# Molecular Organization and Translocation in Nuclear Pore Complexes

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Abstract:

In this talk we will describe theoretical predictions for the molecular structure of yeast Nuclear Pore Complex (NPC) and the translocation of model particles. The theoretical approach that we apply is a molecular theory that accounts for the geometry of the pore and the sequence and anchoring position of the unfolded domains of the nucleoporin proteins (the FG-Nups), which control selective transport through the pore. The theory explicitly models the electrostatic, hydrophobic, steric, conformational and acid-base properties of the FG-Nups. The electrostatic potential within the pore, which arises from the specific charge distribution of the FG-Nups, is predicted to be negative close to pore walls and positive along pore axis. The positive electrostatic potential facilitates the translocation of negatively charged particles and the free energy barrier for translocation decreases for increasing particle hydrophobicity. The above results agree with the experimental observation that transport receptors which form complexes with hydrophilic/neutral or positively charged proteins to transport them through the NPC, are both hydrophobic and strongly negatively charged. The molecular theory shows that the effects of electrostatic and hydrophobic interactions on the translocating potential are cooperative and non-equivalent due to the interaction-dependent reorganization of the FG-Nups in the presence of the translocating particle. The combination of electrostatic and hydrophobic interactions can give rise to complex translocation potentials displaying a combination of wells and barriers, in contrast to the simple barrier potential observed for a hydrophilic/neutral translocating particle. This work demonstrates the importance of explicitly considering the amino acid sequence and hydrophobic, electrostatic and steric interactions in understanding the translocation through the NPC.