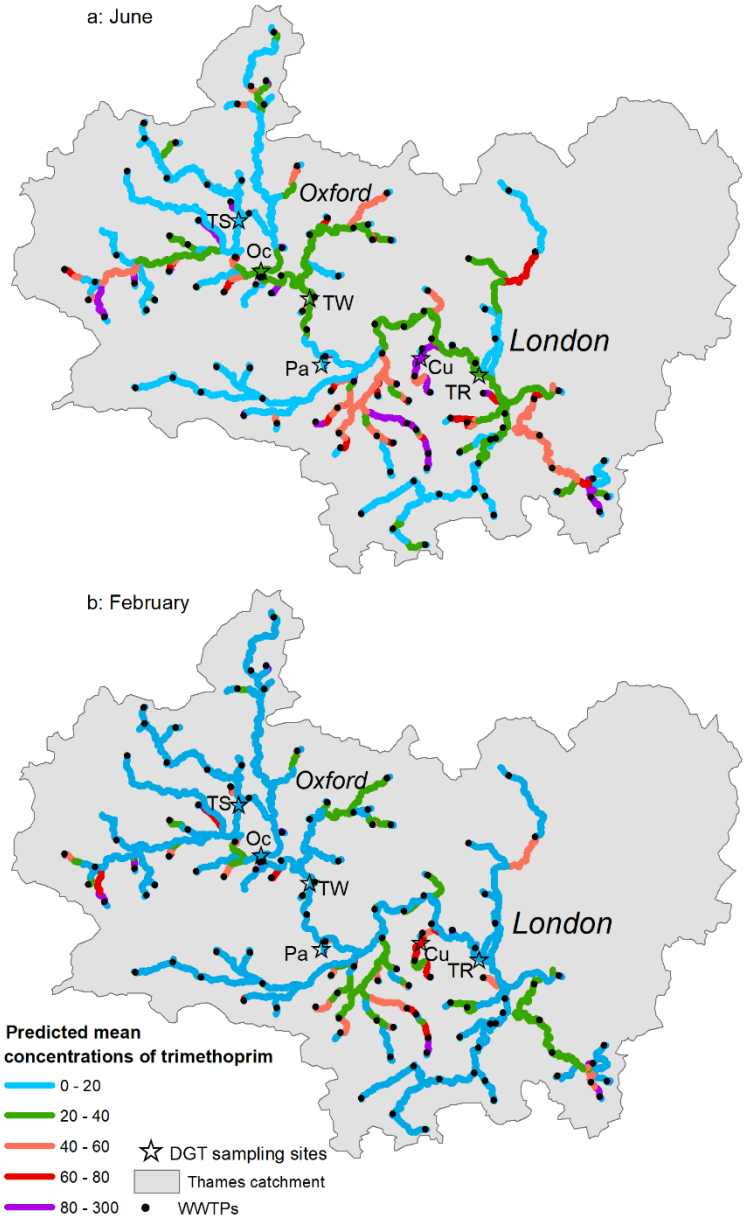

Figure 6.3. Model predicted mean concentrations of trimethoprim (ng/L) in the River Thames catchment. Sources of WWTPs and DGT sampling sites are shown on the map. Site code: Thames at Swinford (TS), Thames at Wallingford (TW), Thames at Runnymede (TR), Ock at Abingdon (Oc), Pang at Tidmarsh (Pa) and the Cut at Paley Street (Cu).

Table 6.5. DGT measured concentrations (DGT-MECs) and predicted mean concentrations (PECmean) of trimethoprim, observed and modelled mean flow at the DGT sampling sites in the two sampling months

Site code	June 2018				Feb 2019			
	DGT-MEC (ng/L)	PECmean (ng/L)	Flow observed (m^3/s)	Flow modelled (m^3/s)	DGT-MEC (ng/L)	PECmean (ng/L)	Flow observed (m^3/s)	Flow modelled (m^3/s)
TS	4.5±0.5	17.5±10.1	3–6	9±6	8.7±0.6	8.3±6.0	18–31	23±21
TW	7.4±0.8	22.3±9.8	7–9	18±32	10.4±0.6	11.3±7.2	29–57	49±57
TR	5.9±0.2	31.3±11.0	18–24	11±27	15.2±1.2	16.1±8.9	57–106	76±110
Oc	4.3±0.3	20.6±12.4	0.6–0.7	0.8±0.4	7.6±0.6	10.9±9.6	2–4	2±2
Pa	<LOQ	0.0	0.4–0.5	0.2±0.1	<LOQ	0.0	0.5–0.7	0.4±0.2
Cu	117.3±7.3	97.6±52.3	0.6–0.8	0.5±0.2	NA	75.3±45.4	NA	0.9±0.5

Site code: Thames at Swinford (TS), Thames at Wallingford (TW), Thames at Runnymede (TR), Ock at Abingdon (Oc), Pang at Tidmarsh (Pa) and the Cut at Paley Street (Cu).
River flow at the sampling site or the nearest gauging station was obtained from the National River Flow Archive (https://nrfa.ceh.ac.uk/data).
LOQ: limit of quantification.

6.3.3 Fate of trimethoprim in the River Thames catchment

This fate discussion is based on the fact that the model predicted concentrations agreed well with DGT measurements across the DGT sampling sites (in respect of concentration and site differences), so it was assumed that the LF2000-WQX did a reasonable job at generating accurate predicted concentrations of trimethoprim across the whole River Thames network. Predicted monthly mean concentrations are used here for the fate discussion, to represent an average scenario. Table 6.6 summarises the distribution of predicted mean concentrations in five bands, expressed as a percentage of total river length modelled (1398 km). In the seven months—from January to May, November and December—over 50% of the total river length was predicted to be ≤20 ng/L and for the other five months the majority of the river length was >20 ng/L. The percentage of the total river length predicted in the low band of trimethoprim (≤20 ng/L) decreased from January to August—with July, August and September at the lowest—and then increased until December. Correspondingly, the percentages of total river length in higher bands (20–40, 40–60, 60–80, and 80–300 ng/L) increased from January—with July, August and September the highest—and then decreased until December. In each river reach modelled, except those concentrations predicted to be 0, the concentration followed the same trend, increasing from January and peaking in one of the three months—July, August and September—and then decreasing (see Figure 6.4). As the emissions from the modelled WWTPs and in-river removal rate were fixed values for the whole year, the monthly variations are due only to changes in river flow.

Figure 6.3 shows concentrations of trimethoprim in river reaches across the River Thames network in two contrasting months (June and February), as a demonstration of spatial range. River reach variations are due to different emissions from the upstream WWTPs and changes in river flow. Influent concentrations of WWTPs were predicted to be 99–598 ng/L (median: 401 ng/L) and effluent concentrations were 54–323 ng/L (median: 217 ng/L). Since the WWTP removal rates used were similar—for biological filter only [(46±37)%] and sewage activated sludge and all tertiary treatments [(45±27)%]—the influent and effluent concentrations are dominated by emissions from the population served and DWF of the WWTP. Upstream tributaries tended to have higher concentrations than the main stream, due to less dilution at low river flow (see Figures 6.3 and 6.4).

This exercise clearly demonstrates that river flow, population served and DWF of the WWTP were dominant factors on trimethoprim distribution in river waters while chemistry factors such as indirect photolysis are less important because the processes are slow relative to flow rates.

Table 6.6. Distribution of predicted mean concentrations in 5 prescribed bands across the River Thames network, expressed as a percentage of total river length modelled and the mean, median and maximum concentrations in each month

Concentration (ng/L)		Jan	Feb	Mar	Apr	May	June	July	Aug	Sept	Oct	Nov	Dec
0–20	% of total river length	73	72	72	66	57	47	39	33	37	48	59	69
20–40		15	16	16	19	23	25	29	34	29	24	23	18
40–60		7	6	6	5	9	14	13	12	14	15	9	6
60–80		3	3	4	4	4	5	7	9	7	4	4	4
80–300		2	3	3	5	7	8	12	13	12	9	6	3
Mean		27	29	29	32	36	42	48	50	48	40	36	30
Median		12	12	12	15	19	24	31	34	31	23	18	14
Maximum		269	267	272	282	283	279	274	274	272	276	270	274

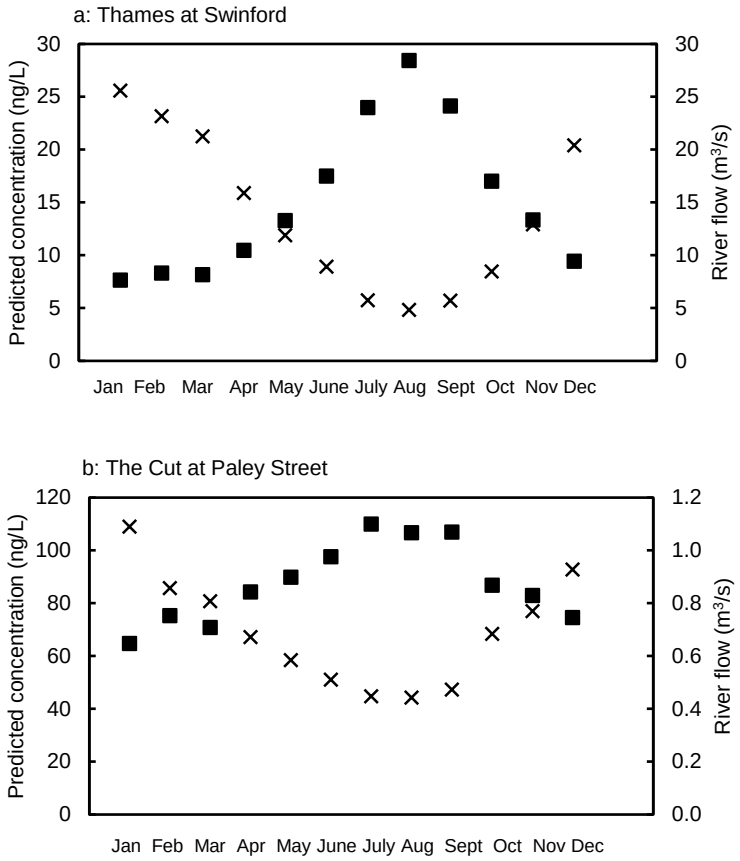

Figure 6.4. The predicted mean concentrations of trimethoprim (square, left y axis) corresponding to the river flow (cross, right y axis) in the two reaches where locate two DGT sampling sites [Figure (a) at the main stream (River Thames) and Figure (b) at a tributary (the Cut)].

6.3.4 Temporal trend of trimethoprim in surface water in England

The United Kingdom had the highest trimethoprim consumption rates at 500 μg capita^{-1} day^{-1} in 1995–2003 of 12 European countries, with an average value of 400 μg across these countries (Straub, 2013). In 2012, the United Kingdom still had the highest trimethoprim consumption of 505 μg capita^{-1} day^{-1} (Straub, 2013). It was calculated that the average individual consumption of trimethoprim was 590 μg day^{-1} in 2014. However, the amount of trimethoprim prescribed, as a proportion of nitrofurantoin and trimethoprim combined, fell from >70% in 2011 gradually to <50% in 2017, after implementing actions to reduce trimethoprim use by the NHS (Croker et al., 2018). This study calculated the average consumption of trimethoprim to be 190 μg capita^{-1} day^{-1} in England, which was about 30% of average consumption in 2014. It is of interest to check if the concentration of trimethoprim in the surface waters in England is decreasing, corresponding to the decreasing per capita emission. A time series of trimethoprim concentrations in influent and effluent of WWTPs and river waters in the United

Kingdom was collated in Table 6.7. It is clear that the concentrations of trimethoprim show a decreasing trend in influent and effluent of WWTPs and river waters in the United Kingdom.

Table 6.7. Concentrations of trimethoprim in influent and effluent of WWTPs and river waters in the United Kingdom

Reference	Concentration of trimethoprim (ng/L)*			Location	Time
	Influent	Effluent	River water		
(Ashton et al., 2004)	NA	<1288 (128)	<42 (12)	England	2002
(Hilton and Thomas, 2003)	NA	83–270	<39	England	2003
(Roberts and Thomas, 2006)	<300	<300	4–19 (9)	England	2004
(Thomas and Hilton, 2004)	NA	NA	<569 (40)	England	2004
(Kasprzyk-Hordern et al., 2009)	464–6796 (2192)	625–3052 (1152)	30–120 (89)	Wales	2009
(Kasprzyk-Hordern et al., 2009)	1514–4673 (2925)	385–1218 (876)	10–183 (62)	Wales	2009
(Straub, 2013)	NA	NA	89–152	Europe^	2013
(Johnson et al., 2017)	88–1022	87–455	NA	England	2012–2015
(Nakada et al., 2017)	<1580 (551)	<500 (313)	<427 (58)	England	2012–2015
This study	NA	NA	<117 (8)*	England	2018
This study#	100–600 (400)	55–320 (220)	0–270 (10)	England	2018

* Median value in the brackets; # concentrations under mean flow are shown; ^including England

6.3.5 Comments on the measurement and modelling comparison exercise

WWTPs appeared to be dominate sources of trimethoprim in the River Thames network. Seasonal variations of trimethoprim concentration are mainly due to flow differences and variations between river reaches are also affected by upstream emissions from the population served through WWTPs and DWF of the WWTPs. The model LF2000-WQX did a reasonable job at generating accurate predicted concentrations of trimethoprim across the whole River Thames network but it did better in winter than in summer. There seemed to be a seasonal factor reducing the environmental concentration (e.g., indirect photolysis) at some of the river reaches in summer. This indicated that the model performance can be improved by improving in-river removal rate, i.e., using different in-river removal rates considering local environmental conditions such as DOC in different river reaches.

