# Antibody binding to anthrax edema factor determined by RosettaDock (v2.3) using flexible loop modeling

Michael A. Dolan, Ph.D.

Office of Cyber Infrastructure and Computational Biology
National Institute of Allergy and Infectious Diseases
U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

# Anthrax (band) = ✓

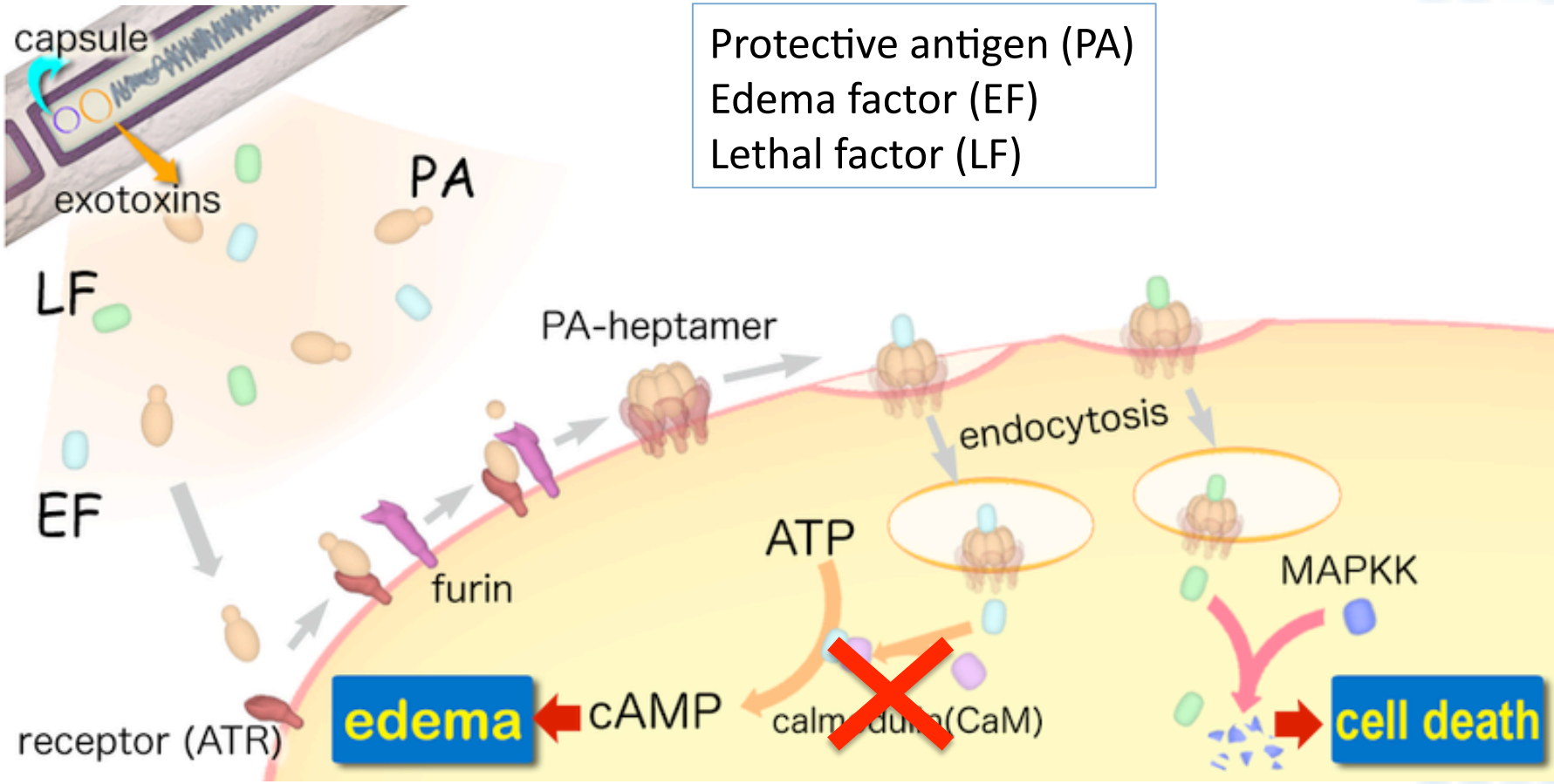
# Anthrax (bacterium) =

"Less than a μg of inhaled anthrax is invariably fatal within five days to a week after exposure."

- FAS (Federation of American Scientists), "Biological Warfare Agents (Partial List)," www.fas.org/nuke/intro/bw/agent.htm, (28 March 2005).

