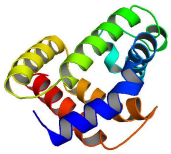
Protein Structure Determination II



Scott McAllister
Princeton University
CS597A, Fall 2005

Outline

- Notable Methods
- ASTRO-FOLD Framework
  - α-helix Prediction
  - β-sheet Prediction
  - Interhelical contact prediction
  - Derivation of Restraints
  - Generation of additional distance bounds
  - Tertiary Structure Prediction
- Results
- Discussion

Protein Structure Prediction

Amino acid sequence [PDB: 1q4sA]

MHRTSNGSHATGGNLPDVASHYPVAYEQTLDGTVGFVIDEMTPERATASVEVTDTLRQRWGLVHGGAYCALAEMLA
TEATVAVVHEKGMMAVGQSNHTSFRRPVKEGHVRAEAVRIHAGSTTWFWDVSLRDDAGRLCAVSSMSIAVRPRRD

Helical structure

MHRTSNGSHATGGNLPDVASHYPVAYEQTLDGTVGFVIDEMTPERATASVEVTDTLRQRWGLVHGGAYCALAEMLA
TEATVAVVHEKGMMAVGQSNHTSFRRPVKEGHVRAEAVRIHAGSTTWFWDVSLRDDAGRLCAVSSMSIAVRPRRD

Beta strand and sheet structure

MHRTSNGSHATGGNLPDVASHYPVAYEQTLDGTVGFVIDEMTPERATASVEVTDTLRQRWGLVHGGAYCALAEMLA
TEATVAVVHEKGMMAVGQSNHTSFRRPVKEGHVRAEAVRIHAGSTTWFWDVSLRDDAGRLCAVSSMSIAVRPRRD

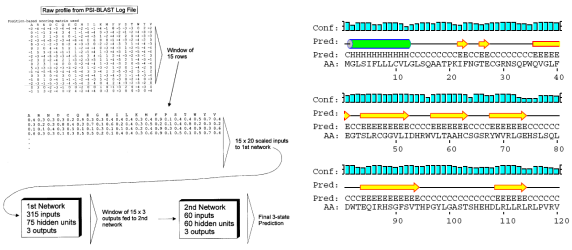
3D Protein Structure

Notable Methods – PSI-PRED

- Prediction of Secondary Structure
- 3 stages:
  - Generation of a sequence profile
    - PSI-BLAST on non-redundant database
    - Creates PSSM for later input
  - Prediction of initial secondary structure
    - Neural network (Feed forward, back propagation)
  - Filtering of the predicted structure
- Web server: http://bioinf.cs.ucl.ac.uk/psipred

Jones, DT. *J. Mol. Biol.* (1999)

Notable Methods – PSI-PRED



Jones, DT. *J. Mol. Biol.* (1999)

Notable Methods - RAPTOR

- Fold recognition method as optimization problem
- Scoring function that accounts for
  - mutation
  - environment
  - gaps
  - secondary structure
  - pairwise interactions

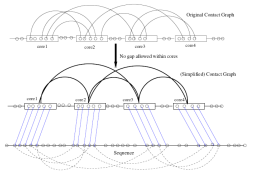


Fig. 1. Template contact graph and an example of alignment between a template and a sequence. A small circle represents a residue. A solid arc in the original contact graph represents an interaction between the two connected residues. A dashed arc means that if two query sequence residues are aligned to two interacting template residues, then the interaction score of these two query sequence residues must be counted in the energy function. The interaction score between two segments of the query sequence is the sum of the interaction scores of two query sequence residues which are aligned by two interacted template residues.

$$\min W_m E_m + W_s E_s + W_p E_p + W_g E_g + W_{ss} E_{ss},$$

Xu, J and M. Li. *J. Bioinf Comput Biol.* (2003)

Notable Methods – Robetta

- Combines template-based and ab initio approach
  - Uses template if available, otherwise starts with ab initio
- Also includes methods to detect domains and model loops

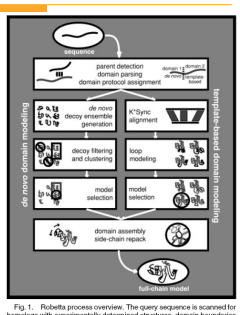


Fig. 1. Robetta process overview. The query sequence is scanned for homologs with experimentally determined structures, domain boundaries are determined, and each domain is modeled separately using either the *de novo* or template-based protocols, assembled into a full-chain model, and side-chains are repacked to produce a full-chain all-atom complete model.

D. Chivian et al. *Proteins*. (2003)

Notable Methods – Skolnick

- Combine aspects of comparative modeling/fold recognition/ab initio
- Apply clustering algorithm to select among conformers

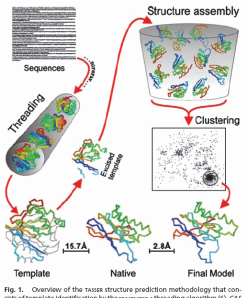
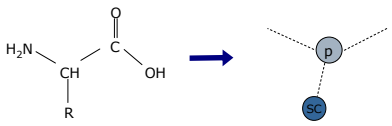


Fig. 1. Overview of the TASSER structure prediction methodology that consists of template identification by the PROSPECTOR_3 threading algorithm (6), CAS fragment assembly, and fold selection by SPICKER clustering (18). The entire process for 1AYD is shown as an example.

Zhang, Y. and J. Skolnick. *PNAS*. (2004)

Notable Methods - UNRES

- United Residue approach
- Represent each protein as unified peptide group and unified side chain



- Minimize with this coarse force field, then refine a detailed atomistic force field

Liwo, et al. *J. Comput Chem.* (1997a,b)

Notable Methods – PREDICT

- Method for the structure prediction of membrane proteins, especially GPCRs
  - Does NOT rely on homology to rhodopsin
- Approach
  - Generation of a large number of protein "decoys"
  - Simultaneous optimization and scoring of decoys
    - Optimization includes helix orientations, helix vertical alignments, helix positions, π-stacking of aromatic residues, helical tilts

Shacham, S. *Proteins*. (2004)

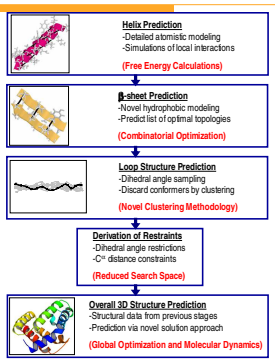
Notable Methods – Available Servers

- 3D Jury (consensus)
  - http://bioinfo.pl
- 3D-pssm/phyre
  - http://www.sbg.bio.ic.ac.uk/~3dpssm/
- 123D+
  - http://123d.ncfcrf.gov/run123D+.html
- FFAS03
  - http://ffas.ljcrf.edu/ffas-cgi/cgi/ffas.pl
- FORESST
  - http://abs.cit.nih.gov/foresst2/

Notable Methods – Available Servers

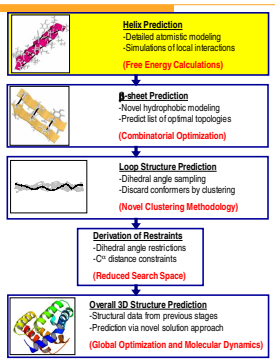
- 3GenesilicoD Jury (consensus)
  - http://genesilico.pl/meta/
- PredictProtein
  - http://cubic.bioc.columbia.edu/predictprotein
- mGenTHREADER/PSIPRED
  - http://bioinf.cs.ucl.ac.uk/psipred/psiform.html
- Robetta
  - http://robetta.bakerlab.org

ASTRO-FOLD



Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

ASTRO-FOLD



Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

Helix Formation

- Physical characteristics
  - Well-defined backbone and hydrogen bonding patterns
- Physical understanding
  - Local forces: Hierarchical folding
  - Non-local forces: Hydrophobic collapse
- Experimental Evidence
  - Helix formation occurs rapidly
  - Sequence is sufficient to identify initiation/termination

Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2002)

Helix Prediction – Key Ideas

Overlapping oligopeptides

> Decompose polypeptide to identify local sites of helix formation and termination

Ensemble of low energy states

> Calculate properties of proteins using data from many low energy states rather than a single state

Free energy calculations Klepeis & Floudas 2000

> Model proteins using detailed energy calculations including entropic and solvation contributions

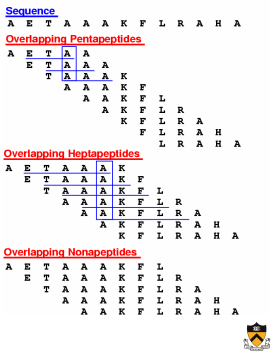
Deterministic global optimization Floudas 2000

> Predict low energy states using powerful global optimization approaches such as aBB

Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2002)

