BINF 731

Protein Structure Analysis

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Regular Expressions

Patterns described in a standard way are known as *regular expressions*

x	ANY		
[ ]	OR	[ILV]	I or L or V
{ }	NOT	{DE}	not D or E
( )	repetitions	x(2,3)	x-x or x-x-x
-	separator		
<	N-terminal		
>	C-terminal		
.	END		

Regular Expressions

[AC]-x-V-x(4)-{ED}.

[Ala or Cys]-any-Val-any-any-any-any-{any but Glu or Asp}

...LKHV**A**Y**V**FQALIYWIK...
...AVEM**A**G**V**KYLQVQHGS...
...LYTG**A**I**V**TNNDGPYMA...
...KEYK**C**K**V**EKELTDICN...

PROSITE Database

Current version contains 1079 documentation entries that describe 1459 different patterns, rules and profiles/matrices

[ST]-x(2)-[DE]
Casein kinase II phosphorylation site

[AG]-x(4)-G-K-[ST]
ATP/GTP-binding site motif A (P-loop)

Y-x-[NQH]-K-[DE]-[IVA]-F-[LM]-R-[ED]
Heat shock hsp90 proteins family signature

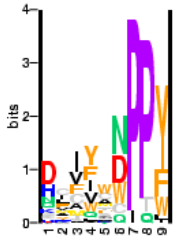
http://www.expasy.ch/prosite

Blocks Database

Blocks are multiply aligned ungapped segments corresponding to the most highly conserved regions of proteins

N-6 Adenine-specific DNA methylases proteins
width=9 seqs=78

```
DMA_VIBCH|Q08318   (85)  SCTQWWPPF 77
HEMK_MYCLE|P45832  (181) DLFVAQPTL 100
MT57_ECOLI|P25240  (111) DGALGNPPF 13
MTC1_CHVN1|Q01511  (172) NFVFLDPPY 8
MTC1_COREQ|P42828  (71)  QLSFSCPPF 49
MTH2_HAEHA|P00473  (32)  KIAFFDPQY 52
MTH3_HAEIN|P43871  (23)  HAIISDIPY 73
MTM1_MICAM|P50190  (306) AAVLTNPPF 14
MTM2_MORBO|P23192  (25)  QLAVIDPPY 10
MTMU_MYCSP|P43641  (37)  QVIYADPPW 13
MTR1_RHOSH|P14751  (60)  QLIICDPPY 8
.....................................
```



http://www.blocks.fhcrc.org/

Pfam Database

Pfam is a large collection of multiple sequence alignments and hidden Markov models covering many common protein domains

Zinc finger, C2H2 type

```
TYY1_HUMAN/383-407   YVCPF.DGCN...KKFAQSTNLKSHILT...H
ZG52_XENLA/61-83     YTCT..QCN...KQFSHSAQLRAHIST...H
KRUP_DROME/306-328   YTCE...ICD...GKFSDSNQLKSHMLV...H
YKQ8_CAEEL/78-102    YKCT...VCR...KDISSSESLRTHMFKQ.HH
DEFI_CHICK/268-292   YECP...NCK...KRFSHSGSYSSHISSK.KC
ZFH1_DROME/389-413   FGCD...NCG...KRFSHSGSFSSHMTSK.KC
YL57_CAEEL/42-65     YLCY...YCG...KTLSDRLEYQQHMLK..VH
ZFA_MOUSE/542-564    FKCD...ICL...LTFSDTKEVQQHALV...H
BASO_HUMAN/719-742   FQCD...ICK...KTFKNACSVKIHHKN..MH
HUNB_DROME/297-319   FQCD...KCS...YTCVNKSMLNSHRKS...H
SFP1_YEAST/598-623   FKCPV.IGCE...KTYKNQNGLKYHRLH..GH
ZG29_XENLA/62-84     FVCT...VCG...KTYKYKHGLNTHLHS...H
```

http://pfam.wustl.edu/

Other Motif Databases

PRINTS : a compendium of protein fingerprints. A fingerprint is a group of conserved motifs used to characterise a protein family
http://bioinf.man.ac.uk/dbbrowser/PRINTS/

DOMO : a protein domain database
http://www.infobiogen.fr/~gracy/domo/home.htm

ProDom : a protein domain database
http://protein.toulouse.inra.fr/prodom.html

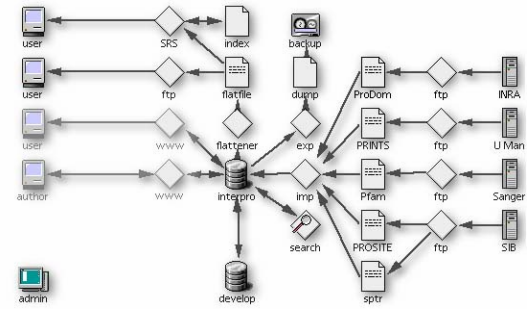
InterPro Database

InterPro : integrated resource for the commonly used signature databases - Pfam, PRINTS, PROSITE, ProDom and SWISS-PROT + TrEMBL.

