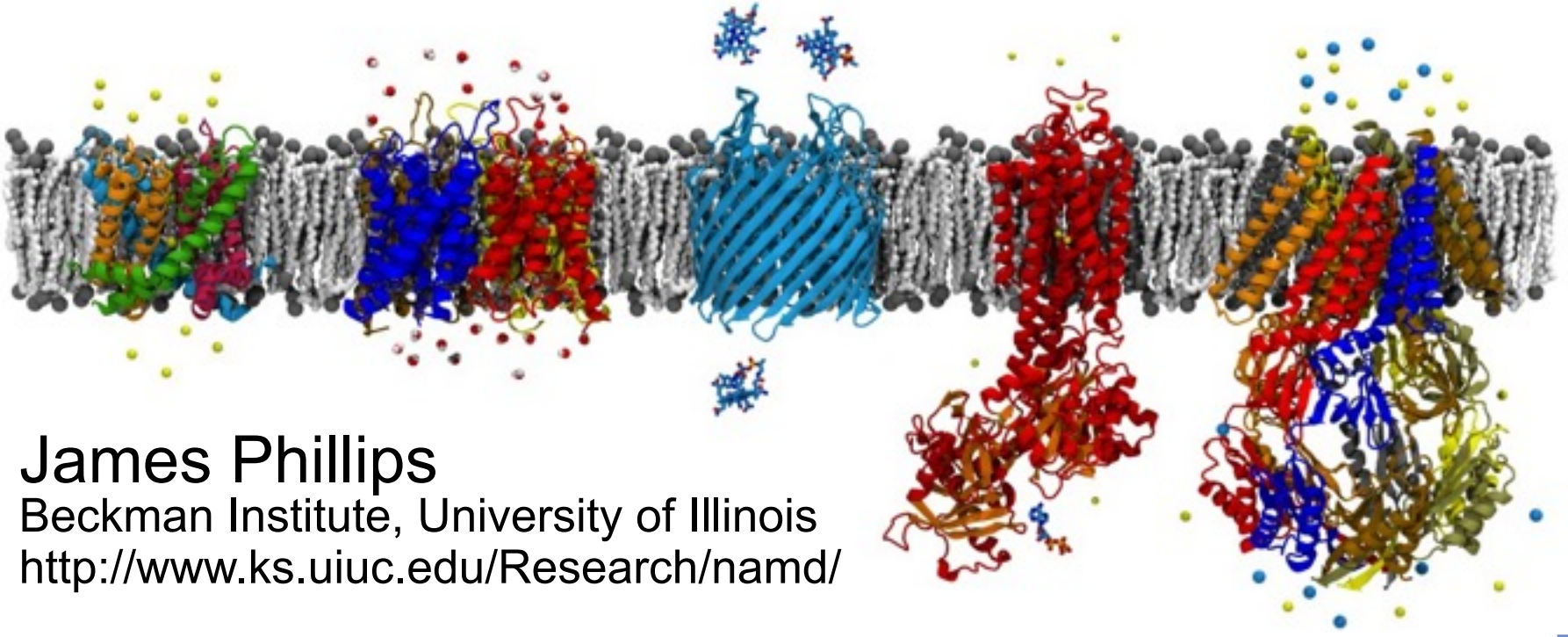
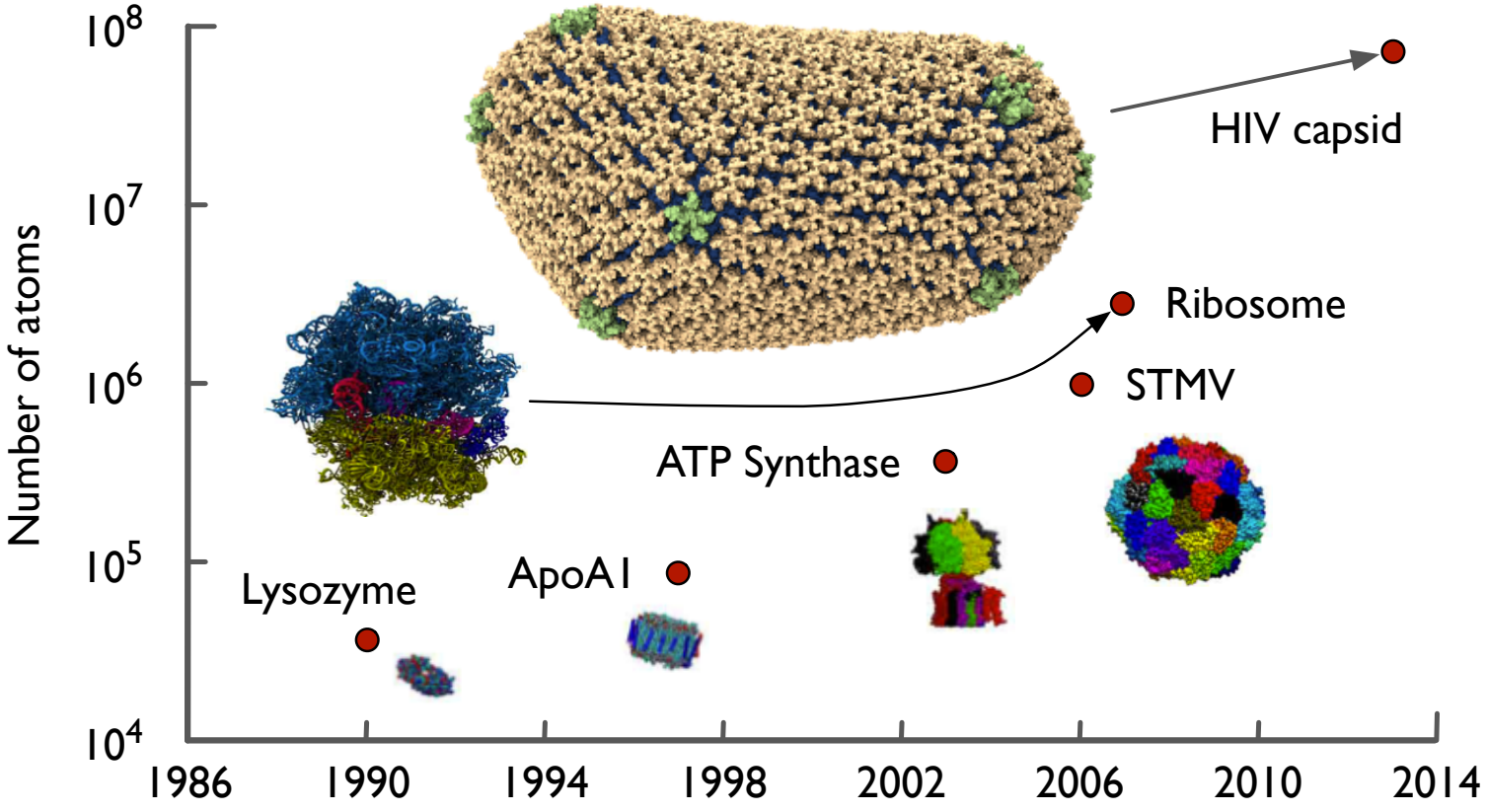
Petascale Bimolecular Simulation with NAMD on Titan, Blue Waters, and Summit

