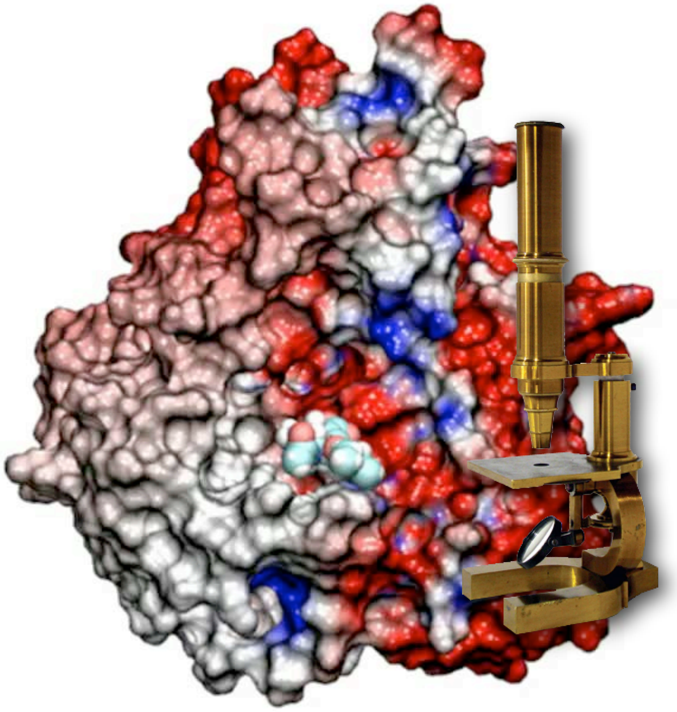
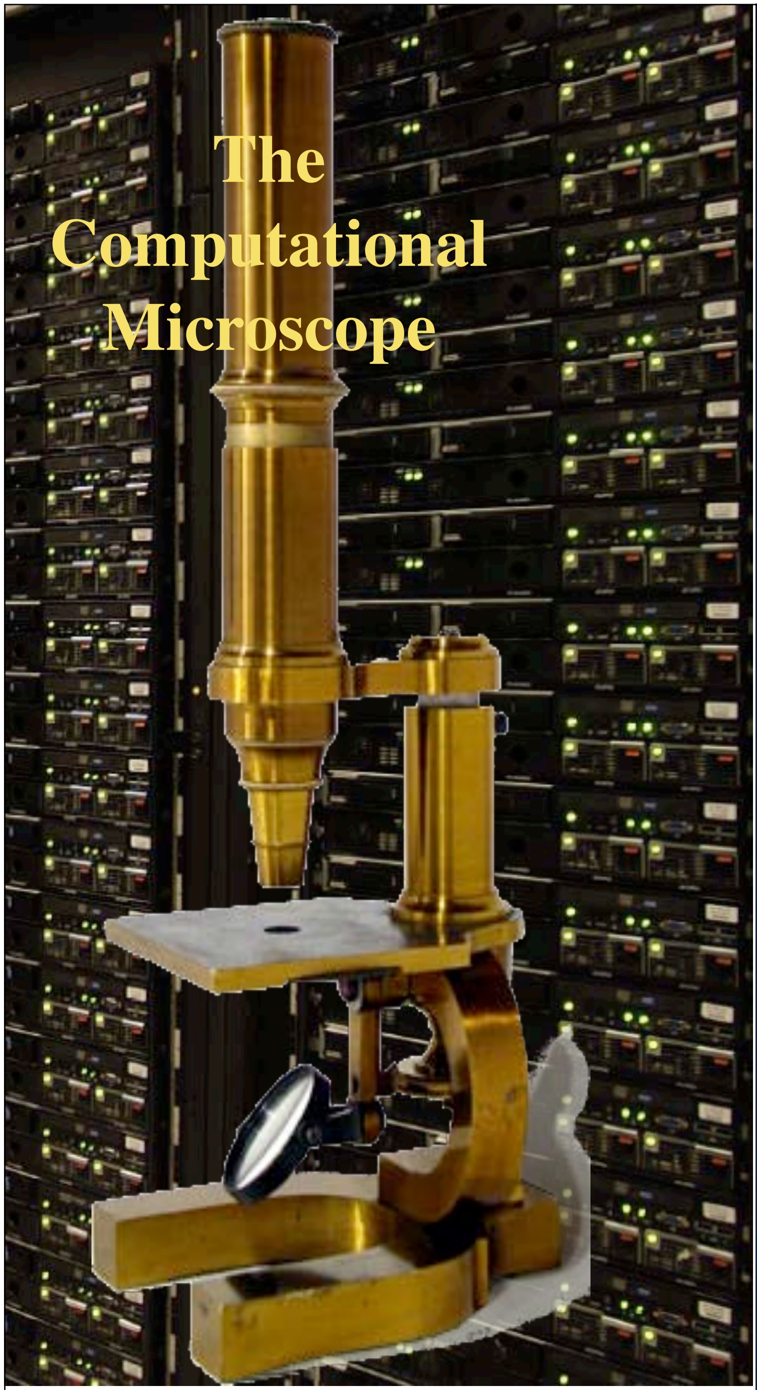
Discoveries Through the Computational Microscope

Accuracy • Speed-up • Unprecedented Scale



Investigation of drug (Tamiflu) resistance of the "swine" flu virus demanded **fast response!**

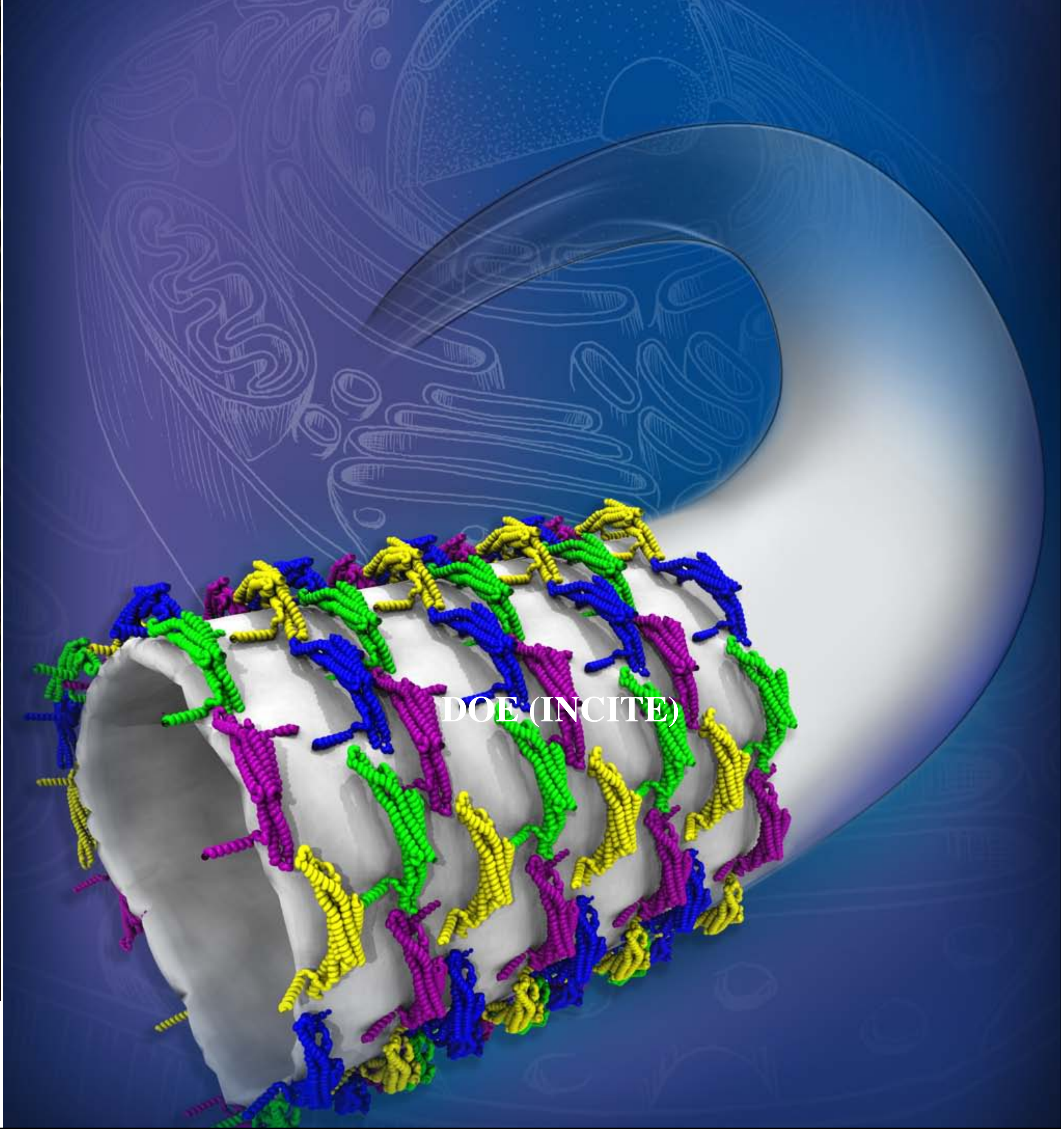
Klaus Schulten
Department of Physics and
Theoretical and Computational Biophysics Group
University of Illinois at Urbana-Champaign



