
**Title:** Comment on “Time-frequency techniques in biomedical signal analysis: A tutorial review of similarities and differences” by M. Wacker and H. Witte

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In commenting on the review by Wacker and Witte [1], we would like to applaud the authors’ emphasis on the importance of being able to treat signals with time-varying properties: this feature is universal in time series derived from measurements on living systems. From a physics perspective, life always corresponds to a thermodynamically open system, for which energy and matter are being exchanged freely with the environment. Consequently, the oscillatory processes associated with life have natural frequencies and amplitudes that are continuously modulated by external influences. From the perspective of mathematics, they are non-autonomous oscillators and must be treated as such.

The authors have provided a systematic review of the main methods currently available for time-frequency analysis of biomedical signals. The continuous wavelet transform has indeed been the main work-horse for the analysis of such time-series, ever since it was introduced for the study of oscillatory processes in e.g. heart rate variability [2,3] and blood flow [4]; and the other methods reviewed [1] certainly have their merits. We would like to point out, however, that there are additional approaches of which the reader should also be aware. We describe some of them below, but first we expand slightly on the physiological and medical applications of the continuous wavelet transform, complementing the mainly EEG-related discussion of [1] by mentioning some applications to signals derived from the cardiovascular system.

Multiresolution wavelet analysis was reported to discriminate between healthy subjects and those with cardiac pathology [5]; the continuous wavelet transform, using the Morlet mother wavelet, enabled the extraction of characteristic frequencies in blood flow [6], and their association with particular physiological processes [7]. The wavelet transform has been used e.g. as a filter for denoising single events [8] and to reveal endothelial dysfunction in diabetes mellitus [9], post-acute myocardial infarction [10], congestive heart failure [11], hypertension [12], and ageing [13,14]. Its great advantage lies in the possibility of logarithmic frequency resolution, enabling a very wide range of frequencies to be encompassed, a feature that is often essential in the analysis of physiological time series. The synchrosqueezed wavelet transform [15] has brought some additional advantages, being especially useful for phase detection [16] as it provides optimal time-frequency localisation.

In dealing with time series from systems whose frequencies and amplitudes vary in time, several distinct, often coexisting problems must be overcome: (i) To identify basic oscillatory components, despite the time-variations; (ii) to discriminate between oscillatory components that may have nearby characteristic frequencies which, with noise and time-variability, may pose a very difficult problem; (iii) furthermore, there may be a mixture of harmonics and basic components, all with nearby frequencies to be distinguished. Where there are several oscillatory components, it may be useful to investigate the interactions that occur between the underlying physiological processes by studying measures of e.g. synchronization, coherence, phase coherence, bispectral density, couplings, coupling functions, and direction of coupling. We will enlarge briefly on these methods.

Ambiguities can arise in the analysis of signals containing oscillatory contributions at different frequencies, as commonly occur in physiological applications. Because of inherent nonlinearities, higher harmonics will be present in addition to basic frequencies, and an observed component may either be due to a real oscillatory process at that frequency or may just represent a harmonic of another lower-frequency process. The distinction can be especially hard to draw when several time-variable frequencies are present, combined with random noise, but a method [17] based on mutual information combined with surrogate testing [18] enables the question to be settled in most cases.
As indicated in [1], wavelet phase coherence analysis [19-21] can be used to establish whether there is a relationship between the oscillatory processes giving rise to two complex signals, even where there is time variability and noise. Time-localised wavelet phase coherence has been applied to test [21] the possible influence of arterial blood pressure on intracranial pressure (ICP) in intensive care, related to the preservation or otherwise of ICP auto-regulation.

Synchronization analysis [22] provides another method that is robust in the face of time-varying frequencies in the presence of noise. It has been applied to investigate the cardio-respiratory interaction by many authors. Where bivariate data are being analysed, it is quite possible for both frequencies to vary together with time, mutually locked at a particular synchronization ratio (which in general is not 1:1). Alternatively, the ratio may evolve discontinuously with time e.g. during the induction of, or awakening from, anaesthesia [23], or during exercise [24]. The ratio can be found either by plotting a synchrogram [22] or by the calculation of synchronization indices [25].

Where two oscillatory processes are tending to synchronise, thus demonstrating an underlying interaction, it is interesting to ask which process is dominant, i.e. which oscillator is mainly the driver and which of them is adjusting its frequency and amplitude mainly on account of being driven? This directionality of interaction can be established either by an analysis of phase dynamics [26], by the use of information theory [27], or by wavelet-based bispectral analysis [28]. For example, evaluation of coupling strengths showed causal interaction between the phases of respiration and δ-waves in the EEG and how it changes in anaesthesia [29]. Arguably, however, one the most complete way of describing the interaction between two oscillatory processes, based on measurements of their time series, is by calculation of their coupling functions [30]. Bayesian inference enables coupling functions to be followed efficiently as they change with time in the presence of noise, as demonstrated by application of this method to study the cardio-respiratory interaction as a function of time [31,32].

In conclusion, we agree with Wacker and Witte [1] that the use of time-frequency methods is virtually mandatory for the meaningful analysis of biomedical time series. It is a rapidly evolving area of scientific endeavour, with a steady stream of new methods being proposed and validated.

References