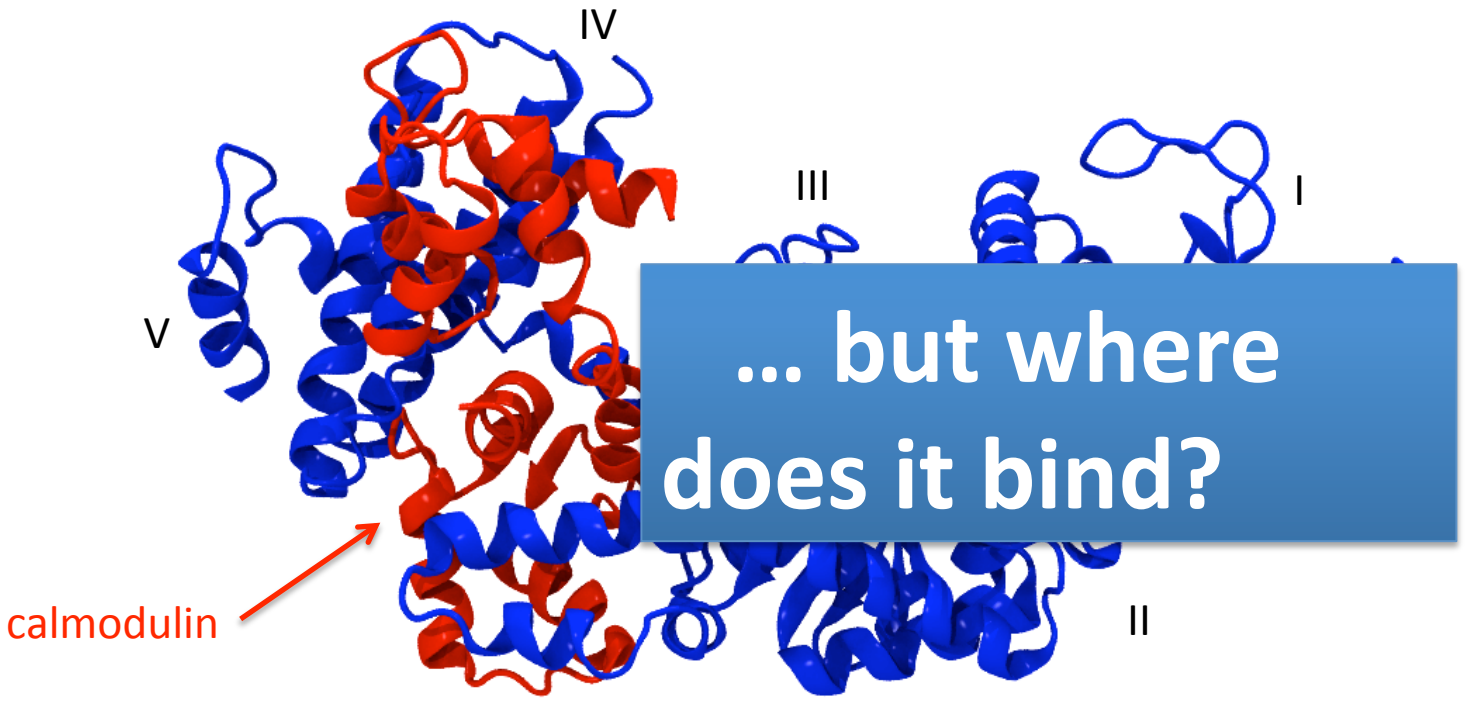
# A three-protein exotoxin

Protective antigen (PA)
Edema factor (EF)
Lethal factor (LF)

