Investigation of drug (Tamiflu) resistance of the “swine” flu virus demanded fast response!

Klaus Schulten
Department of Physics and
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The Computational Microscope

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

100 - 1,000,000 processors
Viewing the Morphogenesis of a Cellular Membrane from Flat to Tubular in 200 μs


Inspecting the mechanical Strength of a blood clot

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

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


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


Longest ever (1 us) SMD simulation closes gap between simulation and experiment!!!!!
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!
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Viewing How Proteins Are Made from Genetic Blueprint

Low-resolution data

High-resolution structure

Close-up of nascent protein
Viewing how Proteins are Made from Genetic Blueprint

Trigger Factor Bound to Translating Ribosome

Trigger factor (TF): ribosome-associated chaperon preventing misfolding of nascent chain

New DBP1-Ribosome effort with collaborator R. Beckmann, U. Munich
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**

- methylated DNA
- un-methylated DNA

- 88 bp copies
- voltage (V)

- hard to move
- easy to move
- methylated DNA
- un-methylated DNA
Recent progress
Building a nanodevice for kinase detection (Collaborator: Logan Liu; UIUC)

- Protein kinases are known to regulate the majority of biochemical pathways in the cell
- Disruption of kinase signaling pathways are frequent causes for diseases, such as cancer and diabetes
- New nanodevice to detect kinase activity

Key points for creating a functional device:
- Phosphorylated peptides must change conformation under different voltage polarities
- Peptide conformation must be sensitive to spectroscopic detection

Sequence insensitive to voltage polarity

All-atom model

MD reveals undesired effects

Optimized sequence responds to voltage polarity

Sequence optimization through MD

BTRC for Macromolecular Modeling and Bioinformatics
http://www.ks.uiuc.edu/