Protein folding

6.885
L15.2
Nov. 3, 2004

- proteins quickly (milliseconds to seconds) fold to a 3D structure ~very consistently
- behavior of protein strongly influenced by this geometry (and flexibility/rigidity in that state)
- thermodynamics hypothesis: proteins fold to minimum-energy state
  - but no consensus on precise energy function & most accurate functions are very hard to minimize

Motivation:

- protein misfolding is cause of several diseases:
  - Alzheimer's
  - mad cow disease
  - cystic fibrosis
  - some forms of cancer
- understanding of protein-folding process may help understand these diseases & help cure them
- more generally, want to design synthetic proteins for drugs to combat unwanted proteins e.g. HIV

Two aspects to folding:

1. mechanics
   - close connection to linkages
   - leads to many interesting problems, only some of which are solved
   - "relatively tractable"
2. energetics
   - folding + optimization (but is it really global?)
   - many possible models ~ fewer clear problems
   - even simple models are largely intractable
   - still some interesting specific unsolved problems