(Aspekte der Thermodynamik in der Strukturbiologie)

Einführung in die Bioinformatik

Wintersemester 2012/13

Peter Güntert

Protein Data Bank (PDB)

Outline

- PDB content overview
- Protein structure classification
- Format and content of PDB entries
- Structure comparison

Protein Data Bank (PDB)

- Contains all publicly available experimentally determined three-dimensional protein structures
- One entry for each structure with an accession code consisting of 1 digit (1–9) and 3 characters (A–Z, 1–9), e.g. 1ABC

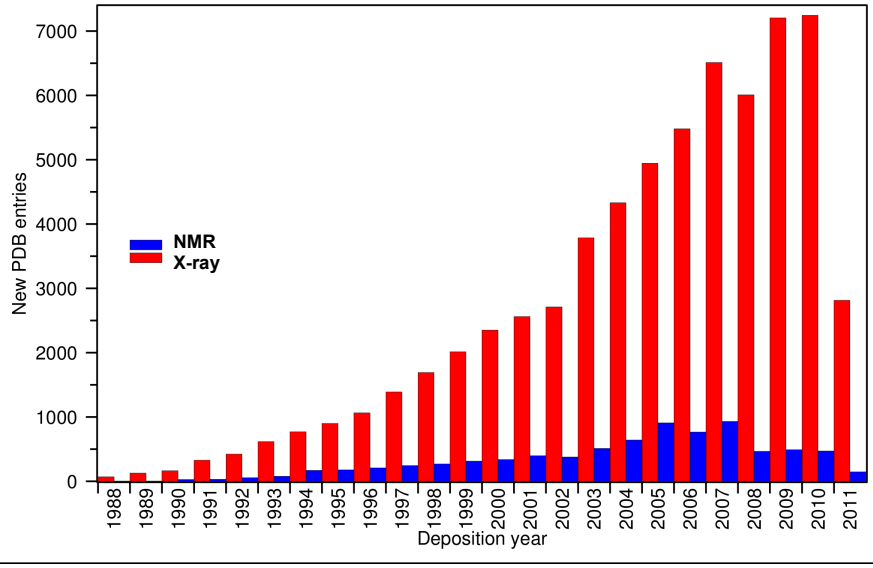
PDB Current Holdings Breakdown 22.01.2013

Exp.Method	Proteins	Nucleic Acids	Protein/NA Complexes	Other	Total
X-RAY	72060	1432	3686	3	77181
NMR	8564	1017	191	7	9779
ELECTRON MICROSCOPY	339	39	123	0	501
HYBRID	45	3	2	1	51
other	147	4	5	13	169
Total	81155	2495	4007	24	87681

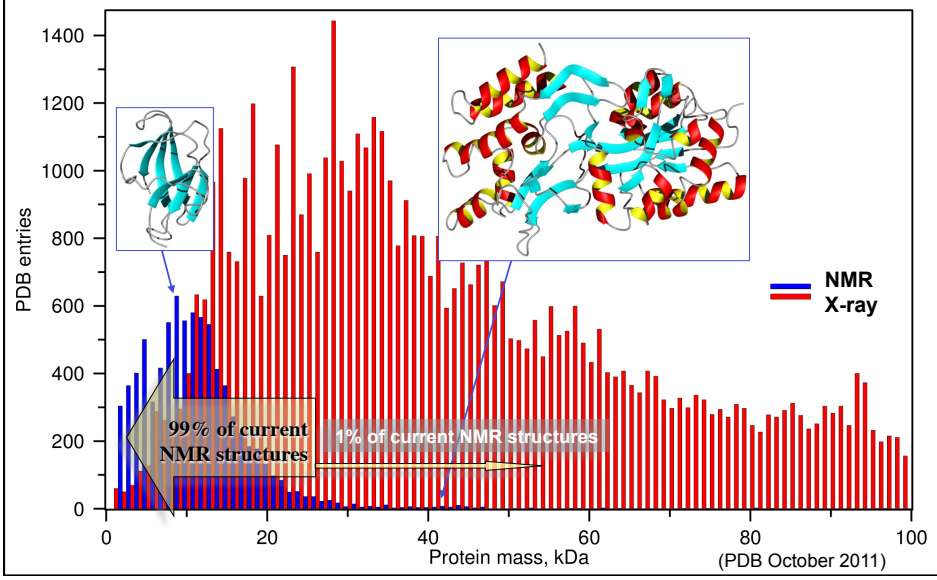
(Click on any number to retrieve the results from that category.)

66634 structures in the PDB have a structure factor file.
7086 structures in the PDB have an NMR restraint file.
844 structures in the PDB have a chemical shifts file.

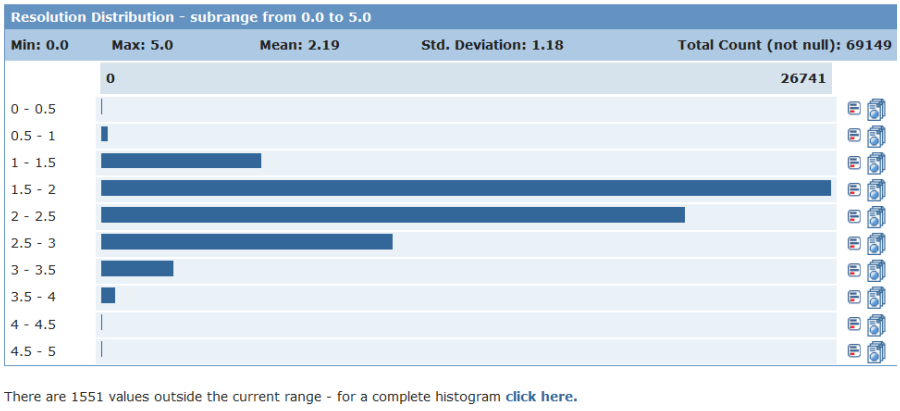
Number of released X-ray and NMR structures in the PDB (October 2011)



