LARGE-SCALE COARSE-GRAINED MOLECULAR SIMULATIONS OF THE VIRAL LIFECYCLE OF HIV-1

Research Challenge

- HIV-1 Gag polyproteins self-assemble into the “immature protein lattice” at an infected cell’s membrane as part of the process of releasing viral particles to spread the infection.
- Disruption of this self-assembly is a potential therapeutic target, but difficult to study in conventional experiments.
- Understanding aggregation and interactions of large numbers of biomolecules at cell membranes can advance fundamental biophysical knowledge.

Methods & Codes

- We created large-scale coarse-grained (CG) molecular models of relevant viral components and the cell membrane to investigate immature protein lattice self-assembly.
- CG models are computationally efficient, enabling otherwise-impossible simulated time- and length-scales.

Results & Impacts

- By combining computer simulations with fluorescence localization experiments, we elucidate the interactions that regulate HIV-1 viral assembly dynamics.
- Aspects of the interactions, difficult to control experimentally, are tractable with our CG models.
- Insights gained through CG analysis can assist in designing new therapeutic approaches.

Why Blue Waters

- These simulations required simulating large numbers of individual molecules over long time scales, under a wide range of biologically-relevant conditions.
- The tightly coupled parallel nature of our simulations made the leadership-class computing capabilities and cutting-edge network hardware of Blue Waters crucial in successfully investigating this and other molecular systems of significant biomedical interest.