

Using nanopores as sensors: a Monte Carlo modeling study



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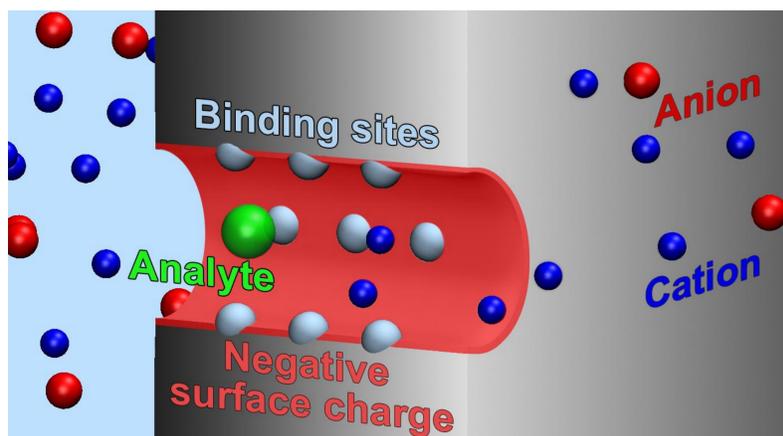
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Introduction

The basic concept of our model nanopore sensor is that the presence of an analyte molecule modulates the ionic current flowing through the pore. The analyte molecule (usually a biomolecule) is detected selectively if it is bound to the nanopore. If the binding is a reversible process involving physical forces that are weaker than chemical bonds, the probability that the analyte molecule binds to the nanopore is proportional to its concentration. From calibration curves (current vs. concentration) the analyte concentration can be determined. We present a modeling study to analyze the device **sensitivity** (defined as I/I_0 , where I and I_0 are the currents in the presence and absence of the analyte, respectively) to the various model parameters: number, strength, and width of the binding sites; properties of the electrolyte and the analyte. Through the calculated concentration profiles, the molecular mechanisms of the system can be understood.

Model

- Nanopore: a cylindrical pore penetrating a membrane of with 6 nm
- Membrane and pore: hard walls
- Cation selective pore: negative charges are located on the pore's wall
- Ions: Primitive Model of electrolytes, charged hard spheres
- Solvent: implicit water model, a constant dielectric continuum
- Binding sites: square-well potential



Schematic figure of the nanopore based model sensor

$$u_{SW}(r) = \begin{cases} 0 & \text{for } r - R_X > d_{SW} \\ -\varepsilon_{SW} & \text{for } r - R_X < d_{SW} \end{cases}$$

where r is the distance of the site and the ion center and R_X is the radius of the analyte (X ion with the valence of z_X). The short-range potential attracts X with ε_{SW} energy once the closest point of the X ion's surface is closer to the site than the distance parameter d_{SW} .

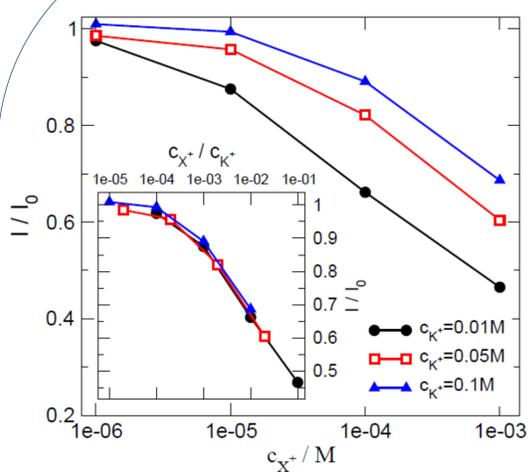
NP+LEMC Method

The ionic flux computed with the Nernst-Planck (NP) equation of electrodiffusion:

$$-kTj_i(r) = D_i(r)c_i(r)\nabla\mu_i(r)$$

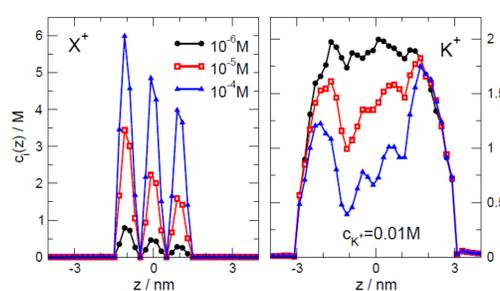
- $j_i(r)$ particle flux density of ionic species i ,
- k Boltzmann's constant
- T temperature
- $c_i(r)$ concentration profile
- $\mu_i(r)$ electrochemical potential profile
- The relation between $c_i(r)$ and $\mu_i(r)$ is established with Local Equilibrium Monte Carlo simulation (LEMC)
- LEMC is a grand canonical MC simulation devised for a non-equilibrium situation.
- The computation domain of the NP system is divided into volume elements with different μ_i values
- The whole system is solved in an iterative way until conservation of mass is satisfied.

