

Ionic Memcapacitive Effects in Nanopores

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ABSTRACT Using molecular dynamics simulations, we show that, when subject to a periodic external electric field, a nanopore in ionic solution acts as a capacitor with memory (memcapacitor) at various frequencies and strengths of the electric field. Most importantly, the hysteresis loop of this memcapacitor shows both negative and diverging capacitance as a function of the voltage. The origin of this effect stems from the slow polarizability of the ionic solution due to the finite mobility of ions in water. We develop a microscopic quantitative model which captures the main features we observe in the simulations and suggest experimental tests of our predictions. We also suggest a possible memory mechanism due to the transport of ions through the nanopore itself, which may be observed at small frequencies. These effects may be important both in DNA sequencing proposals using nanopores and possibly in the dynamics of action potentials in neurons.

KEYWORDS Nanopore, memristor, memcapacitor, sequencing, neurons

A nanopore is an aperture of nanoscale dimensions across an insulating membrane. This way, if immersed in an ionic solution, ions can enter the nanopore, and if subject to an electric field of given strength, they may enter it from one side of the opening and emerge on the other side. The membrane can be made of either biological or solid-state materials. Nanopores are ubiquitous in biological systems as they regulate the flow of ions across cell membranes (of, e.g., neurons). At present, they are also actively investigated for potential applications in DNA sequencing.^{1,2} Despite its apparent simplicity, ion dynamics in nanopores is far from trivial. An example of this is provided by the recently predicted phenomenon of “quantized ionic conductance”, namely the presence of current steps occurring at effective pore radii that match the radii of the water hydration layers that form around the ions.³

Here, we predict another intriguing property of ion dynamics in nanopores, when the latter are subject to a periodic external electric field. In particular, we show that the electric field forces ions to accumulate at the two surfaces of the nanopore membrane, creating an effective capacitor. However, this capacitor shows interesting features as a function of the frequency of the field, namely, a hysteresis loop of the capacitance (memory-capacitance or *memcapacitance* for short⁴) as a function of voltage which diverges at zero voltage and displays negative-capacitance properties. Memcapacitors have been theoretically formulated in ref 4 and belong to the wider class of memory-circuit elements, which includes also memristors and meminductors, namely, resistors and inductors with memory. Following ref 4 we define a voltage-controlled memcapacitive system by the set of equations

$$Q(t) = C(x, V, t)V(t) \quad (1)$$

$$\dot{x} = f(x, V, t) \quad (2)$$

where $Q(t)$ is the charge on the capacitor at time t , $V(t)$ is the voltage across it, and C is the time-dependent *memcapacitance* which depends on the internal state of the system described by a set of n state variables x , with f a continuous n -dimensional vector function. Using all-atom molecular dynamics (MD) simulations, we indeed demonstrate that memory characteristics of nanopores in solution originate from the finite mobility of ions in water with consequent slow polarizability of the ionic solution. We also develop a simple microscopic model that captures the main properties observed in the simulations and allows us to extend our results to regimes beyond the reach of MD simulations. Additionally, we use an equivalent circuit formulation to discuss how ionic transport through the nanopore itself may lead to an additional memory mechanism. We also propose ways our predictions could be tested with available experimental capabilities.

Ionic Memcapacitors. In order to show that a nanopore in solution indeed acts as a memcapacitive system (eqs 1 and 2), let us be more specific and consider the experimental situation as depicted in Figure 1 which we suggest as a way to observe the effects predicted here. An external (time-dependent) voltage $V(t)$ is applied to electrodes which form an effective capacitor with the ionic solution and the nanopore at its interior. In this paper we consider a typical setup for, e.g., DNA sequencing devices^{5–7} with KCl ionic solution and a Si_3N_4 nanopore 25 Å thick and 88 Å wide with a 7 Å radius cylindrical hole drilled through the center of the membrane. However, the specific dimensions of the pore are irrelevant for the overall conclusions of this paper and

