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## Deconstructing nuclear pore complex function by bio-synthetic reconstruction

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Cellular nanomachines are touted to offer novel technological strategies provided that their mechanisms can be replicated outside the cell. This provides the driving impetus in our lab to resolve the *modus operandi* of the nuclear pore complex (NPC), which regulates macromolecular traffic between the nucleus and the cytoplasm. As a physical pore ~50 nm in diameter, the biological marvel of the NPC lies in its ability to restrict or promote cargo translocation via biochemical selectivity and not size exclusion *per se*. Moreover, unlike synthetic nanopores, the NPC does not clog *in vivo* - in spite of the molecular complexity of the cellular environment.

The objective of our lab is to cast a wide net in order to resolve and correlate the pertinent biophysical, biochemical and structural aspects of NPC functionality. These efforts range from (i) applying AFM to studying the nanomechanical force response of the key NPC proteins (i.e., natively unfolded phenylalanine-glycine (FG)-rich domains) on pore-like nanostructures; (ii) to correlating binding-induced conformational changes in the FG-domains to binding affinities using surface plasmon resonance; (iii) to constructing biomimetic nanopores that reproduce the transport selectivity of the NPC.

In my talk, I will describe how these efforts provide new insight into the underlying principles that govern molecular mechanics, selectivity and transport in the NPC. By replacing the NPC machinery with synthetic polymers, I will further demonstrate how NPC-like functionality can be harnessed to target specific proteins from authentic biological environments to site-selective locations with nanoscale precision - in technological systems.

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3. Peleg O. and **Lim R. Y. H.**, Converging on the Function of Intrinsically Disordered Nucleoporins in the Nuclear Pore Complex, *Biological Chemistry* 391 719 (2010)
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