The Computational Microscope

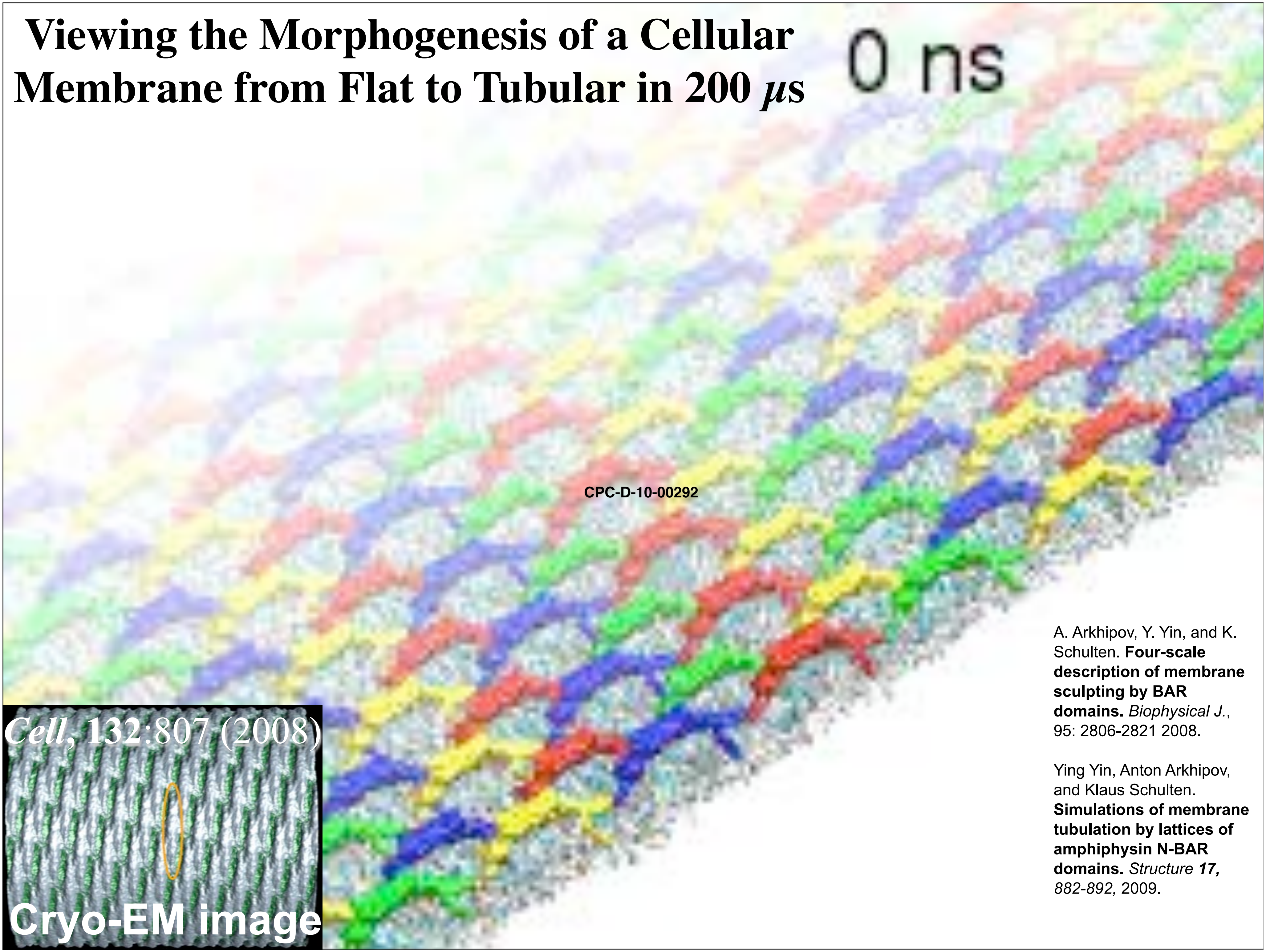
100 - 1,000,000 processors

Viewing the Morphogenesis of a Cellular Membrane from Flat to Tubular in 200 μs



DOE (INCITE)

Viewing the Morphogenesis of a Cellular Membrane from Flat to Tubular in 200 μs



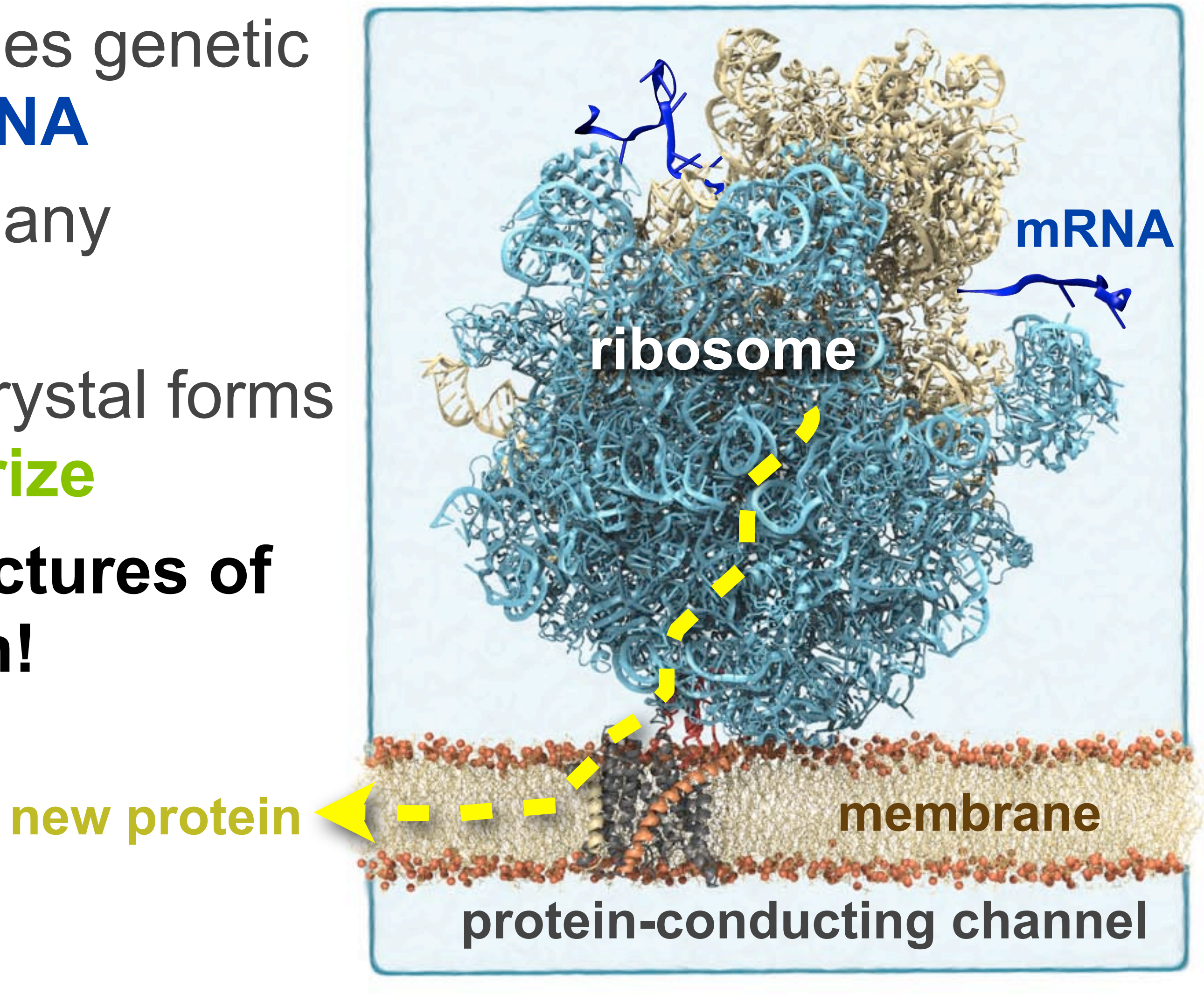
CPC-D-10-00292

A. Arkhipov, Y. Yin, and K. Schulten. **Four-scale description of membrane sculpting by BAR domains.** *Biophysical J.*, 95: 2806-2821 2008.