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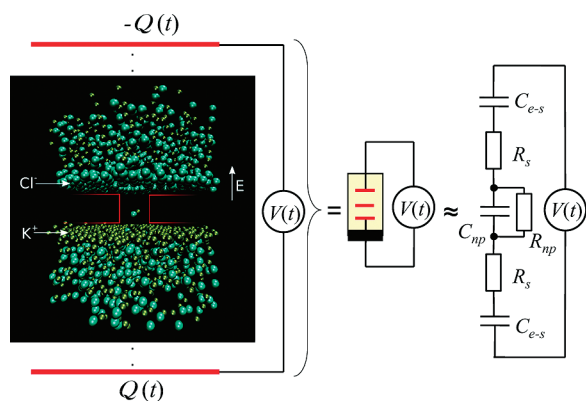


FIGURE 1. (left) A snapshot of the molecular dynamics geometry at a time when a buildup of charges of the opposite sign on each side of the nanopore is observed due to a finite electric field E . The nanopore membrane is located at the center (represented by the red lines) and water is not visible. Top and bottom horizontal red lines represent electrodes (holding plate charges $\pm Q(t)$) of the suggested experimental setup needed to observe the predicted memcapacitive effects. (right) Simplified equivalent circuit model.

similar considerations would apply also to biological pores. When a global time-dependent bias is applied to the system, the ionic solution is polarized and ions are forced to accumulate at the surfaces of the pore (see Figure 1). First, we consider relatively short time scales when ion transport across the nanopore is not significant. (We will discuss toward the end of the paper the effect of ion transport across the pore at longer times.) This implies that the same (and opposite in sign) charge, $Q(t)$, that accumulates on the surfaces of the pore also accumulates on the plates of the capacitor.

In the simplest approximation, the electrical properties of the total nanopore system can be approximated by an equivalent circuit model as shown in Figure 1, where capacitors and resistors (generally, nonlinear) represent different parts of the system. Here, C_{e-s} denotes the external electrode–solution capacitance, R_s is the resistance of the solution, $R_{ss} (\gg R_s)$ is the resistance of the ion current through the pore, and C_{ss} is the capacitance of the membrane. The total voltage drop is then given by

$$2 \frac{Q}{C_{e-s}} + 2R_s \frac{dQ}{dt} + \frac{Q}{C_{ss}} = V(t) \quad (3)$$

Since we are interested in the properties of the pore and solution only, we envision the experimental setup so that $C_{e-s} \gg C_{ss}$. The equation for the charge then takes the form

$$\frac{dQ}{dt} = \frac{V(t)}{2R_s} - \frac{Q}{2R_s C_{ss}} \quad (4)$$

Equation 4 describes a relaxation of Q toward $V(t)/(2R_s)$ with a relaxation time $2R_s C_{ss}$. Generally, due to the finite mobility of ions in water, the charge on the external plates—and hence on the pore—is slow to respond to changes of the bias upon varying $V(t)$. This means that $V(t)$ may be zero when $Q(t)$ is finite and vice versa. Therefore, the capacitance of this whole system, $C = Q(t)/V(t)$, depends on the applied voltage history, shows divergences, and acquires negative values at specific times, similar to what has been recently predicted in some solid-state memcapacitors.⁸ Since these memory effects can be viewed as originating from the history-dependent permittivity of the ionic solution, following the definition of ref 4 (eqs 1 and 2), a nanopore in ionic solution is indeed a memcapacitive system.

Results and Discussion. Let us now demonstrate these memcapacitive effects from a microscopic point of view. For this we employ all-atom MD simulations using NAMD2⁹ and investigate the response of the system to external ac and dc electric fields. According to our previous discussion, in order to calculate the total capacitance of the system we only need the net charge that accumulates at the nanopore surface. We then employ periodic boundary conditions in the direction both perpendicular and parallel to the external field. On each side of the pore, we place a 50 Å long section of water with a 1 M solution of a homogeneous, random distribution of potassium and chlorine ions. The CHARMM27 force field^{10,11} is used for the interaction of water and ions while quantum mechanical parameters¹² are used for the Si_3N_4 pore.¹³

