



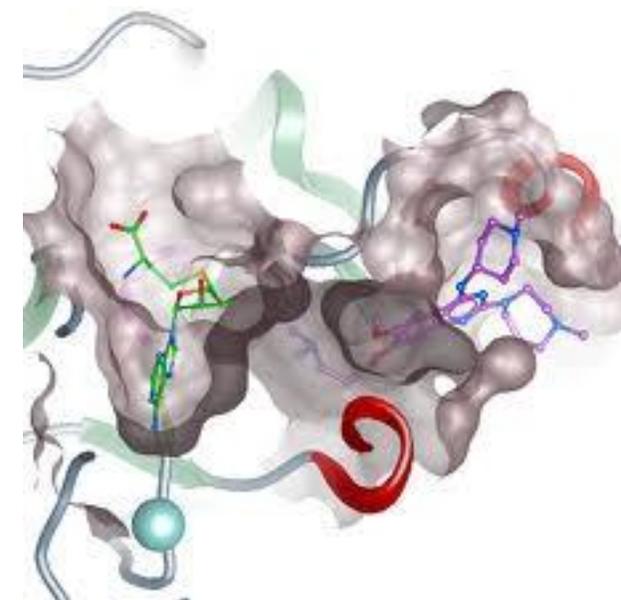
HPC in Drug Discovery

Ashutosh Tripathi, Ph.D.

