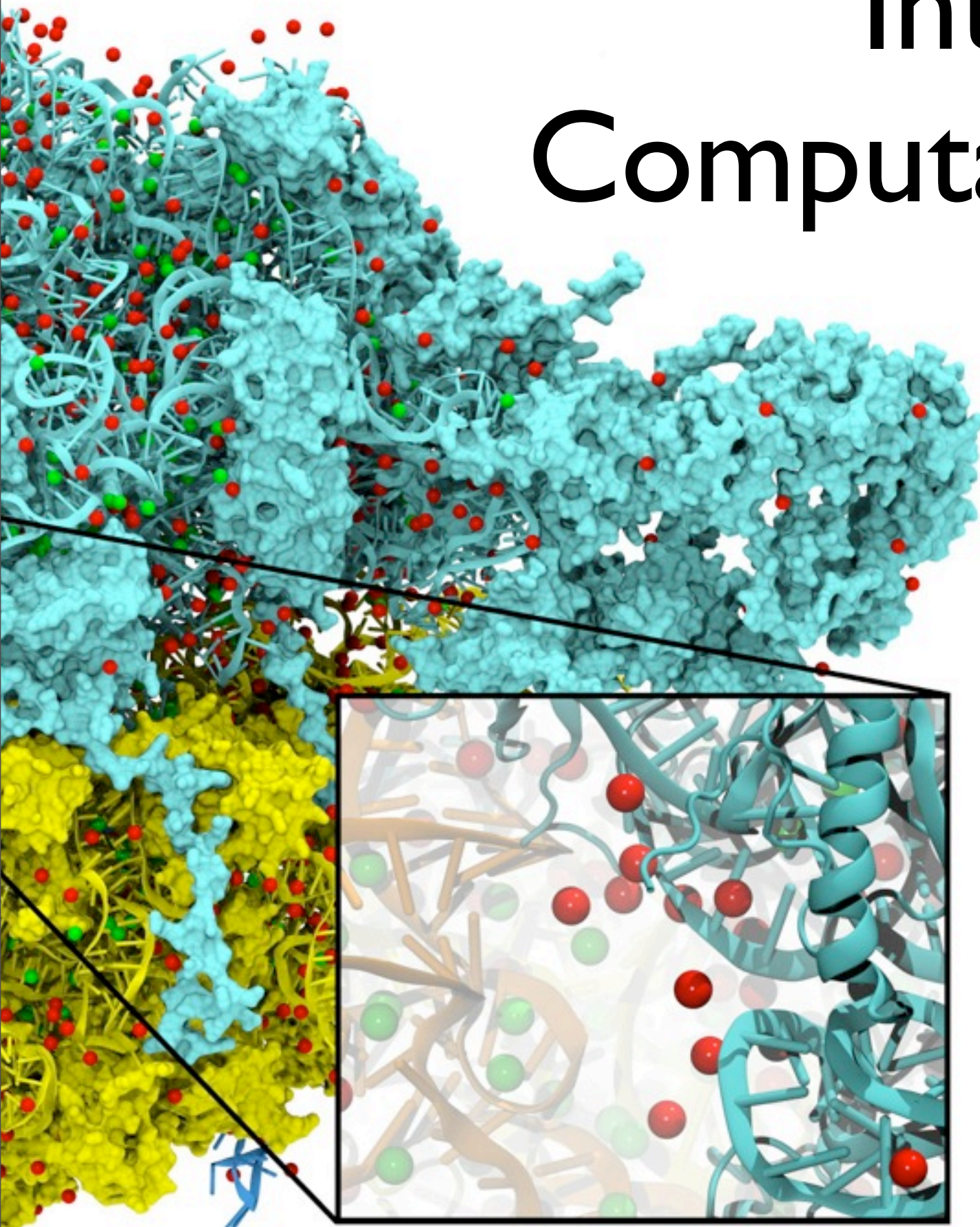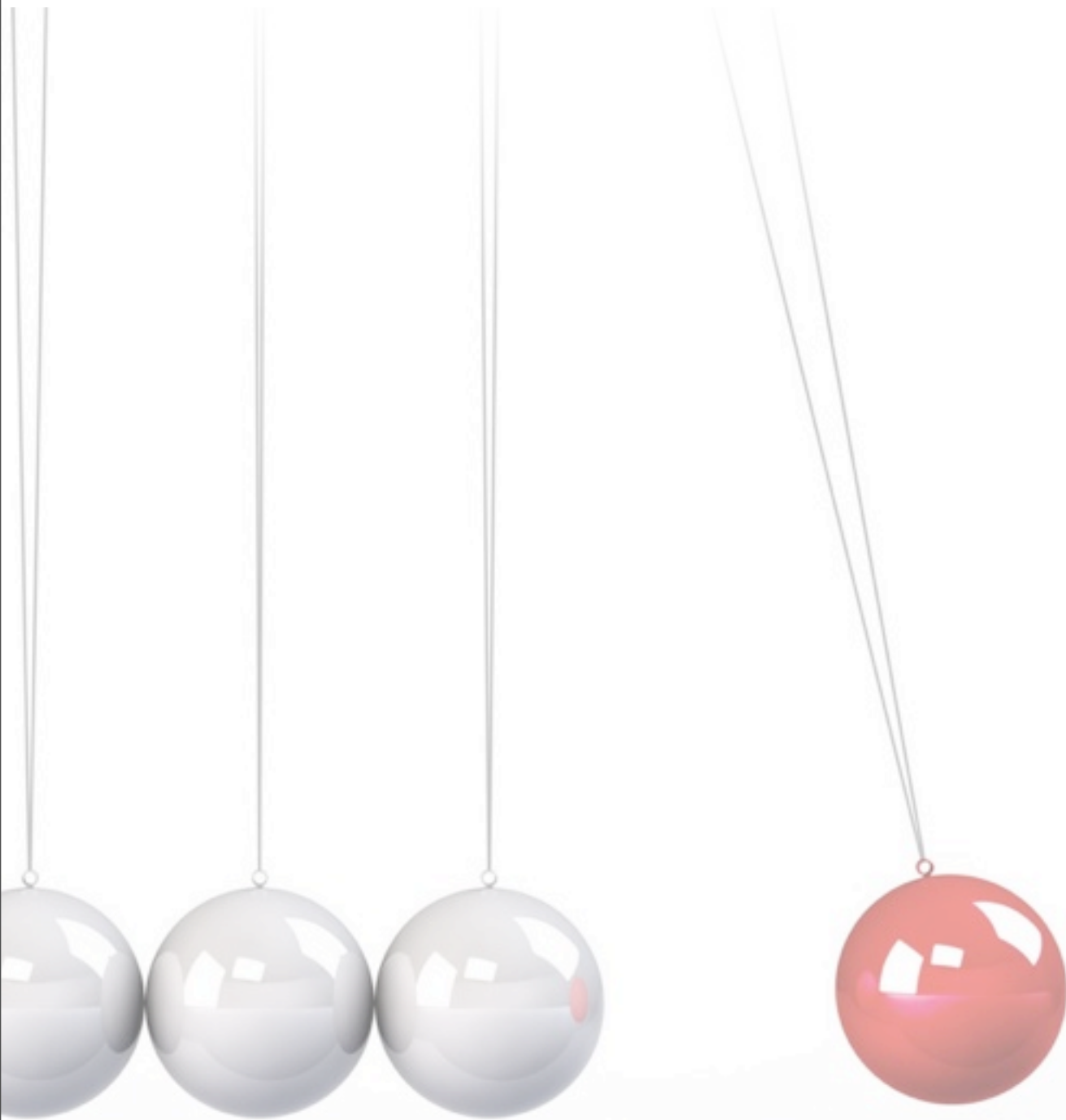