Dividing the problem

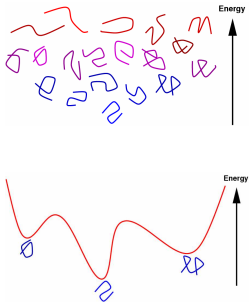
- Decompose sequence into smaller, overlapping oligopeptides
- Captures local interactions
- Free energy calculations on oligopeptides combined to yield overall prediction



Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2002)

Generating an ensemble

- Create low energy states and the global minimum state
- Formulated as a nonconvex optimization problem
  - requires global optimization techniques



Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2002)

Overall Gibbs Free Energy

- **Potential** (Scheraga & coworkers) — F_{vac} —
- **Entropic** — TS_{vac} +
- **Cavity** (Honig & coworkers 1988, 1993, 1995) — F_{cavity} +
- **Polarization** (Honig & coworkers 1988, 1993, 1995) — $F_{solvation}$ +
- **Ionization** (Honig & coworkers 1988, 1993, 1995) — $F_{ionization}$

Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2002)

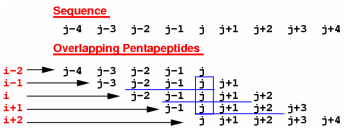
Helix Formation Probability

- Calculate probability of conformer i from free energy

$$p_i = \frac{\exp[-\beta(F_o - F_i)]}{\sum_j \exp[-\beta(F_o - F_j)]}$$

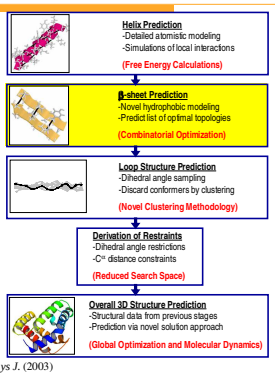
- Use to calculate probability of cluster formation for particular oligopeptide

$$p_{\mathrm{AAA}} = \sum_{i \in \mathrm{AAA}} p_i$$



Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2002)

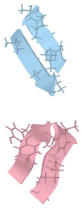
ASTRO-FOLD



Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

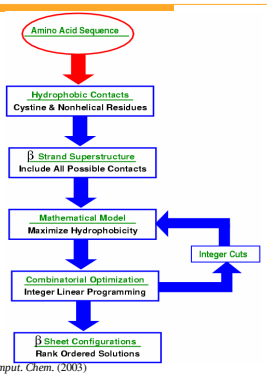
β-sheet Formation

- Major challenge for protein structure prediction
  - β-strand location not accurate
  - Topology prediction not reliable
- Physical understanding
  - Local forces not as important
  - Non-local forces (hydrophobic collapse) dominate
- Experimental evidence
  - Hydrophobic collapse proceeds rapidly



Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2003)

β-sheet Prediction Flowchart



Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2003)

β-sheet Prediction

- Residue-based aspect
  - Identify set of residues i, and the associated hydrophobicity, H_i
  - Binary variables introduced for residue-residue contact

- Strand-based aspect
  - Identify set of strands si, and the associated weight S_{si}
  - Binary variables introduced for strand-strand contacts

Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2003)

B-sheet Formulation: Key Concepts

Binary variables

0-1 variables are used to characterize residue-to-residue and strand-to-strand contacts

Linear objective function

Objective is to maximize the hydrophobic potential as controlled by the binary variables

Linear constraints

Constraints account for different combinations of residue and strand contacts (e.g., parallel/antiparallel)

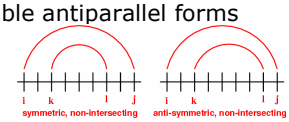
Integer cuts

Iterative addition of these constraints allow for the generation of a ranked list of optimal solutions

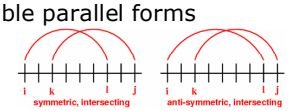
Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2003)

β-sheet Constraints

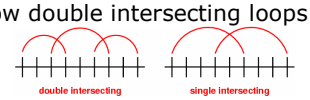
- Allowable antiparallel forms



- Allowable parallel forms



- Disallow double intersecting loops



Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2003)

