Introduction:
Video games for structure prediction and design

CS/CME/Biophys/BMI 371

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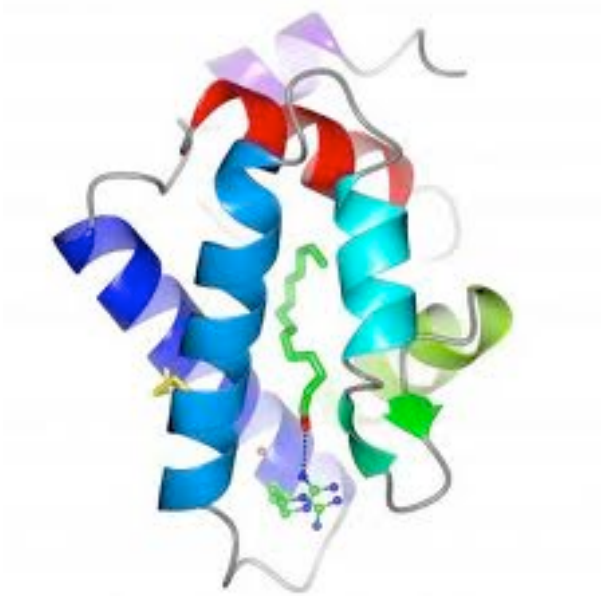
Ron Dror

Protein Structure Prediction

- Goal: given the amino acid sequence of a protein, predict its three-dimensional structure
- Proteins are constantly in motion. We want the *average* structure, which is roughly what's measured experimentally.
- Protein structure prediction is usually done by template-based modeling (also known as homology modeling), which requires a protein with similar sequence whose structure is known
  - If there isn't one, we need to do *ab initio* prediction, which is harder

SVYDAAAQLTADVKKDLRDSW
KVIGSDKKGNGVALMTTLFAD
NQETIGYFKRLGNVSQGMAND
KLRGHSITLMYALQNFIDQLD
NPDSLDLVCS…….

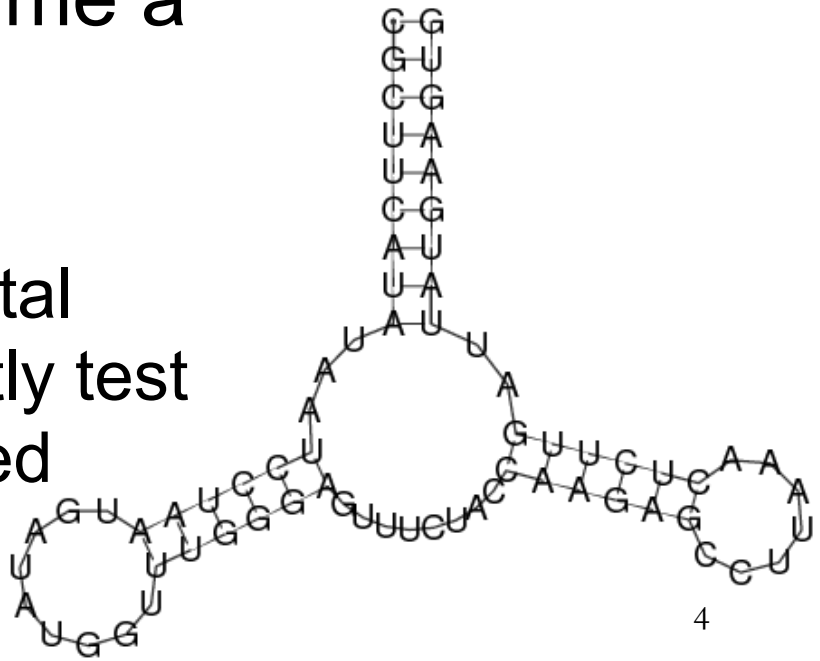


FoldIt: Human-assisted structure prediction

- Rosetta, a popular software package for *ab initio* structure prediction, has two key components:
  - An energy function, which assigns an energy to each possible structure
    - This energy function is inherently an approximation
  - An optimization procedure that searches for global minimum of the energy function
    - Existing optimization procedures are imperfect
- FoldIt lets humans help with the optimization process
  - FoldIt players have discovered clever structural optimization tricks that can be coded on the computer

RNA design

- For RNA, “secondary structure” — that is, how the bases pair — is of primary interest
- Predicting this computationally is usually a tractable problem
- Designing RNAs that will assume a desired secondary structure, however, is still tricky
  - A recently developed experimental procedure allows one to efficiently test whether one achieved the desired structure



http://www.tbi.univie.ac.at/~pkerp/forgi/_images/1y26_ss.png

EteRNA: Human-assisted RNA design

- Goal: design RNA with specified secondary structure
- Players who reach a certain level get to contribute to designs that are tested experimentally on a periodic basis
- Feedback from these experiments helps players improve their designs
- Players have discovered new rules for RNA design

Papers for next Wednesday

- One paper covers FoldIt
- The other two cover EteRNA (developed at Stanford and Carnegie Mellon)

- For background on protein structure prediction, see slides from CS/CME/BioE/Biophys/BMI 279:
  - http://web.stanford.edu/class/cs279/lectures/lecture6.pdf