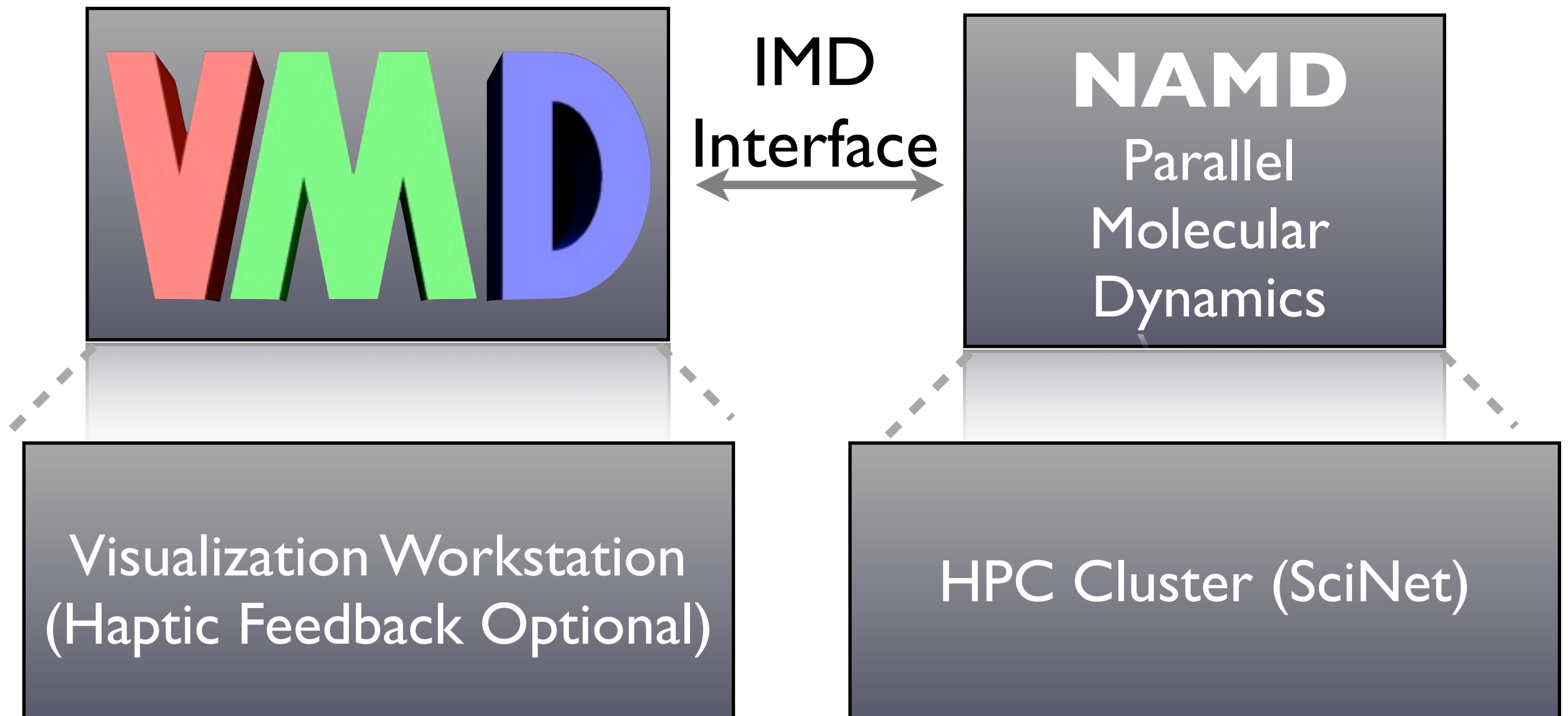# Interactive Computational Biology

