The Pfam and MEROPS databases

EMBO course 2004

Robert Finn (rdf@sanger.ac.uk)

The Wellcome Trust Sanger Institute

Organisation of Tutorial

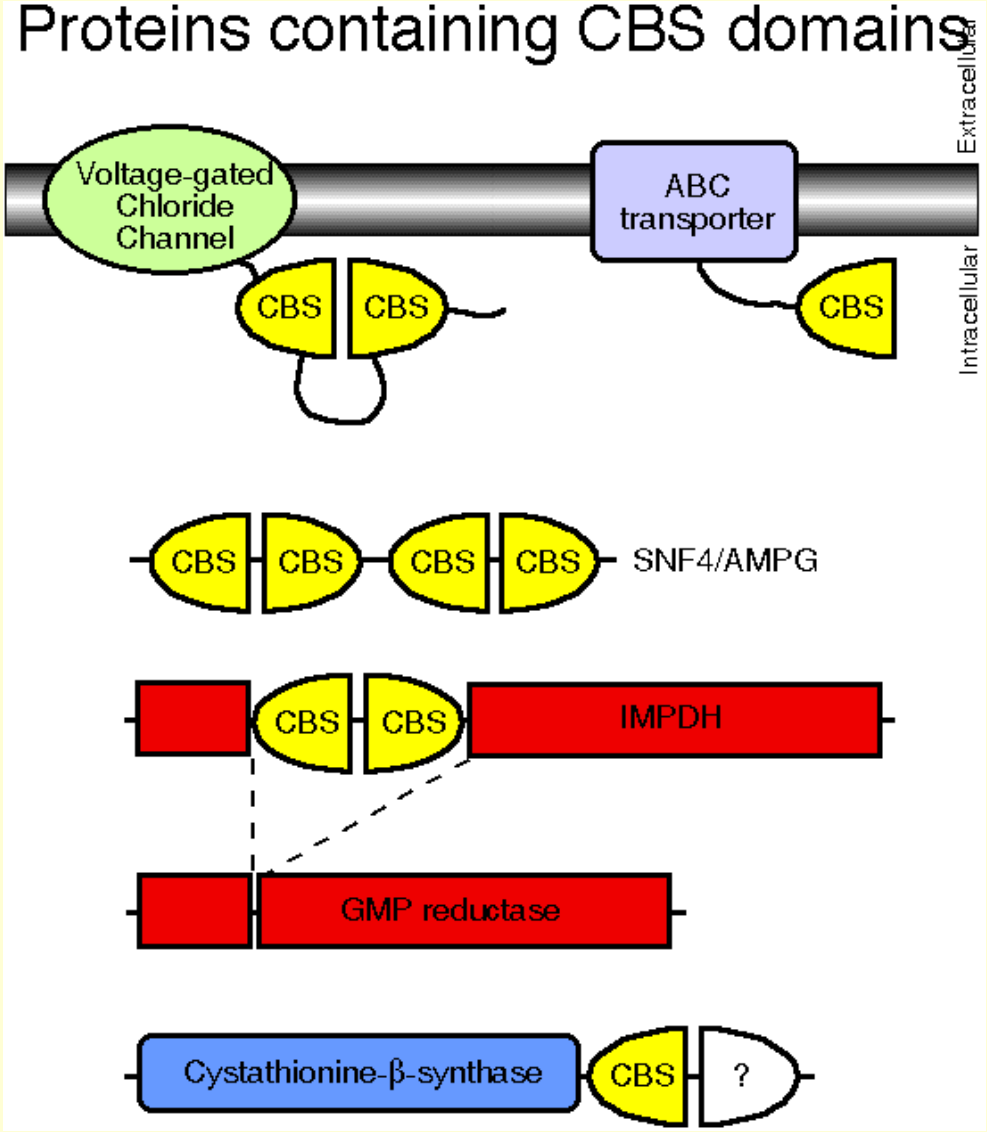
Part 1 – Background and Practical on Pfam

Part 2 - Background and Practical on MEROPS

Summary

- Introduction to Pfam
  - What is Pfam?
  - Sequence Coverage
  - Using Pfam
- More Advanced Topics
  - Pfam and Protein Structures
  - Pfam Clans
  - *i*Pfam

What is Pfam ?



Domains can be considered as building blocks of proteins.

Some domains can be found in many proteins with different functions, while others are only found in proteins with a certain function.

The presence of a particular domain can be indicative of the function of the protein.