Protein structures in the PDB

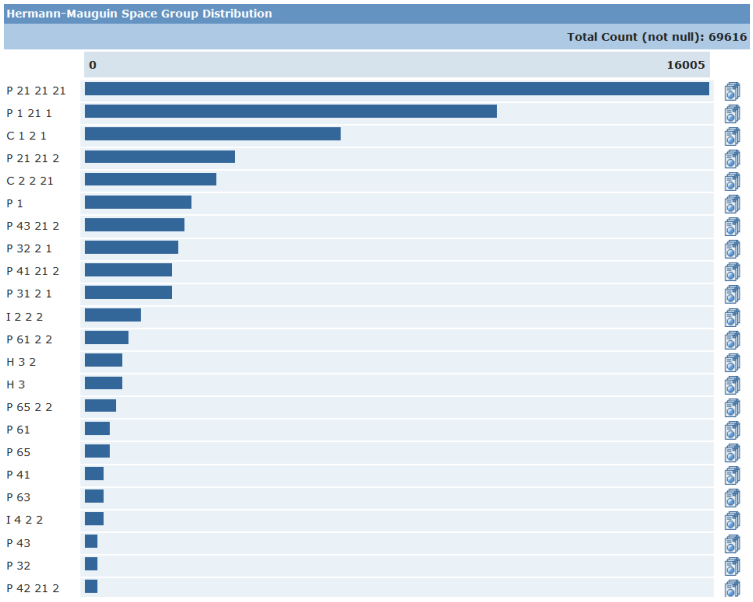


PDB: Resolution distribution

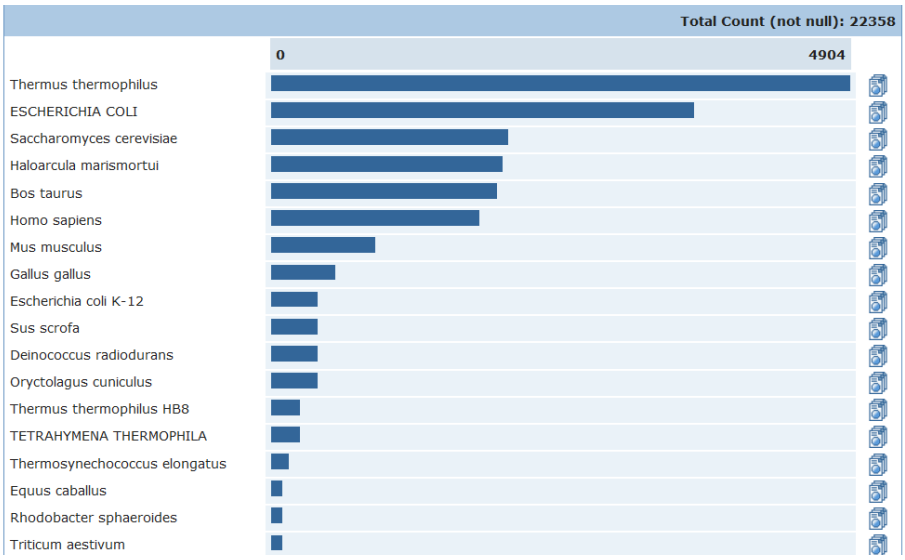


There are 1551 values outside the current range - for a complete histogram **click here.**