SNUG January 2013
Christopher Ing
Pomès Lab
Hospital for Sick Children

Molecular Simulation

- Takes Newton's laws to the limit!

- Vast range of applications.

- Has limitations.

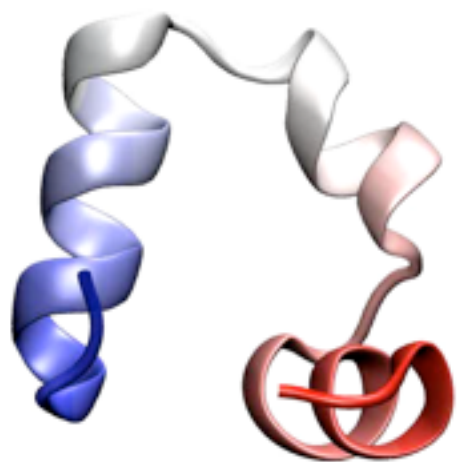- Mature and performance optimized parallel software (Gromacs, NAMD)

Interactive Simulation

VMD

IMD
Interface

NAMD
Parallel
Molecular
Dynamics

Visualization Workstation
(Haptic Feedback Optional)
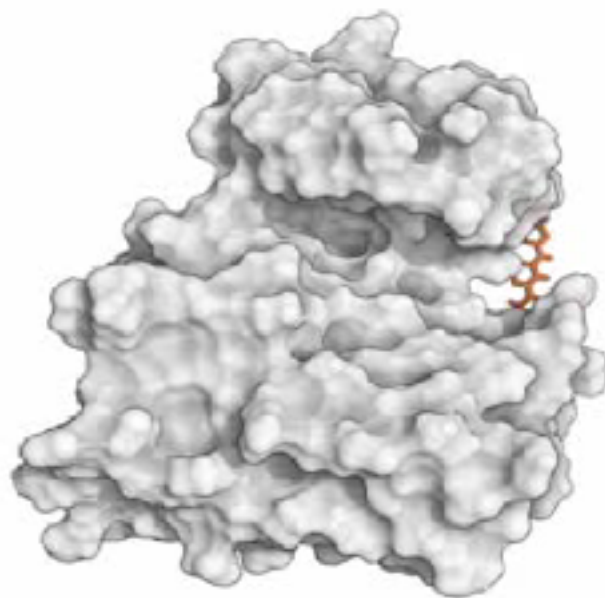
HPC Cluster (SciNet)

Stone, J. E., Gullingsrud, J. & Schulten, K. A system for interactive molecular dynamics simulation. 191–194 (2001).
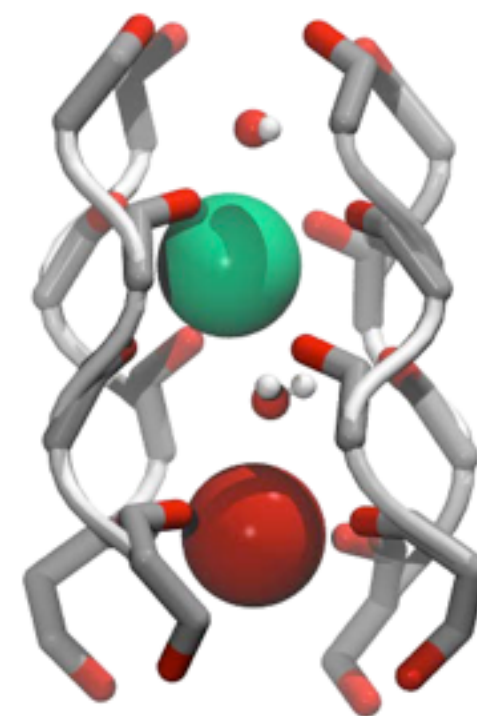
Applications of Molecular Dynamics

Protein Folding   **Ligand Binding**   **Ion Permeation**

1. Freddolino, P. L. & Schulten, K. Common Structural Transitions in Explicit-Solvent Simulations of Villin Headpiece Folding. *Biophysj* **97**, 2338–2347 (2009).
2. Shan, Y. *et al.* How Does a Drug Molecule Find Its Target Binding Site? *J. Am. Chem. Soc.* **133**, 9181–9183 (2011).
3. Jensen, M. O. et al. Principles of conduction and hydrophobic gating in K+ channels. Proceedings of the National Academy of Sciences 107, 5833–5838 (2010).

Protein Folding

- Chicken Villin Headpiece (35 residues, PDB 2F4K) made of 3 alpha helices.

- One of the best studied fast-folding protein domains (~1 microsecond)

Interactive Protein Unfolding

- Use the approach of "FoldIt" by working in reverse: repeated unfolding.