Ying Yin, Anton Arkhipov, and Klaus Schulten. **Simulations of membrane tubulation by lattices of amphiphysin N-BAR domains.** *Structure* ***17,*** *882-892,* 2009.

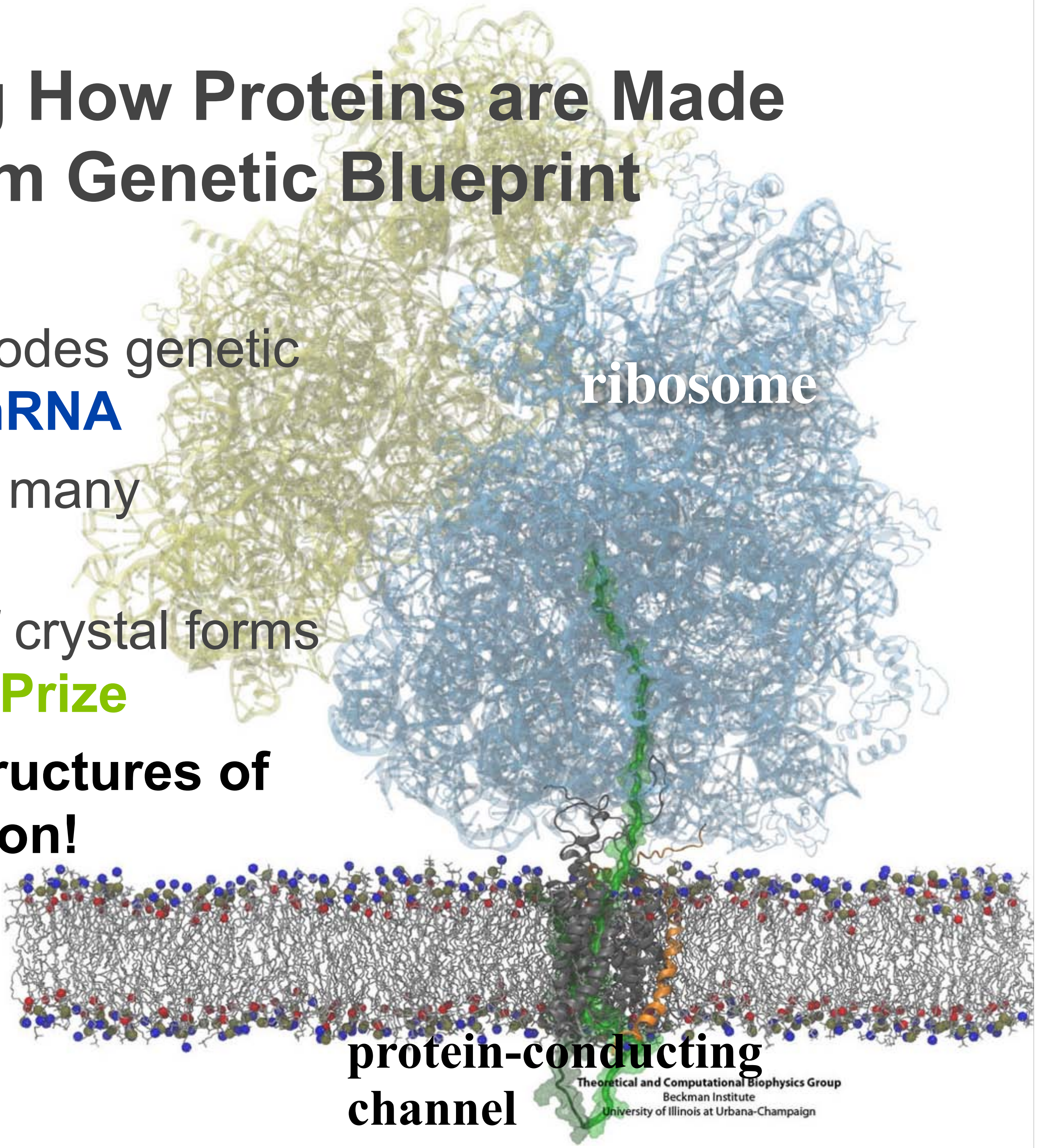
Viewing How Proteins are Made from Genetic Blueprint

- **Ribosome** — Decodes genetic information from **mRNA**
- Important target of many **antibiotics**
- Static structures of crystal forms led to 2009 **Nobel Prize**
- **But one needs structures of ribosomes in action!**



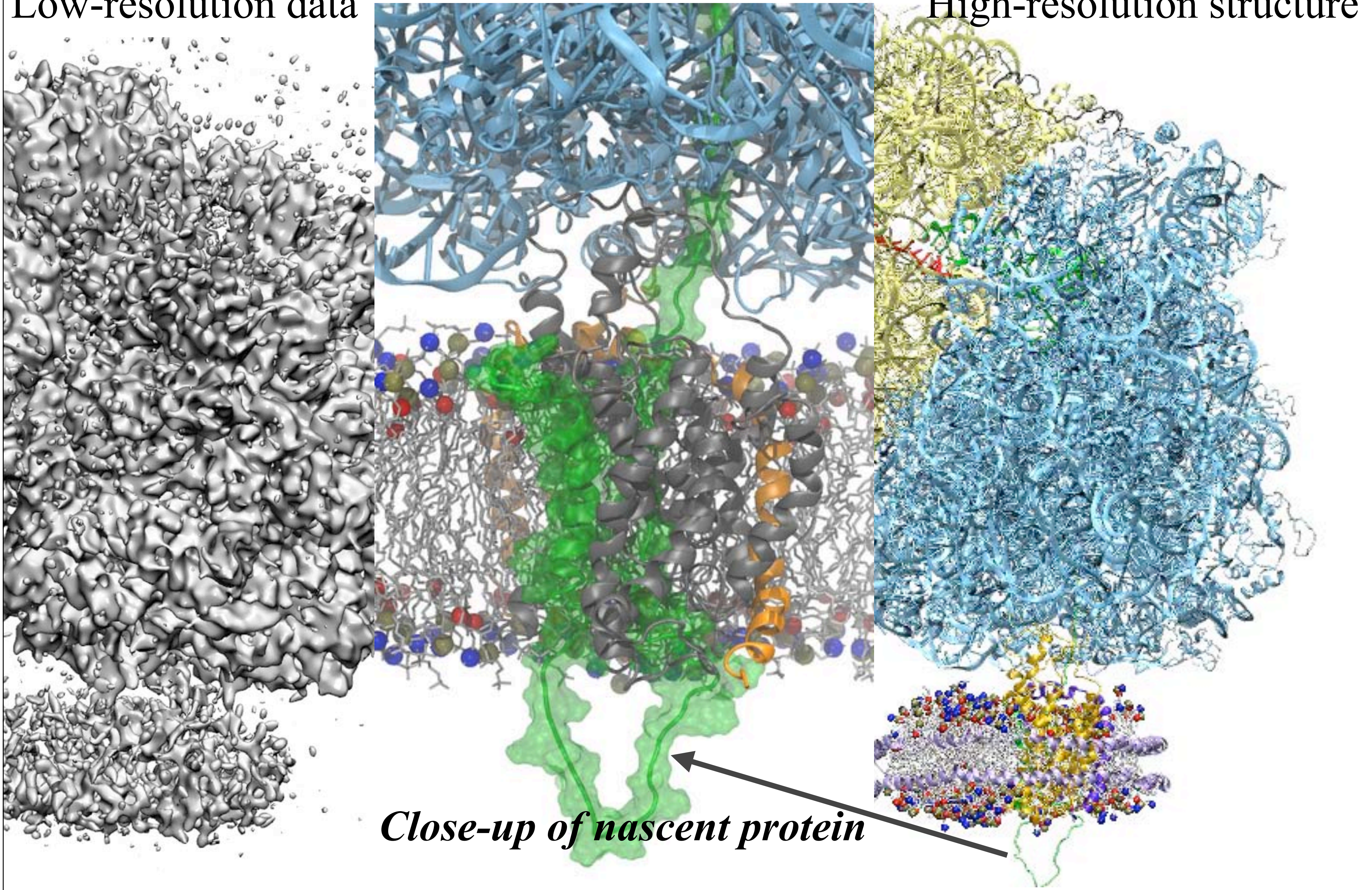
Viewing How Proteins are Made from Genetic Blueprint

