

Molecular Dynamics Simulations

Amedeo Caflisch

Department of Biochemistry

University of Zurich

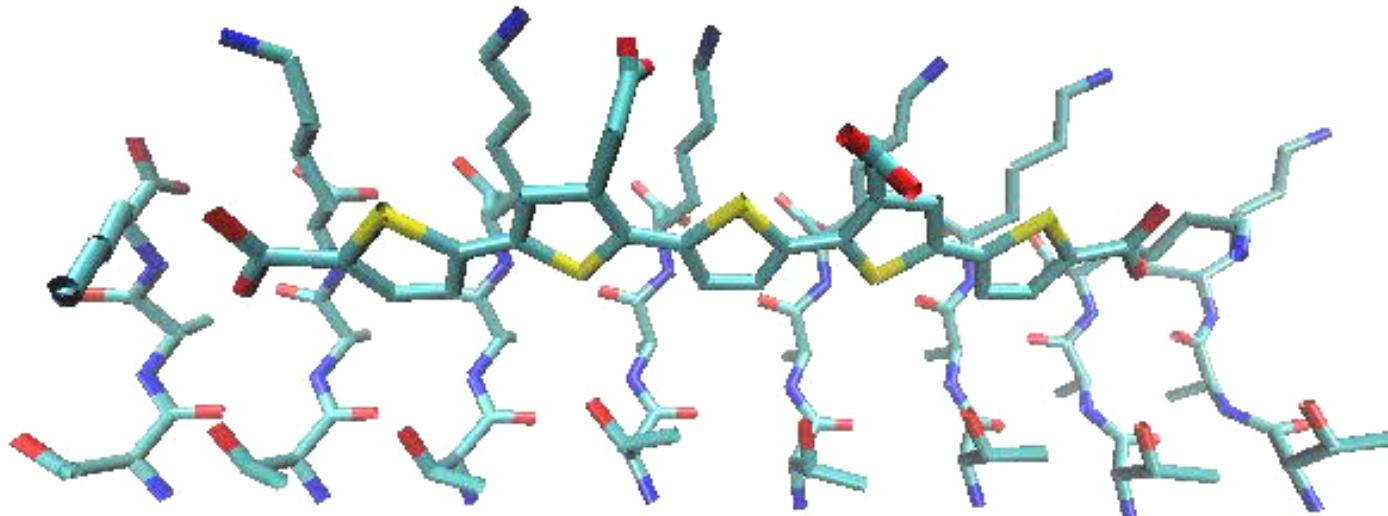
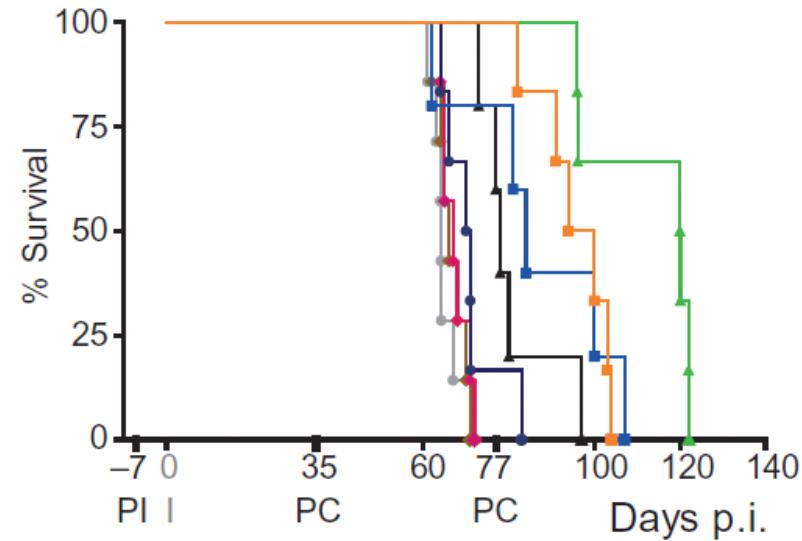
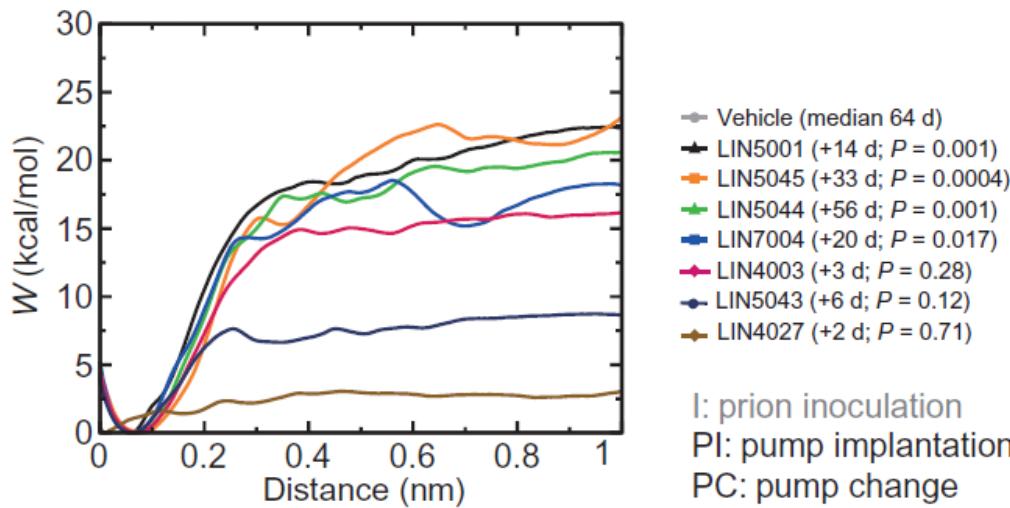
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Structure-based drug design identifies polythiophenes as antiprion compounds

with A. Aguzzi

www.ScienceTranslationalMedicine.org

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Article

Peptide Binding to a PDZ Domain by Electrostatic Steering via Nonnative Salt Bridges

Nicolas Blöchliger,¹ Min Xu,¹ and Amedeo Caflisch^{1,*}

¹Department of Biochemistry, University of Zurich, Zurich, Switzerland

ABSTRACT We have captured the binding of a peptide to a PDZ domain by unbiased molecular dynamics simulations. Analysis of the trajectories reveals on-pathway encounter complex formation, which is driven by electrostatic interactions between negatively charged carboxylate groups in the peptide and positively charged side chains surrounding the binding site. In contrast, the final stereospecific complex, which matches the crystal structure, features completely different interactions, namely the burial of the hydrophobic side chain of the peptide C-terminal residue and backbone hydrogen bonds. The simulations show that nonnative salt bridges stabilize kinetically the encounter complex during binding. Unbinding follows the inverse sequence of events with the same nonnative salt bridges in the encounter complex. Thus, in contrast to protein folding, which is driven by native interactions, the binding of charged peptides can be steered by nonnative interactions, which might be a general mechanism, e.g., in the recognition of histone tails by bromodomains.

$$\overrightarrow{F}_i(t) = m_i \overrightarrow{a}_i(t) = m_i \frac{d^2 \overrightarrow{x}_i(t)}{dt^2}$$

2013 Nobel Prize in Chemistry



Taking the Experiment to Cyberspace

The [Nobel Prize in Chemistry 2013](#) was awarded jointly to [Martin Karplus](#), [Michael Levitt](#) and [Arieh Warshel](#) "for the development of multiscale models for complex chemical systems".

► [Press release](#)



Photo © Harvard University

Martin Karplus

Martin Karplus, U.S. and Austrian citizen. Born 1930 in Vienna, Austria. Ph.D. 1953 from California Institute of Technology, CA, USA. Professeur Conventionné, Université de Strasbourg, France and Theodore William Richards Professor of Chemistry, Emeritus, Harvard University, Cambridge, MA, USA.



Photo: S. Fisch

Michael Levitt

Michael Levitt, U.S., British and Israeli citizen. Born 1947 in Pretoria, South Africa. Ph.D. 1971 from University of Cambridge, UK. Robert W. and Vivian K. Cahill Professor in Cancer Research, Stanford University School of Medicine, Stanford, CA, USA.

► [Have a look at Michael Levitt's](#)



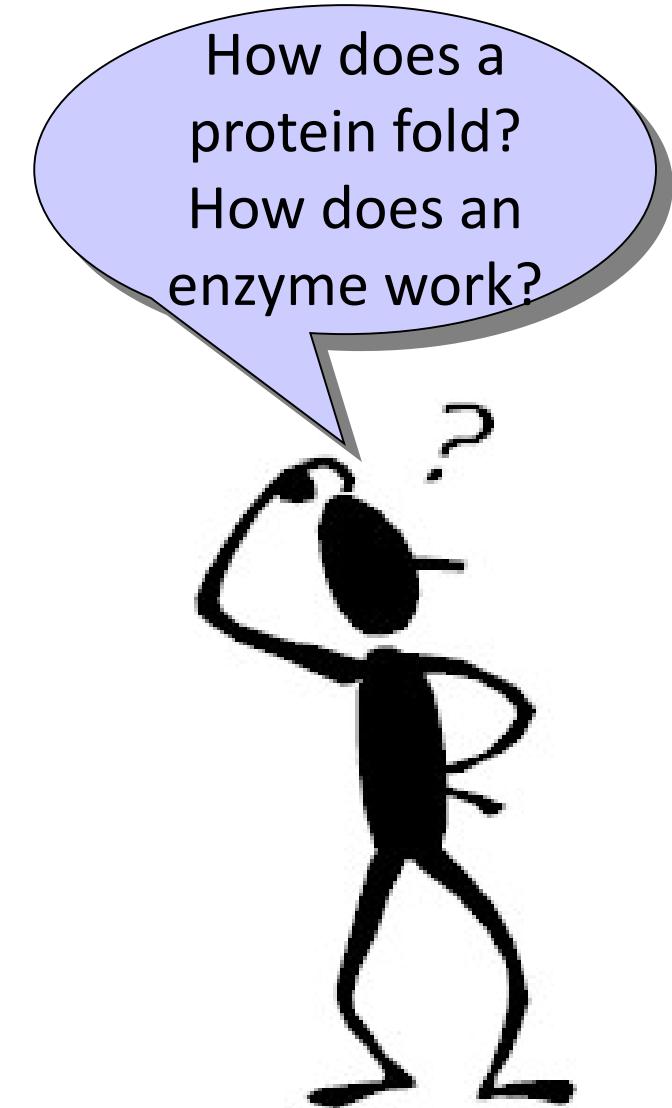
Photo: Wikimedia Commons

Arieh Warshel

Arieh Warshel, U.S. and Israeli citizen. Born 1940 in Kibbutz Sde-Nahum, Israel. Ph.D. 1969 from Weizmann Institute of Science, Rehovot, Israel. Distinguished Professor, University of Southern California, Los Angeles, CA, USA.

► [Interviews with Chemistry](#)

Introduction



How does a
protein fold?
How does an
enzyme work?

To answer these questions (and many others) scientists use appropriate experimental techniques, e.g., single-molecule spectroscopy, NMR spectroscopy , site-directed mutagenesis etc.

In this lecture we will see how we can use a computer to analyze at atomic level of detail the structure, flexibility and function of biological (macro)molecules.

Introduction

- In Molecular Dynamics (MD) simulations the laws of classical physics are used to approximate the interactions and motion of (macro)molecules.
- MD simulations are a multidisciplinary field. The underlying laws and theories stem from mathematics, physics and chemistry; algorithms from various areas of applied mathematics and computer science are implemented in a wide variety of MD software packages.