β-sheet Objective Function

- Maximizing hydrophobic potential

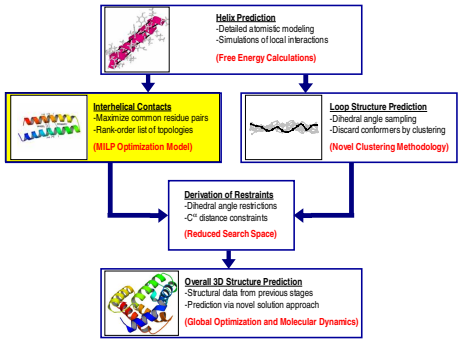
$$\max \quad \sum_i \sum_{j,P(i)+2<P(j)} (H_i + H_j + H_{ij}^{\text{add}}) y_{ij} + \sum_{si} \sum_{sj,Q(si)<Q(sj)} (S_{si} + S_{sj}) w_{si,sj}$$

$$y_{ij} = \begin{cases} 1 & \text{if } i,j \text{ form contact} \\ 0 & \text{if } i,j \text{ do not form contact} \end{cases} \quad \forall i < j$$

$$w_{si,sj} = \begin{cases} 1 & \text{if } si,sj \text{ form contact} \\ 0 & \text{if } si,sj \text{ do not form contact} \end{cases} \quad \forall si < sj$$

Klepeis, JL and Floudas, CA. *J. Comput. Chem.* (2003)

ASTRO-FOLD for α-helical Bundles



McAllister, SR and Floudas, CA. *Proceedings, BIOMAT Conference* (2005).

Dataset Selection

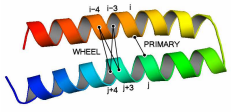
- Protein Sources
  - 229 PDBSelect25[1] database
  - 62 CATH[2] database
  - 20 Zhang et al.[3]
  - 7 Huang et al.[4]
- Restrictions
  - No β-sheets, at least 2 α-helices
  - No highly similar sequences
- Dataset
  - 318 proteins in the database set

[1]Hobohm, U. and C.Sander. *Prot Sci* **3** (1994) 522
[2]Orengo, C.A. et al. *Structure* 5 (1997) 1093.
[3]Zhang, C. et al. *PNAS* 99 (2002) 3581.
[4]Huang, E.S. et al. *J Mol Biol* 290 (1999) 267.

McAllister, SR, et al. (submitted 2005)

Probability Development

- Contact Types
  - PRIMARY contact
    - Minimum distance hydrophobic contact between 4.0 Å and 10.0 Å
  - WHEEL contact
    - Only WHEEL position hydrophobic contacts between 4.0 Å and 12.0 Å
- Classified as parallel or antiparallel contacts



McAllister, SR, et al. (submitted 2005)

Model Overview

- Formulation: Maximize interhelical residue-residue contact probabilities
  - Binary variable $yh^{A}_{m,n}$ indicates antiparallel helical contact
  - Binary variable $w^{m,n}_{i,j}$ indicates residue contact
- Goal: Produce a rank-ordered list of the most likely helical contacts
  - Contacts used to restrict conformational space explored during protein tertiary structure prediction

McAllister, SR, et al. (submitted 2005)

Pairwise Model Objective

- Level 1 Objective
  - Maximize probability of pairwise residue-residue contacts

$$\max \quad \sum_m \sum_n y^a_{mn} \cdot \sum_i \sum_j w^{mn}_{ij} \cdot p^a_{ij;mn} + \sum_m \sum_n y^p_{mn} \cdot \sum_i \sum_j w^{mn}_{ij} \cdot p^p_{ij;mn}$$

$$y^a_{mn}, y^p_{mn}, w^{mn}_{ij} = \{0,1\}$$

McAllister, SR, et al. (submitted 2005)

Pairwise Model Constraints

- Level 1 Constraints
  - At most one contact per position

$$\sum_{j;j>i} w_{ij} + \sum_{j;j<i} w_{ij} \leq 1$$

  - Helix-helix interaction direction

$$y^a_{mn} + y^p_{mn} \leq 1 \quad \forall(m,n)$$

  - Linking interaction variables

$$w^{mn}_{ij} \leq y^a_{mn} + y^p_{mn}$$

$$y^a_{mn} + y^p_{mn} - \sum_i \sum_j w^{mn}_{ij} \leq 0$$

McAllister, SR, et al. (submitted 2005)

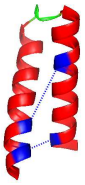
Pairwise Model Constraints

- Level 1 Constraints
  - Limit helical kinks

$$w^{mn}_{ij} + w^{mn}_{i'j'} \leq 1$$

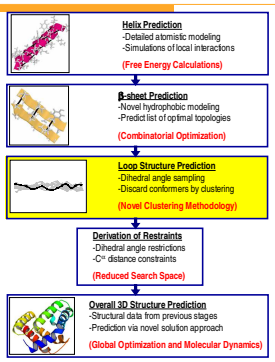
$$\forall(i,i',j,j'): \quad |\text{diff}(i,i')| - |\text{diff}(j,j')| \leq 2$$

$$\text{or either } |\text{diff}(i,i')| \leq 5 \text{ or } |\text{diff}(j,j')| \leq 5$$



McAllister, SR, et al. (submitted 2005)

ASTRO-FOLD



Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

Loop Prediction - Methodology

Create ensemble by dihedral angle sampling

- extracted p(φ,ψ) from ~2500 loops
- sampled p(φ,ψ) at 5ºx5º resolution
- created ensembles of 2000 conformers for each loop

ARG PRO …

Structure optimization with first principles force field

- Dunbrack rotamer library
- ECEPP/3 force field for structure optimization

Clustering to identify conformers that are close to native

Mönnigmann, M. and Floudas, CA. *Proteins.* (2005)

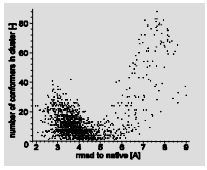
Loop Prediction – New Use of Clustering

- Clustering has been used before to
  - Group conformers
  - Select conformers that represent groups
- New use of clustering
  - Discard conformers that are far from native
- First steps of approach
  - Choose RMSD threshold t
  - Calculate pairwise RMSD values for the ensemble
  - For each conformer, record number of conformers with RMSD $\leq t$

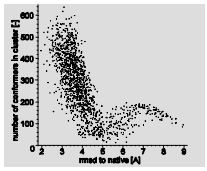
Mönnigmann, M. and Floudas, CA. *Proteins.* (2005)

Loop Prediction – Clustering Example

- threshold t= 3.0Å
- large clusters for small RMSDs unfortunately also for large RMSDs
- not always advisable to consider centroid of largest cluster



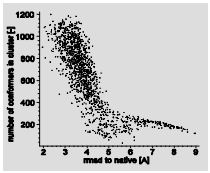
- threshold t= 3.5Å
- increasing threshold shows that clusters with large RMSDs are small basins only
- large clusters with small RMSDs survive



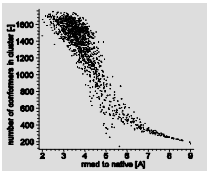
Mönnigmann, M. and Floudas, CA. *Proteins.* (2005)

Loop Prediction – Clustering Example

- threshold t= 4.0Å
- for sufficiently large threshold distribution is monotonous
- tail with large RMSDs becomes apparent



- threshold t= 4.5Å
- distribution more conservative the larger threshold
- for sufficiently large threshold clusters of conformers with large RMSDs can be discarded



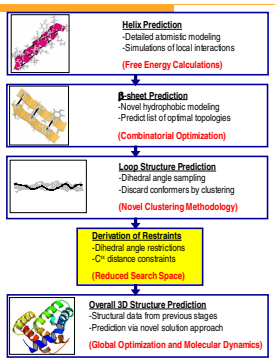
Mönnigmann, M. and Floudas, CA. *Proteins.* (2005)

Loop Prediction – Clustering Algorithm

1. Choose threshold t, choose critical cluster size N_{crit}
2. Calculate cluster sizes N_i for all conformers in ensemble
3. If $N_i > N_{crit}$ for all i, stop
4. Discard conformers that generate clusters of size $N_i < N_{crit}$
5. Go back to step 2

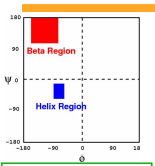
Mönnigmann, M. and Floudas, CA. *Proteins.* (2005)

ASTRO-FOLD

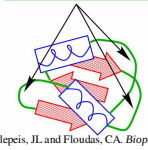


Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

Derivation of Restraints



Connection between two elements of secondary structure



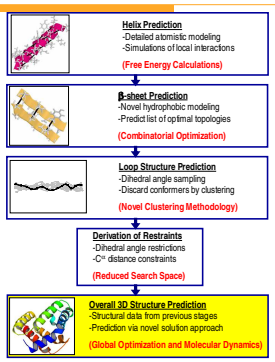
Dihedral angle restraints
- Backbone dihedral angles restrained according to classification of residue as either helix or strand

Distance restraints
- C^{α}-C^{α} distance restraints for hydrogen bond network of helix (residues i and i+4)
- C^{α}-C^{α} distance restraints for predicted interhelical contacts

Bounds on loop residues
- Based on dihedral angle deviation of best identified conformer from loop clustering analysis

Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

ASTRO-FOLD



Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

Tertiary Structure Prediction: Key Ideas

Utilization of helix predictions

Enforce prediction of secondary structure and interhelical distances through rigorous constraint modeling

Mathematical formulation

Formulate tertiary structure prediction problem as a constrained global optimization problem

Energy modeling

Model proteins using detailed atomistic level force field with physically based terms

Global optimization approach

Predict overall tertiary structure using combination of global optimization and torsion angle dynamics

Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

Tertiary Structure Prediction Formulation

$$\min_{\boldsymbol{\theta}} \quad E(\boldsymbol{\theta})$$
$$\text{s.t.} \quad E_{l,\text{distance}}(\boldsymbol{\theta}) \leq E_{l,\text{ref}} \quad l = 1,\ldots,N_{\text{con}}$$
$$\theta_i^L \leq \theta_i \leq \theta_i^U \quad i = 1,\ldots,N_\theta$$

Objective: Nonconvex atomistic level forcefield

$$E = \sum_{i,j \in NB} \epsilon_{ij}\left[\left(\frac{r_{ij}^o}{r_{ij}}\right)^{12} - \left(\frac{r_{ij}^o}{r_{ij}}\right)^{6}\right] + \sum_{i,j \in HB} \epsilon_{ij}\left[\left(\frac{r_{ij}^o}{r_{ij}}\right)^{12} - \left(\frac{r_{ij}^o}{r_{ij}}\right)^{10}\right]$$
$$+ \sum_{i,j \in ES} \frac{332\, q_i q_j}{D r_{ij}} + \sum_{k \in TOR} \frac{A_k}{2}(1 \pm \cos n_k \phi_k)$$

Constraints

- Enforce bounds on backbone variables
- Enforce upper / lower distances through square well constraints

$$E_{\text{distance}} = \sum_{j \in \text{upper}} \begin{cases} A_j (d_j - d_j^U)^2 & \text{if } d_j > d_j^U \\ 0 & \text{otherwise} \end{cases}$$
$$+ \sum_{j \in \text{lower}} \begin{cases} A_j (d_j - d_j^L)^2 & \text{if } d_j < d_j^L \\ 0 & \text{otherwise} \end{cases}$$

Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

Torsion Angle Dynamics

Initialization

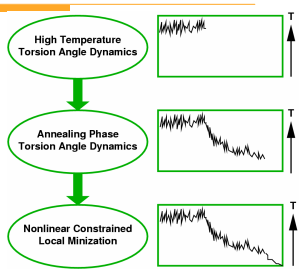
- Difficult to identify low energy feasible structures

Torsion Angle Dynamics

- Identify feasible low energy structures (satisfy constraints)
- Fast evaluation of simplified force field (steric based)
- Unconstrained formulation using penalty functions

Implementation

- Solve equations of motion as **preprocessing** for each constrained minimization



Good Initial Points for Local Optimization

Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

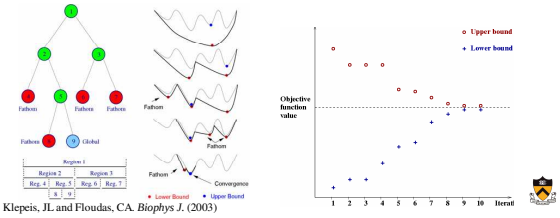
Wuthrich & coworkers

αBB Framework

$$\min_{\mathbf{x}} \quad f(\mathbf{x})$$
$$\text{s.t.} \quad \mathbf{h}(\mathbf{x}) = \mathbf{0}$$
$$\mathbf{g}(\mathbf{x}) \leq \mathbf{0}$$
$$\mathbf{x} \in \mathbf{X} \subset \mathcal{R}^n$$

f, $\mathbf{h}$, $\mathbf{g}$ twice continuously differentiable

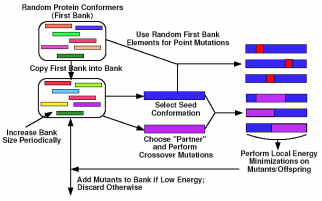
- Based on a branch-and-bound framework
- Upper bound on the global solution is obtained by solving the full nonconvex problem to local optimality
- Lower bound is determined by solving a valid convex underestimation of the original problem
- Convergence is obtained by successive subdivision of the region at each level in the brand & bound tree
- Guaranteed ε-convergence for C^2 NLPs