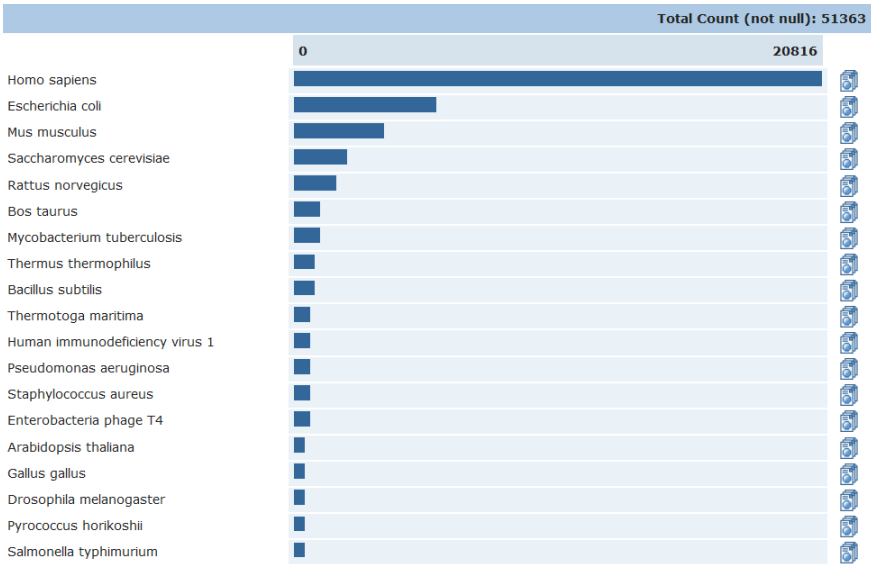
PDB: Distribution by space group



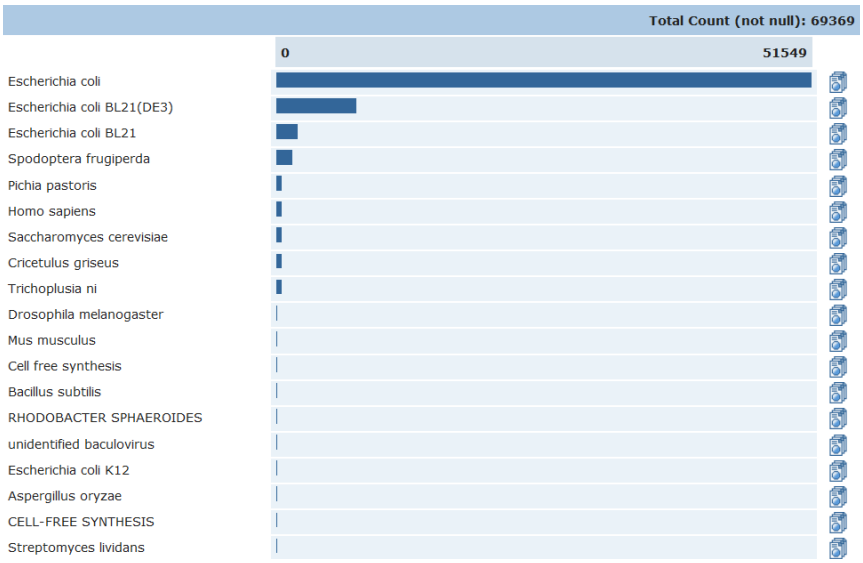
Distribution by natural source organism



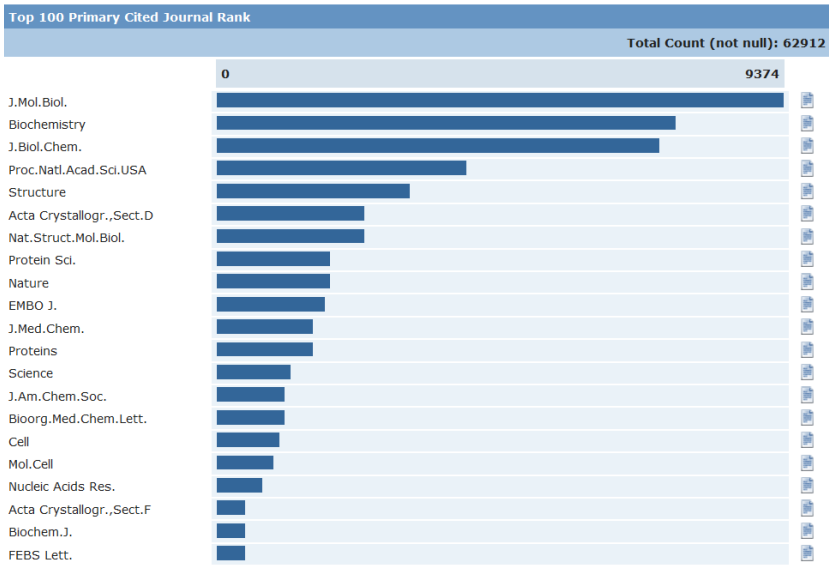
Distribution by gene source organism



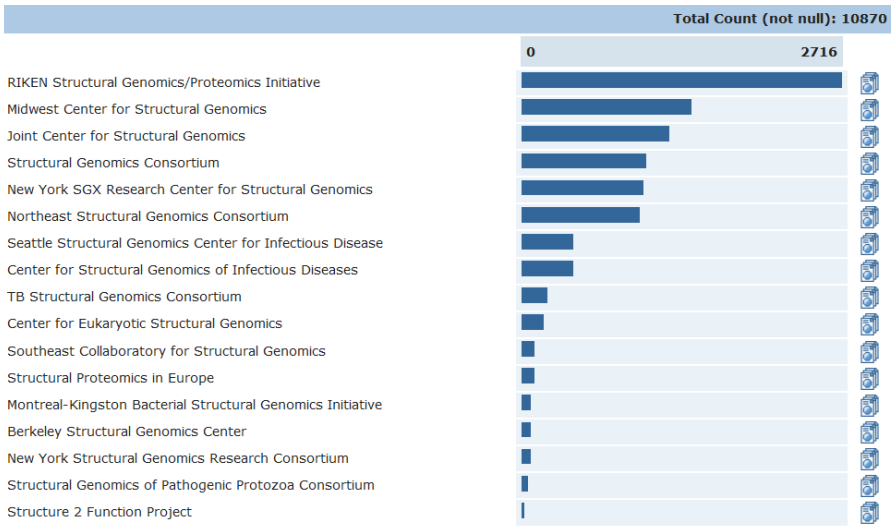
Distribution by expression organism



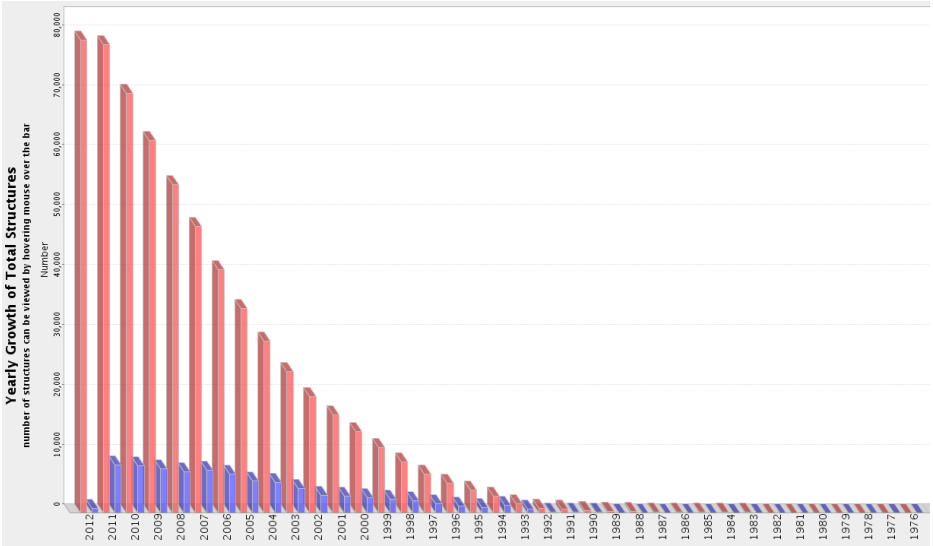
Distribution by primary cited journal



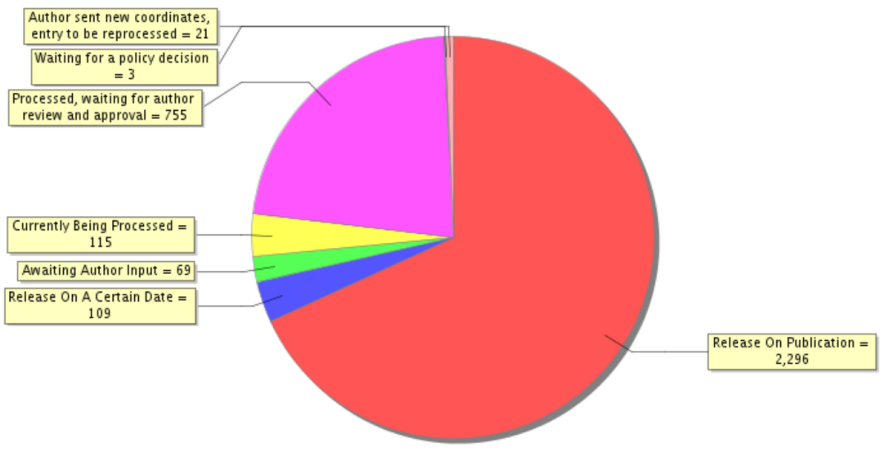
Distribution by structural genomics center



