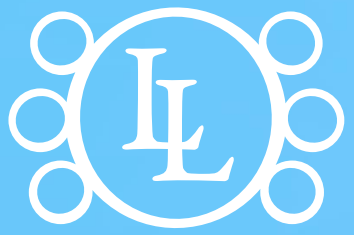


LOSCHMIDT
LABORATORIES

Protein folding, stability and dynamics

Outline

- Revisions
- Protein folding
- Protein stability
- Protein dynamics

Revisions: molecular interactions

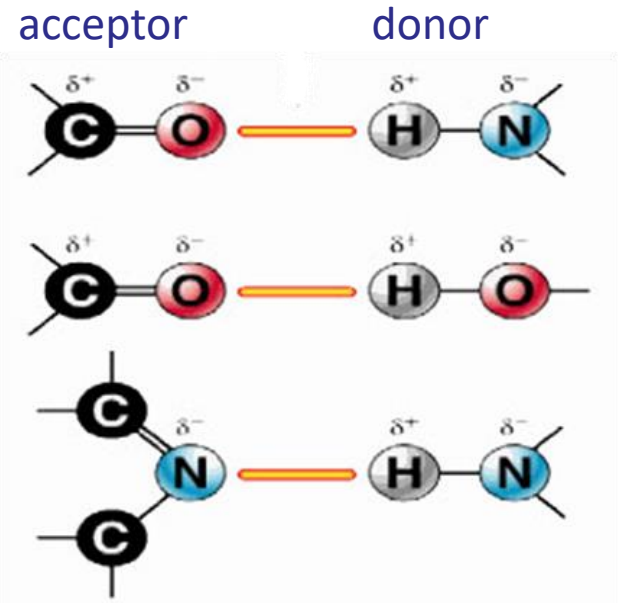
- Covalent interactions
  - sharing of electrons
  - under standard condition – very stable
  - primary structure of proteins
- Non-covalent (weak) interactions
  - electrostatic interactions
  - polar interactions
  - non-polar interactions
  - secondary, tertiary and quaternary structure of proteins

Revisions: electrostatic interactions

- Charge-charge interactions
  - charged residues – Arg, Lys, Glu, Asp and His (low pH)
  - long-range interaction – decrease with r^2
  - environment dependent
    - permitivity (ε):
      - 1 – vacuum
      - 2-20 – interior of proteins, membranes
      - 80 – bulk water -> water shields the chares form each others
    - salt concentration – counter ions close to charged residues
    - pH – change in charge of molecule (His)

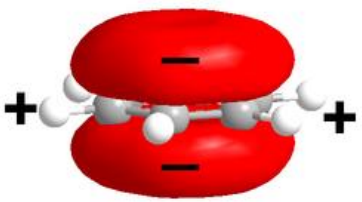
Revisions: polar interactions

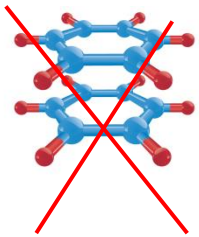
- Hydrogen bonds (H-bonds)
  - donor and acceptor atoms sharing hydrogen
  - polar residues – Ser, Thr, Asn, Gln, Cys, Trp, Tyr and His (high pH)
  - charged residues – Arg, Lys, Glu, Asp and His (low pH)
  - governs formation of secondary structure
  - H-bond distance: 2.8-3.4 Å



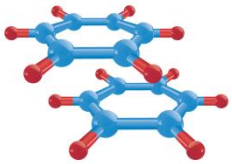
Revisions: polar interactions

- Aromatic (π-π) interactions
  - attractive interaction between aromatic rings
  - aromatic residues – Phe, Trp, Tyr and His
  - distance of centre of mass – about 5 Å

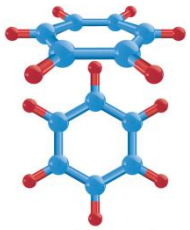




sandwich



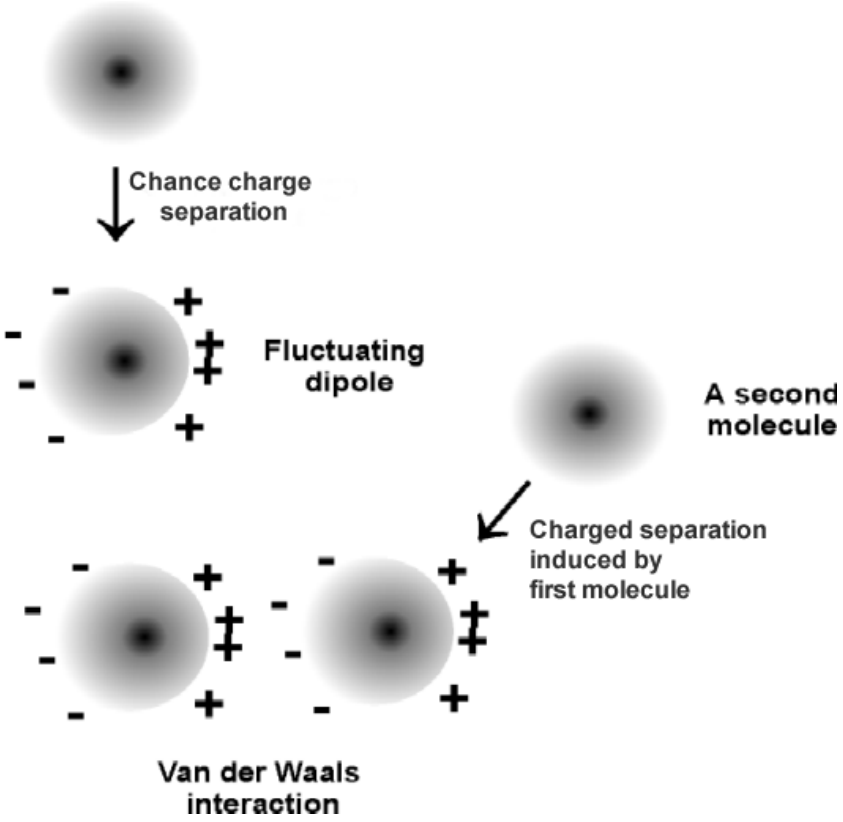
parallel displaced



T-shaped

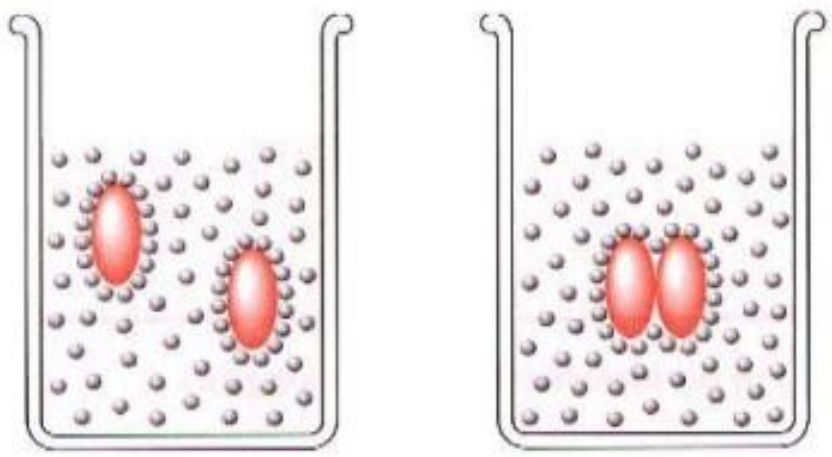
Revisions: non-polar interactions

- van der Waals (vdW) interactions
  - between any two atoms -> all residues
  - short-range interactions
  - negligible beyond 5 Å
  - tertiary structure



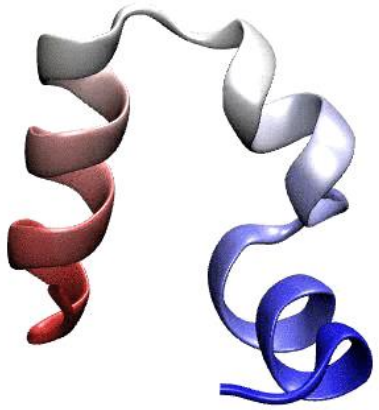
Revisions: non-polar interactions

- Hydrophobic interactions
  - hydrophobic residues – Phe, Pro, Met, Leu, Ile, Val, Ala, and possibly also Tyr and Trp
  - entropic origin – water molecules ordered around hydrophobic residues -> unfavorable
  - hydrophobic packing -> release of some ordered water -> favorable increase of entropy
  - tertiary structure



Protein folding

- Levinthal's paradox
- Anfinsen's thermodynamic hypothesis
- Mechanisms of protein folding
- Energetics of protein folding
- Database of protein folding



0.0 ns

Levinthal's paradox

- **Cyrus Levinthal**
  - 1968 – impossibility of random folding
  - random folding
    - 100 residue protein (average sized)
    - 3 conformation per residue (many more)
    - 0.1 ps sampling time per conformation (much longer)
    - folding time = $3^{100}*10^{-13}$ s ≈ $5*10^{34}$ s ≈
    - 1 634 251 397 552 039 990 billions of years
- **Experimental folding rates**
  - 1 ms to 10 min

Anfinsen's thermodynamic hypothesis

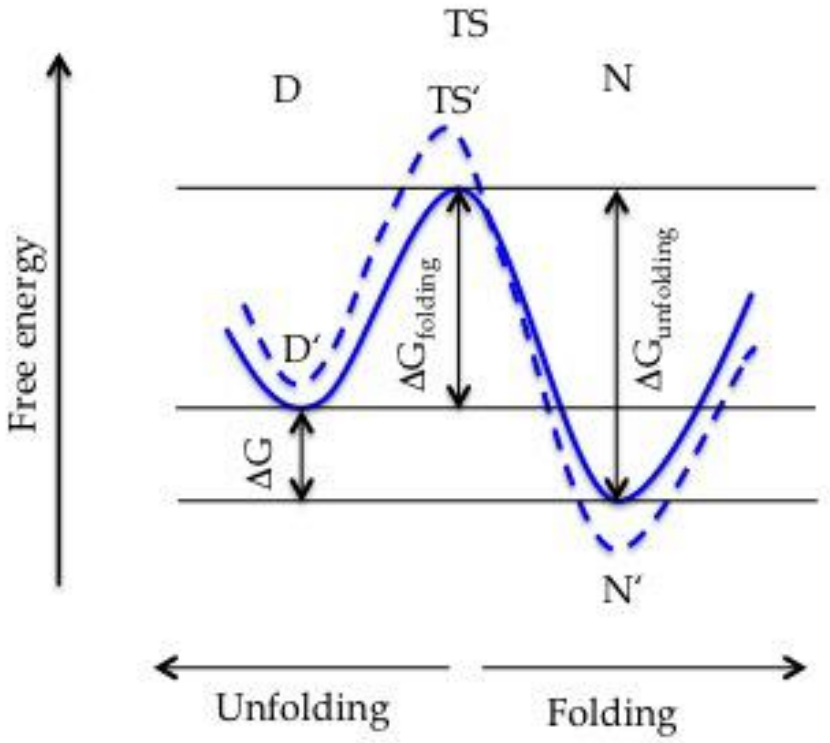
- **Christian Anfinsen**
  - 1973 – protein folding *in vitro*
  - refolding of ribonuclease

- **Findings**
  - native structure of a protein is the thermodynamically stable structure
  - folding depends only on the amino acid sequence and on the conditions of solution, and not on the kinetic folding route