6.3.6 Risk assessment

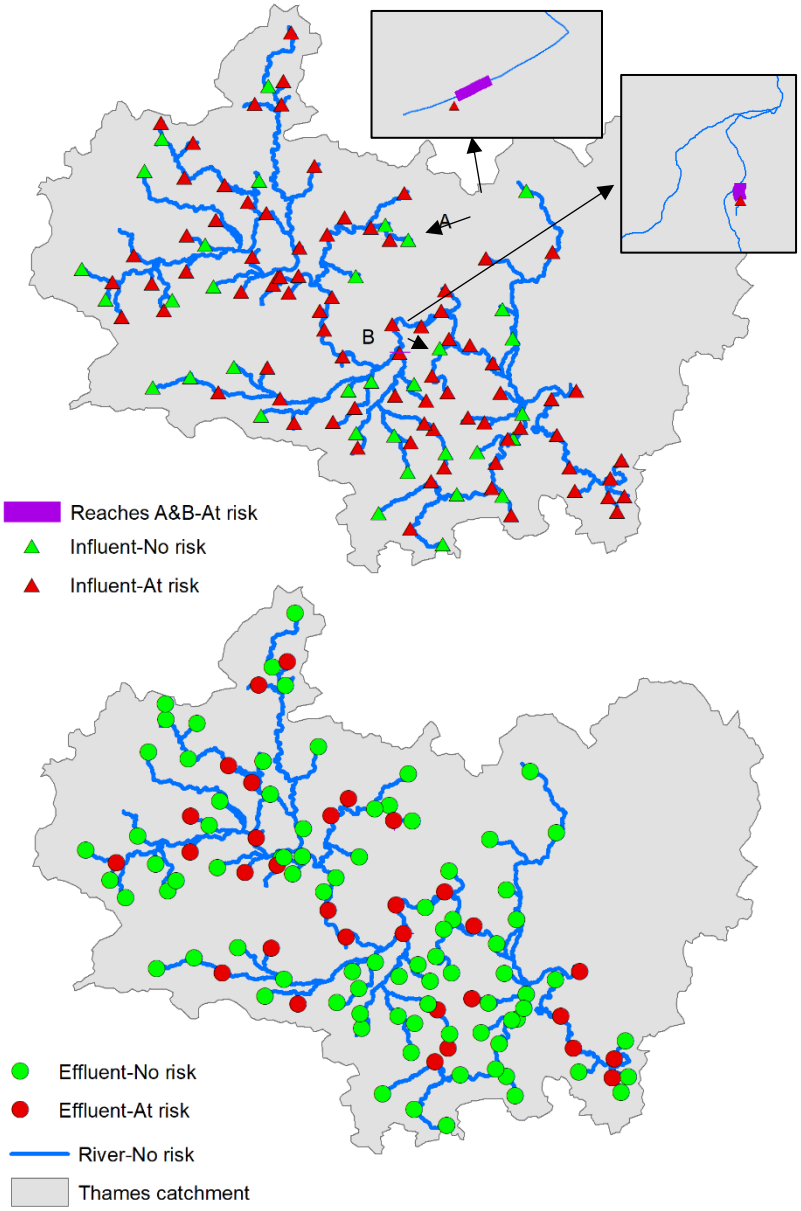

Figure 6.5. Distribution of predicted risk levels (no risk and at risk) in river, influent and effluent waters in the River Thames catchment.

Predicted monthly 95th percentile concentrations (PEC95) of trimethoprim in each river reach and PEC95 values in influent and effluent were used to undertake a 'worst-case-scenario' risk assessment for antimicrobial resistance. When RQ <1 (PEC95 < PNEC, which is 500 ng/L), the host water is marked no risk; when RQ >1, the host water is marked at risk (see Figure 6.5). Influent water in 70% WWTPs modelled were predicted to be at risk. Due to removal effect of WWTP treatment, effluent water in about 30% WWTPs modelled were predicted to be at risk. Two river reaches (A and B) showed at risk. A is a 100 meter reach downstream of WWTP A, with PEC95 ranging from 560 to

610 ng/L, and predicted to be at risk for the whole year. B is a 260 meter reach at the downstream of WWTP B, with PEC95 ranging from 485 to 530 ng/L, and predicted to be at risk for eight months of the year (March, and June to December). In total, less than 0.1% of the total river length modelled was predicted to be at risk. This is a combined effect of emission from the population served, DWF of the WWTP and river flow.

6.4 Conclusions

Water quality models such as LF2000-WQX can be helpful to study environmental fate, undertake risk assessments for ECs and determine the capacity of rivers for ECs based on known environmental standards. They are also particularly useful to check estimates of use/discharge generating predicted environmental concentrations against measurements, and to identify stretches of rivers likely to be most at risk from high concentrations. This study represents the first attempt to combine DGT and water quality models to study the environmental fate of ECs and to use the DGT measurement to assess the ability of the model to predict reasonable concentrations. This study also showed that LF2000-WQX is suitable for point-source ECs as the predicted concentrations agreed well with DGT measurements at the DGT sampling sites across the whole River Thames network. However, modelling ECs can be challenging, as there is still little information available to describe the properties of these chemicals and how they act within the environment. Catchment specific model input parameters can contribute to a more accurate estimation of the model.

Chapter 7: Conclusions and future work

7.1 Conclusions

This project explored the role of DGT in studying trace organic contaminants, especially emerging contaminants. It includes four perspectives: (i) understanding the standard DGT sampler design limitations and constraints to possible organic analytes, (ii) investigating practical constrains of the DGT sampler in the real-world such as biofouling and within-sampler degradation, (iii) applying DGT technique in a dynamic water system to test its reliability and challenges and to understand the transport, sources, and fate of ECs,, and (iv) combining DGT measurements with modeling to study environmental fate of emerging contaminants.

In summary, the following key conclusions were drawn in the studies presented in this thesis:

- The limitation to use the current DGT device for trace organics is adsorption in the diffusion layer, mainly in the membrane filter. However, it is possible to extend the DGT technique for a wider range of chemicals, for example, by replacing the current DGT membrane filter with a new type of membrane filter that does not interact with target analytes.
- A standard procedure is provided to measure lag times (from minutes to days) by exposing a series of DGT samplers in waters until linear mass accumulation in samplers is achieved. For compounds of higher values of K_{OW} or with aromatic rings, knowledge of the lag phase is necessary to optimize sampling times to avoid biasing subsequent laboratory analyses.
- Up to 15-day old biofilms generated at the surface of DGT devices in summer and winter from urban wastewater treatment plants showed no effect on DGT measurements of most ECs.
- Intact DGT samplers can be simply stored in polythene bags at ambient temperature (18–26 °C) with most compounds stable (mass loss <20%) over 1-week, although this practice should be minimized if possible. Keeping binding gels in the solvent stored in the refrigerator (4 °C) gave the best preservation with most chemicals stable up to 2-months.
- DGT is a powerful tool for studying the sources and environmental fate and impact of trace organic contaminants, especially emerging contaminants in terms of (i)

providing high temporal and spatial resolution at reasonable cost, (ii) simpler to end-users in collecting, preserving, transporting and pre-treatment of samples than traditional grab sampling method, and (iii) providing information on bioavailability.

- DGT measurements can be combined with water quality models to provide concentrations of trace organic contaminants at high temporal and spatial resolution at low cost.

7.2 Future perspectives

DGT is more than a passive sampling technique but a powerful research tool. Its research into organics has been growing rapidly but is still in its early stage. The work in this thesis is a step forward to understand some issues of the DGT sampler and to explore its role in studying trace organic contaminants. There is a great research space for the DGT technique in this area.

This work has shown the limitations of the current DGT device for trace organics. Future work can be focused on understanding and controlling losses by sorption, retardation by the membrane filter, possible effects on sampler performance from the biofilm formation, etc., to extend the DGT technique for a wider range of chemicals. Development of the DGT technique for new and emerging contaminants is of interest and encouraged by environmental agencies. For example, the U.S. EPA encourages development of new analytical methods and tools for understanding and managing organic contaminants [e.g., EPA's Per- and Polyfluoroalkyl Substances (PFAS) Action Plan].

Environmental scientists are interested to apply the DGT technique in new situations, such as for drinking water quality assessment, which is a promising direction.

As shown in this thesis, the DGT sampling technique has a number of advantages over traditional grab sampling. However, until now, most environmental monitoring studies are still based on the traditional grab sampling. Relative policies, protocols and effective deployment systems are needed to promote the use of passive sampling techniques for environmental monitoring.

DGT is a powerful tool to predict biouptake or the bioavailable fraction of a chemical, whether in waters, soils or sediments. It can be used to boost the research of bioavailabilty and impact of trace organic contaminants, especially unregulated new and emerging contaminants.

A combination of DGT sampling with bioassays (toxic effects) to assess the toxicity of the mixture organic contaminants in the environment would be another application area.

DGT has been used for one-dimensional and two-dimensional high-resolution measurements (chemical imaging), which is providing new evidence for the micro-scale (millimetre and submillimetre ranges) biogeochemical heterogeneity of soils and sediments. So far, these techniques have not been used for trace organic chemicals, but this is likely to be a productive area for future research.

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Appendix I

List of chemicals tested for DGT technique

List of chemicals tested for DGT technique (* not the first time to appear)

No.	Compound	CAS No.	Reference	Catalogue
1	Sulfamethoxazole	723-46-6	(Chen, Zhang et al. 2012)	Antibiotic
2	Sulfacetamide	144-80-9	(Chen, Zhang et al. 2013)	Antibiotic
3	Sulfachlorpyridazine	80-32-0		Antibiotic
4	Sulfadiazine	68-35-9		Antibiotic
5	Sulfadoxine	2447-57-6		Antibiotic
6	Sulfadimethoxine	122-11-2		Antibiotic
7	Sulfamethazine	57-68-1		Antibiotic
*	Sulfamethoxazole	723-46-6		Antibiotic
8	Sulfameter	651-06-9		Antibiotic
9	Sulfamonomethoxine	1220-83-3		Antibiotic
10	Sulfapyridine	144-83-2		Antibiotic
11	Sulfaquinoxaline	59-40-5		Antibiotic
12	Sulfisoxazole	127-69-5		Antibiotic
13	Sulfathiazole	72-14-0		Antibiotic
14	Sulfanilamide	63-74-1		Antibiotic
15	Sulfamerazine	127-79-7		Antibiotic
16	Sulfaguanidine	57-67-0		Antibiotic
17	Trimethoprim	738-70-5		Antibiotic
18	Ormetoprim	6981-18-6		Antibiotic
19	Ciprofloxacin	85721-33-1		Antibiotic
20	Difloxacin	98106-17-3		Antibiotic
21	Enrofloxacin	93106-60-6		Antibiotic
22	Fleroxacin	79660-72-3		Antibiotic
23	Lomefloxacin	98079-51-7		Antibiotic
24	Norfloxacin	70458-96-7		Antibiotic
25	Ofloxacin	82419-36-1		Antibiotic
26	Pefloxacin	70458-92-3		Antibiotic
27	Carbadox	05/07/6804		Antibiotic
28	Lincomycin	154-21-2		Antibiotic
29	Clarithromycin	81103-11-9		Antibiotic
30	Leucomycin	1392-21-8		Antibiotic
31	Oleandomycin	3922-90-5		Antibiotic
32	Roxithromycin	80214-83-1		Antibiotic
33	Tylosin	1401-69-0		Antibiotic
34	Erythromycin-H2O	23893-13-2		Antibiotic
35	Salinomycin	53003-10-4		Antibiotic
36	Monensin	17090-79-8		Antibiotic
37	Novobiocin	303-81-1		Antibiotic
38	4-chlorophenol	106-48-9	(Dong, Fan et al. 2014)	Phenolic compound
39	Phenol	108-95-2	(Dong, Li et al. 2014)	Phenolic compound
40	Glyphosate	1071-83-6	(Fauvelle, Nhu-Trang et al. 2015)	Herbicide
41	Aminomethyl Phosphonic Acid	1066-51-9		Degradation product of glyphosate
42	Bisphenol A	80-05-7	(Zheng, Guan et al. 2015)	Bisphenol
43	Bisphenol B	77-40-7		Bisphenol
44	Bisphenol F	620-92-8		Bisphenol
45	Adenosine monophosphate	61-19-8	(Mohr, Vogt et al. 2015)	Organic phosphorus
46	Myo-inositol hexakisphosphate	83-86-3		Organic phosphorus
47	Atenolol	29122-68-7	(Challis, Hanson et al. 2016)	Pharmaceutical
48	Atrazine	1912-24-9		Herbicide
49	Carbamazepine	298-46-4		Pharmaceutical
50	Chlorpyrifos	2921-88-2		Pesticide
*	Clarithromycin	81103-11-9		Antibiotic
51	Clofibric acid	882-09-7		Herbicide
52	Clothianidin	210880-92-5		Pesticide
53	Diazinon	333-41-5		Pesticide
54	2,4-D	94-75-7		Herbicide
55	Diclofenac	15307-86-5		Pharmaceutical
*	Erythromycin	114-07-8		Antibiotic
*	17β-Estradiol	50-28-2		Hormone
56	Estrone	53-16-7		Hormone
57	17α-ethynylestradiol	57-63-6		Pharmaceutical
58	Fenoprofen	29679-58-1		Pharmaceutical
59	Fluoxetine	54910-89-3		Pharmaceutical

Continued on next page

List of chemicals tested for DGT technique—Continued

No.	Compound	CAS No.	Reference	Catalogue
60	Gemfibrozil	25812-30-0		Pharmaceutical
61	Ibuprofen	15687-27-1		Pharmaceutical
62	Imidacloprid	138261-41-3		Pesticide
63	Ketoprofen	22071-15-4		Pharmaceutical
64	Metoprolol	51384-51-1		Pharmaceutical
65	Naproxen	22204-53-1		Pharmaceutical
66	Paroxetine	61869-08-7		Pharmaceutical
67	Propranolol	525-66-6		Pharmaceutical
*	Roxithromycin	80214-83-1	(Challis, Hanson et al. 2016)	Antibiotic
*	Sulfachlorpyridazine	80-32-0		Antibiotic
*	Sulfadimethoxine	122-11-2		Antibiotic
*	Sulfamethazine	57-68-1		Antibiotic
*	Sulfamethoxazole	723-46-6		Antibiotic
*	Sulfapyridine	144-83-2		Antibiotic
*	Sulfisoxazole	127-69-5		Antibiotic
68	Thiamethoxam	153719-23-4		Pesticide
*	Trimethoprim	738-70-5		Antibiotic
69	Bentazon	25057-89-0		Pesticide
70	Chlorsulfuron	64902-72-3	(Guibal, Buzier et al. 2017)	Pesticide
71	Ioxynil	1689-83-4		Pesticide
72	Mecoprop	93-65-2		Pesticide
73	Ketamine	6740-88-1		Drug
74	Methamphetamine	537-46-2	(Guo, Zhang et al. 2017)	Drug
75	Amphetamine	300-62-9		Drug
76	Methylparaben	99-76-3		Preservative
77	Propylparaben	94-13-3		Preservative
78	Isopropylparaben	4191-73-5		Preservative
79	Butylparaben	94-26-8		Preservative
80	Benzylparaben	94-18-8		Preservative
81	Heptyl paraben	1085-12-7		Preservative
82	4-Hydroxybenzoic acid	99-96-7	(Chen, Li et al. 2017)	Preservative
83	Antioxidant	25013-16-5		Antioxidant
84	Hydroxytoluene	128-37-0		Antioxidant
85	Ortho-phenylphenol	90-43-7		Disinfectant
86	Triclosan	3380-34-5		Disinfectant
87	Triclocarban	101-20-2		Disinfectant
88	17β-estradiol	50-28-2	(Guo, Van Langenhove et al. 2017)	Oestrogen
*	Sulfadimethoxine	122-11-2		Antibiotic
*	Sulfachlorpyridazine	80-32-0		Antibiotic
*	Sulfamonomethoxine	1220-83-3		Antibiotic
*	Sulfamethazine	57-68-1		Antibiotic
*	Sulfathiazole	72-14-0		Antibiotic
*	Sulfamethoxazole	723-46-6		Antibiotic
*	Sulfadiazine	68-35-9		Antibiotic
*	Sulfapyridine	144-83-2		Antibiotic
89	Azithromycin	83905-01-5		Antibiotic
*	Clarithromycin	81103-11-9		Antibiotic
*	Erythromycin-H_2O	114-07-8	(Xie, H. et al., 2018a)	Antibiotic
*	Ofloxacin	82419-36-1		Antibiotic
*	Enrofloxacin	93106-60-6		Antibiotic
*	Ciprofloxacin	85721-33-1		Antibiotic
*	Norfloxacin	70458-96-7		Antibiotic
90	Florfenicol	73231-34-2		Antibiotic
91	Thiamphenicol	15318-45-3		Antibiotic
92	Chloramphenicol	56-75-7		Antibiotic
*	Lincomycin	154-21-2		Antibiotic
*	Trimethoprim	738-70-5		Antibiotic
*	17β-Estradiol	50-28-2		Oestrogen
93	Estriol	50-27-1		Oestrogen
*	17α-Ethynylestradiol	57-63-6		Oestrogen
*	Atrazine	1912-24-9	(Xie, H. et al., 2018b)	Herbicide
94	Acetochlor	34256-82-1		Acetochlor
*	Bisphenol A	80-05-7		Bisphenol
95	Ethylparaben	120-47-8	(Wei CHEN, personal communication)	Preservative