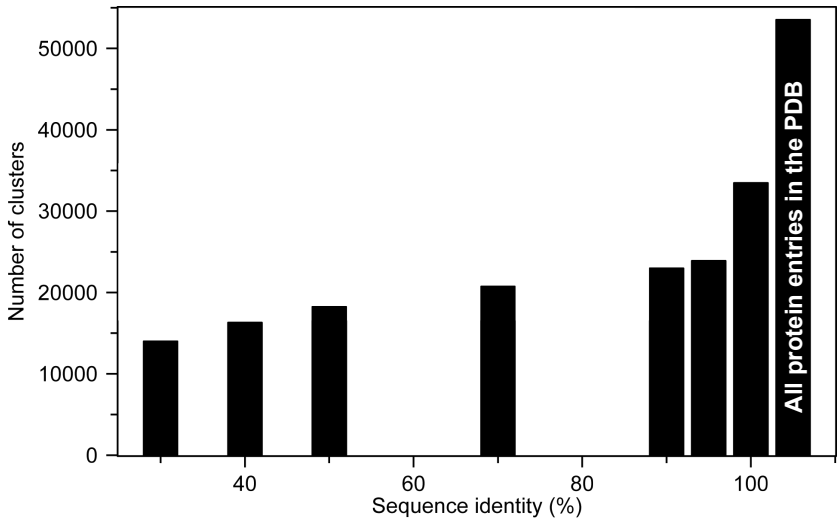
PDB: Total structures



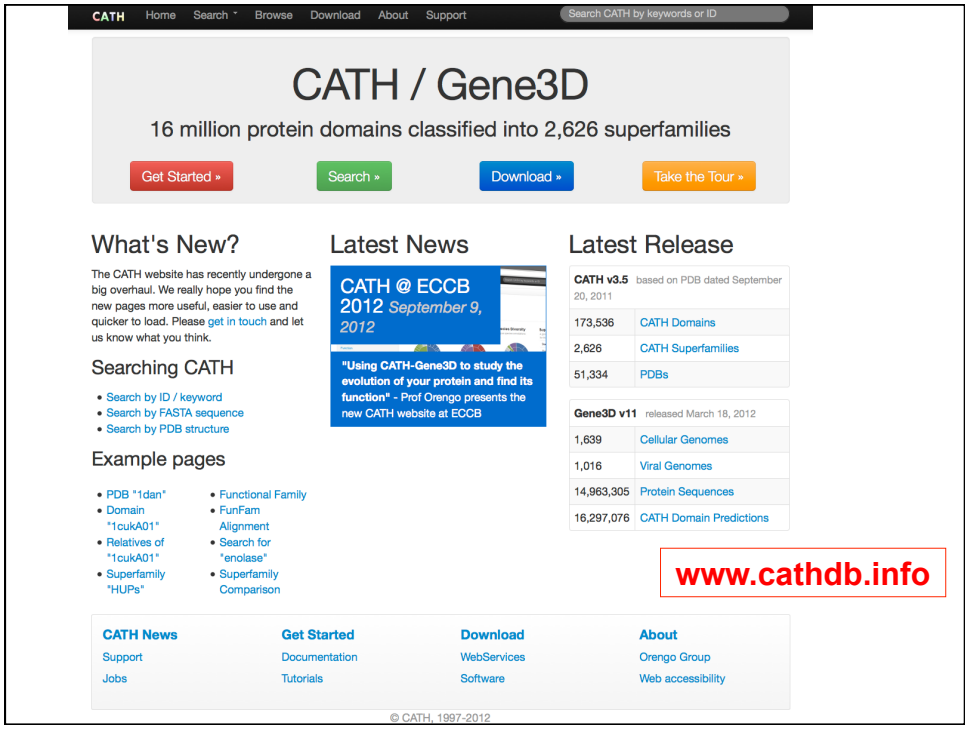
PDB: Status of unreleased entries



PDB redundancy



Structure classification



CATH Protein Structure Classification

- CATH is a manually curated classification of protein domain structures.
- Each protein has been chopped into structural domains and assigned to homologous superfamilies (groups of domains related by evolution).
- This classification procedure uses a combination of automated and manual techniques which include computational algorithms, empirical and statistical evidence, literature review and expert analysis.
- CATH is a tree-like organization of nodes that begins with the class node (i.e. the first branch-point of the tree) and ends with the domain nodes (i.e. the leaves of the tree).
- Each node below the class have a parent that they belong to, e.g. the parent of the **H** level (Homologous superfamily) is the **T** (Topology).
- Additionally, each node above the domains have child nodes that belong to them, e.g. the child nodes of a given **H** (Homologous superfamily) level are the S35 families (domains clustered at > 35% sequence identity).

CATH Hierarchical classification

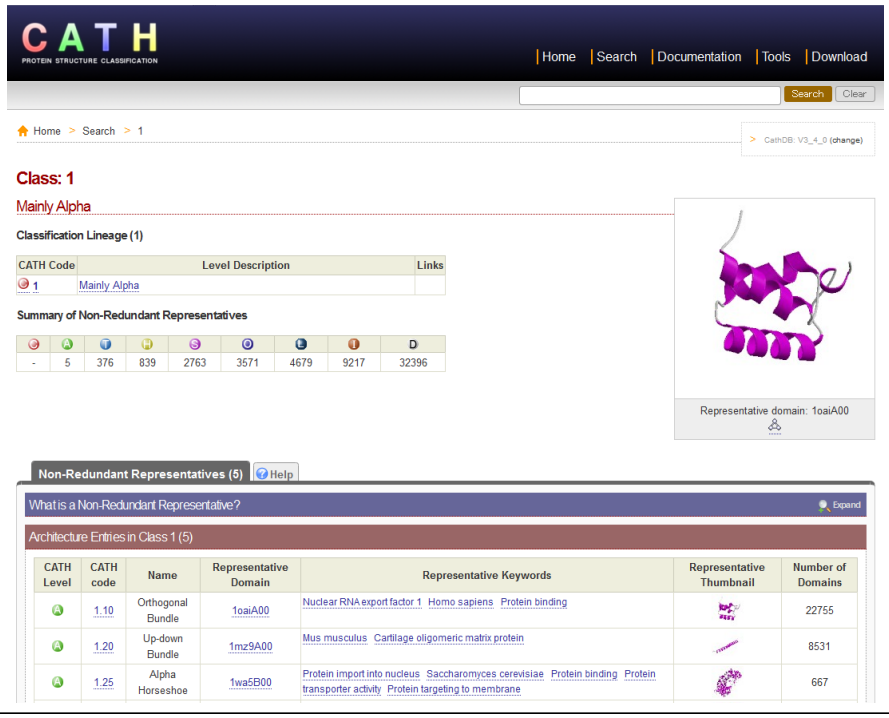
C Class: Class is determined according to the secondary structure composition and packing within the structure. Four major classes are recognized; mainly-alpha, mainly-beta, alpha-beta, and low secondary structure content.

