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Perspective

A Novel Approach for Biomolecular Recognition *via* DNA Nanopores

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DESCRIPTION

Biological membrane channels promote molecular recognition by mediating information exchange between cells. While tuning the shape and function of membrane channels for precision molecular sensing *via* routes is complex, an even more significant challenge is interfacing membrane channels with electronic devices for signal readout, which results in low efficiency of information transfer one of the major barriers to the continued development of high-performance bioelectronic devices. In order to achieve this, they combine membrane-spanning DNA nanopores with bioprotonic contacts to produce programmable, modular, and efficient artificial ion-channel interfaces.

They show that cholesterol-modified DNA nanopores bridge the lipid bilayer generated over the planar bio-protonic electrode surface spontaneously and with remarkable affinity, mediating proton transfer across the bilayer. They demonstrate that this bioprotonic device may be configured for electronic recognition of biomolecular signals such as the presence of Streptavidin and the cardiac biomarker B-type natriuretic peptide without altering the biomolecules. They believe that this robust interface will provide multiplexed electronic measurement and quantification of biomolecules.

Membrane proteins and ion channels operate as size-selective filters or stimulus-responsive molecular valves in biological systems to either passively allow or actively control the flow of ions through the cell membrane. In terms of efficiency, control, and specificity, cellular communication frequently outperforms information processing in electronic devices. The addition of biological components to electronic equipment allows one to access, evaluate, and respond to intercellular information *via* data transduction and signal transmission.

Metal oxide semiconductors with ATPase, carbon nanotubes and silicon nanowires to sense pH, 2D transistors functionalized with gramicidin, organic electrochemical devices with membrane channels and H^+ selective bioprotonic devices with gramicidin, alamethicin, and light sensitive rhodopsins are examples. Synthetic membrane channels with well-defined geometries, durability, resilience, and ease of modification can improve the functionality of these devices. Because of their ease of production, self-assembled synthetic membrane channels are particularly appealing.

Watson-Crick pairing-based hybridization of single-stranded DNA (ssDNA) can be used to rationally and bottom-up design self-assembled DNA nano-structures that resemble membrane proteins with sophisticated architectures and diverse functionalities. In this study, they combine synthetic self-assembled DNA nanopore-based ion-channels with H^+ selective Palladium (Pd)-based electrodes to develop a bioprotonic device that records and regulates H^+ currents traversing the bilayer membrane.

In contrast to previous studies that used single channel ionic current measurements in membrane spanning nanopores our device architecture enables biomolecular recognition as a function of ensemble measurement of the overall conductance change of the membrane, which is an average of many ion-channels spread across several nanopore states. Using programmable DNA nanopores, they demonstrate the device's adaptability in detecting unique biomolecules *via* discrete electronic signals, avoiding the need for extra biomolecule pre-processing.

They successfully showed a programmable bio-protonic device that uses membrane-spanning DNA nanopore ion channels as molecularly precise interconnects to measure and control H^+ transfer across the lipid bilayer interface. They introduced a class of self-assembling membrane-spanning molecular signal transducers by using the programmability of DNA constructs to custom design the nanopores and alter their surfaces. These can connect with bio-protonic contacts to electronically sense specific biomolecules *in-vitro*, eliminating the need for extra biomolecule preprocessing.

They proved with their device architecture that ensemble electronic current signals, rather than single channel recordings, can be employed efficiently for electronic recognition of individual biomolecules. This method allows for the collecting of replies from numerous channels at the same time, which may result in more trustworthy and accurate information on the

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target. Their ensemble method compensates for any fluctuation or outliers in individual channel recordings, resulting in more consistent and trustworthy data, which improves the resilience and reliability in sensing the targets. Furthermore, by eliminating the need for high precision equipment and individual customizing associated with single-molecule devices, this technique considerably simplifies the device production process and signal recording. Furthermore, by conducting ensemble studies and building a dynamic model, they gave valuable insights into the dynamics of DNA nanopores. These findings establish the groundwork for future research into the possible applications of this DNA nanopore architecture in the realm of biosensing.