Wet-lab

Theory/Computer



Experimental information from:

X-ray crystallography

NMR spectroscopy

Electron microscopy

Atomic force microscopy

X-ray, light, and neutron scattering

Fluorescence techniques (FRET, FCS)

Other spectroscopic techniques
(CD, IR, ESR, UV)

Calorimetry (ITC, DSC)

Measurements of pH (titration),
sedimentation (centrifugation),
elution time (chromatography), ...

Development of new theories and models to rationalize and predict experimental observations

Development of (mathematical) models

Development of methods to explore models

Exploration of model phenomenology and properties

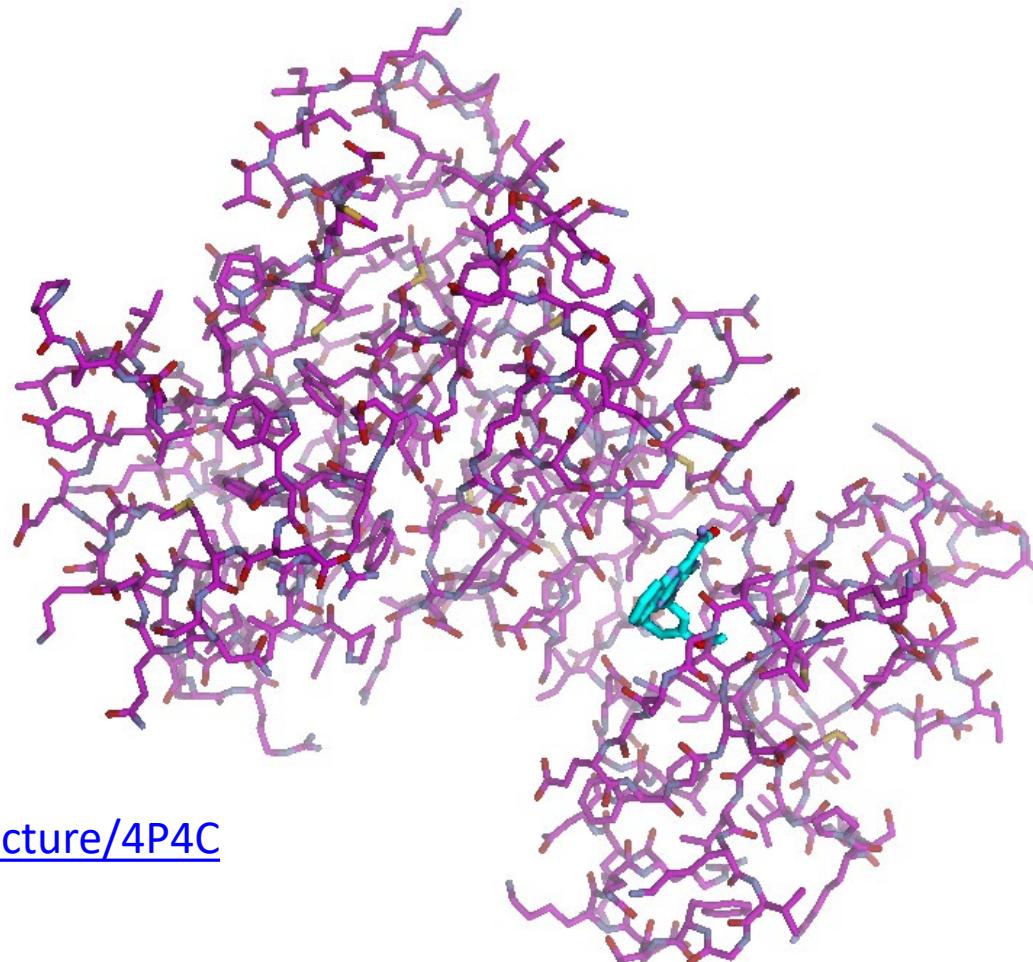


Understanding biomolecular structure, dynamics and function

- Molecule(s) of interest, e.g., protein, DNA, protein/RNA complexes, protein/small molecule complex, protein/membrane
- Solvent (water, ions, alcohol)
- Simulation box

- Instead of expressing (e.g. in *E. coli*) the molecule of interest, we have to supply the computer with the 3D coordinates of the desired molecule(s).
- For proteins and small organic compounds the atomic coordinates can be downloaded from the PROTEIN DATA BANK (www.rcsb.org).
- In the following slides the molecule of interest will always be **protein**, keep in mind though that for other types of (macro)molecules everything works analogously.

An example of a set of atomic coordinates which can be used to run molecular dynamics simulations. Which protein/ligand complex is it?

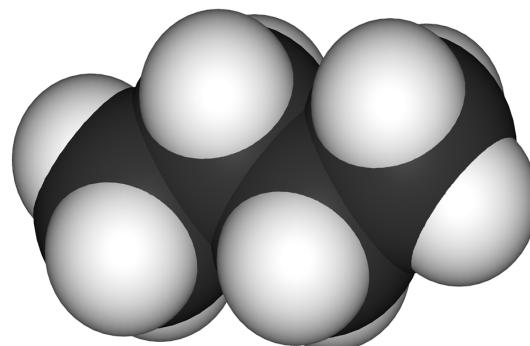
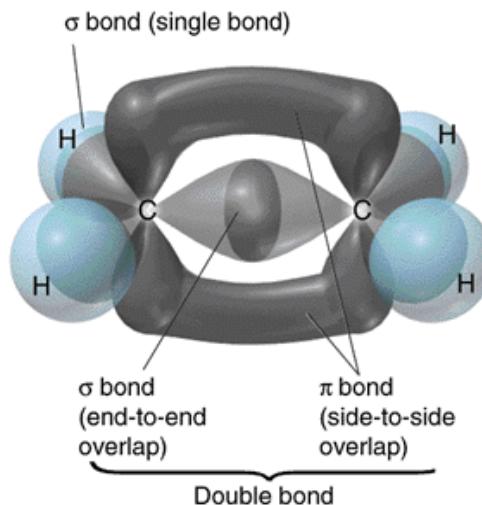


<http://www.rcsb.org/structure/4P4C>

- Furthermore, we need a model to describe the geometry and the physical interactions of the atoms of our protein.
- There are two main approaches:
 - Molecular mechanics, where the atoms are rigid spheres connected by rigid and unbreakable bonds.
 - Quantum mechanics, where also the dynamical evolution of the electrons is taken into account.
- In this course we will discuss the model based on classical mechanics.

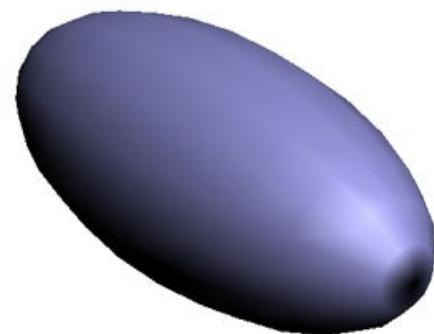
Structural Resolution in the Representation of Biomolecules

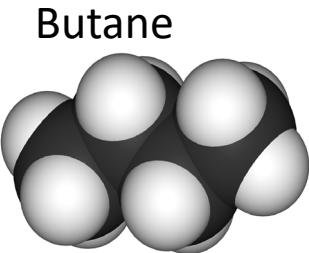
Ethene in electronic structure
level representation (orbitals)



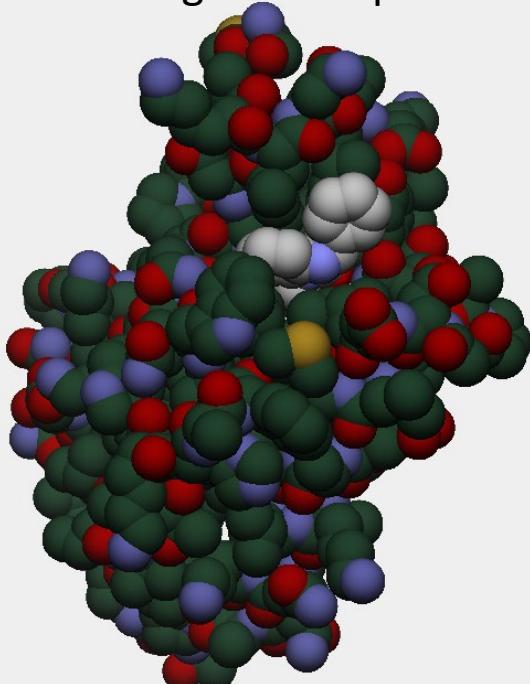
Butane in all-atom molecular
mechanics representation (spheres)

Short linear carbohydrate
in coarse-grained
representation (single
ellipsoidal bead)





Protein-ligand complex



<https://www.rcsb.org/structure/4 pci>

Molecular Mechanics Representation

- Each atom is represented as a sphere.
- The biomolecular force field is what shapes the collection of spheres into things that look like molecules through so-called **bonded** interactions.
- The force field also describes the atom-atom interactions of distal parts within a flexible molecule as well as the interactions between molecules through **nonbonded** interactions.
- Sometimes all-atom representation is simplified to so-called united-atoms (e.g.: a methyl group is a single sphere).
- Electronic structure is in general coarse-grained out and expected to be captured by the force field.

- The force field is an analytical function of the spatial coordinates of the atomic nuclei.
- Several different force fields are commonly available (CHARMM, AMBER, OPLS) . The CHARMM paper contains detailed information

<http://www.biochem-caflisch.uzh.ch/sites/default/files/publist/pdfs/charmm09.pdf>

- In modern force fields:

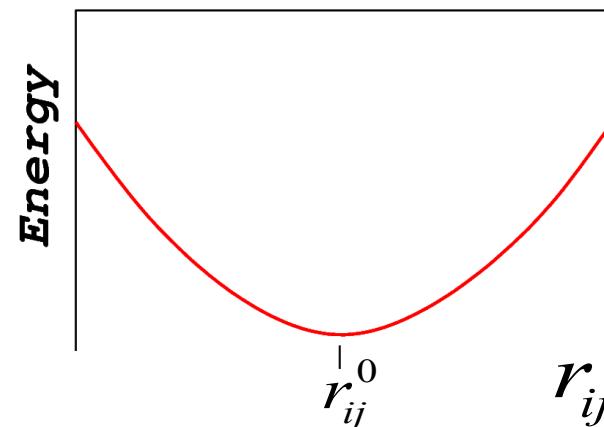
$$E = E_{Bonds} + E_{Angles} + E_{Dihedrals} + E_{Nonbonded}$$

- Let's go through the single terms.

- E_{Bonds} approximates the energy needed to stretch a covalent bond between two atoms by Hooke's law for the potential energy stored in a spring:

$$E_{Bonds}(r_{ij}) = k_{ij}^B (r_{ij} - r_{ij}^0)^2$$

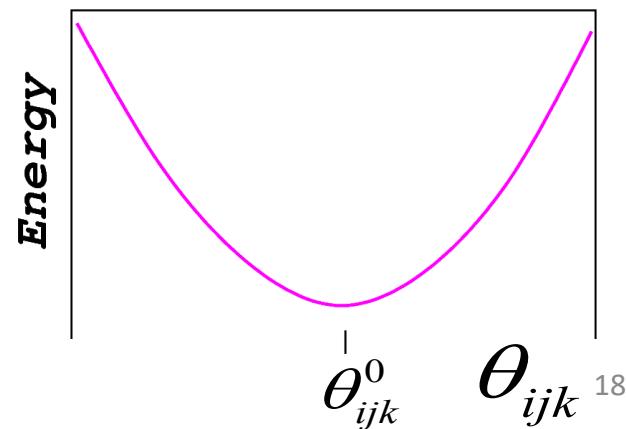
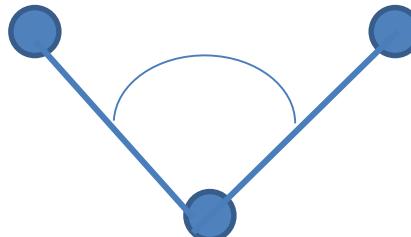
where i and j are two covalently connected atoms and r_{ij} is the distance between them. r_{ij}^0 is the equilibrium bond length and k_{ij}^B is a constant representing the stiffness of the bond.