- **Ribosome** — Decodes genetic information from **mRNA**
- Important target of many **antibiotics**
- Static structures of crystal forms led to 2009 **Nobel Prize**
- **But one needs structures of ribosomes in action!**



Theoretical and Computational Biophysics Group
Beckman Institute
University of Illinois at Urbana-Champaign

Viewing How Proteins Are Made from Genetic Blueprint

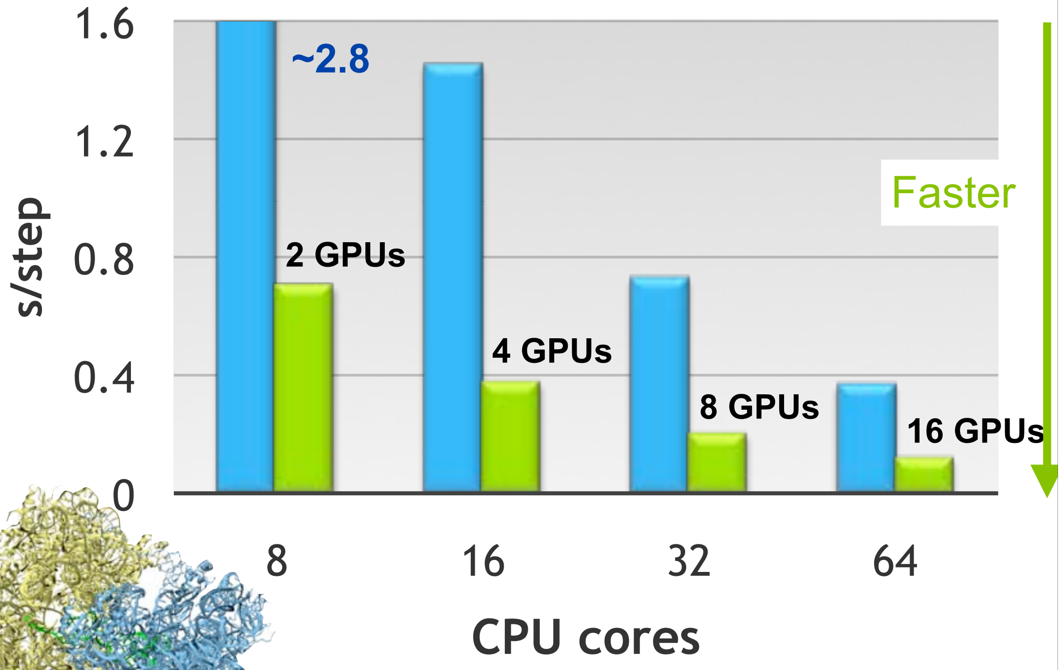


Low-resolution data

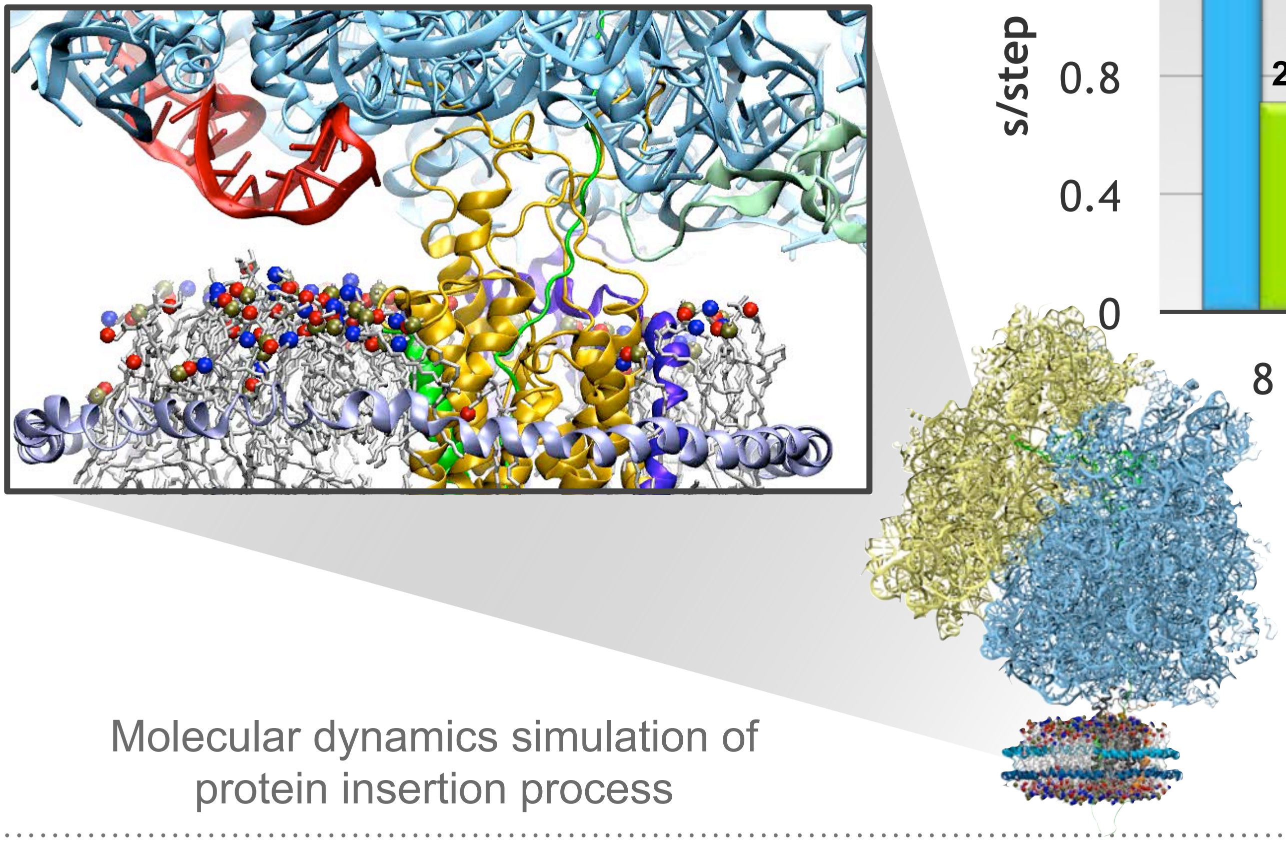
High-resolution structure

Close-up of nascent protein

GPU Solution 3:
Molecular Dynamics Simulations



NCSA Lincoln Cluster performance
(8 Intel cores and 2 NVIDIA Tesla
GPUs per node, 1 million atoms)