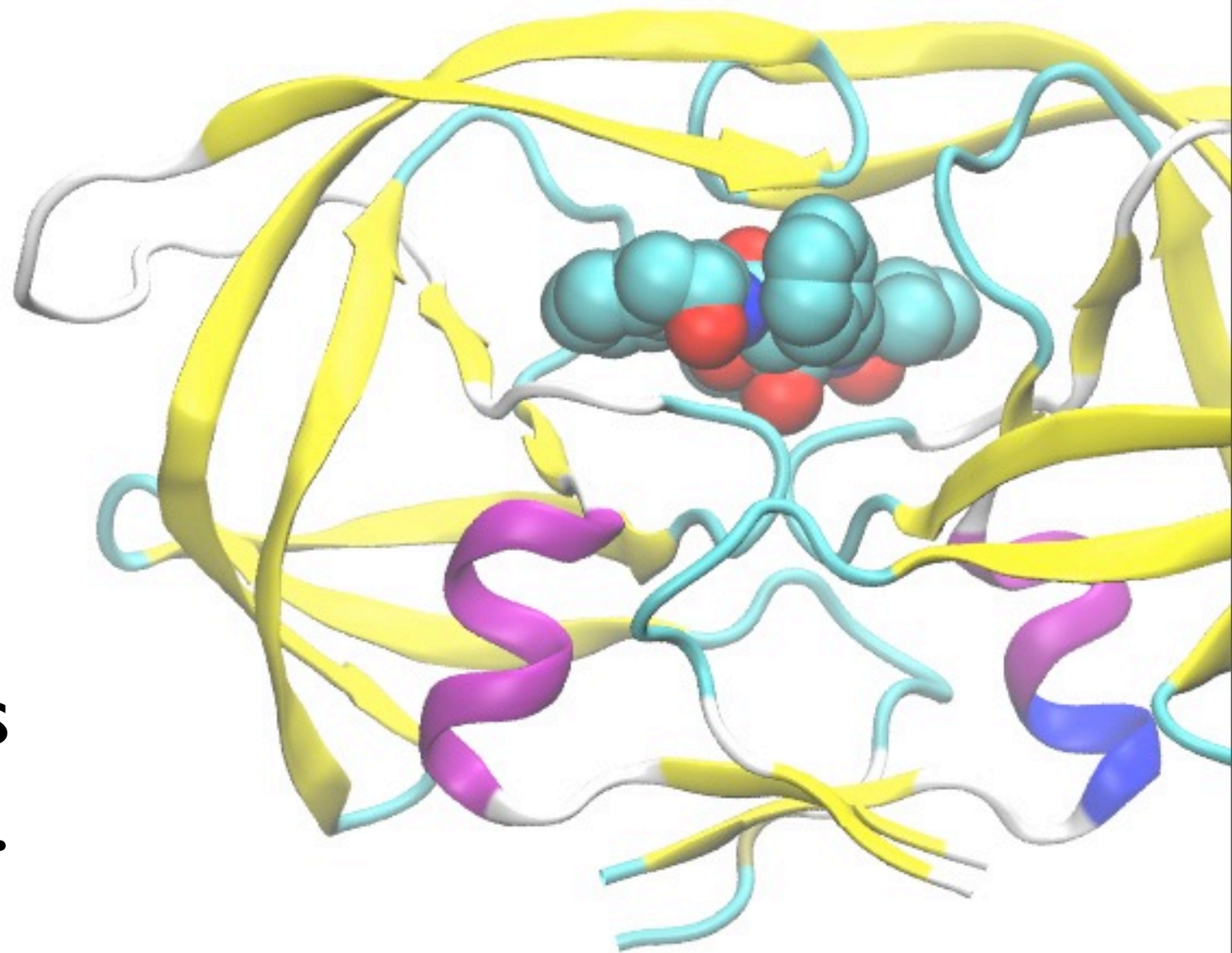- Naively pulling either end of the peptide chain results in unfolding.

Interactive Protein Unfolding

- Use the approach of "FoldIt" by working in reverse: repeated unfolding.

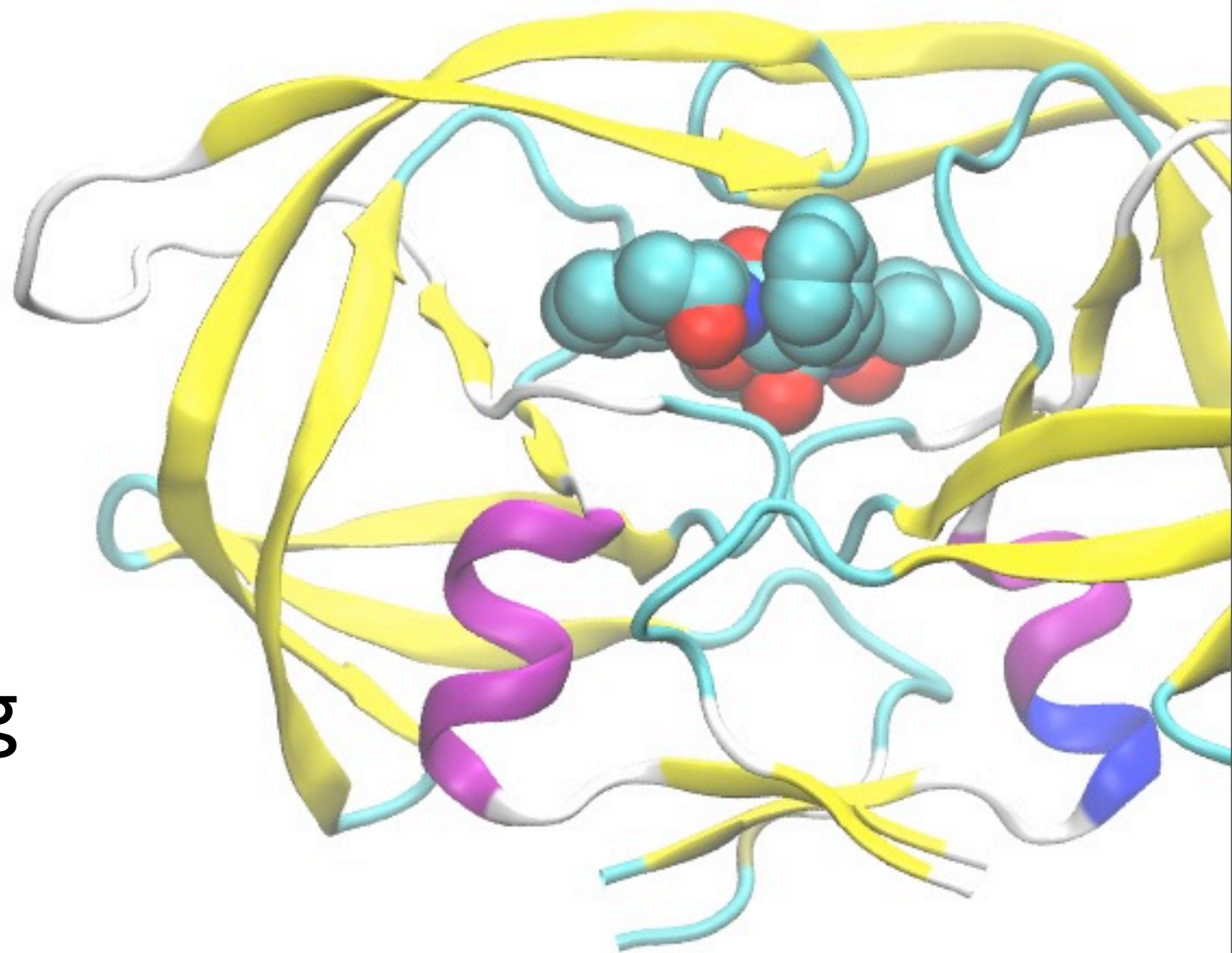- Naively pulling either end of the peptide chain results in unfolding.

