Introduction: Protein–protein interactions

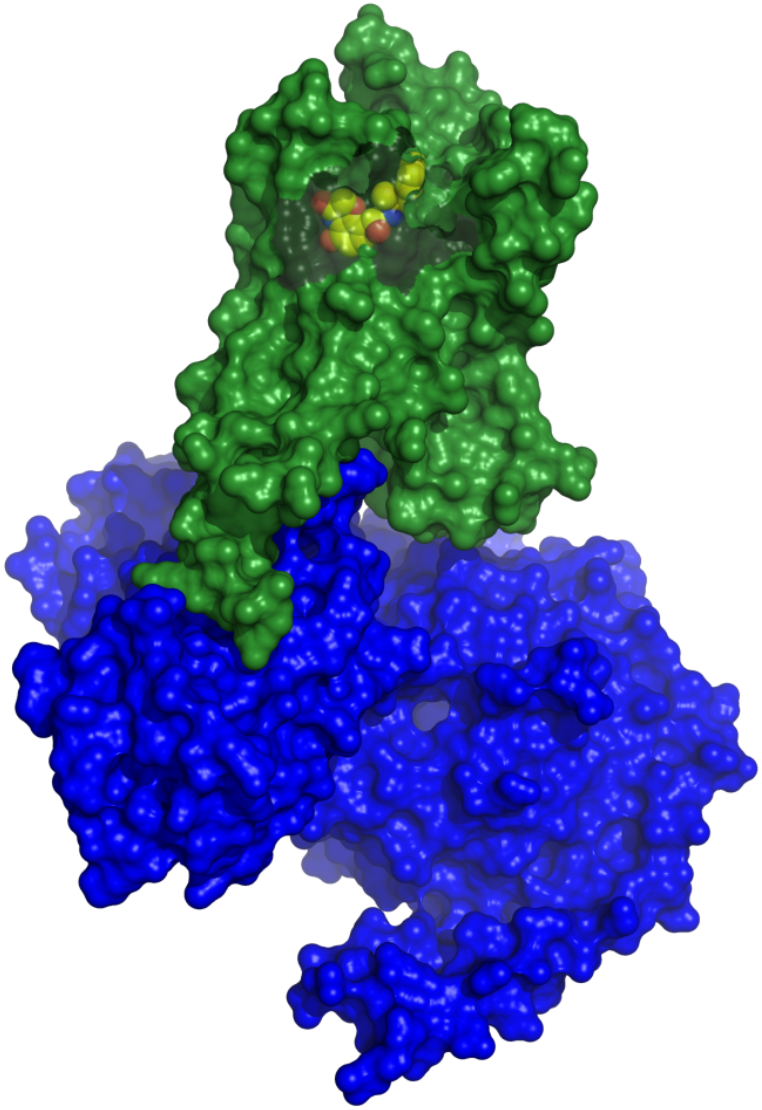
CS/CME/Biophys/BMI 371

Feb. 15, 2017

Ron Dror

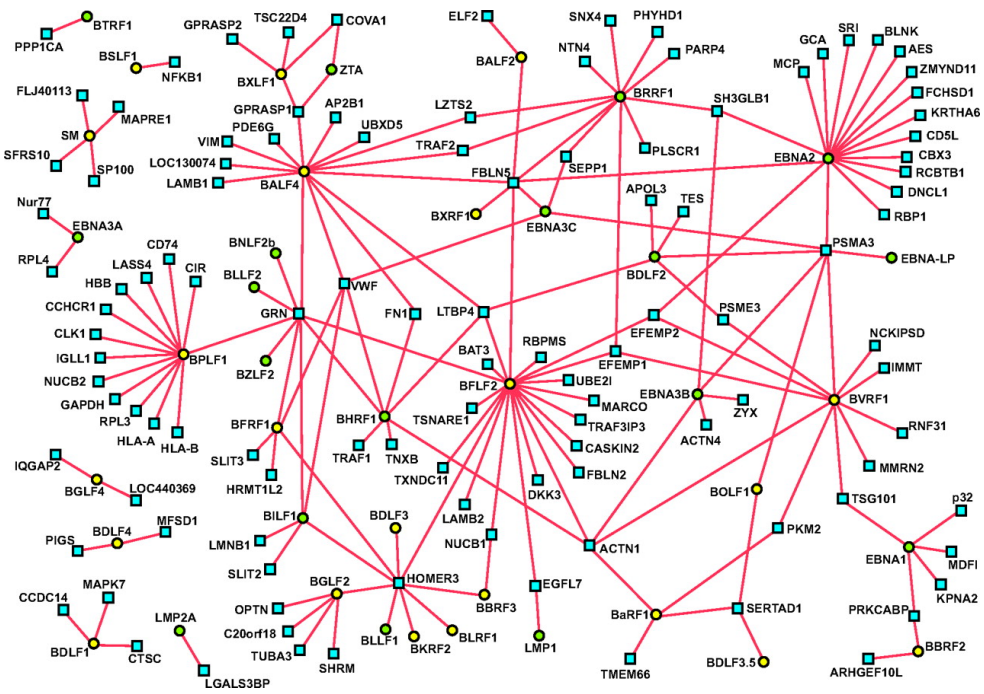
Protein–protein interactions

- Humans have tens of thousands of proteins
- These proteins often interact with one another to form complexes of two or more proteins
  - These interactions are critical to protein function

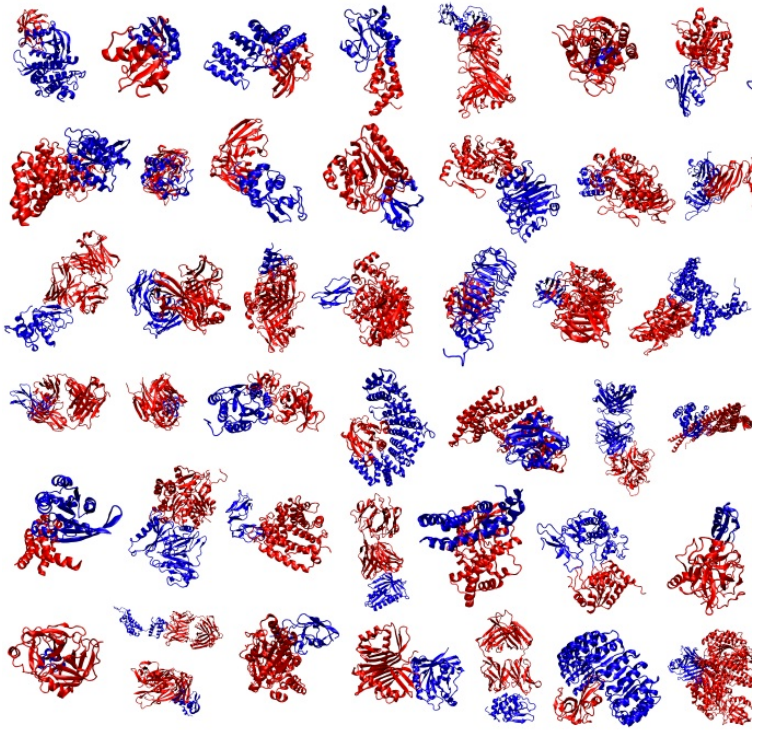


Two challenging computational problems

- These papers address two related problems:
  - Given two (or more) proteins that interact, what is the structure of their complex?
  - Which pairs (or larger sets) of proteins interact to form complexes



Calderwood et al., PNAS 104:7606-11, 2007



http://bmm.crick.ac.uk/~bmmadmin/Affinity/

Why is this challenging?

- Answers are often not available experimentally
  - This is particularly true for structures of protein–protein complexes. There are far more protein–protein complexes than individual proteins, and far fewer solved experimental structures in the Protein Data Bank
- A straight physics-based solution to these problems is difficult
  - Like protein–ligand binding, but worse
- Heuristic protein–protein docking strategies are available, but not particularly reliable

Next Wednesday's papers

- One reports a method that predicts whether or not a pair of proteins interact, taking into account the structures of those proteins and all available structures of protein complexes
- The other uses experimental data, combined with computational analysis, to determine many sets of proteins that form complexes in multiple species
  - They then look at how these protein complexes evolved
  - "Metazoan" = animal
- Both involve machine learning methods

Background information

- Homology modeling = template-based modeling (predicting protein structures “by analogy”)
  - For more detail on homology modeling, see http://web.stanford.edu/class/cs279/lectures/lecture5.pdf