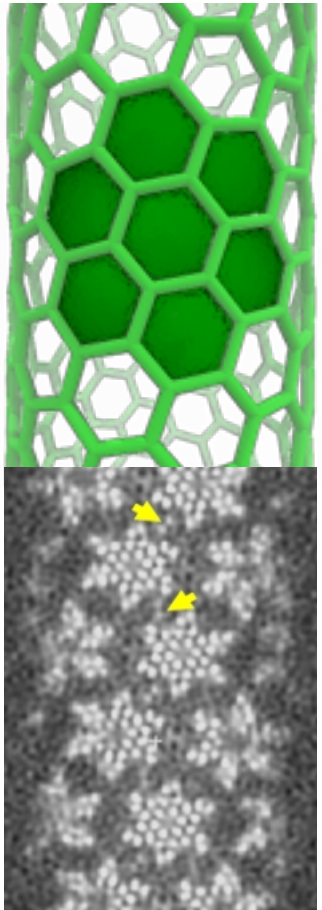


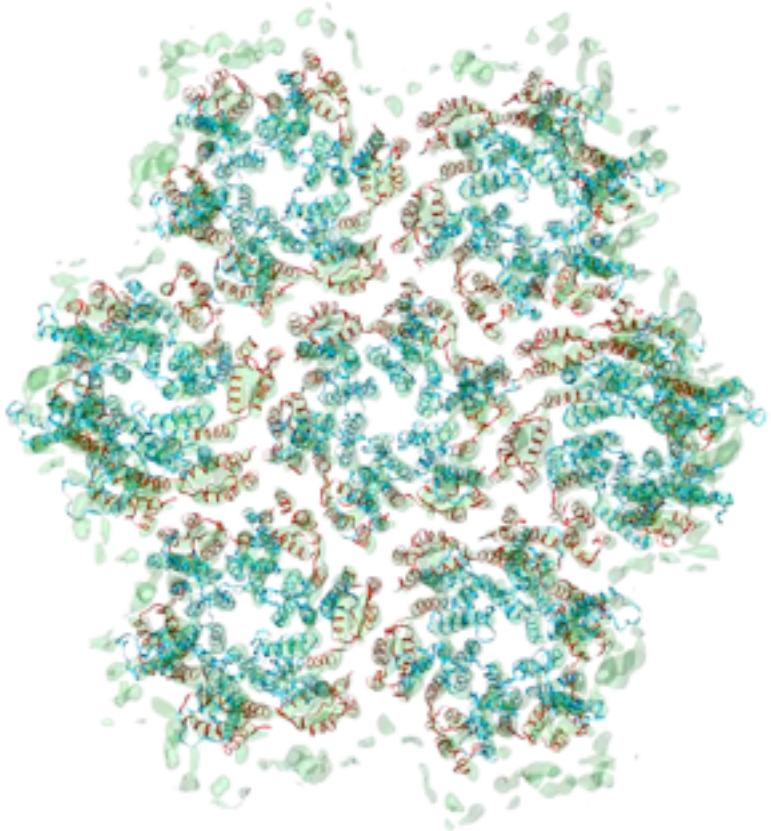
James Phillips
Beckman Institute, University of Illinois
http://www.ks.uiuc.edu/Research/namd/

Need for petascale: Simulation follows structural discovery



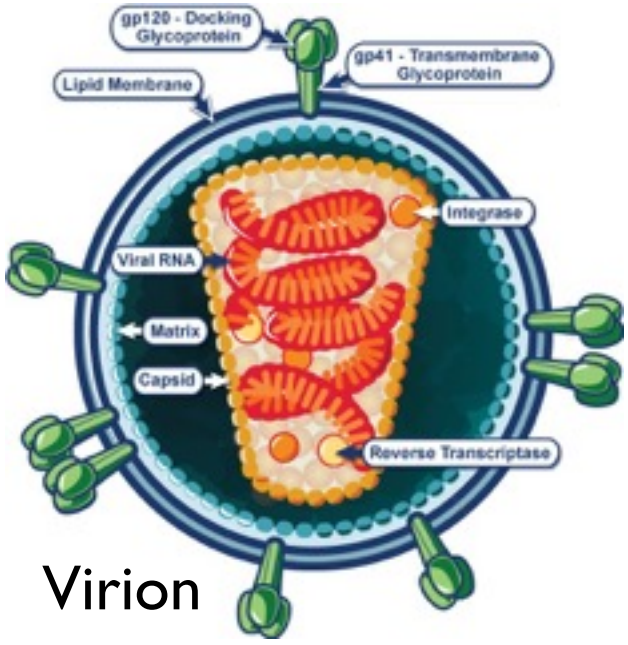
Need for petascale: Simulation **enables** structural discovery

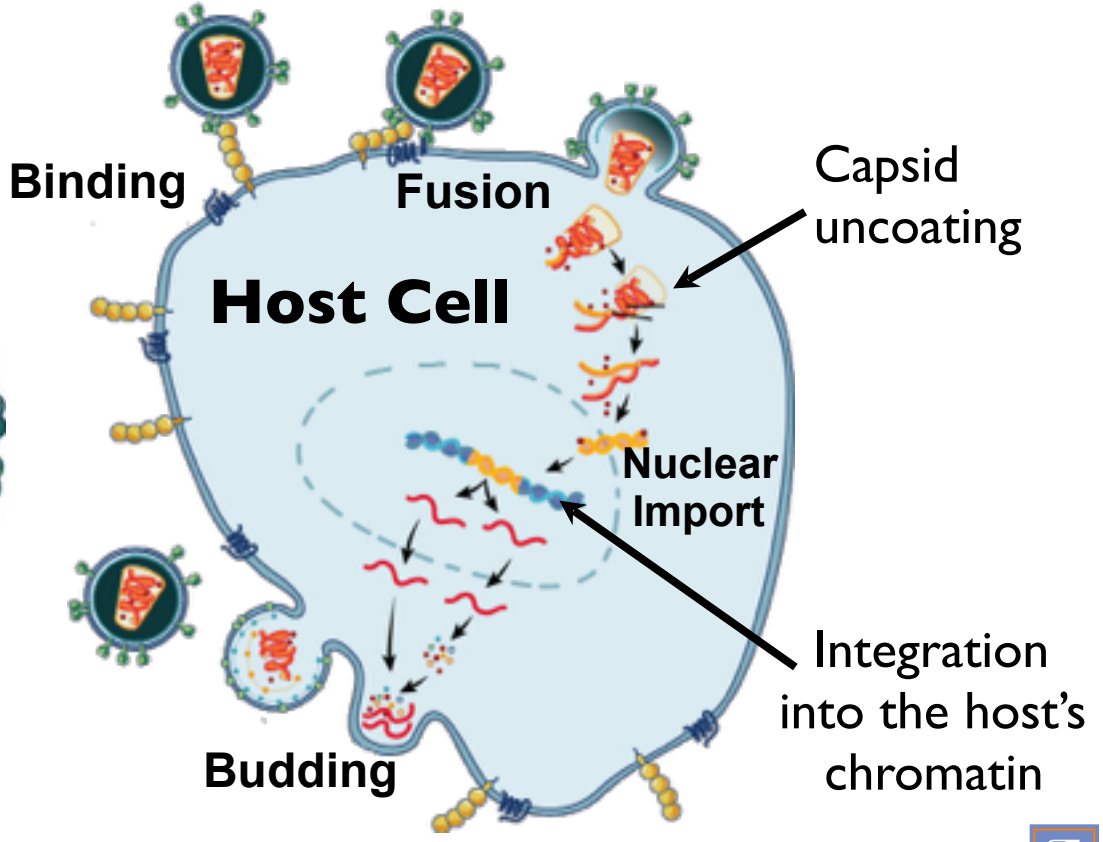




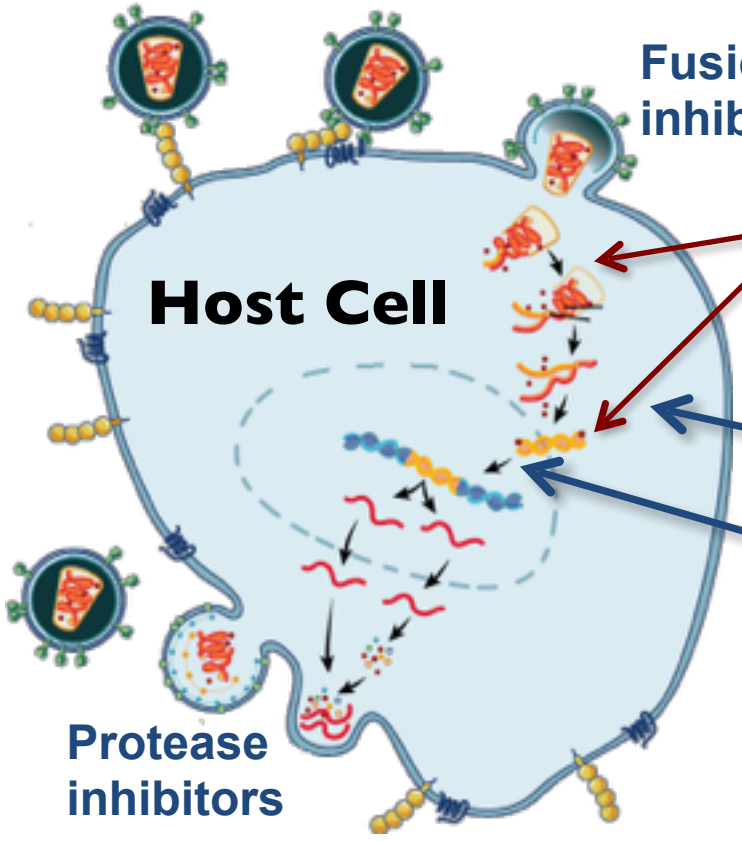
G. Zhao, et al. *Nature* **497** (2013); exp + comp

Capsid is central to HIV infective cycle





How is HIV treated today?