Drug Binding

- HIV-1 Protease (PDB 1EBZ) and inhibitor BEA388.

- Essential for the infectiousness of HIV

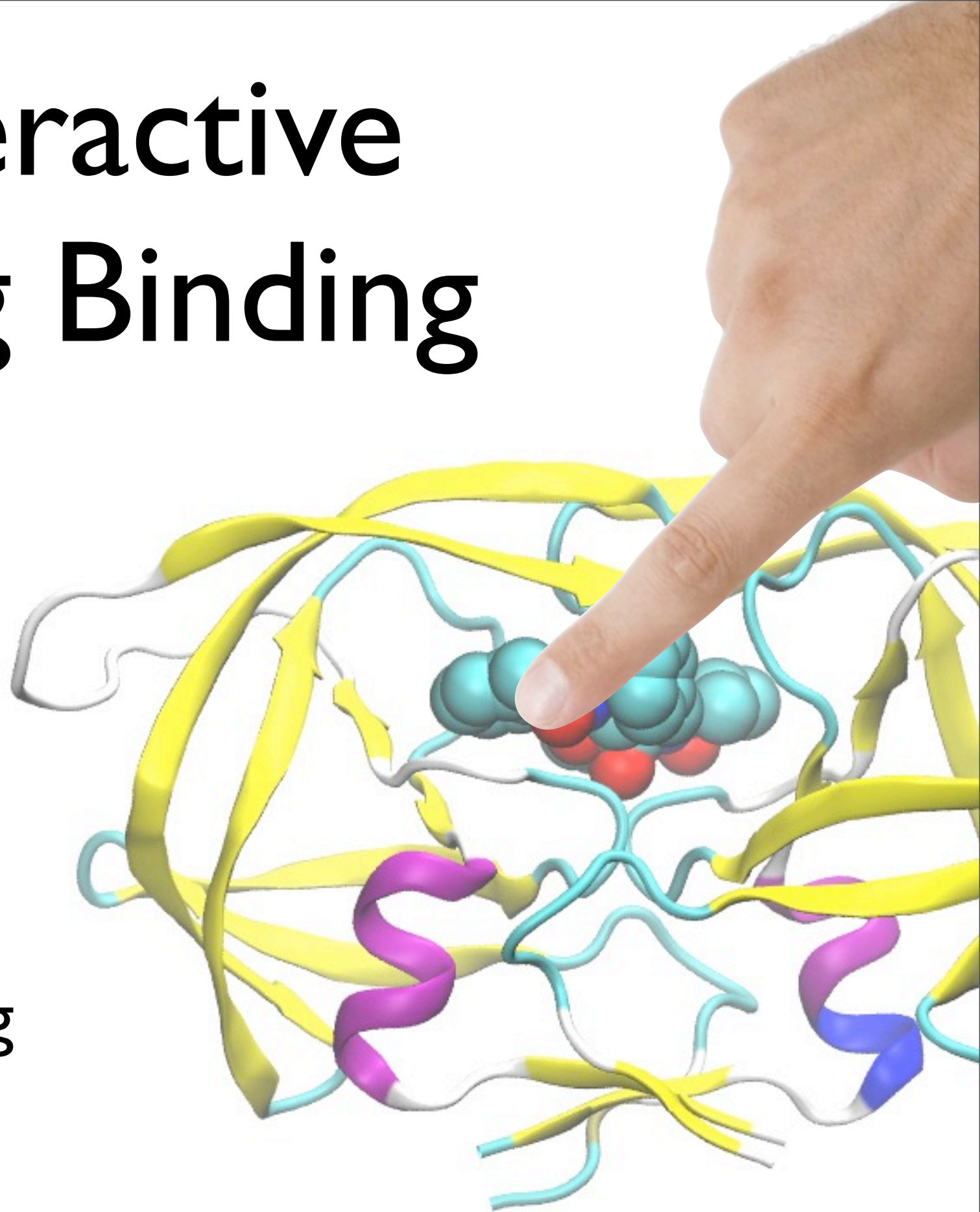- It's active site can be blocked by numerous small drug molecules.