Thermodynamic and kinetic stability

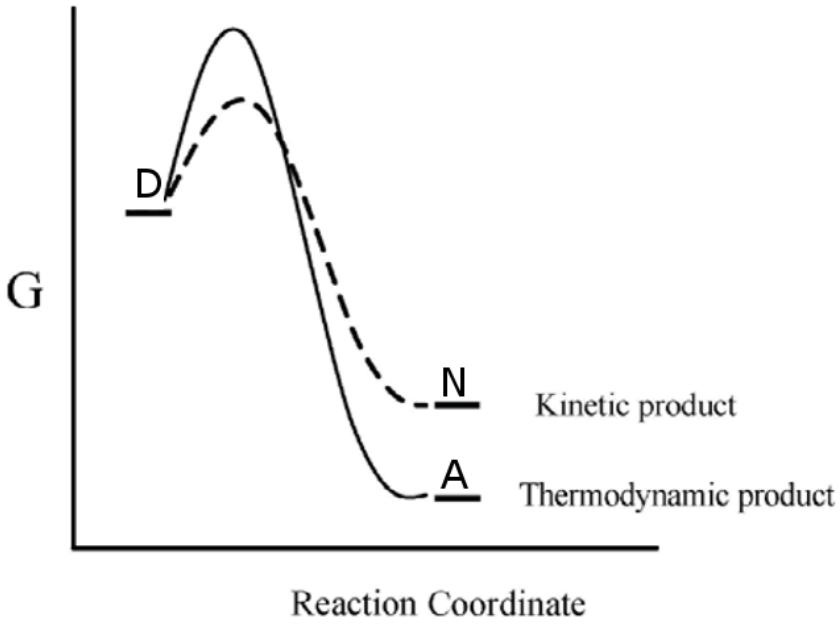
Thermodynamic stability

$$Native \overset{K_{eq}}{\longleftrightarrow} Denatured$$

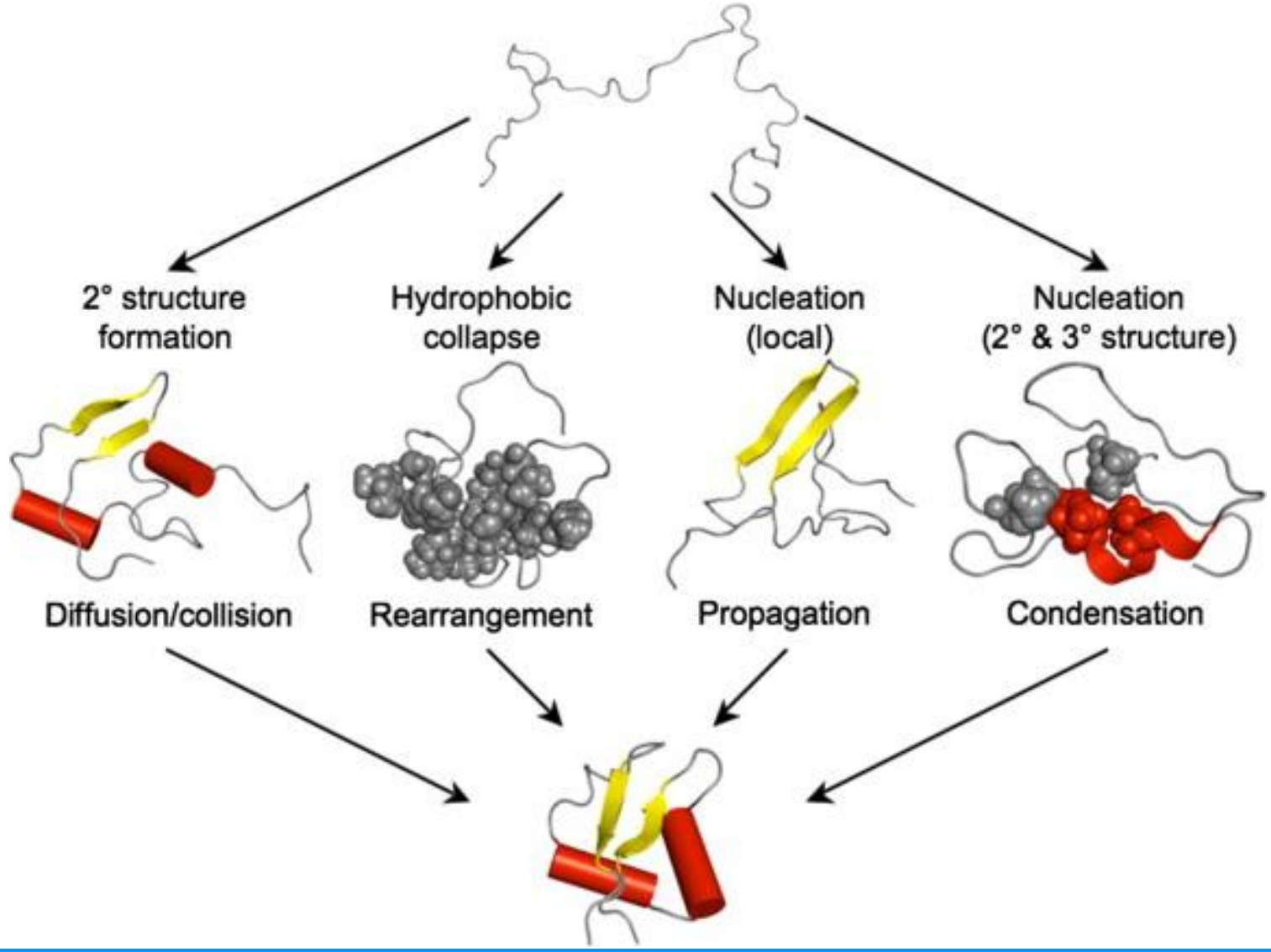


Kinetic stability

$$Native \overset{k}{\rightarrow} Denatured$$



Mechanisms of protein folding



Mechanisms of protein folding

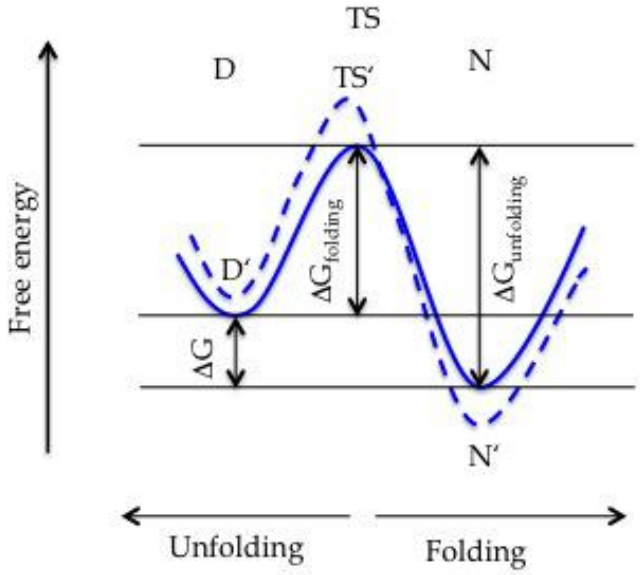
- **Nucleation-growth (propagation) model**
  - continuous growth of tertiary structure from initial nucleus of local secondary structure
  - it did not account for folding intermediates -> model dismissed

Mechanisms of protein folding

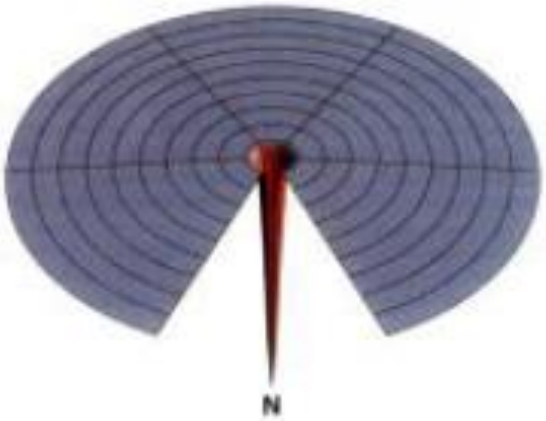
- **Framework model**
  - secondary structure folds first -> coalescence of secondary structural units to the native protein
- **Hydrophobic collapse model**
  - compaction of the protein -> folding in a confined volume -> narrowing the conformational search to the native state
- **Nucleation-condensation model**
  - concerted & cooperative secondary and tertiary structure formation
  - transition state resembles distorted form of the native structure
  - the least distorted part called folding nucleus or molten globule

Energetics of protein folding

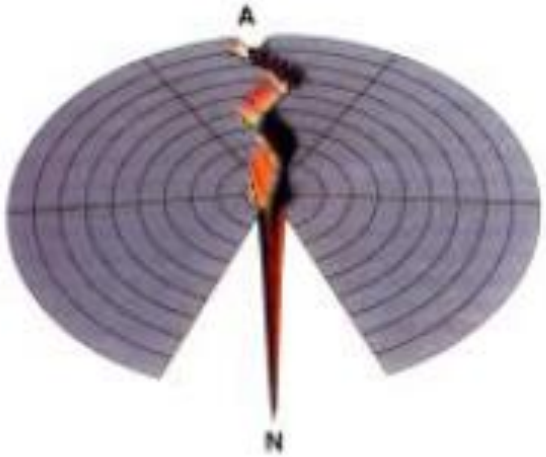
- **Free energy of folding** ($\Delta G_{fold} = \Delta H - T.\Delta S$)
  - protein more structured -> $\Delta S\downarrow$ – unfavorable
  - solvent less structured -> $\Delta S\uparrow$ – favorable
    - hydrophobic interactions are driving “force”
  - more non-covalent interactions -> $\Delta H\downarrow$ – favorable



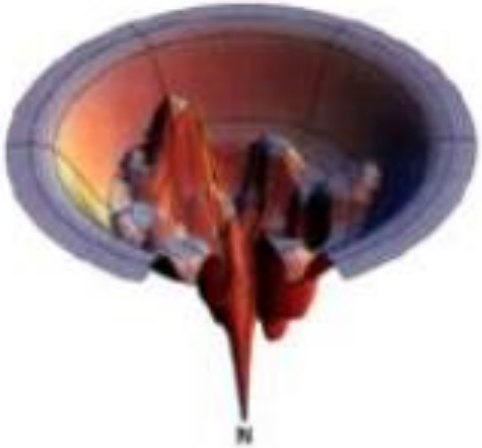
Energetics of protein folding



Flat landscape
(Levinthal paradox)

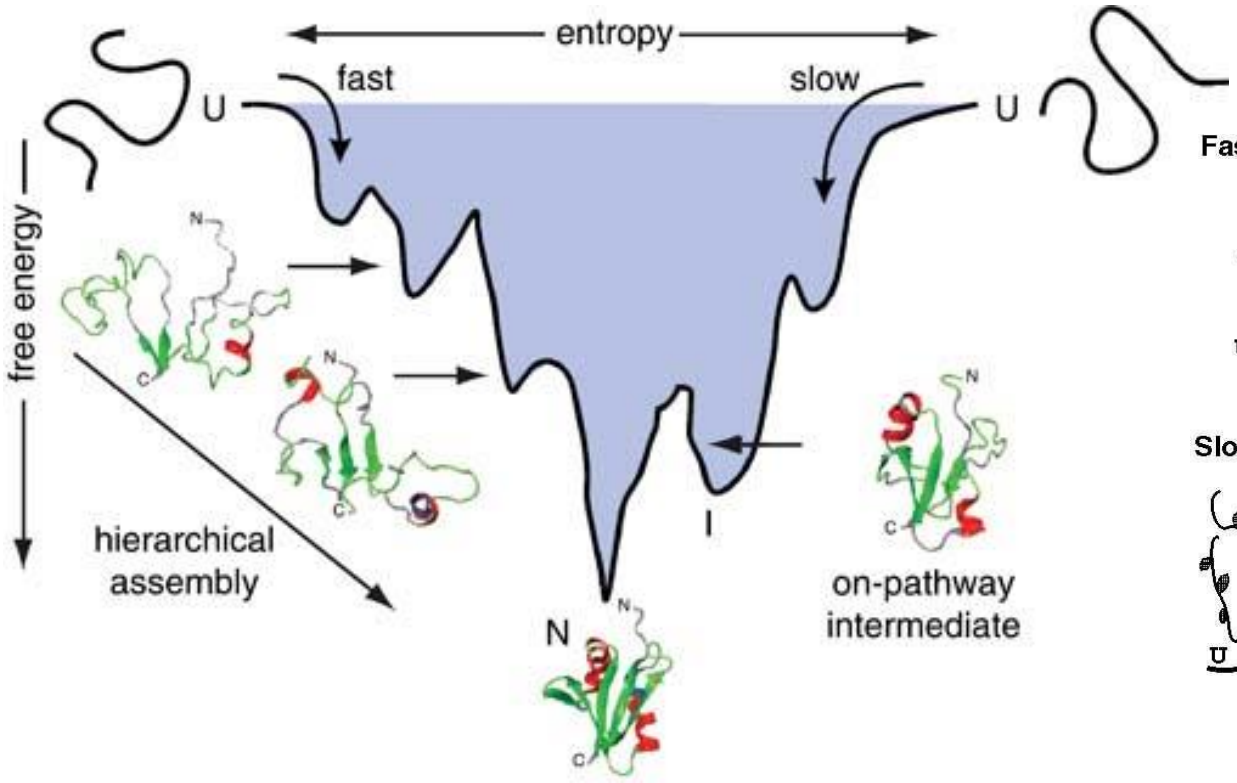


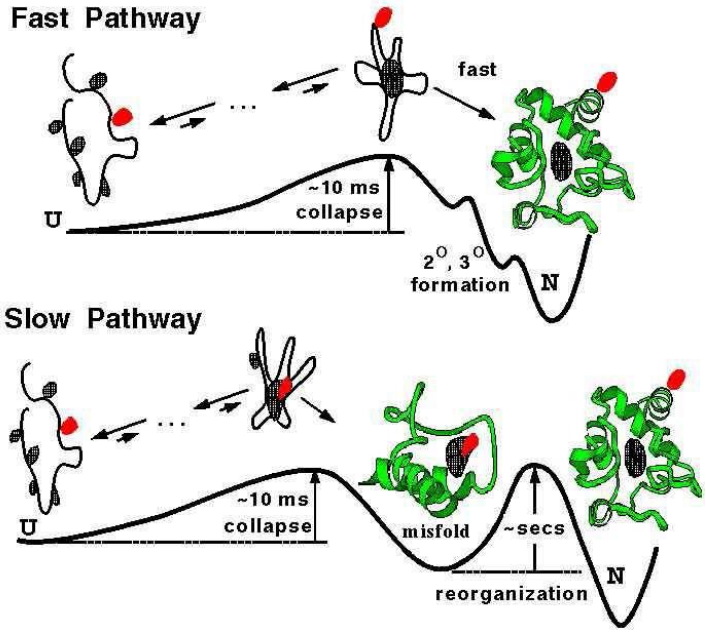
Tunnel landscape
(discrete pathways)



