

# The dynamics of quasiparticles in a toy model of the KcsA biological ion channel

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**Abstract**—We study the highly-concerted motion of ions in a narrow biological ion channel (KcsA) by considering the notion of a quasiparticle, with specific focus on the transition process. Namely, we show that the ion entering or exiting the channel is correlated with the position of the quasiparticle. This result is of importance in the rate theories of ion conduction through narrow channels and artificial nanopores.

**Index Terms**—Ion channel; highly-correlated ionic motion; quasiparticle; effective potential; transition process; Brownian dynamics; statistical physics

## I. INTRODUCTION

The healthy evolution of a biological cell severely depends on the functioning of ion channels – proteins allowing for the passive transport of ions across the otherwise impermeable cellular membrane [1]. Due to its pharmacological importance, this topic has attracted the enormous attention both theoretically and experimentally. The underlying question – how to connect the channel’s function to its structure, – still uncovers new unstudied facets and, consequently, provides challenges and reason for further investigation.

A major challenge is the theoretical description of conductivity and selectivity of a given channel. The permeation of ions through the channel’s pore can be described by a number of methods, depending on the required level of details. Molecular dynamics, arguably the most realistic approach, considers all atoms and ions separately, but due to the pairwise nature of interactions a computation requires a lengthy simulation run. Brownian dynamics avoids this caveat at the cost of implicit inclusion of ion-water collisions via the noise terms. Continuous methods, e.g. the classical Poisson-Nernst-Planck theory [2], represent ions as a continuum, but due to the absence of ion-ion interactions it fails to properly describe correlated ionic motion inside the channel.

Recently, the concept of the quasiparticle (QP) was introduced to describe the highly correlated motion of ions in a narrow ion channel [3], [4]. A quasiparticle represents the center of mass of the ions in the channel. It is the motion of the QP, or equivalently, that of the ions as a whole, that

leads to the electric current through the channel – the main experimental observable.

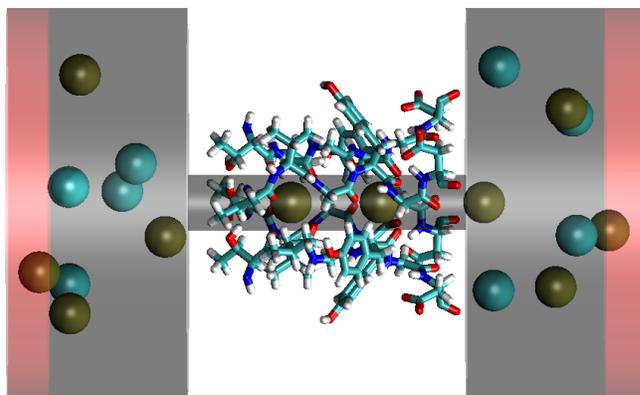


Fig. 1. BD domain. The central narrow tube represents the pore and the biological structure of the selectivity filter is overlaid. The pore is coupled at either boundary to bulk reservoirs and the ions are visualised by coloured golden and blue spheres representing cations and anions respectively.

In the previous work [5], we have connected the QP’s potential landscape and the MD-generated potential of the mean force. Here, we focus on the transitions between channel’s occupancy states using Brownian dynamics (BD) simulations. In many cases, noninteracting ions in the mean field are considered [6], [7] thus omitting the correlations between ions [8]. The latter is of primary importance for the rate theories [9], [10] where generally the entrance / exit probabilities still remain an unsolved problem. Using BD simulations, we provide important insight into the motion of the QP and its connection to the motion of bulk ions close to the channel mouth.

## II. BROWNIAN DYNAMICS

KcsA is a prokaryotic potassium channel [1]. It became one of the first channels whose crystal structure became known [11]. The amino acid sequence of its selectivity filter appears highly conserved amongst potassium channels, and as a result it became one of the most heavily studied channel.

Here, we describe the motion of ions in the KcsA channel using a toy model [3]. The BD domain is shown in Fig. 1. The central narrow tube represents the pore, and the two

PhD Scholarship from the Faculty of Science and Technology of Lancaster University; the Engineering and Physical Sciences Research Council (grants EP/M016889/1 and EP/M015831/1); Leverhulme Trust Research Project Grant RPG-2017-134.

large surrounding cylinders are the bulk reservoirs of radius and length 2nm. We consider a KCl solution with the ions highlighted by the coloured spheres. The pore axis spans along the  $z$  coordinate from -2nm to 2nm. We apply a harmonic radial potential ( $k = 10k_B T / \text{\AA}^2$ ) to ensure the one-dimensional motion of ions within the channel. To prevent ions exiting the domain through a cylindrical boundary, a short-range harmonic repulsive force is applied to approaching ions.