A Architecture: This describes the overall shape of the domain structure as determined by the orientations of the secondary structures but ignores the connectivity between the secondary structures. It is assigned manually using a simple description of the secondary structure arrangement e.g. barrel or 3-layer sandwich. Reference is made to the literature for well-known architectures (e.g the β-propeller or α four helix bundle).

T Topology (Fold family): Structures are grouped according to whether they share the same topology or fold in the core of the domain, that is, if they share the same overall shape and connectivity of the secondary structures in the domain core. Domains in the same fold group may have different structural decorations to the common core.

H Homologous Superfamily, H-level: This level groups together protein domains which are thought to share a common ancestor and can therefore be described as homologous. Similarities are identified either by high sequence identity or structure comparison using SSAP.

S, O, L, I, D Sequence Family Levels: Domains within each H-level are subclustered into sequence families using multi-linkage clustering at S = 35, O = 60, L = 95, and I = 100% sequence identity levels. The D-level acts as a counter within each S100 family.



SCOP Structural Classification of Proteins

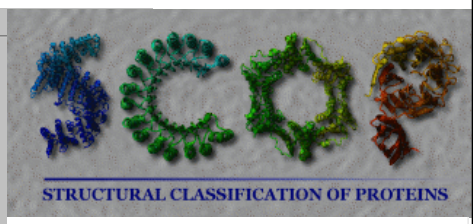
Structural Classification of Proteins

Root: scop

Classes:

1. All alpha proteins [46456] (284)
2. All beta proteins [48724] (174)
3. Alpha and beta proteins (a/b) [51349] (147)
   Mainly parallel beta sheets (beta-alpha-beta units)
4. Alpha and beta proteins (a+b) [53931] (376)
   Mainly antiparallel beta sheets (segregated alpha and beta regions)
5. Multi-domain proteins (alpha and beta) [56572] (66)
   Folds consisting of two or more domains belonging to different classes
6. Membrane and cell surface proteins and peptides [56835] (58)
   Does not include proteins in the immune system
7. Small proteins [56992] (90)
   Usually dominated by metal ligand, heme, and/or disulfide bridges
8. Coiled coil proteins [57942] (7)
   Not a true class
9. Low resolution protein structures [58117] (26)
   Not a true class
10. Peptides [58231] (121)
    Peptides and fragments. Not a true class
11. Designed proteins [58788] (44)
    Experimental structures of proteins with essentially non-natural sequences. Not a true class

Enter search key: 4pti Search



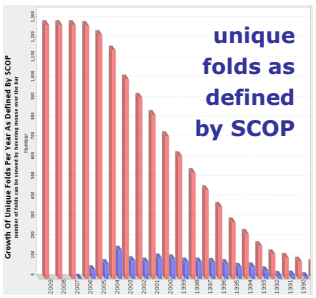
Scop Classification Statistics

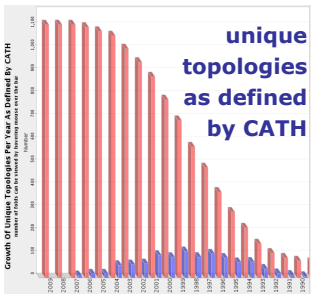
SCOP: Structural Classification of Proteins. **1.75** release
38221 PDB Entries (23 Feb 2009). 110800 Domains. 1 Literature Reference
(excluding nucleic acids and theoretical models)

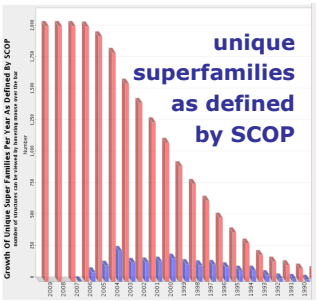
Class	Number of folds	Number of superfamilies	Number of families
All alpha proteins	284	507	871
All beta proteins	174	354	742
Alpha and beta proteins (a/b)	147	244	803
Alpha and beta proteins (a+b)	376	552	1055
Multi-domain proteins	66	66	89
Membrane and cell surface proteins	58	110	123
Small proteins	90	129	219
Total	1195	1962	3902

