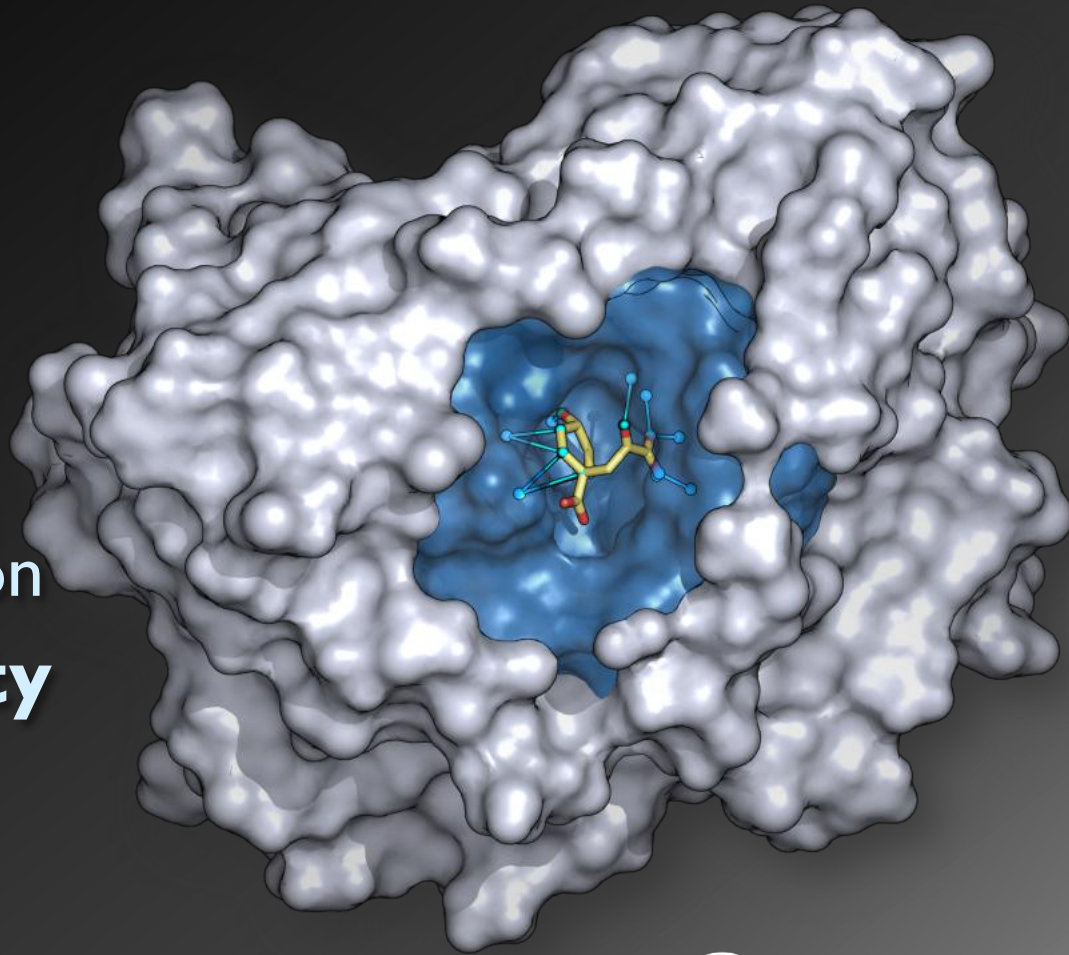




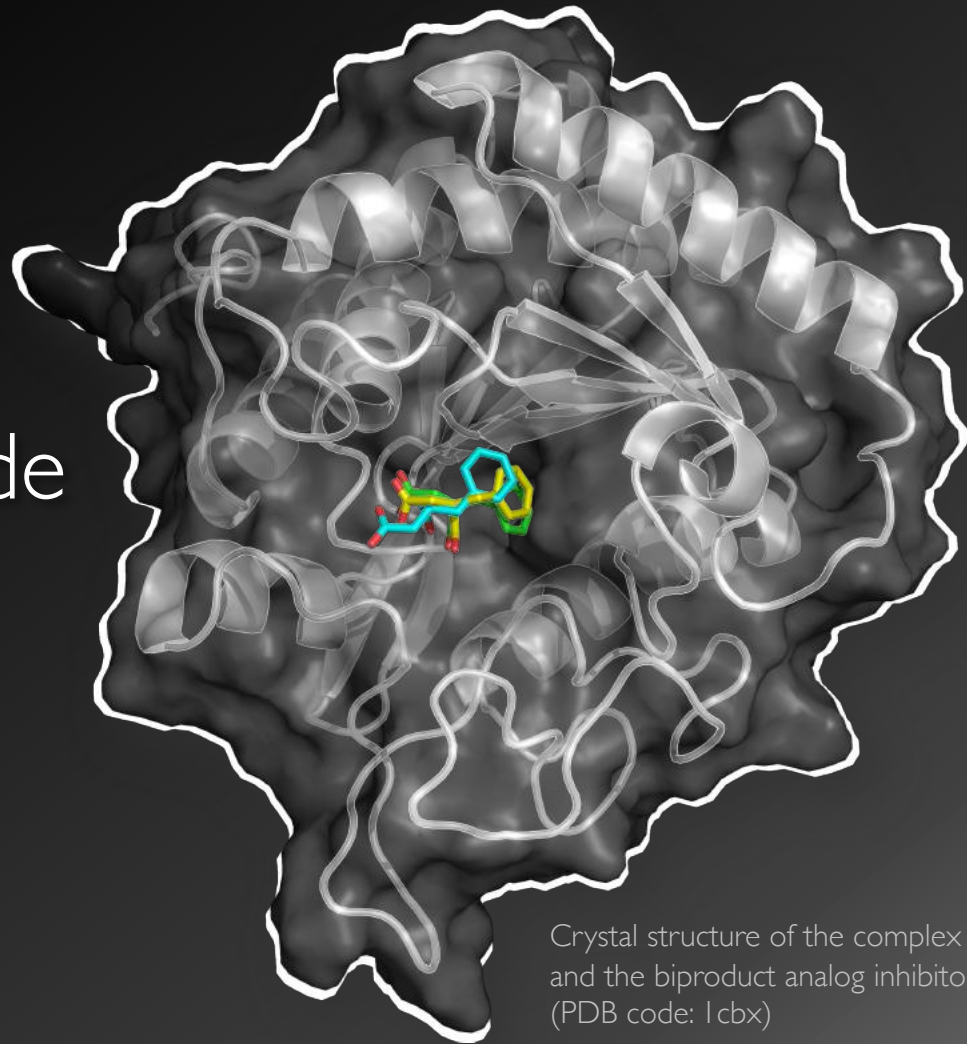
Leslie A. Kuhn Lab
Sebastian Raschka

Detecting the Native Ligand Orientation by **Interfacial Rigidity**



Biochemistry & Molecular Biology
Departmental Retreat October 7, 2016; Okemos Conference Center

Binding Mode Prediction



Crystal structure of the complex between carboxypeptidase A and the biproduct analog inhibitor L-benzylsuccinate (PDB code: 1cbx)