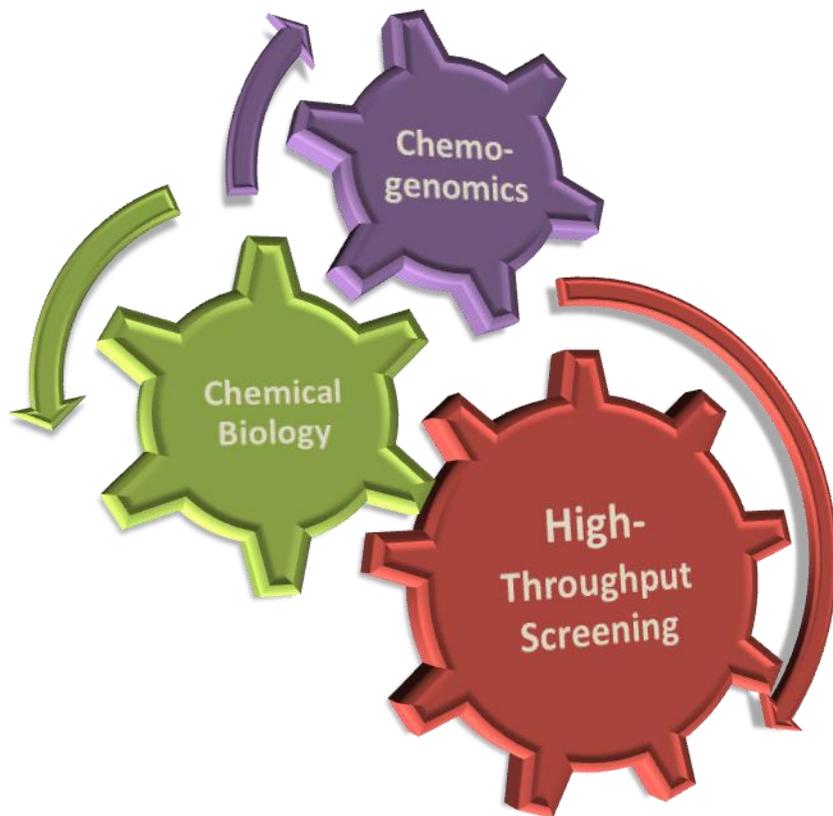
Bankaitis Lab

**Department of Molecular
and Cellular Medicine**

TAMHSC

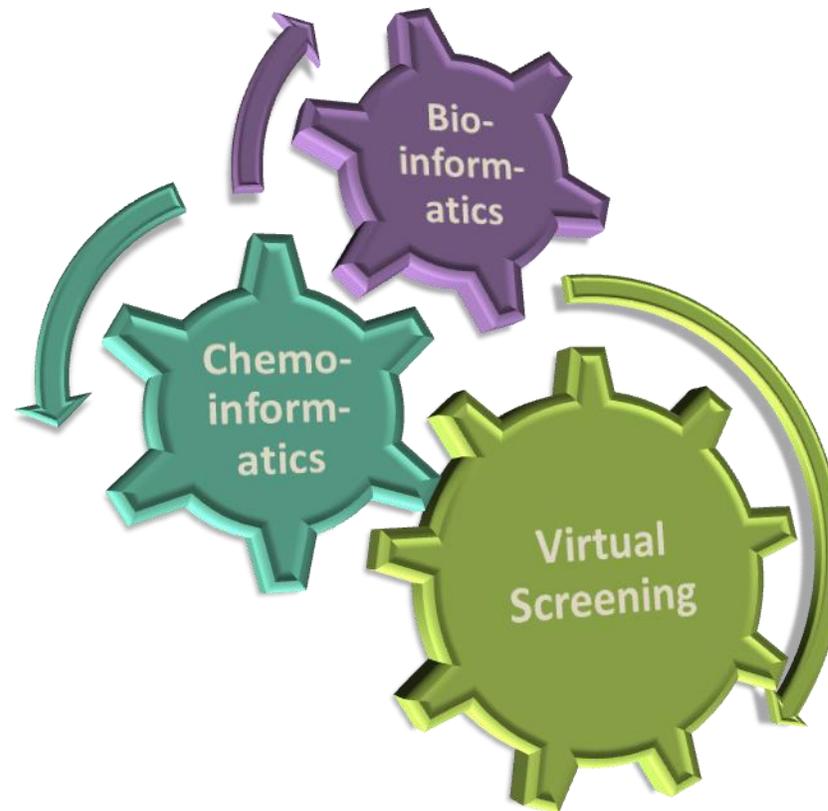


Technologies in Drug Discovery



Chemistry Lab based

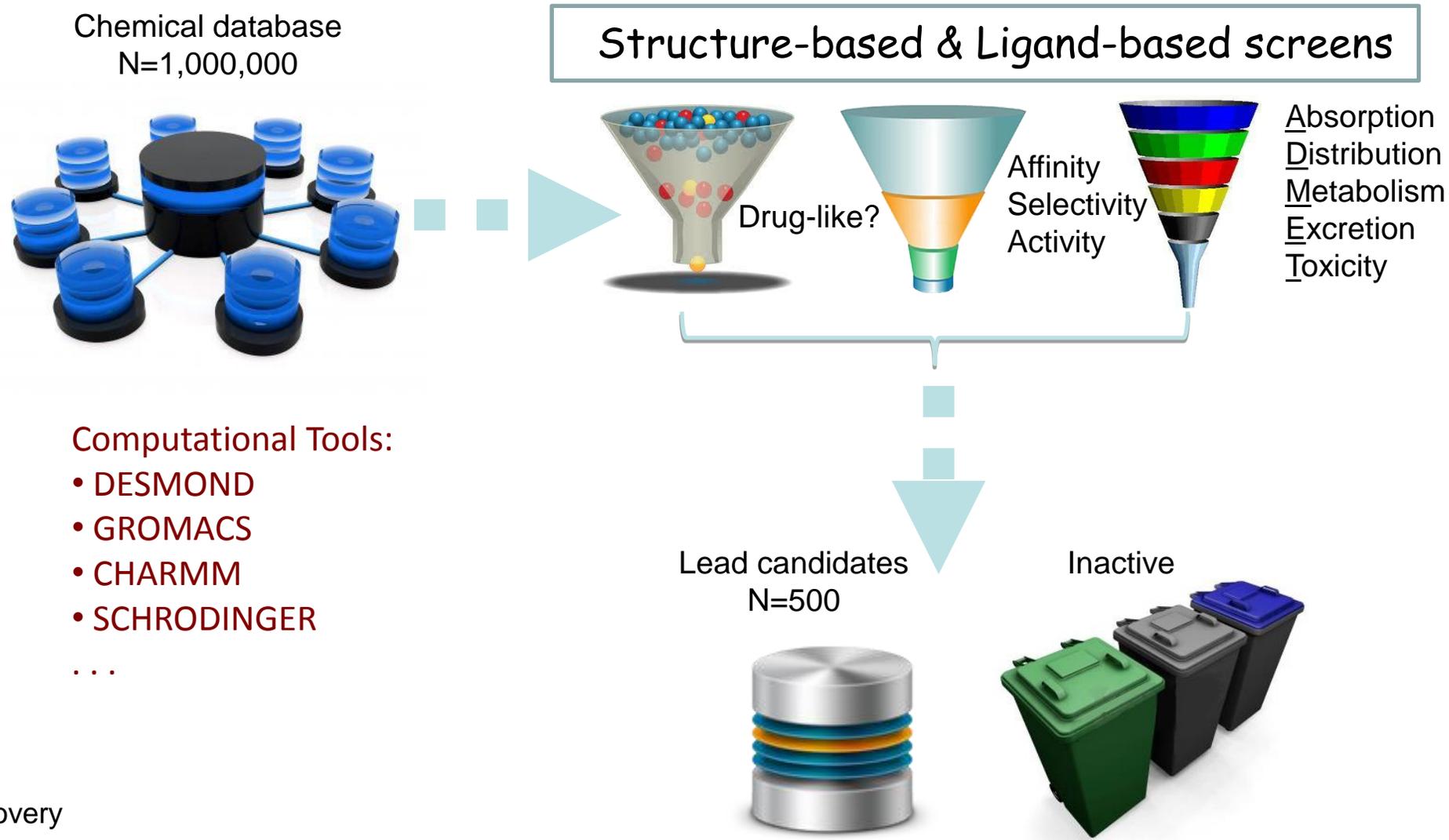
- Expensive
- Protracted
- Difficult



HPC MD-based Simulations

