BINF 731

Protein Structure Analysis

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2015

Structure verification and validation

Anolea
Verify3D
Procheck
WhatIf

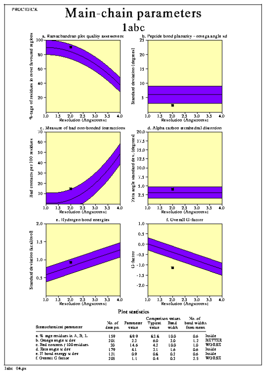
Bond lengths (Procheck)

```
-----------------------------------------------------------------
Bond          | labeling                            | Value | sigma
-----------------------------------------------------------------
C-N           | C-NH1           | (except Pro)      | 1.329 | 0.014
              | C-N             | (Pro)             | 1.341 | 0.016
              |                 |                   |       |
C-O           | C-O             |                   | 1.231 | 0.020
              |                 |                   |       |
Calpha-C      | CH1E-C          | (except Gly)      | 1.525 | 0.021
              | CH2G*-C         | (Gly)             | 1.516 | 0.018
              |                 |                   |       |
Calpha-Cbeta  | CH1E-CH3E       | (Ala)             | 1.521 | 0.033
              | CH1E-CH1E       | (Ile,Thr,Val)     | 1.540 | 0.027
              | CH1E-CH2E       | (the rest)        | 1.530 | 0.020
              |                 |                   |       |
N-Calpha      | NH1-CH1E        | (except Gly,Pro)  | 1.458 | 0.019
              | NH1-CH2G*       | (Gly)             | 1.451 | 0.016
              | N-CH1E          | (Pro)             | 1.466 | 0.015
-----------------------------------------------------------------
```

Bond angles (Procheck)

```
-----------------------------------------------------------------
Angle          | labeling                           | Value | sigma
-----------------------------------------------------------------
C-N-Calpha     | C-NH1-CH1E    | (except Gly,Pro)   | 121.7 | 1.8
               | C-NH1-CH2G*   | (Gly)              | 120.6 | 1.7
               | C-N-CH1E      | (Pro)              | 122.6 | 5.0
               |               |                    |       |
Calpha-C-N     | CH1E-C-NH1    | (except Gly,Pro)   | 116.2 | 2.0
               | CH2G*-C-NH1   | (Gly)              | 116.4 | 2.1
               | CH1E-C-N      | (Pro)              | 116.9 | 1.5
               |               |                    |       |
Calpha-C-O     | CH1E-C-O      | (except Gly)       | 120.8 | 1.7
               | CH2G*-C-O     | (Gly)              | 120.8 | 2.1
-----------------------------------------------------------------
```

Procheck output



a. Ramachandran plot quality - percentage of the protein's residues that are in the **core** regions of the Ramachandran plot.

b. Peptide bond planarity - standard deviation of the protein structure's **omega** torsion angles.

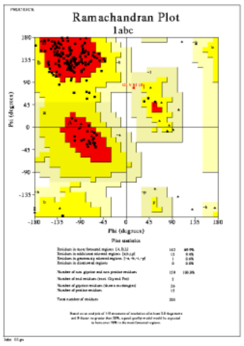
c. Bad non-bonded interactions - number of bad contacts per **100** residues.

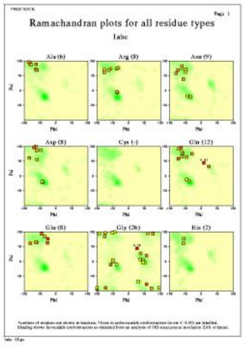
d. Cα tetrahedral distortion - standard deviation of the **ζ torsion angle** (**Cα**, **N**, **C**, and **Cβ**).

e. Main-chain hydrogen bond energy - standard deviation of the **hydrogen bond energies** for **main-chain hydrogen bonds**.

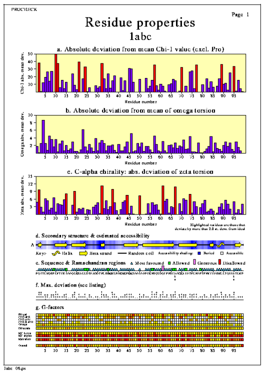
f. Overall G-factor - average of different G-factors for each residue in the structure.