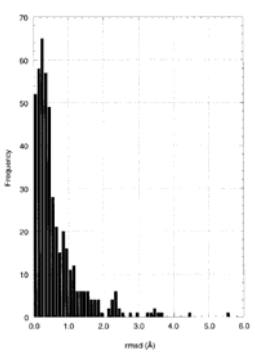
Current release of InterPro (3.2) contains 3939 entries, representing 1009 domains, 2850 families, 65 repeats and 15 post-translational modification sites.

http://www.ebi.ac.uk/interpro

InterPro Database



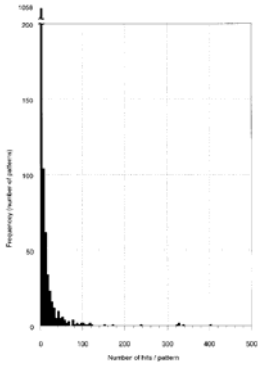
Structural motifs of PROSITE patterns



Distribution of rmsd values for the true hits. The rmsd was calculated from all true hits eliminating false and unidentifed hits for each of the 466 patterns having more than one true hit.

From Kasuya and Thornton (1999)

Structural motifs of PROSITE patterns



Distribution of number of hits per pattern. Each column represents frequency of patterns having sequence matches in the 3D-sequence library. The bin width is 10. There were 1058 patterns having numbers of hits smaller than 10, including 712 patterns with no hits.

From Kasuya and Thornton (1999)

Root mean square deviation

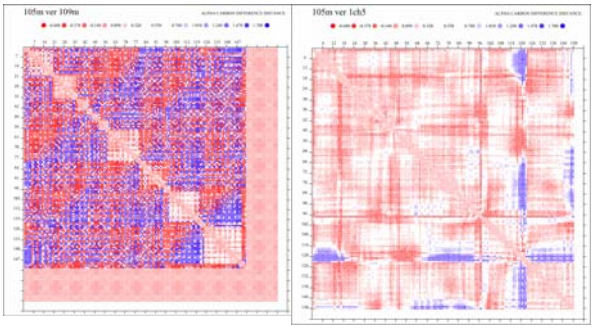
Coordinate based RMSD

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

Distance based RMSD

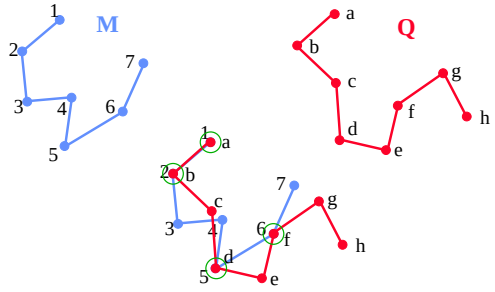
$$RMSd_D(A,B) = \frac{1}{m} \sqrt{\sum_{i=1}^{m} \sum_{j=1}^{m} \left(d_{ij}^A - d_{ij}^B\right)^2}$$

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

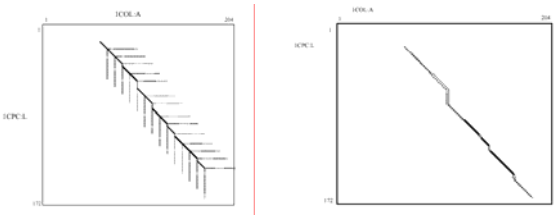
Hash table H is created. It has a bin for each cell in the frame systems. The coordinates of all points in each model frame system are calculated. If there is a point in the cell (p,q) in the frame system with basis (a_i,a_k), then (a_i,a_k) is placed in the bin H(p,q)

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

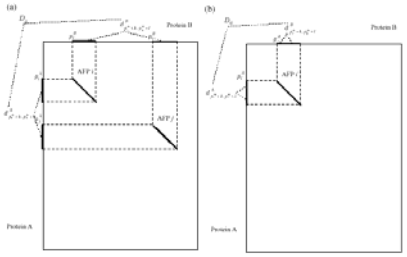
Structure alignment of phycocyanin (1CPC:L) to colicin A (1COL:A).



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.