- Inexpensive
- Very fast
- Useful for early stages

In silico Screening Complements High-throughput Screening

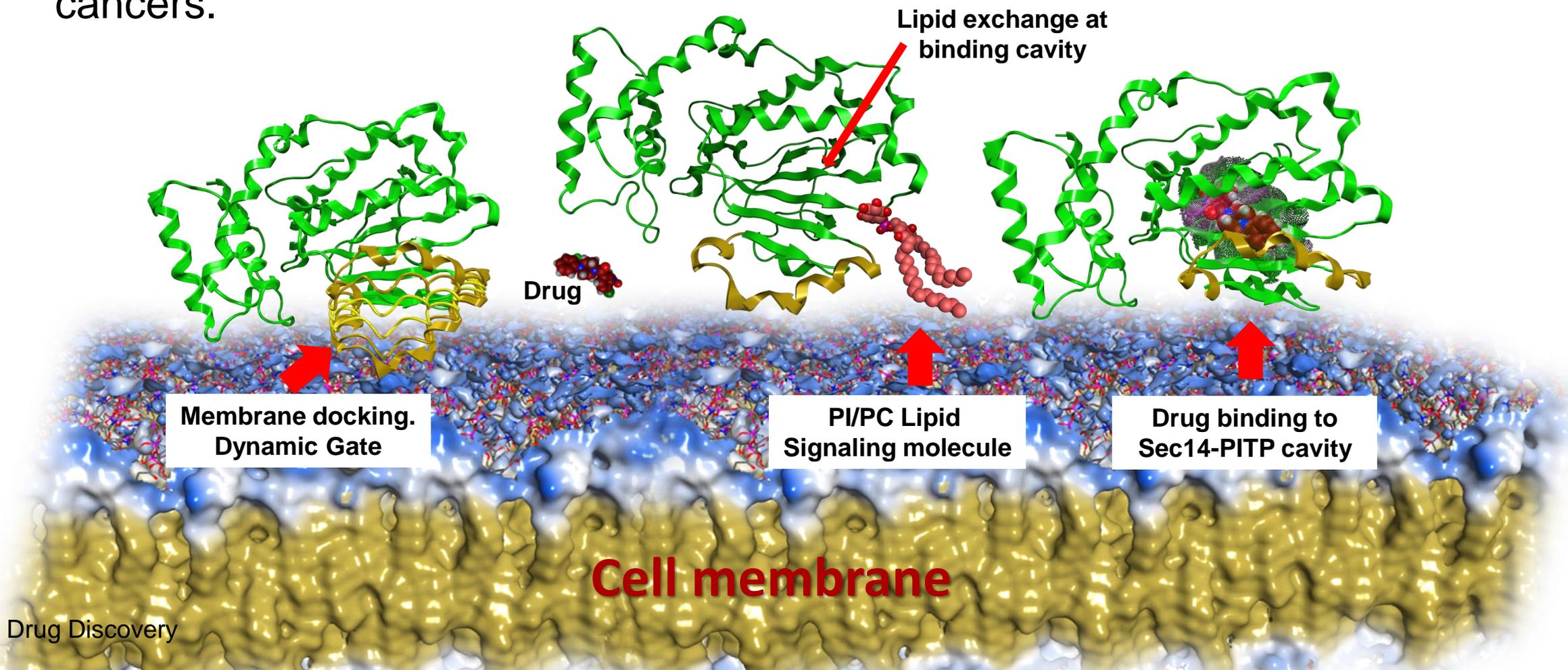


Drug Discovery: Driven by Computation and Experiments



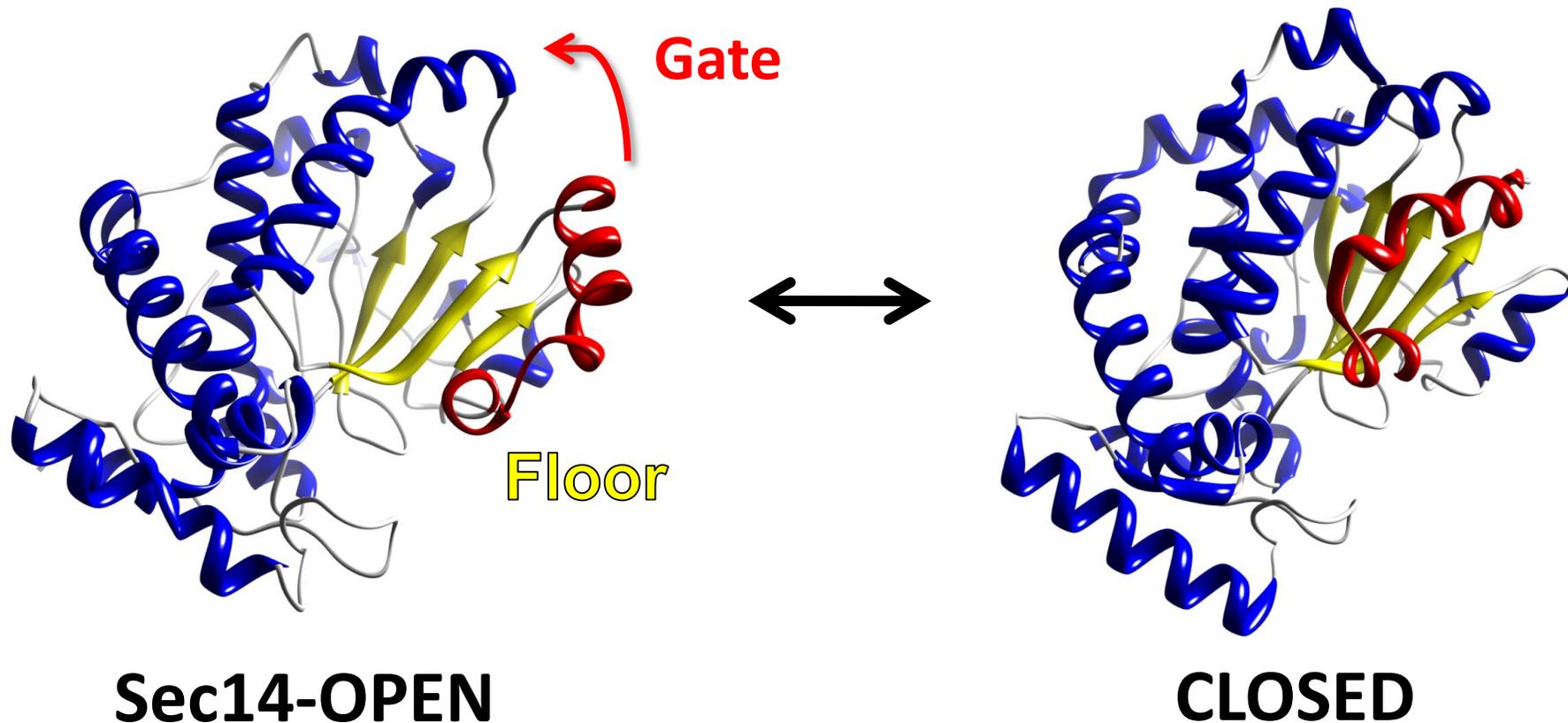
Phosphatidylinositol Transfer Proteins (PITPs) Important in Cell Function

