

A New Method for Molecular Detection and Identification in a Metallic Nanopore

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Statement of Purpose: Nanopore sensors with single-molecule resolution will be the basis for the next generation of fast, long-read DNA sequencers. However, a reliable method of signal transduction is needed in order to extract useful information from molecular and sub-molecular analytes. With this goal, a new type of nanopore sensor was developed with sensitivity to changes in the electrical double layer. By developing this technique, we demonstrate a method of molecular detection that is sensitive to the physical and electrical properties of the analyte and the supporting electrolyte.

Methods: A solid state nanopore was fabricated in a membrane composed of a supporting layer of silicon nitride (Si_3N_4) and a conductive layer of gold. The nanopore was evaluated with a variety of molecular analytes in a range of supporting electrolyte concentrations. An invariable driving potential was applied across the nanopore and the nanopore surface was charged by the application of a small electrical current. A signal detection algorithm was developed to identify transient signals in the electrical potential of the charged nanopore and in the ionic current. Coinciding transient signals in both the charged nanopore potential (the 'double layer potential') and the ionic current were collected and correlated with the properties of the molecular analytes.

A numerical model of the nanopore system was also developed in the continuum regime based on previous work (figure 1). The nanopore was considered as a conical nanopore in aqueous solution. The Nernst-Planck and Stokes equations were solved over the fluid domain and the fully coupled Poisson equation was solved over the entire model. The charged surface of the gold layer was considered to correspond to the charging potential of the electrical double layer (EDL) in a parallel RC circuit. EDL capacitance was iteratively and self-consistently solved. The analyte molecules were considered at the narrowest region of the nanopore with various properties corresponding to the experimental conditions.

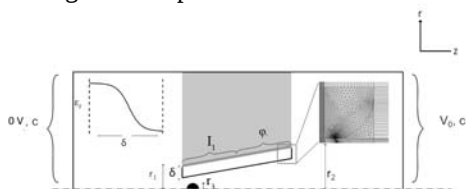


Figure 1. Nanopore model geometry and parameters.

Results: The transient electrical signal detected at the charged gold nanopore was found to be characteristic of the analyte molecules and linearly related to the concentration of the supporting electrolyte (figure 2). Sensitivity to the analyte was reduced at high concentrations due to electrochemical saturation of the solution within the nanopore. Analytes carrying different

valence charges are distinguishable as well as analytes with similar valence charge, but different size and permittivity (eg, oxalic acid and hydroquinone).

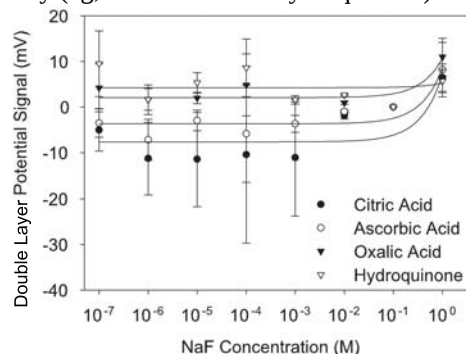


Figure 2. Signal magnitude for analytes in various concentrations of supporting electrolyte.

The results from the numerical model agree very well with the experimental results (figure 3). Further probing in the numerical model indicates that the signal generation is due to disruption of the EDL structure within the nanopore due to analyte charge, size, and permittivity. This EDL disruption resulted in a transient change to the electrochemical potential within the nanopore, which is balanced by the potential of the floating, charged nanopore electrode.

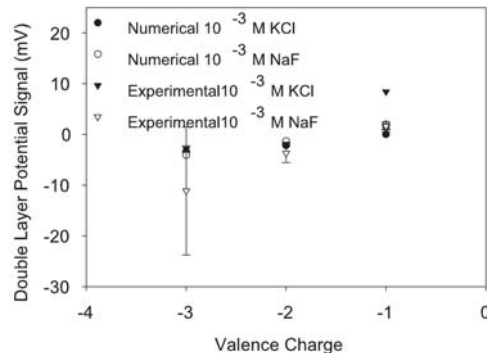


Figure 3. Experimental and numerical results.

Conclusions: We have developed a new method of molecular detection in a nanopore. The magnitude of the signal is correlated to the physical properties of the molecular analytes and the supporting electrolyte concentration. Unlike other nanopore detection methods, this method is insensitive to the molecular transport properties of the nanopore and to analyte orientation. This study demonstrates a sensitive, stable, and robust method for detecting and differentiating single molecule analytes.

References:

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Hückel, E.; Debye, P. The Theory of Electrolytes. I. Lowering of Freezing Point and Related Phenomena. *Phys. Zeitschrift* 1923, 24, 185–206.