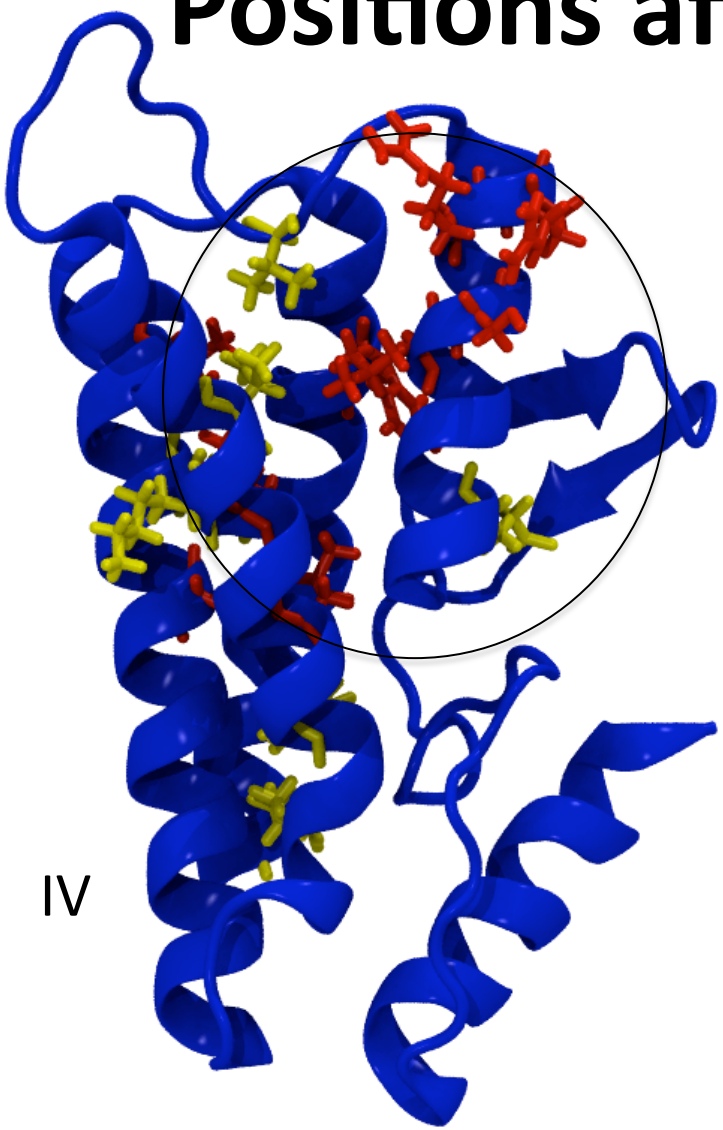


# Monoclonal Ab binds to Edema factor

Chen Z.C., *et al* (2009) Potent neutralization of anthrax edema toxin by a humanized monoclonal antibody that competes with calmodulin for edema factor binding. *Proc Natl Acad Sci USA* ***106(32): 13487-13492***



# Positions affecting Ab binding



IV

Total loss Ab binding
Partial loss Ab binding

| EF position | Amino Acid | PARTIAL BINDING | LOSS OF BINDING |
|---|---|---|---|
| 662 | GLU | x | |
| 667 | LEU | | x |
| 668 | SER | | x |
| 671 | ARG | | x |
| 672 | ARG | | x |
| 678 | VAL | x | |
| 694 | VAL | x | |
| 696 | LYS | x | |
| 697 | ILE | | x |
| 701 | LEU | | x |
| 704 | TYR | x | |
| 728 | ALA | | x |
| 732 | ILE | x | |
| 736 | LEU | | x |
| 748 | TYR | | x |
| 763 | LEU | x | |
| 797 | ILE | x | |

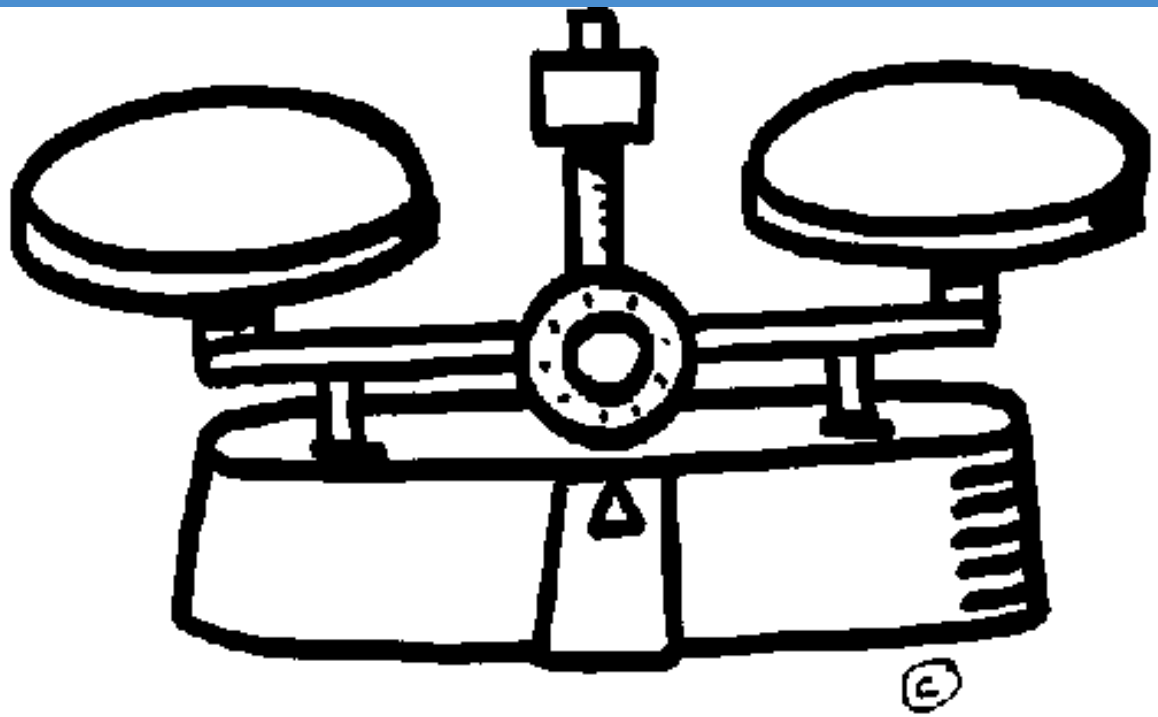
# Rosetta docking

- Ab constructed
  $F_v$ Homology M
- Perturbation, fl
  loop modeling:
  1. H3
  2. L1,L2,L3 a
  3. L1,L2,L3 a
  4. 5. 6. – as
- Only 1 calculati
  agreed with ben