- E_{Angles} models the energy needed to bend the angle formed by two covalent bonds. This term is represented by the following formula:

$$E_{Angles}(\theta_{ijk}) = k_{ijk}^\Theta (\theta_{ijk} - \theta_{ijk}^0)^2$$

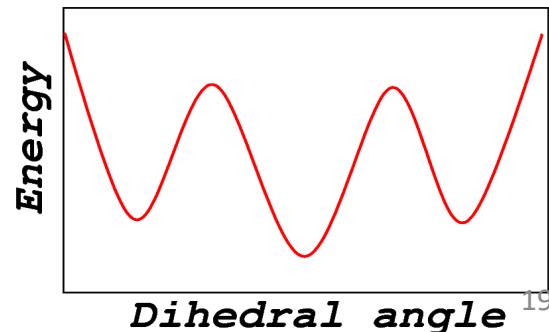
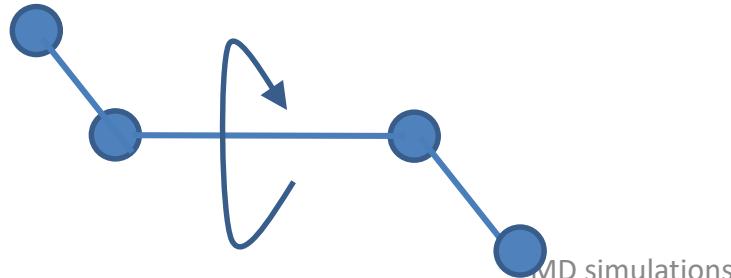
where i, j and k are three covalently connected atoms and θ_{ijk} is the angle between them. θ_{ijk}^0 is the equilibrium angle width and k_{ijk}^Θ represents the rigidity of the angle.



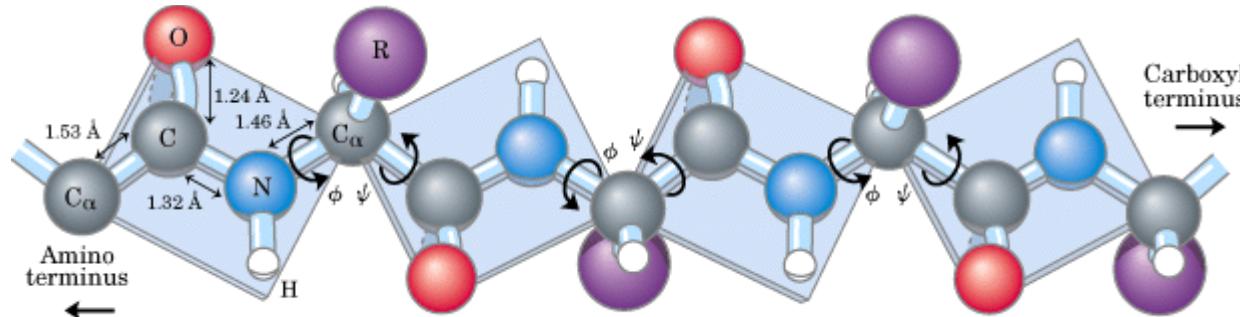
- $E_{Dihedrals}$ models the energy needed to bend the dihedral angle formed by three covalent bonds. This term is represented by the following formula:

$$E_{Dihedrals}(\varphi_{ijkl}) = k_{ijkl}^\Phi [1 + \cos(n\varphi_{ijkl} - \delta)]$$

where i, j, k and l are four covalently connected atoms and φ_{ijkl} is the dihedral angle between them.



- In $E_{Dihedrals}$, the k_{ijkl}^Φ parameter stands for the rigidity of the dihedral, while the parameters n and δ determine the value(s) where the energy has a minimum. For example for the ω dihedral angle of the protein backbone the two minima should always be close to 180° or 0° .



- So far we have treated covalently bonded atoms. What about the interactions between non covalently bonded atoms, i.e., pairs of atoms that are separated by more than two covalent bonds in the same protein or pairs of atoms indifferent proteins?
- In the classical force field representation, these interactions are **pairwise** and modeled with the following formula:

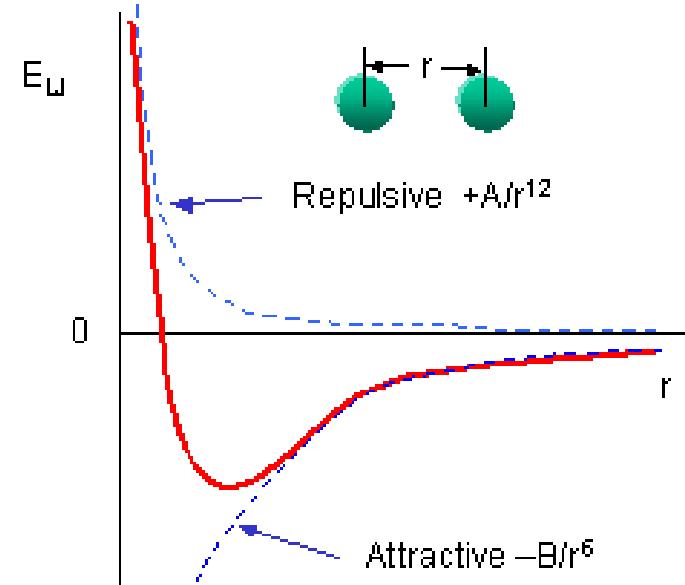
$$E_{Nonbonded} = E_{vdW} + E_{electrostatic}$$

- In principle, $E_{Nonbonded}$ should be calculated for every pair of atoms in the system. In practice, a distance threshold is used, i.e., nonbonding interactions are actually calculated only for atom pairs whose distance is smaller than a threshold (usually about 1.2 nm).

- E_{vdW} is modeled by the following energy function:

$$E_{vdW}(r_{ij}) = E_{\min_{ij}} \left[\left(\frac{r_{\min}}{r_{ij}} \right)^{12} - 2 \left(\frac{r_{\min}}{r_{ij}} \right)^6 \right]$$

- The repulsive term at short distances stems from the energy arising from the Pauli repulsion of overlapping electronic orbitals of different atoms;
- The attractive term at longer distances describes the attractive dispersion interactions.



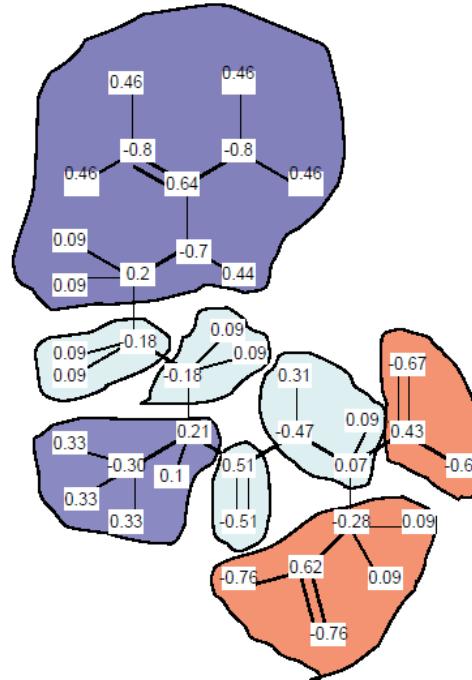
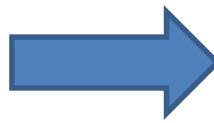
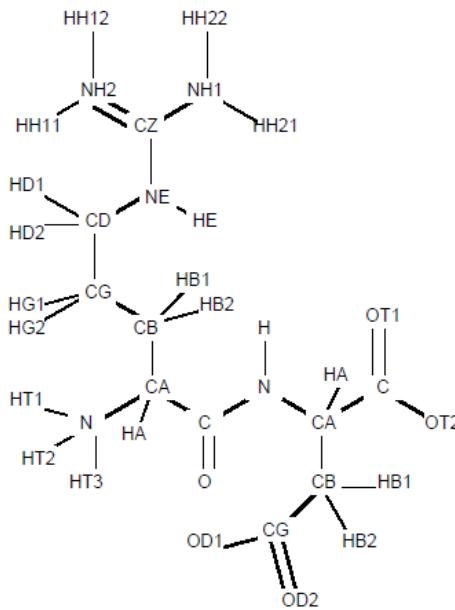
- $E_{electrostatic}$ models the coulombic interactions between partial charges:

$$E_{electrostatic}(r_{ij}) = \frac{q_i q_j}{4\pi\epsilon r_{ij}}$$

where ϵ is the dielectric constant of the surrounding medium.

- What are q_i and q_j ?

- From chemistry we know that the electrons do not evenly distribute along a covalent bond (cfr. electronegativity values).
- In order to reproduce the polarization of a covalent bond, which leads for example to the hydrogen-bonding, a partial charge is assigned to each atom of our protein, depending on the bond partners.



- All the parameters, like the equilibrium values and the spring constants in E_{Bond} or the values of r_{min}^{ij} and E_{min}^{ij} in E_{vdW} have to be calibrated for each desired molecule.
- The parameters are determined by an optimization process, which consists of several steps . At each step, the calculated properties of a protein are compared to experimental results and then the set of parameters is iteratively changed in order to get as close as possible to the experimentally known properties of the examined protein.

An experiment on a computer

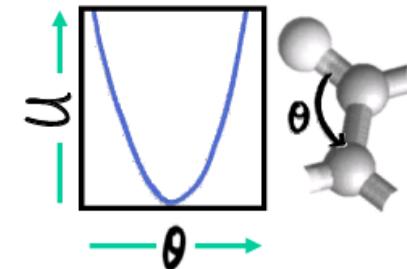
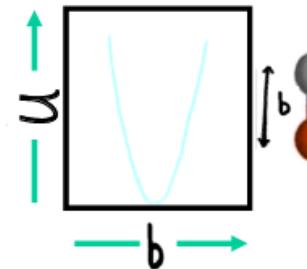
$$E = E_{Bonds} + E_{Angles} + E_{Dihedrals} + E_{Nonbonded}$$

$$= \sum \frac{1}{2} K_b (b - b_0)^2 + \sum \frac{1}{2} K_\theta (\theta - \theta_0)^2$$

All Bonds

Hooke 1635

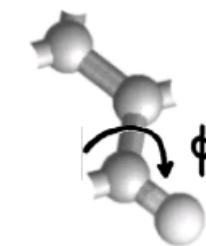
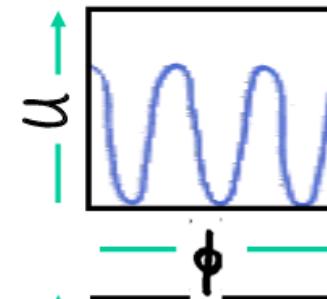
All Angles



$$+ \sum K_\phi [1 - \cos(n\phi + \delta)]$$

All Torsion Angles

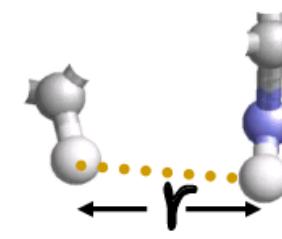
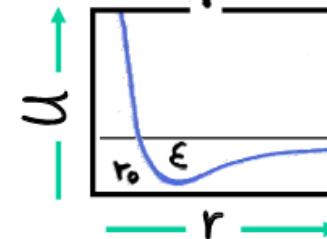
Fourier 1768



$$+ \sum \epsilon \left[\left(\frac{r_0}{r} \right)^{12} - 2 \left(\frac{r_0}{r} \right)^6 \right]$$

All Nonbonded pairs

Van der Waals 1837

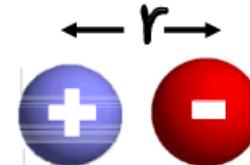
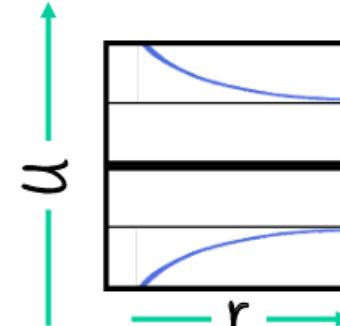


$$+ \sum 332 q_i q_j / r$$

All partial charges

Coulomb 1736

Simple sum over many terms



- “*Everything should be made as simple as it can be but not simpler*” (A. Einstein).
- A force field (model) is never perfect. A model that is not quantitatively fully accurate does **not** preclude one from formulating hypothesis to guide experiments.
- One of the major sources of **systematic error** in classical force fields is the lack of polarization. Partial charges are assigned at the beginning of the calculation (minimization or dynamics) and kept constant.
- It is important to compare **simulation results** to all available **experimental data**.