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List of chemicals tested for DGT technique—Continued

No.	Compound	CAS No.	Reference	Catalogue
*	Estrone	53-16-7	(Chen, Pan et al. 2018)	Oestrogen
*	17β-estradiol	50-28-2		Oestrogen
*	Estriol	50-27-1		Oestrogen
*	17α-ethynylestradiol (Ethinylestradiol)	57-63-6		Oestrogen
*	Bisphenol A	07/05/1980	(Chen, Pan et al. 2018)	Bisphenol
96	Diethylstilbestrol	56-53-1		Oestrogen
97	4-tert-octylphenol	140-66-9		Alkyl-phenol
98	Nonylphenol	84852-15-3		Alkyl-phenol
99	Dosulepin	113-53-1	(Xinli XING, personal communication)	Drug
100	Amitriptyline	549-18-8		Drug
*	Fluoxetine	000002-84-9		Drug
101	Simvastatin	79902-63-9		Drug
102	Diphenhydramine	58-73-1		Drug
103	Codeine	76-57-3		Drug
104	Tramadol	027203-92-5		Drug
105	MDMA(ecstasy)	4254210-9		Drug
106	Cocaine	50-36-2		Drug
*	Clofibric acid	882-09-7		Drug
107	Bezafibrate	41859-67-0		Drug
108	Fenofibric acid	42017-89-0		Drug
109	Pyrimethanil	53112-28-0	(Li et al., 2019a)	Fungicide
110	Ethofumesate	26225-79-6		Herbicide
111	Fluometuron	2164-17-2		Herbicide
112	Chloridazon	1698-60-8		Herbicide
113	Clomazone	81777-89-1		Herbicide
114	Thiabendazole	148-79-8		Fungicide
*	Atrazine	1912-24-9		Herbicide
115	Linuron	330-55-2		Herbicide
116	Pirimicarb	23103-98-2		Insecticide
117	tetracycline	60-54-8	(You, Yao et al. 2019)	Antibiotic
118	oxytetracycline	79-57-2		Antibiotic
119	chlortetracycline	57-62-5		Antibiotic
120	Tris(2-chloroethyl) phosphate	115-96-8	(Zou, Fang et al. 2018)	Flame retardant
121	Tris(2-chloroisopropyl) phosphate	13674-84-5		Flame retardant
122	Tris(1,3-dichloro-2-propyl) phosphate	13674-87-8		Flame retardant
123	Tri-n-propyl phosphate	513-08-6		Flame retardant
124	Tri-n-butyl phosphate	126-73-8		Flame retardant
125	Tris(2-butoxyethyl) phosphate	78-51-3		Flame retardant
126	methcathinone	5650-44-2	(Zhang, Zhang et al. 2018)	Drug
127	ephedrine	299-42-3		Drug
128	o-nitrophenol	88-75-5	(You, Li et al. 2018)	Nitrophenol
129	p-nitrophenol	100-02-7		Nitrophenol
130	2,4-dinitrophenol	51-28-5		Nitrophenol
*	17β-Estradiol	50-28-2	(Xie, Chen et al. 2018)	Estrogen
*	Estriol	50-27-1		Estrogen
*	17α-Ethynylestradiol	57-63-6		Estrogen
*	Atrazine	1912-24-9		Pesticide
*	Acetochlor	34256-82-1		Pesticide
*	Bisphenol A	80-05-7		Bisphenol
*	triclocarban	101-20-2	(Wei, Yang et al. 2018)	Antibacterial agent
*	triclosan	3380-34-5		Antibacterial agent
131	methyl triclosan	4640-01-1		Antibacterial agent
*	ciprofloxacin	85721-33-1	(Sidhu, D'Angelo et al. 2018)	Antibiotic
*	azithromycin	83905-01-5		Antibiotic
*	ciprofloxacin	85721-33-1	(Li, Chen et al. 2018)	Antibiotic
132	monobutlytin	78763-54-9	(Cole, Mills et al. 2018)	Organotin
133	dibutyltin	1002-53-5		Organotin
134	tributyltin	688-73-3		Organotin
135	diphenyltin	6381-06-2		Organotin
136	triphenyltin	17272-58-1		Organotin

Continued on next page

List of chemicals tested for DGT technique—Continued

No.	Compound	CAS No.	Reference	Catalogue
*	ciprofloxacin	85721-33-1	(D'Angelo and Starnes 2016)	Antibiotic
137	triethyl phosphate	78-40-0	(Wang et al., 2019)	Flame retardant
138	triphenyl phosphate	115-86-6		Flame retardant
139	1-chloro-3- nitrobenzene	121-73-3	(Zhang et al., 2019)	Nitrochlorobenzene
140	1-chloro-4- nitrobenzene	100-00-5		Nitrochlorobenzene
141	1-chloro-2 -nitrobenzene	88-73-3		Nitrochlorobenzene
142	1-chloro-2,4- dinitrobenzene	97-00-7		Nitrochlorobenzene
143	hydroxyatrazine	2163-68-0	(Li et al., 2019b)	Metabolites of atrazine
144	deethylatrazine	6190-65-4		Metabolites of atrazine
145	deisopropylatrazine	1007-28-9		Metabolites of atrazine
146	diaminochlorotriazine	3397-62-4		Metabolites of atrazine
147	2-chlorophenol	95-57-8	(Meng et al., 2019)	Chlorophenol
148	2,4-dichlorophenol	120-83-2		Chlorophenol
149	2,4,6-trichlorophenol	88-06-2		Chlorophenol
150	Fluoxetine hydrochloride	56296-78-7	(Fang et al., 2019)	Pharmaceutical
151	Risperidone	106266-06-2		Pharmaceutical
152	Caffeine	58-08-2		Pharmaceutical
153	Clomipramine	303-49-1		Pharmaceutical
154	Fluvoxamine maleate	61718-82-9		Pharmaceutical
155	Mirtazapine	85650-52-8		Pharmaceutical
156	Perphenazine	18052-18-1		Pharmaceutical
157	Amitriptyline	50-48-6		Pharmaceutical
158	Bupropion hydrochloride	31677-93-7		Pharmaceutical
159	Estazolam	29975-16-4		Pharmaceutical
160	Diazapam	439-14-5		Pharmaceutical
161	Temazepam	846-50-4		Pharmaceutical
162	Alprazolam	28981-97-7		Pharmaceutical
163	Oxazepam	604-75-1		Pharmaceutical

Appendix II

Abstract of oral presentation at DGT conference: **Wang, R.**, Jones, K. C. & Zhang, H. Understanding potential limitations of the current DGT passive sampler for organic chemicals in aquatic systems. DGT Conference 2019. Vienna, Austria. September 18–20, 2019.

Understanding potential limitations of the current DGT passive sampler for organic chemicals in aquatic systems

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Abstract: DGT technique has recently been extended from measuring inorganic elements to quantifying in situ concentrations of organic contaminants in waters with appropriate spatial and temporal resolution at low cost. This study addresses the basic requirements and property range of chemicals that can be accurately measured with the present design of DGT device (PTFE membrane filter, agarose gel diffusive layer and HLB binding layer). The effect of biofouling and post-deployment sample storage on DGT measurements were systematically investigated. Organophosphate esters with various functional groups and a wide range of physicochemical properties (log K_{ow} [0.8-9.5], molecular weight [182-435 Da]) compared to previous studies were used in the sorption and DGT performance experiments. It showed compounds with high hydrophobicity and aromatic rings were prone to retention on PTFE polymer filters, slowing the supply of chemical to the binding layer. The current DGT sampler is reliable for measuring hydrophilic (log K_{ow} [0.8-2.6]) and non-aromatic-ring organics. A standard procedure is provided to measure lag times (from minutes to days), to optimise sampling times when necessary. Biofouling may affect the accuracy of DGT measured concentrations due to its thickness and/or biouptake. Effect of the biofilm generated at the surface of DGT sampler in summer and winter from a typical urban wastewater treatment plant were tested with 13 emerging organic pollutants. None of the 8-day or 15-day biofilms (collected from influent or effluent, in summer or winter) affected DGT measurements of most compounds. Samplers were mostly treated immediately after retrieval while for projects covering large areas, it becomes less practical and therefore a sampler storage protocol is needed. Four storage methods up to 2-month were evaluated: samplers sealed in a polyethylene bag at room temperature; binding gels stored in acetonitrile in amber vials at room temperature; samplers stored at 4 °C and binding gels stored in acetonitrile in amber vials at 4 °C. The results showed that keeping intact samplers in refrigerator (4 °C) is the simplest and safest way of preserving compounds up to 2-month, but if no refrigerators were available, keeping binding gels in elution solvent at room temperature would reach comparable effect.

Appendix III

Co-authored paper

Zou, Y. T., Fang, Z., Li, Y., **Wang, R.**, Zhang, H., Jones, K. C., Cui, X. Y., Shi, X. Y., Yin, D., Li, C., Liu, Z. D., Ma, L. Q. & Luo, J. 2018. Novel method for in situ monitoring of organophosphorus flame retardants in waters. *Analytical Chemistry,* 90, 10016-10023.

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Article

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Novel Method for *in Situ* Monitoring of Organophosphorus Flame Retardants in Waters

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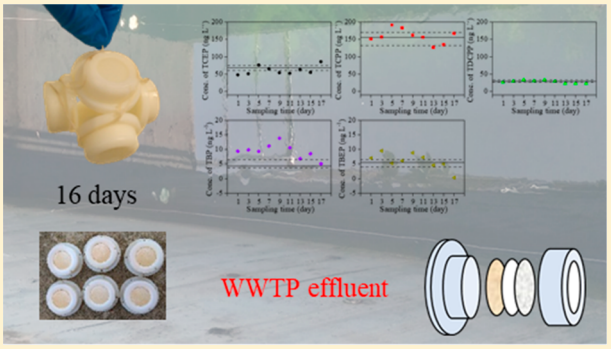
Supporting Information

ABSTRACT: Widespread use of organophosphorus flame retardants (OPFRs) and their ubiquity in water results in the need for a robust and reliable monitoring technique to better understand their fate and environmental impact. *In situ* passive sampling using the diffusive gradients in thin-films (DGT) technique provides time-integrated data and is developed for measuring OPFRs here. Ultrasonic extraction of binding gels in methanol provided reliable recoveries for all tested OPFRs. Diffusion coefficients of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP in the agarose diffusive gel (25 °C) were obtained. The capacity of an HLB binding gel for OPFRs was >115 μg per disc, and the binding performance did not deteriorate with time up to 131 days. DGT performance is independent of typical environmental ranges of pH (3.12−9.71), ionic strength (0.1−500 mmol L^{-1}), and dissolved organic matter (0−20 mg L^{-1}), and also of diffusive layer thickness (0.64−2.14 mm) and deployment time (3−168 h). Negligible competition effects between OPFRs was found. DGT-measured concentrations of OPFRs in a wastewater treatment plant (WWTP) effluent (12−16 days) were comparable to those obtained by grab sampling, further verifying DGT's reliability for measuring OPFRs in waters.



Organophosphorus flame retardants (OPFRs) are emerging contaminants which have been widely utilized in polyurethane foam plastic, resin, paint, textiles, and building materials.[1] OPFRs are relatively water-soluble organic contaminants, and many OPFRs are used as additives incorporated into polymer products, rather than chemically bonded to them. They can therefore easily transfer to environmental media, particularly to water. However, some OPFRs, such as chlorinated compounds tris(2-chloroethyl) phosphate (TCEP), tris(2-chloroisopropyl) phosphate (TCPP), and tris(1,3-dichloro-2-propyl) phosphate (TDCPP), cannot be effectively removed from wastewaters by activated sludge treatment and are quite recalcitrant to an advanced oxidation process.[2] OPFRs concentrations were reported to be around 4 μg L^{-1} in municipal wastewater effluent in Germany,[3] and 7.9−39 μg L^{-1} in sewage treatment plants effluents in Sweden.[4] Consequently, most of these OPFRs were then discharged to the environment through effluent and sludge. OPFRs are therefore ubiquitous in surface water, and have even been reported in tap water and bottled drinking water in many countries.[5−9] The concentrations of OPFRs were around 5000 ng L^{-1} in River Aire in United Kingdom,[9] from 7.3 ± 4.5 ng L^{-1} in Lake Huron to 96 ± 43 ng L^{-1} in Lake Erie in the Great Lakes in America,[10] 190−2820 ng L^{-1} in River Oder in Germany,[11] and around 1 μg L^{-1} in Songhua River in Northeast China.[12] Tris(2-butoxyethyl) phosphate (TBEP) and TCEP are the most prominent OPFR compounds in some aquatic systems.[10,12] Total concentrations of OPFRs have been reported from 85 to 325 ng L^{-1} in tap water and up to 1660 ng L^{-1} in drinking water.[6,13] The most frequently detected compounds in tap water were TBEP and TCPP, and TCEP, TCPP, and TBEP in bottled drinking water.

Although there has been no report on OPFRs regulations in aquatic system in legislative frameworks, many investigations have focused on their negative effects on human health and ecological systems. This suggests that they may become incorporated in regulatory frameworks in the future. TCEP, TCPP, tri-*n*-butyl phosphate (TBP), and TBEP can be bioaccumulated in fish and can be transferred through the aquatic food web.[14−17] Concerns over human exposure to OPFRs have focused on endocrine disruption via disturbing steroidogenesis,[18] inducing oxidative stress,[19] or influencing thyroxine.[20] Hence, accurate measurement and monitoring of

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OPFRs in aquatic systems are necessary to better understand their fate and biogeochemical behavior and to further evaluate their potential effect on ecosystems and human health.