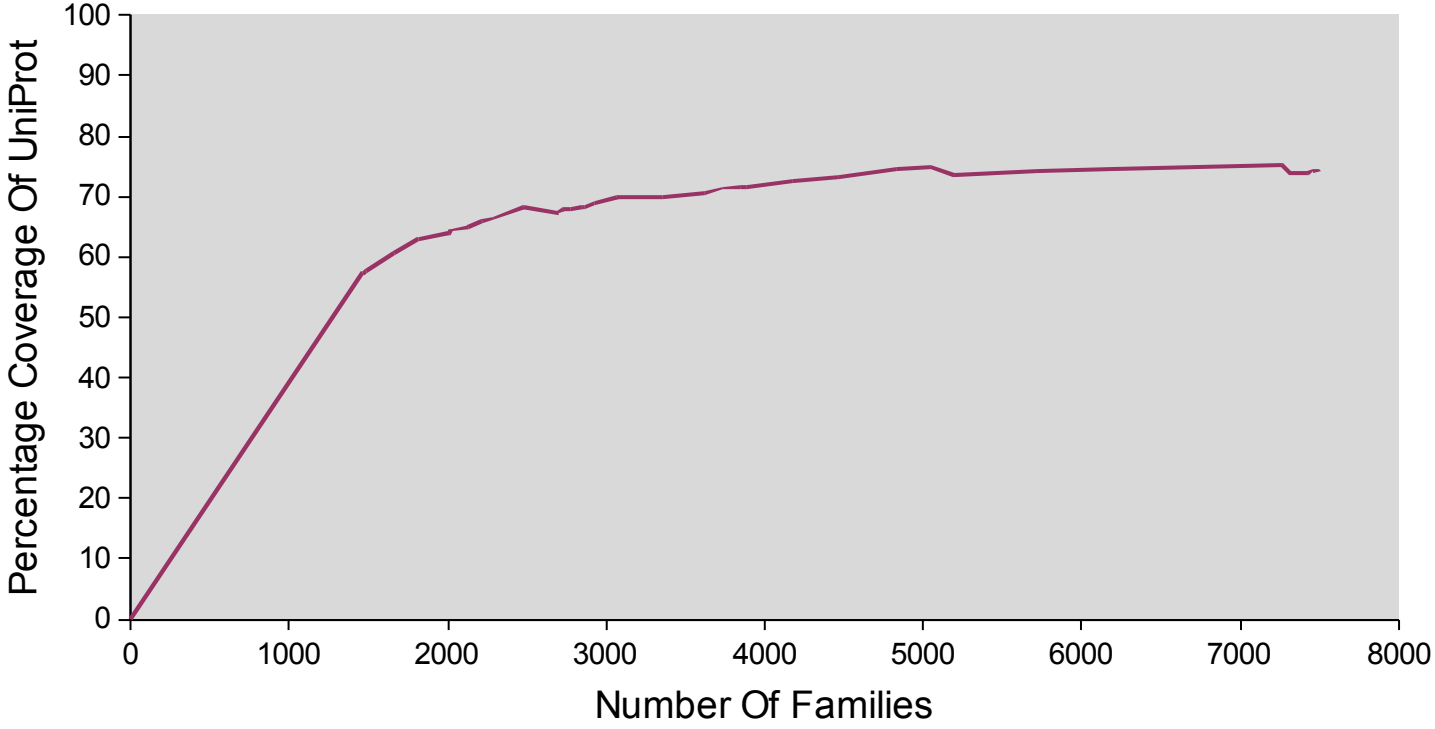
Pfam is a domain database.

Comprised of two parts – Pfam-A and Pfam-B.

Pfam is use by many different groups in many different ways. Originally set up to aid the annotation the *C. elegans* genomes.

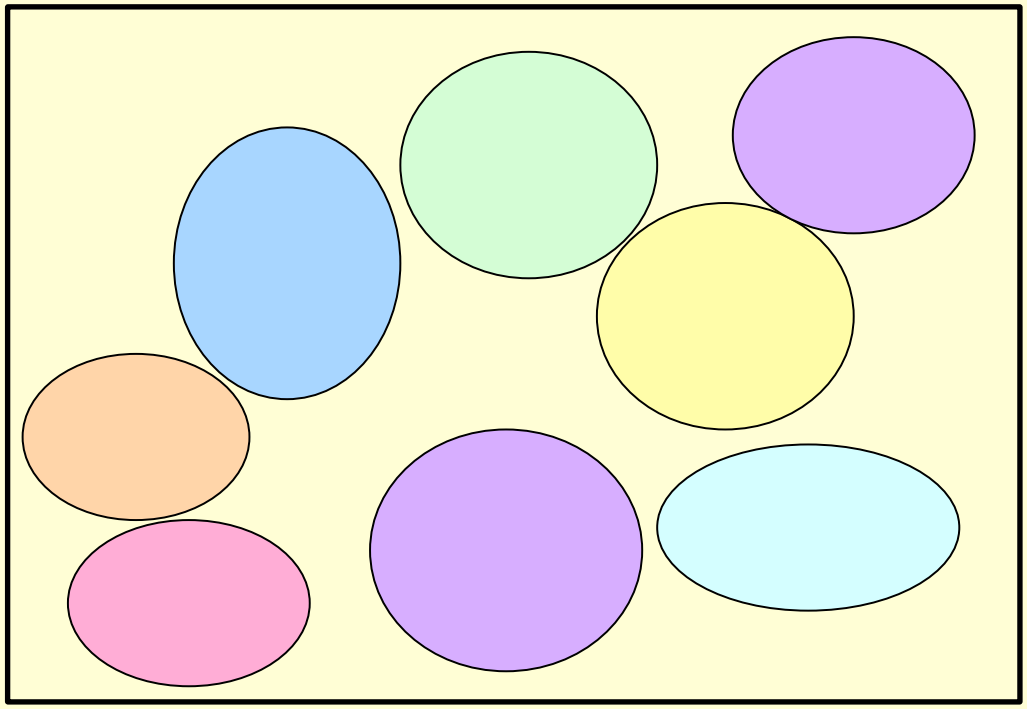
What is a Pfam-A Entry?