Molecular dynamics simulation of
protein insertion process

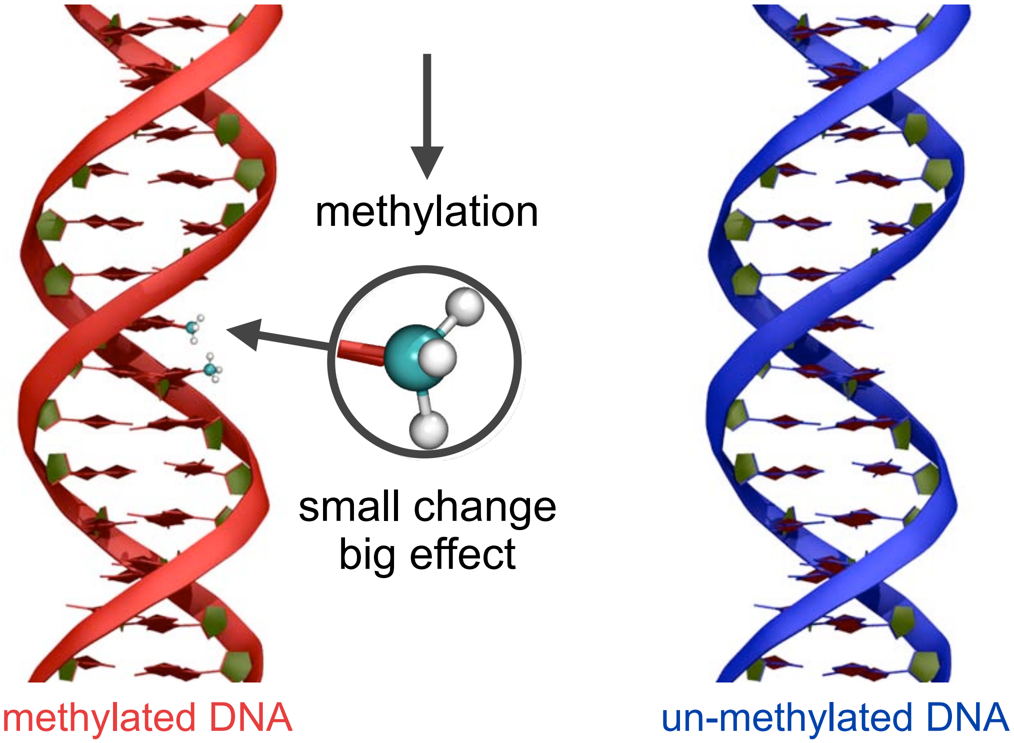
GPUs reduced time for simulation from **two months to two weeks!**

Viewing Nanopore Sensors

Genetics: Genes control our bodies and experiences!

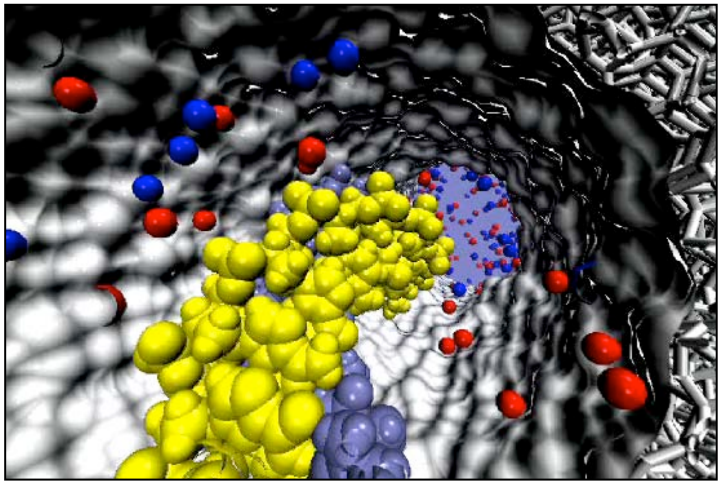
Epigenetics: Our bodies and experiences control the genes!

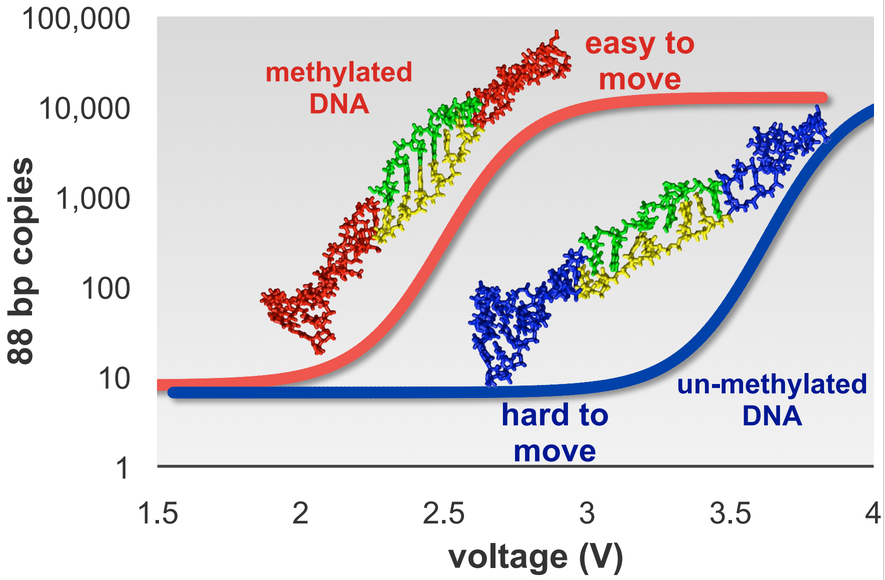
Epigenetics made possible through DNA methylation