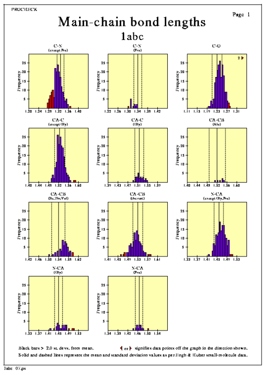
Procheck output



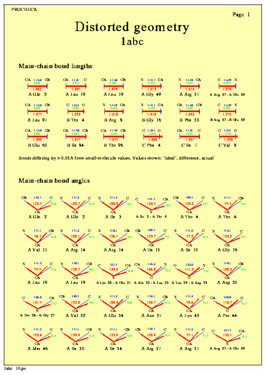


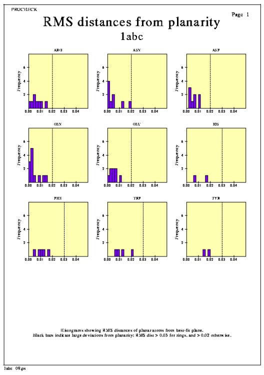
Procheck output



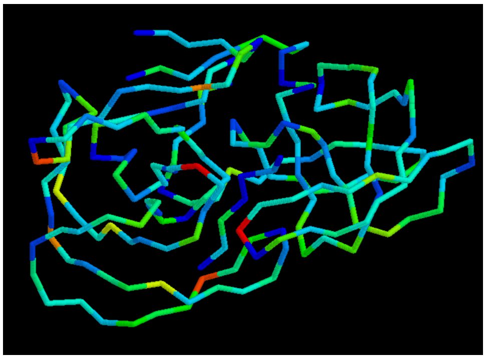


Procheck output

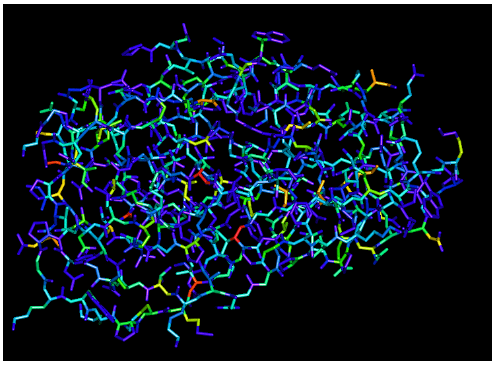




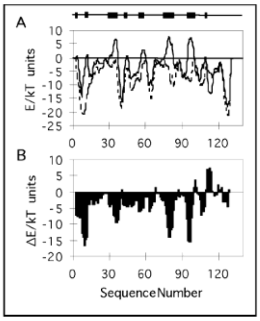
Procheck output - backbone G factors



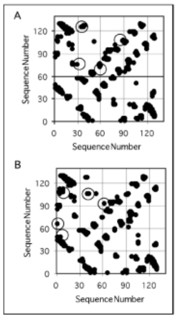
Procheck output - all atom G factors



Anolea



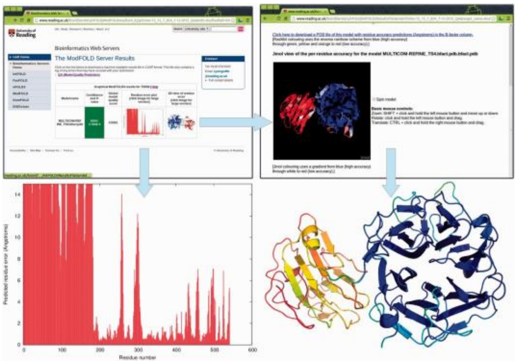
High energy zones



Non-local contact maps

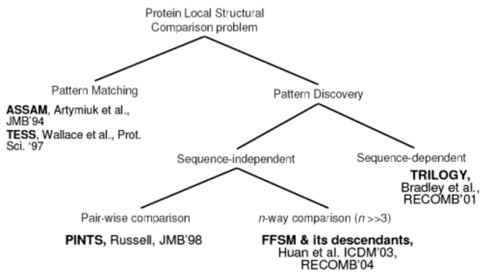
Melo et al., 1997

Model Quality Assessment


University of Reading
Bioinformatics Web Servers
The ModFOLD Server Results
Jmol view of the per-residue accuracy for the model MULTICOM-REFINE_TS4.bfact.pdb.bfact.pdb
Spin model
Basic mouse controls:
Predicted residue error (Angstroms)
Residue number