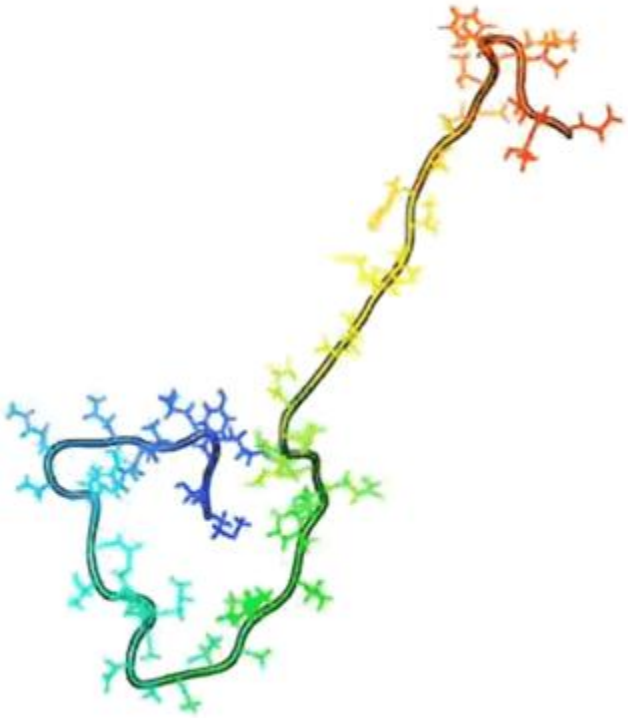
Realistic landscape
("folding funnel")

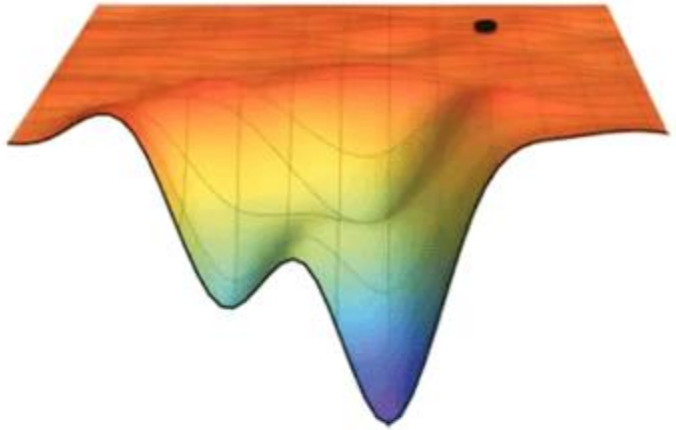
Energetics of protein folding





Energetics of protein folding



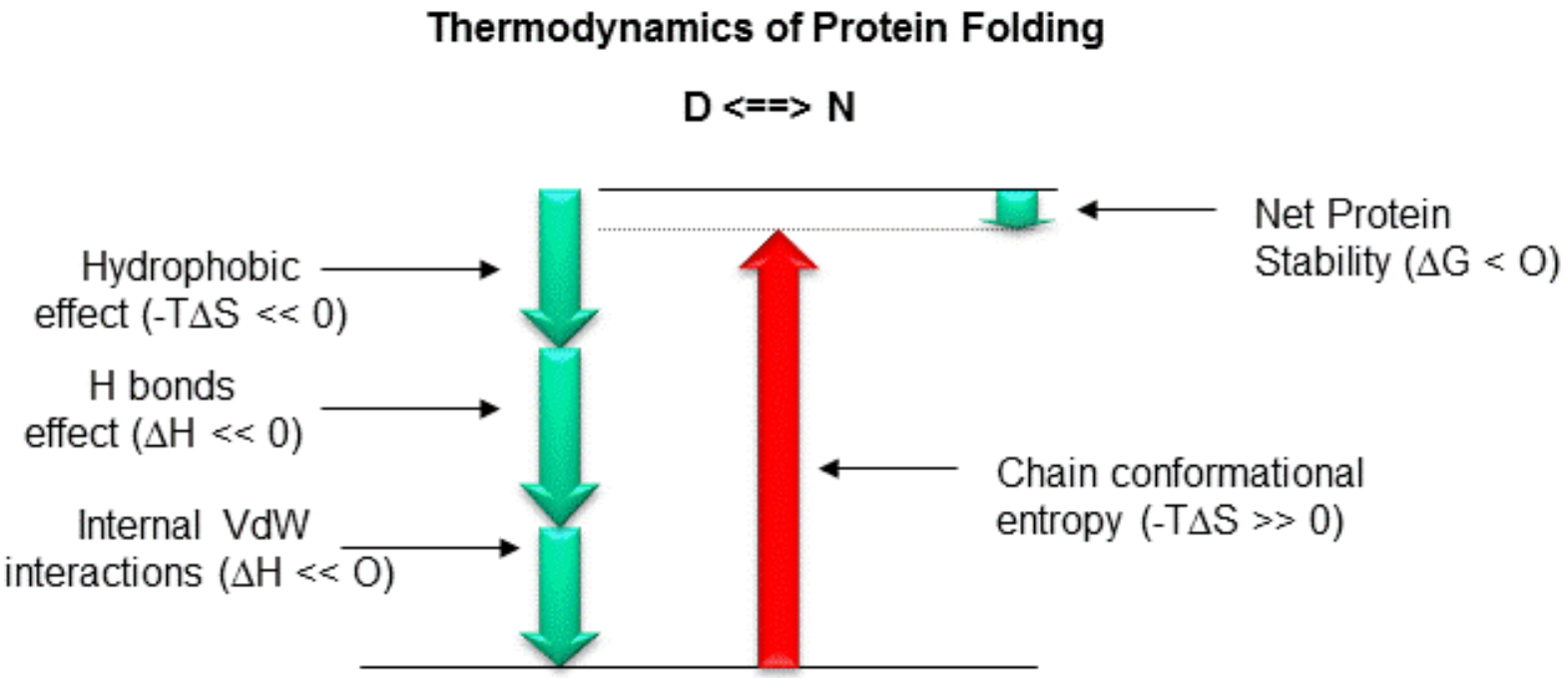


Protein stability

- Basics of protein stability
- Database of protein stability

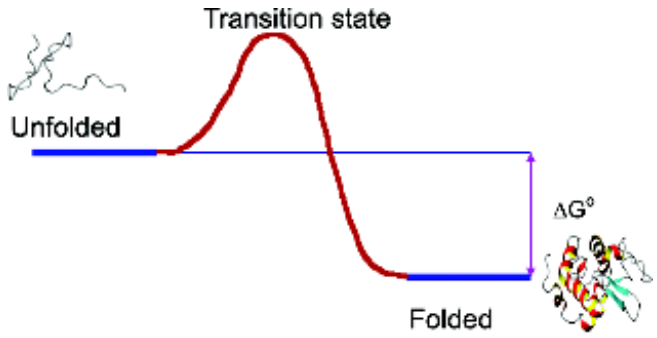
Basics of protein stability

- **Tertiary structure of protein**
  - sum of non-covalent weak interactions *vs* conformational entropy
  - folded protein = thermodynamic compromise
  - folded protein marginally more stable than unfolded (10-80 kJ/mol)



Basics of protein stability

- **Tertiary structure of protein**
  - sum of non-covalent weak interactions *vs* conformational entropy
  - folded protein = thermodynamic compromise
  - folded protein marginally more stable than unfolded (10-80 kJ/mol)



  - Weak interactions are frequently disrupted
    - denaturation - disrupted bonds replaced by bonds with solvent
    - dynamics - disrupted bonds reformed between protein atoms

Database of protein stability

- **ProTherm**
  - https://www.iitm.ac.in/bioinfo/ProTherm/index.html
  - set of 746 unique proteins and 311 proteins with mutants
  - numerical data of thermodynamic parameters for wild type and mutant proteins
- Data
  - Gibbs free energy change, enthalpy change, heat capacity change, transition temperature
  - secondary structure and accessibility for wild type residues
  - experimental conditions, methods and activity information

Database of protein stability

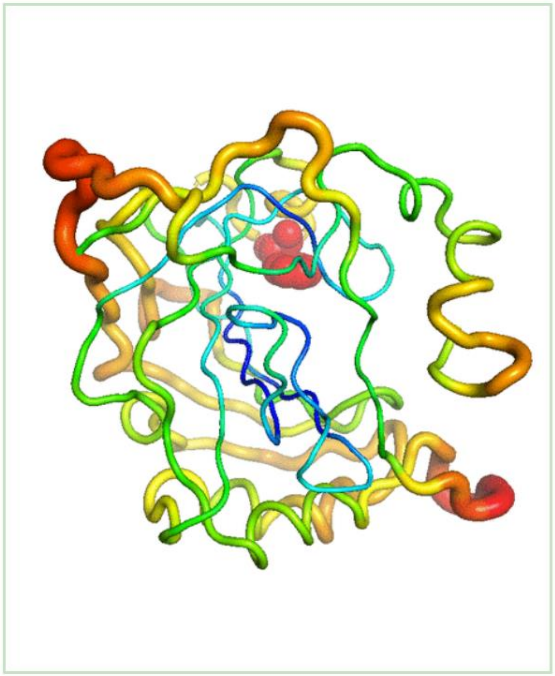
ProThermDB

HOME | BROWSE | STATISTICS | TUTORIAL | UPLOAD | RELATED RESOURCES | DOWNLOADS | CITE US | CONTACT US

OVERVIEW

ProThermDB, thermodynamic Database for Proteins and Mutants (ProThermDB) contains more than 32,000 data of several thermodynamic parameters such as melting temperature, free energy obtained with thermal and denaturant denaturation, enthalpy change, and heat capacity change along with experimental methods and conditions, sequence, structure, and literature information. Besides, the current version of the database includes ~0.12 million thermodynamic data obtained for different organisms and cell lines, which are determined by recent high throughput proteomics techniques using whole-cell approaches. In addition, we provided a graphical interface for the visualization of mutations at sequence and structure levels. ProThermDB is cross-linked with other relevant databases, PDB, UniProt, PubMed, etc.

ProThermDB can be queried through the search options by giving UniProt ID, PDB ID, protein name, mutation, experimental conditions, and author name, etc. Users can check our tutorial to get help in searching the database. Fill the download form provided to download the entire dataset.

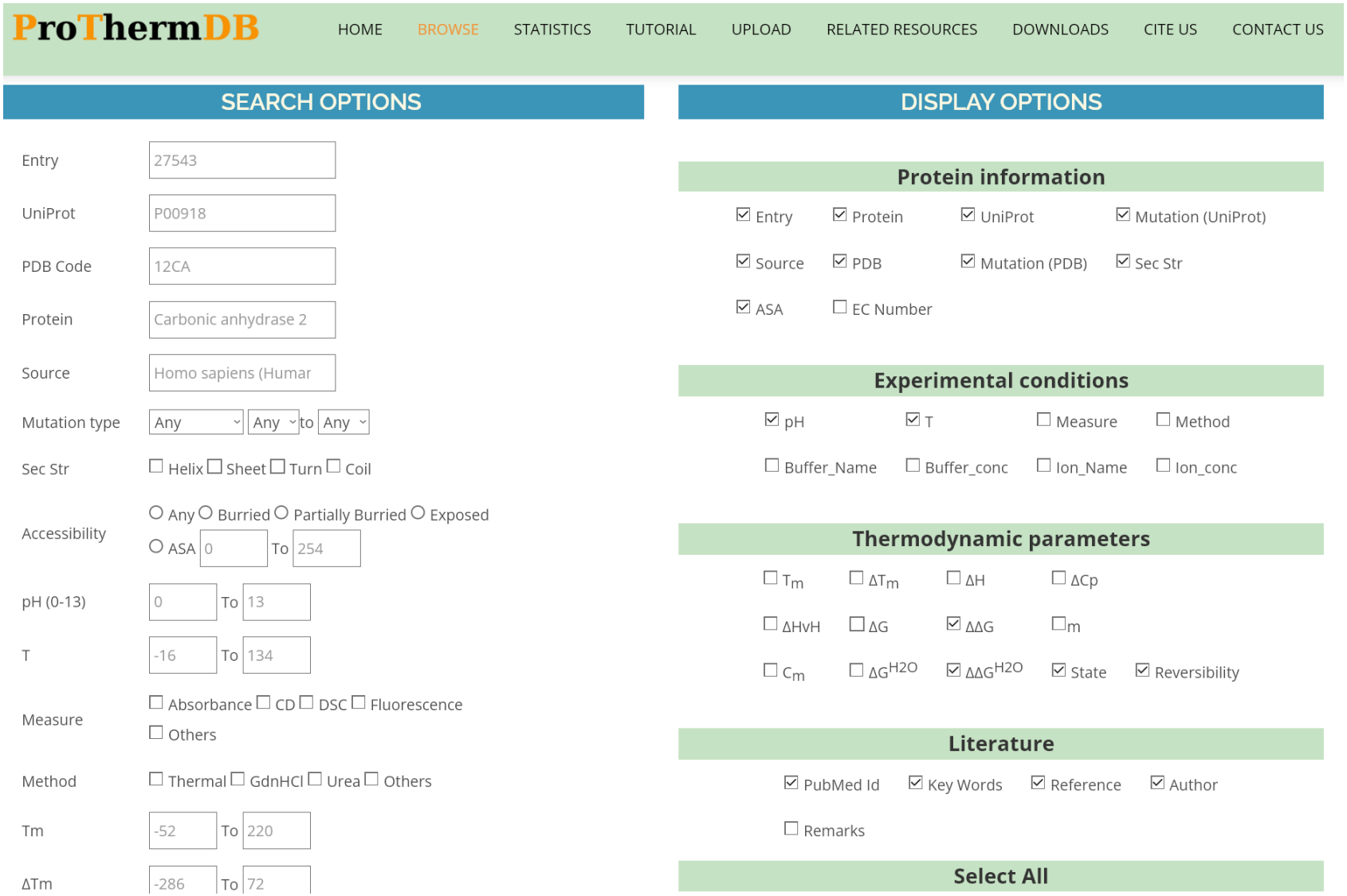


WHAT'S NEW

- ProThermDB is now available
- 7000+ Mutation data are added to ProThermDB
- New features are included in the ProThermDB

rothermdb/index.html

Database of protein stability



Database of protein stability

Entry	Protein	Source	Mutation	Tm	Measure	Reversibility
5	Ribonuclease HI	Escherichia coli	WILD	49.80	CD	YES
6	Ribonuclease HI	Escherichia coli	WILD	52.00	CD	YES
7	Ribonuclease HI	Escherichia coli	K 91 R	49.80	CD	YES
8	Ribonuclease HI	Escherichia coli	K 91 R	52.00	CD	YES
9	Ribonuclease HI	Escherichia coli	D 94 E	49.80	CD	YES
10	Ribonuclease HI	Escherichia coli	D 94 E	52.00	CD	YES
11	Ribonuclease HI	Escherichia coli	K 95 G	49.80	CD	YES
12	Ribonuclease HI	Escherichia coli	K 95 G	52.00	CD	YES
13	Ribonuclease HI	Escherichia coli	K 95 A	49.80	CD	YES
14	Ribonuclease HI	Escherichia coli	K 95 A	52.00	CD	YES
15	Ribonuclease HI	Escherichia coli	K 95 N	49.80	CD	YES
16	Ribonuclease HI	Escherichia coli	K 95 N	52.00	CD	YES
124	Ribonuclease HI	Escherichia coli	WILD	53.00	CD	YES
125	Ribonuclease HI	Escherichia coli	A 52 I	59.20	CD	YES
126	Ribonuclease HI	Escherichia coli	A 52 V	58.50	CD	YES
127	Ribonuclease HI	Escherichia coli	A 52 L	57.30	CD	YES
128	Ribonuclease HI	Escherichia coli	A 52 C	55.50	CD	YES
129	Ribonuclease HI	Escherichia coli	A 52 M	54.60	CD	YES
130	Ribonuclease HI	Escherichia coli	A 52 F	51.50	CD	YES
131	Ribonuclease HI	Escherichia coli	A 52 T	50.30	CD	YES
132	Ribonuclease HI	Escherichia coli	A 52 Q	49.10	CD	YES
133	Ribonuclease HI	Escherichia coli	A 52 E	48.00	CD	YES
134	Ribonuclease HI	Escherichia coli	A 52 P	47.60	CD	YES
135	Ribonuclease HI	Escherichia coli	A 52 S	47.20	CD	YES
136	Ribonuclease HI	Escherichia coli	A 52 N	47.10	CD	YES
137	Ribonuclease HI	Escherichia coli	A 52 D	46.90	CD	YES
138	Ribonuclease HI	Escherichia coli	A 52 Y	45.40	CD	YES
139	Ribonuclease HI	Escherichia coli	A 52 G	44.10	CD	YES
140	Ribonuclease HI	Escherichia coli	A 52 H	41.20	CD	YES
141	Ribonuclease HI	Escherichia coli	A 52 K	33.50	CD	YES

Database of protein stability

- **FireProtDB**
  - https://loschmidt.chemi.muni.cz/fireprotdb/
  - numerical data of thermodynamic parameters for wild type and mutant proteins
  - More than 16,000 experimental stability data on ~ 300 proteins
  - Manual curation
- Data
  - Gibbs free energy change, enthalpy change, heat capacity change, transition temperature
  - experimental conditions and methods

Database of protein stability

FIREPROT DB v1.1 | Mutational data for protein stability

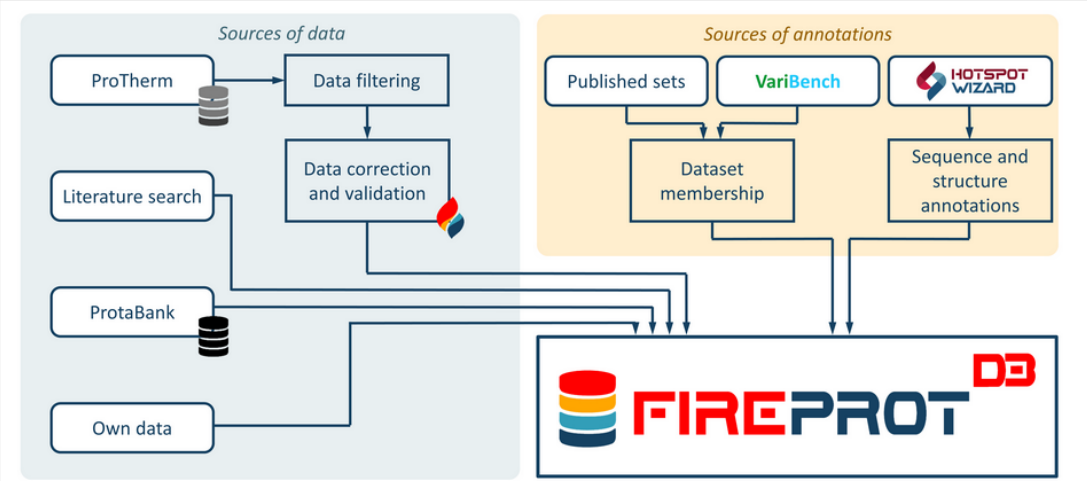
Search | Enter search phrase... | ADVANCED

Home | Help | Show all | Use cases | Acknowledgement

FireProtDB is a comprehensive, manually curated database of the protein stability data for single-point mutants.

Proteins find their use in numerous biomedical and biotechnological applications. Naturally occurring proteins usually cannot withstand harsh industrial environments since they have evolved to function under mild conditions. Increasing protein stability is one of the key determinants of protein applicability. The predictive power of the current computational tools is compromised by the limited experimental data that would allow a rigorous training and testing.

This database combines the published datasets from ProTherm and ProtaBank, the data extracted from the recent literature, and the measurements collected in our laboratory. The annotations were obtained from VariBench and HotSpot Wizard. The graphical user interface is designed to facilitate both types of the expected use: (i) the interactive explorations of individual entries on the level of a protein or a mutation and (ii) the construction of highly customized, machine learning-friendly datasets using advanced searching and filtering.



Database of protein stability

FireprotDB search results

Export CSV

Stabilizing Destabilizing Neutral

Protein	Curated	Mutation	ΔΔG (kcal/mol)	ΔTm (°C)
Halohydrin dehalogenase	★	E64A	-	1
Halohydrin dehalogenase	★	S22A	-	-0.5
Halohydrin dehalogenase	★	N113H	-	-3.5
Halohydrin dehalogenase	★	N113H	-	-2
Halohydrin dehalogenase	★	D96H	-	-9
Halohydrin dehalogenase	★	A29L	-	3
Halohydrin dehalogenase	★	P253G	-	-0.5
Halohydrin dehalogenase	★	P253G	-	-2.5
Halohydrin dehalogenase	★	T134I	-	-1
Halohydrin dehalogenase	★	T134I	-	0.5

Protein dynamics

- Basics of protein dynamics
- Characteristics of protein motions
- Dynamics and protein function
- Approaches to study dynamics
- Databases of dynamics
- Protein dynamics in biology

Introduction to protein dynamics

- **Origin of dynamics** – disruption of weak interactions by
  - thermal kinetic energy (k_b.T)
  - binding interactions (ligands or other proteins) – induced fit

- Protein atoms fluctuates around their average positions
  - in tightly packed interior – movement restricted
  - near surface – movement promoted by solvent movements
  - -> proteins considered as "semi-liquids"

Characteristics of protein motions

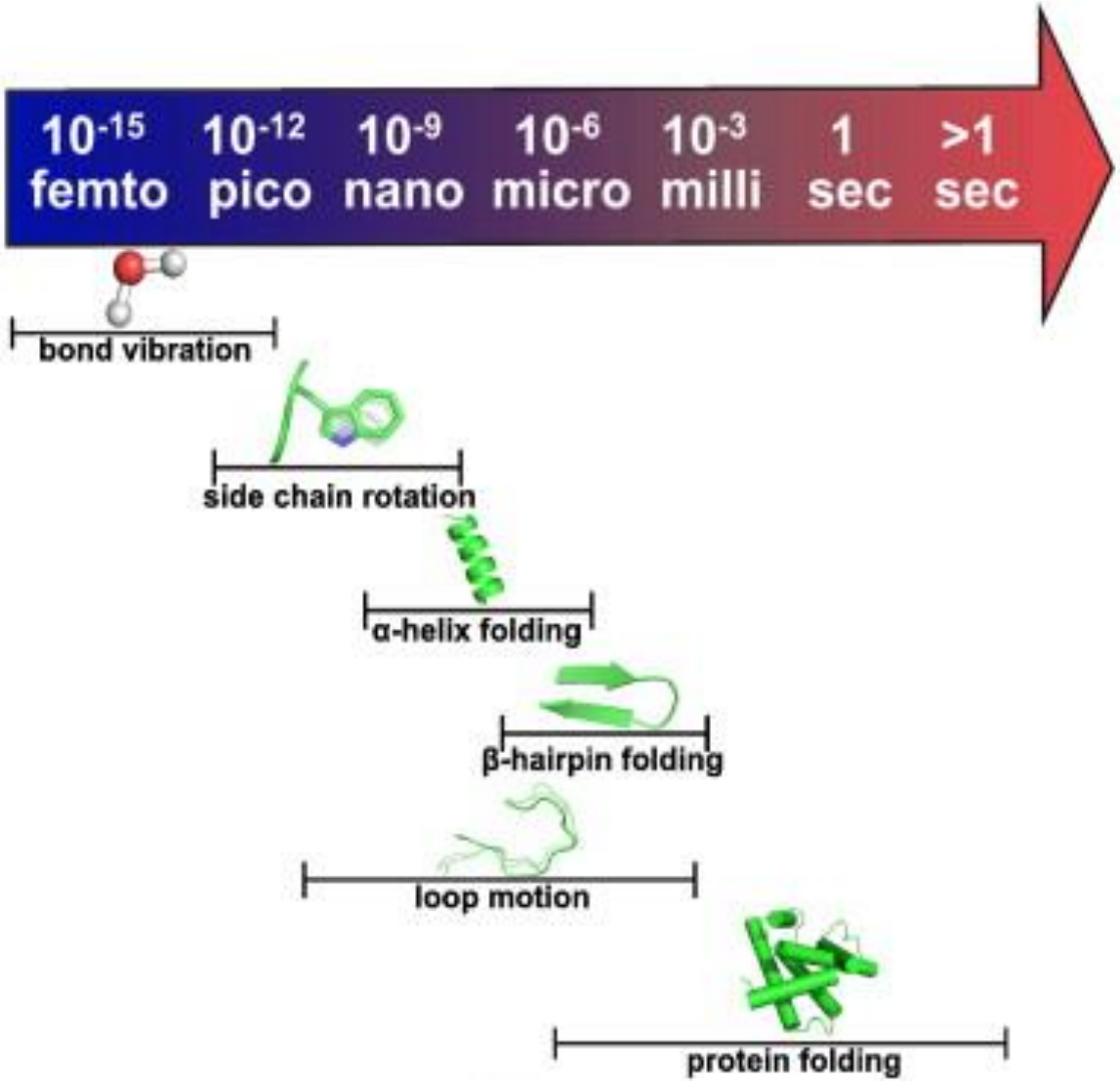
- **Divisions of protein motions**

Type of motion	Moving moiety	Functionality
Local	atoms; side-chains	bond vibration; ligand flexibility; temporal diffusion pathways
Medium-scale	secondary structures	active site conformational changes; motion of hinge; peptide bond rotation;
Large-scale	domains	hinge facilitated domain movements; allosteric transition
Global	subunits	helix-loop transition; folding/unfolding

Amplitudes of protein motions

- **Fluctuations**
  - less than 1 Å
  - local motions
- **Collective motions**
  - 1-10 Å
  - medium and large-scale motions
- **Triggered conformational changes**
  - more than 10 Å
  - global motions

Time scales of protein motions



Time scales of protein motions

- **Time scales governed by local environment**
  - interior – motions coupled due to packing restraints
  - surface – no coupling of motions

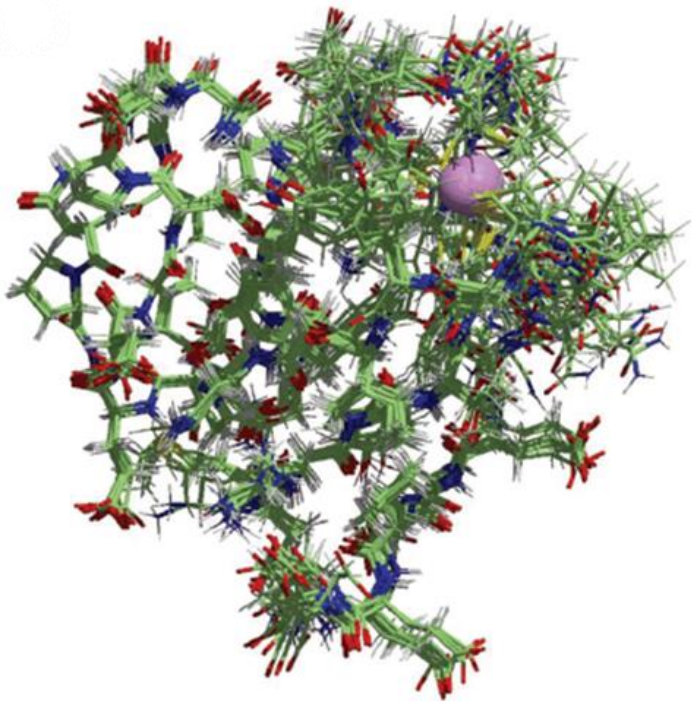
- Example: aromatic ring flipping
  - can occur on ps time scale, but often observed on ms time scale
  - aromatic residues -> hydrophobic -> inside protein -> tightly packed
  - -> low probability of synchronized movement of surrounding atoms
  - -> prolonged time scale

Approaches to study dynamics

- NMR spectroscopy
- High resolution X-ray crystallography
- Computational
  - Normal mode analysis (NMA)
  - Molecular dynamics (MD)

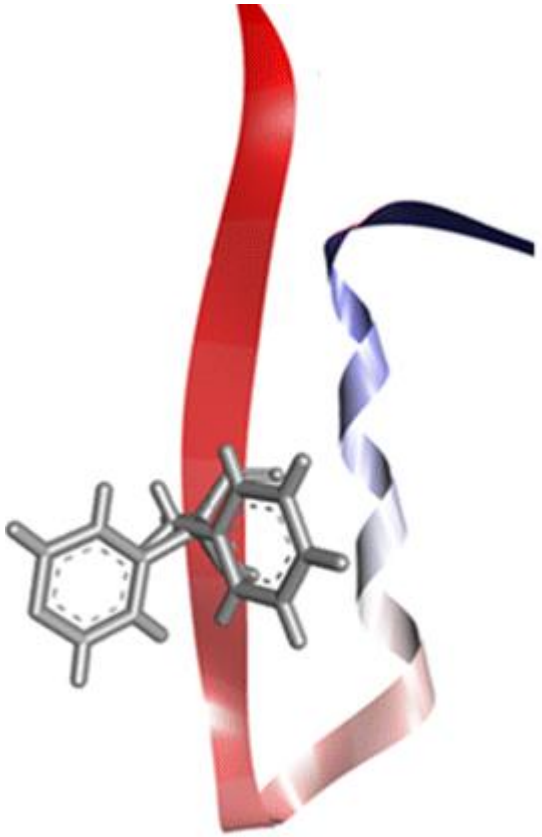
NMR spectroscopy

- **Ensemble of possible low energy conformations**
- Directly shows possible amplitudes of motion
- Limited applicability to larger proteins
- **Does not describe**
  - very fast motions & transition states
  - time scales & energetics of motions



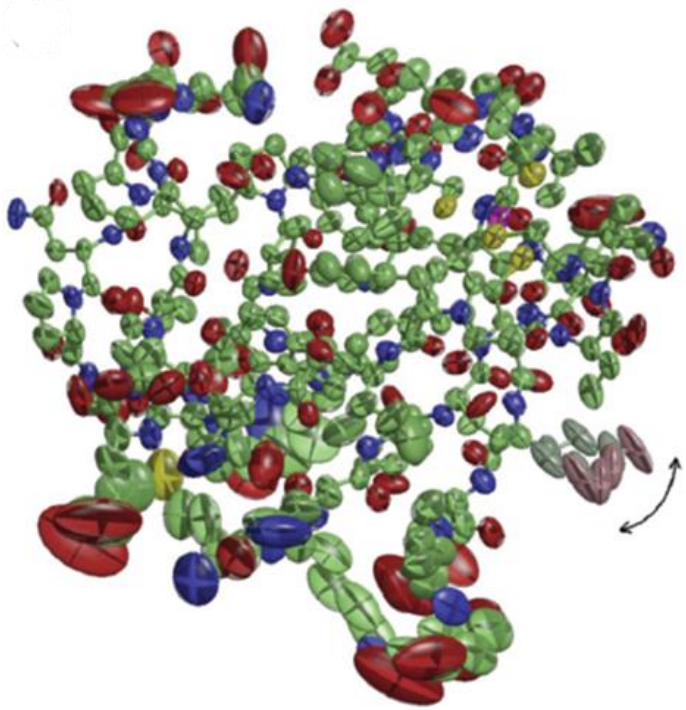
High resolution X-ray crystallography

- **Average low energy structure** - more conformations:
  - in one structure only if both are separated by barrier
  - in multiple structures



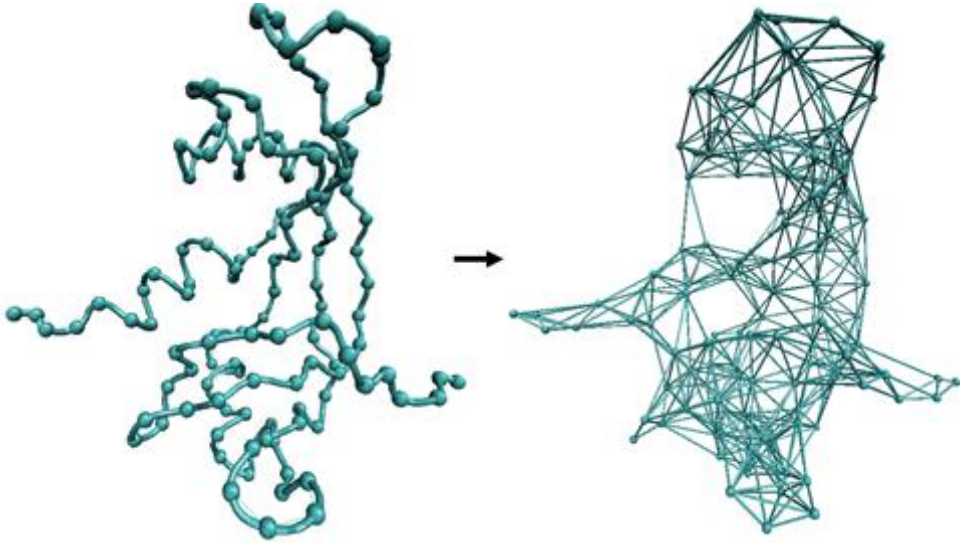
High resolution X-ray crystallography

- **Average low energy structure** - more conformations:
  - in one structure only if both are separated by barrier
  - in multiple structures
- Crystalline state
  - non-native contacts
  - artificially lower amplitudes of motions
- Range of fluctuations – B-factors
- **Does not describe**
  - very flexible regions
  - collectiveness of motions
  - time scales & energetics of motions



Normal mode analysis

- **Principle**
  - motion of system as harmonic vibration around a local minimum
  - Coarse-grained model, residues connected with springs
- Small number of low-frequency normal modes
  - shows directionality, collectiveness and sequence of global motions
- **Does not describe**
  - local movements
  - amplitudes & time scales
  - energetics of motions



Molecular dynamics

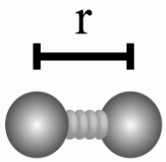
- **Principle**
  - physical description of interactions within system (force field)
  - Newton's laws of motions
  - forces acting on all atoms due to all atoms
  - small time-step ~ 2 fs

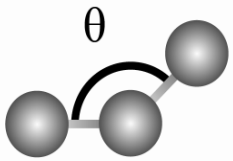
$$E_{total} = \sum_{bonds} K_r(r - r_{eq})^2 + \sum_{angles} K_\theta(\theta - \theta_{eq})^2 + \sum_{dihedrals} \frac{V_n}{2}[1 + \cos(n\phi - \gamma)] + \sum_{i<j} \left[\frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^{6}} + \frac{q_i q_j}{\epsilon R_{ij}} \right]$$

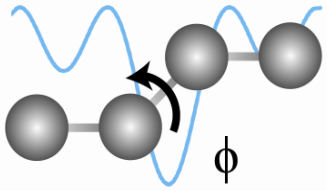
Molecular dynamics

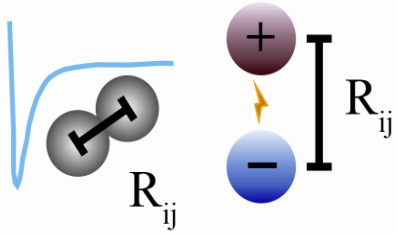
- **Principle**
  - physical description of interactions within system (force field)
  - Newton's laws of motions
  - forces acting on all atoms due to all atoms
  - small time-step ~ 2 fs

$$E_{total} = \underbrace{\sum_{bonds} K_r(r - r_{eq})^2 + \sum_{angles} K_\theta(\theta - \theta_{eq})^2 + \sum_{dihedrals} \frac{V_n}{2}[1 + \cos(n\phi - \gamma)]}_{\text{Bonded}} + \underbrace{\sum_{i<j} \left[\frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^{6}} + \frac{q_i q_j}{\epsilon R_{ij}} \right]}_{\text{Non-bonded}}$$