Hypothesis

“bad” docking
→ flexible binding pocket

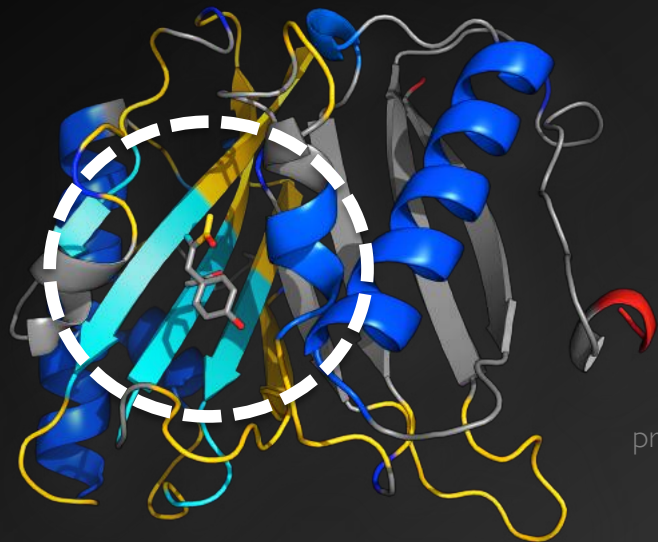


near-native binding mode
→ rigid binding pocket

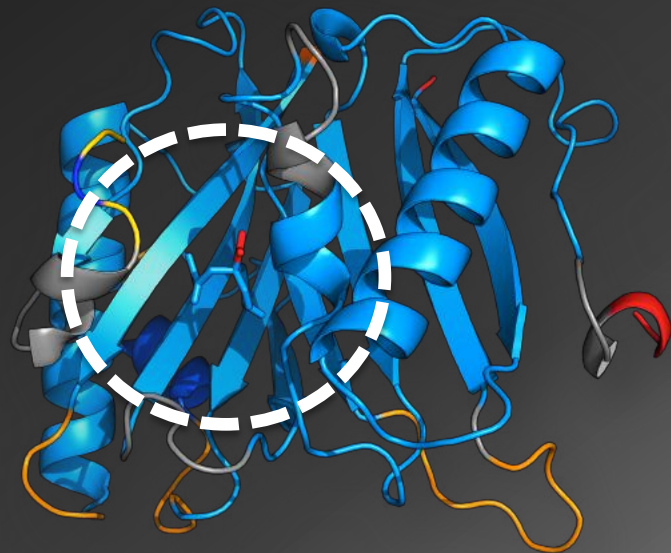
“bad” docking
→ flexible binding pocket



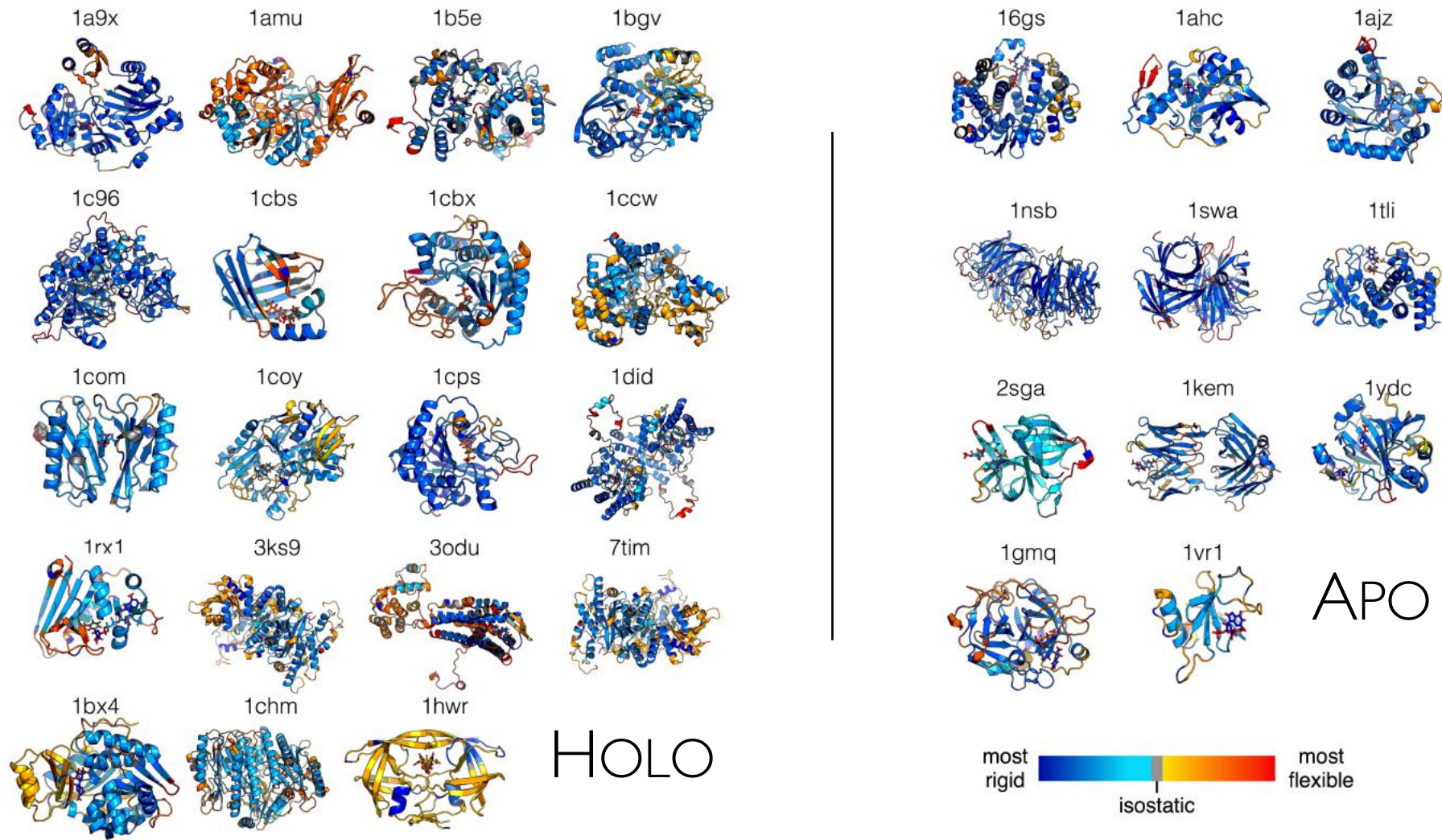
near-native binding mode
→ rigid binding pocket

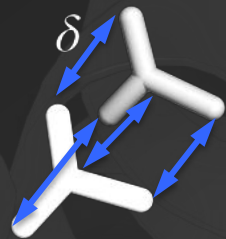


Chorismate mutase and
prephenate (PDB code: 1com)

