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Self-regulating mechanisms of bi-directional transport through the Nuclear Pore Complex

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Nuclear Pore Complex (NPC) is a biomolecular "nanomachine"that controls nucleocytoplasmic transport in eukaryotic cells. The key component of the functional architecture of the NPC is the assembly of the polymer-like intrinsically disordered proteins that line its passageway and play a central role in the NPC transport mechanism. Due to paucity of experimental methods capable to directly probe the morphology and the dynamics of this assembly in intact NPCs, much of our knowledge about its properties derives from in vitro experiments interpreted through theoretical and computational modeling. Remarkably, despite their molecular complexity, much of the behavior of these assemblies and their selective permeability with respect to cargo-carrying transport proteins can be understood based on minimal complexity models relying on the statistical physics of molecular assemblies on the nanoscale.
Due to the unstructured nature of the proteins in the NPC passageway, it does not possess a molecular "gate" that transitions from an open to a closed state during translocation of individual cargoes. Rather, its passageway simultaneously contains multiple transport proteins carrying different cargoes in both directions. Although this feature increases NPC throughput, it remains unclear how the NPC maintains selective and efficient bi-directional transport under such crowded conditions. I will present of a coarse-grained computational model of the NPC transport and will discuss various proposed solutions to the crowding problem in light of the model results and the available experimental data.

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