Usually OPFRs monitoring is by grab collecting large-volume water samples followed by preconcentration using solid-phase extraction. However, this only provides snapshots of OPFR concentrations at a certain sampling time.[6−8,13] The sample treatment is time-consuming and costly. The measurements cannot reflect any daily or weekly concentration fluctuations.[21] Passive sampling techniques, which preconcentrate analytes from water to binding agents *in situ* during field deployment, can overcome these drawbacks[21] and provide time-averaged concentrations, which better reflect environmental contamination levels and contribute to a more accurate risk assessment of ecosystems and human health. The polar organic chemical integrative sampler (POCIS) has been applied to monitoring organic contaminants, including organophosphate pesticides and EDCs, in waters.[22,23] However, a significant limitation of POCIS is that its sampling rates largely depend on hydrodynamic conditions. Calibration carried out in the laboratory, which was used to assess the sampling rate in field conditions, cannot reflect the field conditions.

The diffusive gradients in thin-films (DGT) technique is independent of hydrodynamic conditions, and hence, no calibration is needed for *in situ* measurements.[24] (The principles of the DGT technique are given in the Supporting Information.) DGT is well established for measuring various inorganic species in aquatic systems.[24−34] Recently, DGT has been extended to measuring organic pollutants, such as antibiotics,[35,36] bisphenols,[37] pesticides,[38] household and personal care products (HPCPs),[39] and some polar chemicals in wastewater treatment plants.[40] These developments have made it feasible to use DGT for measuring OPFRs in waters.

HLB (hydrophilic−lipophilic-balanced) resin (*N*-vinylpyrrolidone and divinylbenzene copolymer) has been widely used in cartridges to extract polar organics.[6,8] Here DGT devices containing HLB resin incorporated in agarose gel as binding phase were prepared to effectively sample six frequently detected or studied OPFRs, i.e., TCEP, TCPP, TDCPP, tri-n-propyl phosphate (TPrP), TBP, and TBEP for the first time. DGT was evaluated for its performance characteristics under various pH values, ionic strengths, and dissolved organic matter concentrations which cover the range typically found in the environment. The possible effects of binding kinetics, capacity of the binding gels, deployment time, competition among different OPFRs, storage time of the HLB binding gels, and diffusive gel thickness were also studied. DGT was deployed in wastewater treatment plant effluent in Nanjing, China, to evaluate its performance in field conditions.

METHOD AND MATERIALS

Gel Preparation. A standard DGT device consists of a binding gel, a diffusive gel, and a filter membrane held in a plastic molding (DGT Research Ltd., UK).[37] Diffusive gels were prepared using agarose solution following previously published procedures.[36,37] Information on the evaluation of possible adsorption of OPFRs onto filter membranes, diffusive gels, and DGT moldings is given in the Method and Materials and Results and Discussion sections of the Supporting Information.

Binding gels were prepared by adding 3.6 g (wet weight) of HLB resins into 18 mL of 2% agarose solution (dissolving 0.36 g of agarose in 18 mL of MQ water) when the solution was heated to transparent. The resulting solution was then pipetted into preheated glass plates separated by a 0.50 mm thick PTFE spacer. The diffusive gels were made following the same procedure without the resin. When gels were set at room temperature, they were then cut into discs of 2.5 cm diameter and stored in 0.01 M NaCl solution at 4 °C.

Uptake Kinetics and Elution Efficiencies of HLB Gels. Preparations of reagents, materials, and solutions used in the following sections are detailed in the Supporting Information. HLB gel discs were immersed in 10 mL of 100 μg L^{-1} OPFRs solutions and shaken horizontally for various times, from 0.5 min to 24 h. The masses of OPFRs adsorbed by the HLB gel discs were calculated by the difference between the original concentration and the remainder in each sample.

Elution efficiencies of OPFRs were assessed by eluting HLB gels preloaded with various amounts of OPFRs with 10 mL of methanol. Hence, HLB gels were immersed in 10 mL of 10, 20, 50, 100, and 200 μg L^{-1} OPFRs solutions containing 0.01 M NaCl, and shaken horizontally for 24 h. The OPFRs-loaded HLB gels were extracted using 10 mL of methanol in an ultrasonic bath for 30 min. The elution and immersion solutions were then filtered using PTFE filter membranes with 0.22 μm pore size and analyzed using UPLC−MS/MS (Qsight 210, PerkinElmer). Detailed information on instrumental analysis was summarized in Supporting Information.

Diffusion Coefficients. Diffusion coefficients of OPFRs were measured following a previously widely described method, but with a slight modification.[27,29,41] In brief, they were measured with two stainless steel compartments connected with a 1.5 cm diameter circle window holding a 0.75 mm thick diffusive gel. The source compartment was filled with 50 mL of 0.01 M NaCl solution containing 1 mg L^{-1} OPFRs, while the receptor compartment contained 50 mL of 0.01 M NaCl solution without any OPFRs. The solution pH in both compartments was the same (5.91 ± 0.23). An aliquot of 0.2 mL was removed to glass vials, for further instrumental analysis, from both compartments at intervals of 30 min each time. The experiments were performed at 22.1 ± 0.2 °C for 270 min. Diffusion coefficients, D_{cell}, measured in this way were calculated using eq 1:

$$D_{cell} = \text{slope}\frac{\Delta g}{CA} \quad (1)$$

Here, Δg is the thickness of agarose diffusive gel, C means concentrations of OPFRs in the source compartment, and A represents the area of the window connecting the two compartments. The slope was obtained by plotting the diffused masses of OPFRs versus diffusion time.

Diffusion coefficients, D_{DGT}, of OPFRs were also measured by deploying 8 DGT devices in 2.5 L of 20 μg L^{-1} well-stirred OPFRs solutions for 24 h, assuming that DGT-measured concentrations of OPFRs were equal to solution concentrations. D_{DGT} was calculated using a previously reported equation (eq 2):[37]

$$D_{DGT} = \frac{M\Delta g}{CAt} \quad (2)$$

Here, M is the mass accumulated on the HLB binding gels, Δg is the thickness of the diffusive layer (a diffusive gel and a filter), C is the solution concentration of OPFRs, A is the area of exposure window of the DGT device (2.51 cm^2), and t is the deployment time.

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DGT Performance under Different Conditions. Standard DGT devices containing a 0.5 mm thick HLB binding gel, a 0.75 mm thick agarose diffusive gel, and a 0.14 mm thick, 0.45 μm pore size hydrophilic PTFE filter membrane were deployed in various OPFRs solutions for 24 h to evaluate the effects of pH, ionic strength, and dissolved organic matter on DGT performance. The solutions were (a) 2.5 L of 20 μg L^{-1} OPFRs solutions containing 0.01 M NaCl with a range of pH from 3.1 to 9.5; (b) 2.5 L of 20 μg L^{-1} OPFRs solutions containing various NaCl concentrations ranging from 0.0001 to 0.5 M; and (c) 2.5 L of 20 μg L^{-1} OPFRs solutions (C_{NaCl} = 0.01 M) with a range of humic acid (Aladdin, fulvic acid ≥90%) concentrations, from 0 to 20 mg L^{-1}.

To test the effect of deployment time on DGT performance, the DGT devices were deployed in 6 L of 20 μg L^{-1} OPFRs solutions containing 0.01 M NaCl and retrieved at different times (from 3 to 168 h). To explore the dependence of mass taken up by DGT on diffusive gel thicknesses, DGT devices with various thicknesses of agarose diffusive gels were immersed in 2.5 L of 20 μg L^{-1} OPFRs solutions containing 0.01 M NaCl for 24 h.

Capacity and Competition Effect. To measure the capacity of DGT to accumulate OPFRs, the DGT devices were deployed in 2.5 L of well-stirred solutions containing 0.01 M NaCl with OPFR concentrations ranging from 20 to 1800 μg L^{-1} for 24 h.

To investigate the potential competition effect among OPFRs, six studied OPFRs were divided into 2 groups: alkyl OPFRs (TBP, TBEP, and TPrP) and chlorinated alkyl OPFRs (TCEP, TCPP, and TDCPP). DGT devices were immersed in various mixed solutions: (a) alkyl OPFRs were at 20 μg L^{-1}, while the others were at 100 or 1000 μg L^{-1}, respectively; (b) alkyl OPFRs were at 100 μg L^{-1}, while the others were at 20 or 1000 μg L^{-1}, respectively; and (c) alkyl OPFRs were at 1000 μg L^{-1}, while the others were at 20 or 100 μg L^{-1}, respectively.

DGT Tests *in Situ* in Field Trials. To further test the robustness of DGT for measuring OPFRs in the real environment, the devices were applied to monitor concentrations of OPFRs in a wastewater treatment plant (WWTP), which was mainly for treating domestic sewage with the anaerobic−anoxic−oxic (A^2O) treatment process in Nanjing. The capacity of sewage treatment is about 100 000 m^3 day^{-1}. The DGT deployments were carried out for 12−16 days. Six DGT devices were assembled into hexahedral units to allow each DGT device to have the same chance to accumulate OPFRs from water.[27,37,42] A temperature button data logger was set with each hexahedral unit to record the water temperature every 180 min. On retrieval, DGT devices were immediately transported to the laboratory; HLB binding gels were eluted with 10 mL of methanol in an ultrasonic bath for 30 min. Water samples (0.5 L) were collected from each sampling site every 2−3 days during the DGT deployment and concentrated with HLB cartridges (Waters, 6 cc 150 mg), followed by elution twice with 5 mL of methanol. The two eluents were merged. Both HLB binding gel eluents and cartridge eluents were evaporated to near dryness under a gentle stream of nitrogen, and then redissolved with 0.5 mL of methanol for further instrumental analysis.

RESULTS AND DISCUSSION

Uptake Kinetics of OPFRs onto HLB gels. Accumulated OPFRs on HLB binding gels increased almost linearly with time in the first 30 min. More than 80% of OPFRs were bound onto the HLB gels after 60 min (Figure 1and Figure S3). The average binding rates of the analytes over the first 30 min were

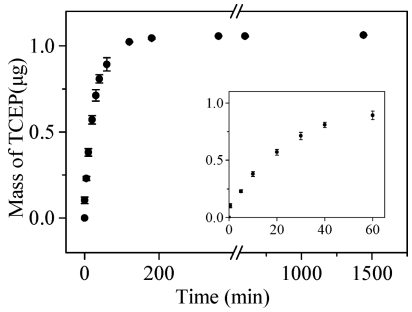

Figure 1. Mass of TCEP accumulated by HLB gels in 10 mL solutions containing 0.01 M NaCl and 100 μg L^{-1} tested OPFRs for 0.5 min to 24 h.

2.42, 2.20, 2.02, 2.06, 1.79, and 1.55 ng min^{-1} cm^{-2} for TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP, respectively. They were much higher than those calculated from DGT devices deployed in 200 μg L^{-1} OPFRs solutions for 24 h at 24 °C (1.02, 0.70, 0.73, 0.86, 0.74, and 0.66 ng min^{-1} cm^{-2} for TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP, respectively). This suggests that HLB gels can adsorb OPFRs rapidly enough to ensure OPFRs concentration at the interface between the diffusive gel and HLB binding gel is effectively zero, which is a requirement for the DGT technique.[24]

Elution Efficiencies of OPFRs Loaded on HLB Gels. Reliable elution efficiencies of OPFRs are required for accurate calculation of DGT-measured concentrations using eq S1. Consistent and stable elution efficiencies of 100% were obtained for the OPFRs using 10 mL of methanol across a series of exposure concentrations (10−200 μg L^{-1}) by extraction in an ultrasonic bath for 30 min (Table S3). High elution efficiencies here are consistent with XAD 18 binding gels for antibiotics[35] and MIP binding gels for 4-chlorophenol.[43] They are also comparable to HLB binding gels for HPCPs[39] and pesticides,[38] but higher than AC binding gels for bisphenols (52−62%)[37] and MAX binding gels for pesticides (46−86%).[38]

DGT Blanks and Method Quantitation Limits. Table 1 summarizes DGT blank concentrations, instrument quantitation limits (IQLs), and DGT method quantitation limits (MQLs) of OPFRs. DGT blank concentrations of OPFRs were achieved by measuring the mass of the analytes on HLB binding gels retrieved from DGT devices which were assembled and left for 24 h without deployment. Table 1 shows that 4 of the studied OPFRs were detected in the HLB gels with quite low concentrations (0.01−0.22 ng per disc), with a little higher detection of TCEP and TCPP (0.75 ± 0.32 and 1.51 ± 0.34 ng per disc). External standard calibration with six OPFRs (0.01−50 μg L^{-1}) were used for quantification. IQL was defined as the lowest point on the calibration curve which could be accurately measured within ±20% of its nominal value. MQLs were calculated from IQLs, assuming that a DGT device with a 0.75 mm thick diffusive gel and a 0.14 mm thick filter membrane was deployed for 14 days at 25 °C. MQLs of the DGT method ranged from 0.25 to 0.32 ng L^{-1} for the studied OPFRs (Table 1). OPFRs in fresh water were 7.3−96 ng L^{-1} in the North American Great Lakes,[10] 0.6−0.8 μg L^{-1} in the River Tiber (Italy),[5] and ∼1 μg L^{-1} in the Songhua River, China.[12] In WWTPs, reported concen-

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Table 1. DGT Blank, Instrument Quantitation Limits (IQLs) of OPFRs Detected by UPLC−MS/MS, and Method Quantitation Limits (MQLs) for Both Water and DGT Samples During Field Application

compd	blank, ng per disc, (mean ± SD), n = 12	IQL[a], μg L^{-1}	recoveries of SPE, % (average ± SD), n = 3	D at 25 °C[b], 10^{-6} cm^2 s^{-1}	MQL[c], ng L^{-1}	
					water	DGT
TCEP	0.75 ± 0.32	0.1	88.2 ± 8.2	5.87	0.11	0.25
TCPP	1.51 ± 0.34	0.1	102 ± 12.1	5.56	0.10	0.26
TDCPP	0.15 ± 0.07	0.1	93.9 ± 3.8	5.11	0.11	0.29
TPrP	0.22 ± 0.07	0.1	69.5 ± 4.1	5.53	0.14	0.26
TBP	0.11 ± 0.05	0.1	66.6 ± 1.7	4.99	0.15	0.29
TBEP	0.01 ± 0.00	0.1	82.4 ± 5.7	4.58	0.12	0.32

[a]IQLs: the lowest point of the calibration curve which can be accurately evaluated within ±20%. [b]D: D_{cell} values were used for assessing MQLs here. [c]MQLs were calculated using following equation for DGT: MQL = $\frac{IQL}{R \times CF}$. R is the recovery of the SPE method for water and elution efficiency (1.0) for DGT. CF (concentration factor) was 1000 for water and calculated using the following equation: CF = $\frac{DAt}{V\Delta g}$. The assumption is that DGT with a 0.14 mm thick PTFE filter membrane, a 0.75 mm thick agarose-based diffusive gel, and a 0.5 mm thick HLB-based binding gel is deployed in waters for 14 days at 25 °C. V is 0.5 mL for DGT.

trations of OPFRs were 3.67−150 μg L^{-1} in Spain,[2] 3.3−16.3 μg L^{-1} in Germany,[8] and 0.8−1.4 μg L^{-1} in China.[44] Given the much lower values of the MQLs for OPFRs than reported concentrations in surface water and WWTPs, DGT coupled with UPLC−MS/MS has the required sensitivity for measurement of OPFRs in waters. If the concentrations of OPFRs in some samples were < MQLs, a longer deployment time or merging two or more HLB binding gels into one sample will improve the measurable mass and reduce the MQLs.

