Using nanopores as sensors: a Monte Carlo modeling study

Eszter Mádai¹, Mónika Valiskó¹ and Dezső Boda¹,²
¹Institute of Chemistry, Department of Physical Chemistry, University of Pannonia, Veszprém, Hungary
²Institute of Advanced Studies Kőszeg (iASK), Kőszeg, Hungary

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 \(I/I_{NP}\)) where \(I\) and \(I_{NP}\) 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

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

where \( r \) is the distance of the site and the ion center and \( R_i \) is the radius of the analyte (X ion with the valence of \( z_x \)). The short-range potential attracts \( X \) with \( \varepsilon_{SW} \) 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:

\[-kT \frac{\partial j_i(r)}{\partial x_i} = D_i(r)c_i(r)\mu_i(r)\]

- \( k \) Boltzmann’s constant
- \( T \) temperature
- \( \mu_i \) electrochemical potential profile
- \( c_i \) concentration profile
- \( D_i \) diffusion coefficient

The relation between \( c_i(r) \) and \( \mu_i(r) \) is established with Local Equilibrium Monte Carlo simulation (LEMC)

The diffusion current \( I \) is given by the number of analyte molecules entering the pore per unit time and is obtained from the Nernst-Planck equation (NP) and the local equilibrium model (LEMC) by minimizing the free energy of the system. The free energy is given by the sum of the chemical potential and the electrochemical potential of the analyte, as well as the contributions from the electrical potential and the osmotic pressure.

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 \( c_{SW} = \text{10}kT_d, d_{SW} = 0.2\text{nm}, N_{X_i} = 3, \]

\[ \quad R_{\text{pore}} = 1\text{nm}, U = 200\text{mV}, R_{\text{K}^+} = 0.3\text{nm}, \text{and } z_x = 1. \]

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 \( c_{K^+} = 0.01 \text{M}. \)

Summary

Sensor sensitivity can be improved:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>With increasing</th>
<th>With decreasing</th>
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<tbody>
<tr>
<td>Model</td>
<td></td>
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<tr>
<td>( c_{SW} )</td>
<td>( d_{SW} )</td>
<td>( N_{X_i} )</td>
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<td>Analyte</td>
<td>( R_x )</td>
<td>( c_x )</td>
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<tr>
<td>Experimentally controllable</td>
<td>( R_x )</td>
<td>( c_x )</td>
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- The sensor can detect the analyte molecules that are present in the sample in very low concentrations
- Our calibration curves show scalability: the \( c_{K^+}/c_{X^-} \) ratio determines the current reduction \((I/I_{NP})\) independent of \( c_{X^-} \)
- 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


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