- Most of the experiments in biochemistry are performed in aqueous solvent. Therefore we need to model the interactions of our protein with the aqueous environment.
- There are two different ways to model the protein/solvent interactions:
 - Explicit solvent representation:
Water molecules and ions are modeled considering all of their nuclei as interaction centers and degrees of freedom.
 - Implicit solvent representation:
The interactions of the examined protein with the surrounding solvent are described by a mean field framework.

Explicit Water Representation

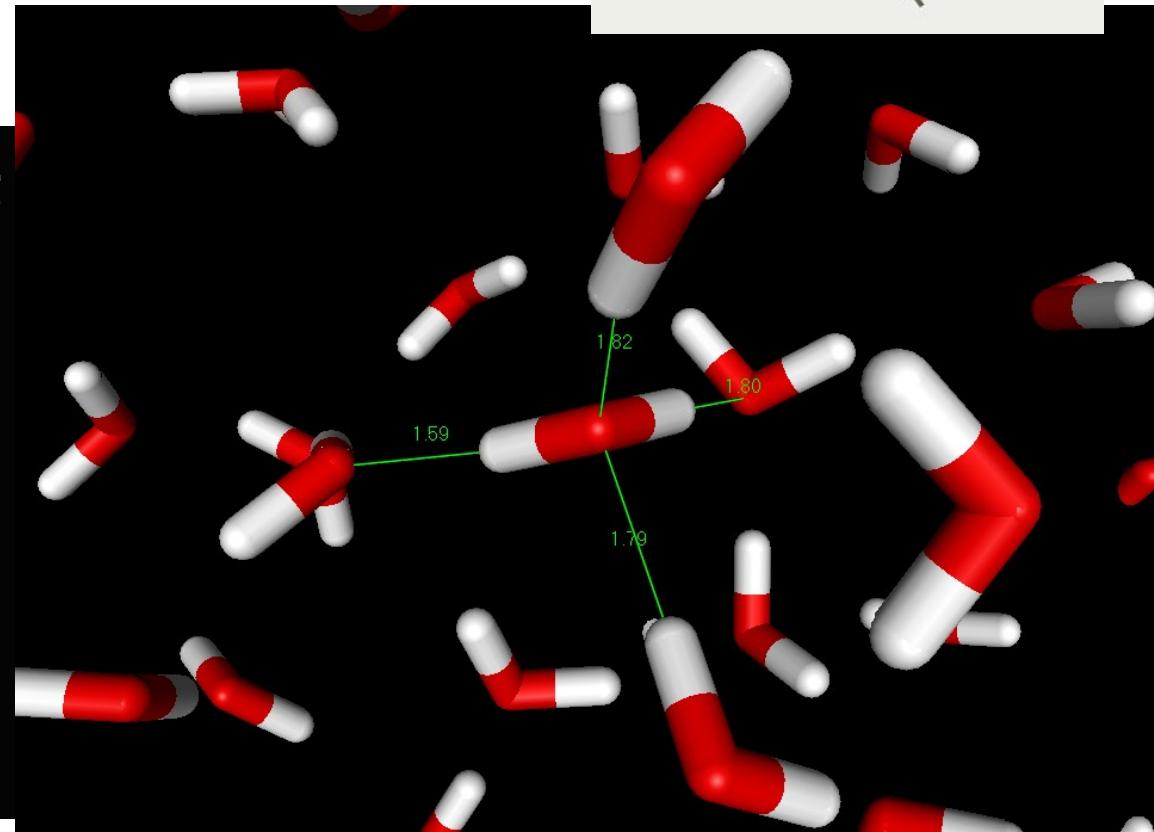
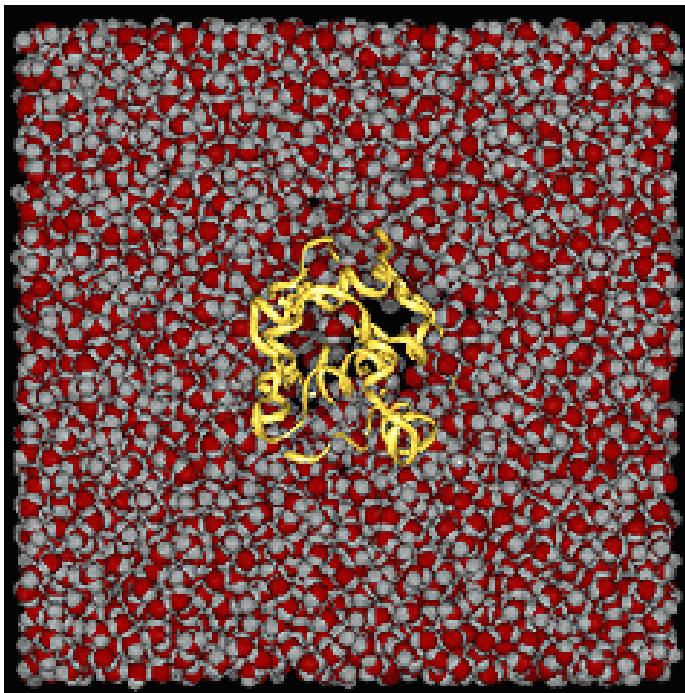
- The description of the water molecules is based on the same principles aforementioned for the protein.
- Water molecule's geometry is described with spheres connected by rigid and unbreakable bonds.
- The interactions of the water molecules with each other and with the examined protein are given by the following term of the force field:

$$E_{Nonbonded} = E_{vdW} + E_{electrostatic}$$

An experiment on
a computer

SOLVENT
SOLVENT

Explicit Water Representation



Implicit Water Representation

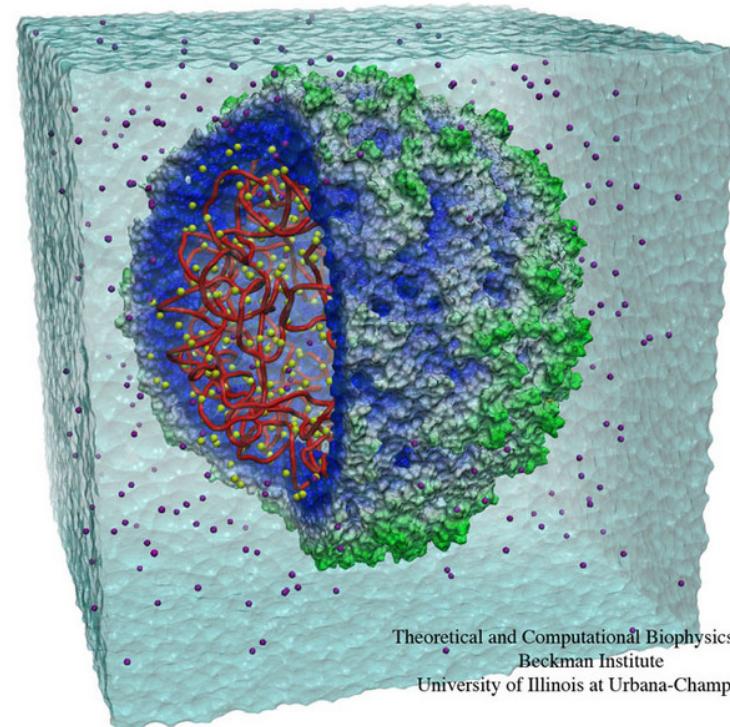
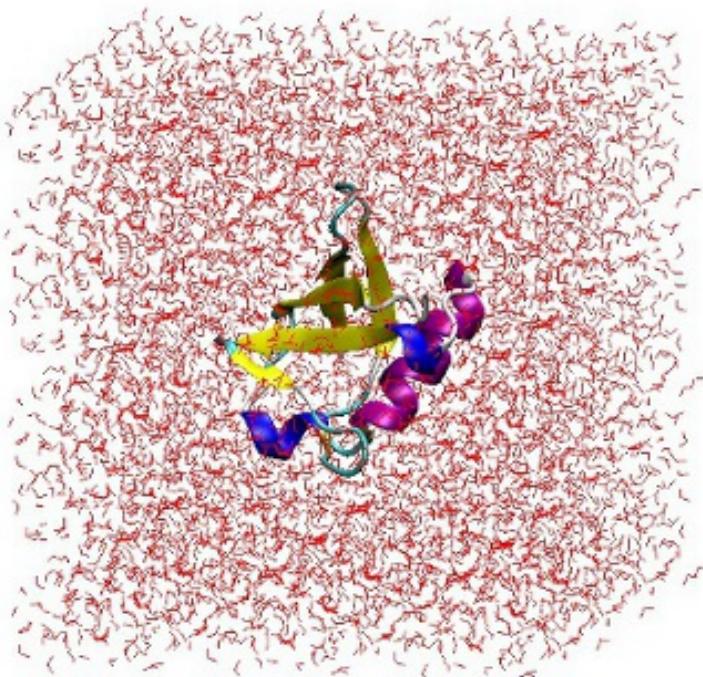
- From the pictures in the previous slide it stands out that usually the protein is much “bigger” than a water molecule.
- Consider a boat on the Lake of Zurich: in order to study the motion of the boat on the water we do not need to consider the interactions of it with all the single water molecules surrounding it.
- Analogously, we can avoid representing each water molecule in our simulation, given that we have a function that models the mean interaction of the aqueous solvent with the examined protein. This is what is meant by Implicit Water Representation