Measurement of Diffusion Coefficient. For use of the DGT method, it is vital to accurately measure diffusion coefficients of targeted analytes. The measurements were carried out, and good linear relationships (r^2 = 0.98−0.99) of diffused masses versus time were obtained (Figure S4) using the diffusion cell device. D_{cell} was calculated using eq 1 and calibrated to 25 °C using eq 3:[36]

$$\log D_t = \frac{1.37023(t-25) + 8.36 \times 10^{-4}(t-25)^2}{109 + t} + \log \frac{D_{25}(273+t)}{298} \quad (3)$$

The D_{cell} diffusion coefficients at 25 °C were 5.87 × 10^{-6}, 5.56 × 10^{-6}, 5.11 × 10^{-6}, 5.53 × 10^{-6}, 4.99 × 10^{-6}, and 4.58 × 10^{-6} cm^2 s^{-1} for TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP, respectively. They are similar to the values of D_{DGT} (6.37 × 10^{-6}, 5.34 × 10^{-6}, 4.63 × 10^{-6}, 5.82 × 10^{-6}, 5.32 × 10^{-6}, and 4.06 × 10^{-6} cm^2 s^{-1} for TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP, respectively) using DGT devices in a well-stirred OPFRs solutions for 24 h. The ratios of D_{cell} to D_{DGT} for all selected OPFRs were in the range 0.89−1.09 (Table S4), indicating the accuracy of diffusion coefficients measured by diffusion cell.

Previous studies demonstrated that diffusion coefficients of chemicals are influenced by their octanol−water partition coefficient (log K_{ow}).[36,41] The K_{ow} reflects the hydrophilicity of analytes, which can influence the diffusion process through diffusion layers. Thus, we further explored the relationship between D and log K_{ow}. A good linear relationship (eq 4, r^2 = 0.98) was obtained for chlorinated alkyl OPFRs (TCEP, TCPP, and TDCPP) and two alkyl OPFRs (TPrP and TBP) (Figure 2), which have similar chemical structures (Figure S1).

$$D_{cell} = 6.411 - 0.344 \log K_{OW} \quad (4)$$

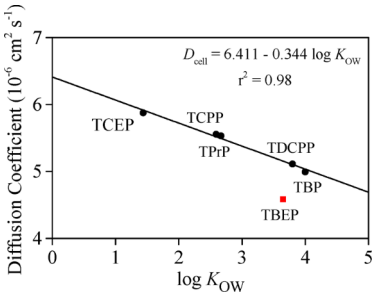

Figure 2. Dependence of diffusion coefficients on log K_{OW}. Solid line was obtained from the linear regression between diffusion coefficients and log K_{OW} values of TCEP, TCPP, TDCPP, TPrP, and TBP.

This relationship may apply to the calculation of D for other OPFRs, which were not included in our study but have similar chemical structures. However, OPFRs with different structures, such as TBEP, did not satisfy this equation.

DGT Performance under Different Conditions. Solution pH could potentially influence adsorbent surface properties and the diffusion of the target analytes and thus affect the DGT measurement. Although changing solution pH (3.12−9.71) did not significantly affect the DGT measurement of OPFRs, with C_{DGT}/C_{soln} ranging from 0.87 to 1.09 (Figure 3), the variability of DGT measurement increased at either end of the pH range, especially at pH 9.71. This could be caused by changes of OPFRs species and accompanying diffusion coefficient change or uncertain effects on adsorbent surface. Results indicate that DGT can accurately measure OPFRs, but more attention should be paid when deployment solutions are relatively acid or alkaline and more replicates (not less than 3) are recommended.

The effect of ionic strength (IS) on DGT performance for measuring OPFRs is demonstrated in Figure S5. The result indicates that most of the OPFRs studied were not significantly influenced by IS in solutions containing 0.0001−0.1 M NaCl, with most ratios of C_{DGT}/C_{soln} in the range 0.9−1.1 (Figure S5). When IS concentration increased to 0.5 M, the ratios of C_{DGT}/C_{soln} for TCEP, TPrP, and TBP remained in the range 0.9−1.1 but for other tested chemicals were slightly lower than expected. No significant reduction in C_{DGT}/C_{soln} was observed (ANOVA, p < 0.05). IS could potentially change the charge density and thus influence the diffusion process of tested chemicals.[26] TDCPP and TBEP, with more chlorine atoms and

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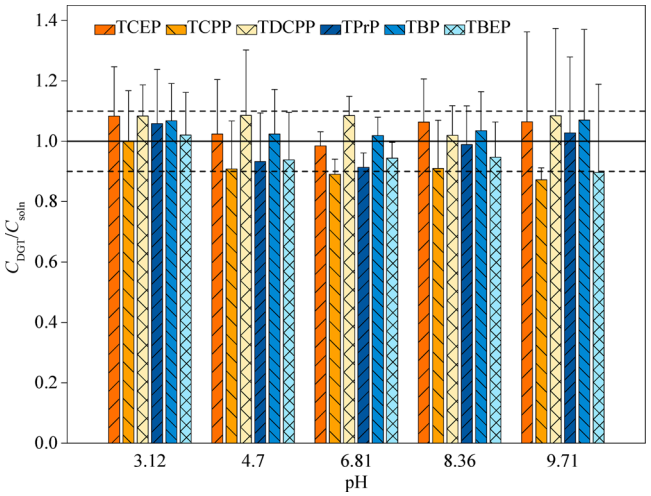

Figure 3. Effects of pH on the ratio of DGT-measured OPFRs concentrations, C_{DGT}, to their concentrations in the bulk solution, C_{soln}. All experiments were performed in solutions of nominally 20 μg L^{-1} OPFRs, containing 0.01 M NaCl. The solid lines represent the target value of 1.00. Values were expressed as mean ± standard deviation of at least three replicates.

oxygen atoms, are more susceptible to charge density change. A similar phenomenon was previously observed when XAD gels were used for illicit drugs, and the possible reason was the reduced hydrophilicity of tested chemicals at high IS.[45]

No significant effect of DOM on DGT measurement was observed in this study. The ratios of C_{DGT}/C_{soln} for most of the tested OPFRs in solution containing 0–20 mg L^{-1} DOM were between 0.9 and 1.12 (Figure S6). DOM tends to bind more hydrophobic organic compounds with higher log K_{ow},[46,47] resulting in bound analytes with larger chemical structures which are difficult to pass through the diffusion layer. Tested OPFRs are relatively hydrophilic with lower log K_{ow} (Table S1) and thus were less influenced. Similar phenomena were observed in Chen et al.'s[39] study on DGT performance for HPCPs, where the ratios of C_{DGT}/C_{soln} of five HPCPs still stay within an acceptable range when DOM concentration increased. Our study indicates that DGT is an effective tool for measuring OPFRs under typical environmental conditions covering a wide range of pH, IS, and DOM.

Effect of Diffusive Gel Thickness and Deployment Time. Accumulated masses of OPFRs by DGT devices containing diffusive gels of different thickness correlated with the reciprocal of the thickness (0.64–2.14 mm) of the diffusive layers (Figure S7). The data points are very close to the theoretical line for all the compounds tested. This indicates that the concentrations of OPFRs can be measured accurately using the DGT technique.

Longer-time deployment of DGT can be used when relatively low concentrations may occur in aquatic systems.[36,37,39,45] The robustness and reliability of DGT in long-time deployment is vital. DGT-measured masses of OPFRs had a linear correlation with the increasing deployment time (3–168 h) and fitted well with the theoretical lines calculated from the known concentrations of deployment solutions using eq S1 (Figure S8). The results are in accordance with Chen et al.'s study on HPCPs with DGT devices containing HLB gels, where the accumulated masses of HPCPs increased linearly with increasing deployment time over 120 h.[39]

Binding Capacity and Competition among OPFRs. Enough capacity is critical for deployments of a long time or in heavily polluted areas. Accumulated masses of OPFRs measured by DGT linearly increased with their increasing solution concentrations. As shown in Figure 4, DGT devices can simultaneously accumulate 25.5, 25.0, 19.9, 18.8, 12.9, and 11.9 μg of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP, respectively, when the deployment solution concentrations reached around 1800 μg L^{-1}. The capacity of HLB gels for binding OPFRs is much higher than 115 μg per disc, which is comparable to that of XAD 18 gels for antibiotics (0.18 mg per disc)[35] and AC gels for bisphenols (140–194 μg per disc).[37] The total capacity for OPFRs here is higher than reported capacities of HLB gels and MAX gels for anionic pesticides (52 and 50 μg per disc for HLB gel and MAX gel, respectively) prepared by Guibal et al.[38] The maximum effective capacities in this study were not reached. If the total concentration of OPFRs at deployment sites is 30 μg L^{-1}, DGT could theoretically be deployed for about 10 months. However,

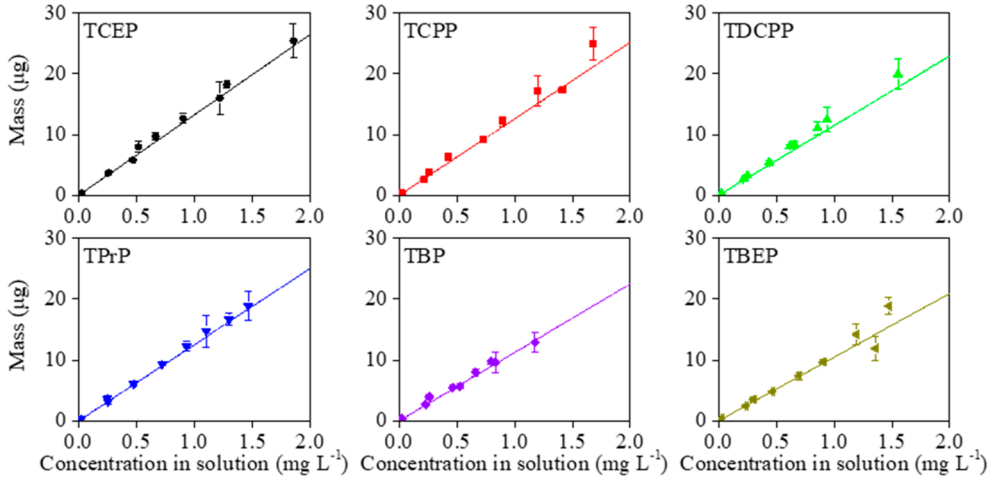

Figure 4. Measured masses of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP accumulated by HLB binding gels within DGT devices deployed in well-stirred solutions at a wide range of concentrations (20–1800 μg L^{-1}), containing 0.01 M NaCl. The solid line represents the theoretical values predicted from the known solution concentrations using eq S1. Error bars were calculated from at least three replicates.

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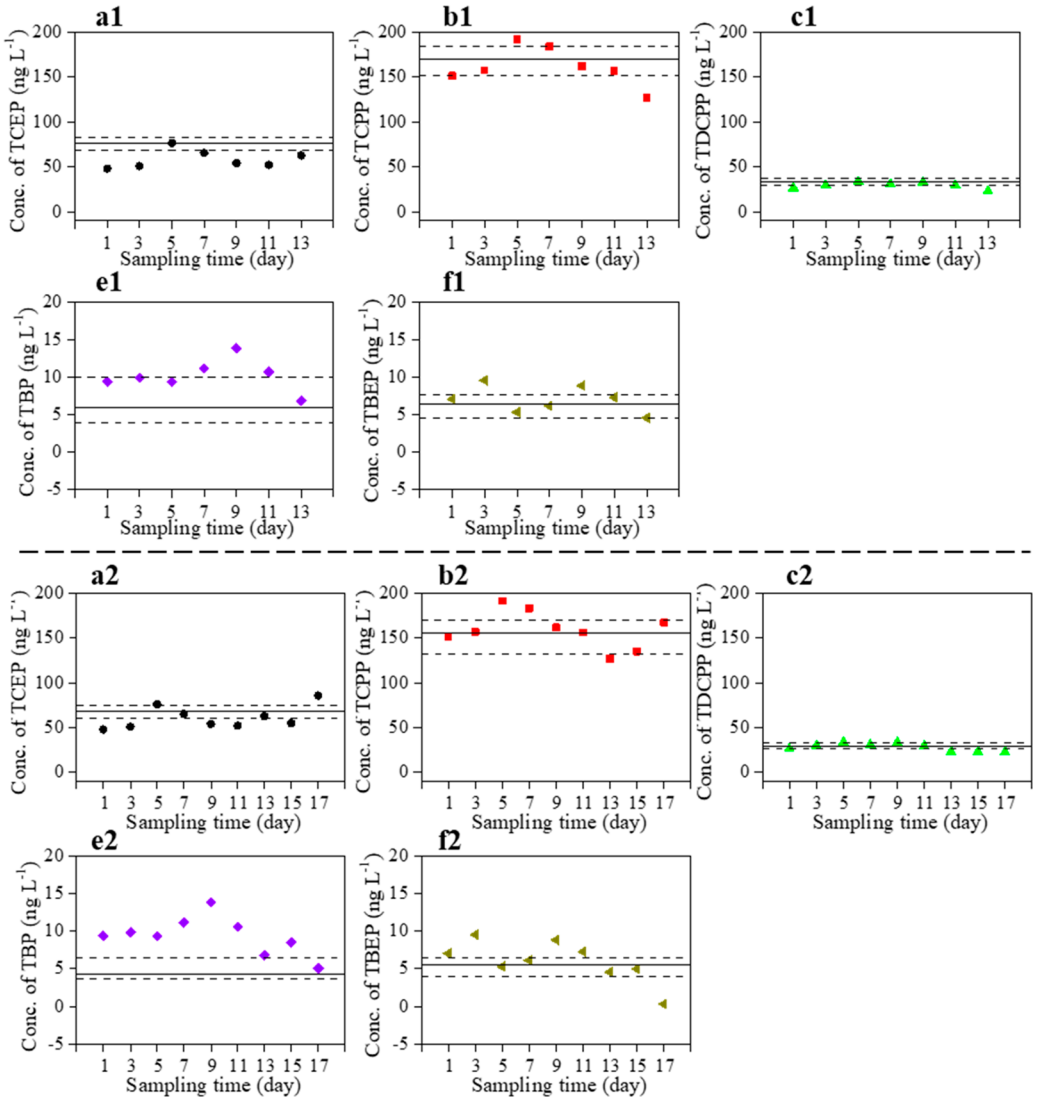

Figure 5. Concentrations of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP in a wastewater treatment plant in Nanjing measured by grab sampling method and DGT over a 12 or 16 d sampling and deployment campaign. The solid line represents the average concentrations of analytes measured by DGT. The upper and the lower dashed lines represent the maximum and minimum concentrations of analytes measured by DGT, respectively. The dots in different shapes and colors represent the concentrations of different analytes measured by the grab sampling method at different times. Data in parts a1−f1 represent the 12 day DGT-measured concentrations of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP, respectively. Data in parts a2−f2 represent the 16d DGT-measured concentrations of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP, respectively. TPrP was not detected by neither grab sampling nor DGT deployment.

given that long-term deployments may be hampered by practical problems, such as biofilm growth on filter membranes, it is suggested that deployment times should be shorter than the theoretical 10 months. When the total concentration of OPFRs is up to 300 μg L^{-1}, DGT can perform for 4 weeks. Reported concentrations of OPFRs were usually at ng L^{-1} levels in surface waters[5,10,12] and from ng L^{-1} to several μg L^{-1} level in WWTPs.[8,9,44] Therefore, the measured binding capacities of DGT devices are enough for monitoring OPFRs in aquatic systems.