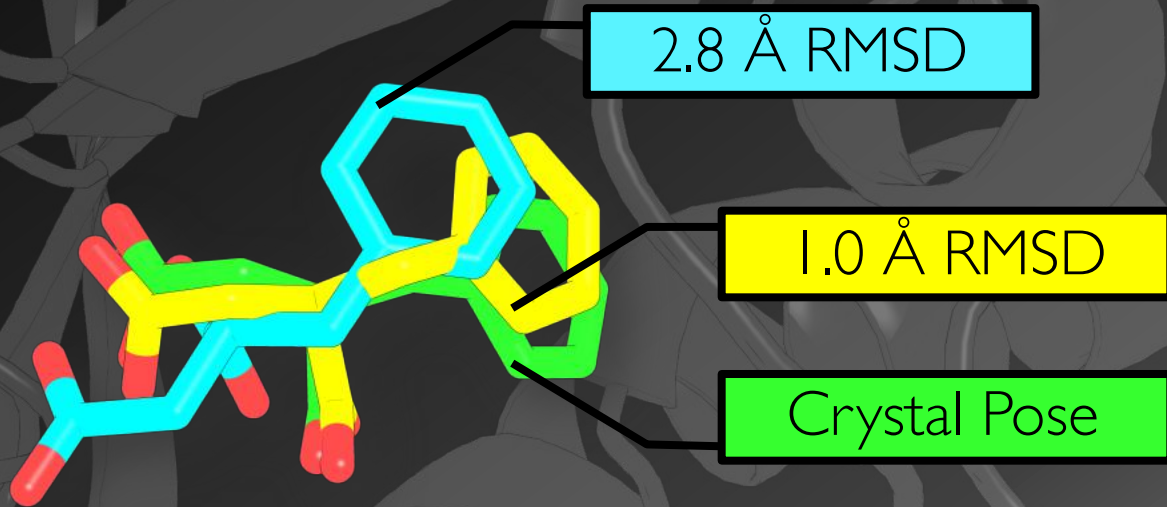


ProFlex: D. J. Jacobs, A. J. Rader, L. A. Kuhn, and M. F. Thorpe (2001)
Protein Flexibility Predictions Using Graph Theory. *Proteins*: 44, 150-165