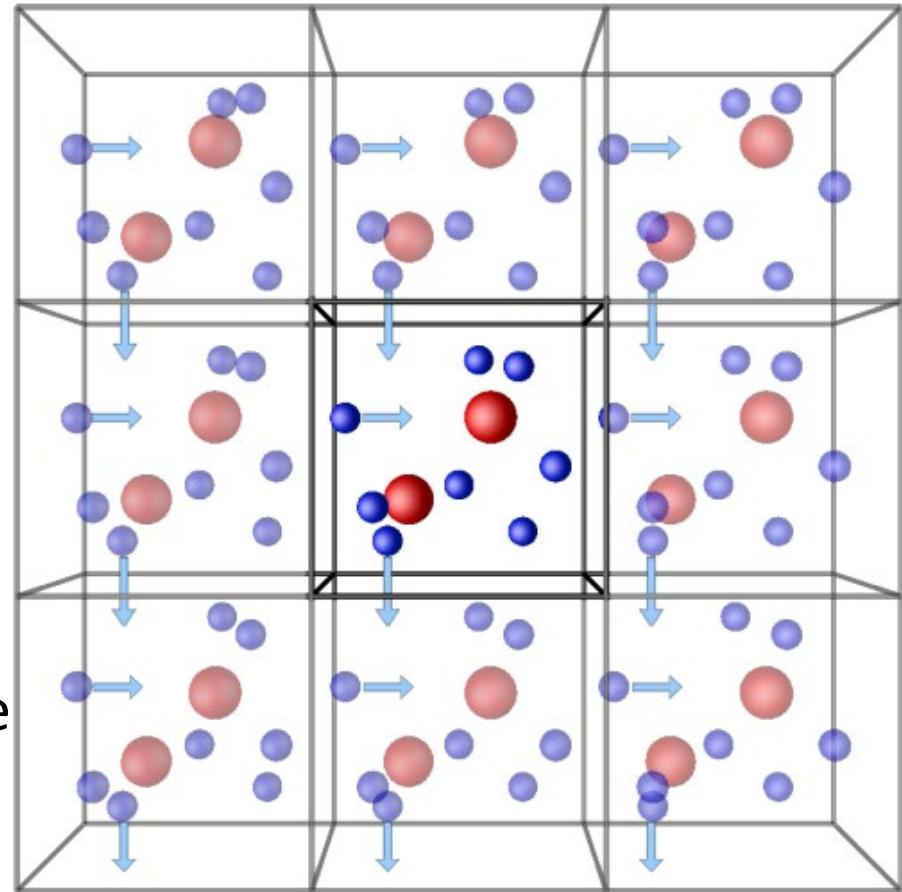
An experiment on a computer

SIMULATION BOX

- We have seen how to model the protein and the solvent, now we have to “place” them somewhere.
- Where in experiments you would use a cuvette, in simulation we use a virtual box of a given geometry (cubic, orthorombic, truncated octahedron, etc.)



- To avoid finite-size effects and prevent molecules from leaving the box, Periodic Boundary Conditions (PBC) are usually applied.
- The actual simulation box is replicated so that it is fully surrounded by “image” boxes.
- Special algorithms deal with the interactions between the “real” molecules and their images.



- Once we have our protein properly solvated in a simulation box, we can start our experiment .
- In our approximation, the evolution in time of our system will be dictated by the Newton's equation:

$$\vec{F}_i(t) = m_i \vec{a}_i(t) = m_i \frac{d^2 \vec{x}_i(t)}{dt^2}$$

where for atom i, $\vec{F}_i(t)$ is the force acting on it at time t , m_i is the mass, $\vec{a}_i(t)$ is the acceleration at time t and $\vec{x}_i(t)$ is the position at time t.

- At $t = 0$, the positions of each atom are given from the PDB structure.
- To each atom we assign an initial velocity, taken from a Gaussian distribution.
- From the energy of the system, we can calculate the force acting on each atom at a certain time t :

$$-\frac{\partial \vec{E}(t)}{\partial \vec{x}_i} = \vec{F}_i(t) = m_i \vec{a}_i(t)$$

Remember: to calculate the energy at time t , we just need to plug in the coordinates of all the atoms at time t in the force field function!

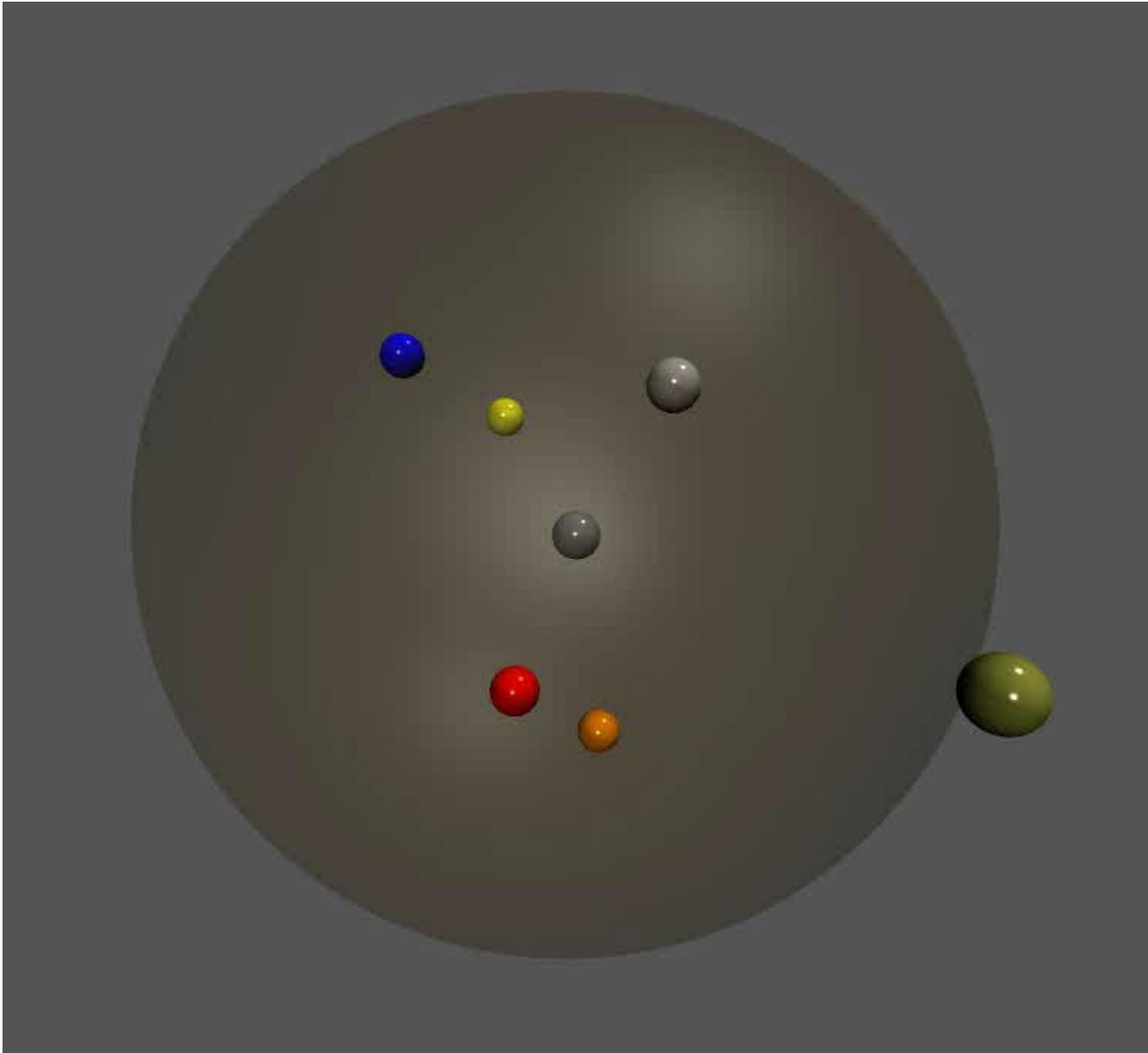
- Knowing the acceleration, the velocity and the position at time t for all the atoms, we can calculate the positions at time $(t + \Delta t)$:

$$\vec{x}_i(t + \Delta t) = \vec{x}_i(t) + \vec{v}_i(t)\Delta t + \frac{1}{2}\vec{a}_i(t)\Delta t^2$$

while the velocities are given by the equation:

$$\vec{v}_i(t + \Delta t) = \vec{v}_i(t) + \vec{a}_i(t)\Delta t$$

Usually, the time step is chosen to be $\Delta t = 2$ fs.



Changing the ensemble

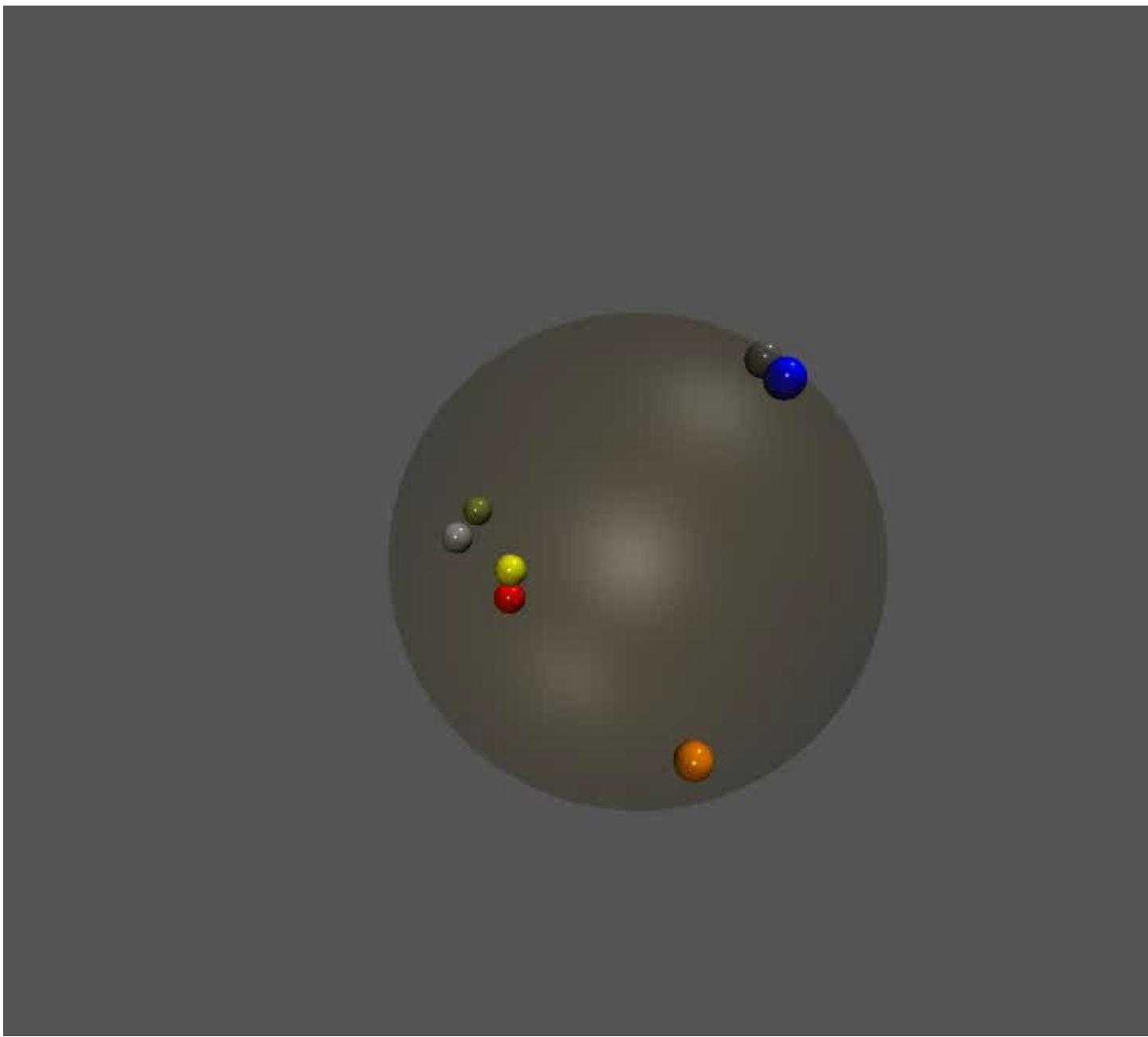
- The system we have put together has constant number of particles, constant volume and constant energy. The simulation samples then what in statistical mechanics is called a **microcanonical ensemble (NVE)**.
- Often, it will be necessary to **match the conditions of a simulation to that of an experiment** or to something that is physically more suitable to the problem.
- **NVE → NVT**: Add a thermostat; in essence an auxiliary process that modifies particle velocities (common: Berendsen, Nose-Hoover, Andersen, Bussi-Parrinello)
- **NVE → NPT**: Add a manostat and a thermostat; in essence, a manostat is an auxiliary process that rescales the volume of the system in response to the difference between internal and external pressure (common: Berendsen, Parrinello-Rahman, Langevin piston)
- **NVE → $\mu_m VT$** : Add a thermostat and a chemostat (particle bath); in essence, a chemostat is a reservoir of “bath” particles that allows the concentration of particles in the explicitly represented volume to fluctuate (remember aquaporins).