L.J.McGuffin et al., 2013

Local structure comparison algorithms



Protein Local Structural Comparison problem

Pattern Matching

ASSAM, Artymiuk et al., JMB'94

TESS, Wallace et al., Prot. Sci. '97

Pattern Discovery

Sequence-independent

Sequence-dependent

TRILOGY, Bradley et al., RECOMB'01

Pair-wise comparison

PINTS, Russell, JMB'98

n-way comparison (*n* >>3)

FFSM & its descendants, Huan et al. ICDM'03, RECOMB'04

Huan, 2006

Root mean square deviation

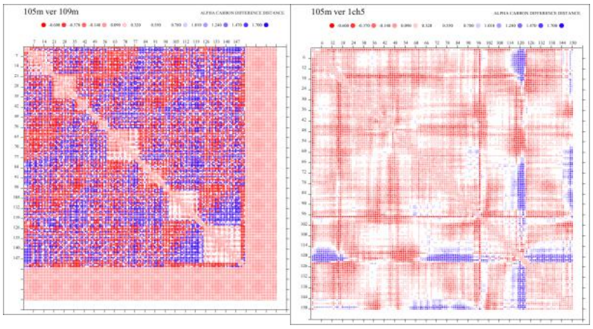
Coordinate based RMSD

$$RMSd(A,B) = \min_T \sqrt{\sum_{i=1}^{m} (A_i - TB_i)^2}$$

Distance based RMSD

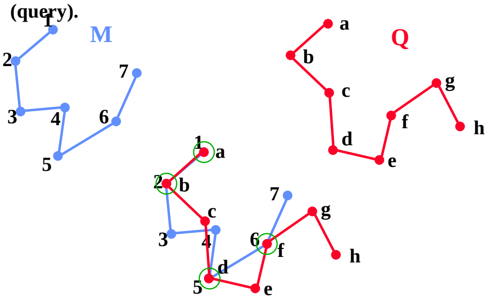
$$RMSd_D(A,B) = \frac{1}{m}\sqrt{\sum_{i=1}^{m}\sum_{j=1}^{m}\left(d_{ij}^A - d_{ij}^B\right)^2}$$

Difference Distance Matrix Plot (DDMP)



Geometric Hashing

Find common subsets, invariant under rotation and translation in two point sets M (model) and Q (query).



Finding the maximum coincidence set is an NP-hard problem

Geometric Hashing

Reference frames

- **Two points (basis pair) define a reference frame**
- **The coordinates of all points are computed in the reference frame (reference frame system)**
- **There will be pairs of points (from M and Q) with the same coordinates**
- **The number of such pairs depends on selection of reference frame and reference frame system resolution**

Geometric Hashing Algorithm

Preprocessing

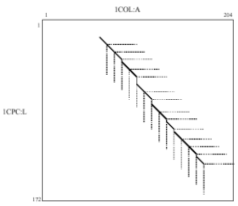
Hash table H is created. It has a bin for each cell in the frame systems. The coordinates of all points in each model frame system are calculated. If there is a point in the cell (p,q) in the frame system with basis (a_i,a_k), then (a_i,a_k) is placed in the bin H(p,q)

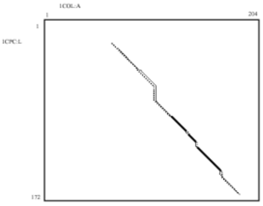
Recognition

A pair of points in the query is chosen as basis, and the coordinates of the other points are calculated. These coordinates are used as indices for H, and for each cell being indexed, a vote is given for the (model) basis pairs in the cell. The number of votes for a model basis pair is the number of coinciding points to the query (using the specified query basis pair)

Combinatorial Extension (CE) Algorithm

Structure alignment of phycocyanin (1CPC:L) to colicin A (1COL:A)

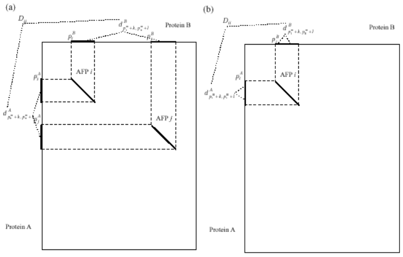




The solid line represents the optimal path built from AFPs. The dotted line represents the search area at every step of path extension.

The thick solid line represents alignment overlap both before and after optimization.