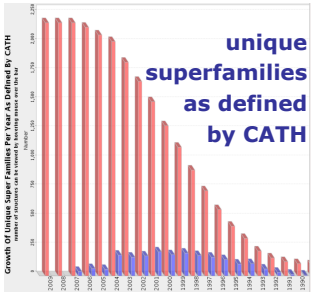
http://scop.mrc-lmb.cam.ac.uk/scop

New folds in the PDB

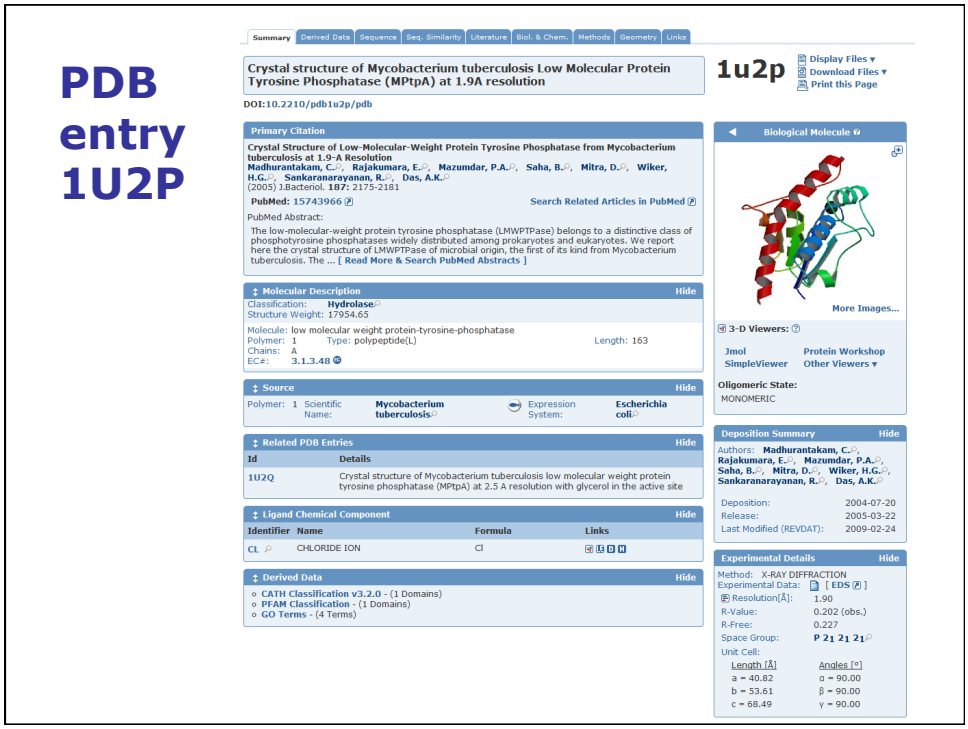


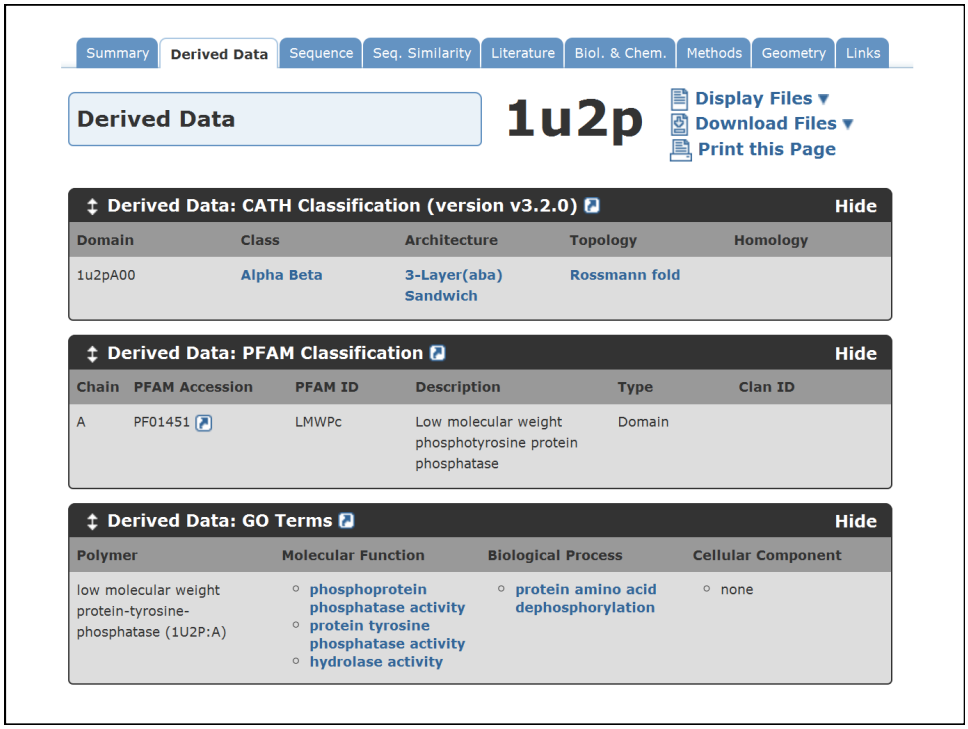


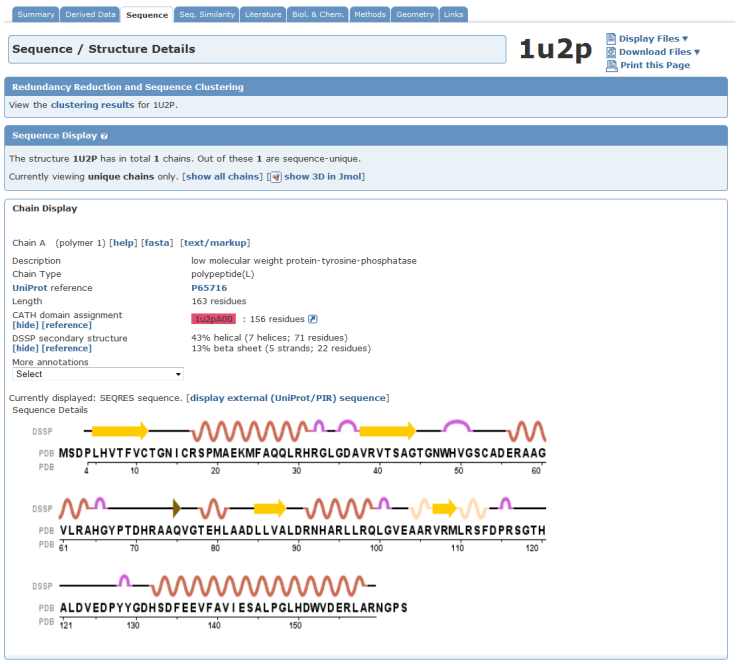




PDB entry 1U2P







PDB entry 1U2P: Header, source

```
HEADER    HYDROLASE                               20-JUL-04   1U2P
TITLE     CRYSTAL STRUCTURE OF MYCOBACTERIUM TUBERCULOSIS LOW
TITLE    2 MOLECULAR PROTEIN TYROSINE PHOSPHATASE (MPTPA) AT 1.9A
TITLE    3 RESOLUTION
COMPND    MOL_ID: 1;
COMPND   2 MOLECULE: LOW MOLECULAR WEIGHT PROTEIN-TYROSINE-
COMPND   3 PHOSPHATASE;
COMPND   4 CHAIN: A;
COMPND   5 SYNONYM: PTPASE;
COMPND   6 EC: 3.1.3.48;
COMPND   7 ENGINEERED: YES
SOURCE    MOL_ID: 1;
SOURCE   2 ORGANISM_SCIENTIFIC: MYCOBACTERIUM TUBERCULOSIS;
SOURCE   3 ORGANISM_TAXID: 1773;
SOURCE   4 GENE: MPTPA;
SOURCE   5 EXPRESSION_SYSTEM: ESCHERICHIA COLI;
SOURCE   6 EXPRESSION_SYSTEM_TAXID: 562;
SOURCE   7 EXPRESSION_SYSTEM_STRAIN: SG13009;
SOURCE   8 EXPRESSION_SYSTEM_VECTOR_TYPE: PLASMID;
SOURCE   9 EXPRESSION_SYSTEM_PLASMID: PQE30
KEYWDS    HYDROLASE, TYROSINE PHOSPHATASE, MYCOBACTERIUM
```