Interactive Drug Binding

- Use the approach of the new "Fit2Cure" game

- Guiding a drug molecule to block an active site, attempting to optimize it's fit.
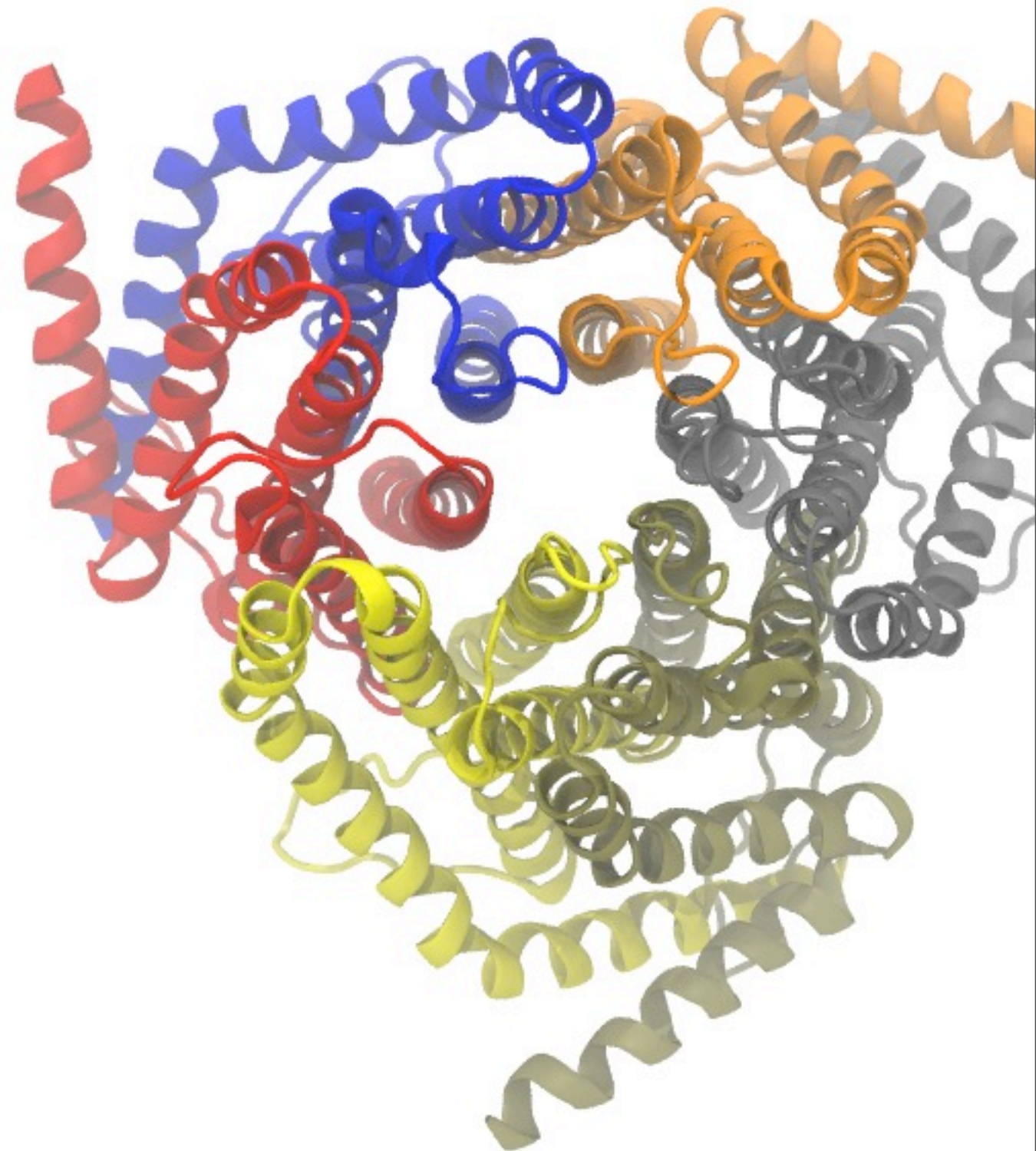
Interactive Drug Binding

- Use the approach of the new "Fit2Cure" game

- Guiding a drug molecule to block an active site, attempting to optimize it's fit.
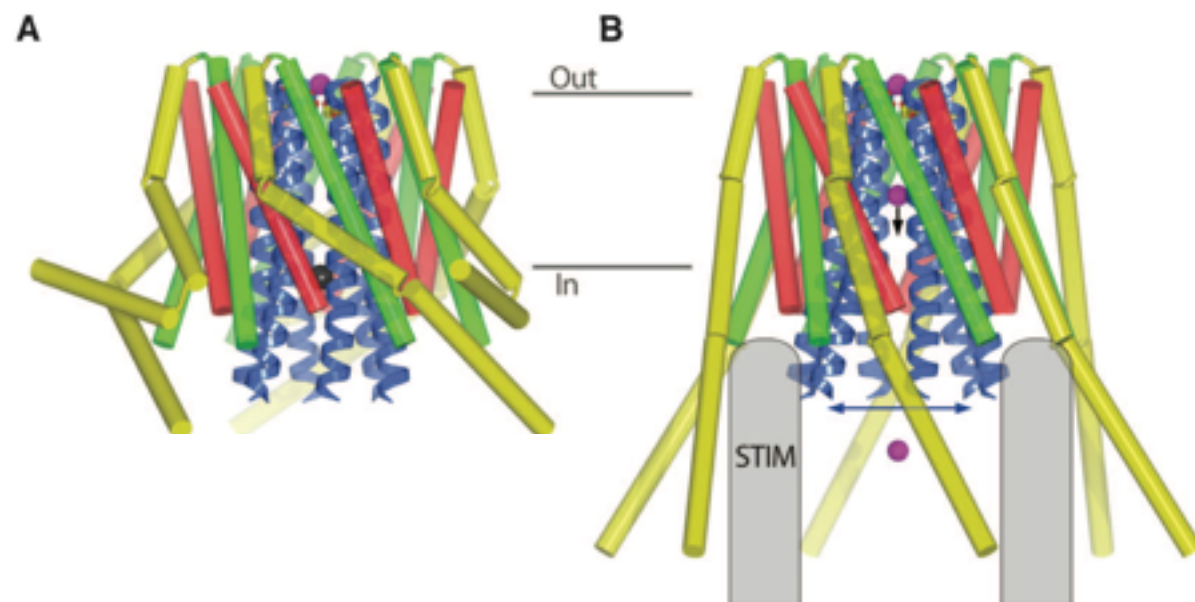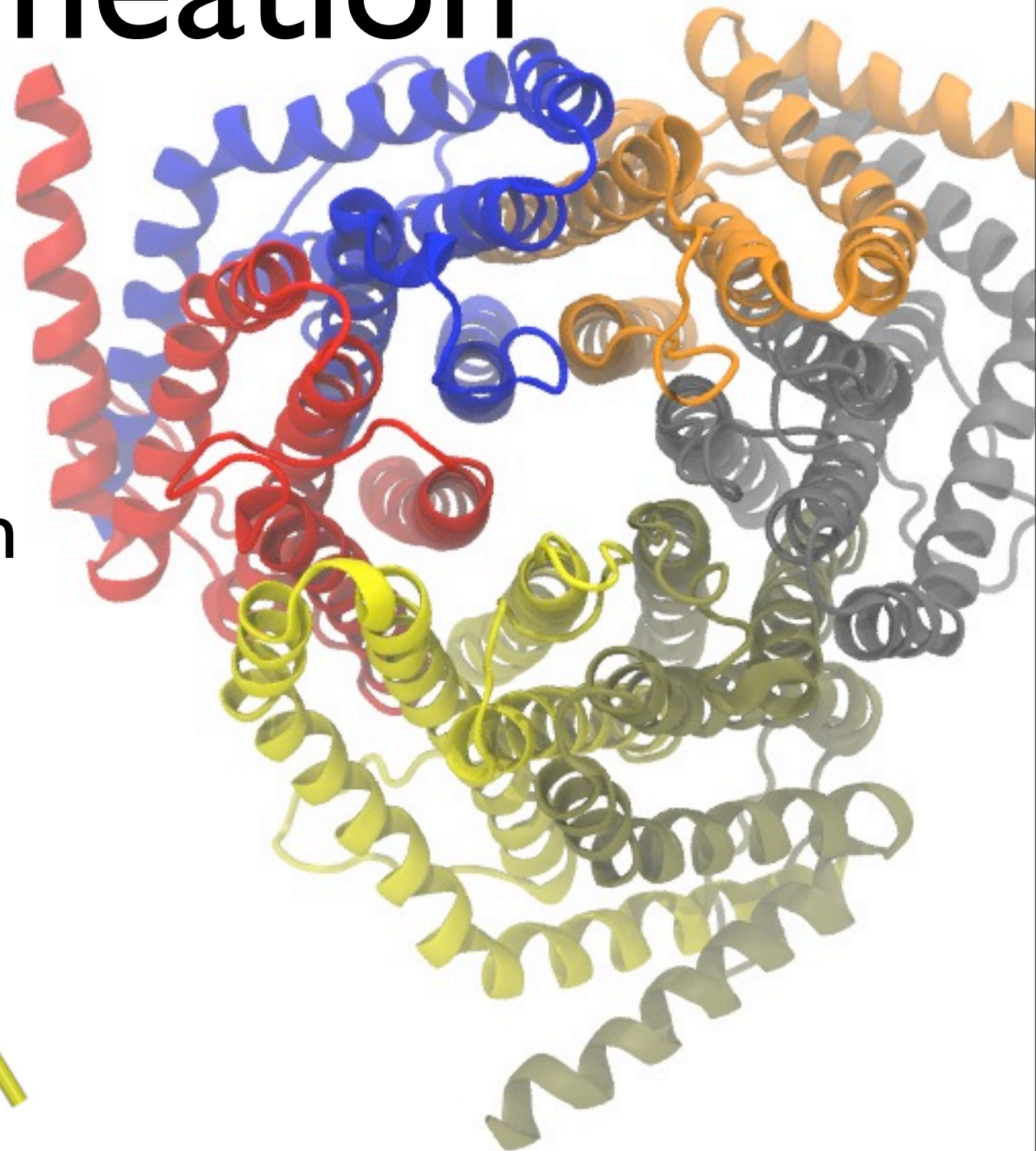
Ion Permeation

- Orai1 Calcium Release Activated Channel (PDB 4HKR).