Langevin's Equation of Motion

- Alternatively to Newton's equation, Langevin's equation of motion can be used to reproduce the time evolution of our system. For each (classical) atom, we have a modified differential equation:

$$m_i \vec{a}_i(t) = \vec{F}_i(t) + \sqrt{2\gamma_i k_B T m_i} \vec{R}(t) - m_i \gamma_i \vec{v}_i(t)$$

- Newton's equation is “extended” by two terms: a random force relying on a stationary and normalized random (Wiener) process, and a friction term that is velocity-dependent.
- The rate of kinetic energy dissipation (friction) and the magnitude of the random force resulting from equilibrium fluctuations are fundamentally linked because they are caused by the same underlying process: assumed collisions with “bath” particles.
- Because the system is coupled explicitly to an (assumed) bath, energy is not conserved and one naturally obtains **a canonical ensemble (NVT)** when using Langevin's equations of motion to propagate a dynamical system.

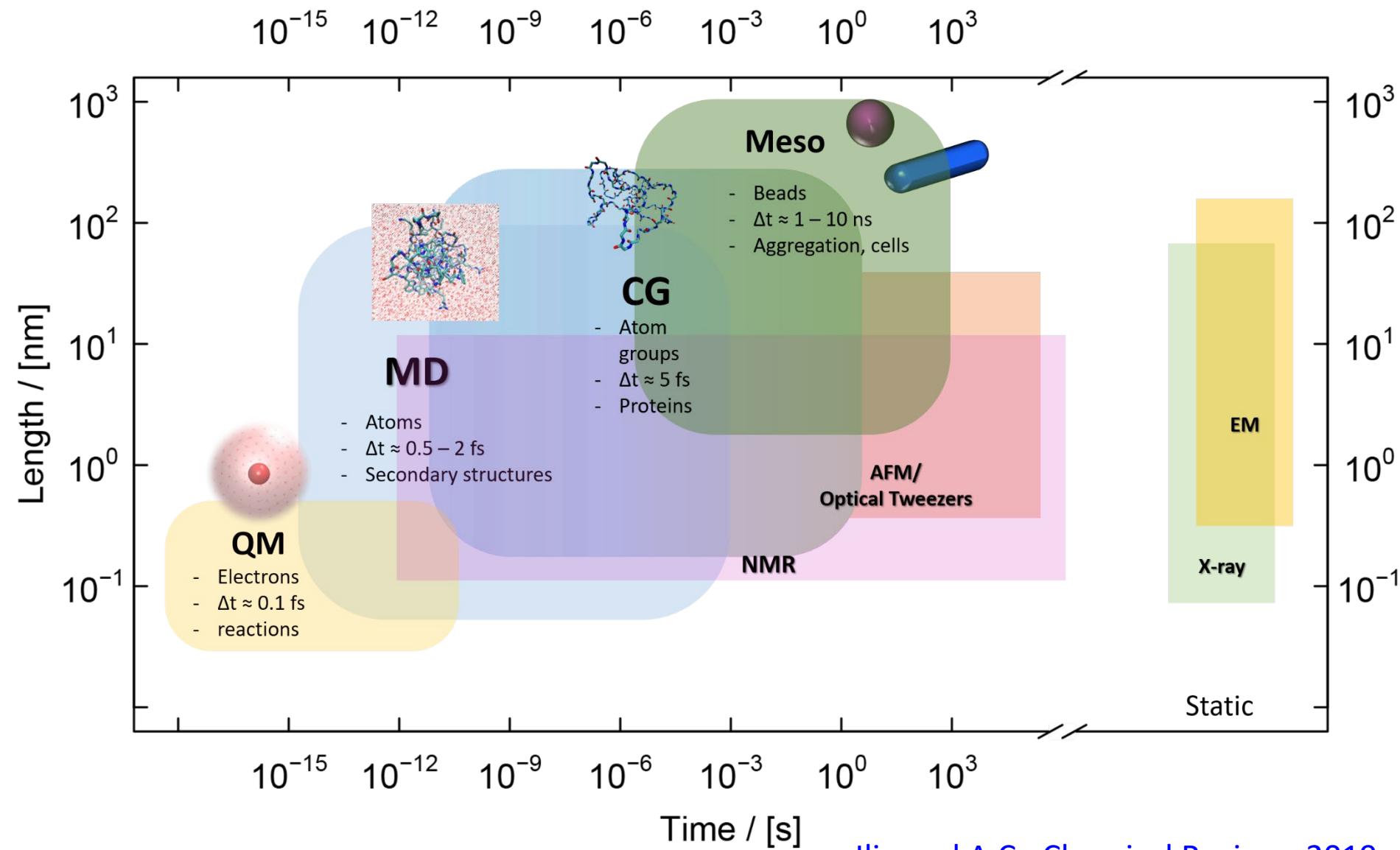


- Since modelling all atoms explicitly is computationally expensive, representations with lower resolution (coarse graining) have been developed to simulate processes that take place on longer time scales.
- Coarse graining can reduce the **statistical error** (i.e., can reach longer time scales because of less degrees of freedom and longer time step) but increases the **systematic error**.

System	Time scale
Ligand unbinding of a weak binder from the binding pocket on a protein	~ 10 ns
Structural rearrangements of a domain of ~ 100 a.a. in the native state in explicit water	~ns to μ s
Reversible folding of a miniprotein ~ 20 a.a. in implicit water	~ μ s
Aggregation of a model peptide in coarse-grained representation	~10 μ s

An experiment on a computer

DYNAMICS



Ilie and A.C., Chemical Reviews 2019

- The simulation packages produce an output file called *trajectory*, that contains the coordinates of all the atoms at specific time intervals decided by the user, e.g. every 2-20 ps depending on the type of simulation and on the studied system.
- From the trajectory, we can calculate time evolution or averages over time of quantities like radius of gyration, internal energy, secondary structure propensity, interaction energy, root mean square deviation (RMSD) of the protein(s).

Simulations of PDZ3 of PSD-95/SAP90 in native state:

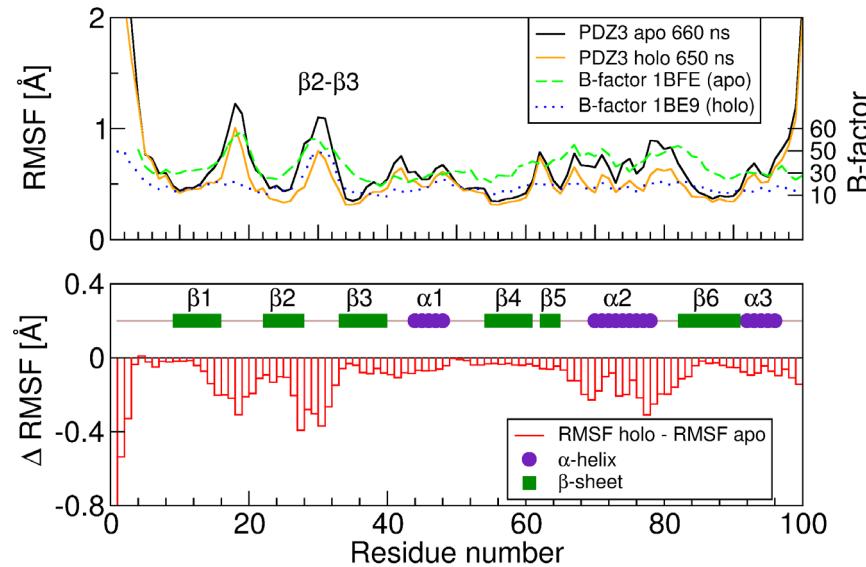
Over the complete MD trajectory we can compute the root mean square fluctuations (RMSF) for specific atoms.

The formula for the RMSF of an atom i is the following :

$$RMSF = \sqrt{\frac{1}{T} \sum_{t_j=1}^T (x_i(t_j) - \tilde{x}_i)^2}$$

where T is the time over which one wants to average, $x_i(t_j)$ is the position of atom i at time t_j and \tilde{x}_i is the reference position for atom i (i.e. average position over time).

The plot of RMSF of the Ca's of each residue of PDZ3 shows that loop regions fluctuate much more than secondary structure elements. The profile of RMSF along the sequence can be compared with the crystallographic B-factors.



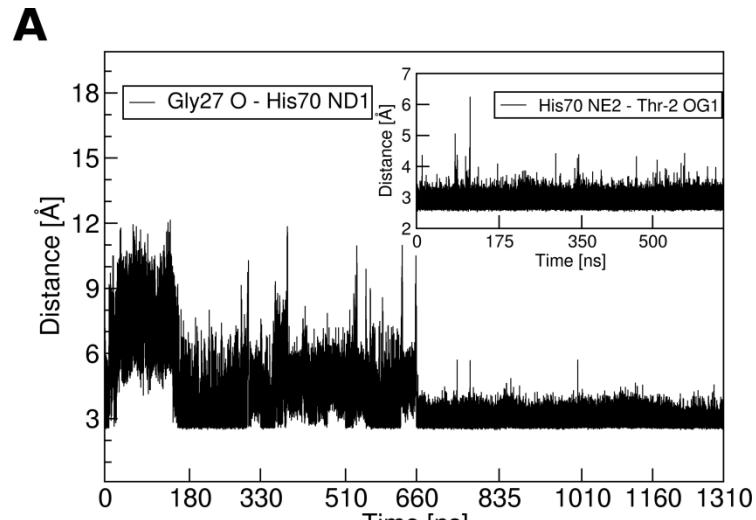
From: [Steiner & Caflisch, Proteins. 80\(11\): 2562-72 \(2012\)](#)

An experiment on a computer

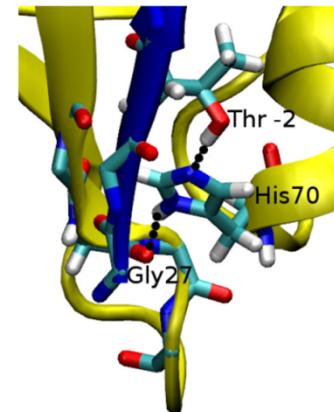
ANALYSIS

Since the MD trajectory allow us to follow the position of every single atom over time, we can also follow certain interactions over time.

If we plot the distances of the Donor and Acceptor of each hydrogen bond over time, we can see when and how often these bonds are formed during the simulation (remember that for H-bonds Donor-Acceptor distance is usually around 3 Å).