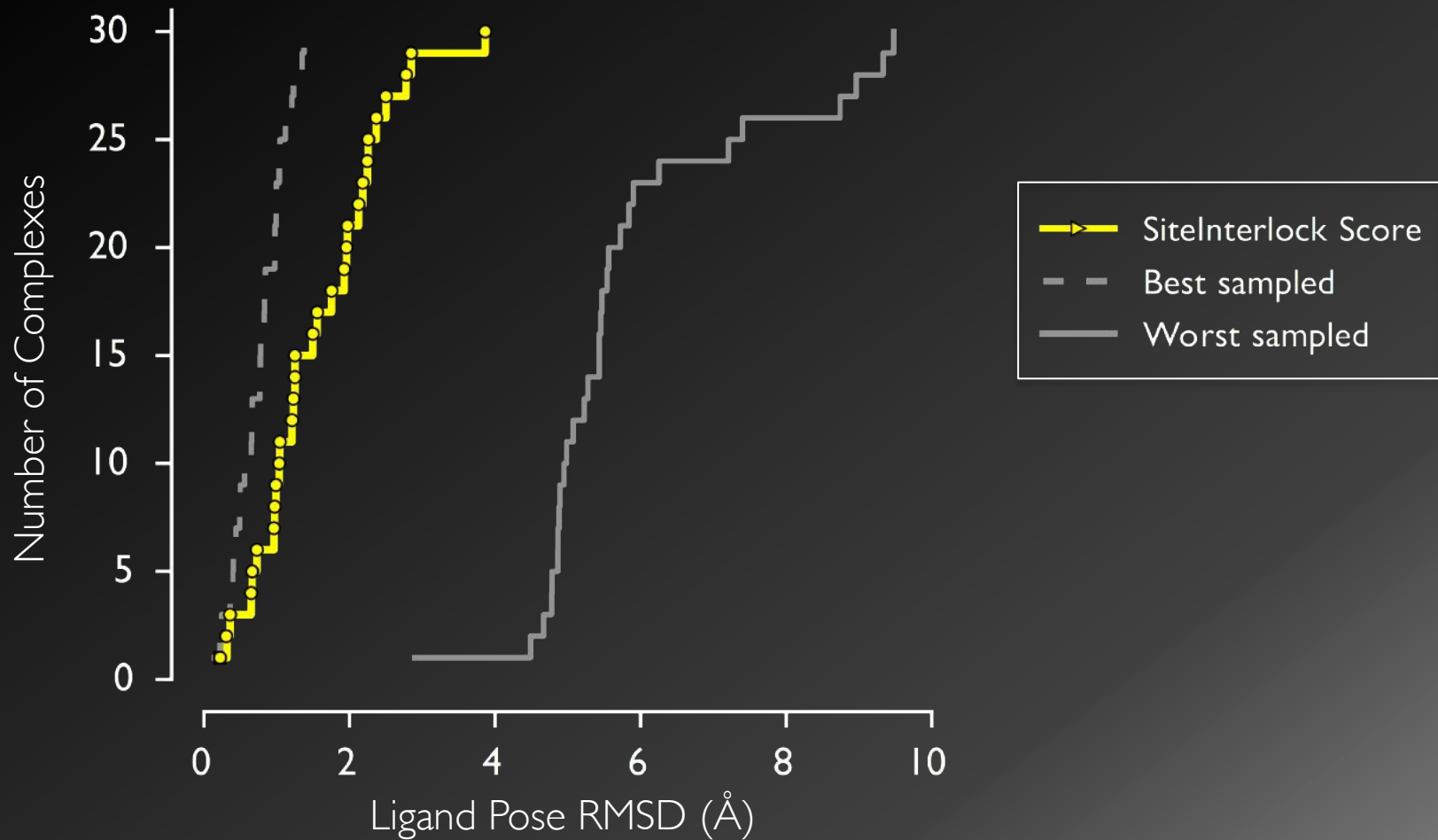


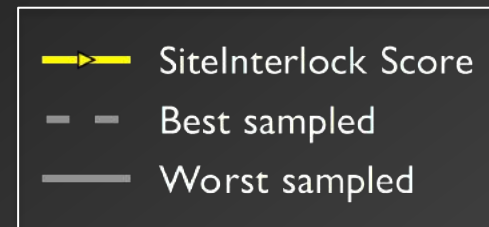