Related pathologies: obesity, depression, cancer

Detect methylation with **nanopores**

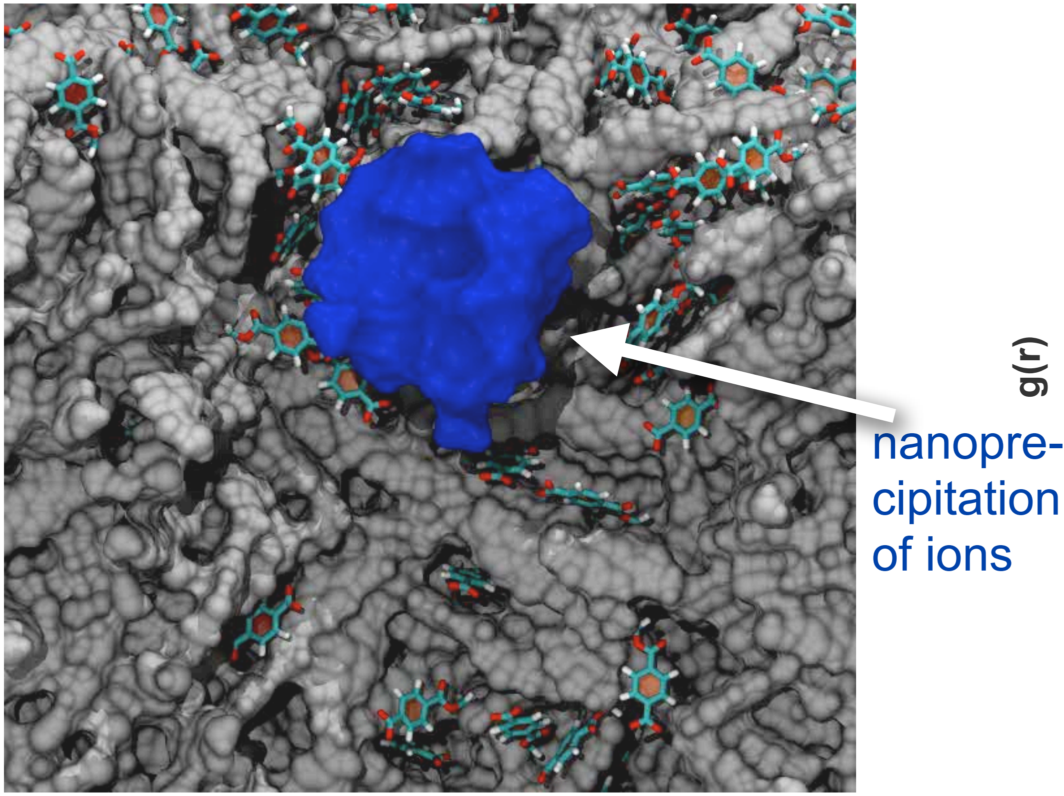




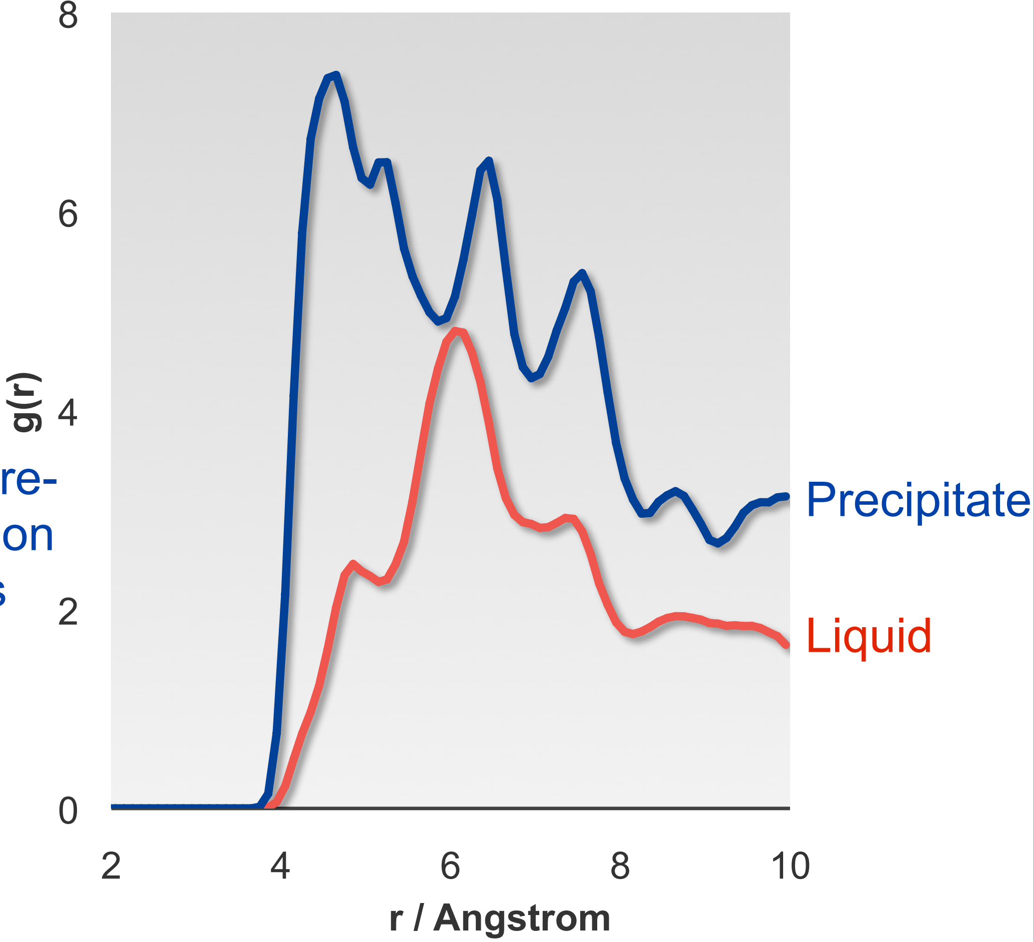
Viewing Nanopore Sensors

Create a **Better Nanopore** with Polymeric Materials

New materials, new problems: Nanoprecipitation

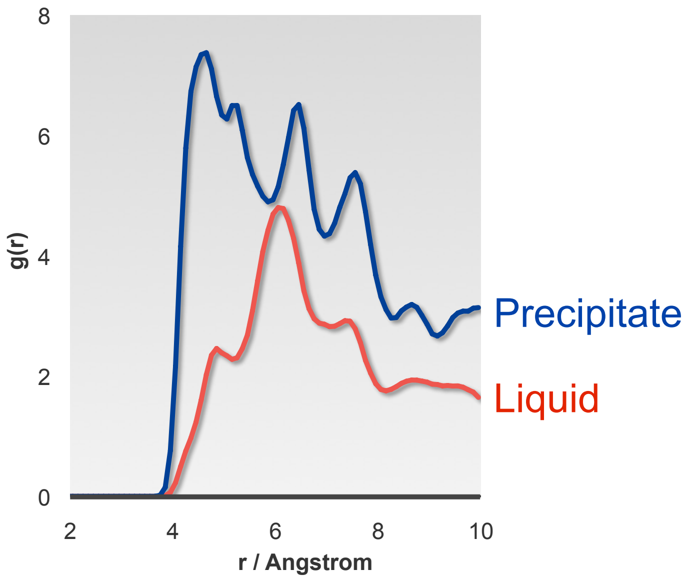


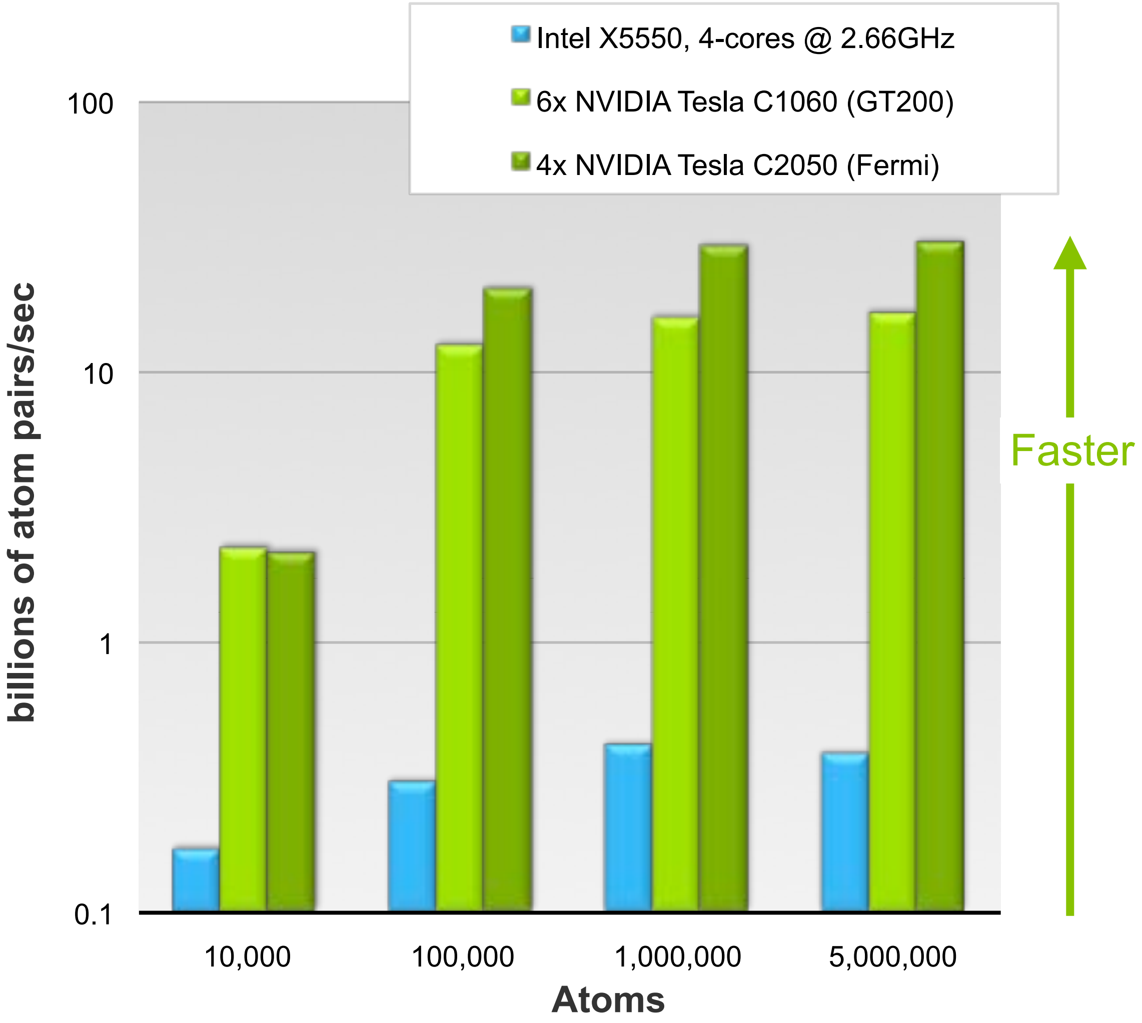
Radial distribution functions
identify nanoprecipitation



GPU Solution 4:
Computing Radial Distribution Functions

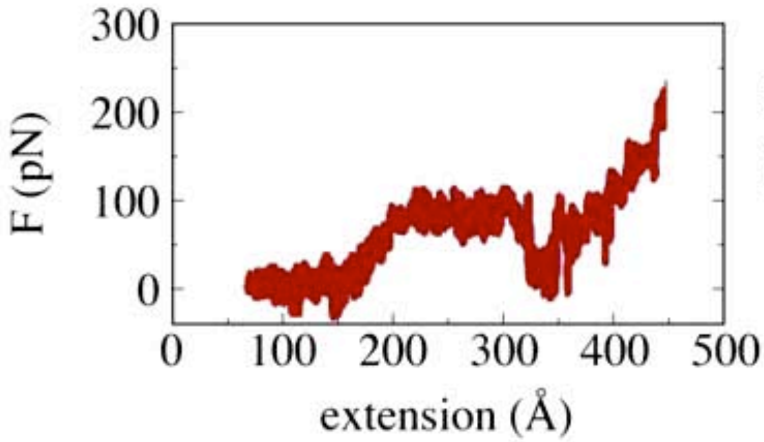
- 4.7 million atoms
- 4-core Intel X5550 CPU: **15 hours**
- 4 NVIDIA C2050 GPUs: **10 minutes**
- Fermi GPUs ~3x faster than GT200 GPUs: larger on-chip shared memory