B

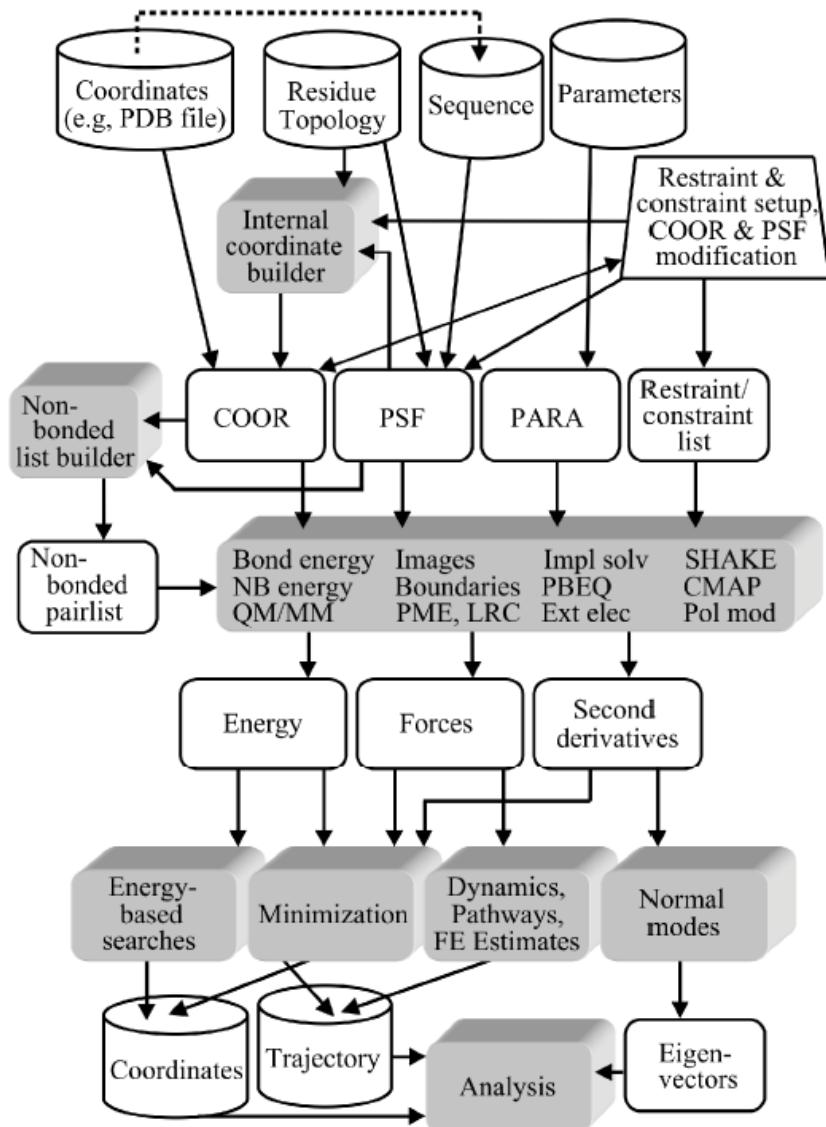


From: [Steiner & Caflisch, Proteins. 80\(11\): 2562-72 \(2012\)](#)

An experiment on a computer

Software Packages: CHARMM

CHARMM
SOFTWARE



Link to paper <[click here](#)>

Input files (force field, molecular topologies, coordinates)

Software setup of structural representation

Setup and use of force field

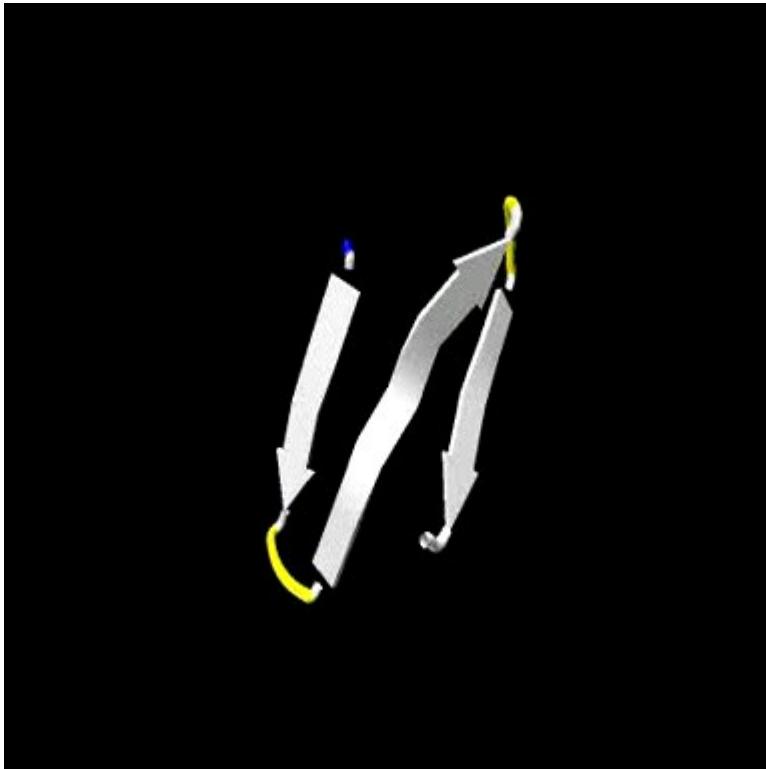
Implementation of sampling algorithms

Simulation data and their analysis

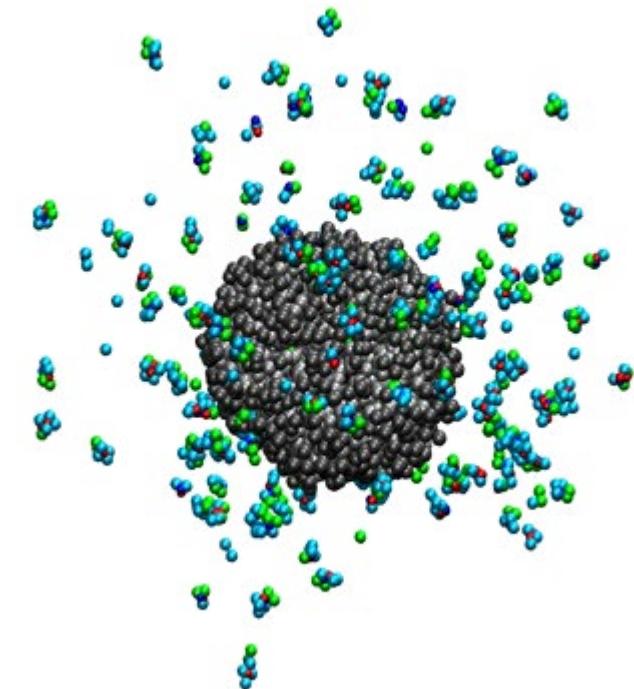
Dynamics Software Packages

- CHARMM (co-development of ~20 research groups around the world over past few decades, originated at Harvard under Martin Karplus, 2013 Nobel laureate in Chemistry)
 - Developed over the last three decades with a primary focus on molecules of biological interest, including proteins, peptides, lipids, nucleic acids, carbohydrates and small molecule ligands.
 - Solution, crystals, and membrane environments.
 - Energy minimization, normal mode analysis, molecular dynamics, Monte Carlo sampling, umbrella sampling, free energy perturbation, large set of analysis techniques, and model-building capabilities.
 - Different energy functions and models including classical potential energy (force field), mixed quantum mechanical-molecular mechanical approach, and interface to ab initio quantum chemistry.
 - Explicit solvent and various boundary conditions, several implicit solvent models (surface based, generalized Born, finite-difference Poisson).
- AMBER (originated at UCSF)
- GROMACS (originated at University of Groningen)
- NAMD, DESMOND, and many more ...

- Typical applications:
 - Reversible **folding** of a miniprotein in implicit water
 - Amyloid **aggregation** on the surface of a lipid vesicle



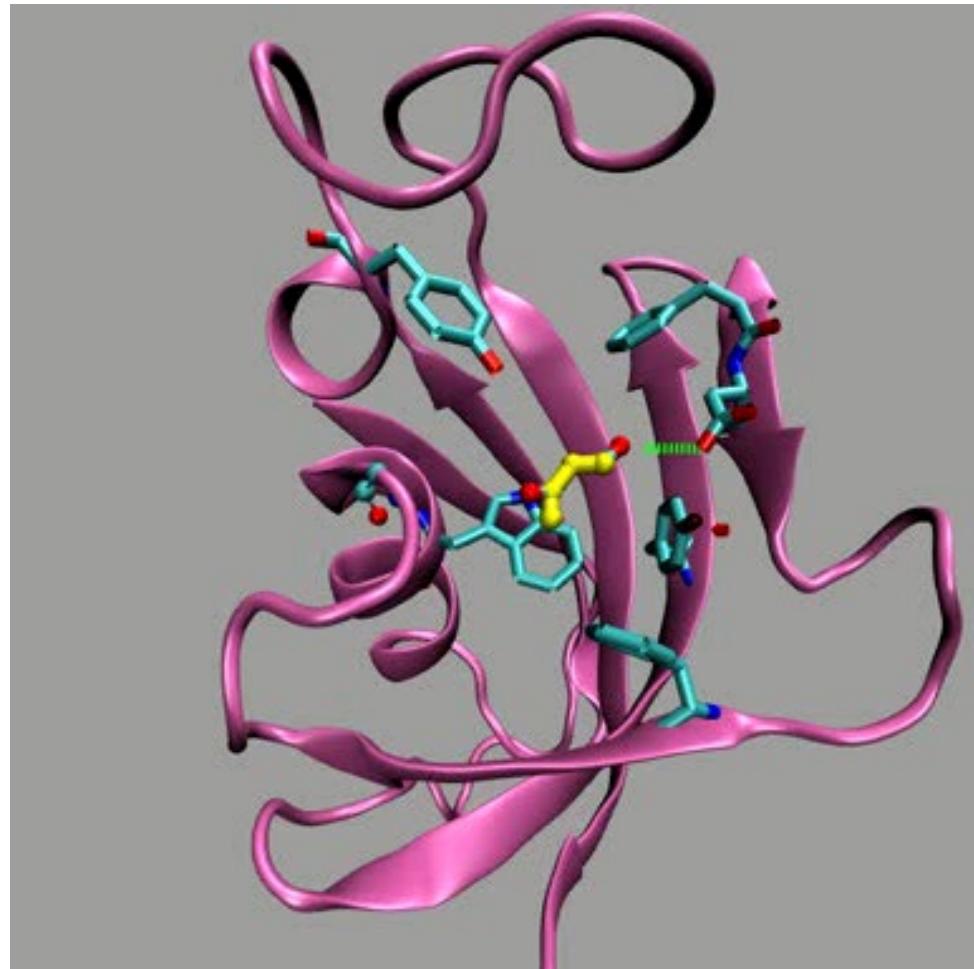
www.biochem-caflisch.uzh.ch/movies/0001/



www.biochem-caflisch.uzh.ch/movies/0005/

- Typical applications:
 - Small molecule **unbinding**

Experimental approaches to the study of fragment binding to proteins have limitations in resolution. Molecular dynamics simulations of small molecule binding and unbinding provide femtosecond temporal resolution and full spatial resolution.