DGT devices were deployed in a series of synthetic solutions with different concentration ratios (20−1000 μg L^{-1}) of OPFRs to evaluate whether they would interfere with each other through competitive binding. Table S5 lists the C_{DGT}/C_{soln} values of the studied OPFRs in solutions containing different concentration ratios of OPFRs. No evident interferences among tested chemicals were found, indicating that potential competition effects between OPFRs are probably negligible for conditions tested.

Field Trial at a WWTP Effluent. For field deployment, the storage of the DGT devices was investigated for up to 131 days. DGT performance was not affected by the storage time (Table S6). To verify DGT field performance, the devices were deployed *in situ* in the effluent of a WWTP in Nanjing, China, for 12−16 days in this study (24 °C, pH 7.14). All tested chemicals, except TPrP, were detected in the effluent of the WWTP (Figure 5). Total OPFR concentrations obtained by grab sampling during 12 and 16 day deployment campaigns were 267.9 ± 31.2 and 265.4 ± 30.9 ng L^{-1}, respectively, indicating a relatively stable state of OPFRs concentrations in the effluent of the WWTP. The concentrations of OPFRs are much lower than those reported for other WWTPs, including WWTPs in Spain (μg L^{-1} level),[2] Sweden (7.9−39 μg L^{-1}),[4] and Austria (several μg L^{-1}).[48] This could be because the

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selected WWTP was located in a rural area and received less polluted discharges than the industrial wastewaters received by other WWTPs reported with high concentrations of OPFRs.[3,4] However, OPFR concentrations in selected WWTP effluent are comparable to that in an industrial WWTP in Germany (397 ng L^{-1}).[3] Most of the DGT measured concentrations were within the maximum and minimum grab sampling measured values (Figure 5), demonstrating that DGT is suitable for measuring OPFRs in effluents of WWTPs.

CONCLUSIONS

This work established a novel method for *in situ* monitoring of OPFRs in waters and WWTP using a DGT technique. The method provides stable and reliable time-integrated recoveries for all tested OPFRs and is not limited by pH, ionic strength, and dissolved organic matters, showing capability for a wide range of environmental conditions. The capacity of the DGT device is large enough for long-time deployment without any competition effect or deterioration. Method quantitation levels of sub-ng L^{-1} make it an appropriate technique for measuring OPFRs in areas with ultralow concentrations. Compared to other passive samplers, the ease-of-use due to their independence of flow rate and no calibration needed would make the DGT method an applicable technique for *in situ* monitoring OPFRs in various types of waters and aquatic systems. The DGT method is rarely dependent on sample matrix and thus can further be applied to various complicated environments, including highly polluted wastewater and even seawaters.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.analchem.8b02480.

Detailed principles of DGT technique and detailed information on tested chemicals, analytical methods, and QA/QC; detailed information on methods to check potential adsorption onto materials and aging effect; results and discussion on potential adsorption onto materials and aging effect; and tables and figures of potential adsorption onto materials, elution efficiencies, diffusion coefficients, uptake kinetics, effects of IS, DOM, diffusive gel thickness, deployment time, binding gel storage time, and competition binding (PDF)

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Notes

The authors declare no competing financial interest.

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Supporting Information for

Novel method for *in situ* monitoring of organophosphorus flame retardants in waters

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Chemical analysis.

Evaluation of potential adsorption onto filter membranes, diffusive gels and DGT moldings.

Aging effect.

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3. Results and Discussion

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Aging effect of HLB binding gels.

Table S1. Physiochemical properties of selected analytes

Table S2. Optimal instrumental parameters of ultra performance liquid chromatography tandem mass spectrometry used in this study.

Table S3. Elution efficiencies (%) of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP for different loaded masses of the analytes bound onto HLB gels eluted with 10 mL methanol for 30 min in an ultrasonic bath. (n=3)

Table S4. Diffusion coefficients of six tested OPFRs and the ratios of D_{cell} to D_{DGT} of corresponding analytes.

Table S5. The ratio of concentrations of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP measured by DGT to concentrations in solutions with different concentration ratios of

OPFRs.

Table S6. The ratio of concentrations of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP measured by DGT with HLB gels stored for different time to concentrations in solutions.

Figure S1. Chemical structures of tested OPFRs and HLB resin.

Figure S2. Adsorption of OPFRs onto three different filter membranes, two different diffusive gels and DGT moldings. Error bars were calculated from the standard deviations of three replicates..

Figure S3. Mass of TCPP, TDCPP, TPrP, TBP, and TBEP accumulated by HLB gels in 10 mL solutions containing 0.01 M NaCl and 100 μg L^{-1} tested OPFRs for 0.5 min to 24 h. Error bars represent the standard deviation of three replicates.

Figure S4. Diffused masses of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP in the acceptance compartment through 0.75 mm thick agarose diffusive gel at different time in a stainless diffusion cell device with 1.0 mg L^{-1} analytes at the source compartment at the beginning.

Figure S5. Effects of ionic strength on the ratio of DGT-measured OPFRs concentrations, C_{DGT}, to their concentrations in the bulk solution, C_{soln}.

Figure S6. Effects of dissolved organic matters on the ratio of DGT-measured OPFRs concentrations, C_{DGT}, to their concentrations in the bulk solution, C_{soln}.

Figure S7. Masses of TCEP, TCPP, TDCPP, TPrP, TBP and TBEP accumulated by HLB gels in DGT devices with different diffusive gel thickness (0.5–2.00 mm) deployed in well-stirred solution of nominally 20 μg L^{-1} OPFRs, containing 0.01 M

NaCl.

Figure S8. Measured masses of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP accumulated by HLB binding gels within DGT devices deployed in well-stirred solutions at different times (3-168h), containing 0.01 M NaCl.

Figure S9. SEM images of HLB gel. Scale at 100 μm (left) and 500 μm (right).

1. Detailed principles of DGT technique

DGT technique is based on Fick's first law of diffusion. The transport of analytes from water to binding agents in DGT sampler is solely controlled by the chemical potential difference along the diffusion passway.[1] Derived from the existing formulas, the analyte concentration measured by DGT, C_{DGT}, is calculated using eq. S1.[1]

$$C_{\mathrm{DGT}}=\frac{M\cdot(\Delta g+\delta)}{D\cdot A\cdot t} \tag{S1}$$

While M is the mass of target pollutants accumulated on the binding gel, Δg expresses the thickness of the diffusion layer, δ is the diffusive boundary layer (DBL) thickness, D represents the diffusion coefficient of target pollutants, A means the area of DGT device exposed to bulk solution and t is the deployment time. In most cases, the thickness of DBL is much smaller than that of a diffusion layer.[2,3] So external environmental conditions has little influence on DGT measurement and DBL thickness is often neglected under well stirred conditions.

2. Method and Materials

Reagents, materials, and solutions. Standards for tris(2-chloroethyl) phosphate (TCEP), tris(2-chloroisopropyl) phosphate (TCPP), tris(1,3-dichloro-2-propyl) phosphate (TDCPP), tri-n-propyl phosphate (TPrP), tri-n-butyl phosphate (TBP), and tris(2-butoxyethyl) phosphate (TBEP) were purchased from Dr. Ehrenstorfer GmbH (Germany). Surrogate standard, deuterated tributyl phosphate (d_{27}-TBP, 98–99%), was obtained from Cambridge Isotope Laboratories. Detailed information of analytes on physicochemical properties is listed in Table S1. (See structures of tested OPFRs in Figure S1) Stock solutions of TCEP, TCPP, TDCPP, TBP, or TBEP were prepared at 2500 mg L^{-1}, while TPrP at 1000 mg L^{-1} in methanol (Merck, HPLC grade) and stored at –20 °C in sealed amber glass bottles. Mixture solution of the six tested OPFRs were prepared at 100 mg L^{-1} for each chemical by diluting stocking solutions and stored at 4 °C in sealed amber glass bottles. All experiments were performed with Milli-Q (MQ, 18.2 MΩ·cm, Millipore, United States) water except for field deployment. Standard DGT moldings were made of acetonitrile-butadiene-styrene (ABS) and purchased from DGT Research Ltd, UK. Glass-made containers (2–6 L) and stainless steel holders were used for laboratory deployment experiments. HLB resins used for binding gel making were extracted from Oasis-HLB SPE cartridges (6g, Waters, USA). HLB resins were thoroughly conditioned with methanol and stored in MQ water before use. (See HLB resin structure in Figure S1) Hydrophilic polytetrafluoroethylene (PTFE) and cellulose acetate (CA) filter membranes were purchased from Shanghai Anpel Scientific Instrument Co. China, while polyether

sulfone (PES) filter membranes were purchased from Pall Co., USA. All filter membranes were with diameters of 25 mm and pore sizes of 0.45 μm.

Chemical analysis. All OPFRs eluents were filtered with 0.22 μm PTFE filters before analyzed with UPLC–MS/MS. OPFRs analyses were performed with PerkinElmer A30 Altus™ UPLC system coupled with PerkinElmer Qsight™ 210 triple quadrupole mass spectrometer. Two solvents (mobile phase A: MQ water containing 0.1% formic acid; mobile phase B: acetonitrile) flowed through an Brownlee SPP C18 column (2.1 × 100mm, 2.7μm) at 300 μL min^{-1} to separate different analytes. Xbridge™ BEH C18 column (2.1 × 100mm, 3.5μm) was placed in-line between the solvent mixer and the injector as an isolator column to reduce the instrument background. Mobile phase gradients were set as follows:0–0.5 min 40–40% B; 0.5–5 min: 40–95% B; 5–6 min: 95–95% B; 6–6.1 min: 95–40% B; 6.1–9 min: 40–40% B. Detailed parameters of instrument and analytes were shown in Table S2.

Evaluation of potential adsorption onto filter membranes, diffusive gels and DGT moldings. In order to check the potential adsorption of OPFRs onto different parts of DGT device, three kinds of filter membranes including polyether sulfone (PES), cellulose acetate (CA), and polytetrafluoroethylene (PTFE), and two types of diffusive gels including polyacrylamide gels cross-linked with an agarose derivative (APA), and pure agarose gels (AGE) were soaked in 10 ml of 100 μg L^{-1} OPFRs solutions and then shaken horizontally for 24 h, while DGT moldings were soaked in 100 ml of 100 μg L^{-1} OPFRs solutions due to their relatively larger geometrical volumes. All samples were in triplicate. Concentrations of OPFRs before and after

exposure and the concentrations of OPFRs in control samples were measured to obtain the potential adsorbed mass by filter membranes, diffusive gels and DGT moldings.

Aging effect. DGT devices incorporated with HLB binding gels stored in 0.01 M NaCl solutions at 4 $^{\circ}$C for different times (60, 81, 116, and 131 d) were immersed in 2.5 L of well-stirred 20 μg L^{-1} OPFRs solutions containing 0.01 M NaCl for 24 h.

Quality assurance and quality control. All DGT deployments in laboratory were performed in at least triplicates and the results were expressed as the means ± standard deviations of the replicates. When performing deployment experiments, at least 3 HLB gels in DGT devices without deployment were retrieved and eluted as blanks. To validate the analytical procedure of water samples, 500 mL MQ water samples were spiked with 10 ng standards of selected OPFRs. The recoveries of all water samples were satisfactory, ranging from 67 to 102% with deviations ranging among 1.7–12.1%. In addition, 10 ng of surrogate standard, d_{27}-TBP, was added to all water samples before performing solid-phase extraction. Acceptable recoveries were obtained for both MQ water samples (70.6 ± 7.2%) and field water samples (67.9 ± 8.9%). Consistent recoveries of d_{27}-TBP between MQ water samples and field water samples indicate appropriate pretreatments for every sample.

3. Results and Discussion

Possible sorption onto filter membranes, diffusive gels and DGT moldings. In order to assure good performance of DGT on measuring OPFRs, it is necessary to select components with low sorption ability of OPFRs for DGT device making except binding gels. From Figure S2, all three filter membranes exhibited adsorption on TDCPP to a certain degree while CA filters almost adsorbed all of the six studied analytes (>90% on average). Considering large amount of analytes in the environment and long deployment time, this deviation could be acceptable. The studied OPFRs adsorbed by APA or AGE were almost all less than 5% (Figure S2), declaring both can be used as the diffusive gels. Given that OPFRs have larger pore sizes than inorganic metal species, [4] AGE would be better for organics. As shown in Figure S2, DGT moldings rarely adsorbed the selected OPFRs except TDCPP. Preliminary experiments (data not shown) demonstrated that DGT moldings are less capable of accumulating OPFRs than HLB binding gels. Hence, once the analytes were bound to the HLB gels, they would never transfer to DGT moldings. Yet, this phenomenon might have some effects on performance characterization of TDCPP in laboratory due to limited volume of solutions, but not on field deployment since the volume of natural waters was large enough to offset the loss of TDCPP induced by DGT moldings.

Aging effect of HLB binding gels. The performance of DGT devices containing HLB gels, which had been stored in 0.01 M NaCl solution for 60, 81 116, and 131 days from preparation, are listed in Table S6. No significant differences (ANOVA, $p >$

0.05) of the C_{DGT}/C_{soln} values were observed for most studied OPFRs. These findings are indicative of HLB binding gel's reliable performance on monitoring OPFRs for up to 4 months. HLB binding gels were protected by DGT moldings (a cap and a base) and filter membranes during field deployment, so they were rarely influenced by external factors. Thus, although the aging effect test only considered synthetic solutions, these results are of great reference value to DGT deployment in the actual environment.