Fusion/Entry inhibitors

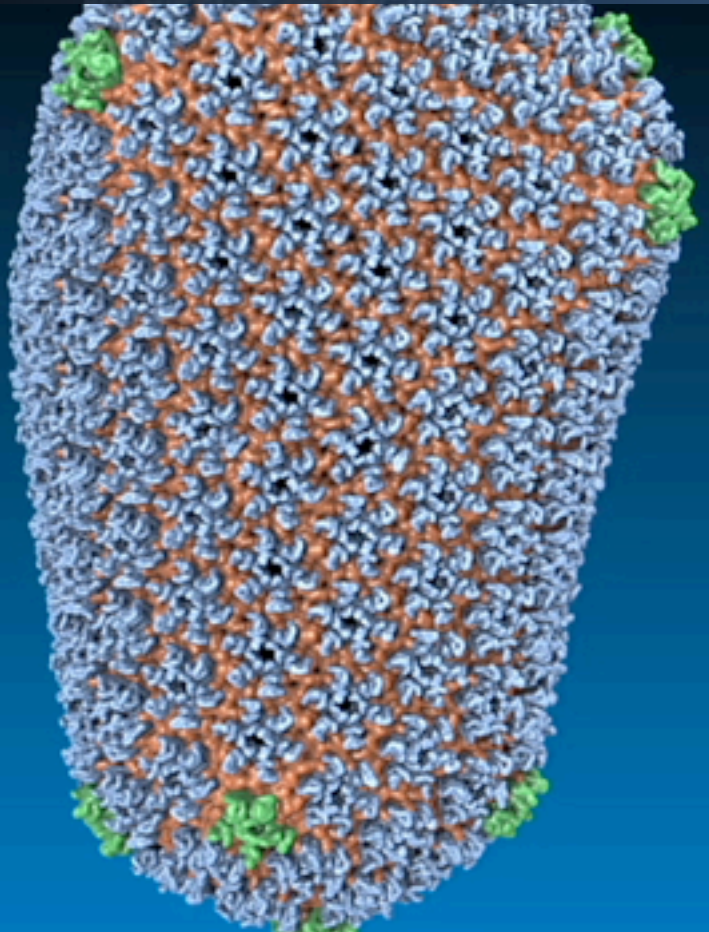
Currently no drug targets *capsid uncoating* or *nuclear import* !

Reverse Transcription (RNA to DNA) inhibitors

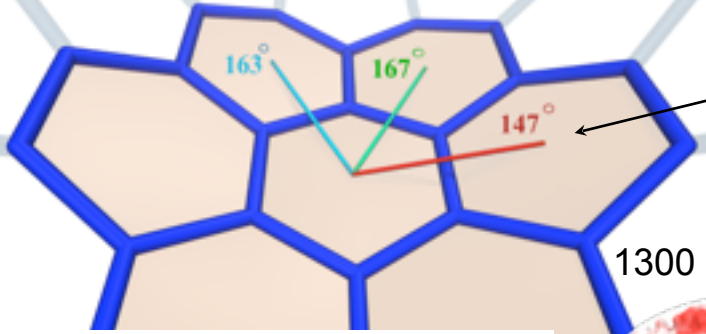
Integrase inhibitors

Protease inhibitors

HIV capsid contains 186
1300+ proteins,

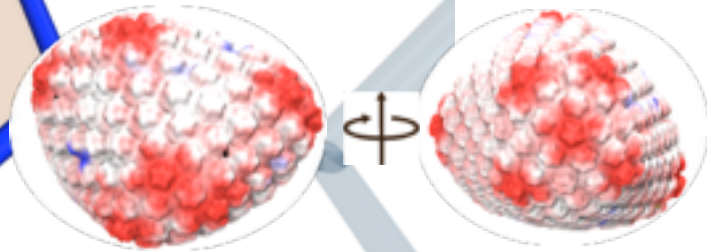


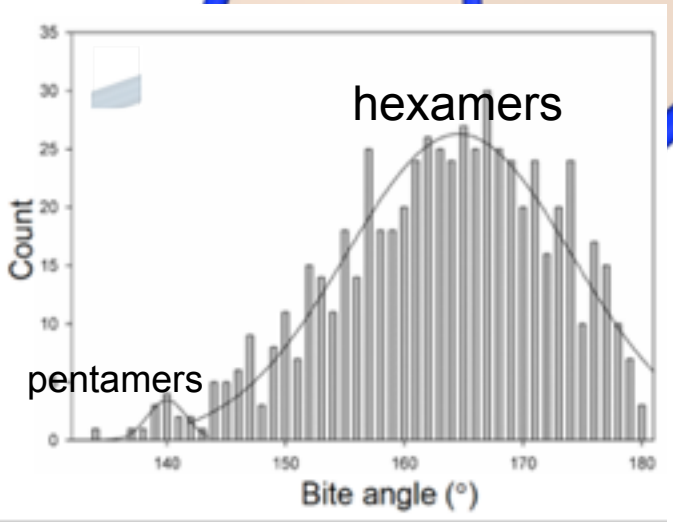
Complex structure from a single building block



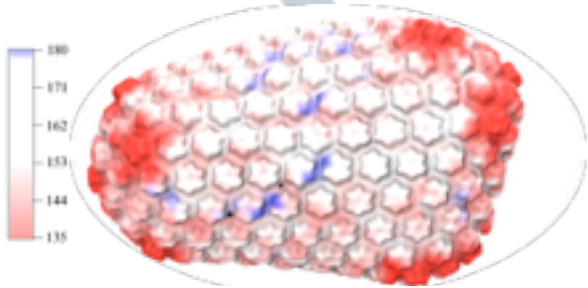
Hexamer of hexamers bite angles along chiral axis