PDB entry 1U2P: Authors

```
EXPDTA    X-RAY DIFFRACTION
AUTHOR    C.MADHURANTAKAM,E.RAJAKUMARA,P.A.MAZUMDAR,B.SAHA,D.MITRA,
AUTHOR   2 H.G.WIKER,R.SANKARANARAYANAN,A.K.DAS
REVDAT   2   24-FEB-09 1U2P    1       VERSN
REVDAT   1   22-MAR-05 1U2P    0
JRNL        AUTH   C.MADHURANTAKAM,E.RAJAKUMARA,P.A.MAZUMDAR,B.SAHA,
JRNL        AUTH 2 D.MITRA,H.G.WIKER,R.SANKARANARAYANAN,A.K.DAS
JRNL        TITL   CRYSTAL STRUCTURE OF LOW-MOLECULAR-WEIGHT PROTEIN
JRNL        TITL 2 TYROSINE PHOSPHATASE FROM MYCOBACTERIUM
JRNL        TITL 3 TUBERCULOSIS AT 1.9-A RESOLUTION
JRNL        REF    J.BACTERIOL.                  V. 187  2175 2005
JRNL        REFN                   ISSN 0021-9193
JRNL        PMID   15743966
JRNL        DOI    10.1128/JB.187.6.2175-2181.2005
REMARK   1
REMARK   2
REMARK   2 RESOLUTION.    1.90 ANGSTROMS.
REMARK   3
REMARK   3 REFINEMENT.
REMARK   3   PROGRAM     : CNS 1.1
REMARK   3   AUTHORS     : BRUNGER,ADAMS,CLORE,DELANO,GROS,GROSSE-
REMARK   3               : KUNSTLEVE,JIANG,KUSZEWSKI,NILGES, PANNU,
REMARK   3               : READ,RICE,SIMONSON,WARREN
```

PDB entry 1U2P: Refinement

```
REMARK   2 RESOLUTION.    1.90 ANGSTROMS.
REMARK   3
REMARK   3 REFINEMENT.
REMARK   3   PROGRAM     : CNS 1.1
REMARK   3   AUTHORS     : BRUNGER,ADAMS,CLORE,DELANO,GROS,GROSSE-
REMARK   3               : KUNSTLEVE,JIANG,KUSZEWSKI,NILGES, PANNU,
REMARK   3               : READ,RICE,SIMONSON,WARREN
REMARK   3
REMARK   3  REFINEMENT TARGET : ENGH & HUBER
REMARK   3
REMARK   3  DATA USED IN REFINEMENT.
REMARK   3   RESOLUTION RANGE HIGH (ANGSTROMS) : 1.90
REMARK   3   RESOLUTION RANGE LOW  (ANGSTROMS) : 24.96
REMARK   3   DATA CUTOFF            (SIGMA(F)) : 0.000
REMARK   3   DATA CUTOFF HIGH         (ABS(F)) : 1161871.740
REMARK   3   DATA CUTOFF LOW          (ABS(F)) : 0.0000
REMARK   3   COMPLETENESS (WORKING+TEST)   (%) : 99.6
REMARK   3   NUMBER OF REFLECTIONS             : 12309
REMARK   3
REMARK   3  FIT TO DATA USED IN REFINEMENT.
REMARK   3   CROSS-VALIDATION METHOD          : THROUGHOUT
REMARK   3   FREE R VALUE TEST SET SELECTION  : RANDOM
REMARK   3   R VALUE            (WORKING SET) : 0.202
REMARK   3   FREE R VALUE                     : 0.227
REMARK   3   FREE R VALUE TEST SET SIZE   (%) : 5.000
REMARK   3   FREE R VALUE TEST SET COUNT      : 616
REMARK   3   ESTIMATED ERROR OF FREE R VALUE  : 0.009
```

PDB entry 1U2P: Missing residues

```
REMARK 465 MISSING RESIDUES
REMARK 465 THE FOLLOWING RESIDUES WERE NOT LOCATED IN THE
REMARK 465 EXPERIMENT. (M=MODEL NUMBER; RES=RESIDUE NAME; C=CHAIN
REMARK 465 IDENTIFIER; SSSEQ=SEQUENCE NUMBER; I=INSERTION CODE.)
REMARK 465
REMARK 465   M RES C SSSEQI
REMARK 465     MET A     1
REMARK 465     SER A     2
REMARK 465     ASP A     3
REMARK 465     ASN A   160
REMARK 465     GLY A   161
REMARK 465     PRO A   162
REMARK 465     SER A   163
```

PDB entry 1U2P: Ramachandran plot outliers

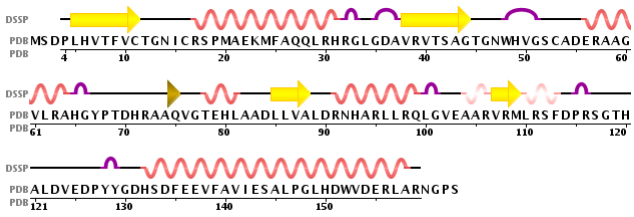
```
REMARK 500 GEOMETRY AND STEREOCHEMISTRY
REMARK 500 SUBTOPIC: TORSION ANGLES
REMARK 500
REMARK 500 TORSION ANGLES OUTSIDE THE EXPECTED RAMACHANDRAN REGIONS:
REMARK 500 (M=MODEL NUMBER; RES=RESIDUE NAME; C=CHAIN IDENTIFIER;
REMARK 500 SSEQ=SEQUENCE NUMBER; I=INSERTION CODE).
REMARK 500
REMARK 500 STANDARD TABLE:
REMARK 500 FORMAT:(10X,I3,1X,A3,1X,A1,I4,A1,4X,F7.2,3X,F7.2)
REMARK 500
REMARK 500 EXPECTED VALUES: GJ KLEYWEGT AND TA JONES (1996). PHI/PSI-
REMARK 500 CHOLOGY: RAMACHANDRAN REVISITED. STRUCTURE 4, 1395 - 1400
REMARK 500
REMARK 500  M RES CSSEQI        PSI       PHI
REMARK 500    CYS A  16      -83.04   -122.74
```