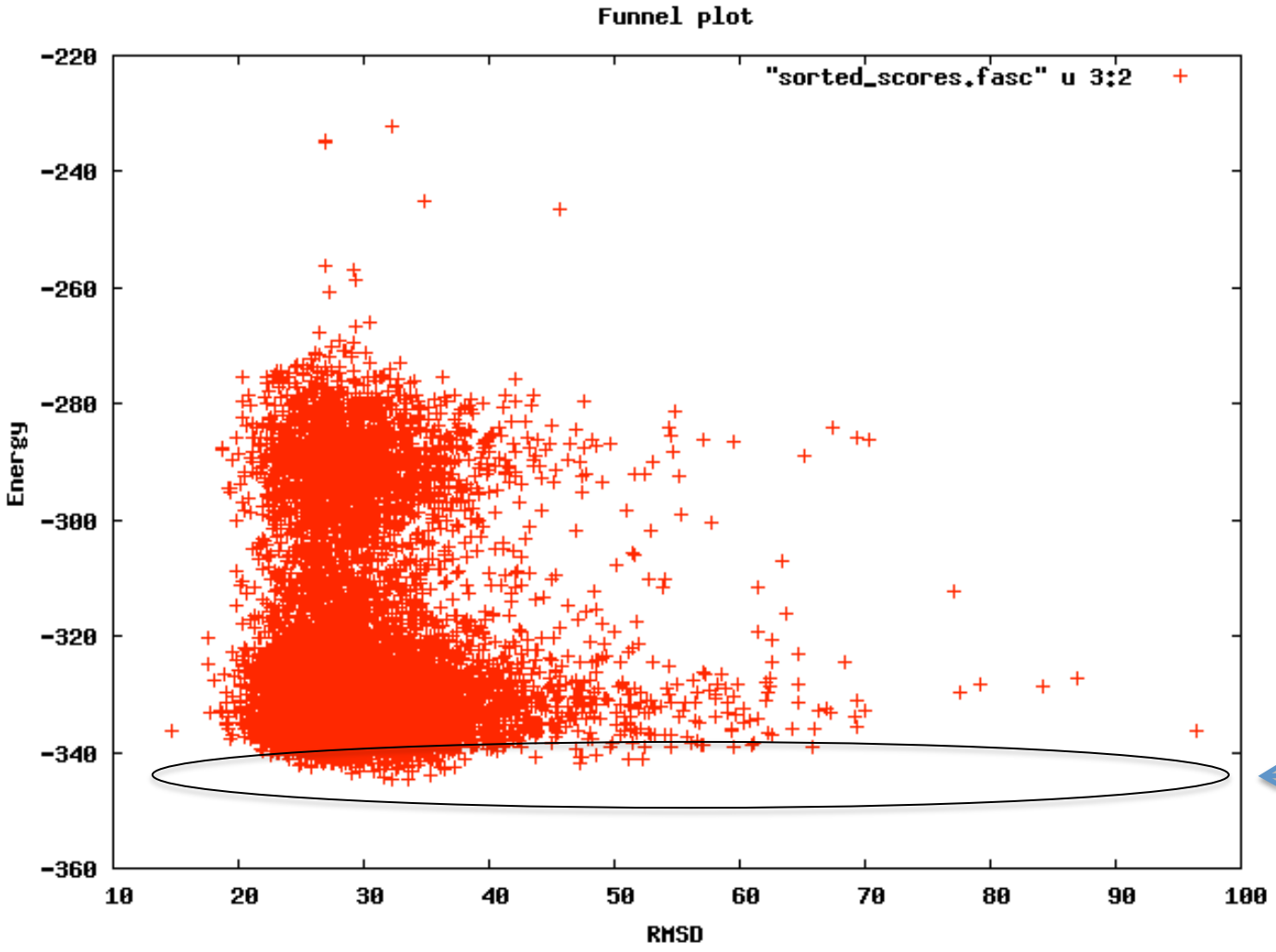
Underscores nee
interpreting resu
the trick.)

FLEXIBILITY

WILL I BE DEAD
WHEN THE
CALCULATION FINISHES??