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



Phosphatidylinositol Transfer Proteins (PITPs) Critical in Cell Function

- 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



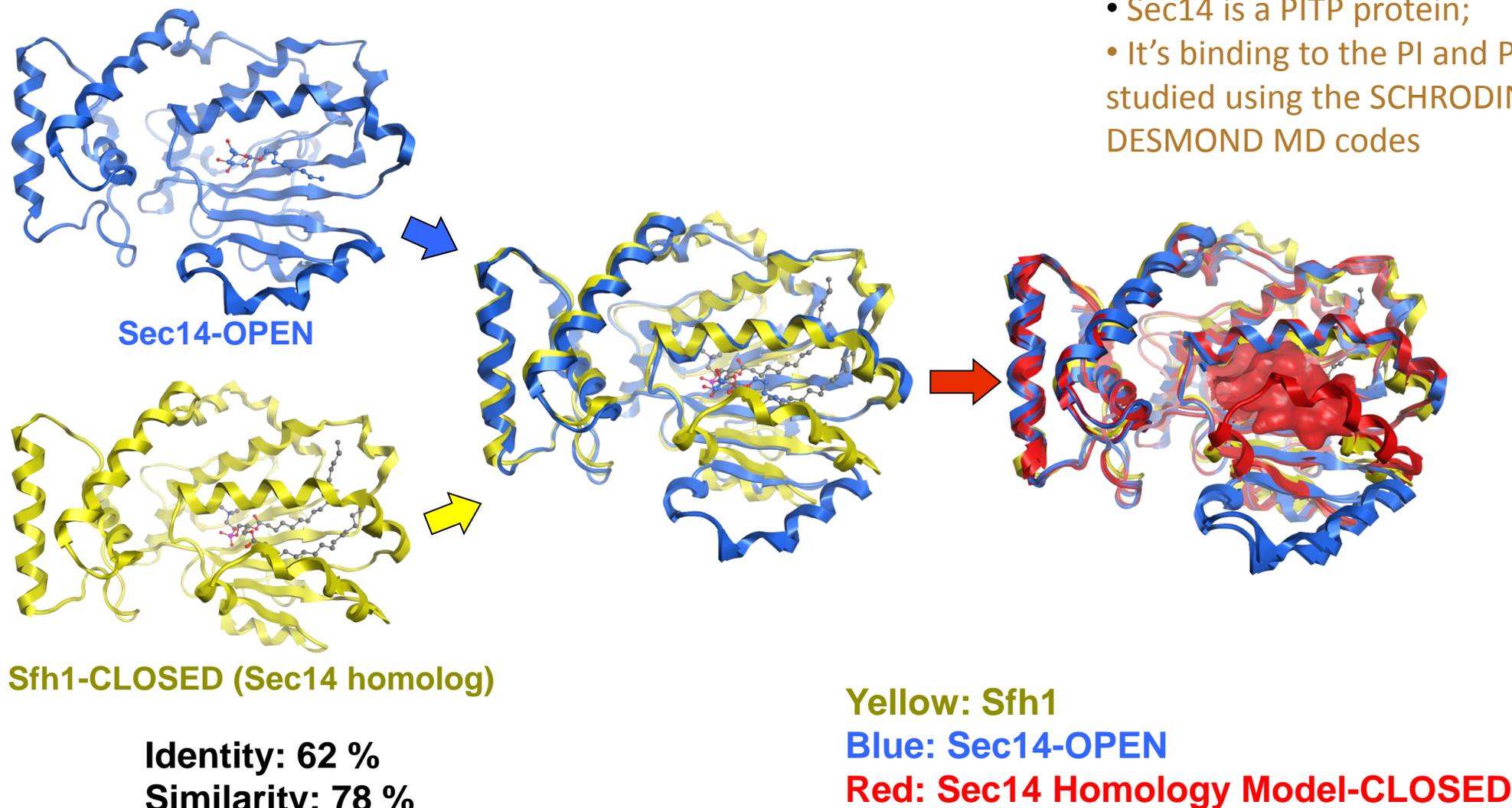
Sec14-OPEN

'Transition state'?