1300 proteins in different conformations



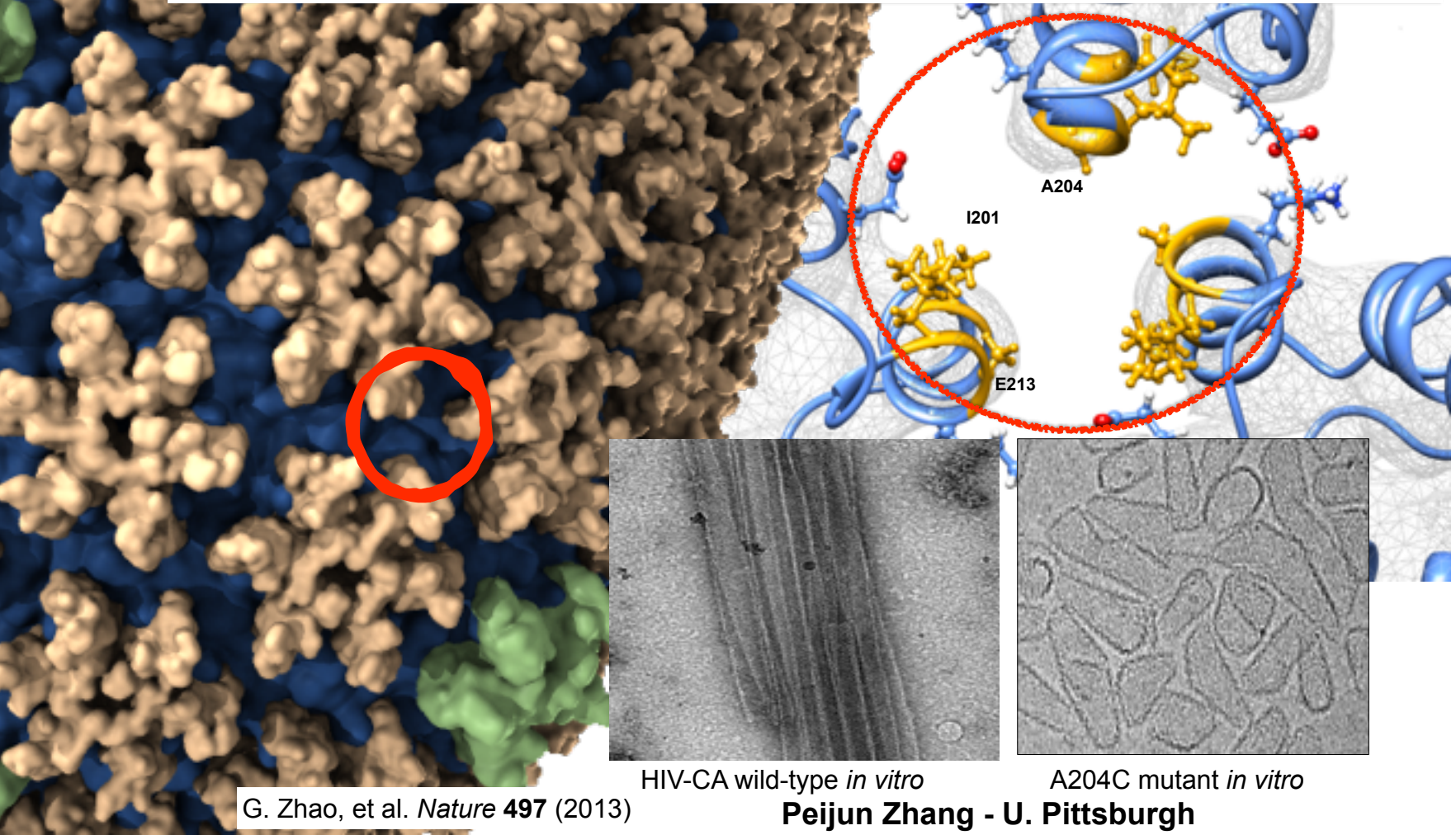


G. Zhao, et al. *Nature* **497** (2013)



Native capsid bite angle distribution

Curvature is regulated by the trimer interface at the atomic level



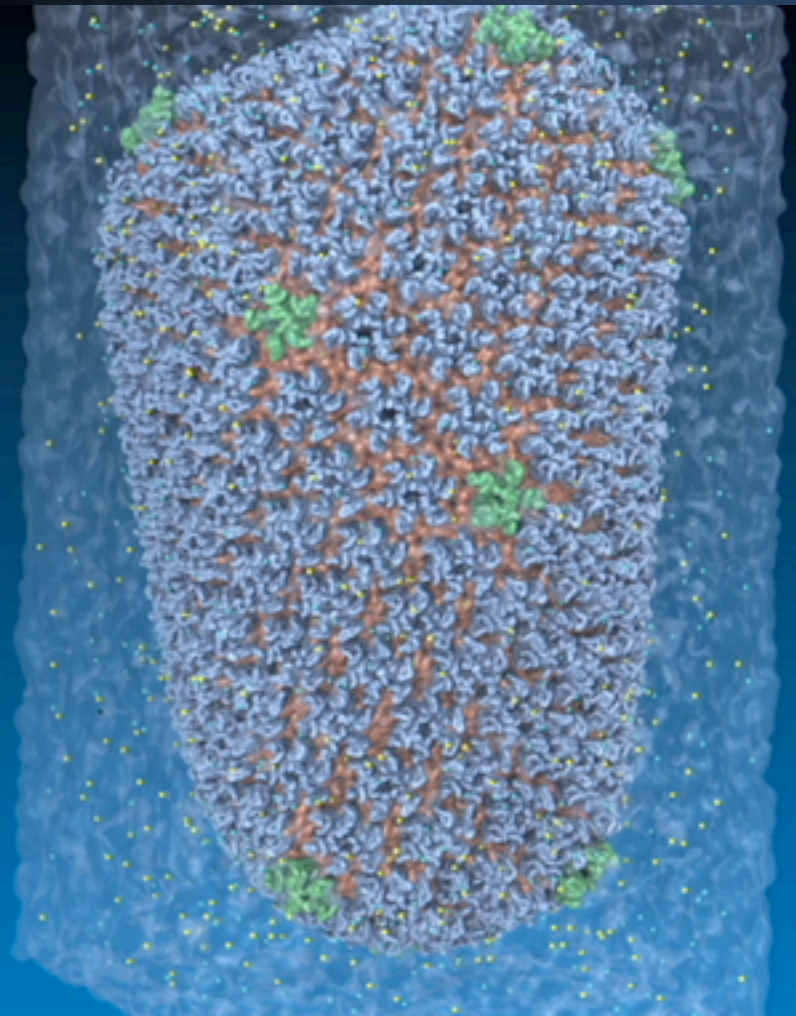
HIV-CA wild-type *in vitro*

A204C mutant *in vitro*

G. Zhao, et al. *Nature* **497** (2013)

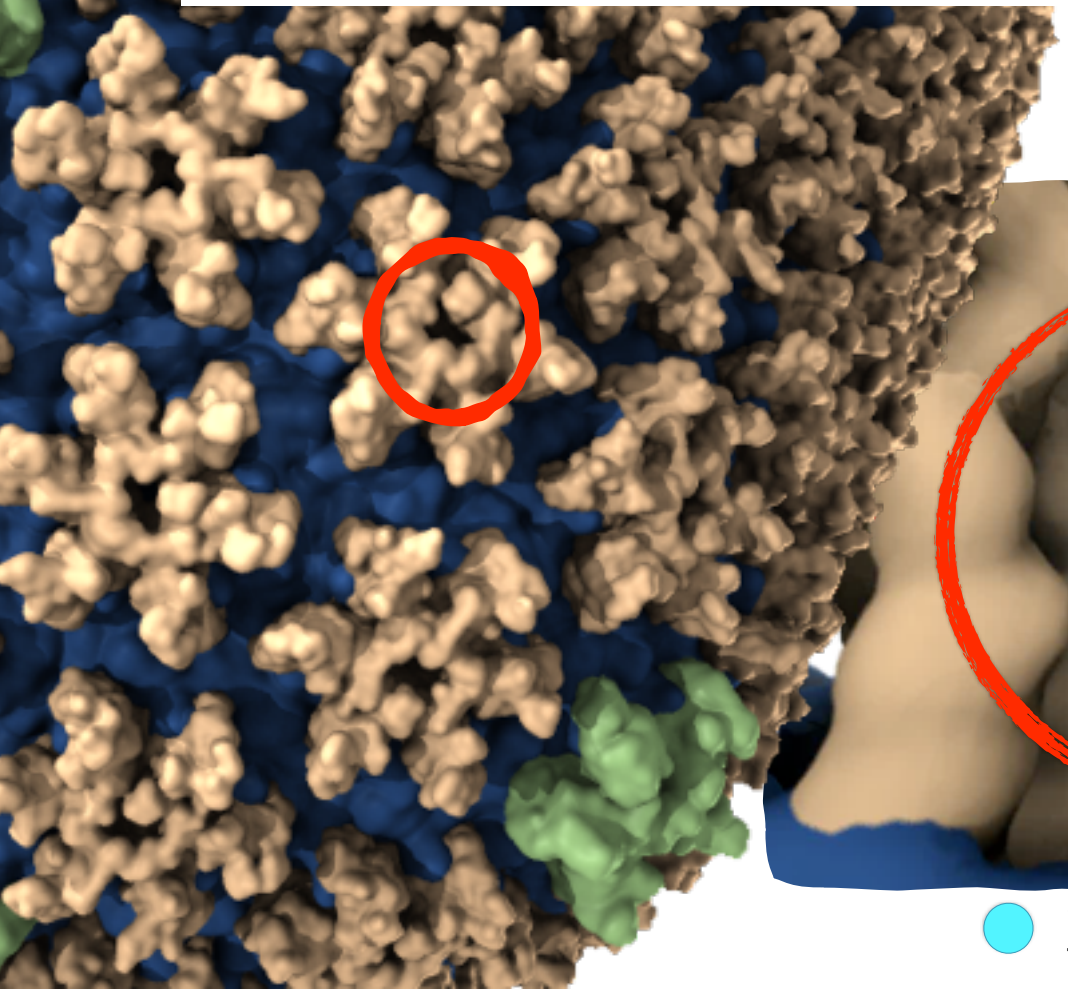
Peijun Zhang - U. Pittsburgh

One-Microsecond Simulation Includes 64 Million Atoms