Table S1. Physiochemical properties of selected OPFRs.[5]

Analyte name	Abbreviation	CAS number	Formula	Solubility (mg L^{-1})	Log Kow	Mw (g/mol)
Tris(2-chloroethyl) phosphate	TCEP	115-96-8	$C_6H_{12}O_4PCl_3$	7000	1.44	285.5
Tris(2-chloroisopropyl) phosphate	TCPP	13674-84-5	$C_9H_{18}Cl_3PO_4$	1600	2.59	327.6
Tris(1,3-dichloro-2-propyl) phosphate	TDCPP	13674-87-8	$C_9H_{15}Cl_{16}O_4P$	1.5	3.8	430.9
Tri-n-propyl phosphate	TPrP	513-08-6	$C_9H_{21}O_4P$	827	2.67	224.2
Tri-n-butyl phosphate	TBP	126-73-8	$C_{12}H_{27}PO_4$	280	4.00	266.3
Tris(2-butoxyethyl) phosphate	TBEP	78-51-3	$C_{18}H_{39}O_7P$	1200	3.65	398.5

Table S2. Optimal instrumental parameters of ultra performance liquid chromatography tandem mass spectrometry used in this study.

Compound	Q1 mass	Q2 mass	EV(V)	CCL2(V)	CC(eV)	Retention time (min)
TCEP	284.9	63.2	15	-70	-47	1.79
	284.9	161.1	15	-70	-22	1.79
TCPP	329.1	99.0	15	-84	-50	3.73
	327.0	99.0	15	-84	-49	3.73
TDCPP	430.8	99.0	15	-84	-49	4.64
	432.8	99.0	15	-88	-50	4.64
TPrP	225.0	99.0	15	-64	-39	3.23
	225.0	140.9	15	-44	-13	3.23
TBP	267.1	99.0	15	-76	-40	4.92
	267.1	155.1	15	-56	-13	4.92
TBEP	399.2	199.1	15	-84	-19	5.27
	399.2	299.1	15	-80	-17	5.27
D27-TBP	294.20	101.80	15	-76	-32	4.83
	294.20	166.10	15	-64	-15	4.83

Table S3. Elution efficiencies (%) of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP for different loaded masses of the analytes bound onto HLB gels eluted with 10 mL methanol for 30 min in an ultrasonic bath. (n=3) S.D. means standard deviation.

Exp. Conc./ μg L^{-1}	TCEP	TCPP	TDCPP	TPrP	TBP	TBEP
10	100±3.5	109±4.8	93.2±5.7	96.6±3.5	112±4.3	98.1±10.2
20	106±3.2	95.0±7.6	100±6.1	95.4±4.7	105±5.0	94.9±9.9
50	95.9±2.2	93.4±2.8	92.3±1.2	94.4±2.3	103±1.5	104±6.6
100	102±1.6	95.9±1.4	96.4±4.3	98.6±1.9	106±1.5	104±8.3
200	107±1.7	103±1.1	101±3.5	105±2.9	102±1.1	104±0.9
Mean	102	99.4	96.5	98.0	106	101
S.D.	4.4	6.7	3.9	4.3	3.8	4.1

Table S4. Diffusion coefficients of six tested OPFRs and the ratios of D_{cell} to D_{DGT} of corresponding analytes.

Diffusion Coefficient /10^{-6} cm^2 s^{-1}	TCEP	TCPP	TDCPP	TPrP	TBP	TBEP
D_{cell}	5.87	5.56	5.11	5.53	4.99	4.58
D_{DGT}	6.37	5.34	4.63	5.82	5.32	4.06
D_{DGT}/Dcell	1.09	0.96	0.91	1.05	1.07	0.89

Table S5. The ratio of concentrations of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP measured by DGT to concentrations in solutions with different concentration ratios of OPFRs. Values were expressed as mean ± standard deviation of at least three replicates.

Solutions	TCEP	TCPP	TDCPP	TPrP	TBP	TBEP
20 μg L^{-1} ClOPFRs, 100 μg L^{-1} alkyl OPFRs	1.14±0.16	0.97±0.15	1.04±0.16	1.12±0.14	1.17±0.17	1.07±0.17
20 μg L^{-1} ClOPFRs, 1000 μg L^{-1} alkyl OPFRs	0.95±0.02	0.88±0.07	0.90±0.07	0.94±0.06	1.05±0.07	0.93±0.09
100 μg L^{-1} ClOPFRs, 20 μg L^{-1} alkyl OPFRs	1.04±0.17	0.93±0.16	0.99±0.17	1.06±0.19	1.05±0.23	0.91±0.18
100 μg L^{-1} ClOPFRs, 1000 μg L^{-1} alkyl OPFRs	0.99±0.03	1.00±0.02	0.76±0.02	0.88±0.03	1.04±0.02	1.03±0.01
1000 μg L^{-1} ClOPFRs, 20 μg L^{-1} alkyl OPFRs	0.95±0.10	0.92±0.06	0.95±0.06	0.84±0.05	0.78±0.05	0.66±0.05
1000 μg L^{-1} ClOPFRs, 100 μg L^{-1} alkyl OPFRs	0.83±0.11	0.82±0.09	0.80±0.15	0.88±0.06	1.09±0.12	1.02±0.21

ClOPFRs is short for chlorinated alkyl OPFRs, including TCEP, TCPP, and TDCPP. Alkyl OPFRs include TPrP, TBP, and TBEP.

Table S6. The ratio of concentrations of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP measured by DGT with HLB gels stored for different time to concentrations in solutions. Values were expressed as mean ± standard deviation of at least three replicates.

Time (d)	TCEP	TCPP	TDCPP	TPrP	TBP	TBEP
131	1.06±0.10	0.80±0.08	0.84±0.12	0.89±0.09	0.99±0.11	0.82±0.09
116	0.97±0.14	0.69±0.09	0.81±0.13	0.86±0.12	0.89±0.12	0.77±0.11
81	1.15±0.14	0.97±0.16	0.97±0.15	1.09±0.15	1.08±0.15	0.90±0.15
60	1.01±0.17	0.86±0.15	0.80±0.16	0.96±0.16	0.96±0.18	0.74±0.11

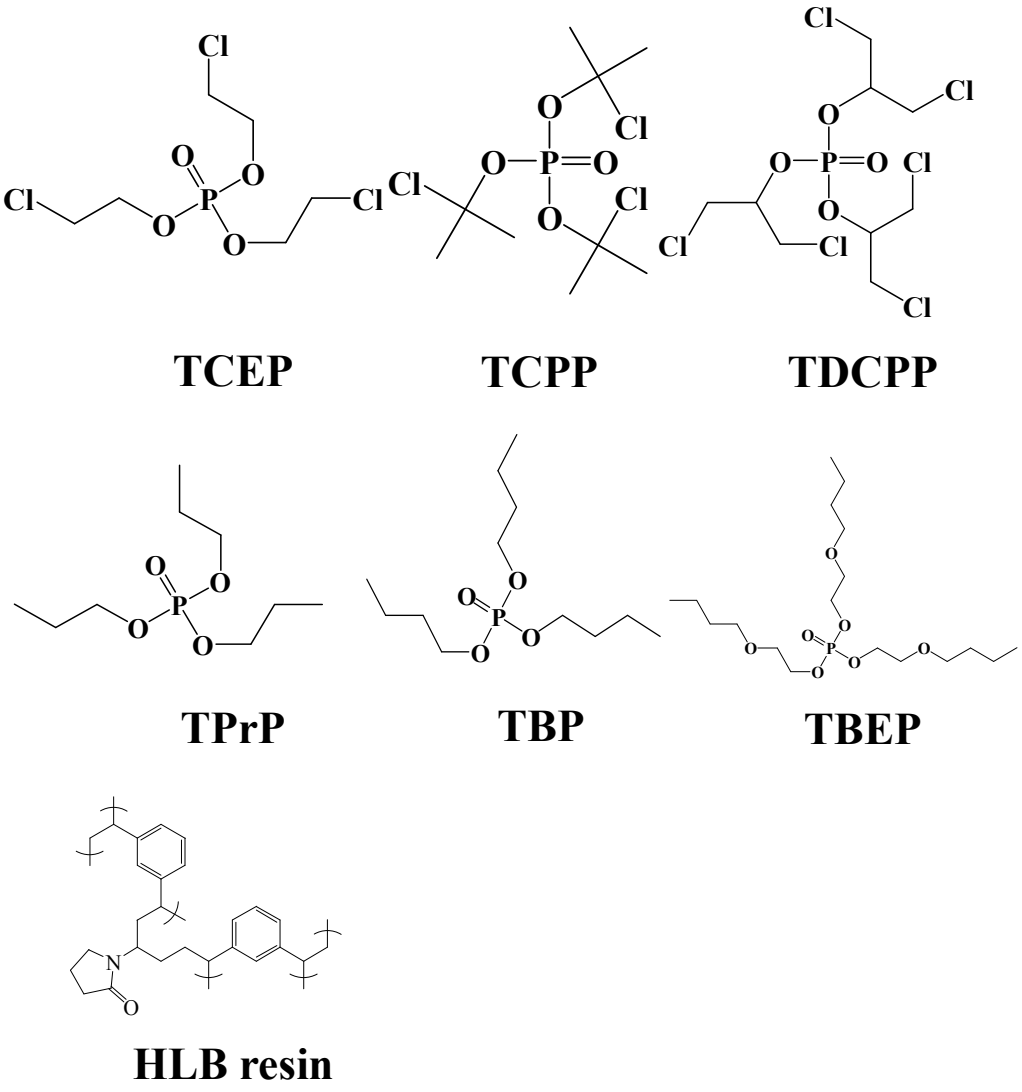

Figure S1. Chemical structures of tested OPFRs and HLB resin.

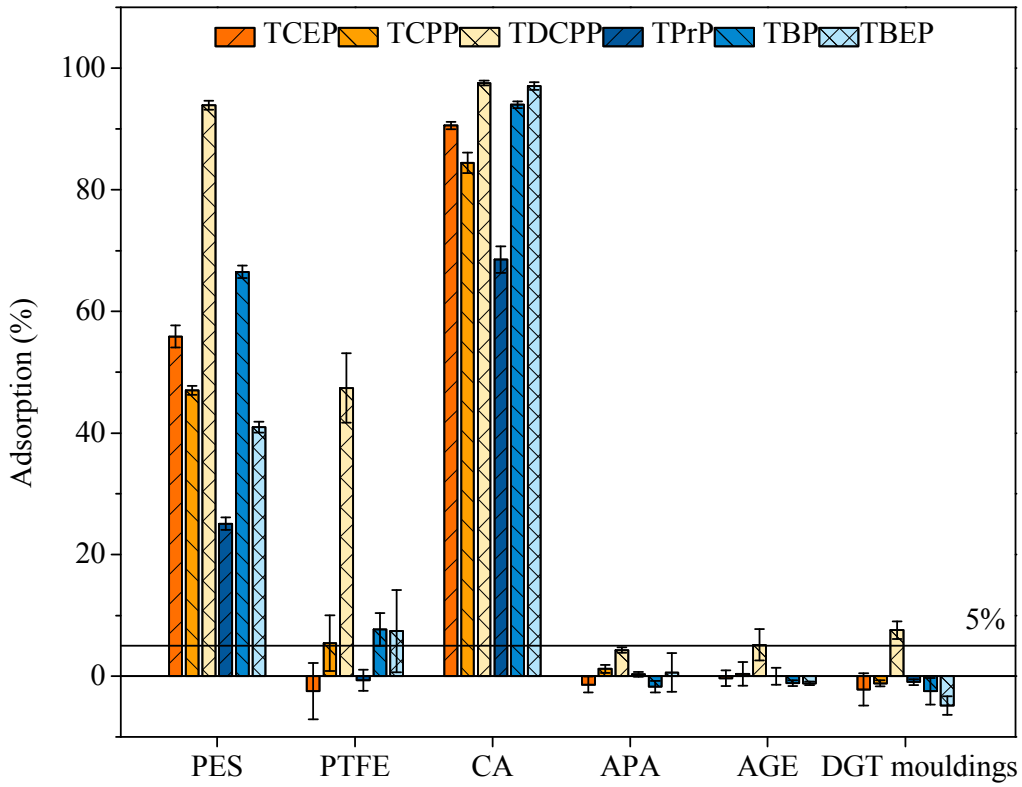

Figure S2. Adsorption of OPFRs onto three different filter membranes, two different diffusive gels and DGT moldings. Error bars were calculated from the standard deviations of three replicates.

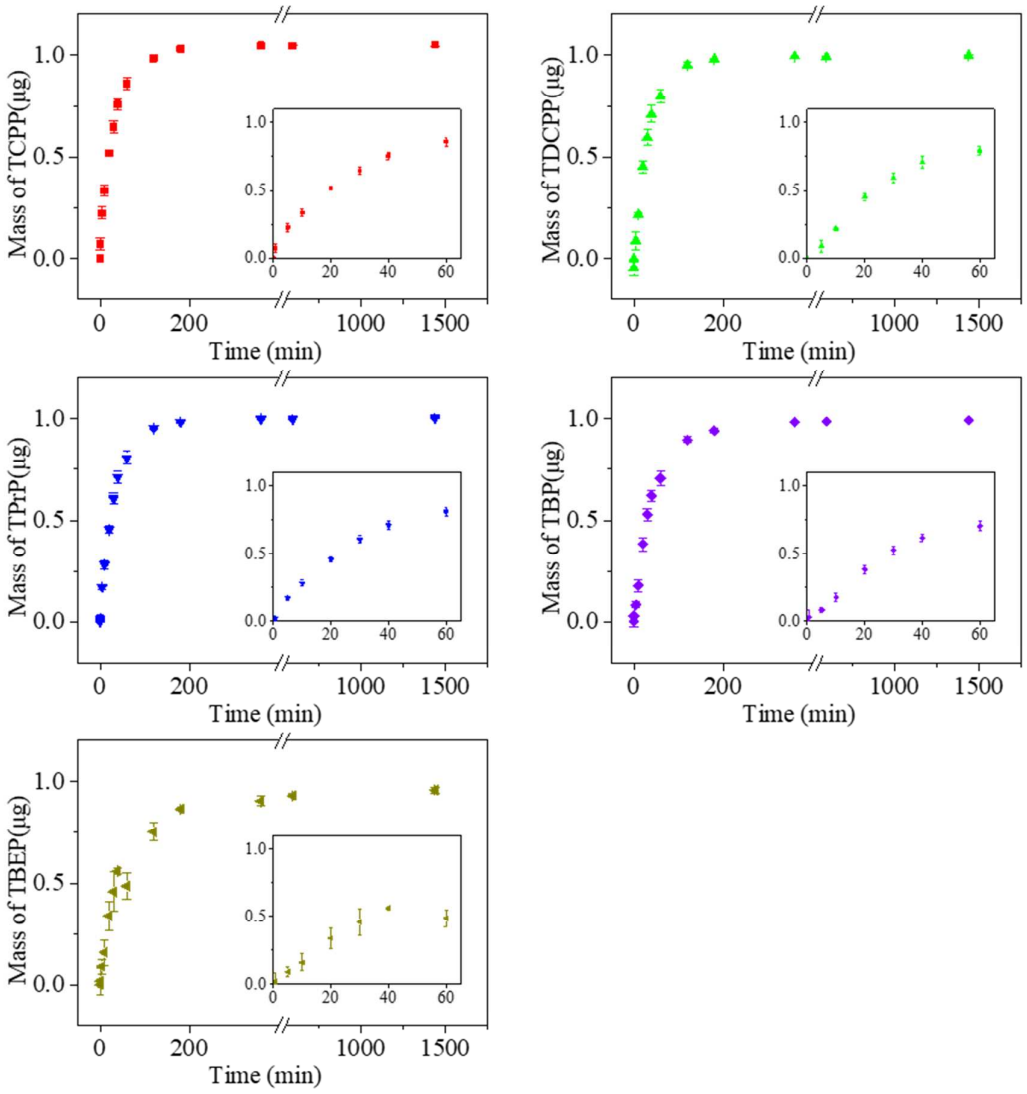

Figure S3. Mass of TCPP, TDCPP, TPrP, TBP, and TBEP accumulated by HLB gels in 10 mL solutions containing 0.01 M NaCl and 100 μg L^{-1} tested OPFRs for 0.5 min to 24 h. Error bars represent the standard deviation of three replicates.