- A SEED alignment – contains a set or representative sequences
- HMM – built using the SEED alignment
- A full alignment – contains all (detectable) sequences in the family
- A description of the family, includes thresholds you to create the full alignment
- Rules – No false positives. A family is not allowed to overlap with any other family



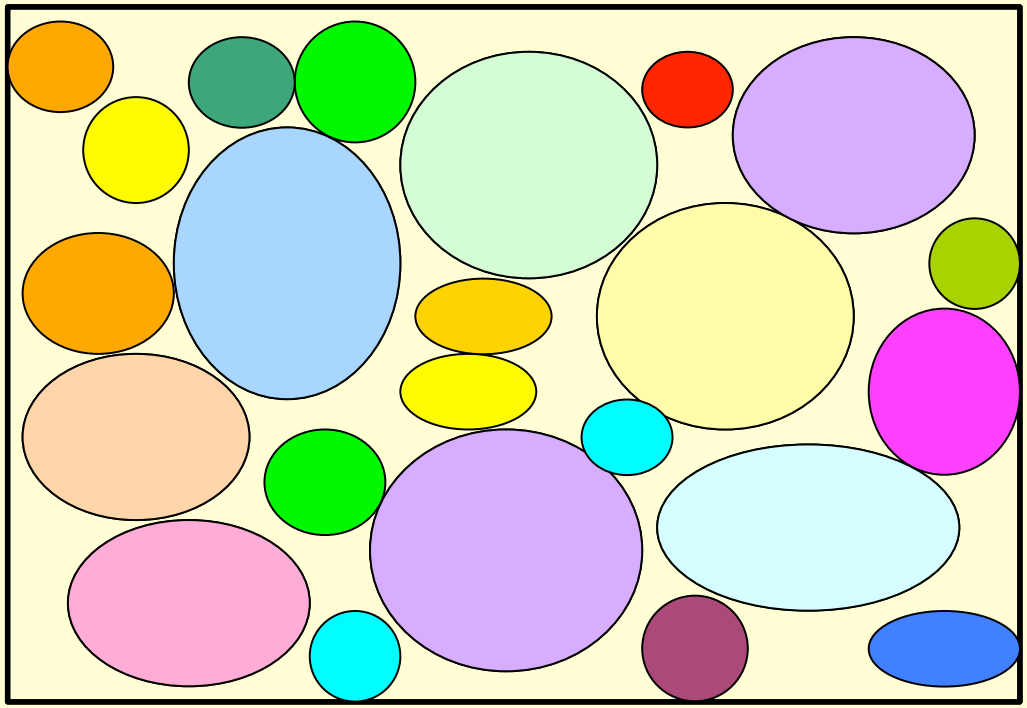
- First 2000 families covered ~ 65% of UniProt
- Currently, 7503 families cover 74% of UniProt

Pfam Sequence Coverage



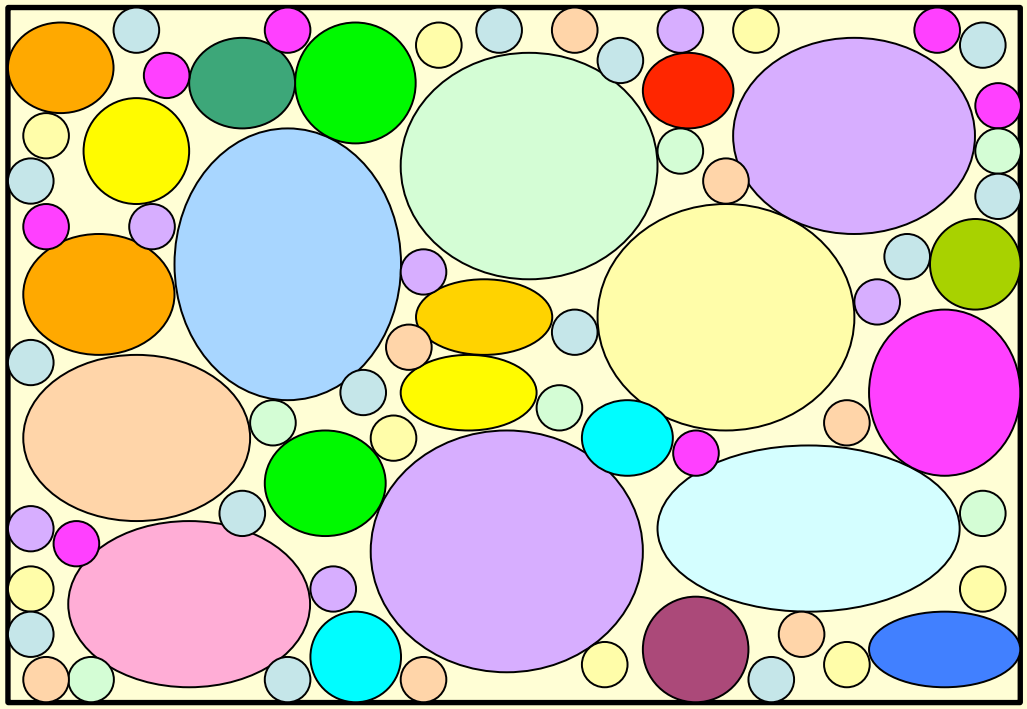
So why does the curve look logarithmic ?

Pfam Sequence Coverage



So why does the curve look logarithmic ?

Pfam Sequence Coverage



So why does the curve look logarithmic ?

Pfam-B

- Pfam-A covers about 74% of sequences
- To be comprehensive we have Pfam-B
- There are over 140,000 Pfam-B
- They cover 24% of UniProt (not covered by Pfam-A)
- Automatically generated clusters that are derived from Prodom

Pfam – Nuts and Bolts

- Collection of sequence alignments and profile hidden Markov models (HMMs)
- Over 7,500 families
- mySQL database
- Bi-Monthly Releases - flatfiles and relational tables
- Current Release – 15.0
- Mirrored around the World

Searching Pfam

- Two Fundamental Ways of Searching Pfam
  - By Sequence
    - Website – Demonstrated in the practical
    - Download HMM libraries and Run Locally
  - By Domain
    - Website – Demonstrated in the practical
    - Flatfiles & RDB

YFD is absent from Pfam.....

