20.1: Models for Simulating Folding

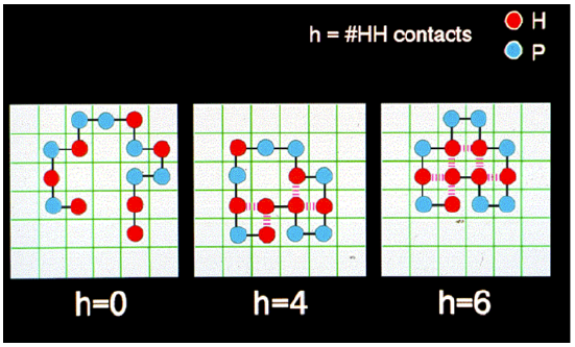
Our study of folding mechanism and the statistical mechanical relationship between structure and stability have been guided by models. Of these, simple reductionist models guided the conceptual development from the statistical mechanics side, since full atom simulations were initially intractable. We will focus on the simple models.

- Reductionist Mod
  - Lattice Models
  - Gō Models
  - Coarse Grained
- Atomistic
  - Force fields

Increasing level of molecular detail

HP Model[1]

- Chain of beads. Self-avoiding walk on square lattice.
- 2 types of beads: Hydrophobic (H) and polar (P).
- H-H contacts are energetically favorable to H-P contacts. more H → collapse to compact state, but many collapsed structures more P → well-solvated, doesn't fold ~1:1 H:P optimal
- Can be used for folding mechanism using Monte Carlo.



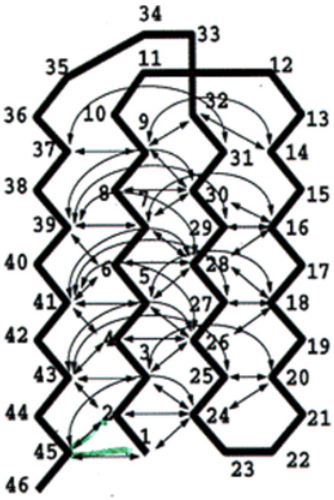
Coarse-Grained Models[2]

Hierarchy of various models that reduce protein structure to a set of interacting beads.

Gō Models[3]

Gō models and Gō-like models refer to a class of coarse-grained models in which formation of structure is driven by a minimalist interaction potential that drives the system to its native structure. The folded state must be known

- Coarse grained
  - Original: one bead per AA
  - "Off-lattice model"
- Native-state biasing potential
  - Multiple forces in single interaction potential
  - Need to know folded structure
  - Increased simulation speed
  - Doesn't do well metastable intermediates or non-native contacts



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2. V. Tozzini, Coarse-grained models for proteins, Curr. Opin. Struct. Biol. 15, 144-150 (2005).
3. Y. Ueda, H. Taketomi and N. Gō, Studies on protein folding, unfolding, and fluctuations by computer simulation. II. A. Three-dimensional lattice model of lysozyme, Biopolymers 17, 1531-1548 (1978).