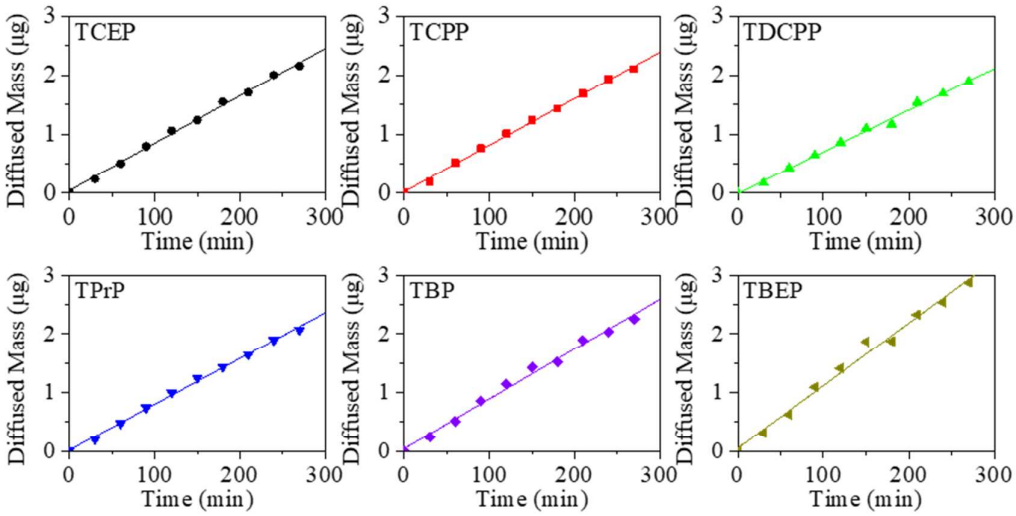

Figure S4. Diffused masses of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP in the acceptance compartment through 0.75 mm thick agarose diffusive gel at different time in a stainless diffusion cell device with 1.0 mg L^{-1} analytes at the source compartment at the beginning. Conditions: pH = 5.9 ± 0.2; temperature = 22.1 ± 0.2 °C, ionic strength = 0.01 M NaCl.

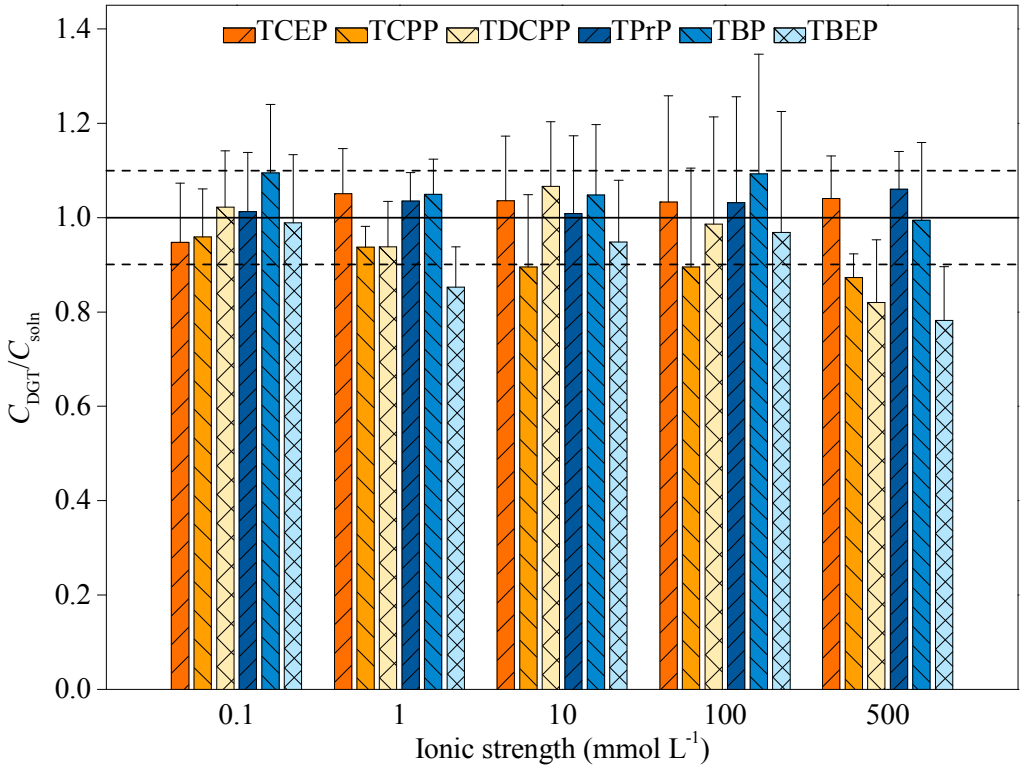

Figure S5. Effects of ionic strength on the ratio of DGT-measured OPFRs concentrations, C_{DGT}, to their concentrations in the bulk solution, C_{soln}. All experiments were performed in solutions of nominally 20 μg L^{-1} OPFRs. The solid line represents the target value of 1.00. Values were expressed as mean ± standard deviation of at least three replicates.

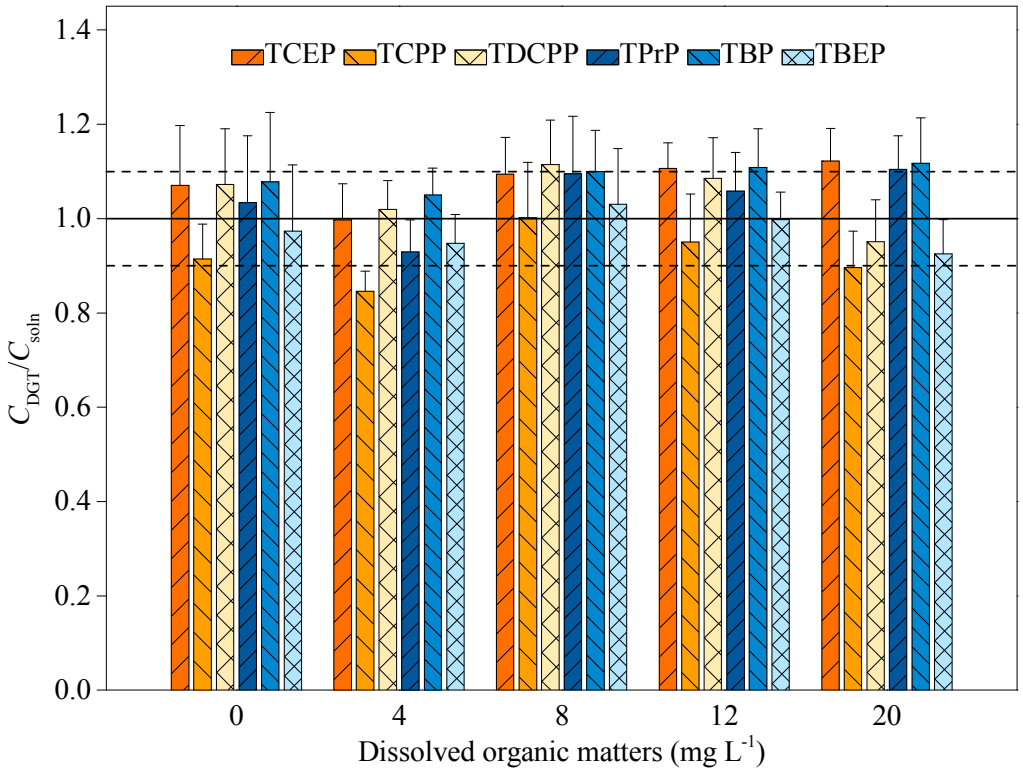

Figure S6. Effects of dissolved organic matters on the ratio of DGT-measured OPFRs concentrations, C_{DGT}, to their concentrations in the bulk solution, C_{soln}. All experiments were performed in solutions of nominally 20 μg L^{-1} OPFRs, containing 0.01 M NaCl. The solid line represents the target value of 1.00. Values were expressed as mean ± standard deviation of at least three replicates.

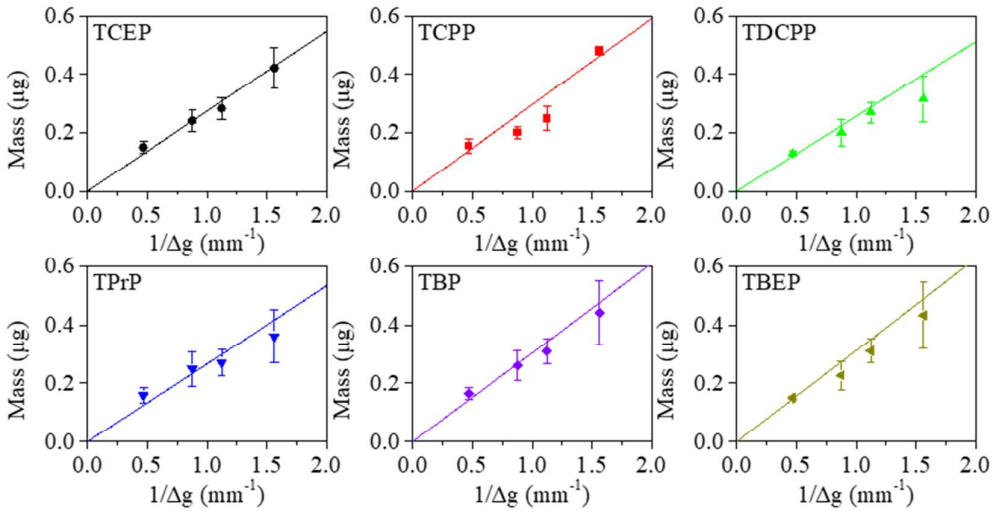

Figure S7. Masses of TCEP, TCPP, TDCPP, TPrP, TBP and TBEP accumulated by HLB gels in DGT devices with different diffusive gel thickness (0.5–2.00 mm) deployed in well-stirred solution of nominally 20 μg L^{-1} OPFRs, containing 0.01 M NaCl. The solid lines represent the theoretical values predicted from eq. S1. Error bars were calculated from three replicates.

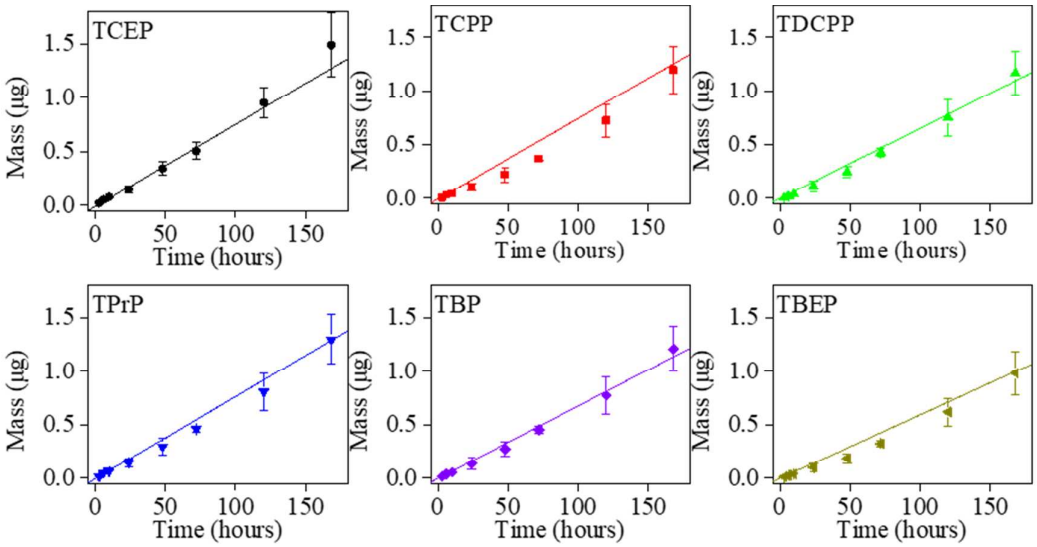

Figure S8. Measured masses of TCEP, TCPP, TDCPP, TPrP, TBP, and TBEP accumulated by HLB binding gels within DGT devices deployed in well-stirred solutions at different times (3-168h), containing 0.01 M NaCl. The solid line represents the theoretical values predicted from the known solution concentrations using eq. S1. Error bars were calculated from three replicates.

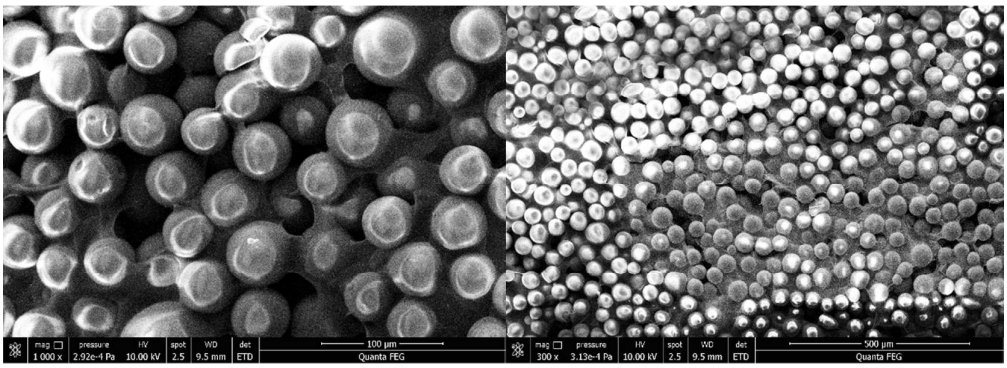

Figure S9. SEM images of HLB gel. Scale at 100 µm (left) and 500 µm (right).

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