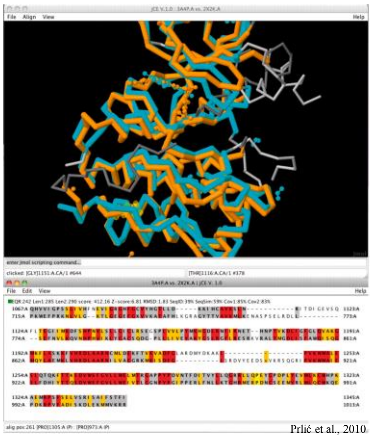
Combinatorial Extension (CE) Algorithm



Calculation of distance

***Dij* for two AFPs *i* and *j* from the path**

***Dii* for single AFP *i* from the path.**



enter Jmol scripting command...

clicked: [GLY]1151:A.CA/1 #644 [THR]1116:A.CA/1 #378

3A4P.A vs. 2X2K.A | jCE V. 1.0

```
EQR:242 Len1:285 Len2:290 score: 412.16 Z-score:6.81 RMSD:1.83 SeqID:39% SeqSim:59% Cov1:85% Cov2:83%
1067:A QHVVIGPSSGIVHFNEVIGRGHFGCVYHGTLLD-----KKIHCAVKSLN------------EITDIGEVSQ 1123:A
715:A  PKWEFPKKNLVLG--KTLGEGEFGKVVKATAFHLKGRAGYTTVAVKMLKENASPSELRDLL---------- 773:A

1124:A FLTEGIIMKDFSHPNVLSLLGICLRSEGSPLVVLPYMKHGDLRNFIRNETHNPTVKDLIGFGLQVAKG 1191:A
774:A  --SEFNVLKQVNHPHVIKLYGACSQDG-PLLLIVEYAKYGSLRGFLRESRKVRALLMGDLISFAWQISQG 861:A

1192:A MKFLASKKFVHRDLAARNCMLDEKFTVKVADFGLARDMYDKAKE----------------FVKWMALE 1253:A
862:A  MQYLAEMKLVHRDLAARNILVAEGRKMKISDFG-----------LSRDVYEEDSYVKRSQGRIPVKWMAIE 921:A

1254:A SLQTQKFTTKSDVWSFGVLLWELMTRGAPPYPDVNTFDITVYLLQGRRLLQPEYCPDPLYEVMLKCWHPK 1323:A
922:A  SLFDHIYTTQSDVWSFGVLLWEIVTLGGNPYPGIPPERLFNLLKTGHRMERPDNCSEEMYRLMLQCWKQE 991:A

1324:A AEMRPSFSELVSRISAIFSTFI 1345:A
992:A  PDKRPVFADISKDLEKMMVKRR 1013:A
```

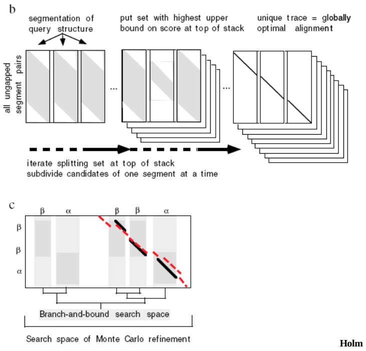
alig pos: 261 [PRO]1305:A (P) : [PRO]971:A (P)

Prlić et al., 2010

jCE and jFATCAT tool at RCSB

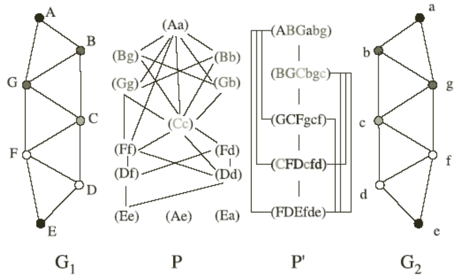
Pairwise structure alignment and pre-calculated 3D structure comparisons for the entire PDB

DaliLight algorithm for protein structure comparison


b
segmentation of query structure
put set with highest upper bound on score at top of stack
unique trace = globally optimal alignment
all ungapped segment pairs
...
...
iterate splitting set at top of stack
subdivide candidates of one segment at a time
c
β
α
β
β
α
β
β
α
Branch-and-bound search space
Search space of Monte Carlo refinement

Holm and Park, 2000

Search for common substructures by clique detection


A
B
G
C
F
D
E
(Aa)
(Bg)
(Bb)
(Gg)
(Gb)
(Cc)
(Ff)
(Fd)
(Df)
(Dd)
(Ee)
(Ae)
(Ea)
(ABGabg)
(BGCbgc)
(GCFgcf)
(CFDcfd)
(FDEfde)
a
b
g
c
f
d
e
G_1
P
P'
G_2