Results

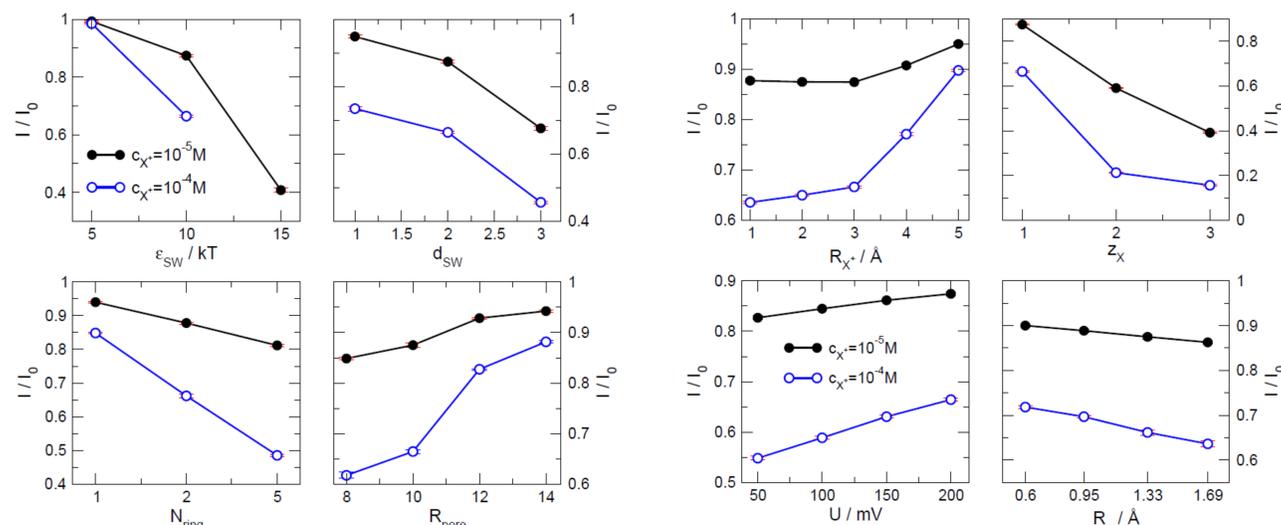


Calibration curves: currents relative to the currents in the absence of X^+ as functions of c_{X^+} for different values of c_{K^+} . The model parameters are $\varepsilon_{SW} = 10kT$, $d_{SW} = 0.2\text{nm}$, $N_{ring} = 3$, $R_{pore} = 1\text{nm}$, $U = 200\text{mV}$, $R_{X^+} = 0.3\text{nm}$, and $z_{X^+} = 1$.

The inset shows the same data, but as a function of the X^+ concentration relative to the K^+ concentration.



Concentration profiles of X^+ and K^+ ions for various values of c_{X^+} with $c_{K^+} = 0.01\text{M}$.



Dependence of the relative current on model parameters for two concentrations of analyte

Dependence of the relative current on external parameters R_{X^+} , z_{X^+} , U , and R_+ for two concentrations of analyte

Summary

Sensor sensitivity can be improved:

Parameters	With increasing	With decreasing
Model	ε_{SW} , d_{SW} , N_{ring}	U , R_{pore}
Analyte	z_X	R_{X^+}
Experimentally controllable	R_+	c_+

- The sensor can detect the analyte molecules that are present in the sample in very low concentrations
- Our calibration curves show scalability: the c_X/c_{K^+} ratio determines the current reduction (I/I_0) independent of c_{K^+} .
- Implicit water model makes it possible to handle low ion concentrations (as opposed to explicit water model studied with MD)
- The NP+LEMC methodology makes it possible to handle finite size of ions and ion correlations (as opposed to continuum theories, such as PNP)

References

B. Matejczyk *et al.*, *J. Chem. Phys.* 146, 124125, 2017.
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