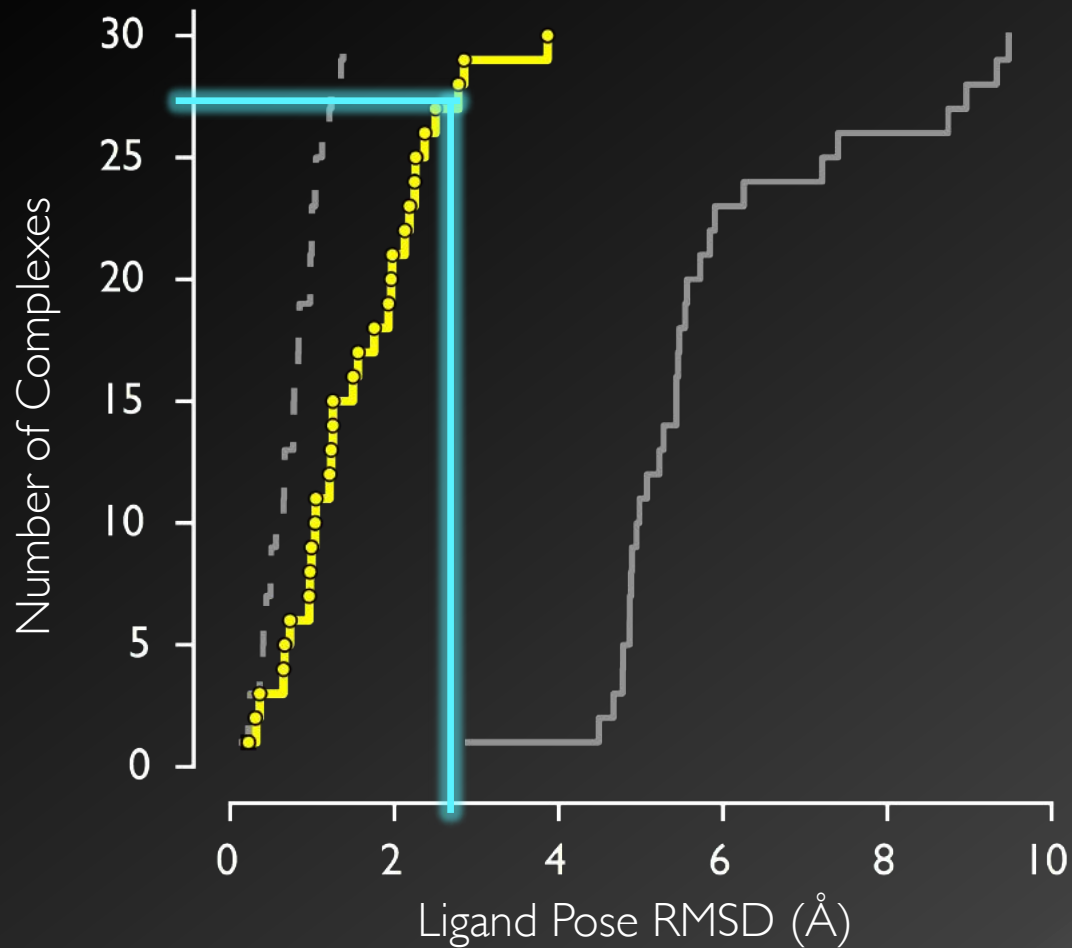