PDB entry 1U2P: Sequence

```
DBREF  1U2P A    1   163  UNP    P65716   PTPA_MYCTU       1    163
SEQRES   1 A  163  MET SER ASP PRO LEU HIS VAL THR PHE VAL CYS THR GLY
SEQRES   2 A  163  ASN ILE CYS ARG SER PRO MET ALA GLU LYS MET PHE ALA
SEQRES   3 A  163  GLN GLN LEU ARG HIS ARG GLY LEU GLY ASP ALA VAL ARG
SEQRES   4 A  163  VAL THR SER ALA GLY THR GLY ASN TRP HIS VAL GLY SER
SEQRES   5 A  163  CYS ALA ASP GLU ARG ALA ALA GLY VAL LEU ARG ALA HIS
SEQRES   6 A  163  GLY TYR PRO THR ASP HIS ARG ALA ALA GLN VAL GLY THR
SEQRES   7 A  163  GLU HIS LEU ALA ALA ASP LEU LEU VAL ALA LEU ASP ARG
SEQRES   8 A  163  ASN HIS ALA ARG LEU LEU ARG GLN LEU GLY VAL GLU ALA
SEQRES   9 A  163  ALA ARG VAL ARG MET LEU ARG SER PHE ASP PRO ARG SER
SEQRES  10 A  163  GLY THR HIS ALA LEU ASP VAL GLU ASP PRO TYR TYR GLY
SEQRES  11 A  163  ASP HIS SER ASP PHE GLU GLU VAL PHE ALA VAL ILE GLU
SEQRES  12 A  163  SER ALA LEU PRO GLY LEU HIS ASP TRP VAL ASP GLU ARG
SEQRES  13 A  163  LEU ALA ARG ASN GLY PRO SER
HET     CL  A 164       1
HETNAM      CL CHLORIDE ION
FORMUL   2   CL    CL 1-
FORMUL   3  HOH   *152(H2 O)
```

PDB entry 1U2P: Secondary structure

```
HELIX    1   1 CYS A   16  ARG A   32  1                                  17
HELIX    2   2 ASP A   55  HIS A   65  1                                  11
HELIX    3   3 GLY A   77  ALA A   82  1                                   6
HELIX    4   4 ASP A   90  LEU A  100  1                                  11
HELIX    5   5 GLU A  103  ALA A  105  5                                   3
HELIX    6   6 ARG A  111  ASP A  114  5                                   4
HELIX    7   7 ASP A  131  ARG A  159  1                                  29
SHEET    1   A 4 VAL A  38  GLY A  44  0
SHEET    2   A 4 LEU A   5  CYS A  11  1  N  LEU A   5   O  ARG A  39
SHEET    3   A 4 LEU A  85  ALA A  88  1  O  VAL A  87   N  THR A   8
SHEET    4   A 4 VAL A 107  MET A 109  1  O  ARG A 108   N  LEU A  86
SITE     1 AC1  4 THR A  12  GLY A  13  ARG A  17  HOH A 171
```



Secondary structure assignment: DSSP algorithm

Kabsch, W., Sander, C. *Biopolymers* 22, 2577–2637 (1983)

The definitions of H-bonded features form a hierarchy:

1.H-bonds are defined.
2.Based on them, turns and bridges.
3.Based on them, α-helices and β-ladders, including common imperfections such as helical kinks and β-bulges.

Each structural feature is defined independently of the others and structural overlaps are resolved by defining a secondary structure summary that assigns a single state to each residue.

DSSP-Algorithm: H-bonds

Hydrogen bonds in proteins have little wave-function overlap and are well described by an electrostatic model. We calculate the electrostatic interaction energy between two H-bonding groups by placing partial charges on the C,O *($+q_1$, $-q_1$) and N,H ($-q_2$,$+q_2$) atoms, i.e.,*

$$E = q_1 q_2 (1/r(\mathrm{ON}) + 1/r(\mathrm{CH}) - 1/r(\mathrm{OH}) - 1/r(\mathrm{CN}))*f$$

with q_1 = *0.42e and* q_2 = *0.20e,* e being the unit electron charge and *r*(AB) the interatomic distance from A to B. In chemical units, *r* is in Å, the dimensional factor *f* = 332, and *E* is in kcal/mol. A good H bond has about -3 kcal/mol binding energy. We choose a generous cutoff to allow for bifurcated H bonds and errors in coordinates and assign an H bond between C=O of residue *i* and N-H of residue *j* if *E* is less than the cutoff, i.e.,

"Hbond(ij)=: [E < -0.5kcal/mole]."

PDB entry 1U2P: Crystal data

```
CRYST1   40.816   53.610   68.486  90.00  90.00  90.00 P 21 21 21    4
ORIGX1      1.000000  0.000000  0.000000        0.00000
ORIGX2      0.000000  1.000000  0.000000        0.00000
ORIGX3      0.000000  0.000000  1.000000        0.00000
SCALE1      0.024500  0.000000  0.000000        0.00000
SCALE2      0.000000  0.018653  0.000000        0.00000
SCALE3      0.000000  0.000000  0.014602        0.00000
```

Experimental Details Hide

Method: X-RAY DIFFRACTION
Exp. Data:
Structure Factors
EDS
Resolution[Å]: 1.90
R-Value: 0.202 (obs.)
R-Free: 0.227
Space Group: P 21 21 21
Unit Cell:

Length [Å]	Angles [°]
a = 40.82	α = 90.00
b = 53.61	β = 90.00
c = 68.49	γ = 90.00

PDB entry 1U2P: Coordinates

```
ATOM      1  N   PRO A   4       6.719 -12.134  26.603  1.00 18.91      N
ATOM      2  CA  PRO A   4       6.735 -10.746  27.122  1.00 18.45      C
ATOM      3  C   PRO A   4       6.209  -9.735  26.108  1.00 16.72      C
ATOM      4  O   PRO A   4       6.701  -9.658  24.983  1.00 16.64      O
ATOM      5  CB  PRO A   4       8.174 -10.427  27.495  1.00 20.82      C
ATOM      6  CG  PRO A   4       8.942 -11.387  26.584  1.00 20.17      C
ATOM      7  CD  PRO A   4       8.093 -12.664  26.557  1.00 22.00      C
ATOM      8  N   LEU A   5       5.207  -8.963  26.521  1.00 16.15      N
ATOM      9  CA  LEU A   5       4.605  -7.937  25.674  1.00 14.51      C
ATOM     10  C   LEU A   5       5.700  -6.960  25.244  1.00 14.38      C
ATOM     11  O   LEU A   5       6.564  -6.600  26.042  1.00 15.34      O
ATOM     12  CB  LEU A   5       3.513  -7.204  26.458  1.00 13.81      C
ATOM     13  CG  LEU A   5       2.639  -6.180  25.737  1.00 14.69      C
ATOM     14  CD1 LEU A   5       1.815  -6.864  24.656  1.00 15.29      C
ATOM     15  CD2 LEU A   5       1.725  -5.506  26.754  1.00 15.24      C
```

Keyword | Atom index | Atom name | Residue name | Chain identifier | Residue number | *x* coordinate | *y* coordinate | *z* coordinate | Occupancy | *B*-factor | Element

Unterlagen zur Vorlesung

http://www.bpc.uni-frankfurt.de/guentert/wiki/index.php/Teaching