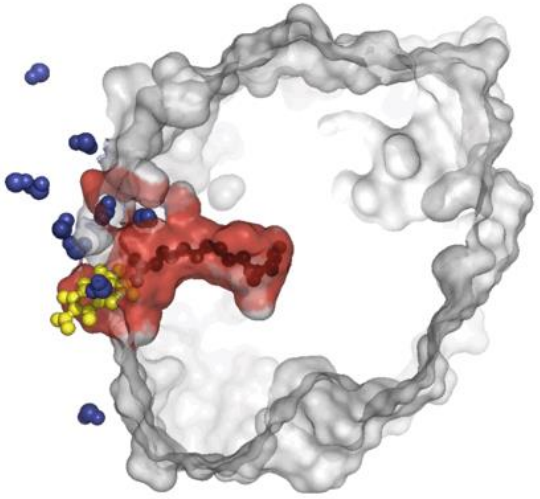






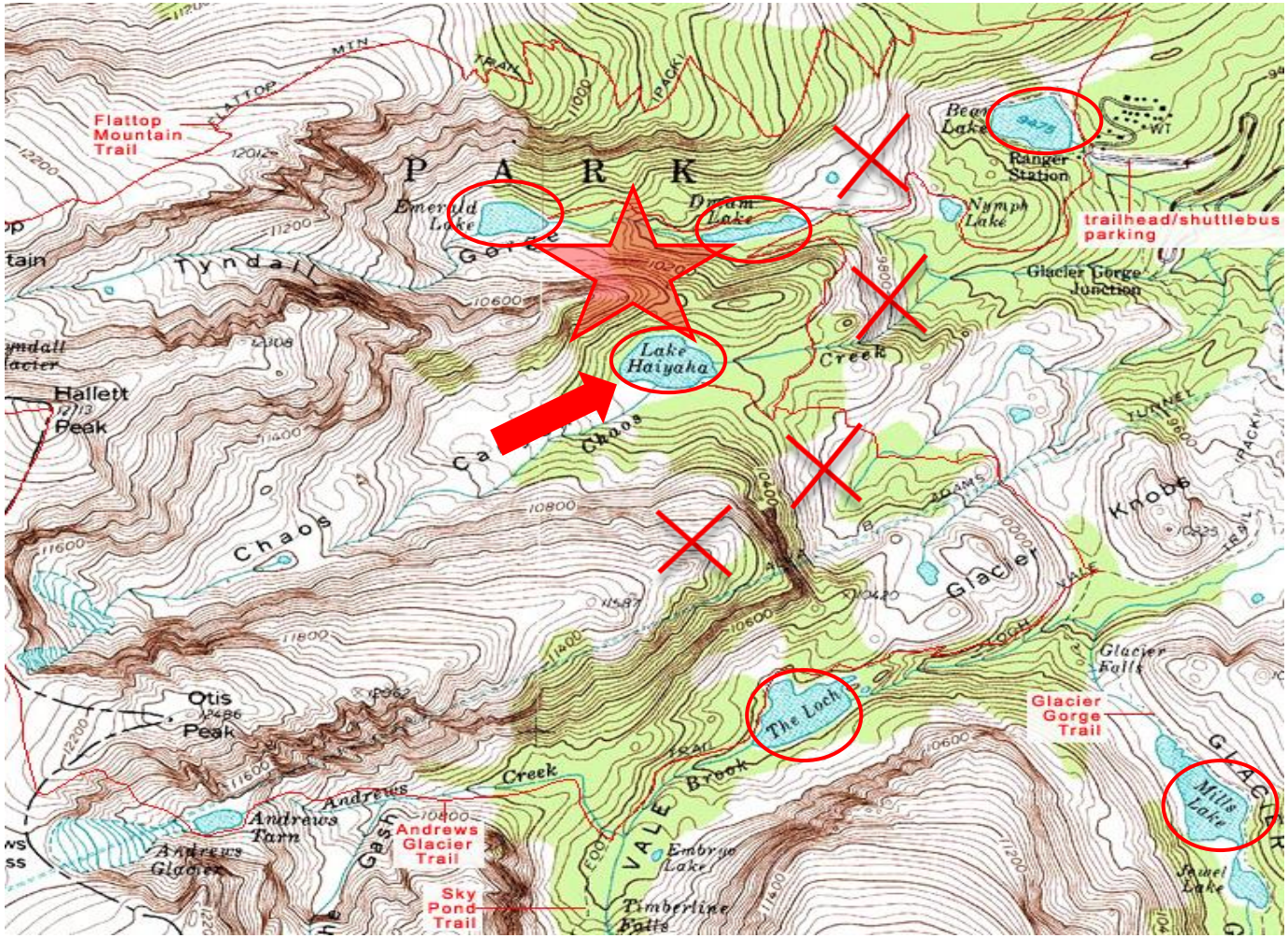
Molecular dynamics

- **Principle**
  - physical description of interactions within system (force field)
  - Newton's laws of motions
- Provides information on energetics, amplitudes and time scales of local motions on atomic level
- **Does not describe**
  - slower large scale motions (> ms)



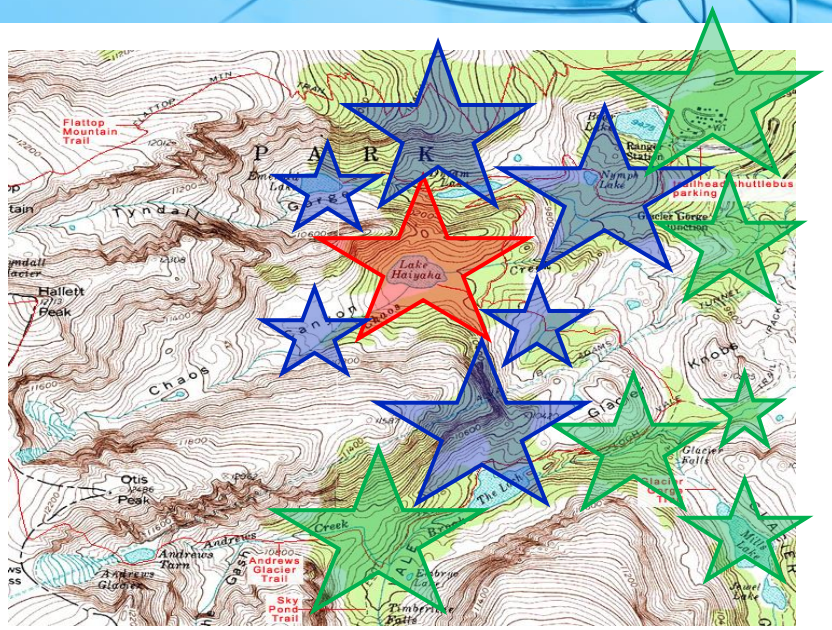
Molecular dynamics

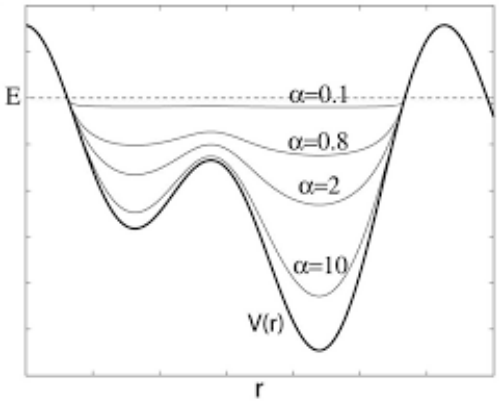
- **Classical MD**



Molecular dynamics

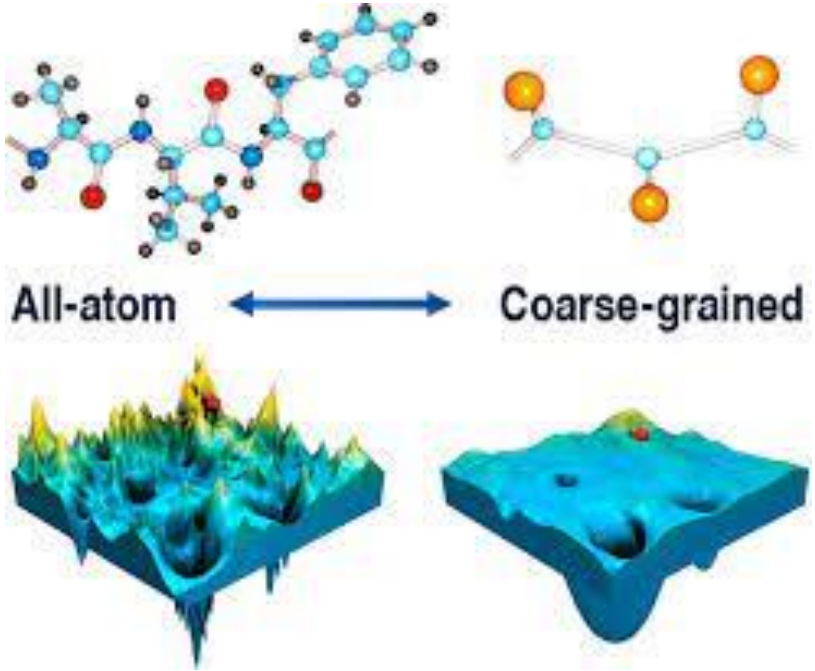
- **Classical MD**
- **Enhanced sampling**
  - Adaptive sampling
  - Metadynamics
  - Accelerated MD
  - Umbrella sampling



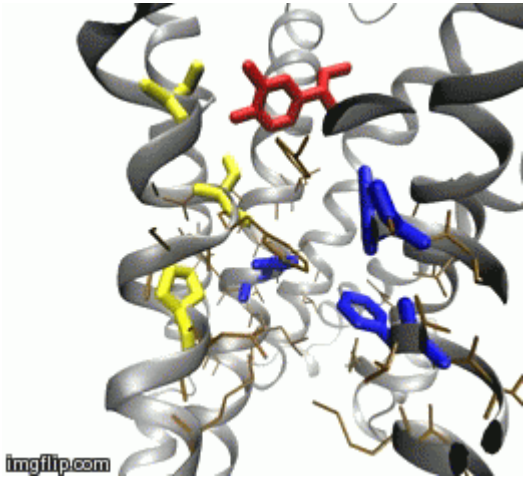


Molecular dynamics

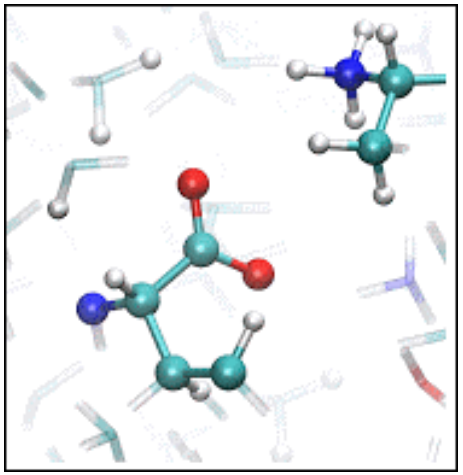
- **Classical MD**
- **Enhanced sampling**
  - Adaptive sampling
  - Metadynamics
  - Accelerated MD
  - Umbrella sampling
- **Coarse-grained molecular dynamics**