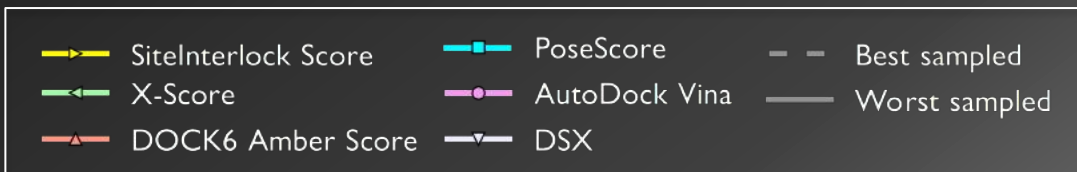
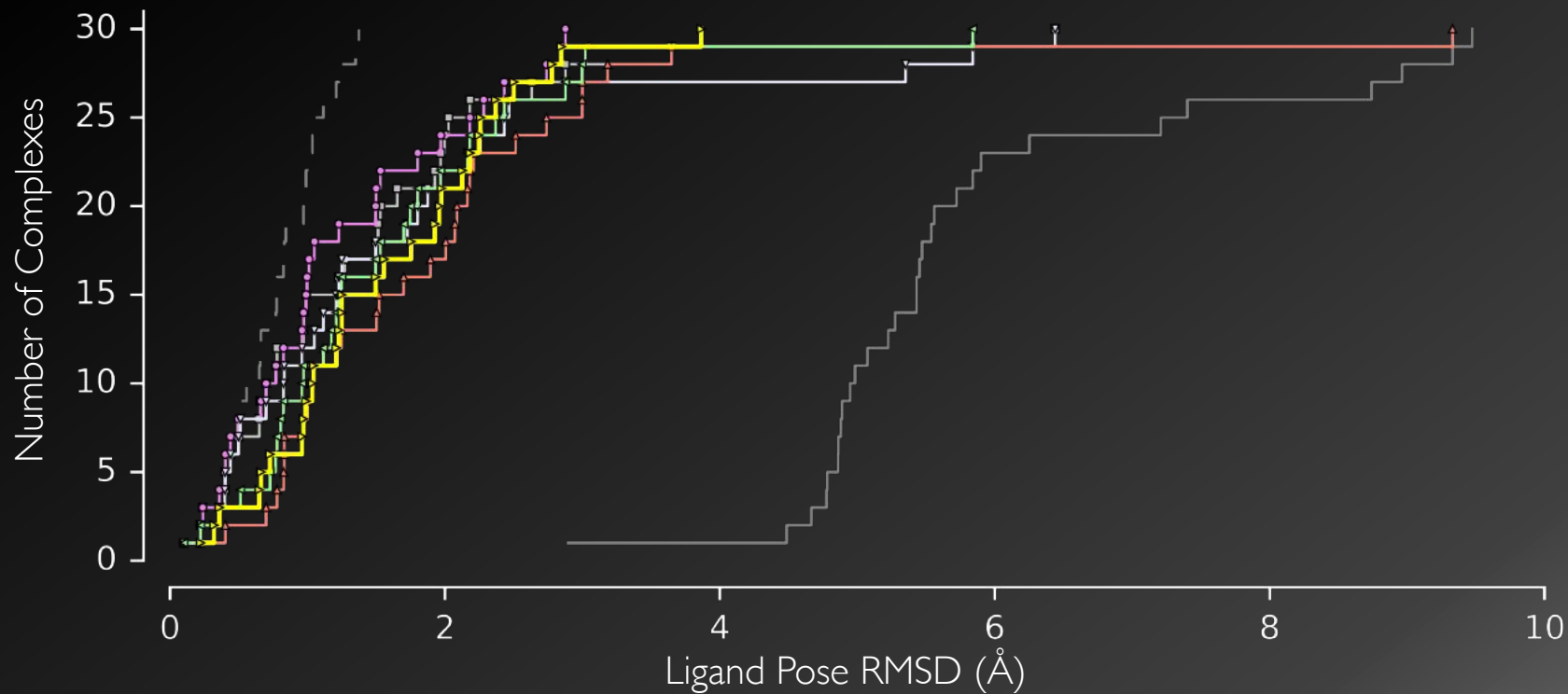
$$RMSD = \sqrt{\frac{1}{N} \sum_{i=1}^N \delta_i^2}$$

