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Single-molecule conductance measurements of biomolecule translocation across biomimetic nuclear pores[1]

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After a brief overview of our recent work on solid-state nanopores, I will present single-molecule transport data across biomimetic nanopores that contain the key regulating parts of the nuclear pore complex (NPC). The mechanism for the remarkable selectivity of NPCs has remained unclear in a large part due to difficulties in designing experiments that can probe the transport at the relevant length and time scales. Building and measuring on biomimetic NPCs provides new opportunities to address this long-standing problem. covalently tether the natively unfolded Phe-Gly rich domains (FG-domains) of human nuclear binding proteins to a solid-state nanopore (a 10-100 nm sized hole in a SiN membrane). Ionic current measurements provide a probe to monitor single molecules that traverse the pore. Translocation events are observed for transport receptors (Impβ), whereas transport of passive molecules (BSA) is found to be blocked. Interestingly, a single type of nuclear pore proteins appears already sufficient to form a selective barrier for transport. A translocation time of about 2.5 ms is measured for Impβ. This time is found to be similar for transport across Nup153 and Nup98 coated pores, although the observed ionic conductance differs between these two types of pores. We compare two simple models for the pore conductance and find, for both Nups, that the data fits best to a model with an open central channel and a condensed layer along the outer circumference of the pore. reproducing the key features of the NPC, our biomimetic approach opens the way to study a wide variety of nucleo-cytoplasmic transport processes at the single-molecule level in vitro.

[1]Work carried out by my graduate student Stefan W. Kowalczyk at Delft and in collaboration with Larisa Kapinos and Roderick Y. H. Lim at the University of Basel.