We have performed extensive MD simulations of the process of polarization of the ionic solution in proximity to the nanopore membrane. As a general observation, within the parameters used, a delay between the formation of ionic polarization and *both* the external ac electric field and the voltage across the pore has been observed. This is evident in Figure 2 where the net charge of ions on one side of the nanopore is plotted as function of time together with the voltage drop across the membrane. The latter is obtained by doing a full electrostatics calculation from MD simulations.¹⁴ At this point we remark that in all our simulations we have found that the net charge induced by the external field is always located within 10 Å from the membrane surface and that the voltage drop across the membrane is very close in value to the external applied voltage, whatever the strength and frequency of the latter. This last observation is consistent with previous studies.¹

Next, we fit these MD simulation results employing the equivalent circuit model given by eq 4. Using microscopic parameters, eq 4 can be rewritten as

$$\frac{dQ(t)}{dt} = 2eA\mu nE(t) - \frac{Q(t)}{\tau} \quad (5)$$

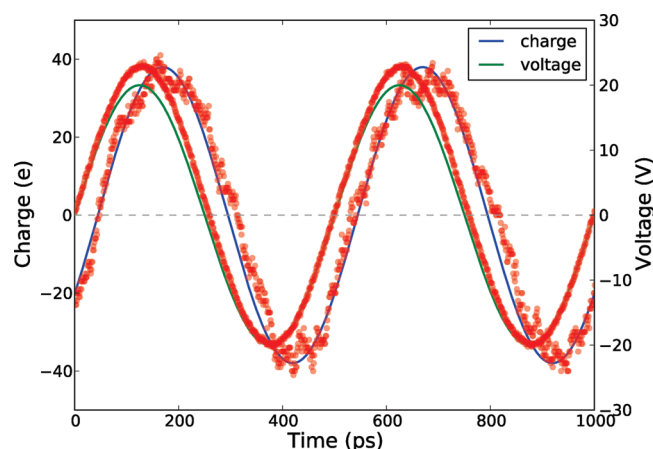


FIGURE 2. Net charge on the surface of the nanopore (equal to system's plate charge) and voltage across the nanopore (which is very close to the external voltage, solid line) plotted as a function of time. The solid line for the charge corresponds to the model we discuss in the text. One can clearly see that the net charge lags behind in time with respect to *both* the external voltage and the voltage at the pore.

where A is the area of the membrane surface, μ is the ion mobility which is similar for both types of ions and we take to be $7.12 \times 10^{-8} \text{ m}^2 \text{ V}^{-1} \text{ s}^{-1}$,¹⁵ e the ion charge, n the density of ions in the bulk, and $\tau = 2R_s C_{ss}$ is the relaxation time. The factor of 2 takes into account the conductivity of both channels (K^+ and Cl^-). Using dc-field simulations, we were able to extract τ . We do this by first applying a constant electric field (with the same magnitude as the amplitude of our ac field simulations) which forces ions to accumulate in the vicinity of the membrane as it is shown in Figure 1. The total net charge within 10 \AA from the nanopore surface is integrated to obtain the capacitor charge.¹⁶ Then we turn off the field and monitor the decay of this charge back into the bulk (see Figure 3). From this we obtain the relaxation time τ . We find that this time is slightly dependent on the amplitude of the initially applied electric field, becoming slightly longer as the applied field decreases. For voltages as low as 5 V across the membrane, we get from our simulations a relaxation time $\tau \sim 75 \text{ ps}$.¹⁷

Solving eq 5 for $Q(t)$ with an ac electric field $E(t) = E_0 \sin(\omega t)$ of amplitude E_0 and angular frequency $\omega = 2\pi f$, we obtain the long-time limit solution

$$Q(t) = \frac{2A\mu enE_0 \sin(\omega t)}{\left(1 + \frac{1}{\omega^2 \tau^2}\right)\omega^2 \tau} - \frac{2A\mu enE_0 \cos(\omega t)}{\left(1 + \frac{1}{\omega^2 \tau^2}\right)\omega} \quad (6)$$

which amounts to a sine function with a phase shift, namely, $Q(t) = Q_0 \sin(\omega t - \delta)$, where

$$Q_0 = \left[\left(\frac{2A\mu enE_0}{\left(1 + \frac{1}{\omega^2 \tau^2}\right)\omega} \right)^2 + \left(\frac{2A\mu enE_0}{\left(1 + \frac{1}{\omega^2 \tau^2}\right)\omega^2 \tau} \right)^2 \right]^{1/2} \quad (7)$$

