BLUE WATERS
SUSTAINED PETASCALE COMPUTING

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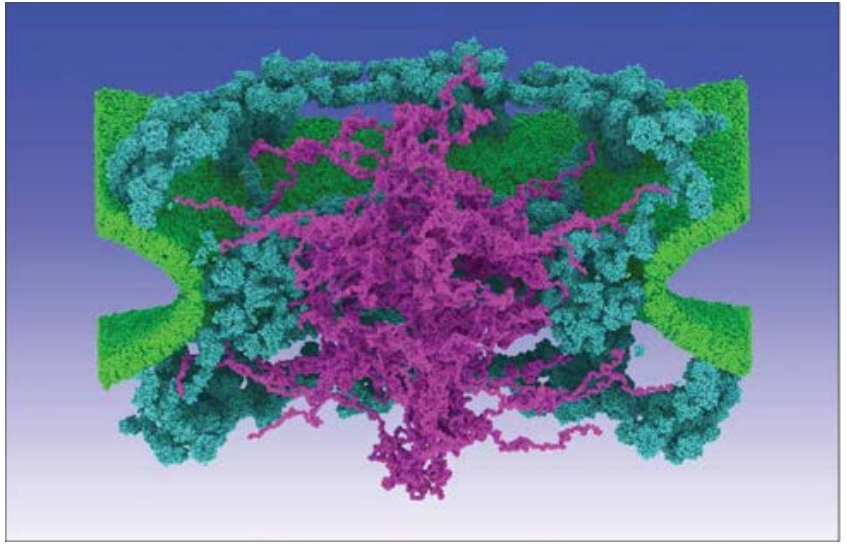
Biology, Chemistry & Health

MOLECULAR MECHANISM OF NUCLEAR TRANSPORT

Research Challenge

The nuclear pore complex (NPC) regulates the transport of all ribonucleic acid (RNA) and proteins across the nuclear envelope of eukaryotic cells, in which the well-defined chromosomes (bodies containing the hereditary material) are located. Simulations will be conducted to gain new insight into the physical mechanism of nuclear transport, with important implications for several human diseases and the development of novel gene therapies.



An atomic model of the entire nuclear pore complex, 140 M atoms in total (water omitted for clarity). Colors highlight the outer scaffolding (in cyan), the disordered central channel of nups (in purple), and the nuclear envelope (in green).

Methods & Codes

We performed explicit-solvent all-atom MD simulations with the latest version of NAMD2 of a solution of nucleoporin (nup) fragments and varied the protein volume fraction within a confined volume. Simulations with an applied electric field were performed to calculate ionic conductivity as a function of nup density. We used atomic-resolution Brownian dynamics (ARBD) and traditional all-atom MD to model the entire NPC

Results & Impact

We characterized the structural fluctuations and electrical properties of a solution of nups varying in protein density. We measured the ionic current of each system in the presence of an applied electric field and observed a transition from conducting to not-conducting ions at a critical nup density, matching a key experimental result. This project may offer new insights into the molecular origin of diseases (e.g., cancer, viral infections, and neurodegenerative diseases) with implications for developing gene therapy treatments.

Why Blue Waters

Explicit-solvent all-atom MD simulations are needed to characterize the structural fluctuations and electrical properties of the disordered central channel of the NPC. MD simulations the size of the entire NPC—140 Million atoms—are only possible with the computational power of Blue Waters. The large number of XK nodes with GPU accelerators and fast Gemini interconnect makes it one of the best publicly available systems for performing simulations of the entire NPC.