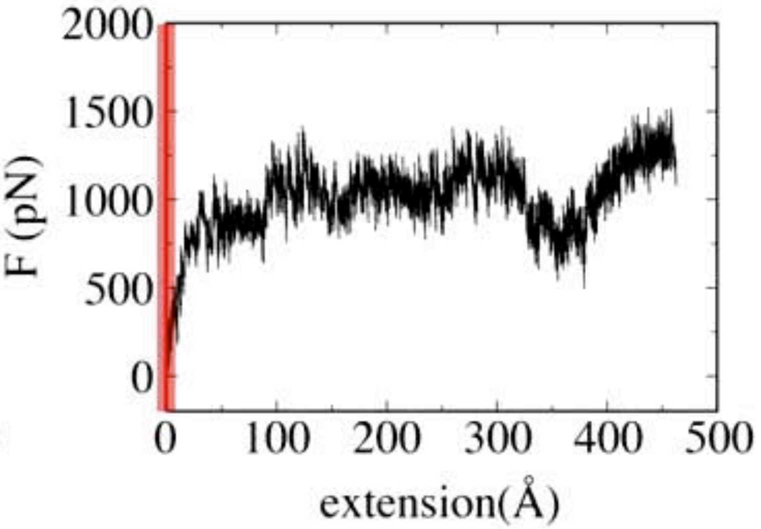




Inspecting the mechanical Strength of a blood clot

Collaborator: Bernard C. Lim (Mayo Clinic College of Medicine)





A Blood Clot

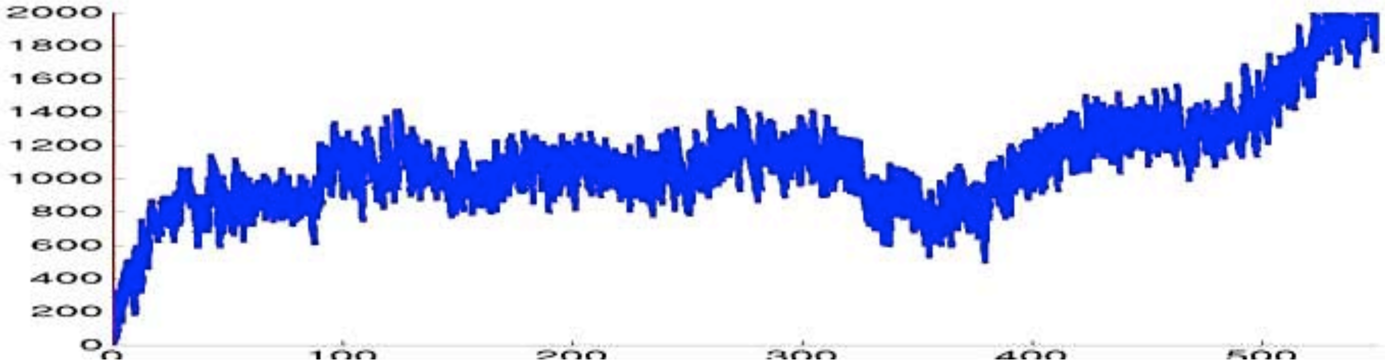
Red blood cells within a network of fibrin fibers, composed of polymerized fibrinogen molecules.

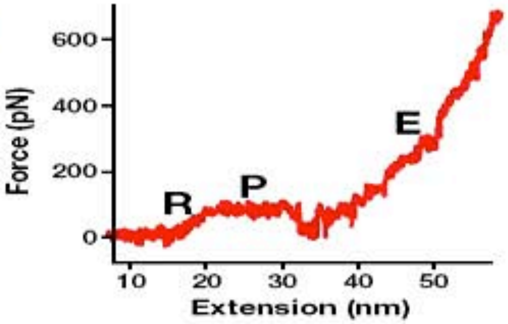
20ns SMD Simulation of <u>fibrinogen,</u> ***1.06 million atoms, 1.2 ns/day with pencil decomposition, 15 days on PSC XT3 Cray (1024 processors)***

B. Lim, E. Lee, M. Sotomayor, and K. Schulten. **Molecular basis of fibrin clot elasticity.** *Structure*, 16:449-459, 2008.

Inspecting the mechanical Strength of a blood clot

Collaborator: Bernard C. Lim (Mayo Clinic College of Medicine)





20ns SMD Simulation of <u>fibrinogen,</u> ***1.06 million atoms, 1.2 ns/day with pencil decomposition, 15 days on PSC XT3 Cray (1024 processors)***

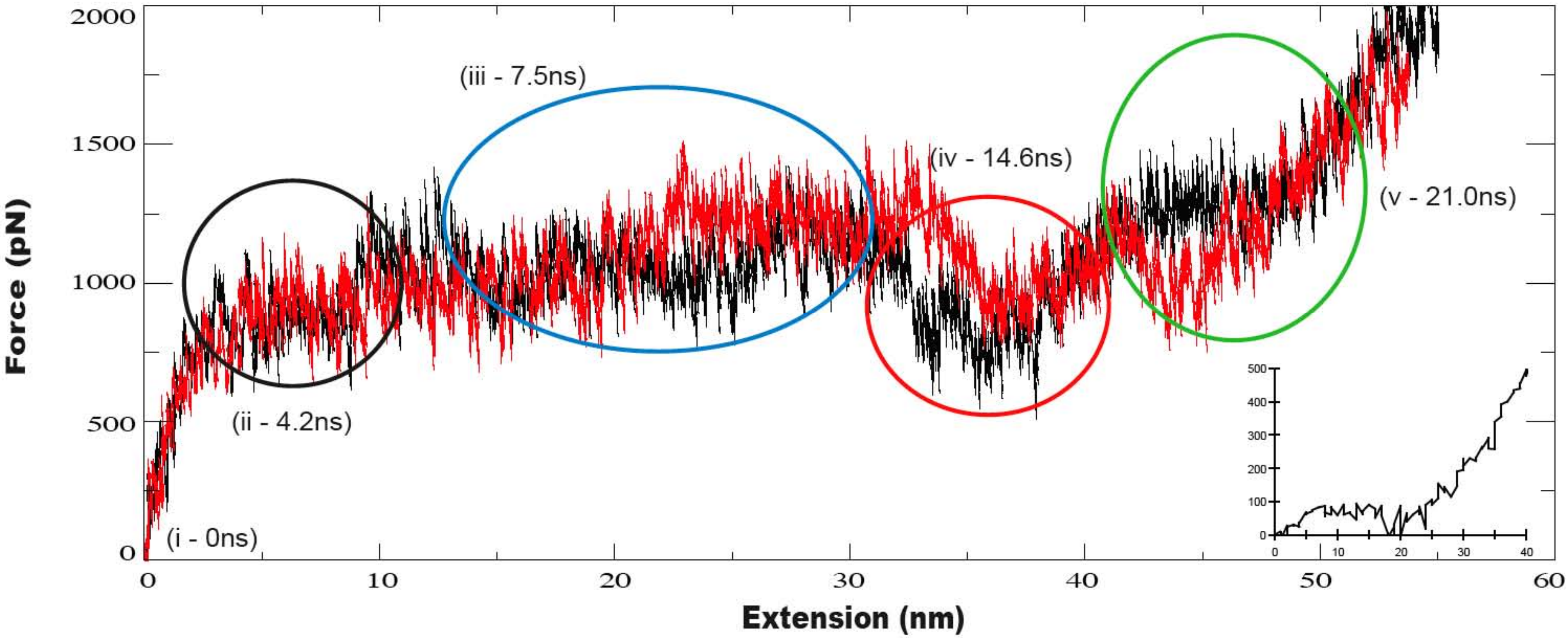
B. Lim, E. Lee, M. Sotomayor, and K. Schulten. **Molecular basis of fibrin clot elasticity.** *Structure*, 16:449-459, 2008.