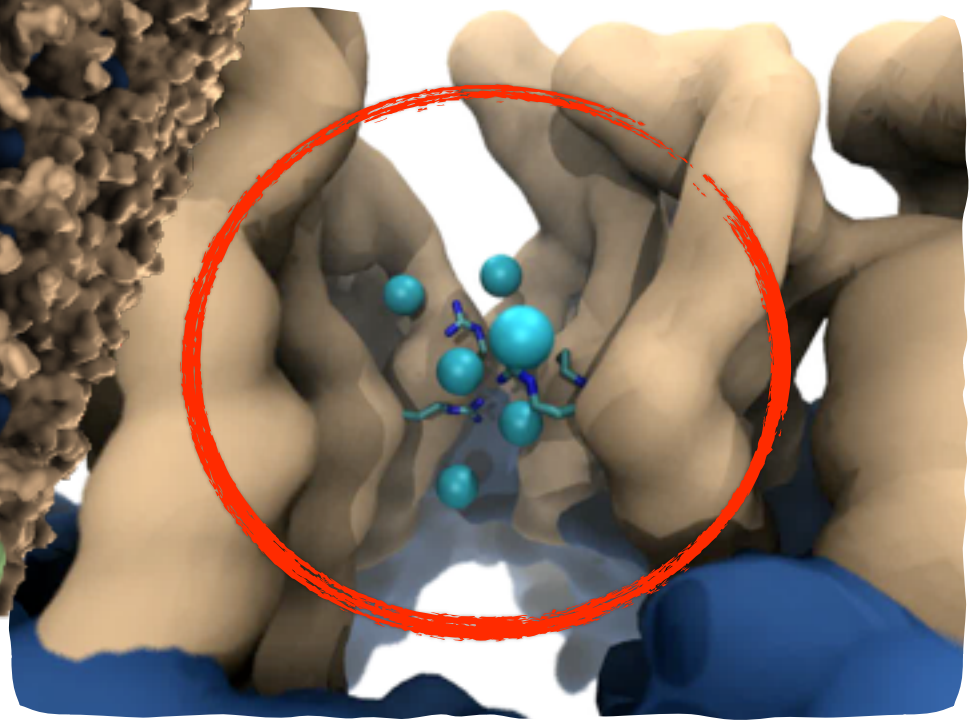


Key person:
Juan Perilla
(UIUC)

Simulation reveals osmotic regulation by capsid

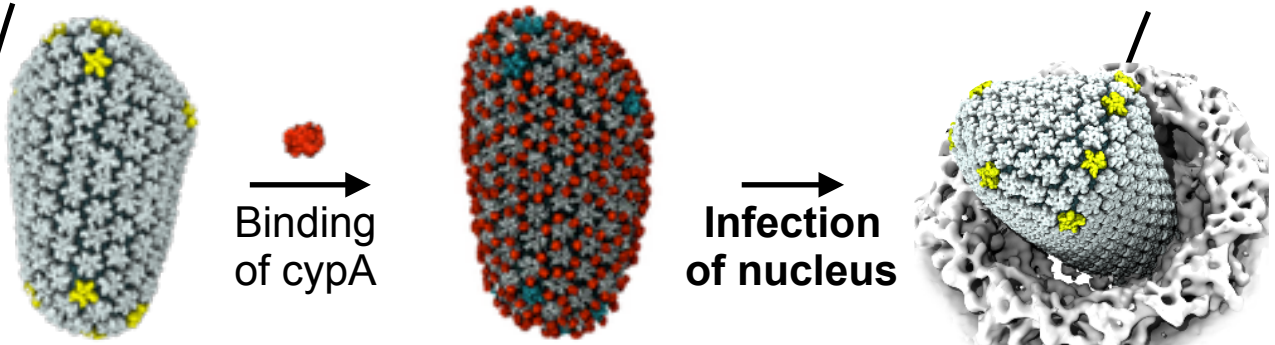


Results from 64 M atom, 1 μs molecular dynamics simulation!



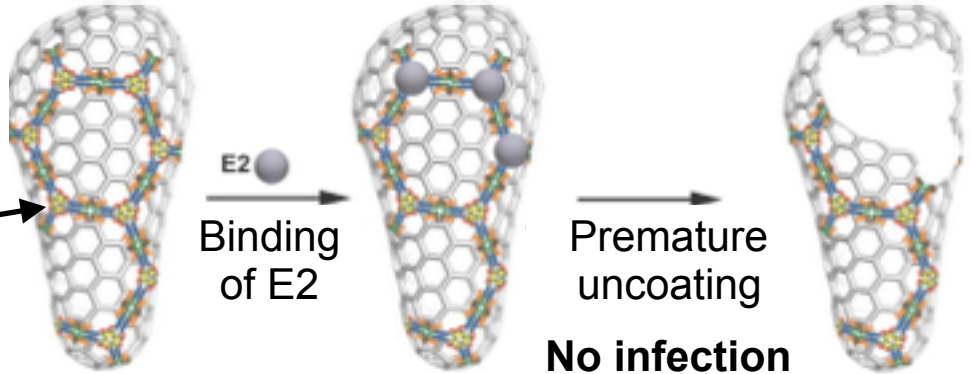
Chloride ions permeate through the hexameric center

HIV uncoating relies on cell factor CypA



Outside
of Cell

cypA binding pattern prevents TRIM binding, but leaves nuclear pore interactions intact