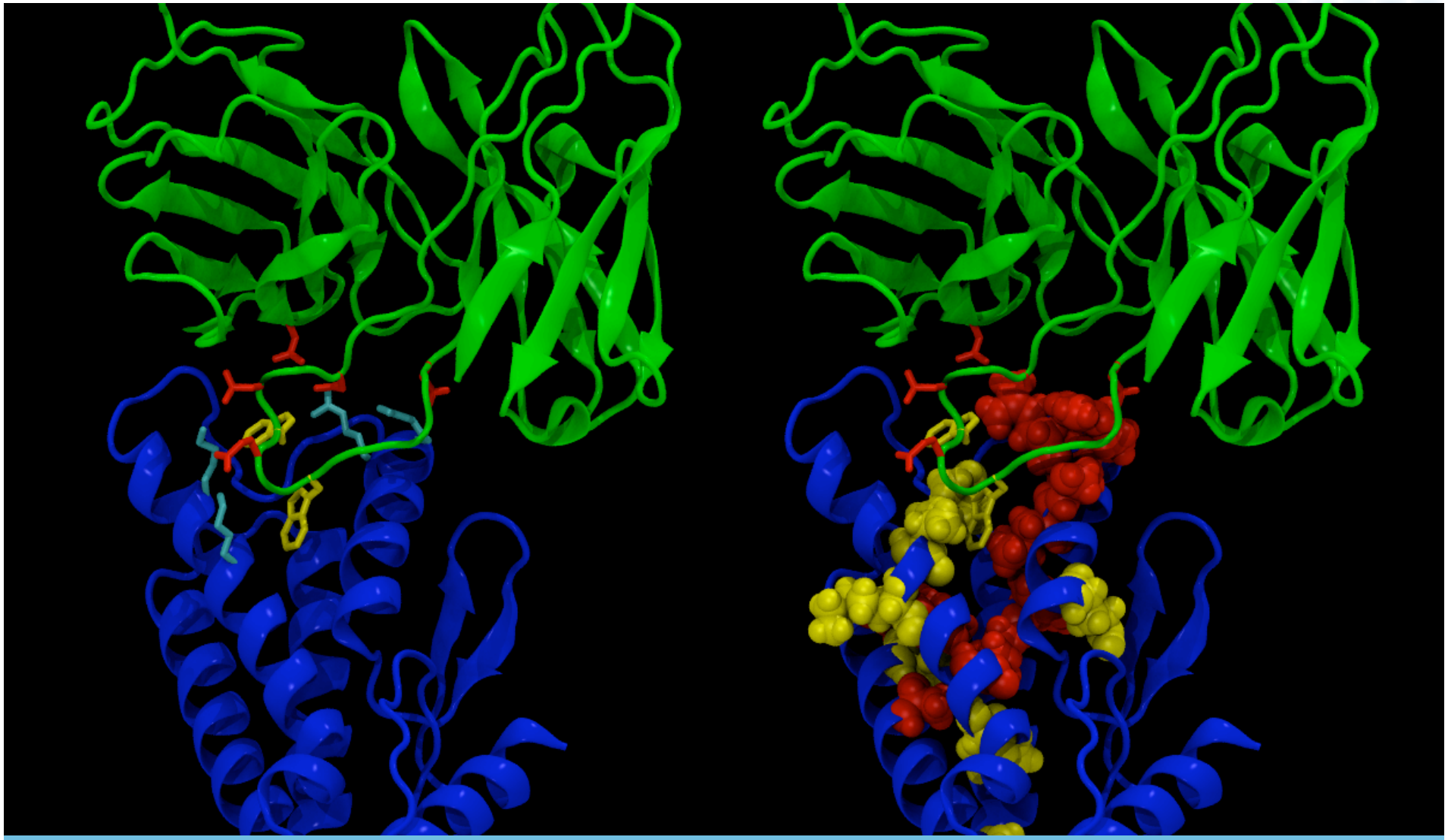


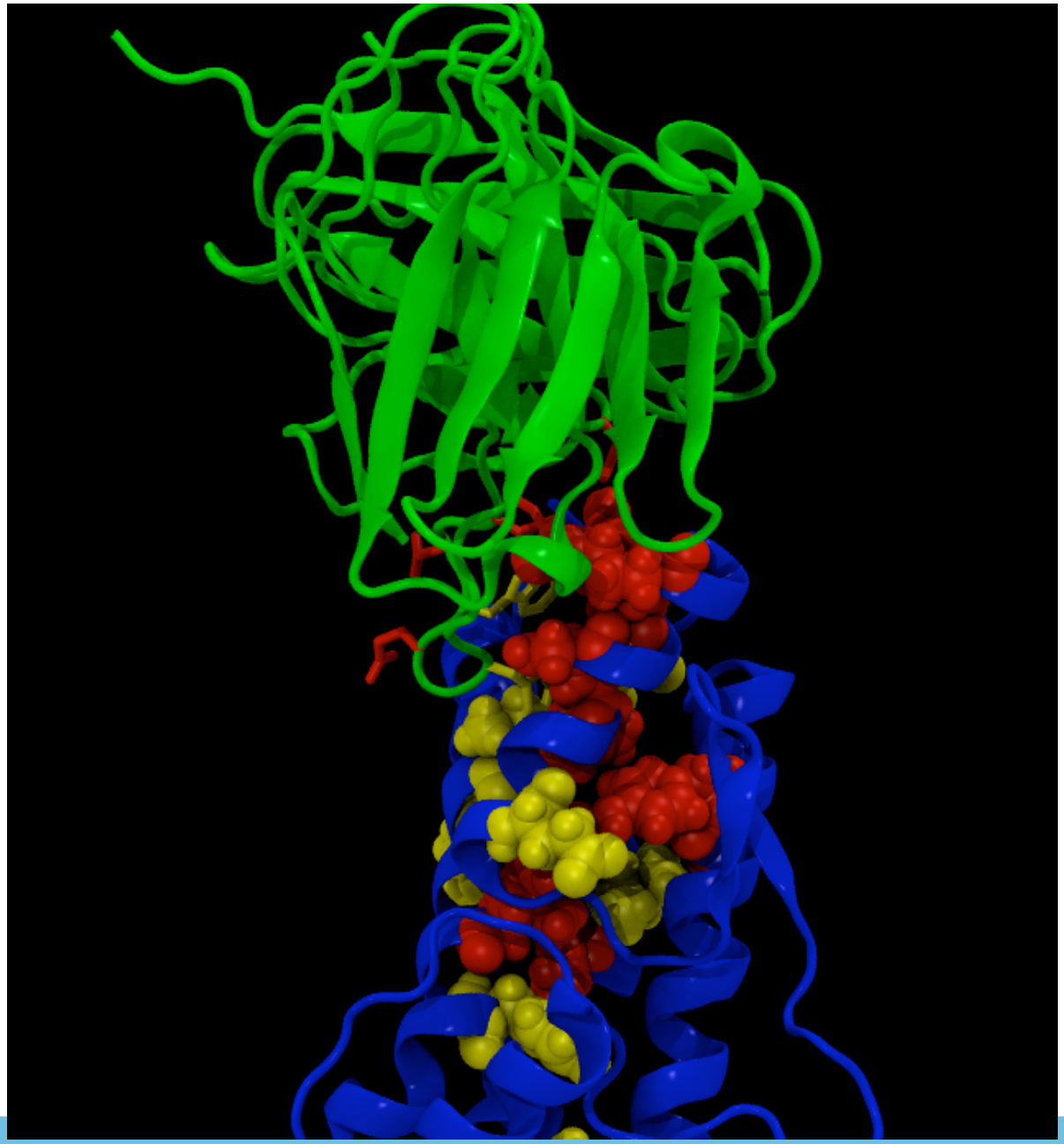
# “Funnel” plot



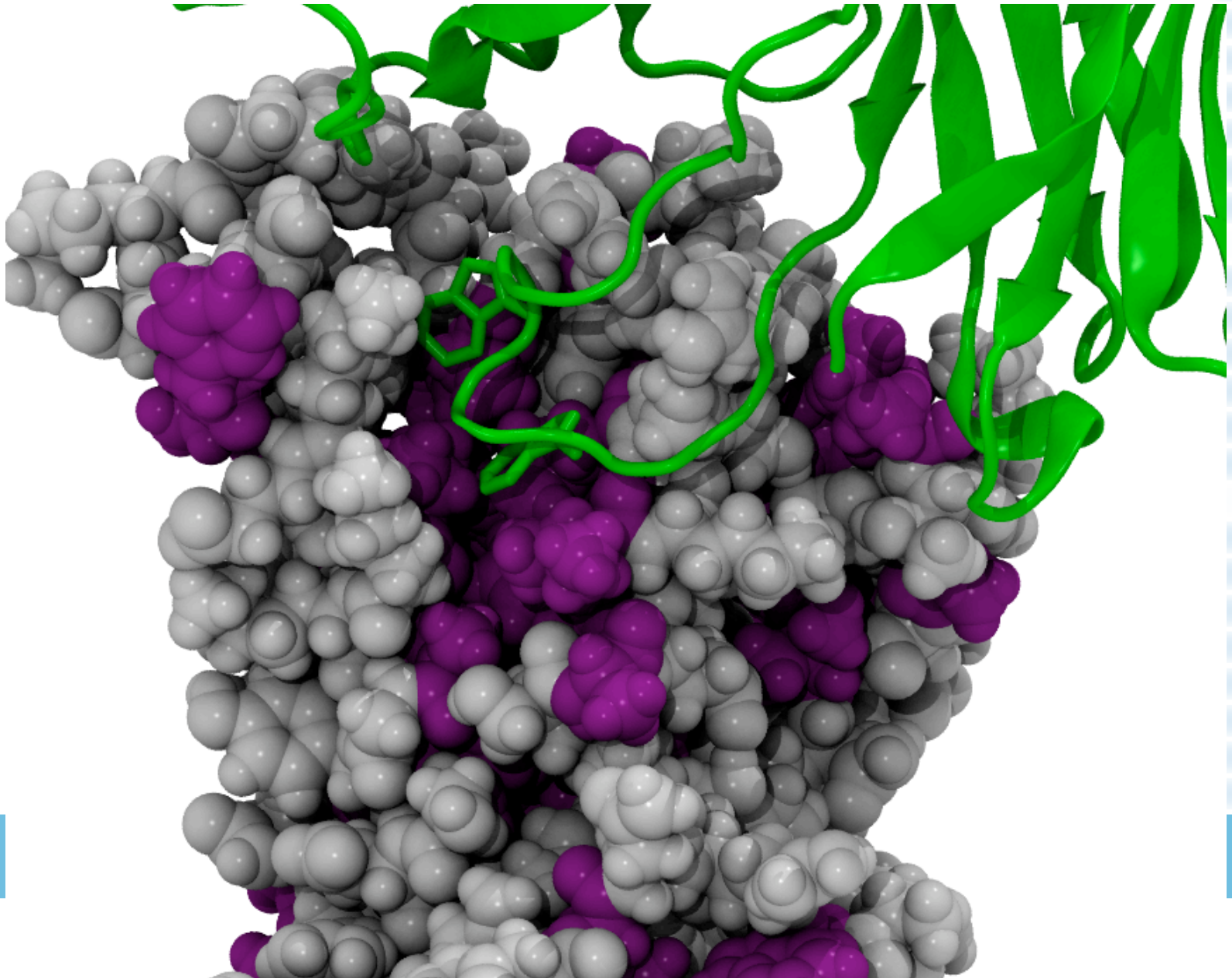

lowest energy conformations used for clustering

