BINF 731

Protein Structure Analysis

Iosif Vaisman

2004

Protein Modeling Methods

- ***Ab initio* methods**
- **Energy-based methods**
- **Knowledge-based methods**

Protein Modeling Methods

- ***Ab initio* methods:**
  solution of a protein folding problem
  search in conformational space
- **Energy-based methods:**
  energy minimization
  molecular simulation
- **Knowledge-based methods:**
  homology modeling
  fold recogniion

Ab initio Methods

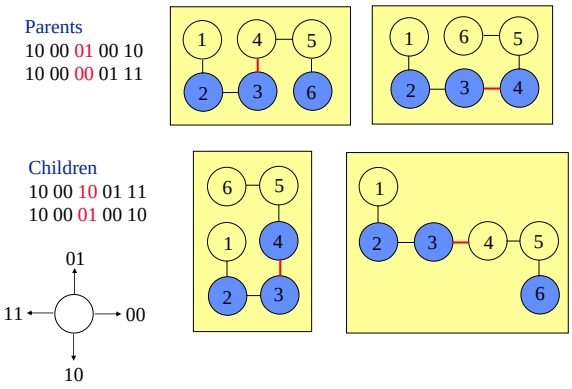
Simplified models
- simplified alphabet (HP)
- simplified representation (lattice)

Build-up techniques

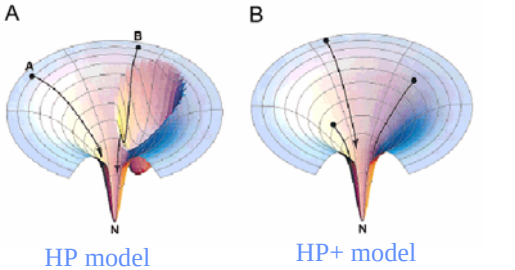
Deterministic methods
- quantum mechanics
- diffusion equations
- DFT

Stochastic searches
- Monte Carlo
- genetic algorithms

Genetic Algorithms Applications



HP Lattice Models



HP model

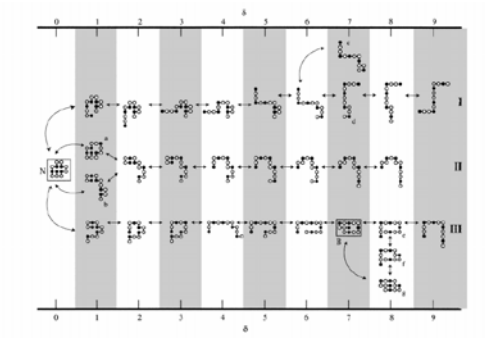
HH	ε < 0
HP	ε = 0
PP	ε = 0

HP+ model

HH	ε < 0
HP	ε = 0
PP	ε = 0
NNC	ε > 0

Chan & Dill, 1998

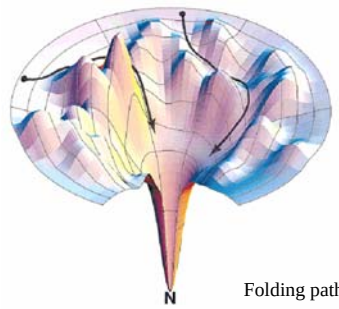
HP Lattice Models



Folding pathways

Chan & Dill, 1998

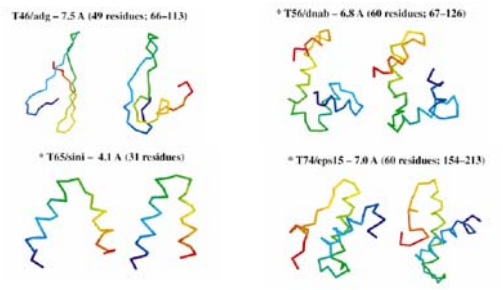
HP Lattice Models



Folding pathways

Chan & Dill, 1998

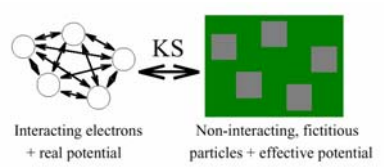
Hierarchical *ab initio* prediction



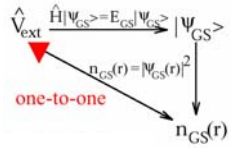
Lattice models
Knowledge-based scoring functions

Samudrala et al., 1999

Density Functional Theory

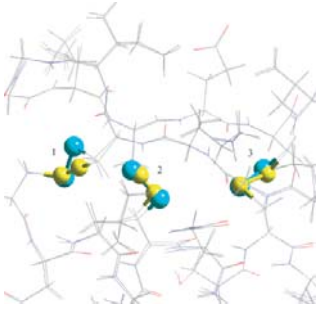


HK theorem: Each local one-particle potential corresponds to exactly one ground state density.



Adopted fromWilfried Aulbur, OSU

Density Functional Theory



DFT optimization of NMR structure (1PNH)

Andreoni et al., 1999

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Knowledge

Knowledge is a.pattern that exceeds certain threshold of interestingness.

Factors that contribute to interestingness:

- coverage
- confidence
- statistical significance
- simplicity
- unexpectedness
- actionability

Knowledge-based methods

Finding patterns in known structures

Deriving rules (usually in the form of PMF)

Applying the rules