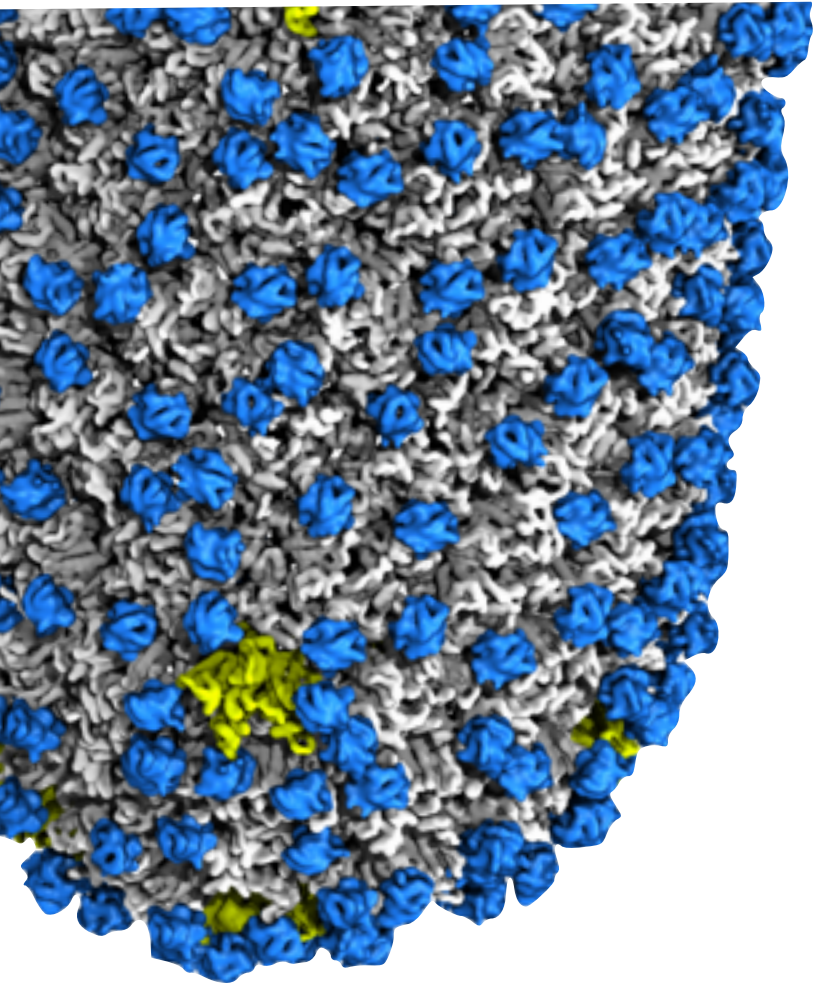
TRIM lattice

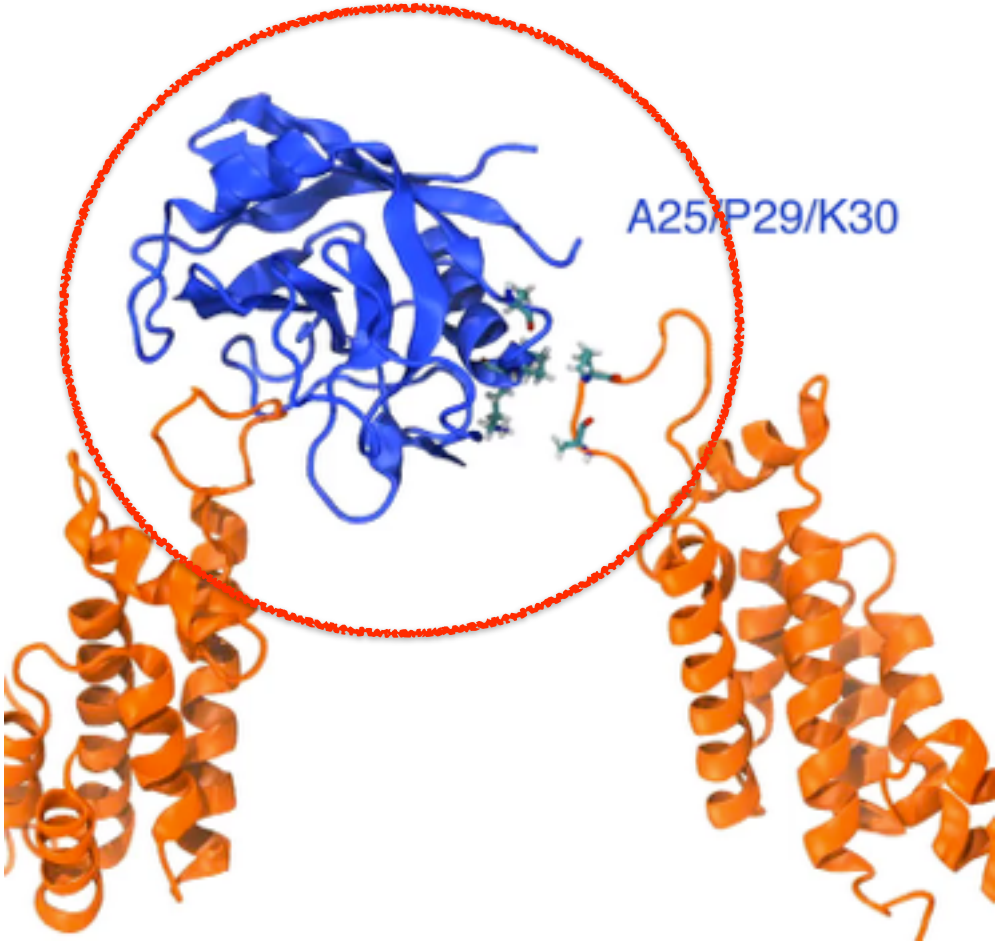
No infection

Cell
Nucleus

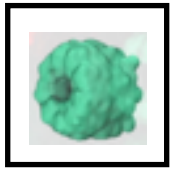
F. Diaz-Griffero, *Viruses* (2011)

Simulation reveals how CypA stabilizes capsid

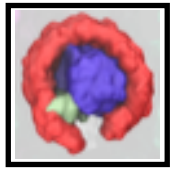




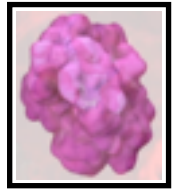
Light Harvesting for ATP Production in the Chromatophore



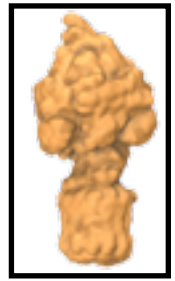
LH2



LH1-RC



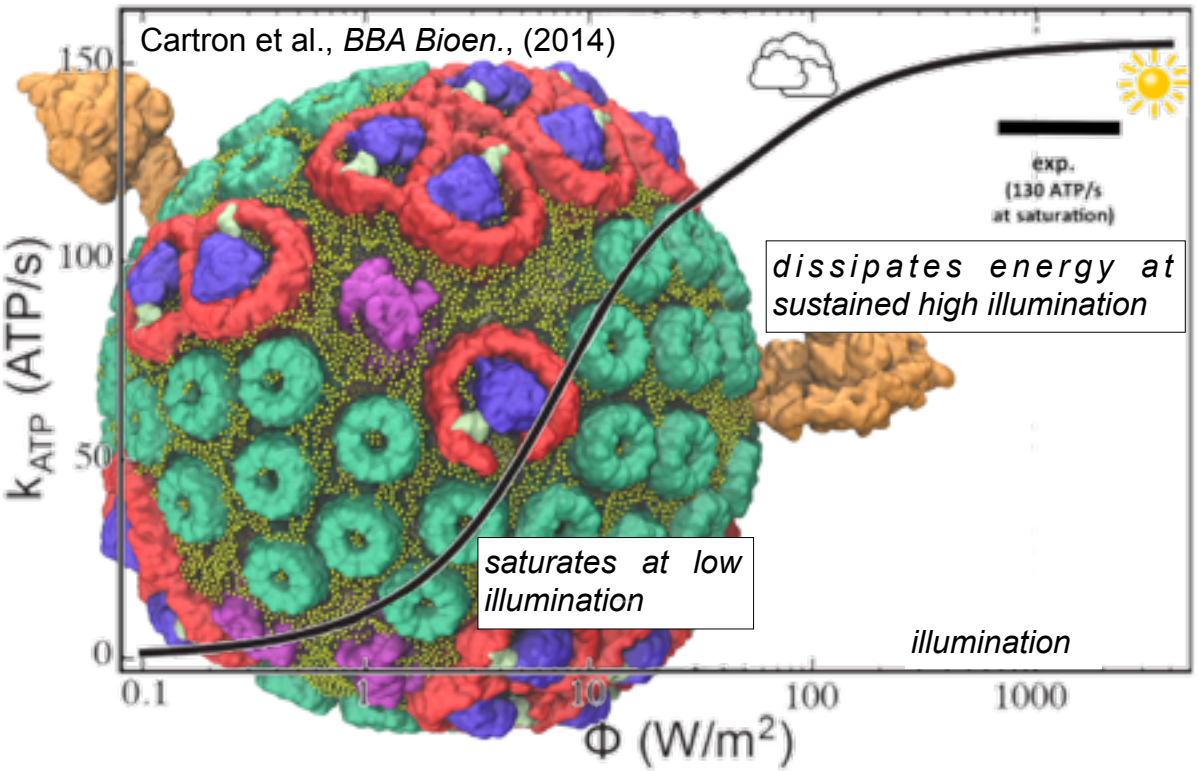
bc1 complex



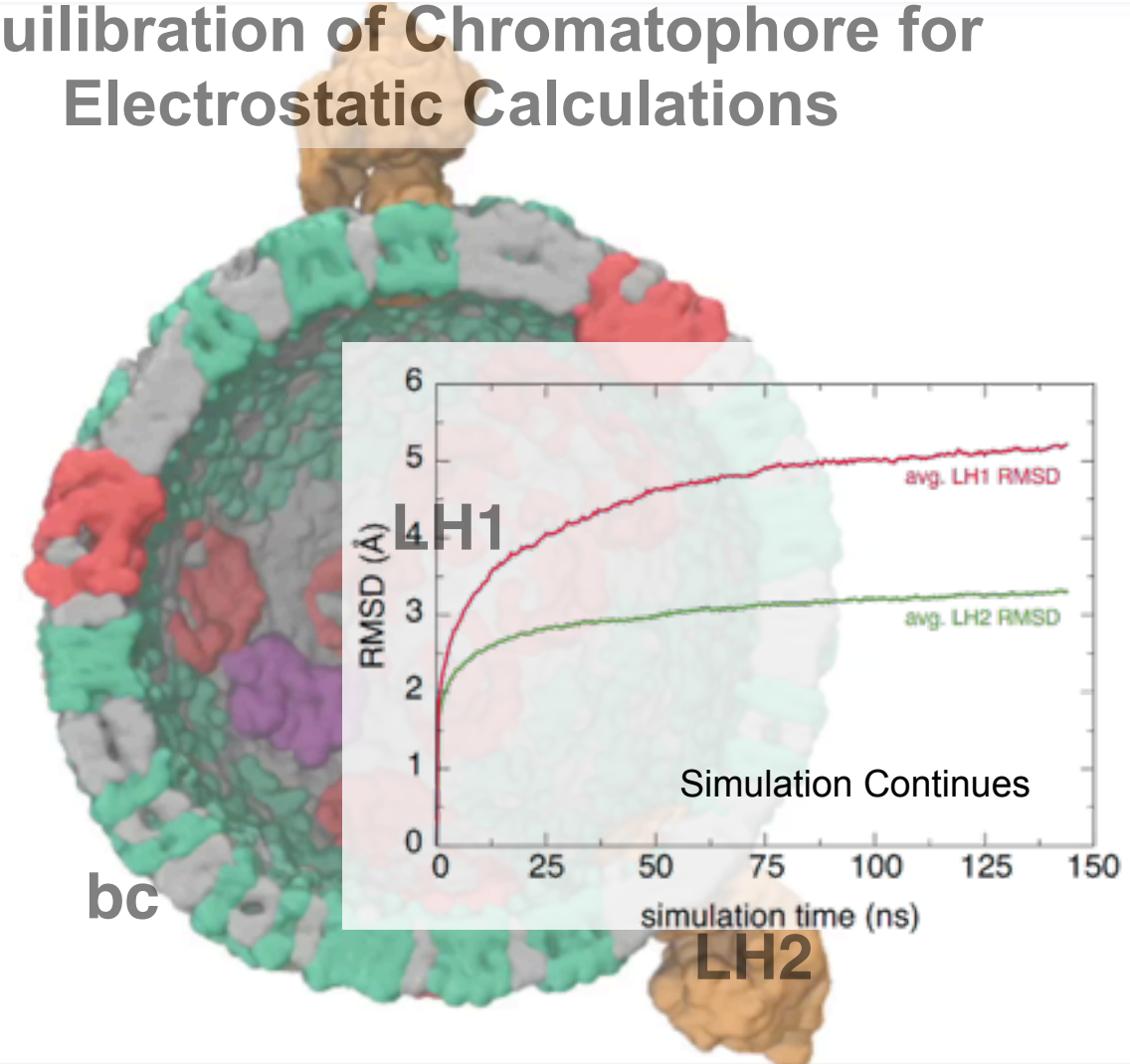
ATP synthase

$$k_{ATP}(I) = \frac{1}{2} I q \left(1 + \frac{1}{2} I q \tau_{RC}(I) \frac{1}{n_{RC}}\right)^{-1}$$

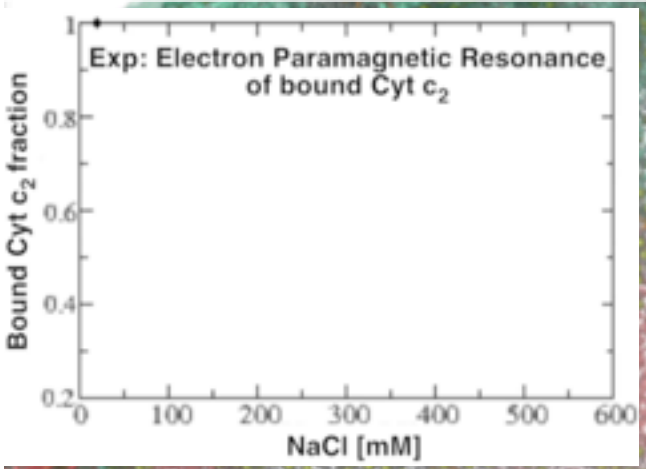
light harvesting efficiency
n_{RC}: number of reaction centers
τ_{RC}: cycling time of quinones at reaction cent.



