HPC in Drug Discovery

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TAMHSC
Chemistry Lab based
• Expensive
• Protracted
• Difficult

HPC MD-based Simulations
• Inexpensive
• Very fast
• Useful for early stages
In silico Screening Complements High-throughput Screening

Chemical database
N=1,000,000

Structure-based & Ligand-based screens

Drug-like?
Affinity Selectivity Activity
Absorption Distribution Metabolism Excretion Toxicity

Lead candidates
N=500

Inactive

Computational Tools:
• DESMOND
• GROMACS
• CHARMM
• SCHRODINGER

HPC in Drug Discovery
Drug Discovery: Driven by Computation and Experiments
Phosphatidylinositol Transfer Proteins (PITPs) Important in Cell Function

- Important in Lipid-mediated cell signaling and metabolism.
- Derangement in Signaling: Neurodegenerative diseases and many forms of cancers.

Cell membrane
• Important in Lipid-mediated cell signaling and metabolism.
• Derangement in Signaling: Neurodegenerative diseases and many forms of cancers.
• Undergoes Conformational Changes: Helical Gate Mediates Lipid Access/Exchange

Sec14-OPEN  ‘Transition state’?  CLOSED

Sec14 is a PITP protein; it’s binding to the PI and PC lipids is studied using the SCHRODINGER & DESMOND MD codes.
Docking-Based Virtual Screening

Decoys: known or presumed non-binders to the target protein.
Sec14 Homology Model: All-Atom MD Simulation
Simulation of Drug Binding to Protein Using DESMOND MD Code
All-Atom Simulation of Sec14 in Explicit Water Molecules (used DESMOND MD Code)
Small molecule (drug) vibrating in Sec14 binding pocket (Used DESMOND MD Code)
Conclusion
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Research Interest

- Computer-aided drug design.
- Algorithm and software development for designing new drugs.
- Cancer therapeutics.
- Clinical informatics.
- ADME/Tox QSAR modeling.