New materials that control specific biomolecular transport will be central to numerous technologies including biosensors, bioseparations, and tissue engineering. Natural systems such as nuclear pores routinely regulate molecular transport with remarkable specificity (>99.9% of proteins rejected) and speed (1,000 proteins per second per pore), but the biophysical mechanisms underlying selective nuclear transport remain unclear. The central channel of the nuclear pore is filled with a disordered matrix of nucleoporin proteins, which inspired the development of a selective transport model based on protein binding, diffusion, and solubility in a polymer network.

In this seminar, I will present a continuum-scale transport model used to investigate the selective transport phenomena exhibited by nucleoporins. The transport model accounts for binding and diffusion of biomolecules in a polymer network. Specifically, target biomolecules exhibit diffusive behavior in bound and unbound molecular states, in comparison to inert biomolecules that exist only in an unbound state. Calculation of the flux ratio of target and inert molecules across a broad parameter space reveals key requirements for selective transport to occur in polymer networks. The model predicts two key principles for selective biomolecular transport by a polymer network: (1) entropic repulsion of non-interacting molecules and (2) affinity-mediated permeation of interacting molecules through a walking mechanism. These principles guide the design and synthesis of artificial, nucleopore-inspired polymer gels that replicate the selective transport function of nuclear pore proteins. Biophysical characterization reveals the importance of entropic size exclusion, moderate binding affinity, and bound-state diffusion processes in selective hydrogel permeability and transport, in agreement with predictions of the selective transport model. Overall, this work presents a new paradigm for selective transport that critically enables the design of polymer hydrogels to control the transport of multi-receptor biomolecules including therapeutic proteins, immunoglobulins, and broad classes of biotoxins.