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Smooth DNA Transport through a Narrowed Pore Geometry

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Voltage-driven transport of double-stranded DNA through nanoscale pores holds much promise for potential applications in quantitative molecular biology and biotechnology, yet the microscopic details of translocation have proven to be challenging to decipher. Earlier experiments showed strong dependence of transport kinetics on pore size: fast regular transport in large pores (>5 nm diameter), and slower yet heterogeneous transport time distributions in sub-5 nm pores, which imply a large positional uncertainty of the DNA in the pore as a function of the translocation time. In this paper, we show that this anomalous transport is a result of DNA self-interaction, a phenomenon which is strictly pore-diameter dependent. We identify a regime in which DNA transport is regular, producing narrow and well-behaved dwell time distributions that fit a simple drift-diffusion theory. A systematic study of the dependence of dwell times on DNA length reveals a power law scaling of 1.37 in the range of 35 - 20,000 bp. We highlight the resolution of our nanopore device by discriminating via single pulses 100 bp and 500 bp fragments in a mixture with >98%accuracy. Our observation of smooth DNA translocation paves the way for high-resolution DNA mapping and sizing applications in genomics.

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Ultra-Precision Nanopore Tool to Study Enzymes at Work

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The protein pore Mycobacterium smegmatis porin A (MspA) is enabling single-molecule nanopore DNA sequencing. In nanopore sequencing an electric field causes an ion current to flow through a single nano-meter sized pore embedded in a membrane. The electric field also draws single-stranded DNA through the pore. DNA bases inside the pore specifically modulate the measured ion current. We use molecular motors to regulate DNA's translocation speed through MspA. Here, we use this system to examine these motors by measuring the movement of DNA. With MspA, we can detect DNA motion as low as 35 picometers on sub millisecond timescales. To demonstrate the sensitivity of MspA we studied the detailed motions of DNA moved by a Super Family II helicase.

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Solid-State Nanopore Characterization of Single-Strand DNA-SSB Interactions

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Single strand binding protein (SSB) plays a central role in genome replication by binding single-strand (ss) regions of DNA to prevent hybridization and nuclease digestion. Here, we study ssDNA-SSB interactions using solid-state nanopores. We show that a systematic increase in the molar ratio of SSB to ssDNA results in increased translocation event depth until DNA saturation is reached. These results are recapitulated in a bulk electromobility shift assay and indicate the weak cooperativity in SSB binding under high ionic strength conditions. We demonstrate that the strong selectivity of SSB for ssDNA over double-strand molecules can be used to differentiate a heterogeneous mixture and use comparisons of linearized and circular ssDNA data to suggest structural characteristics of SSB binding at high salt.

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Label-Free Optical Detection of Biomolecular Translocation through Nanopore Arrays

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In recent years, nanopores have emerged as exceptionally promising single-molecule sensors due to their ability to detect biomolecules at subfemtomole levels in a label-free manner. Development of a high-throughput nanopore-based biosensor requires multiplexing of nanopore measurements. Electrical detection, however, poses a challenge, as each nanopore circuit must be electrically independent, which requires complex nanofluidics and embedded electrodes. Here, we present an optical method for simultaneous measurements of the ionic current across an array of solid-state nanopores, requiring no additional fabrication steps. Proof-of-principle experiments are conducted that show simultaneous optical detection and characterization of ssDNA and dsDNA using an array of pores. Through a comparison with elec-

trical measurements we show that optical measurements are capable of accessing equivalent transmembrane current information, albeit in the current design access to sub-ms timescales is limited.

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Engineered Material Gradients for Biologically Integrated Stretchable Electronics

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Flexible and stretchable electronics have emerged in a pallet of new technologies for realizing smart sensors and actuators for biologically relevant applications. One of these application areas is skin sensors for measuring temperature, sweat, heart rate, and muscle activity. In order to get better functionality, these sensors should be attached on skin. Skin is soft and stretchable, and muscle contraction and expansion can generate huge strains on the surface of the skin, so sensors must tolerate high strains. Also, the material of these sensors must be compatible with the skin. A current solution for making these sensors is based on thinning the electronic sensors and then embedding them in soft polymers. However, thinning sensors and electronics is challenging while simultaneously maintaining high computational and low power capabilities. We are developing a new platform for stretchable electronics with capability of embedding thick electronic and sensing devices (50 µm). When the thickness of the embedded device increases, the risk of delamination from the polymer rises. This delamination issue is addressed by engineering polymer layers around the electronic part in order to gradually change material properties from a highly rigid material (Si) to a highly soft material (PDMS). We envision our approach being applicable to a range of biologically integrated applications.

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An Inexpensive and Effective Device for Diagnosis of Sickle Cell Disease Christopher Brown, Alexey Aprelev, Frank A. Ferrone.

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The life-span of the 300,000 African newborns with sickle cell disease is typically less than 5 years, and the World Health Organization estimates that "70% of SCD deaths in Africa are preventable with simple, cost-effective interventions such as early identification of SCD patients by newborn screening and the subsequent provision of comprehensive care." In contrast, early and regular care has extended the life-span to around 40 years for the 100,000 total number with SCD in the United States. Present techniques for diagnosing sickle cell disease require resources not necessarily readily available in susceptible areas of the world or fail to give correct response under certain conditions. To address these issues we have developed a capillary-based device to determine the presence of sickle blood. The device, assembled from off-the-shelf components at very low cost, performs the test based on the known rigidity of deoxygenated sickle cells. In the device, a packed bed of glass beads is trapped between two narrow glass capillaries. Capillary action will draw whole blood into the device, but deoxygenated sickle blood, as it occludes the inter-bead spaces, rises into the capillary more slowly than oxygenated sickle blood, which forms the local control for the test. The performance of the device will be described, as well as its potential future use in assessment of the clinical status of patient who have sickle cell disease.

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Controlled Delivery of Dopamine Hydrochloride using Surface Modified Carbon Dots for Neuro Diseases

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Marine Biotechnology, National Sun Yat Sen university, Kaohsiung, Taiwan. Delivery of therapeutic moieties using water soluble Carbon dots (C-dots) have been pivotal to control the release of the drugs under physiological condition due to their high biocompatibility. Controlled Dopamine hydrochloride (DA), a potential neurotransmitter using C-dots as carriers is studied in the present work, in order to highlight its potential to deliver drugs related with neurological disorders such as Alzheimer's and Parkinson's disease. The tenure of the DA release under the considered environment at pH 7.4 was extended to 60 h after conjugation to C-dots, in comparison to bare DA under the same environment. The DA release was as per Hixson-Crowell model. In order to understand the impact of the C-dots-DA conjugate under physiological conditions, Nero 2A cells were taken under consideration. The conjugate was found to have least impact as far as the toxicity of the nanoparticles is concerned. Microtomy of tissue section of vital organs was also performed to see the internal effect of conjugate drug. No inimical effect of the conjugate was found on internal organs of experimental models during histological studies. Less toxicity