BLUE WATERS
SUSTAINED PETASCALE COMPUTING

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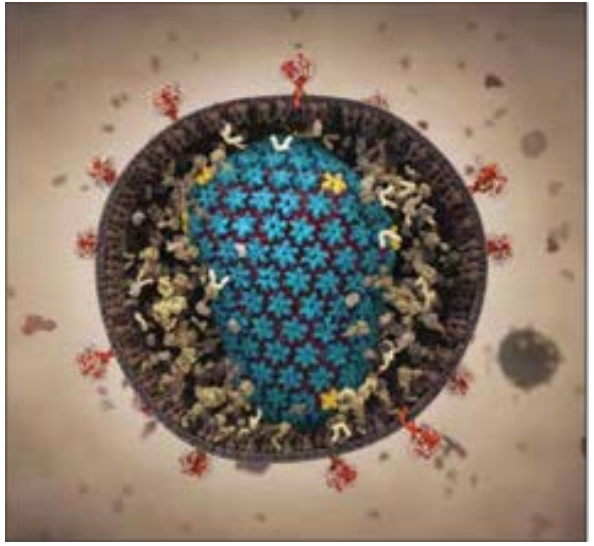
Biology, Chemistry & Health

STUDYING CELLULAR PROCESSES THROUGH THE COMPUTATIONAL MICROSCOPE

Research Challenge

Infectious viral pathogens such as the human immunodeficiency virus type 1 (HIV-1) and the hepatitis B virus (HBV) are major risks to public health, and millions of people die annually due to a lack of effective anti-viral treatments. Developing novel drug compounds that can target viruses depends heavily on characterizing components of virus structure and the roles these components play in facilitating infection. One such component key to virus function is the capsid, a protein shell that packages the viral genome and regulates its delivery to the host cell nucleus. Virus capsids are currently of great pharmacological interest as drug targets.



At the core of the HIV-1 virion lies its capsid. Composed of repeating copies of proteins, the capsid protects the viral genome and performs key functions throughout the viral life cycle that are essential to successful infection.

Methods & Codes

Molecular Dynamics (MD) simulation provides a powerful technique to investigate the structure and properties of virus capsids. All-atom simulations are capable of capturing subtle effects on capsid structure and dynamics induced by bound drug molecules. While simulation of capsids comes at great computational expense, access to the NAMD simulation software on Blue Waters has revealed new insights into capsids, as well as to suggest mechanisms by which drug molecules can disrupt them.

Results & Impact

A simulation characterizing the dynamical behavior of the HIV-1 capsid system (64 million atoms) over the timescale of 1 µs, indicate new avenues for the development of drugs that seek to disrupt the capsid by altering its complex biophysical properties. Extensive unbiased simulations have characterized the dynamical behavior of the HBV capsid system (6 million atoms) in the presence and absence of three distinct drug compounds over timescales of 1 µs.

Why Blue Waters

Due to their formidable computational expense, these simulations of virus capsids are only possible on a machine like Blue Waters. Further, analysis of the data sets generated by these simulations is feasible only through access to the massively parallel computing power and high-performance Lustre filesystem provided by a resource like Blue Waters. The exciting discoveries revealed by this project underscore the essential role for Blue Waters in the development of anti-viral treatments, and demonstrate that access to leadership-class computing facilities holds the potential for significant impact on overall public health.