Introduction: Video games for structure prediction and design

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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 \textit{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: