Threading – LOOPP laboratory

- **LOOPP parameters**
- **Basics of using LOOPP**
- **Examples**
  - Threading complements sequence to sequence alignment
  - Performance of the model on known structures
  - Using the program to identify unknown structures
- **Combinatorial extension**

Using LOOPP

- LOOPP Web server: http://ser-loopp.tc.cornell.edu/cbsu/loopp.htm
- E-mail notifications (status, Web page with results)
- Input sequence format FASTA

Download FASTA from PDB http://www.rcsb.org/pdb/

LOOPP input parameters

- **BLASTP search for sequence homologs**

  1. **Max. number of homolog sequences**

     1 = no BLASTP search

     N>1 = keeps N homologs including the original sequence

  2. **Customized min./max. seq. identity between query and homolog**.

- **Secondary Structure Predictor (JNET)**: post alignment filtering

  -ve scores : bad correlation with LOOPP's secondary structure predictions

  0.0 as threshold

LOOPP alignment options

- **Alignments from homologs and/or query sequence:** all accepted from LOOPP results for homologs; they are translated to query seq. align. using BLAST results.
- **Alignments from homologs and/or query sequence, query sequence preferred:** all accepted from LOOPP results for homologs; corresponding query seq. LOOPP align. will be reported if available, otherwise homolog align. will be translated to query seq. align. using BLAST.
- **Alignments from query sequence only:** only align. above threshold in query seq. are accepted from LOOPP res. for homologs; corresponding query seq. LOOPP align. will be reported

More LOOPP parameters

- **Maximum length difference:** maximum allowed difference in length (% of query length) between query and homolog.
- Maximum number of outputted matches.
- Type of the output format

A Quantitative Trait Locus Key to the Evolution of Tomato Fruit Size

Anne Frary, T. Clint Nesbitt, Amy Frary, Silvana Grandillo, Esther van der Knaap, Bin Cong, Jiping Liu, Jaroslaw Meller, Ron Elber, Kevin B. Alpert, and Steven D. Tanksley

Science 2000 July 7; 289: 85-88

LeORFX (L. pannellli ORFX alleles)

http://www.tc.cornell.edu/research/cbsu/webresources/tmp/blastuser/loopp_108/LeORF.out.htm

http://www.tc.cornell.edu/research/cbsu/webresources/tmp/blastuser/loopp_106/LeORFX.out.htm

LpORFX (L. esculentum ORFX alleles)

http://www.tc.cornell.edu/research/cbsu/webresources/tmp/blastuser/loopp_109/LpORFX.out.htm

http://www.tc.cornell.edu/research/cbsu/webresources/tmp/blastuser/loopp_105/LpORFX.out.htm

Example: Mioglobin (1mbc)

1mbc LOOPP results, default parameters (10 homologs)

http://www.tc.cornell.edu/research/cbsu/webresources/tmp/blastuser/loopp_90/1mbc.out.htm

1mbc LOOPP results (no BLASTP)

http://www.tc.cornell.edu/research/cbsu/webresources/tmp/blastuser/loopp_97/protein.out.htm

Combinatorial Extension (CE) Method

Protein Engineering, Vol 11, 739-747

CE: Algorithm that involves a combinatorial extension of AFPs

AFP: aligned fragment pairs from the two proteins based on local geometry.

Other approaches involving dynamic programming and Monte Carlo optimizations attempt global optimization of the alignment.

Combinatorial Extension (CE) - continuing

http://cl.sdsc.edu/ce.html

Threshold for structure similarity: 3.5
Root Mean Square Deviation (RMSD) between C alpha atoms over the length of the alignment), maximum: 5.0

http://www.tc.cornell.edu/research/cbsu/webresources/tmp/blastuser/loopp_90/1mbc.out.htm

TWO CHAINS: 1mbc and 2vhb:A
CE z-score = 5.7, Rmsd = 1.7 A
1mbc and 1vre:A
CE z-score = 6.1, Rmsd = 2.3 A

LOOPP in CAFASP

Critical Assessment of Fully Automated Structure Prediction

Servers: http://www.cs.bgu.ac.il/~dfischer/CAFASP3/servers.html

Summary: http://www.cs.bgu.ac.il/~dfischer/CAFASP3/summaries/index.html

T0138

http://www.tc.cornell.edu/research/cbsu/webresources/tmp/blastuser/cloopp_59/fp7504.out.htm

CE (1dbw:A – 2fsp): Rmsd = 2.6Å, Z-Score = 6.1

T0147

http://www.tc.cornell.edu/research/cbsu/webresources/tmp/blastuser/cloopp_69/fp7703.out.htm

CE (1byk:A – 1spb:S) Rmsd = 3.1Å Z-Score = 4.1

CE: http://cl.sdsc.edu/ce.html