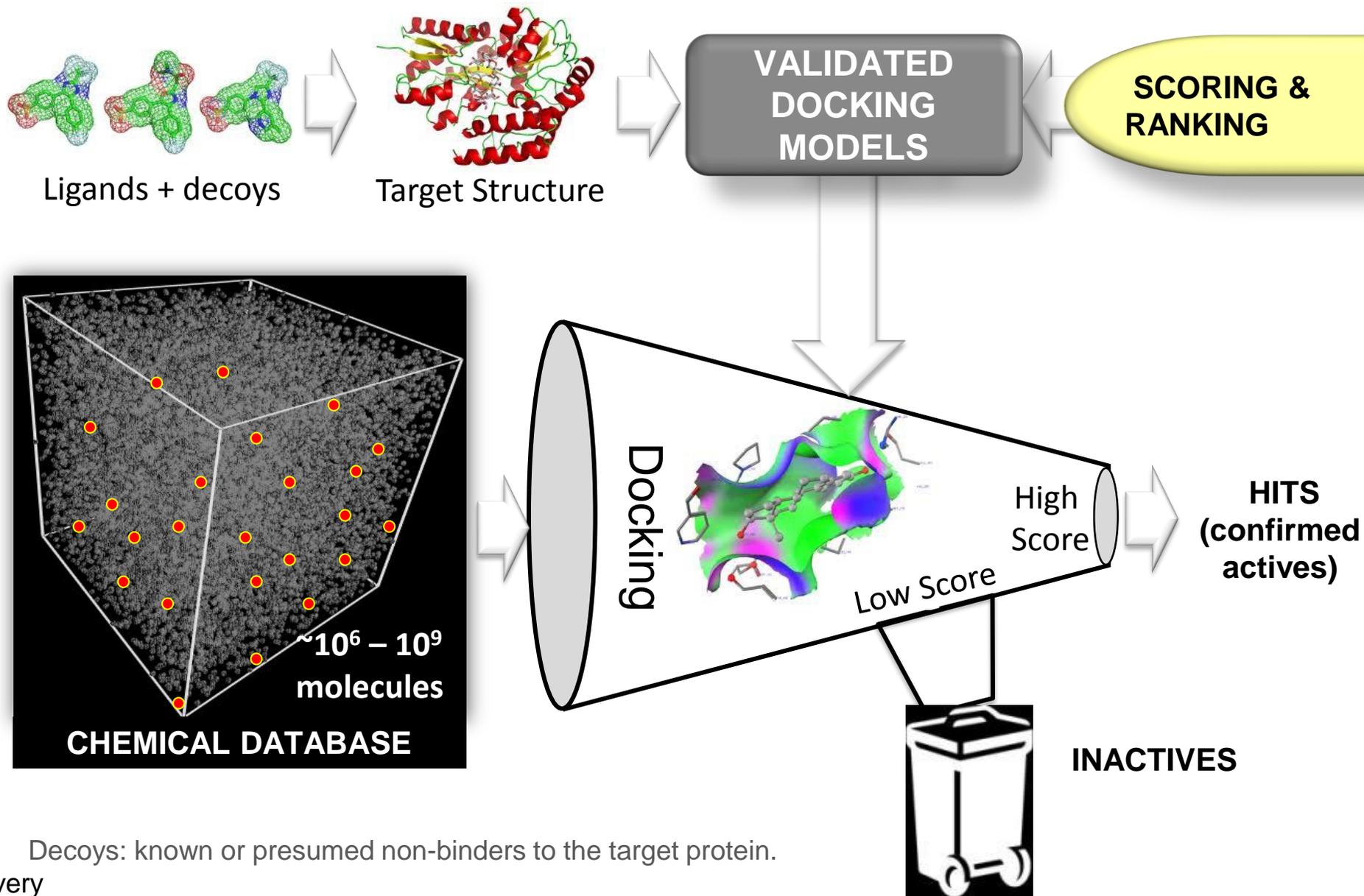
CLOSED

Schaaf et. al. *Mol. Cell.* (2008)

Homology Modeling of Sec14 (Closed Conformation)