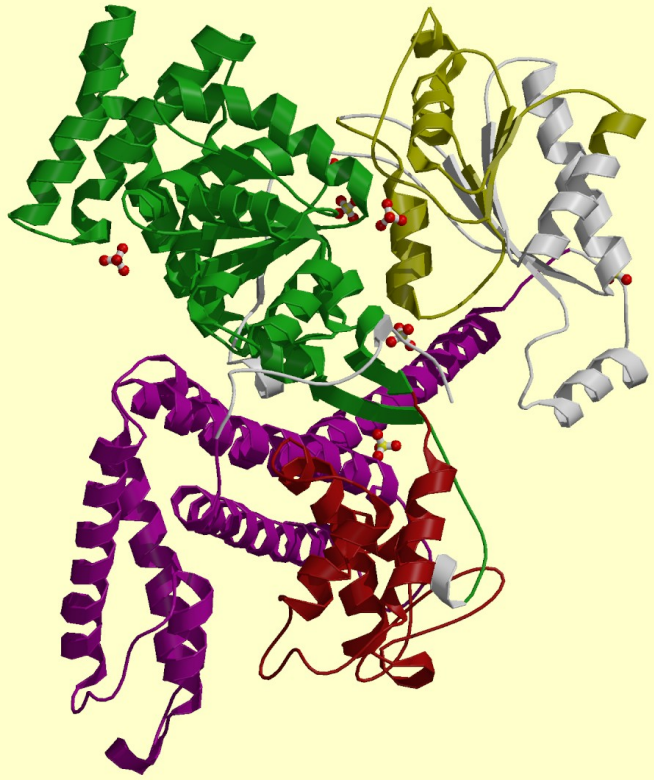
- Send us an Alignment and Some Annotation and we will, in most cases, add it to Pfam.
- Build Your Own HMM and use of to search a sequence database.

More Advanced Topics.....

Pfam & Structure

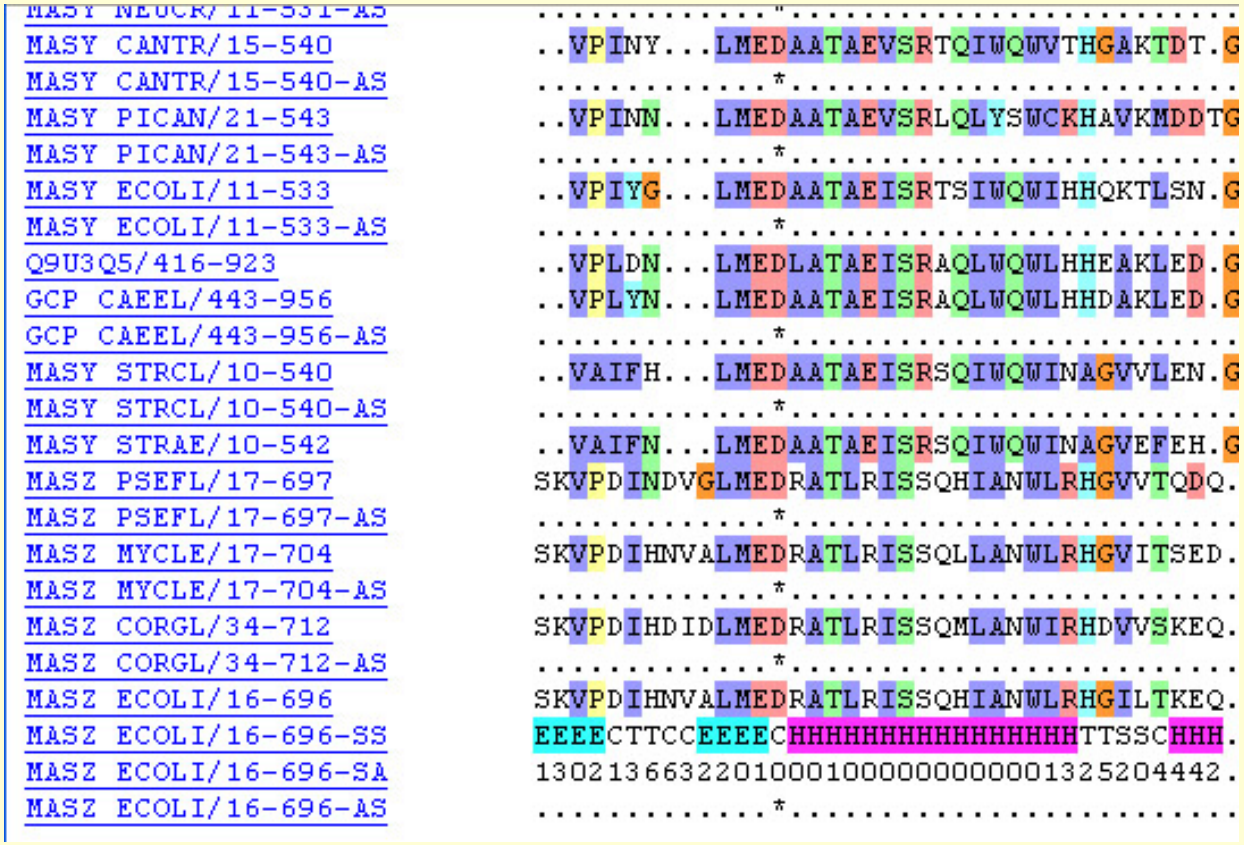
- Part of a collaborative Project called eFamily
  - Structural Markups
  - Alignment Markup
  - Domain Comparison

Structural Markup



- 1m6n – SecA Translocation ATPase
  - Domain Chain Start End
  - SecA_DEAD A 1 382
  - SecA_PP_bind A 226 338
  - Helicase_C A 448 530
  - SecA_SW A 568 780
- This is also applied to structures

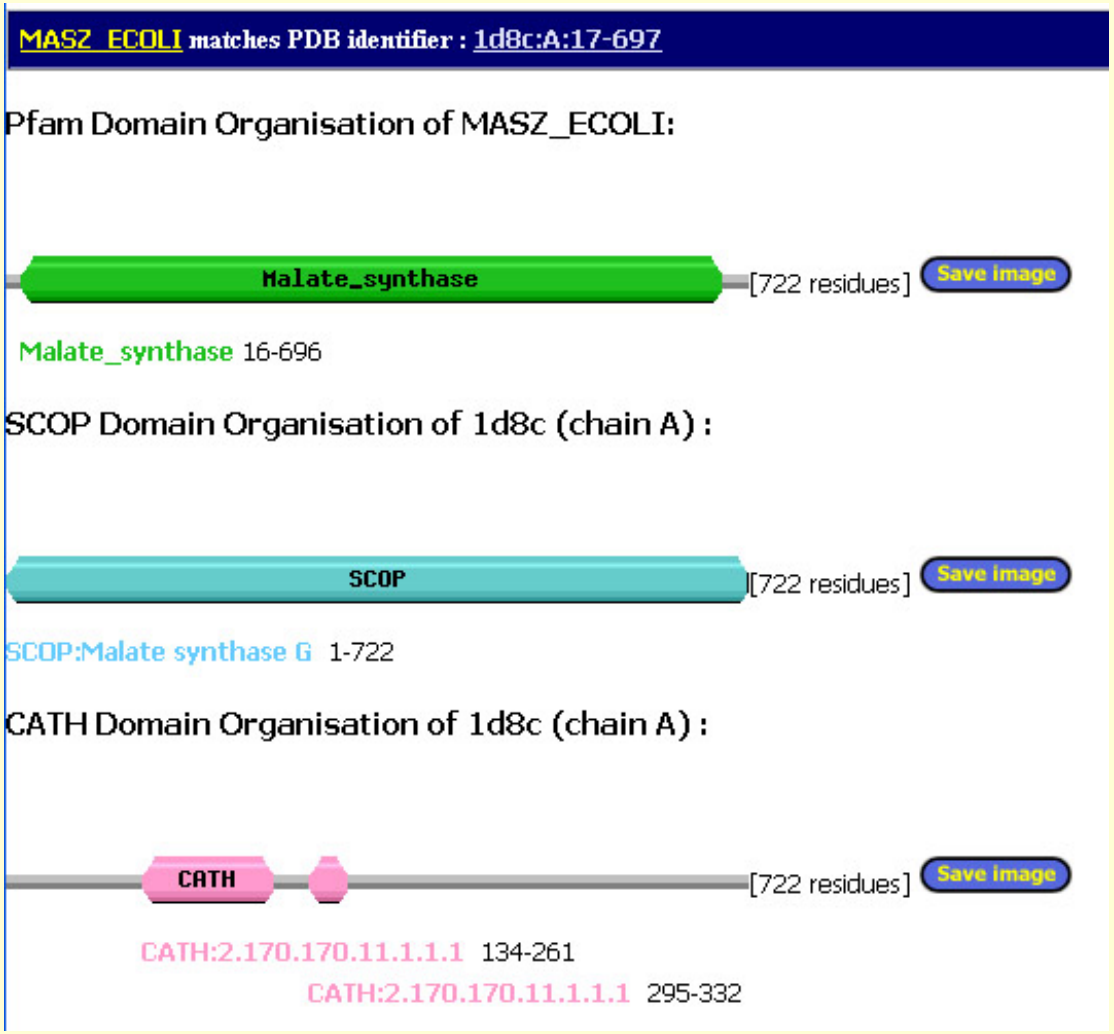
Alignment Markup



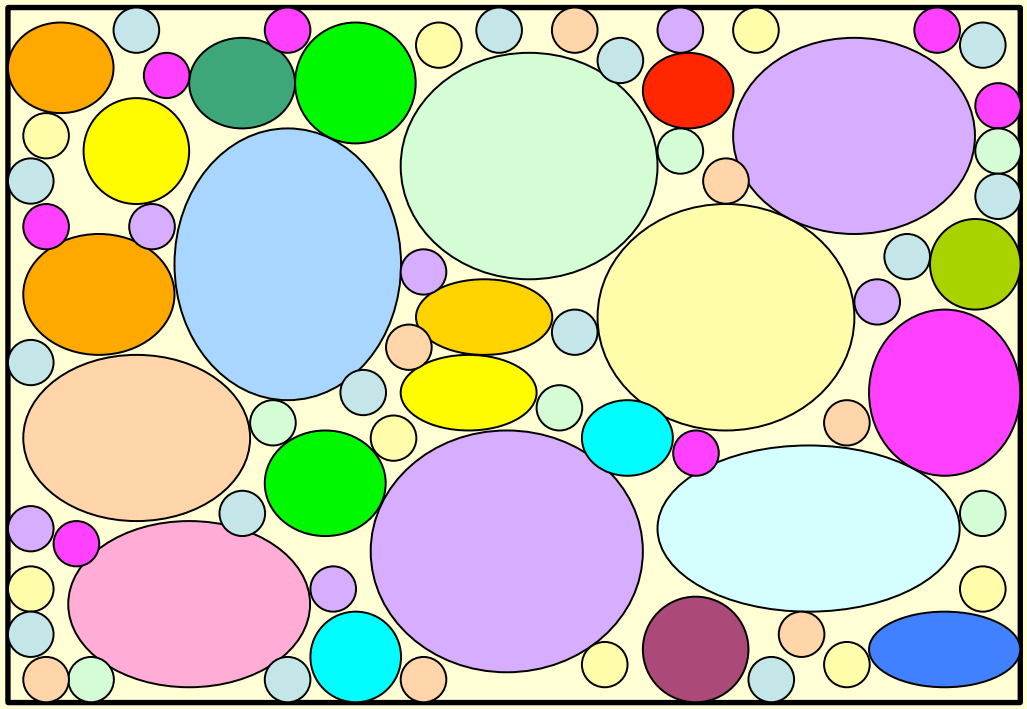
- AS – active site
- SS – secondary structure
- SA – solvent accessibility
- DSSP is used to calculate SS and SA
- MSD-UniProt Mapping used for the markup

Domain Comparison

- Often it is useful to compare Pfam domains to other domain databases
- Pfam provides a convenient tool for comparing domains between Pfam, CATH and SCOP
- Domains can be compared in 2D or 3D
- Explored Further in parctical



Pfam Sequence Coverage



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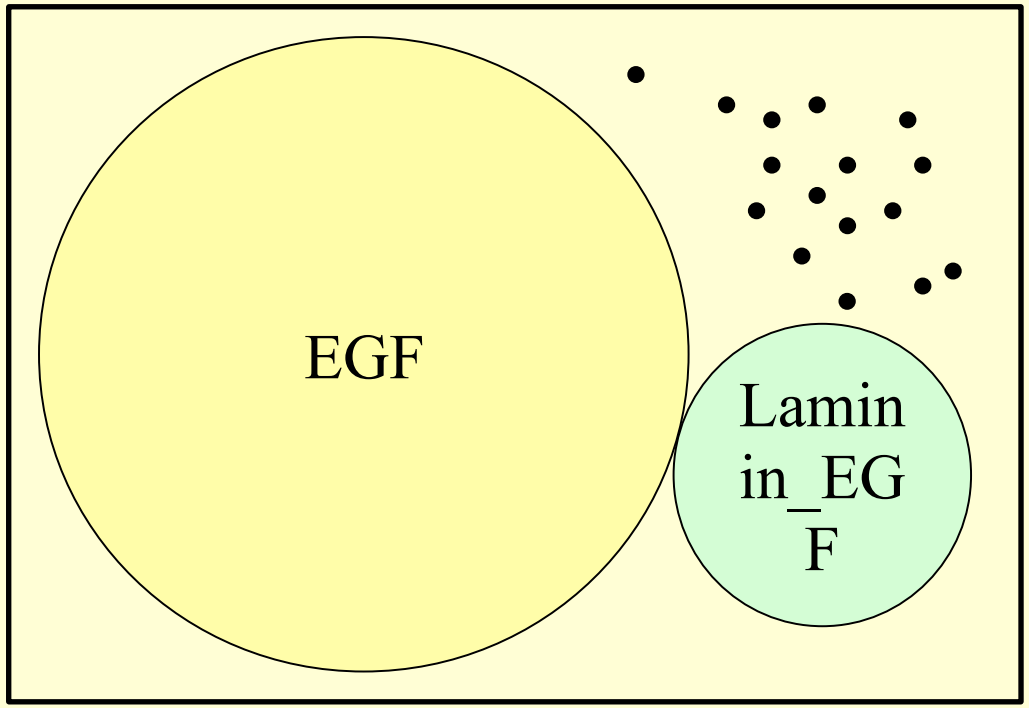
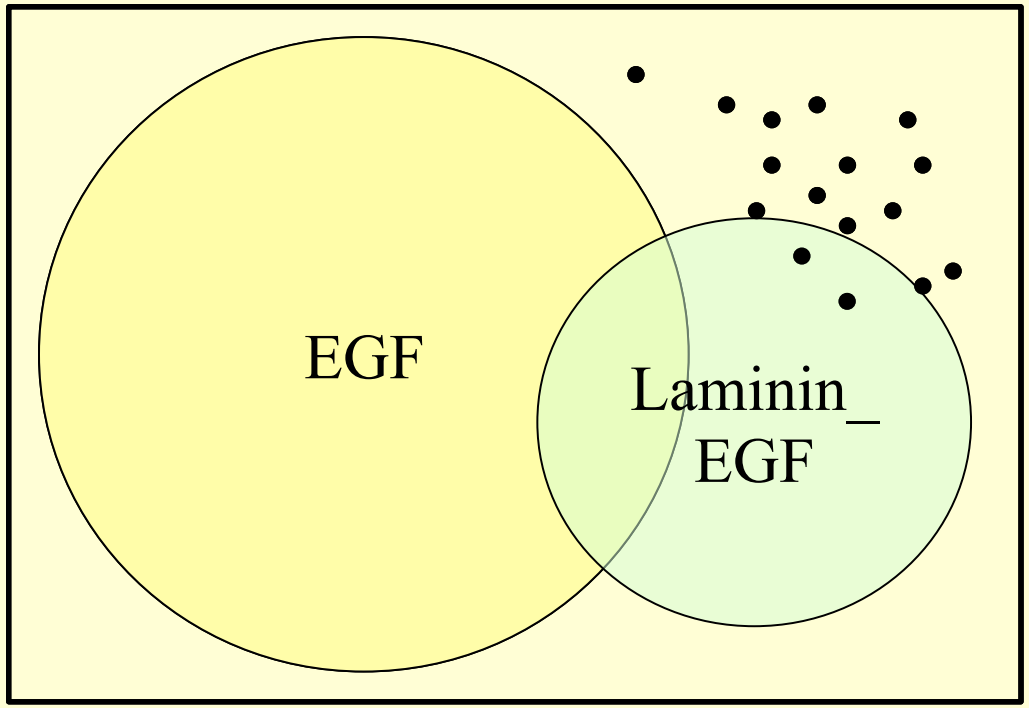
Pfam Clans

- Lets focus in.....
- Two related families in Pfam



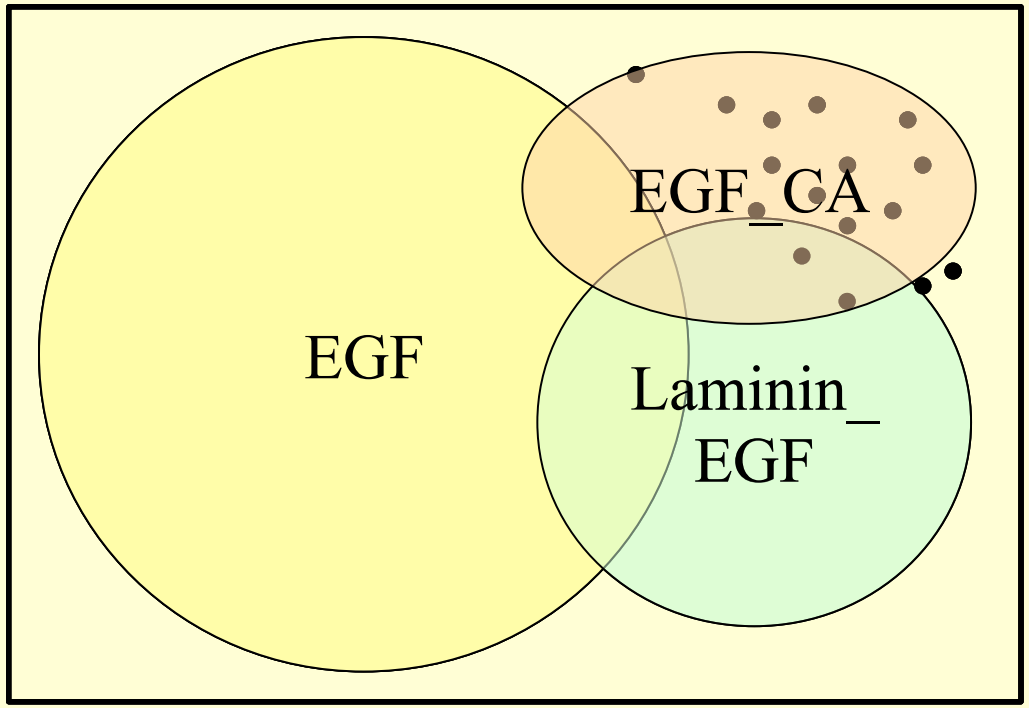
Pfam Clans

- **Two related families in Pfam, but now they overlap**



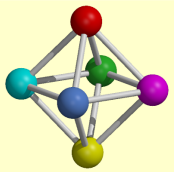
Pfam Clans

- **Add a new family to the Clan to get missing sequences**



Clan Entry Page

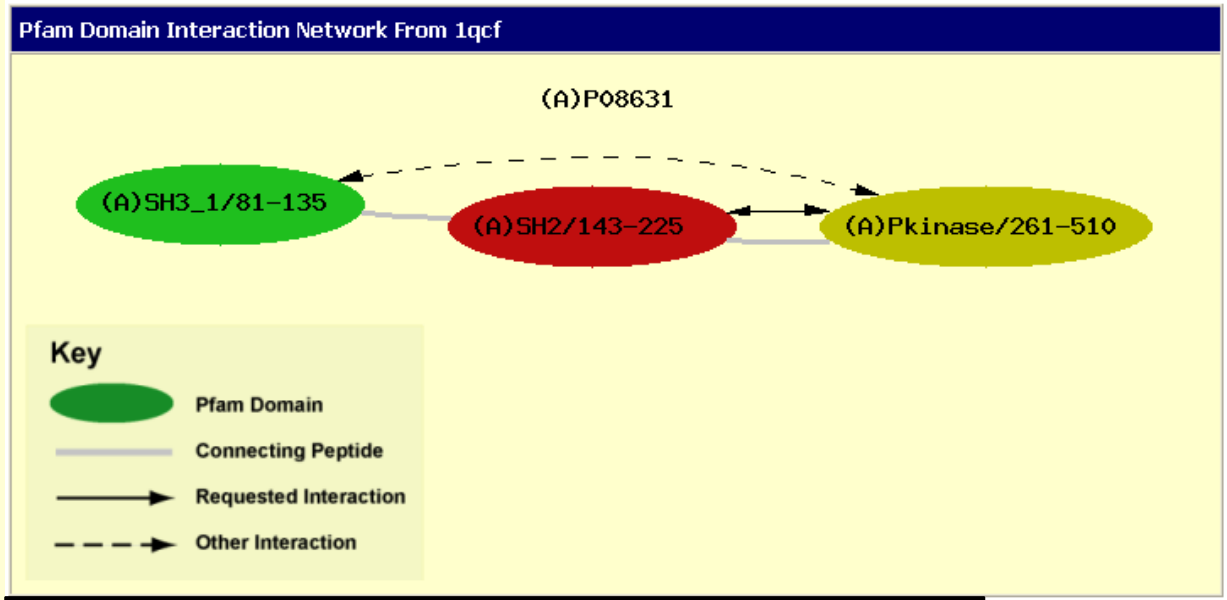
EGF superfamily	
Author:	Finn RD, Bateman A
Comment:	Members of this clan all belong to the EGF superfamily. This particular superfamily is characterised as having least 6 cysteines residues. These cysteine form disulphide bonds, in the order 1-3, 2-4, 5-6, which are essential for the stability of the EGF fold. These disulphide bonds are stacked in a ladder-like arrangement. The Laminin EGF family is distinguished by having an an additional disulphide bond. The function of the domains within this family remains unclear, but they are though to largely perform a structural role. More often than not, there domains are arranged a tandem repeats in extracellular proteins.
Member families:	Laminin_EGF, EGF_CA, EGF
Literature references:	1 Structure and function of epidermal growth factor-like regions in proteins. FEBS Lett 1988;231:1-4. Appella E, Weber IT, Blasi F; 2 Domain structure and organisation in extracellular matrix proteins. Matrix Biol 2002;21:115-128. Hohenester E, Engel J;