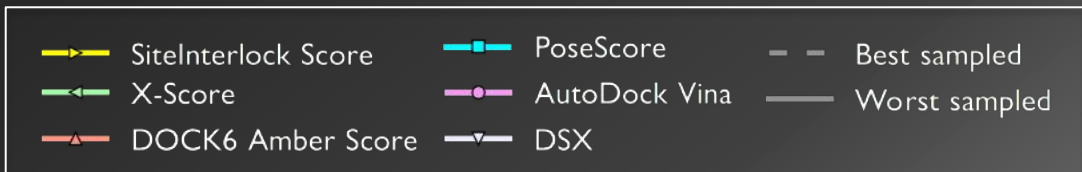
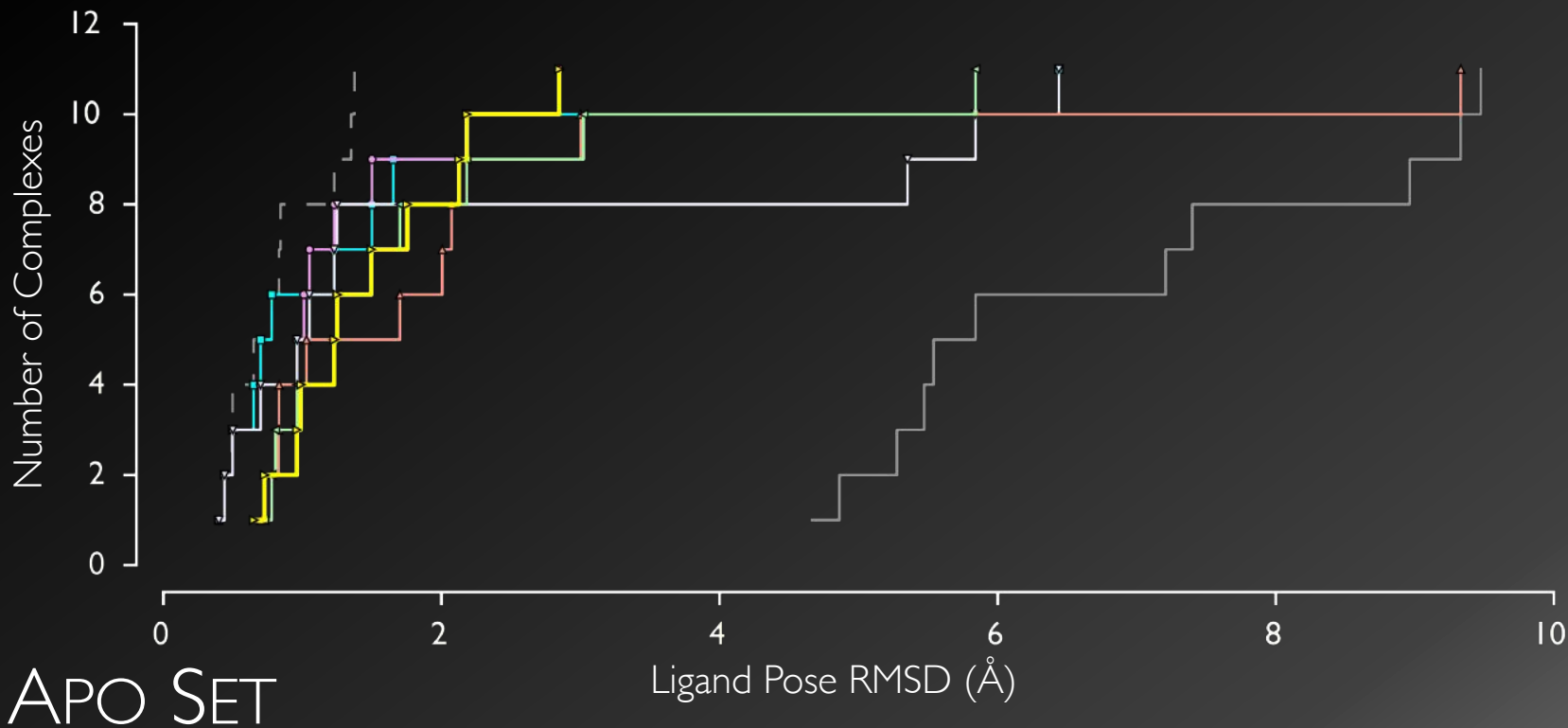


Crystal structure of the complex between carboxypeptidase A and the biproduct analog inhibitor L-benzylsuccinate (PDB code: 1cbx)









1. Competitive scoring function for binding mode prediction / docking
2. Robust, no “bad” predictions
3. New information / signal (cooperativity)

The logo for Site Interlock features the text "Site Interlock" in a sans-serif font. "Site" is in white, and "Interlock" is in light blue. The text is framed by a series of overlapping, curved lines that resemble a stylized wave or a series of interlocking shapes. A single light blue arc is positioned above the "Site" portion, while a series of white arcs are positioned below the "Interlock" portion, creating a sense of depth and structure.