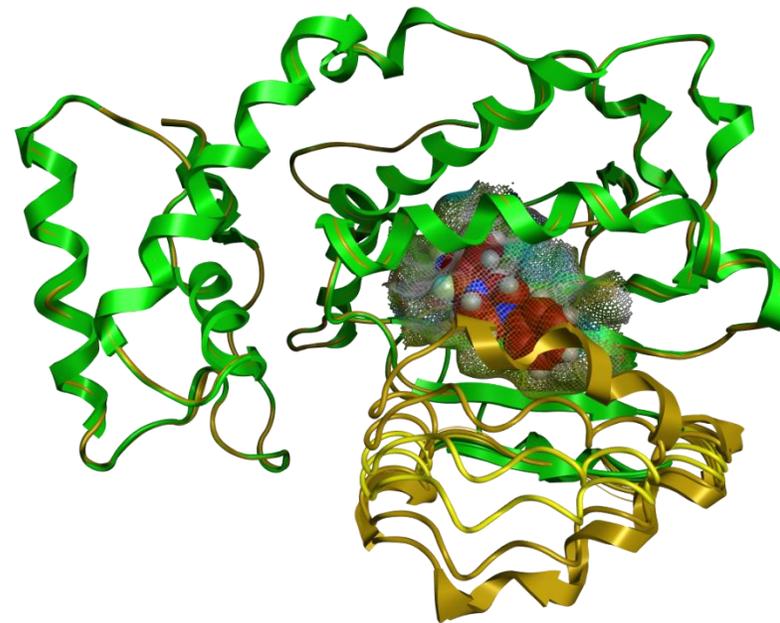
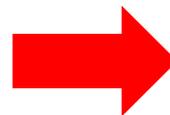
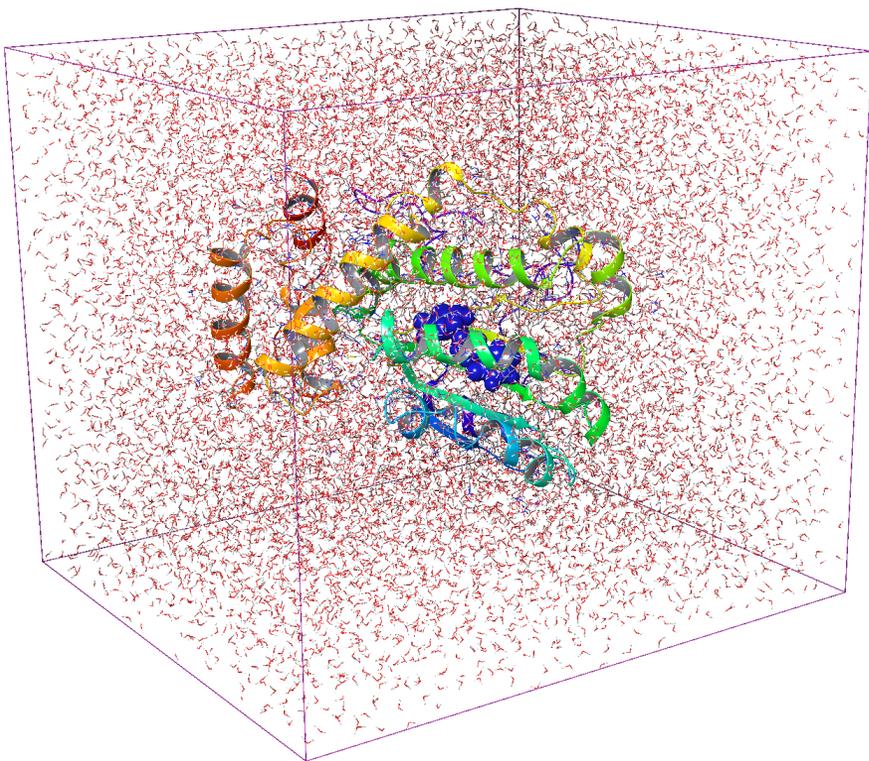