Database references:	CATH; SCOP;

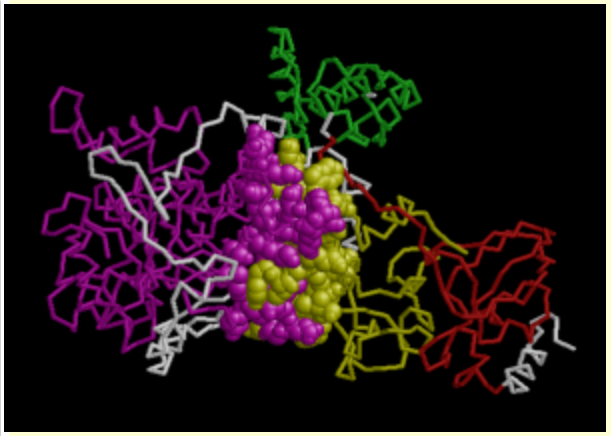


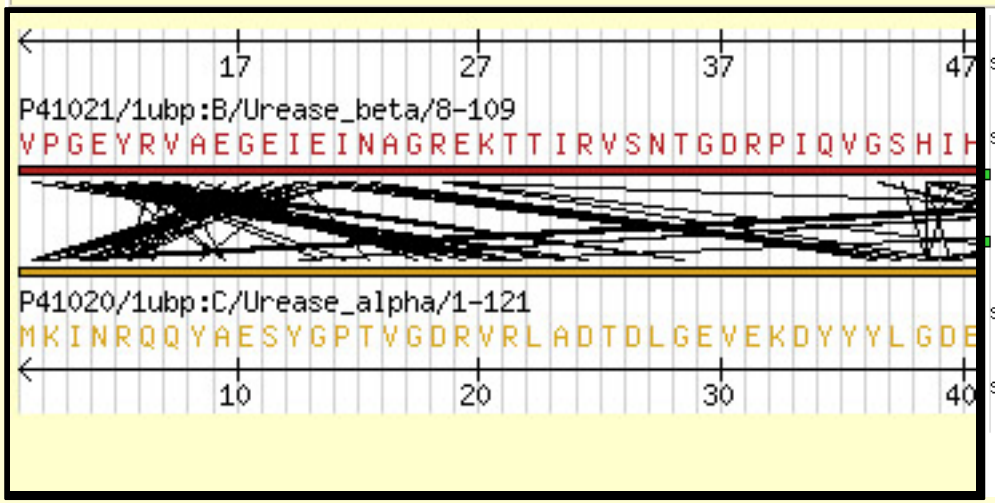
*i*Pfam

- **What is *i*Pfam?**
  - **A database of Pfam domain interactions in known structures**
  - **Interaction information is contained at the level of domains, residues and atoms.**
  - **Information is available from the view point of PDB structure or UniProt Sequence**

iPfam







Further Reading

- Bateman A, Coin L, Durbin R, Finn RD, Hollich V, Griffiths-Jones S, KhannaA, Marshall M, Moxon S, Sonnhammer EL, Studholme DJ, Yeats C, Eddy SR. The Pfam protein families database. Nucleic Acids Res. 2004 Jan 1;32 Database issue:D138-41. PMID: 14681378
- The Pfam website contains many help pages and answers to FAQ
- pfam@sanger.ac.uk - will answer specific queries
- There is a section in Current Protocols in bioinformatics that explains in detail how to use Pfam.
- Biological Sequence Analysis: Probablistic Models of Proteins and Nucleic Acids ~ Richard Durbin, et al
- Stockholm Format - http://www.cgr.ki.se/cgb/groups/sonnhammer/Stockholm.html
- Efamily - http://www.efamily.org.uk

Pfam Practical

Now go to the following page:

http://www.sanger.ac.uk/Users/rdf/EMBO/section1.html