and $\delta = \tan^{-1}(\omega\tau)$. Using the appropriate values of A , n , and τ as obtained from the numerical simulations, this model agrees very well with the results of our MD simulations as it is evident from Figure 2. In particular, it is clear that the net charge and voltage on the capacitor are phase shifted by the amount δ . This means that when the voltage is zero the charge on the capacitor is not necessarily zero, and vice versa. This is shown in Figure 4a where the net charge is plotted as a function of the voltage across the capacitor. This gives rise to diverging and negative values of capacitance.

To see this, we write the external voltage across the whole system as $V(t) = V_0 \sin(\omega t)$, with $V_0 = -E_0 d$ where d is the size of the simulation cell along the direction of the electric field. From $C = Q(t)/V(t)$ and (6) we then obtain the long-time limit of the capacitance

$$C(t) = \frac{2A\mu en}{\left(1 + \frac{1}{\omega^2 \tau^2}\right)\omega^2 \tau d} - \frac{2A\mu en}{\left(1 + \frac{1}{\omega^2 \tau^2}\right)\omega d} \cot(\omega t) \quad (8)$$

This represents the main result of our paper. It shows that the capacitance of the whole nanopore system is history-dependent, diverges when the voltage crosses its zero value,

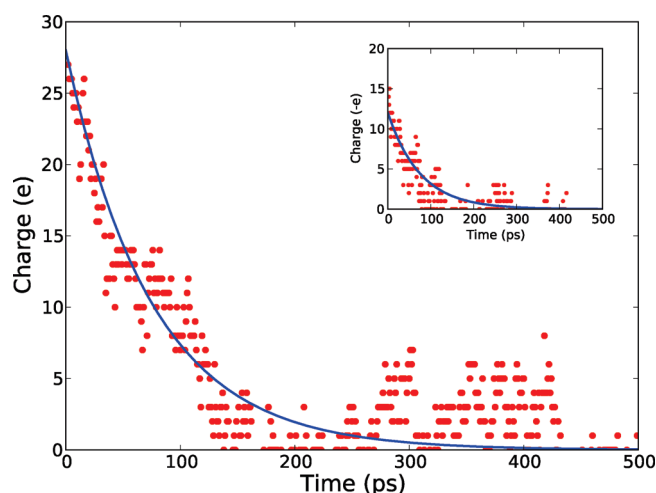


FIGURE 3. Net charge of the positively charged side of the capacitor vs time when a constant 20 V applied voltage responsible for the accumulation of the charges on the surface of the pore is turned off. A decay time scale of 75 ps is obtained by fitting the simulation results with an exponential decay curve, i.e., $Q(t) = Q_{\max} e^{-t/\tau}$. Due to the nearly equal mobilities of K^+ and Cl^- ,¹⁵ we find similar results for the negatively charged side and different field strengths as well. This is shown in the inset with initial voltage of 5 V.