A Blood Clot

Red blood cells within a network of fibrin fibers, composed of polymerized fibrinogen molecules.

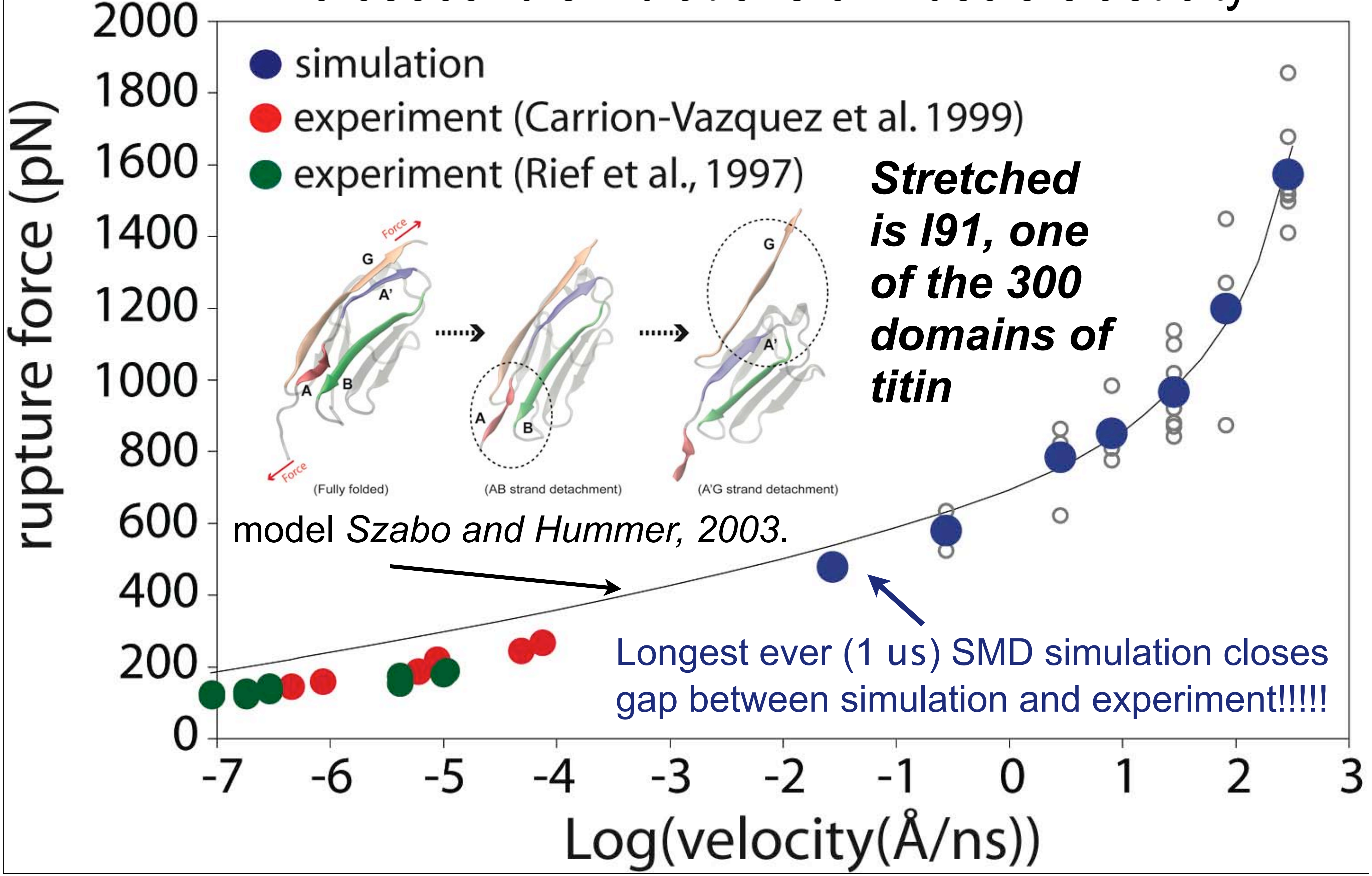
Petascale simulations will Permit Sampling

For Example Carrying out a Second Simulation Required by a Referee



Reaching for Overlapping Time Scales

Microsecond simulations of muscle elasticity



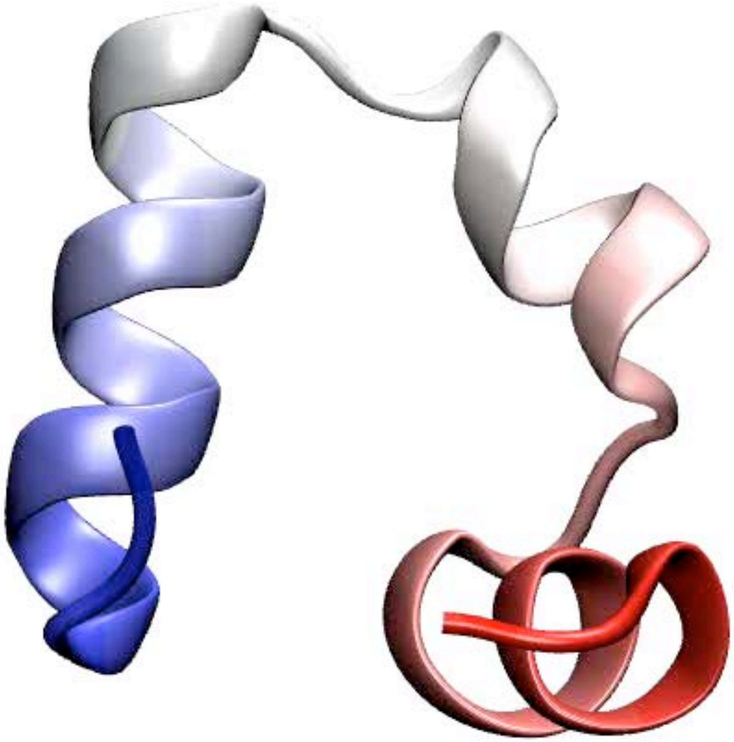
Stretched is I91, one of the 300 domains of titin

model *Szabo and Hummer, 2003*.

Longest ever (1 us) SMD simulation closes gap between simulation and experiment!!!!!

Viewing Protein Folding

- Protein **misfolding** responsible for diseases:
  - Alzheimer’s
  - Parkinson’s
  - Huntington
  - Mad cow
  - Type II diabetes
  - ...

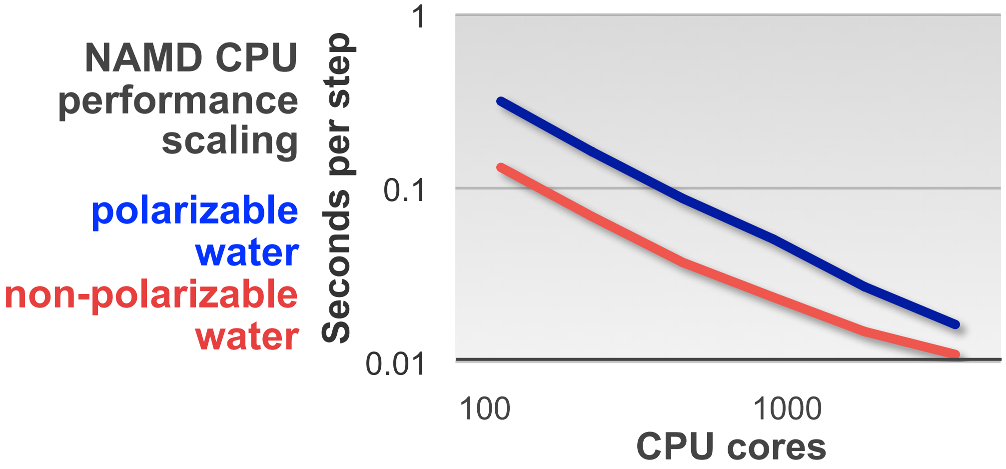


villin headpiece
3 months on 329 CPUs

Observe folding process in unprecedented detail

Science 6: Protein Folding

- Atomic polarizability increases computation by 2x…
- …but, the additional computations are perfectly suited to the GPU!
- For now, NAMD calculates atomic polarizability on CPUs only...soon we will also use GPUs



Atomic polarizability of water, highly accurately simulated through additional particles (shown in green)