By reduction of their contact area, we were able to reduce the measurement noise sufficiently to perform single molecule translocation and even nanopore force spectroscopy experiments. We applied this technique to the translocation of DNA hairpin molecules, but also to a G-quadruplex DNA structure, which has not been characterized using nanopore force spectroscopy before. From the data, the unfolding rates of these DNA structures are extracted and compared with those obtained with other single molecule techniques.

3116-Pos

Studying Voltage Dependent Noise in Polymer and Solid State Nanopores

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Studying the noise properties of ion currents in nanopores can improve detection limits for nanopore sensors as well as give insight into behavior of transport at the nanoscale. We focused on the so-called 1/f noise that is observed in the low frequency regime of the ion current power spectra. We found that 1/f noise in single conically shaped nanopores in polymer films exhibits voltage-dependent noise properties, which are not observed for cylindrical pores. The current passing through the nanopore in the low conductance state shows equilibrium 1/f noise, similar to the noise observed in solid state nanopores. Equilibrium fluctuations are defined as the voltage independent power spectrum magnitude normalized by the current squared. The high conductance state causes the 1/f noise to increase exponentially with increased applied voltage, showing a non-equilibrium 1/f noise. Therefore we can switch between the equilibrium and non equilibrium behavior simply by adjusting the voltage. The current in the high conductance state is about 5 times higher then the current in the low conductance state but the noise at 1 Hz is over 100 times higher. Cylindrically shaped nanopores in polymer and solid-state films do not show current rectification and show equilibrium 1/f noise. We discuss these results and give a comparison of the nanopore noise in these various systems. We hypothesize that the non-equilibrium current fluctuations originate from structural fluctuations of flexible polymer pores. The hypothesis is tested by comparison of noise properties between polymer and silicon nitride pores studied at different electrolyte concentrations.

3117-Pos

Slowing DNA Translocation through Nanopores using Organic Salt Solutions

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One of the key challenges to nanopore DNA sequencing is to slow down DNA translocation. Here, we report that the translocation velocities of various DNA homo- and co-polymers through protein pores could be significantly decreased by using electrolyte solutions containing organic salts. Using a butylmethylimidazolium chloride solution instead of the commonly used KCl solution, DNA translocation rates on the order of hundreds of microseconds per nucleotide base were achieved. The much enhanced resolution of the nanopore coupled with the different event blockage amplitudes produced by different nucleotides permits the convenient differentiation between various DNA molecules.

3118-Pos

Electrophysiological Method for Quantification of the Number of phi29 DNA Packaging Nanopore in Planar Bilayer Membrane

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Bacterial virus phi29 uses one of the strongest DNA packaging nanomotors to package its micron-length genomes into a pro-capsid. After re-engineering, whether the DNA nano-motor can be used to pump drugs, DNA, RNA or other therapeutic molecules into specifically targeted cells represent a great challenge in nanomedicine. We have recently successfully embedded the connector, a core component of phi29 DNA package motor, into a planar bilayer membrane (BLM). Under an electric field, double-stranded DNA translocated through the connector channel.

The application of phi29 connector array as a stochastic sensor requires knowledge of the number of channels on each membrane. We herein report a method for precise counting of the number of channels on each membrane by electrophysiological approach. Generally, the number of channels is determined by the conductance of total channels and conductance per single channel. Using a derived empirical equation, we can calculate the conductance per single channel at any salt concentration using conductivity of respective conducting buffer. The total conductance of total channels can be measured by ionic current through all the channels under an applied ramp voltage. Comparison of calculated and true values established this as a feasible, reliable and reproducible approach.

3119-Pos

Ultrathin Nanopores for Nucleic Acid Analysis

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Over the past decade, synthetic nanopores in solid-state membranes have gained reputation as platforms for studying the biophysical properties of biopolymers. In this presentation, the precise fabrication of ultrathin nanopores and their utility for analyzing complex nucleic acid samples will be discussed, with major emphasis on their resolution capabilities for different biopolymers. The membrane thickness was found to play an important role on the signal obtained from different biopolymers. These findings are critical for developing ultrasensitive nanopore assays which profile biopolymer structure, important for genomics and other biophysical studies.

3120-Pos

Single Channel Sensing of dsDNA using the Membrane- Adapted Nanopore of phi29 DNA Packaging Motor

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The bacteriophage phi29 DNA-packaging motor, geared by six pRNA molecules, contains a truncated cone shape connector channel that is 3.6nm in diameter at its narrow end and 6nm in diameter at its wide end. This channel allows dsDNA to enter and exit the virus procapsid during virus maturation and infection, respectively. We modified the genes that code for the core of the phi29 DNA packaging motor in order to change the amino acid sequence of its protein for membrane incorporation. The modified connector was reconstituted into liposomes and fused into a planar lipid bilayer membrane. Distinctive current jumps were found for each connector insertion. The conductance of each connector channel was measured and found to be uniform (4.8nS in 1M KCl). The membrane embedded connector channel was found to be able to translocate dsDNA. The translocations were recorded as blockage events of the current. The blockages were equal for each of the individual channels, generating a clean, homogenous and uniform signal representing DNA translocation.

The connector channel is larger than the previously studied ion channels, which could only let ssDNA pass. The robust property of the connector in ion and dsDNA tranlocation has extensive potentials in microelectromechanical sensing, microreactors, gene delivery, drug loading and DNA sequencing. Single molecule and low concentration sensing can be achieved using this membrane embedded connector system. Additionally, the available crystal structure of the connector protein makes it easy to modify the channel for specific applications and the established large scale purification procedure of the connector will facilitate its practice.

3121-Pos

Fingerpriting of DNA and RNA using the Channels of Bacteriophage phi29 DNA Packaging Motor

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Living systems contain a wide variety of nanomachines and highly-ordered structures of macromolecules that could serve as modules, tool boxes or building blocks in nanotechnology. The ingenious design of the bacteriophage phi29 DNA packaging motor with an elegant and elaborate channel has inspired its application for single molecule detection and sensing. The central component of the phi29 motor is the connector composed of twelve copies of the protein gp10, which form a dodecamer channel. The connector after incorporation into a lipid bilayer can serve as a detector for extremely sensitive, reliable, and precise sensing and fingerprinting of ions and macromolecules at the single molecule level (Nature Nanotechnology, in press). Double stranded and single stranded DNA can be electrophoretically driven through the channel in a concentration and voltage dependent manner. Information about the structure, length and conformational dynamics can then be deduced by their characteristic dwell time during translocation and by their relative percentage in current blockades. This protein nanopore system with explicit engineering capability has potential technological applications such as rapid DNA sequencing, gene therapy and controlled drug delivery.

3122-Pos

Inhibition of the Voltage-Gated Sodium Current and Opening of Nanopores By Ultra -Short Electric Pulses

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Exposure of mammalian cells to high-voltage, ultra-short electric pulses (USEP) leads to formation of membrane nanopores and alters multiple physiological processes, including function of voltage-gated channels. However, it is not known if USEP affect the channels directly, or the effects are mediated