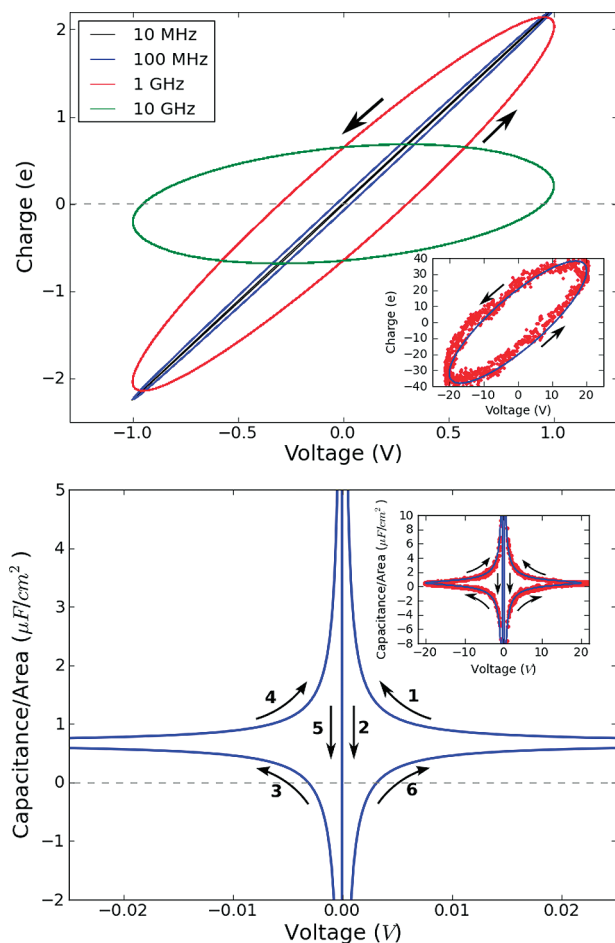


FIGURE 4. (upper panel) Net charge Q versus a periodic voltage of amplitude $V_0 = 1$ V and different frequencies as obtained from eq 6. The inset shows the same quantity for 2 GHz and $V_0 = 20$ V compared with the charge obtained directly from our MD simulations. (lower panel) Capacitance versus a periodic voltage of frequency $f = 10$ MHz and amplitude $V_0 = 1$ V as obtained from eq 8. In the inset we show the same quantity for $f = 2$ GHz and $V_0 = 20$ V compared with the capacitance obtained directly from our MD simulations. It is seen that C can be both negative and diverges as the voltage approaches zero. The arrows indicate the direction the voltage is swept in time and the numbers show the order in which the trace is generated.

and acquires negative values within a certain voltage range. This is plotted in Figure 4 where both the charge on the capacitor and the capacitance are plotted as a function of voltage across the capacitor. From Figure 4 it is evident that at low frequencies, this ionic memcapacitor behaves almost like a regular capacitor. At higher frequencies, memory effects in the capacitance manifest in a hysteresis loop characteristic of memcapacitors. However, unlike typical memcapacitors that show a pinched hysteretic loop,⁴ ionic memcapacitors have a nonvanishing (diverging) zero-bias capacitance.

Memory at Small Frequencies. At small enough frequencies, there will be enough ion transport through the pore to play a role in the dynamics. In fact, it is no longer correct to assume that the charge associated with C_{e-s} is the same as

the charge associated with C_{ss} . Using Kirchoff's loop rule, we get an equation similar to eq 3

$$2 \frac{Q_{e-s}}{C_{e-s}} + 2R_s \frac{dQ_{e-s}}{dt} + \frac{Q_{ss}}{C_{ss}} = V(t) \quad (9)$$

except now we differentiate between the two charges, Q_{e-s} (on the external plates) and Q_{ss} (on the pore). Applying Kirchoff's junction rule we then get

$$\frac{dQ_{e-s}}{dt} = \frac{dQ_{ss}}{dt} + \frac{V_{ss}}{R_{ss}} \quad (10)$$

where due to C_{ss} and R_{ss} being in parallel, V_{ss} is simply the voltage on the C_{ss} capacitor, Q_{ss}/C_{ss} , and we can approximate the conductance across the pore as $1/R_{ss} = 2A_p en\mu/L_p$ where $A_p = \pi r_p^2$, with r_p the pore radius, e the electronic charge, n the ion density, μ the ion mobility, and L_p the length of the nanopore. We approximate C_{ss} as that of a parallel plate capacitor, i.e., $C_{ss} = \epsilon A/L_p$ with ϵ the permittivity of Si_3N_4 , and A is again the area of the membrane surface. We can solve eq 9 for Q_{ss} and plug it into eq 10 to arrive at the following second-order equation for Q_{e-s}

$$2R_s C_{ss} \frac{d^2 Q_{e-s}}{dt^2} + \left(1 + 2 \frac{C_{ss}}{C_{e-s}} + 2 \frac{R_s}{R_{ss}}\right) \frac{dQ_{e-s}}{dt} + 2 \frac{Q_{e-s}}{R_{ss} C_{e-s}} = \frac{V(t)}{R_{ss}} + C_{ss} \frac{dV(t)}{dt} \quad (11)$$

For an ac field, this equation can be solved analytically but the solution is a bit involved. We then just plot it for different frequencies in Figure 5. As anticipated, we see that direct transport across the pore leads to an additional memory mechanism at specific frequencies, much smaller than the ones due to the polarization of the ionic solution.