Equilibration of Chromatophore for Electrostatic Calculations



Salinity mediates selective



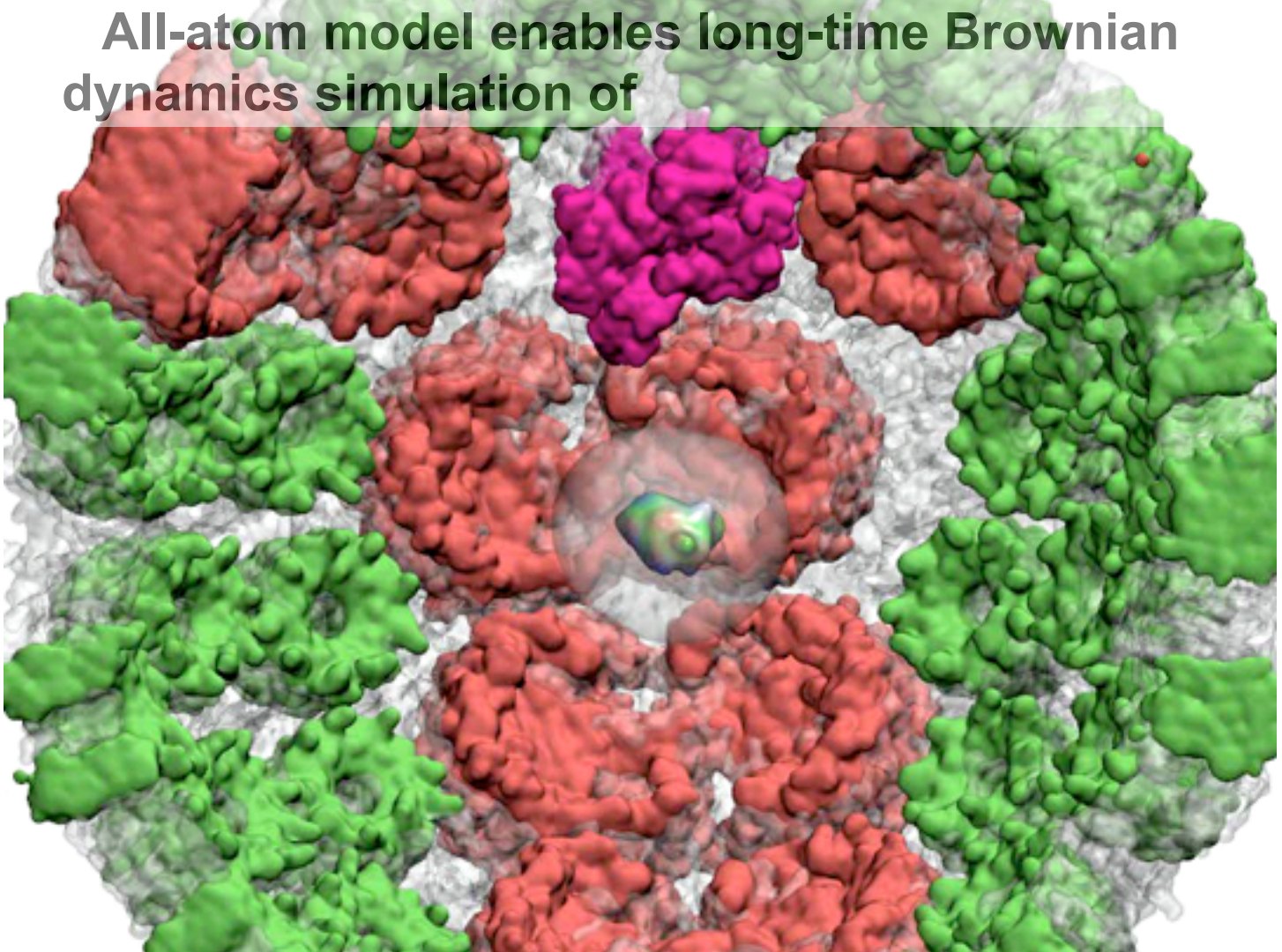
LH1

Complementary potential of the cytochrome c

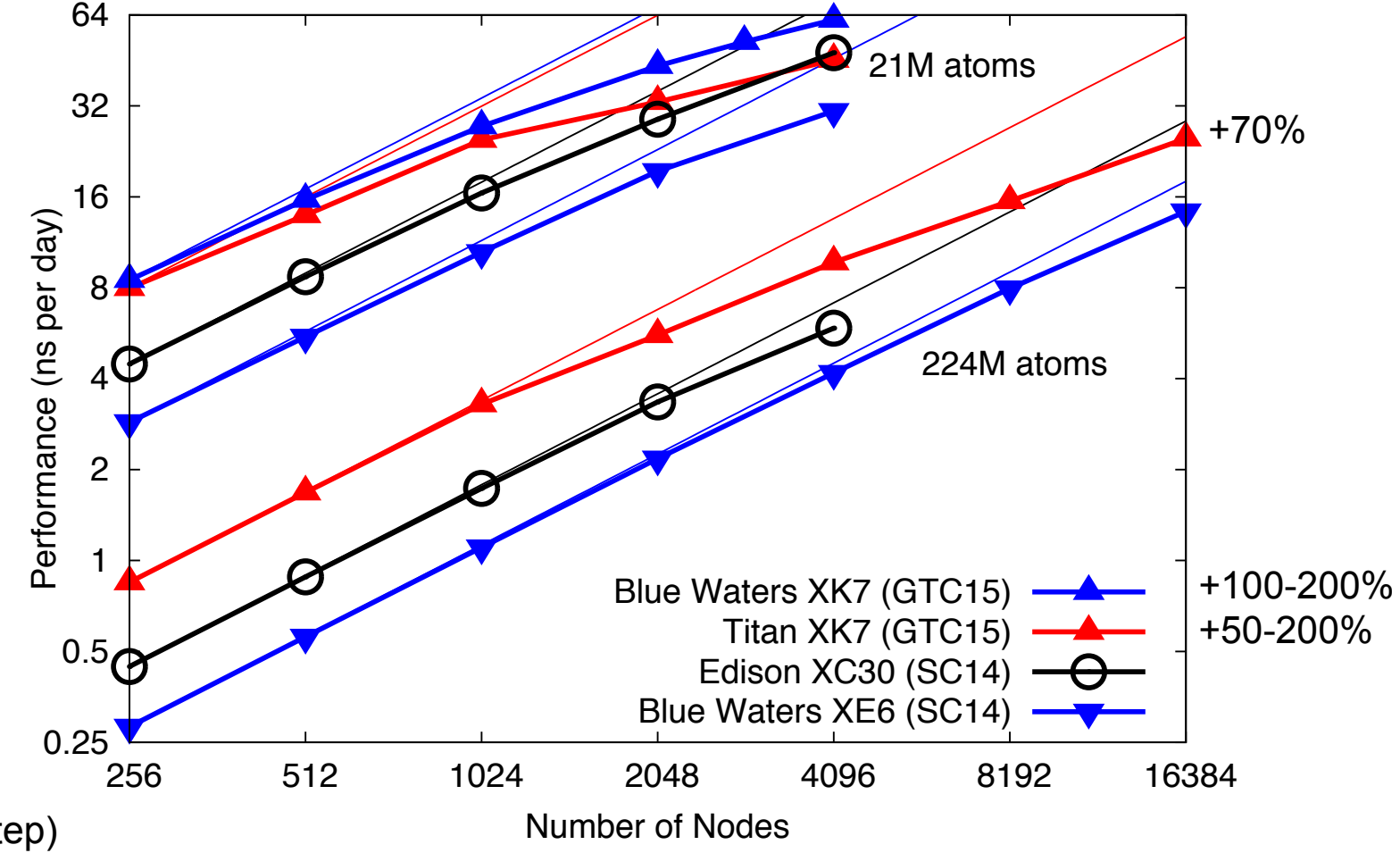
bc

LH2

All-atom model enables long-time Brownian dynamics simulation of



GPUs enable faster, more efficient simulations



(2fs timestep)

GPUs are critical for visualization and analysis

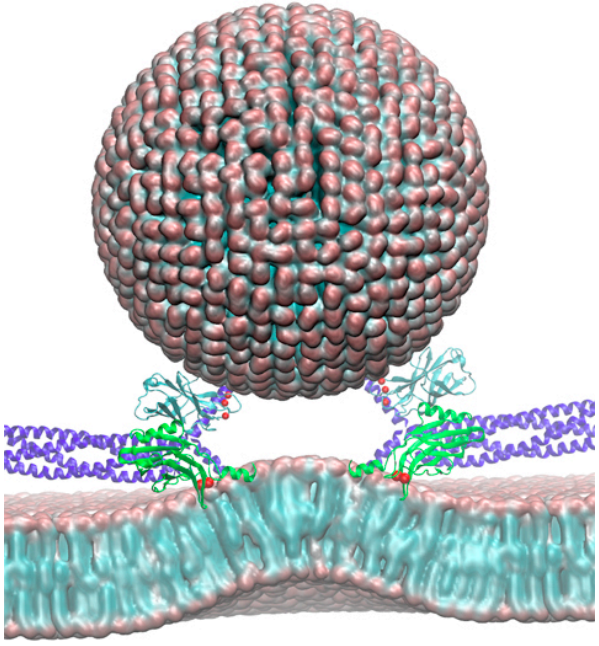
Large memory GPU-accelerated workstations can be accessed remotely from our facility today, but for future machines must be ***embedded at supercomputer centers***.

Compressed Video

1 Gigabit Network

Looking forward to Summit

- Highest throughput: Volta GPU
- Fastest single-thread: Power 9
- Fastest data transfer: NVLink
- Fewer, fatter nodes: Only 3,400
- Five times Titan performance
- Potential for remote visualization
- “Molecular Machinery of the Brain” early science project



Synaptic vesicle and pre-synaptic membrane

NIH Biomedical Technology Research Center for Macromolecular Modeling and Bioinformatics

Developers of the widely used computational biology software **VMD** and **NAMD**

250,000 registered **VMD** users
77,000 registered **NAMD** users

Renewed 2012-2017 with 10.0 score (NIH)

research projects include: virus capsids, ribosome, photosynthesis, protein folding, membrane reshaping, animal magnetoreception

600 publications (since 1972)
over **54,000** citations

Achievements Built on People

5 faculty members
8 developers
1 systems administrator
17 postdocs
46 graduate students
3 administrative staff

Tajkorshid, Luthey-Schulten, Stone, Schulten, Phillips, Kale, Mallon