Docking-Based Virtual Screening

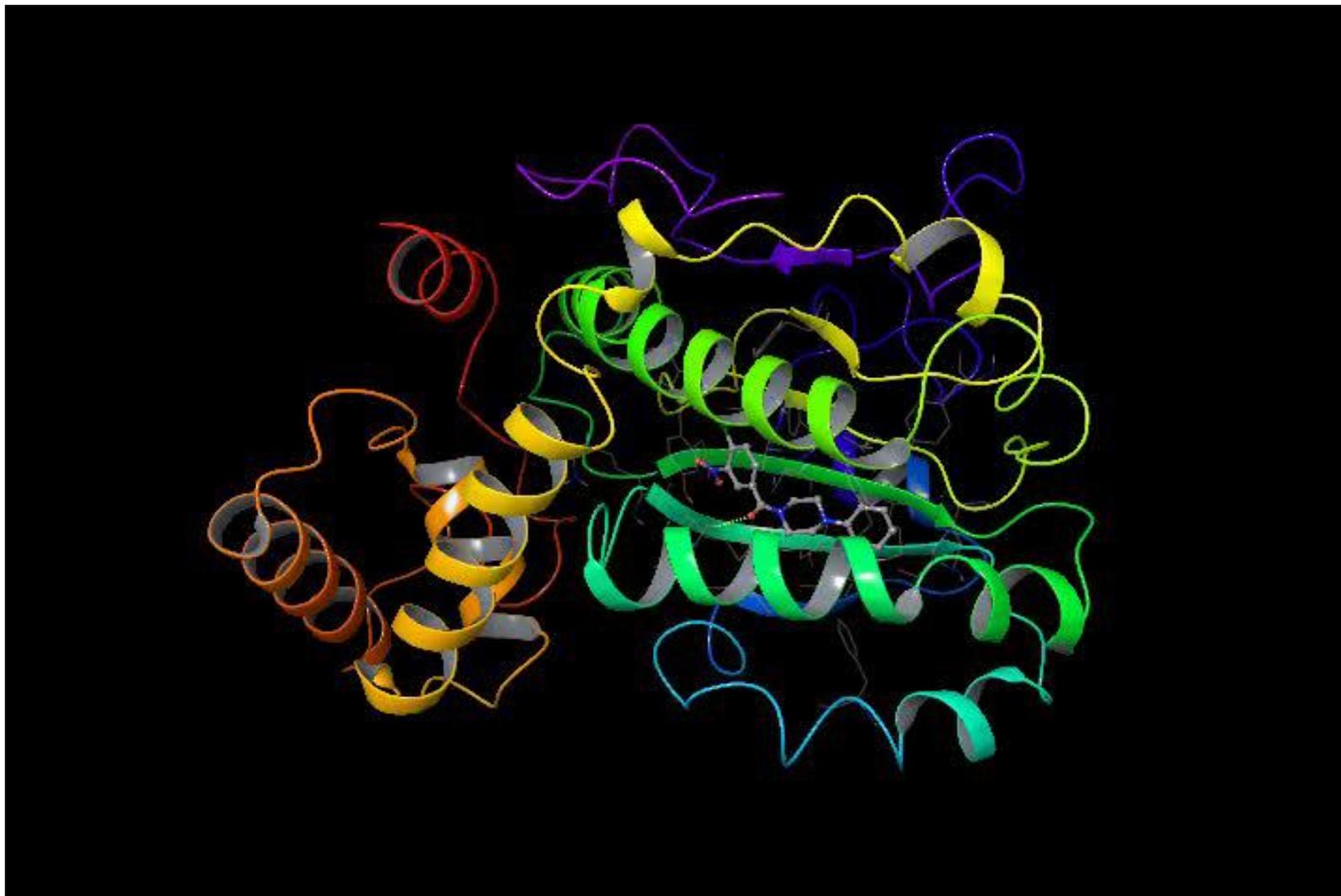


Decoys: known or presumed non-binders to the target protein.

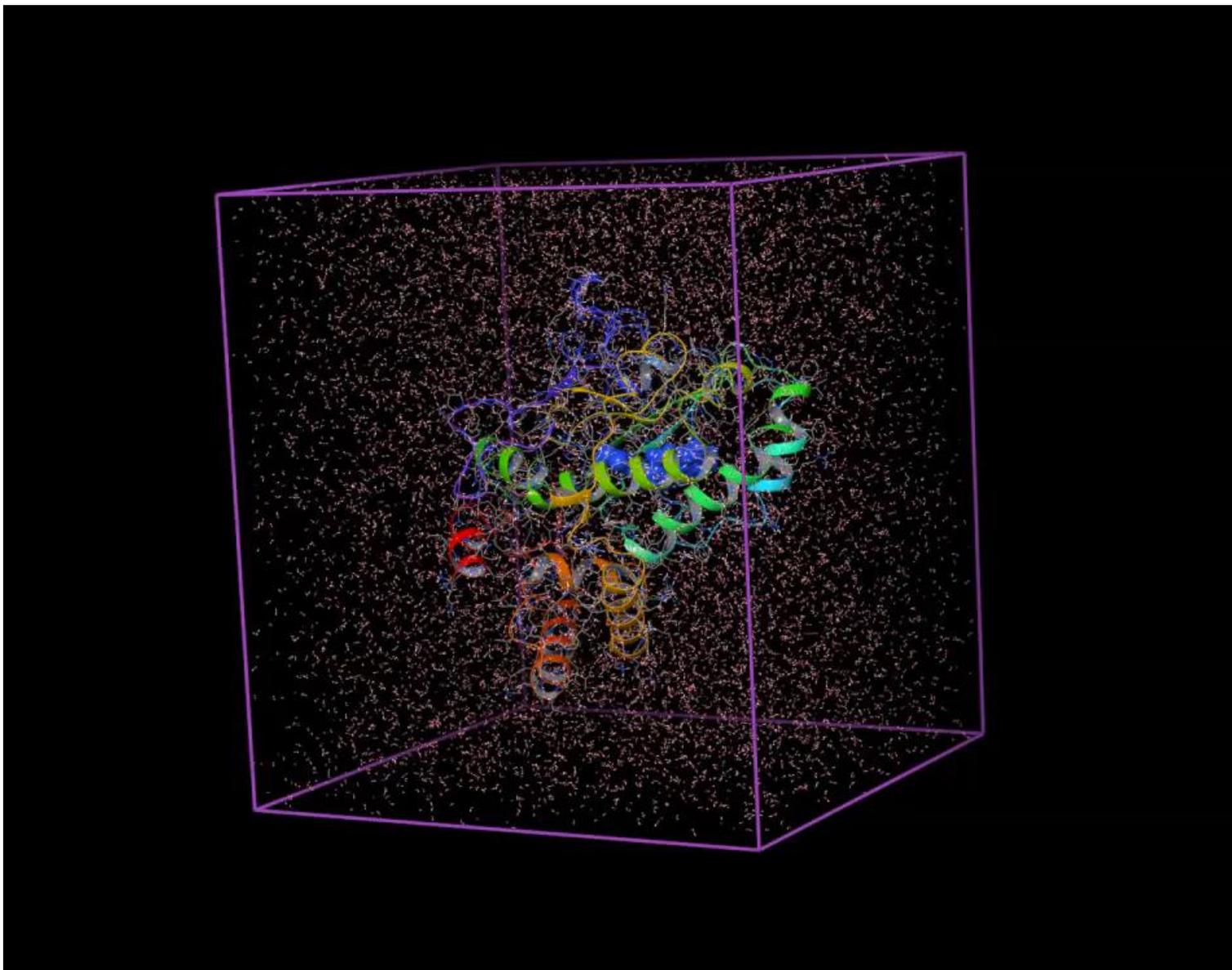
Sec14 Homology Model: All-Atom MD Simulation



