Marc Morais, PhD
Associate Professor
Biochemistry & Molecular Biology

A Viral Genome Packaging Motor Transitions Between Cyclic and Helical Symmetry to Translocate dsDNA

The Morais laboratory uses a combination of structural, biophysical, biochemical, and computational approaches to study the structures and functions of complex macromolecular assemblies and machines. By integrating results from X-ray crystallography, cryo-electron microscopy, small angle X-ray scattering, and traditional biochemical/biophysical methods with molecular simulations, we are able to probe how changes in molecular structure give rise to biological function. In particular, we interested in understanding the rules that govern self-assembly of viral capsids, as well as how various components in molecular motors coordinate their activities to efficiently generate force. By understanding the structure-function relationship at the atomic scale, we hope to apply this knowledge towards the development of therapeutics and the rational design of novel nano-motors and machines.

Abstract: Molecular segregation and biopolymer manipulation require the action of molecular motors to do work by applying directional forces to macromolecules. The additional strand conserved E (ASCE) ring motors are an ancient family of molecular motors responsible for diverse tasks involving biological polymer manipulation (e.g. protein degradation and chromosome segregation). Viruses also utilize ASCE segregation motors to package their genomes into their protein capsids against considerable energetic barriers. Indeed, they are the most powerful molecular motors in nature, and thus provide a unique window into the mechanochemistry of force-generation found in this broad class of molecular motors. We show by CryoEM focused image reconstruction that ASCE ATPases in viral dsDNA packaging motors adopt helical symmetry complementary to their dsDNA substrates. In contrast results from X-ray crystallography showing these ATPases can also adopt planar ring conformations. Taken together with complementary long time-scale MD simulations, these results suggest that viral dsDNA packaging motors translocate dsDNA via stepwise helical-to-planar ring transitions that are tightly coordinated by ATP binding, hydrolysis, and release.

University of Texas Medical Branch at Galveston