<http://www.biochem-caflisch.uzh.ch/movies/0012/>

- Typical applications:
 - Ligand **optimization**

Molecular dynamics simulations can be used to guide the optimization of hit compounds by medicinal chemistry;
example of a paper

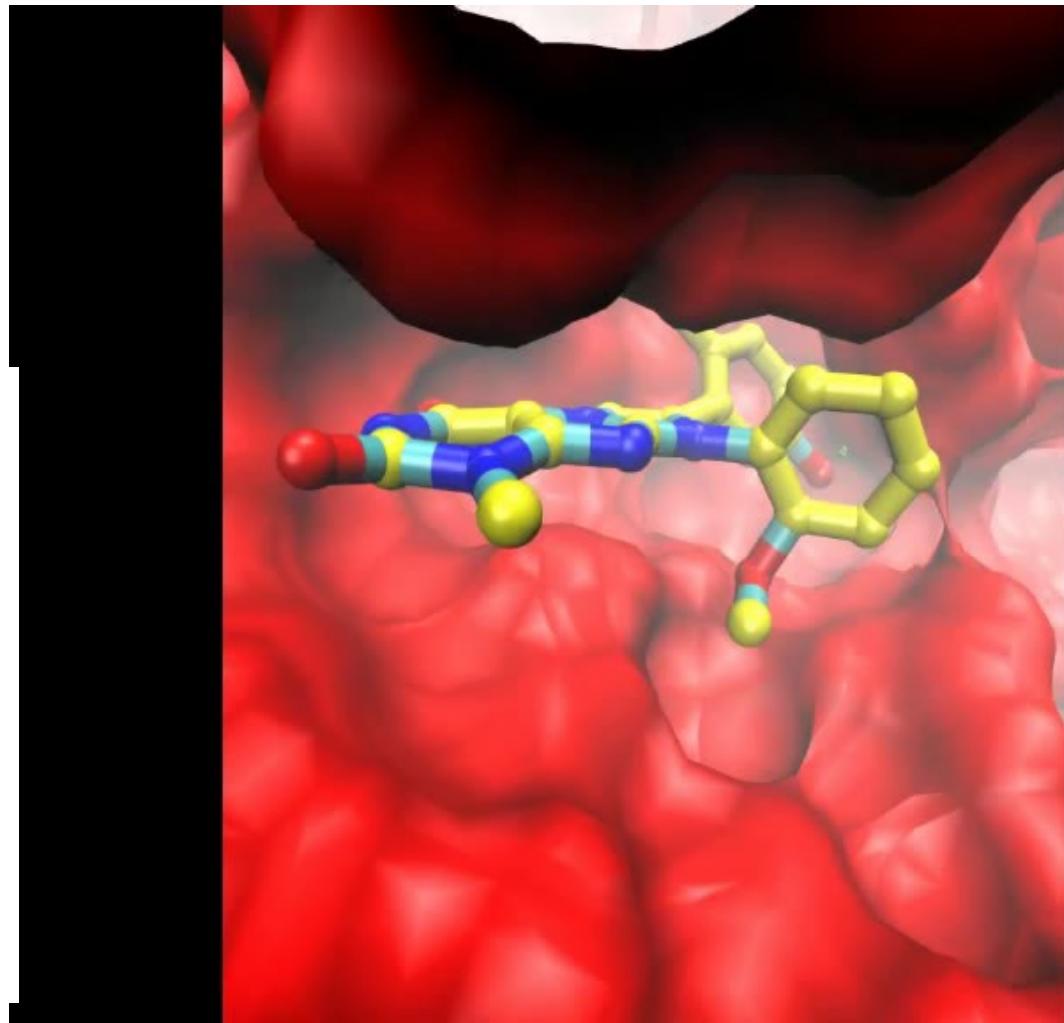
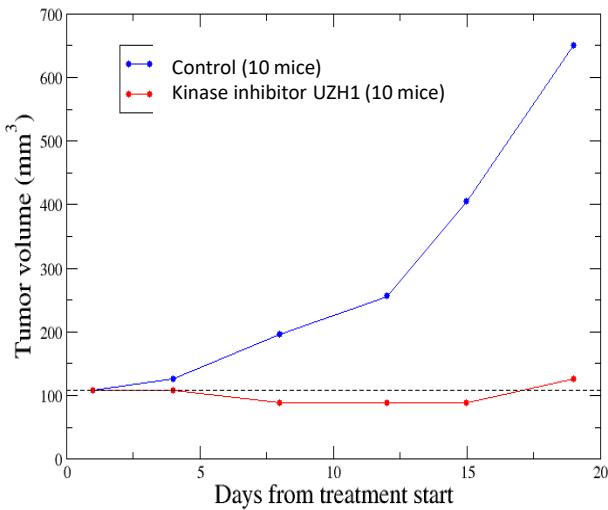
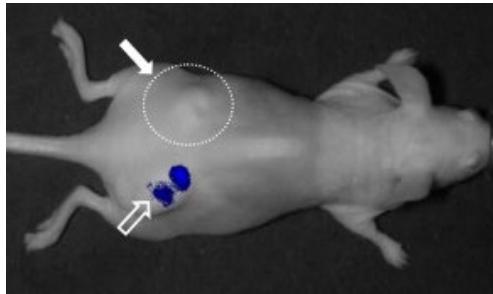
http://www.biochem-caflisch.uzh.ch/sites/default/files/publist/pdfs/Xu_Unzue_JMedChem2016.pdf

Example of a movie



<http://www.biochem-caflisch.uzh.ch/movies/0028/>

- Drug design:



[Unzue et al., J. Med. Chem. 2014, 57, 6834–6844](#)

<http://www.biochem-caflisch.uzh.ch/movies/0010/>

Movies

<http://www.biochem-caflisch.uzh.ch/movies/>

Kinetic response of a photoperturbed allosteric protein

Brigitte Buchli^{a,1}, Steven A. Waldauer^{a,1}, Reto Walser^{a,1}, Mateusz L. Donten^a, Rolf Pfister^a, Nicolas Blöchliger^b, Sandra Steiner^b, Amedeo Caflisch^b, Oliver Zerbe^a, and Peter Hamm^{a,2}

Departments of ^aChemistry and ^bBiochemistry, University of Zurich, CH-8057 Zurich, Switzerland

Edited by Hans Frauenfelder, Los Alamos National Laboratory, Los Alamos, NM, and approved June 3, 2013

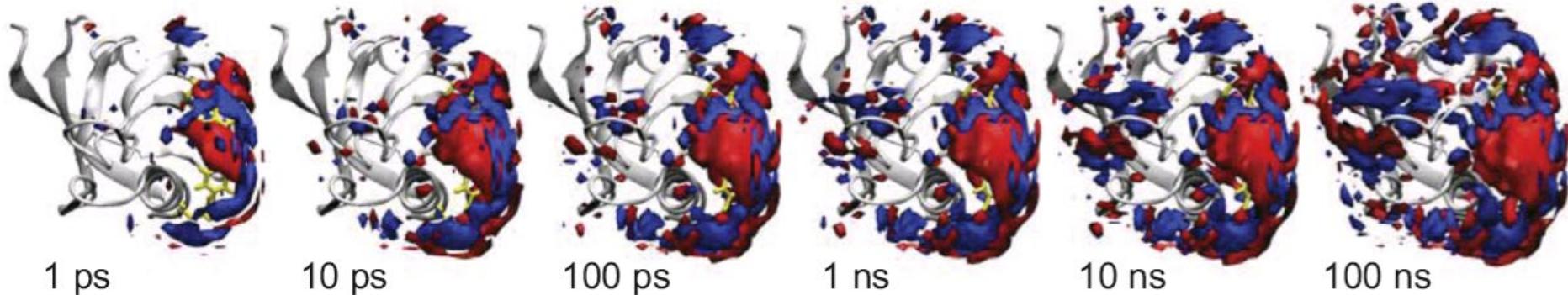
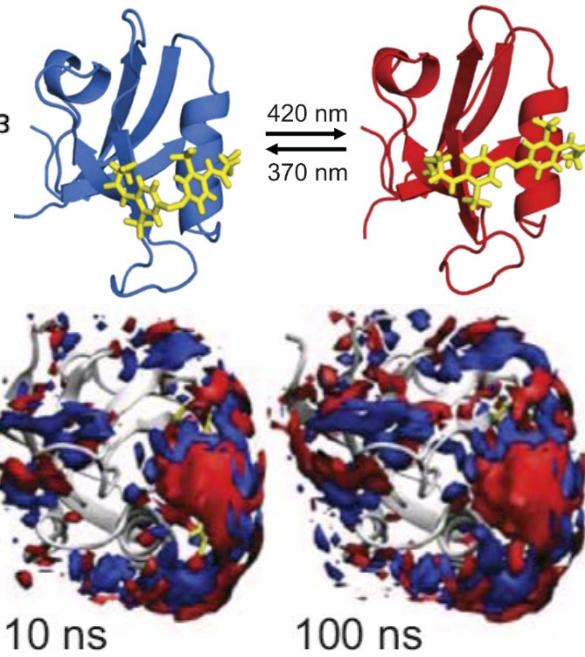


Fig. 5. Change of water density as a function of simulation time, compared with that just before switching. Red depicts increased density and blue decreased density. The contour surfaces correspond to changes of ± 0.01 water/ \AA^3 (for comparison, the bulk water density is ~ 0.033 water/ \AA^3). The protein is shown as a gray ribbon and the photoswitch (visible only in part) is shown in yellow. See also [Movie S1](#).

Interested in a position?

<http://www.biochem-caflisch.uzh.ch/jobs>

The screenshot shows the homepage of the Amedeo Caflisch Research Group at the University of Zurich. The top navigation bar includes links to Home, Research, Group Members, Publications, Movie Gallery, Structure Gallery, Software Download, Chemical Probes, Lectures, Miscellanea, Open Positions, and Contact. The University of Zurich logo is in the top right. Below the navigation, it says "Amedeo Caflisch Research Group" with a small logo. The main heading is "COMPUTATIONAL STRUCTURAL BIOLOGY". A welcome message reads: "Welcome to the Website of the Research Group of Amedeo Caflisch at UZH. We are a multidisciplinary research group situated at the interface of (human) biology and molecular physics. We are part of the Department of Biochemistry at the University of Zurich in beautiful Switzerland. The people working with us are diverse in background, having degrees in any of the natural sciences or even in computer science or mathematics." It continues: "Broadly speaking, we use computers to understand processes of biological interest at a molecular level, for example those implicated in Alzheimer's disease. Similarly, we try to make testable predictions, for example in the discovery of drug candidates for pharmaceutical research. You can find more information on the various activities in the group on our [RESEARCH PAGE](#)." A note at the bottom says: "Please use the top level menu to navigate this website. If you have suggestions or complaints regarding the content on this site, do not hesitate to contact us." To the right of the text is a colorful ribbon diagram of a protein structure. At the bottom is a photo of a group of people sitting around a table in a restaurant.

Home | Research | Group Members | Publications | Movie Gallery | Structure Gallery | Software Download | Chemical Probes | Lectures | Miscellanea | Open Positions | Contact

Amedeo Caflisch Research Group

COMPUTATIONAL STRUCTURAL BIOLOGY

Welcome to the Website of the Research Group of Amedeo Caflisch at UZH

We are a multidisciplinary research group situated at the interface of (human) biology and molecular physics. We are part of the Department of Biochemistry at the University of Zurich in beautiful Switzerland. The people working with us are diverse in background, having degrees in any of the natural sciences or even in computer science or mathematics.

Broadly speaking, we use computers to understand processes of biological interest at a molecular level, for example those implicated in Alzheimer's disease. Similarly, we try to make testable predictions, for example in the discovery of drug candidates for pharmaceutical research. You can find more information on the various activities in the group on our [RESEARCH PAGE](#).

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MD simulations