importance for diverse areas of applied biology, medicine and technology. One of the mainstream lines of development of nanofluidic systems and applications today is creation of biosensors capable of sensing single molecules and manipulating them in a controllable manner. Molecules can be detected based on the measurements of ionic currents through appropriately sized channels: entry into a channel of a molecule with the effective cross-dimension comparable to that of the channel lumen is accompanied by decrease of the ionic current recorded at a given transmembrane potential. The transport properties of such channels can be modulated by coating their walls with lipid bilayers, two-dimensional fluids capable of sustaining transport processes within them. In our present work, we made use of this property of the membranes to develop a method for detecting and controllably transporting single-stranded DNA molecules through channels formed by lipid membrane cylinders with the luminal radius of 5-7 nm. Entry of a DNA molecule into such a channel in the conditions of low (~10 mM) ion strength proved to be accompanied by detectable increase of its ionic conductivity in a manner dependent on the direction of the electric field gradient. The amplitude of the conductivity increment can be credibly used to quantify the number the DNA molecules within the channel. Besides that, adsorption of DNA molecules on the lipid bilayer surface was shown to render the membrane cylinder the properties of a voltage-dependent channel with ion selectivity. The work was financially supported by the Russian Science Fund No 17-75-30064.

3405-Pos Board B613

Asymmetric Dynamics and Current Signals of DNA Entering and Exiting a Strongly Confining Nanopore

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In nanopore sensing, changes in ionic current are used to analyse single molecules in solution. The translocation dynamics of polyelectrolytes is of particular interest given potential applications such as DNA sequencing. In this study, we determine how the dynamics and current signatures of voltage driven DNA translocation can be affected by the nanopore geometry and hence the available configurational space for the DNA. Using the inherent geometrical asymmetry of a conically shaped nanopore, we examine how DNA dynamics and current signals depend on the directionality of transport. The total translocation time of DNA when exiting the extended conical confinement is significantly larger compared to the configuration where the DNA enters the pore from the open reservoir. By using specially designed DNA molecules with positional markers, we demonstrate that the translocation velocity progressively increases as the DNA exits from confinement. We show that a hydrodynamic model can account for these observations. The current signatures also depend on the DNA translocation direction and we used a finite simulation method to explain the observed current signatures. Our analysis shows that over a wide range of geometries, voltages, and salt concentrations, we are able to understand the ionic current signals and dynamics of DNA in asymmetric nanopores, enabling signal optimization in molecular sensing applications.

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3406-Pos Board B614

Amplification-Free Detection of Micrornas Related to Clear Cell Renal Cell Carcinoma Utilizing a Novel Nanopore-Based Sensor

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MicroRNAs (miRs) are small noncoding RNAs that play an important role in gene regulation. Recent studies have shown the correlation of the miRs expression level to carcinogenesis. Currently, qRT-PCR technology is considered as the 'gold standard' for miR detection due to its high sensitivity and specificity. However, this technique requires time-consuming and expensive amplification steps along with labeling and enzymatic reactions. In this work, a new nanopore-based detection scheme utilizing a borosilicate micropipette and an assay of complementary gamma-peptide nucleic acid (γ-PNA) probes conjugated to polystyrene beads have been reported for the detection of miR-204 and miR-210 related to the clear cell Renal Cell Carcinoma (ccRCC). Electroosmotic flow (EOF) was induced as the driving force to transport PNA-beads harboring target miRs to the tip of the pore (sensing zone) which resulted in pore blockades with unique and easily distinguishable serrated shape electrical signals. However, in the case of the control experiments ionic current blockades with right-angled shape were detected. The results showed 1 to 10 fM concentration detection limit and 97.6% detection accuracy in 87 experiments. This simple, PCR-free, and robust platform has a technological appeal to be evolved into a quantitative measurement tool for analysis of miR biomarkers in basic and clinical research by correlating the dwelling time of the particles translocation through the pore with the concentration of the RNA oligomers bound to their surface.

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Probing MspA Porin with PEGs: Size-Dependent Partitioning vs. Specific Binding

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We evaluate the effect of differently sized poly(ethylene)glycols, PEGs, on conductance of *Mycobacterium smegmatis* porin A (D90N/D91N/D93N/D118R/E139K/D134R mutant, M2 MspA), designed as a nanopore sensor for DNA sequencing. Unlike other cases of beta-barrel pores, such as alpha-hemolysin and mitochondrial VDAC, M2 MspA pore is characterized by a smooth dependence of PEG partitioning into its lumen on the polymer molecular weight. Asymmetry of M2 MspA channel manifests itself in asymmetric polymer partitioning from the opposite channel entrances, with the characteristic cutoff sizes of PEGs with molecular mass of 8000 and 2000. This is in good agreement with the crystallography data indicating ~4.5 nm and ~2.5 nm diameters for the corresponding channel openings. We note that PEG interaction with the M2 MspA pore is more pronounced when the polymer is applied from the side of the narrow opening. This is observed as a gradual increase of current noise with the PEG molecular weight. Applying buffer conditions that induce high polymer-pore attractions, we resolve individual events of PEG molecule retention in the M2 MspA pore. Overall, our data provide for better understanding of the M2 MspA pore geometry and describe another model system for probing polymer dynamics in confined nano-volumes.

3408-Pos Board B616

Model-Free Observation of Polypeptide Translocation Success Rate through a Nanopore

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Elucidating the motion of uniformly charged polymers in voltage-biased nanoscale channels has been a scientifically and technologically fruitful enterprise. Non-uniformly charged polymers such as polypeptides present a new set of challenges and opportunities, as they do not in general move through a nanopore unidirectionally or translocate the channel-containing membrane with unity probability. Here we demonstrate a single-molecule, model-free experimental technique to track the motion of a polypeptide in a channel and determine whether each polypeptide ultimately translocates through, or retracts from, the channel. The technique relies on the heterogeneity of the charge density along the polypeptide and its effect on the selectivity of the channel. In a nanopore under an electrolyte concentration gradient, the modulation of the channel selectivity is observable in real time as a change in the ionic conductance. For a polypeptide with different charge densities at the N- and C-termini, the ionic current at the end of a single molecule capture ''event'' reports on which end of the molecule exits the nanopore, and hence the direction of escape. As a demonstration, we report experimental observations of the interaction of a ''diblock copolymer''-like neuronal intrinsically disordered protein, α-synuclein, with mitochondrial voltage-dependent anion channel (VDAC). The voltage-dependent translocation probability derived from the experiments shows that α-synuclein is bound to membrane surfaces with a distribution of binding energies that strongly depends on lipid species. These results have broad