The motion of the ions is governed by the Langevin equation [12]

$$m \frac{d\mathbf{v}_k}{dt} = -\gamma m \mathbf{v}_k + \mathbf{F}_N(\mathbf{r}_k) + \sqrt{2m\gamma k_B T} \xi(t), \quad (1)$$

where  $m$  is ion's mass,  $\gamma$  is its friction coefficient which is coupled to its diffusivity  $D$  by the Einstein relation  $D = k_B T / m\gamma$ ,  $\mathbf{v}_k$  is the ion's velocity,  $k_B$  is Boltzmann's constant,  $T$  represents the absolute temperature, and  $\xi$  is three-dimensional white noise of unit intensity ( $\langle \xi \rangle = 0$ ,  $\langle \xi(t+\tau)\xi(t) \rangle = \delta(\tau)$ ). A third-order algorithm [12] was used to numerically solve Eq. (1) with a timestep  $\Delta t = 0.2\text{ps}$ .

The forces  $\mathbf{F}_N(\mathbf{r}_k) = -\frac{\partial W(\mathbf{r})}{\partial \mathbf{r}}$  acting on the ion located at  $\mathbf{r}$  arise from the potential

$$W(\mathbf{r}) = U(\mathbf{r}) + \sum_m V(|\mathbf{r} - \mathbf{r}_m|), \quad (2)$$

where the sum runs over all other ions in the system.  $U$  stands for the potential of the interaction between the ion and the pore [3]

$$U = -U_0 e^{-(z/a)^2}, \quad (3)$$

and  $U_0 = 10.5k_B T$ ,  $a = 9\text{\AA}$ . We note that this is a toy model reflecting only the overall potential landscape along the pore. For instance, the presence of negatively charged amino acids in the selectivity filter of the channel leads to a potential well. A more detailed description should include the binding sites, and is available via the potential of the mean force (PMF) for the individual ions in the channel [13].

$V$  represents the screened Coulomb potential with a short-range repulsive term

$$V = \frac{c_1 c_2 e^{-r/d}}{4\pi\epsilon_0\epsilon r} + \frac{F_0 r_0}{9} \left(\frac{r_0}{r}\right)^9. \quad (4)$$

Here  $c_m$  represents ion's valence,  $e$  stands for the proton's charge,  $d = 2.8\text{\AA}$  is a screening constant [3],  $\epsilon_0$  and  $\epsilon$  are the dielectric permittivities of vacuum and the pore, respectively,  $F_0 = 2 \times 10^{-10}\text{N}$  and  $r_0 = 2.8\text{\AA}$ . The last term represents the soft-wall [14] repulsive potential acting at short distances.

The presence of the strong repulsive term in Eq. (4) prevents ions from approaching each other too closely. Occasionally the ion-ion distance becomes small  $\leq 2.8\text{\AA}$  and consequently this term provides a strong force that results in a large displacement of the ions, known as long jumps exceptions [15]. We apply an adaptive time step method to overcome these unphysical artifacts, as described in [5] in more details. The fraction of corrected steps was less than one per thousand steps.

To maintain a constant number of ions in the simulation, the standard periodic boundary conditions were used [16].

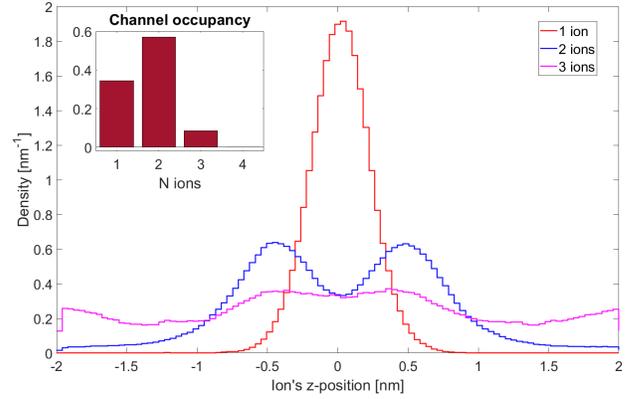


Fig. 2. Distribution of 1, 2, and 3 ions inside the pore. The inset displays the probability of each occupancy state.

Thus an ion that leaving the domain through the left (right) domain side will reappear on the rightmost (leftmost) position of the domain. These are the cheapest method for equilibrium simulations in the absence of an electrochemical gradient (cf. [17]).