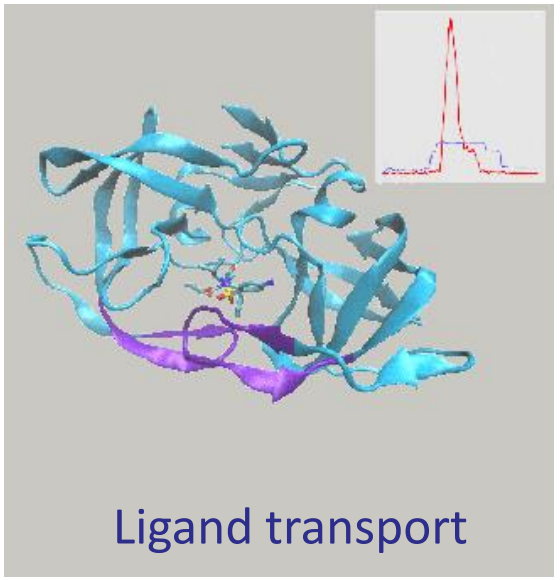
Molecular dynamics



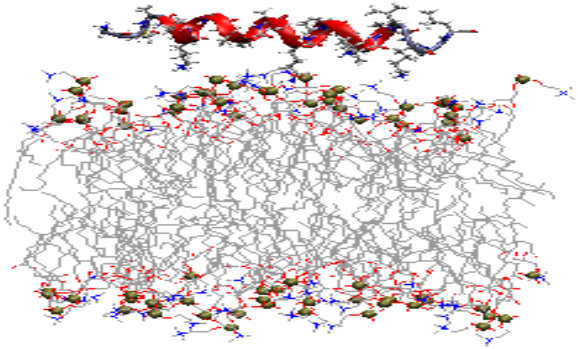
Analysis of interactions



Ligand conversion



Ligand transport



Interaction with membrane

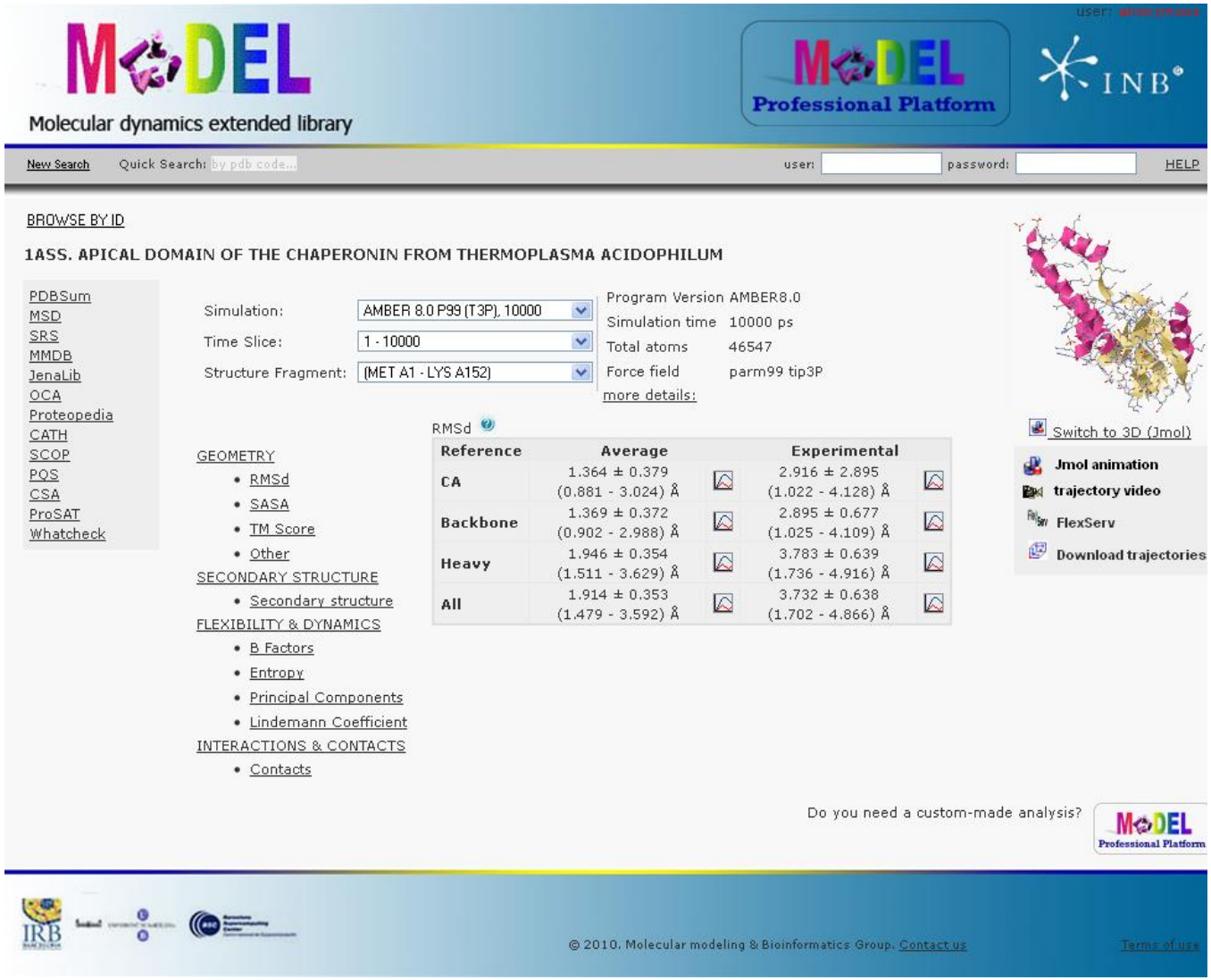
Databases of dynamics

- Molecular Dynamics Extended Library (MoDEL)
- Dynameomics
- Molecular Movements Database (MolMovDB)
- ProMode-Elastic

MoDEL

- http://mmb.pcb.ub.es/MoDEL/
- >1,700 MD simulations of proteins representatives of all monomeric soluble structures in PDB
- 10 ns trajectories from MD simulations
- Data
  - pre-computed analysis of geometry, secondary structure, flexibility and inter-residue contacts
  - trajectory video
  - downloadable trajectories

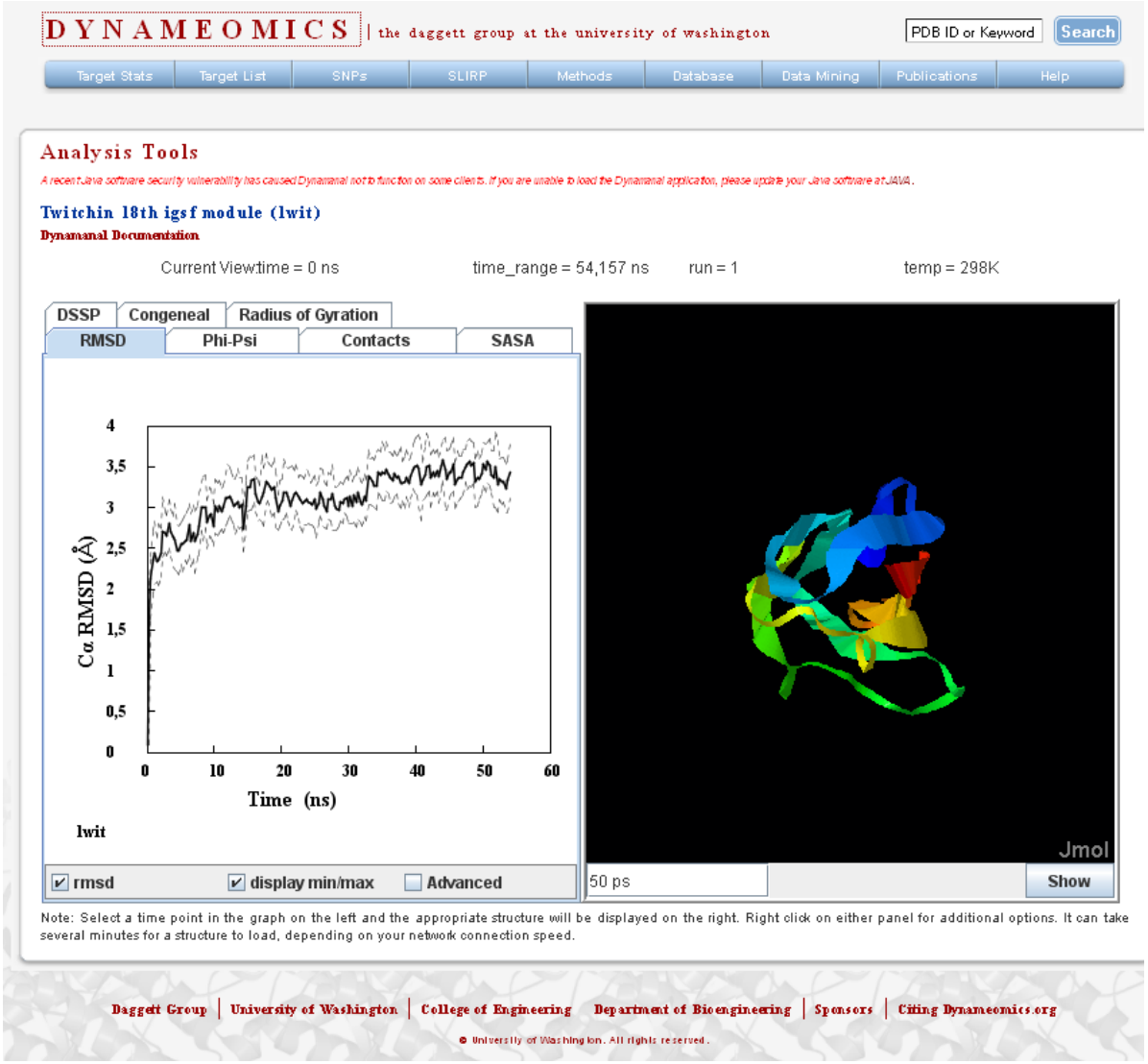
MoDEL


MoDEL
Molecular dynamics extended library
MoDEL
Professional Platform
INB
New Search
Quick Search: by pdb code...
user:
password:
HELP
BROWSE BY ID
1ASS. APICAL DOMAIN OF THE CHAPERONIN FROM THERMOPLASMA ACIDOPHILUM
PDBSum
MSD
SRS
MMDB
JenaLib
OCA
Proteopedia
CATH
SCOP
PQS
CSA
ProSAT
Whatcheck
Simulation: AMBER 8.0 P99 (T3P), 10000
Time Slice: 1 - 10000
Structure Fragment: (MET A1 - LYS A152)
Program Version AMBER8.0
Simulation time 10000 ps
Total atoms 46547
Force field parm99 tip3P
more details:
Switch to 3D (Jmol)
Jmol animation
trajectory video
FlexServ
Download trajectories
GEOMETRY
RMSd
SASA
TM Score
Other
SECONDARY STRUCTURE
Secondary structure
FLEXIBILITY & DYNAMICS
B Factors
Entropy
Principal Components
Lindemann Coefficient
INTERACTIONS & CONTACTS
Contacts
RMSd
Reference
Average
Experimental
CA
1.364 ± 0.379 (0.881 - 3.024) Å
2.916 ± 2.895 (1.022 - 4.128) Å
Backbone
1.369 ± 0.372 (0.902 - 2.988) Å
2.895 ± 0.677 (1.025 - 4.109) Å
Heavy
1.946 ± 0.354 (1.511 - 3.629) Å
3.783 ± 0.639 (1.736 - 4.916) Å
All
1.914 ± 0.353 (1.479 - 3.592) Å
3.732 ± 0.638 (1.702 - 4.866) Å
Do you need a custom-made analysis?
MoDEL
Professional Platform
IRB
© 2010. Molecular modeling & Bioinformatics Group. Contact us
Terms of use

Dynameomics

- www.dynameomics.org
- MD simulations of over 800 proteins
- Longer trajectories (> 31 ns)
- Data
  - pre-computed analysis of RMSD, SASA, Phi-Psi, and contacts
  - trajectory video
  - visualization of individual snapshots
  - downloadable trajectories on request

Dynameomics

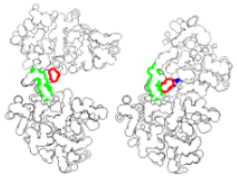


MolMovDB

- http://www.molmovdb.org/
- Collection of over 178 molecular motions
- Based on morphing – interpolation of motion between two experimental crystal structures
- Data
  - classification scheme for molecular motions
  - movements animations
  - hinge identification, structural analysis tools, references to experimental crystal structures
  - downloadable morphs as multi-model PDB

MolMovDB

molmovdb.org



Molecular Movements Database

This outline presents the current database classified by any classification scheme for which data has been compiled. The original schema which separates motions by type of movement is defined on the help page. Thumbnail images appear for motions which have available movies, and link to the best morph for that particular protein.

Many more movies can be seen here, including structures not represented on this page. The movies page also allows searches for protein names or specific PDB IDs.

Switch to CATH survey

I. Motions of Fragments Smaller than Domains

A. Motion is predominantly shear

F-s-2. Proteins for which two or more conformations are known


Adenosylcobinamide Kinase [motion] [morph]


Small G-protein Arf6 [motion] [morph]


Bacteriorhodopsin (bR) [motion] [morph]


Calbindin [motion] [morph]


Dihydrofolate Reductase (DHFR) [motion] [morph]


Histidine-Containing Phosphocarrier Protein [motion] [morph]

ProMode-Elastic

- https://pdbj.org/promode-elastic
- Normal mode analysis of PDB data – on PDB database
- Data
  - fluctuation of atoms and dihedral angles
  - correlation between fluctuating atoms
  - distance map between residues
  - animation of fluctuating molecules
  - displacement vectors

ProMode-Elastic

PDBj ProMode Elastic

Database of normal mode analysis of PDB data using elastic network model in torsional angle space

Home | What is ProMode-Elastic | Help Japanese

No.of entries 103529

PDB code (4 chars) 1cqw Find Example 1a00

Select from a list of entries

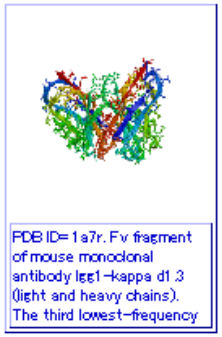
Submission of your data to be analyzed.

Download of software.

ProMode-Elastic is a database of normal mode analysis of **PDB** data. The normal mode analysis is performed by the program PDBETA we have developed. PDBETA is a program of Elastic-network-model based normal mode analysis in **T**orsional **A**ngle space for PDB data. PDBETA can describe molecular structures with relatively smaller number of degrees of freedom, and take into computation not only proteins but also DNA, RNA, and ligand molecules (hydrogen atoms and water molecules are excluded currently to suppress the number of variables).

In each protein page its characteristic dynamic features can be observed through animation and displacement vectors on a viewer such as jV and Jmol. We hope that a user learns more about dynamics from these pages than a static three-dimensional structure image of PDB data.

Reference: Hiroshi Wako and Shigeru Endo, "Ligand-induced conformational change of a protein reproduced by a linear combination of displacement vectors obtained from normal mode analysis." Biophys. Chem. vol.159, pp.257-266, 2011 [DOI:10.1016/j.bpc.2011.07.004]



PDB ID= 1a7r. Fv fragment of mouse monoclonal antibody Igg1-kappa d1.3 (light and heavy chains). The third lowest-frequency

*Click on image for an enlarged image and more information.

TOPICS

14/5/2012 ProMode-Elastic server has been moved to PDBj, IPR, Osaka University. URL was also changed.
9/10/2010 ProMode-Elastic first version is released.
12/12/2009 ProMode-Elastic test version is released.