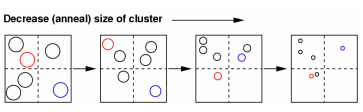


Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

Conformational Space Annealing

- Variation types
  - Single random
  - Backbone random
  - Group crossover
  - Connected crossover
- Annealing
  - Gradual reduction in space
  - Cluster members in low energy regions





Klepeis, JL, et al. *Biophys J.* (2003)

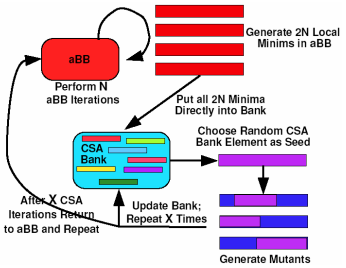
Hybrid Algorithm Motivation

- αBB Features
  - Global minimum guarantee
  - Rigorous upper and lower bounds
  - Rigorous termination
  - Slow performance
- CSA Features
  - Stochastic global minimum search
  - Provides upper bound on solution
  - Heuristic termination
  - Faster performance

Klepeis, JL, et al. *Biophys J.* (2003)

Alternating Hybrids

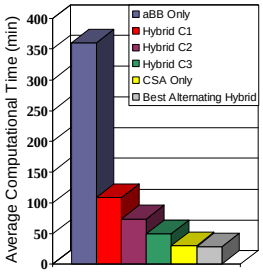
- Approach
  - Use output of a series of αBB runs to fill the CSA bank
  - A number of CSA iterations are performed before refilling the bank with additional aBB solutions



Klepeis, JL, et al. *Biophys J.* (2003)

Hybrid Performance

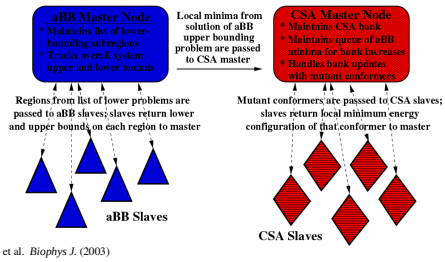
- Runs on met-enkephalin
  - Hybrids identified global minimum structure (rigorous)
  - Best alternating hybrid faster than CSA only!



Klepeis, JL, et al. *Biophys J.* (2003)

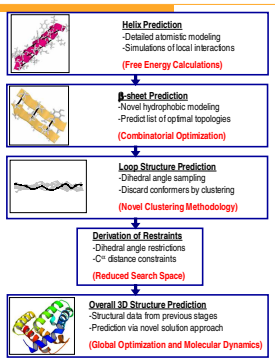
Parallelization

- Protein runs scale as $(N_{res})^{2-4}$
- Implement as distributed method
  - Two "master" nodes: αBB and CSA



Klepeis, JL, et al. *Biophys J.* (2003)

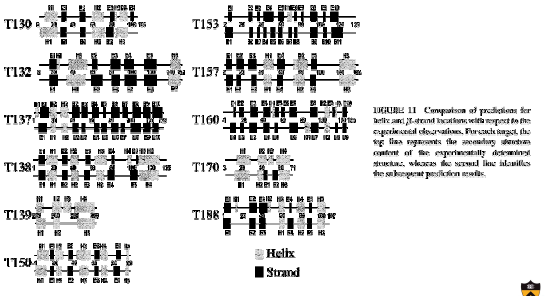
ASTRO-FOLD



Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

Secondary Structure Prediction Results

- Applied to a number of CASP5 targets

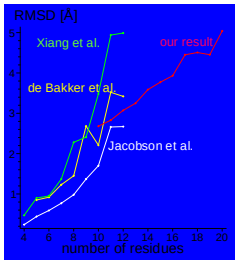


Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

Loop Prediction – Results Comparison

Comparison difficult
- flexible stem residues
- fixed stems in all previous results
- → we solve harder problem
- number of residues includes 3+3 stem residues in our case
- stem residues have tighter probability distributions

Results of comparison
- Jacobson et al. result with fixed stems better
- → use information on stem geometry, if available
- new method results in very favorable slope
- new method is better than or only slightly worse than methods for fixed stems

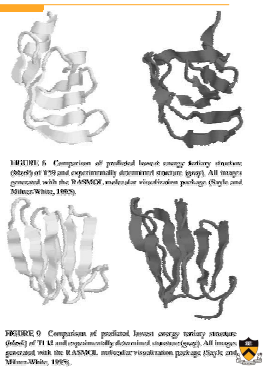


Mönnigmann, M. and Floudas, CA. *Proteins.* (2005)