We consider 0.5mM KCl solutions in both bulks with no applied voltage. This allows us to consider the equilibrium ionic transitions in and out of the pore.

#### A. Quasiparticles

The strong correlation of ionic motion in the pore allows us to introduce the quasiparticle (QP) – the center of mass of  $N$  ions located at  $z_m$  in the pore, – according to Ref. [3]

$$q_N = \frac{\sum_m^N z_m}{N} \quad (5)$$

The Langevin equation (1) can be further simplified [5] to describe the diffusive motion of the QP in the pore

$$\dot{q}_N = -\frac{D_N^*}{k_B T} \frac{\partial U_N^{eff}}{\partial q_N} + \sqrt{2D_N^*} \xi(t) \quad (6)$$

In this equation, the index “ $N$ ” reflects the fact that the QPs consist of different number of ions  $N$  ( $N=1,2,3$ ), and thus different physical properties. The effective potential  $U_N^{eff}$ , faced by the QP, can be derived from the PMF [5]. Likewise, the transport diffusivity  $D_N^*$  differs from the product  $N \cdot D$  due to the ion-ion interactions [18].

### III. RESULTS AND DISCUSSION

Figure 2 shows the distribution of 1, 2, and 3 ions inside the pore. For 1 ion, this is given by the Boltzmann distribution  $P \sim e^{-U(q)/k_B T}$  as in this case the ion and quasiparticle coincide. When two ions occupy the pore the ion-ion repulsion creates a two-headed distribution at approximately  $\pm 0.5\text{nm}$ . With three occupying ions, the outermost ion gains the freedom to reach the edge of the pore and eventually leave it.

The probabilities of each occupancy state are shown by the inset. The pore primarily accommodates 1 - 3 ions, with a negligible chance of a 4-th ion entering. This occupancy

distribution in fact represents the probability to find each individual QP inside the pore. Switching from one QP to another suggests an ion leaving or entering the channel, and thus produces electric current – the main experimental observable. For a better understanding let’s consider the individual ions’ trajectories and these of the QPs.

A typical trajectory of the ions and the QPs are shown in Fig. 3. Individual ions move inside the channel revealing a high level of correlation [5]. An ion (green trace) approaches the channel from the bulk and enters at  $t \approx 550ns$ . This immediately transforms the QP from  $q_2$  (black line) into  $q_3$  (orange line) with an immediate jump to a new position. After that, the quasiparticle diffuses until another jump at a later moment  $t \approx 555ns$  when the outermost ion leaves the channel. The QP  $q_3$  transforms into  $q_2$  with a new location again. Overall, this process, known as the knock-on conduction, corresponds to the diffusion of the QP within the channel and switching its type in a jump-like manner.

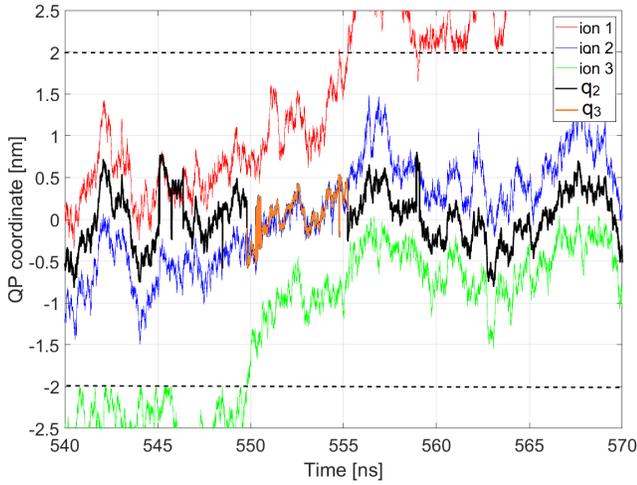


Fig. 3. Dynamics of ions and the QP. An ion (green trace) approaches the channel from the bulk and enters at  $t \approx 550ns$ . This immediately the QP (black line) into a new one (orange line) at a new position. At a later moment  $t \approx 555ns$ , the outermost ion (black line) leaves the channel accompanied by another jump and transition of the QP. Overall, this process is known as knock-on conduction. Dashed lines demarcate the edges of the channel.

The transition processes describing either an ion entering the pore from the bulk, or exiting from the pore, need further clarification. With that in mind, we introduce a cylinder of radius and height  $5\text{-\AA}$  at each end of the channel, representing the channel’s mouths. Thus the dynamics of the entering and leaving processes can be monitored. The inset of Fig. 4 shows the distribution of residence times (identically, of the *cis* trajectories [19]), showing how long on average an ion stays in the mouth.