Experimental Test. The results presented in this paper show that there are two very distinct memory regimes for nanopores in solution. To observe the first memory mechanism due to the polarization of the ionic solution, ideally, one would need high frequencies (on the order of 1 GHz). On the other hand, much smaller frequencies (on the order of 1 kHz) are necessary to observe the additional memory effect due to transport through the pore. This indicates that the second memory mechanism would be the easiest one to detect. However, in both cases we have shown that the capacitance acquires diverging (and also negative) values. This result appears to hold also at frequencies that are relatively smaller than those required to observe the first memory regime, namely, at frequencies that are on the order of tens of megahertz or less (see Figure 4). Therefore,

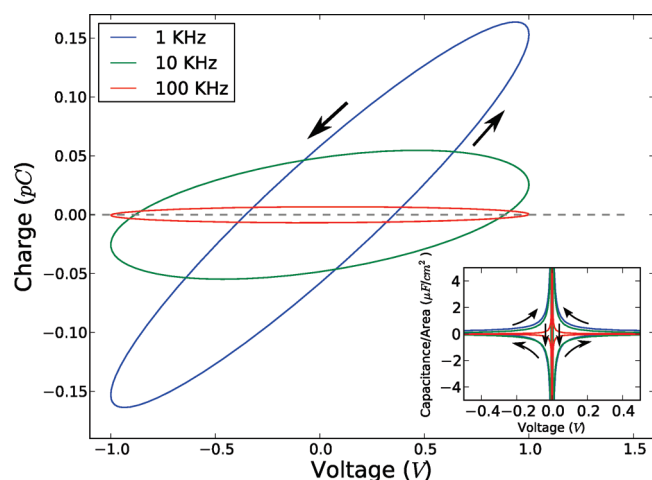


FIGURE 5. Memcapacitive effects due to ionic transport across the pore. Main panel shows the charge on the external capacitor plates plotted versus the voltage across it for various frequencies of the electric field with $V_0 = 1.0$ V, $A = 10 \mu\text{m}^2$, $L_p = 25$ Å, $r_p = 7$ Å, $\epsilon = 7.5\epsilon_0$, $C_{ss} = \epsilon A/L_p$, and $C_{e-s} = 10C_{ss}$ for a 1 M concentration of ions. The inset shows the capacitance plotted versus the voltage for the same frequencies. Memory effects due to ionic transport across the pore occur at much lower frequencies than those due to the polarization of the ionic solution.

with appropriate control of the external circuit, at these frequencies one should at least be able to observe nontrivial changes (manifested, e.g., in fast jumps between positive and negative values) of the capacitance when the bias crosses its zero value. We thus expect that by simultaneously measuring the electric charge on the external electrodes as shown in Figure 1 (or, equivalently, the current at the electrodes) in the presence of an applied time-dependent voltage should allow a direct verification of our predictions for both types of memory.

Conclusions. We have shown, using molecular dynamics simulations, that a nanopore sequencing setup acts as a memcapacitor, namely, a capacitor with memory.⁴ The latter is due to two types of effects and thus arises at very different frequencies of the external bias. At high frequencies the finite mobility of ions in water and hence the slow polarizability of the ionic solution give rise to one type of memory. Memcapacitive effects, however, may also occur as a result of the ion transport through the pore at very low frequencies. These processes occur internally in the system and, from the point of view of an external circuit, the whole system behaves as an unusual capacitor. These effects may potentially play a role in nanopore DNA sequencing proposals, especially those based on ac electric fields,¹⁸ as well as in other nanopore sensing applications. Moreover, the effect of the charge buildup on the nanopore surface may influence

DNA translocation and its structure in proximity to the pore. Finally, due to the ubiquitous nature of nanopores in biological processes, these results may be relevant to specific ion dynamics when time-dependent fields are of importance, such as in the action potential formation and propagation during neuronal activity. We thus hope this work will motivate studies in this direction.¹⁹

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