Tertiary Structure Prediction Results

- Successful on a number of small protein systems
- Able to address difficult structures from CASP5 targets

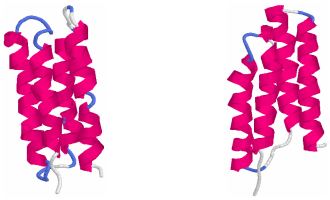
Protein	# of AA	RMSD
1gb1	56	4.2
bpti	58	4.1
3ci2	63	5.4
r69	68	6.2
t59	75	5.4
t114	87	4.5
t105	95	5.8
t52	101	6.9



Klepeis, JL and Floudas, CA. *Biophys J.* (2003)

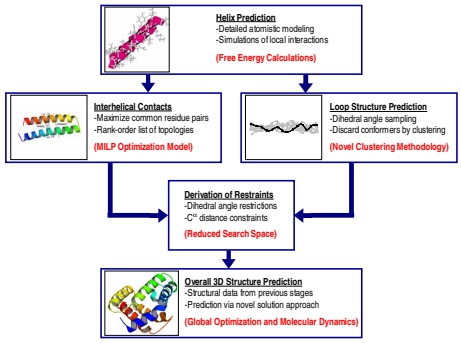
Results – Blind Structure Prediction

- PDB:1p68 (Prof. M. Hecht, Princeton Univ.)
- No information about secondary/tertiary structure
- α-helix: 5-21, 30-49, 56-75, 80-100
- Distance restraints: 63 intrahelical
- Best energy: -846 kcal/mol RMSD: 5.1Å



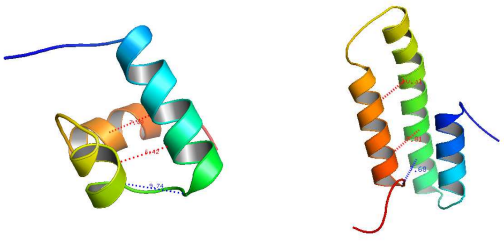
Klepeis, JL, et al. *Proteins.* (2005)

ASTRO-FOLD for α-helical Bundles



McAllister SR and Floudas, CA. *Proceedings, BIOMAT Conference* (2005).

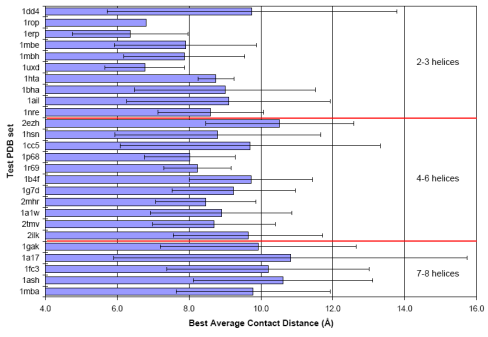
Results – 2-3 helix bundles



PDB:1mbh in PyMol PDB:1nre in PyMol

McAllister et al. (submitted 2005)

Results – Contact Prediction Summary

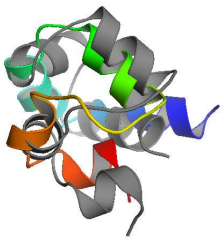


McAllister et al. (submitted 2005)

Results – Tertiary Structure Prediction

- PDB:1r69
  - 63 amino acid protein
  - Top 5 conformers

Conformer	Energy (kcal/mol)	RMSD (Å)
1	-358.77	6.05
2	-351.92	7.95
3	-347.71	6.72
4	-337.80	5.88
5	-337.52	8.04
157	-210.13	4.68



PDB:1r69 in PyMol

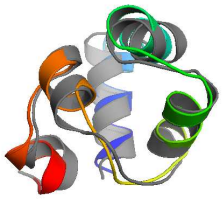
  - +/- 20° on dihedral angles of loop predictions

McAllister SR and Floudas, CA. *Proceedings, BIOMAT Conference* (2005).

Results – Tertiary Structure Prediction

- PDB:1r69
  - 63 amino acid protein
  - Top 5 conformers

Conformer	Energy (kcal/mol)	RMSD (Å)
1	-381.54	3.72
2	-376.10	3.40
3	-375.17	4.45
4	-363.77	2.03
5	-356.85	4.91



PDB:1r69 in PyMol

  - +/- 10° on dihedral angles of experimental loops

McAllister SR and Floudas, CA. *Proceedings, BIOMAT Conference* (2005).

Discussion

?