However, these times should also depend on the location of the QP. To provide some preliminary insight into this question, we fix a pair of ions at a  $2nm$  separation inside the channel and analyze the corresponding changes in the distribution near the pore’s edges. This mimics the ionic configuration at a

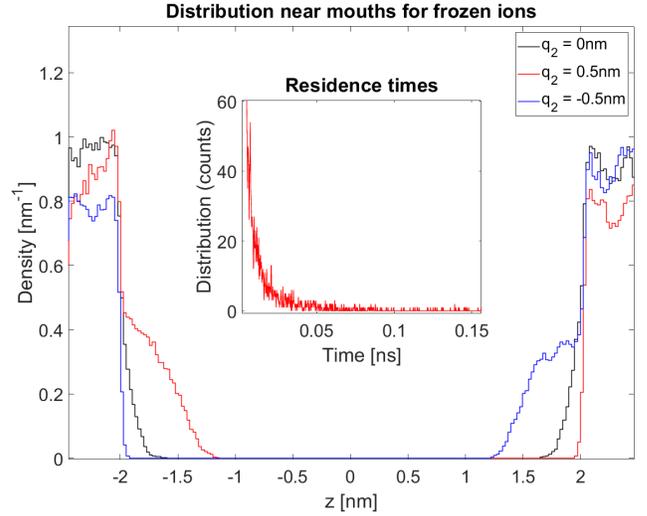


Fig. 4. Distribution of the mobile ions in the channel and the mouths when a pair of ions in the pore is kept immobile. Thus the QP’s location  $q_2$  is fixed. Inset: distribution of the residence times in the mouth.

specific position of the QP analogous to Fig. 2. For clarity, we consider three values of  $q_2 = \{-0.5, 0, 0.5\}nm$ . Eventually, the number density of  $K^+$  ions in the mouths and the channel is measured.

One can see that once the QP is localised closer to the left (right) edge of the channel, ions do not enter the channel from that side, but penetrate from the “free” right (left) mouths of the channel. If the QP is at the centre of the pore then it provides an equal probability of entrance by an ion from either mouth. The increased distribution in the channel or near the mouths suggests an increased probability of entry, and therefore higher probability of permeation.

These findings can be understood in light of the screened Coulomb interaction Eq. (4) between the ions. Thus, the bulk ions can be influenced by ions in the channel at a finite distance ( $\sim d$  in our simulations).

This interaction between bulk and channel ions defines which transition occurs. If the QP approaches the edge of the pore it prevents an ion entering from the bulk on this side but allows an ion to enter on the opposite side. When an ion enters it pushes the remaining ions such that the outermost ion leaves the channel (knock-on conduction). This is an example of a *trans* trajectory [19], [20].

These transitions are vital to understanding the channel’s permeation mechanism. One often assumes noninteracting ions moving in a mean field [6], [7], [10], based on the unconditional probability densities [8], [20]. However, this approach evidently ignores the correlations between ions emerging from their interaction. A more sophisticated analysis requires the application of the conditional probability densities [8] that are closely related to the pair-distribution functions [8]. This improved description of the transition process under arbitrary experimental conditions – voltage, concentrations, and chemical composition [2] – can thus pave the way to a more adequate

definition of the transition rates in the kinetic [9], [10], [21] theories.

#### IV. CONCLUSIONS

We have considered the motion of the quasiparticle (QP) in a narrow ion channel with a specific emphasis on the transition process. We show that the motion of the QP and the bulk ions in the mouths is correlated. Namely, the presence of the QP near one of the channel's edges suggests a higher exit probability from that edge and a higher entering probability on the opposite side. This applies to kinetic and rate theories where the transition process is the key to successive description of conduction and selectivity.

In further work we plan to consider a more realistic description of the channel. First, it is desirable to estimate the forces from the potentials of the mean force (PMF) obtained from Molecular Dynamics (MD). This is proven to be successful in the translocation of DNA through nanopores [22]. Secondly, it's important to extend the analysis for a system far from equilibrium. Finally we plan to run a full scale MD simulation to verify the predictions of this paper.

It is also believed that the concept of quasiparticles can turn out useful in constructing a functionalised nanotubes with prescribed properties. The latter appears at the front end of the research towards efficient water desalination atomically thin membranes [23].

#### ACKNOWLEDGEMENTS

We are grateful to Robert S. Eisenberg, Aneta Stefanovska, and the late Igor Kh. Kaufman for helpful discussions.

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