Site Interlock

<http://www.kuhnlab.bmb.msu.edu/software>
<https://psa-lab.github.io/siteinterlock>

Raschka, Bemister-Buffington, and Kuhn 2016.
Proteins. DOI:10.1002/prot.25172. (In press.)



PROTEIN STRUCTURE AND ANALYSIS LAB

<http://www.kuhnlab.bmb.msu.edu>



Dr. Leslie Kuhn
(Lab. Director)

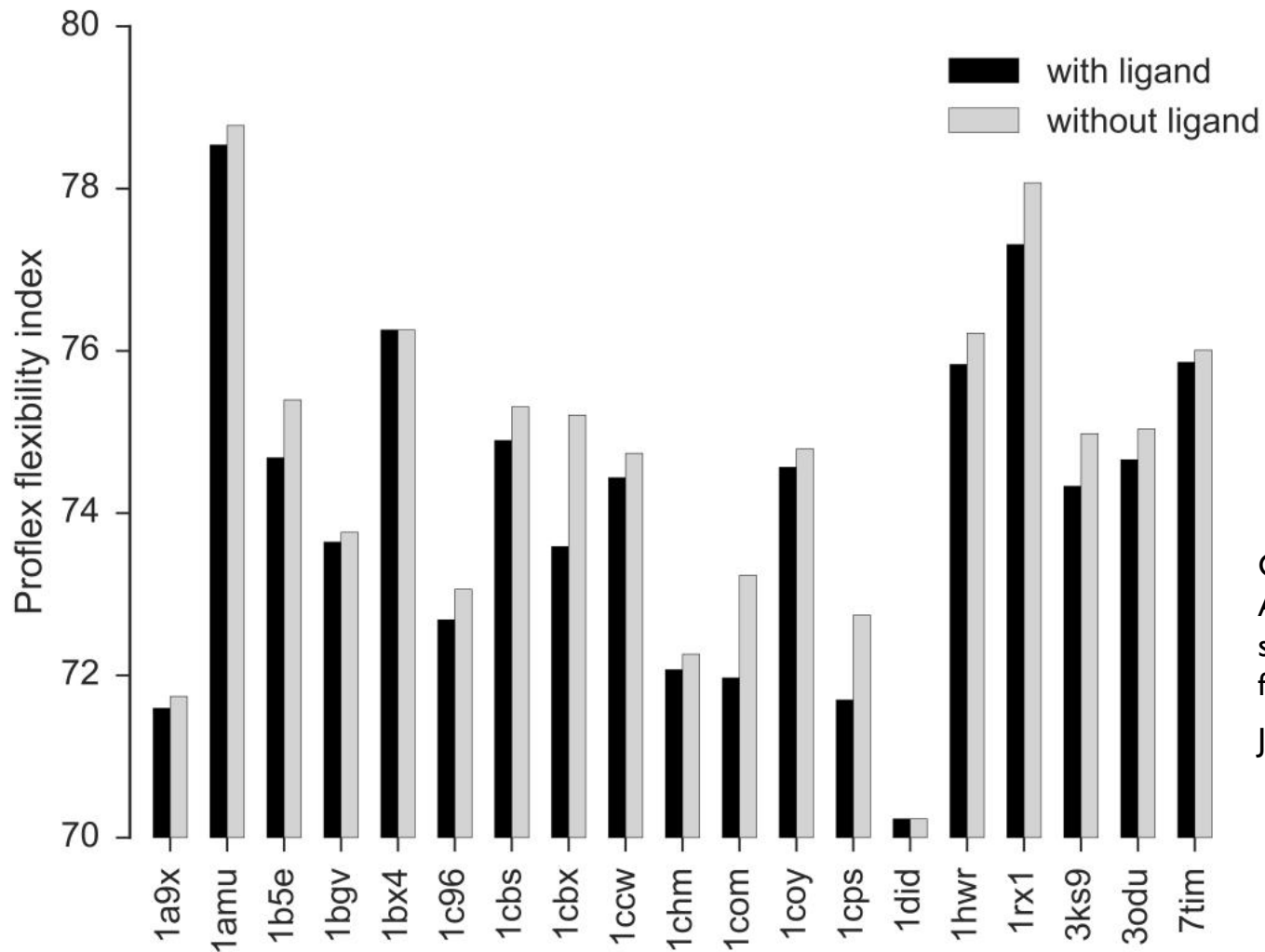


Joseph Bemister-Buffington
(Undergrad. Researcher)



Alex Wolf
(Undergrad. Researcher)

THANK YOU



Chao-Yie Yang R, Wang A, Wang S.
A Systematic analysis of the effect of
small-molecule binding on protein
flexibility of the ligand- binding sites.
J Med Chem 2005;5648–5650.