- Crucial for the immune system response in T-cells, disruption can cause autoimmune disease or inflammation.
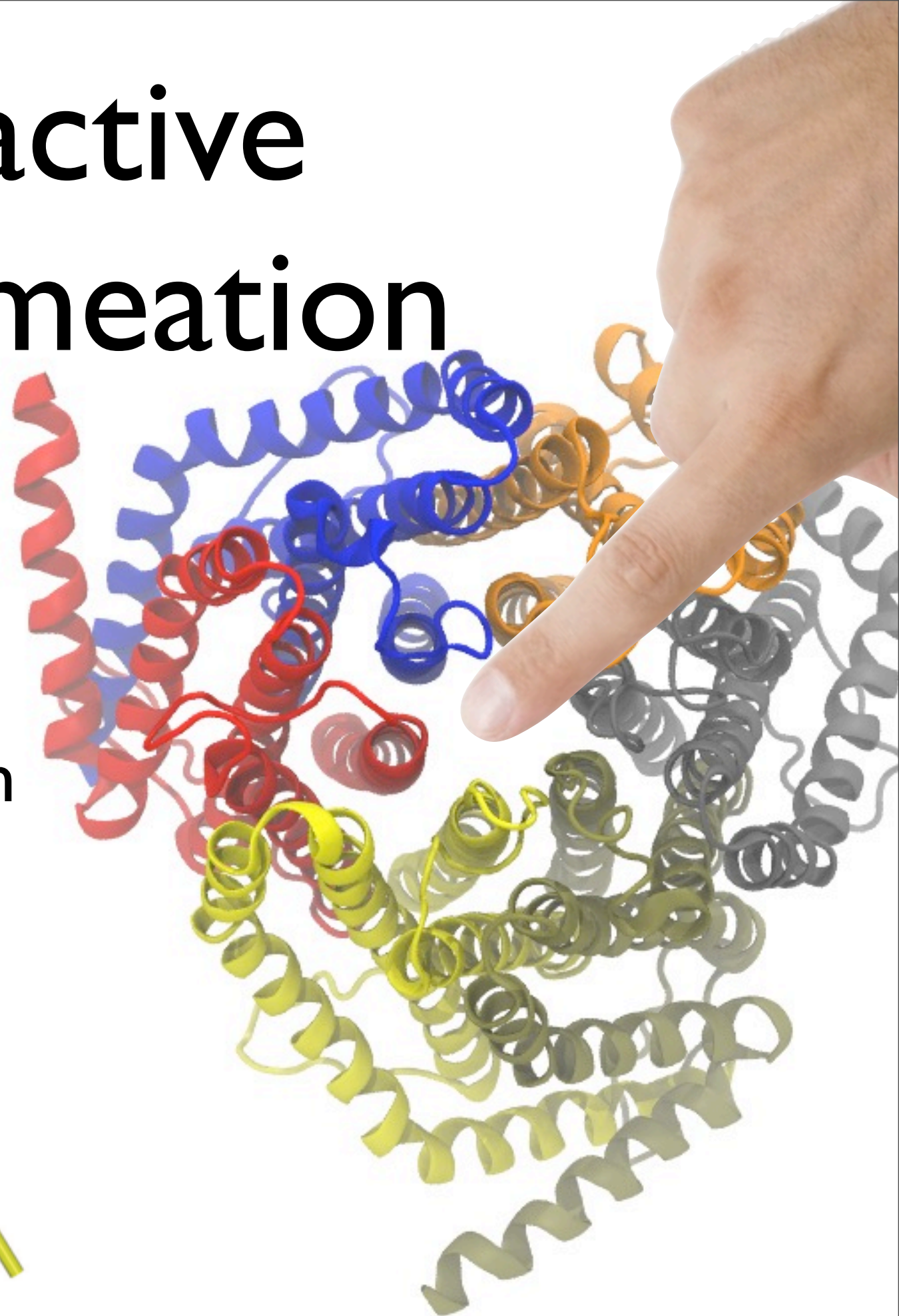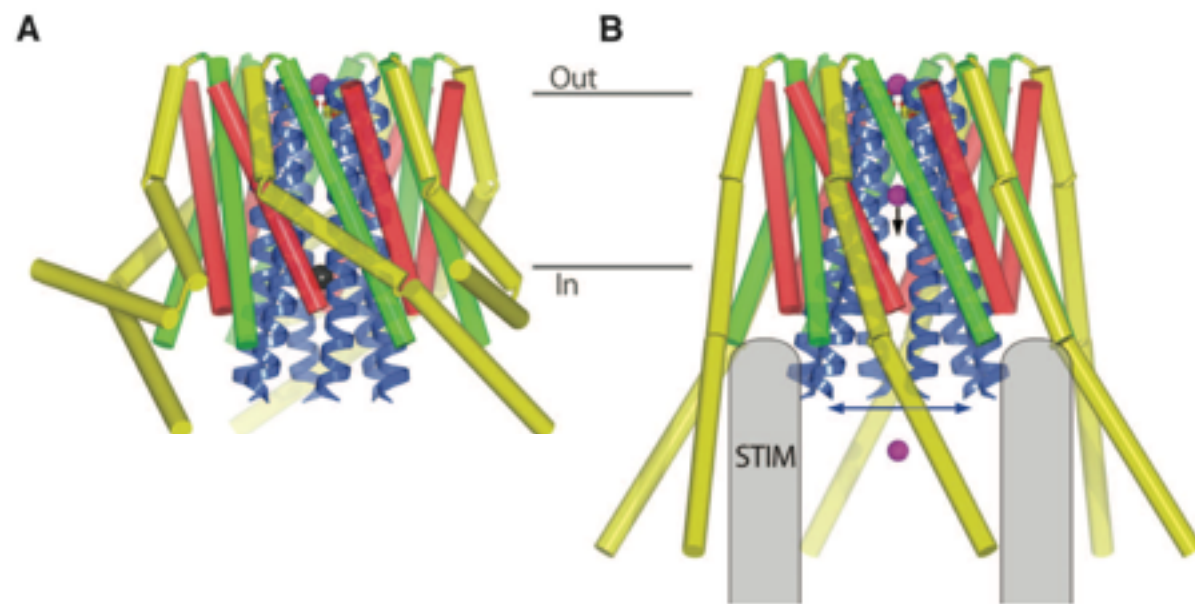
Interactive Ion Permeation

- Forcing atoms through the pore one at a time.

- Opening the pore may require pulling on certain helices.

Interactive Ion Permeation

- Forcing atoms through the pore one at a time.

- Opening the pore may require pulling on certain helices.

Demonstration Time

Only Quad-cores

Mouse as Input

No Network Communication

Future Improvements

3D Glasses

Haptic
Input Device

Game Mechanics