PageTop | Back

(Latest update 2012.07.30)

PDBj ProMode Elastic

Database of normal mode analysis of PDB data using elastic network model in torsional angle space

Home | What is ProMode-Elastic | Help Japanese

Go to PDB code 1cqw Go

Select from a list of entries

1cqw

```
HEADER    HYDROLASE                               11-AUG-99   1CQW
TITLE     NAI COCRYSTALLISED WITH HALOALKANE DEHALOGENASE FROM A
TITLE    2 RHODOCOCCUS SPECIES
COMPND    MOL_ID: 1;
COMPND    2 MOLECULE: HALOALKANE DEHALOGENASE; 1-CHLOROHEXANE
COMPND    3 HALIDOHYDROLASE;
COMPND    4 CHAIN: A;
COMPND    5 EC: 3.8.1.5;
COMPND    6 ENGINEERED: YES;
COMPND    7 OTHER_DETAILS: COCRYSTALLIZED WITH NAI
SOURCE    MOL_ID: 1;
```

1cqw in other DBs >>> PDB PDBj PDBsum SCOP CATH FSSP

3D molecular view of vibration Help

Choose a mode and then click on a Viewer button to launch a viewer.
It may take a while to load data files.

Displacement vectors (Choose up to three modes.)

Mode 1 Mode 2 Mode 3 Mode 4 Mode 5
Mode 6 Mode 7 Mode 8 Mode 9 Mode 10

PDBj Viewer | Jmol Viewer

Animation (Choose one mode.)

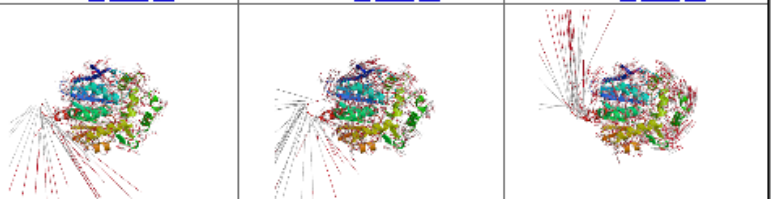
Mode 1 Mode 2 Mode 3 Mode 4 Mode 5
Mode 6 Mode 7 Mode 8 Mode 9 Mode 10

PDBj Viewer | Jmol Viewer

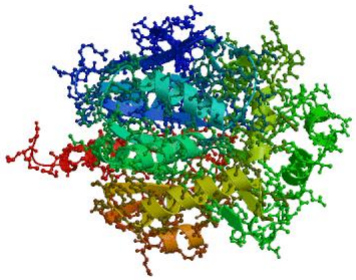
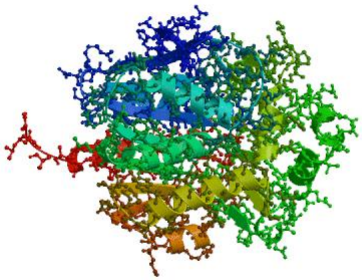
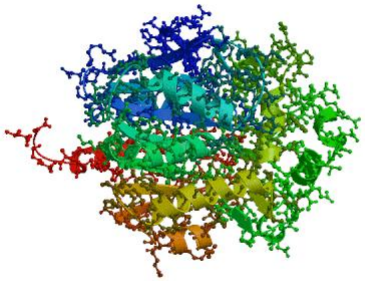
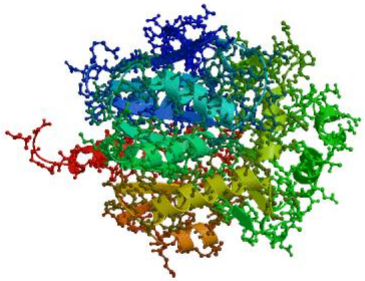
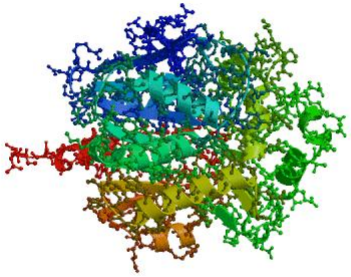
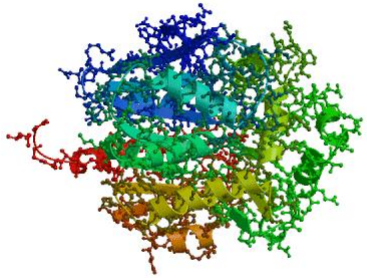
Still image of displacement vectors and GIF animation

Click on All, MainC or GIF for large image or GIF animation
Displacement vectors: All=All atoms and MainC=Main chain atoms. GIF=GIF animation

Mode 1 All MainC GIF | Mode 2 All MainC GIF | Mode 3 All MainC GIF



ProMode-Elastic

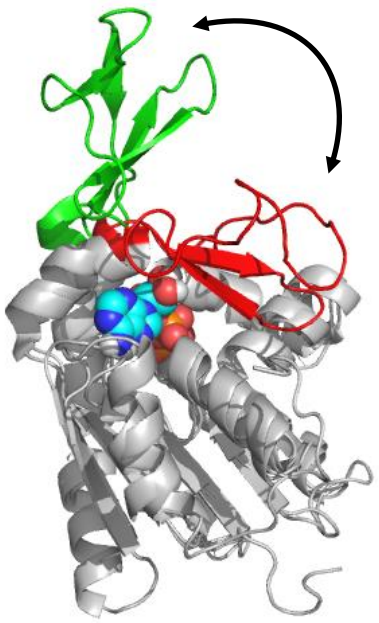







Protein dynamics in biology

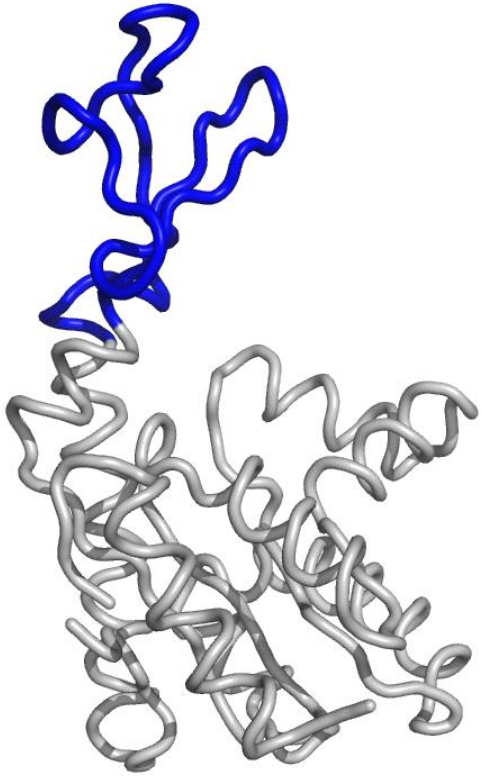
- Adenylate kinase
- Motor proteins

Adenylate kinase

- Biological processes
  - catalyzes interconversion of ATP + AMP ⇔ 2 ADP
- Large conformational change
  - 90 degrees rotation of whole domain, up to 30 Å amplitude
  - induced by binding of ATP
  - shielding of bound substrate from solvent



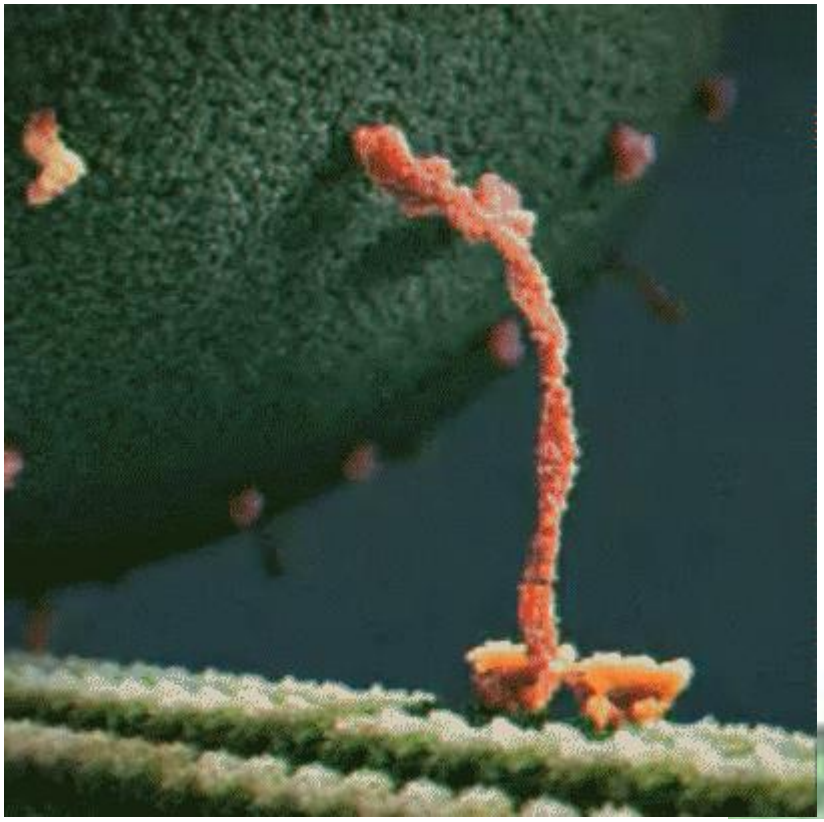
Adenylate kinase

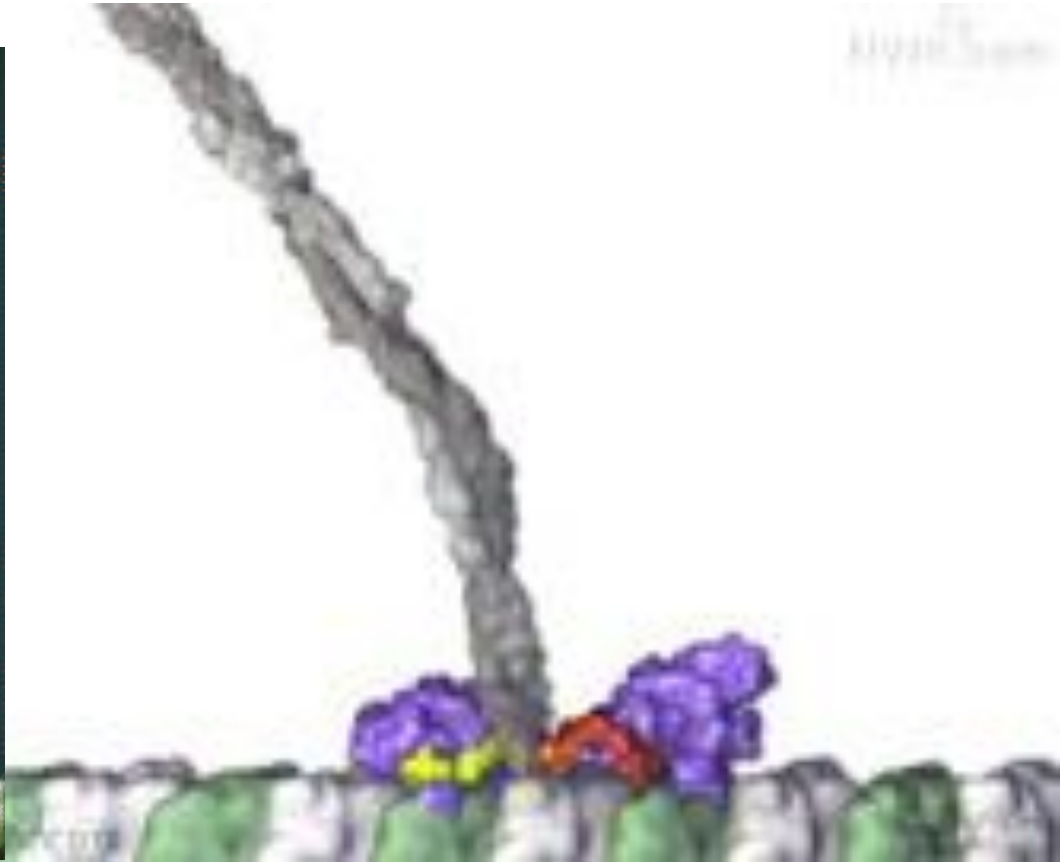


Motor proteins

- Biological processes
  - myosin movement along actin filament
  - kinesin movement along microtubule
- Motor head
  - ATPase domain – binding of ATP
  - linker domain – changes conformation upon ATP binding
- One step
  - moves a motor head for about 160 Å
  - moves an attached cargo for about 80 Å

Motor proteins





References

- Gu, J. & Bourne, P. E. (2009). **Structural Bioinformatics, 2nd Edition**, Wiley-Blackwell, Hoboken.
- Petsko, G. A. *&* Ringe, D. (2004). **Protein Stucture and Function**, New Science Press, London.
- Schwede, T. & Peitsch, M. C. (2008). **Computational Structural Biology: Methods and Applications**, World Scientific Publishing Company, Singapore.
- Daggett, V. & Fersht, A. R. (2003). Is there a unifying mechanism for protein folding? *Trends in Biochemical Sciences* **28**: 18-25.
- Dill, K. A. *et al.* (2008). The protein folding problem. *Annual Review of Biophysics* **37**: 289-316.