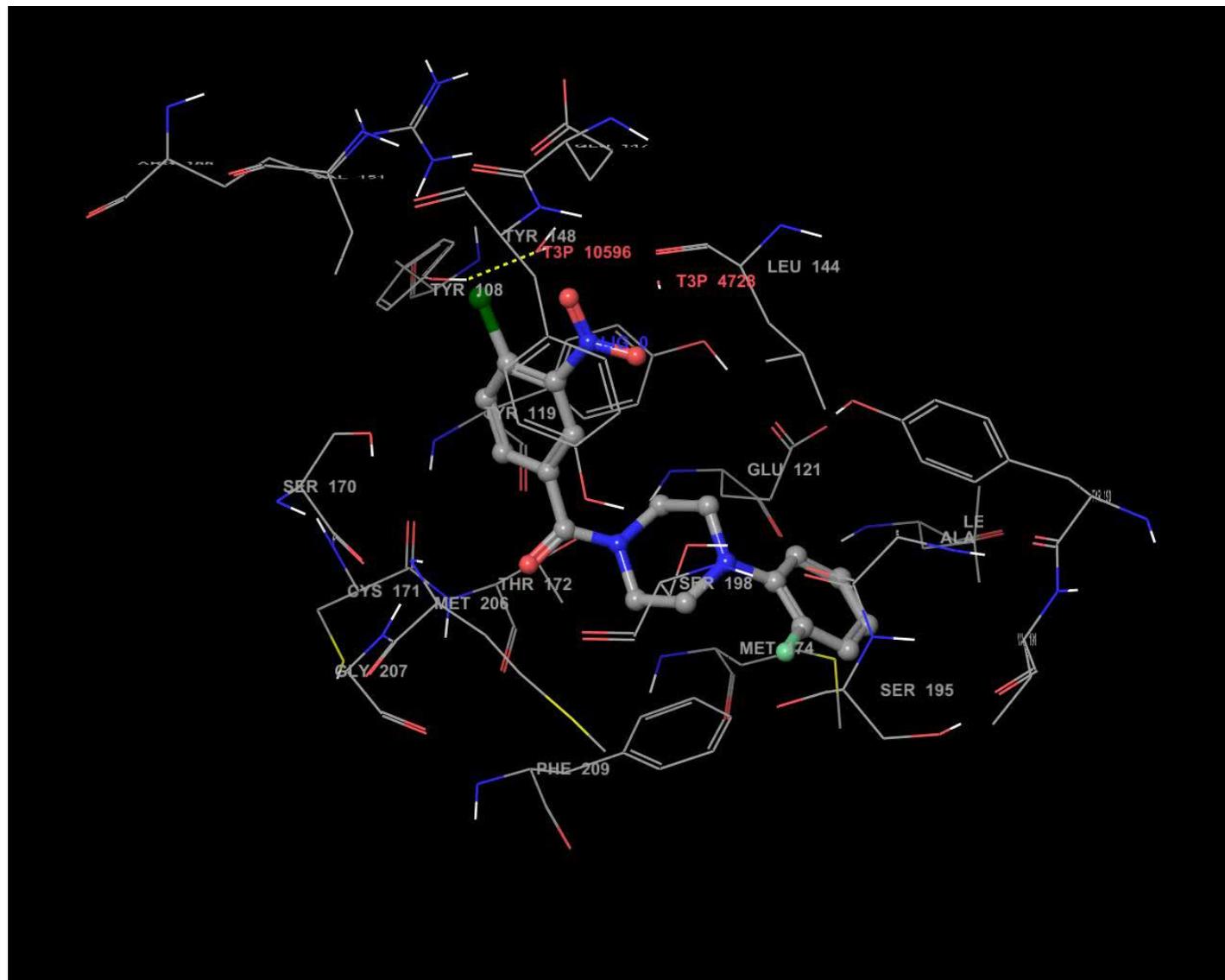
Simulation of Drug Binding to Protein Using DESMOND MD Code



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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- Bachelor of Pharmacy, Institute of Engineering and Technology, M.J.P. Rohilkhand University, India.



Research Interest

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