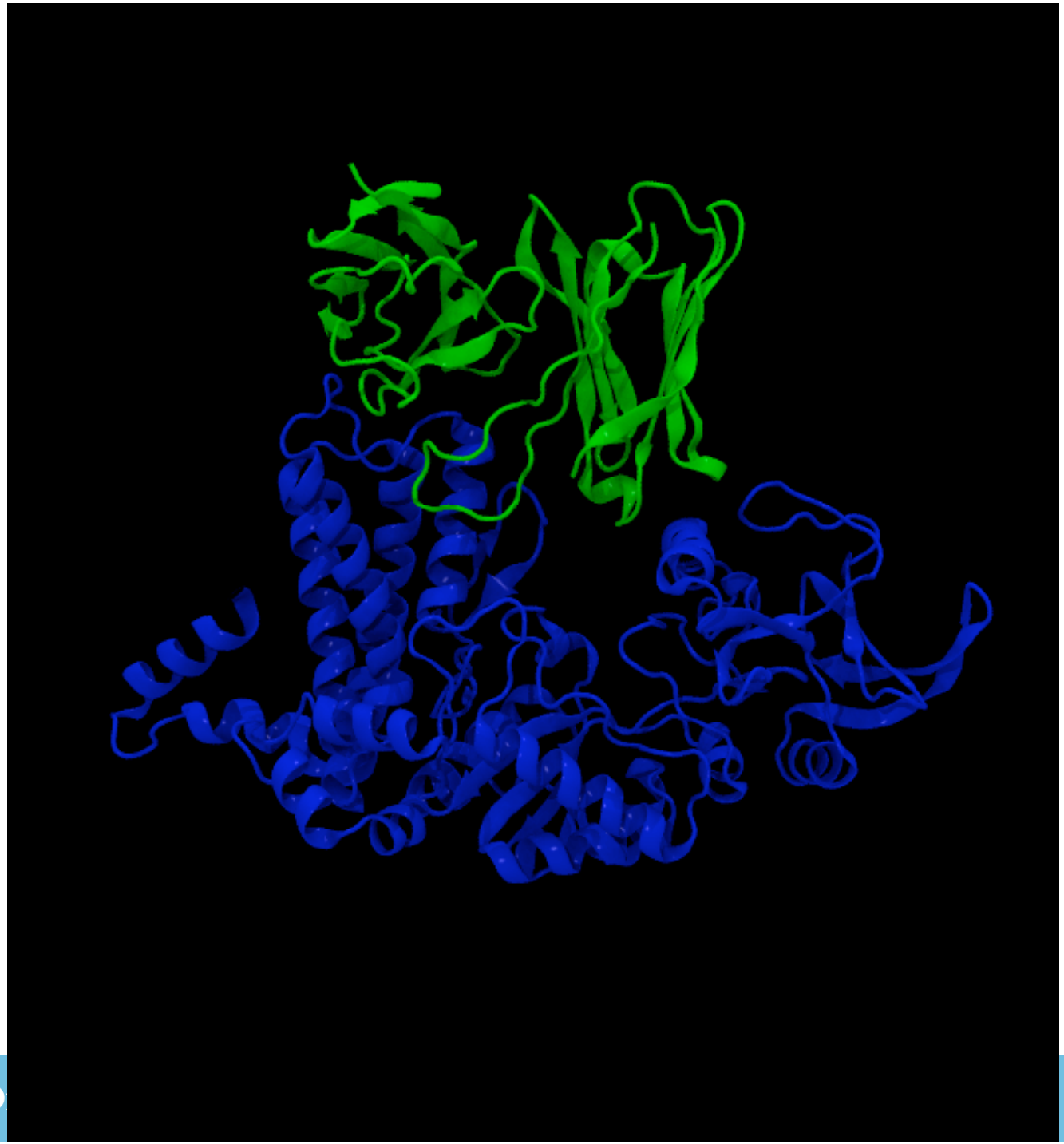
# Detailed contacts



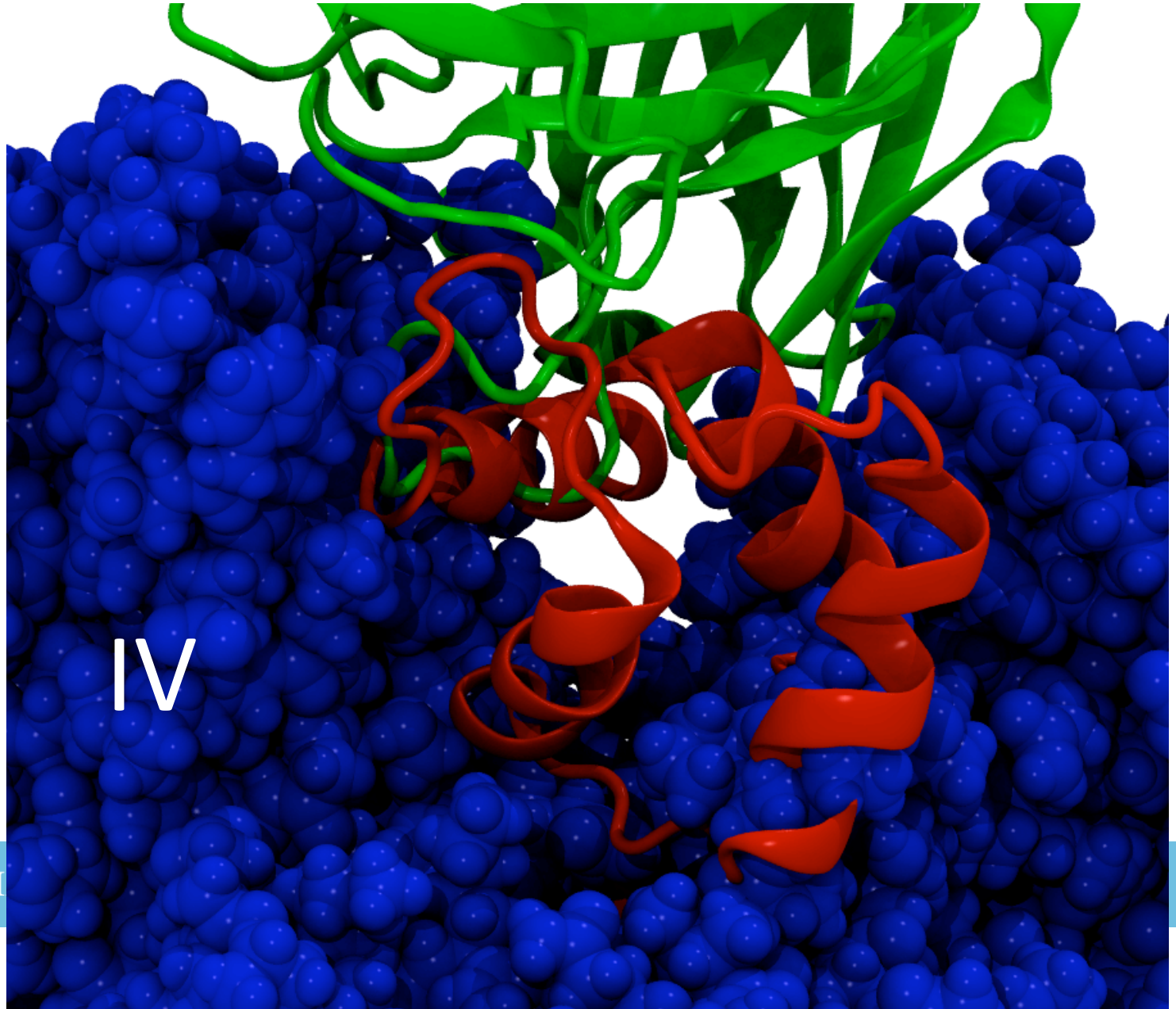


# Post-molecular dynamics





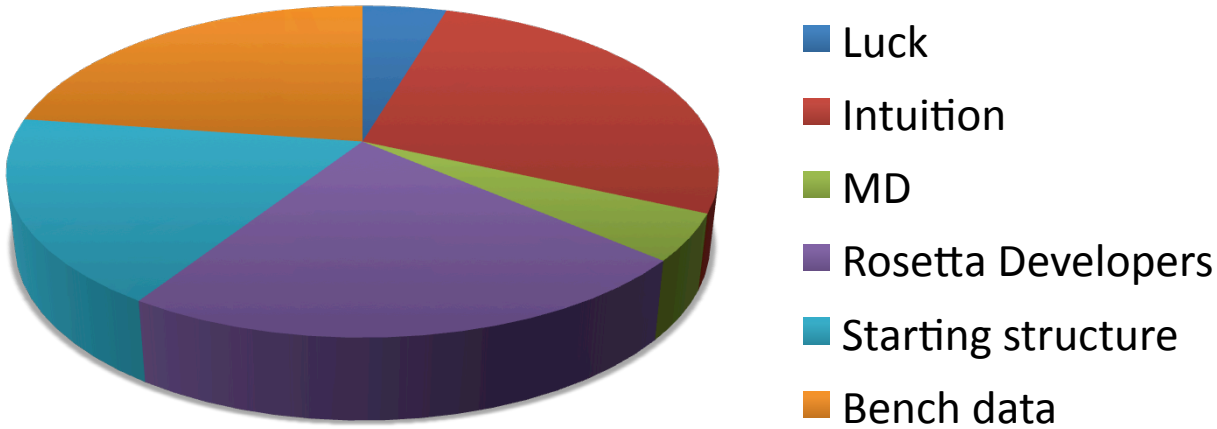
# Anti-EF/calmodulin overlap



# Conclusions

- A little bit of bench data goes a long way
- Constraints (.cst file) not needed
- MD finds lower energy conformation (more native than Rosetta results?)

**What is needed to produce a good, docked solution**



# Future work

Additional EF domain IV and/or anti-EF H3 loop mutations to verify docking results

# Acknowledgements

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