Computational Science and Engineering

Field of Specialization:

Chemistry

Contact:

Prof. Philippe Hünenberger

Prof. Markus Reiher

Prof. Sereina Riniker

Presented by:

Salomé Rieder

Molecular modeling/simulation in (bio)chemistry

Understand (and predict) the workings of (bio)molecular systems using physics-based models

*Simulation can **replace** experiment when:*

- the process **cannot** be studied experimentally
- the process is **dangerous** to study experimentally
- the process is **expensive** to study experimentally

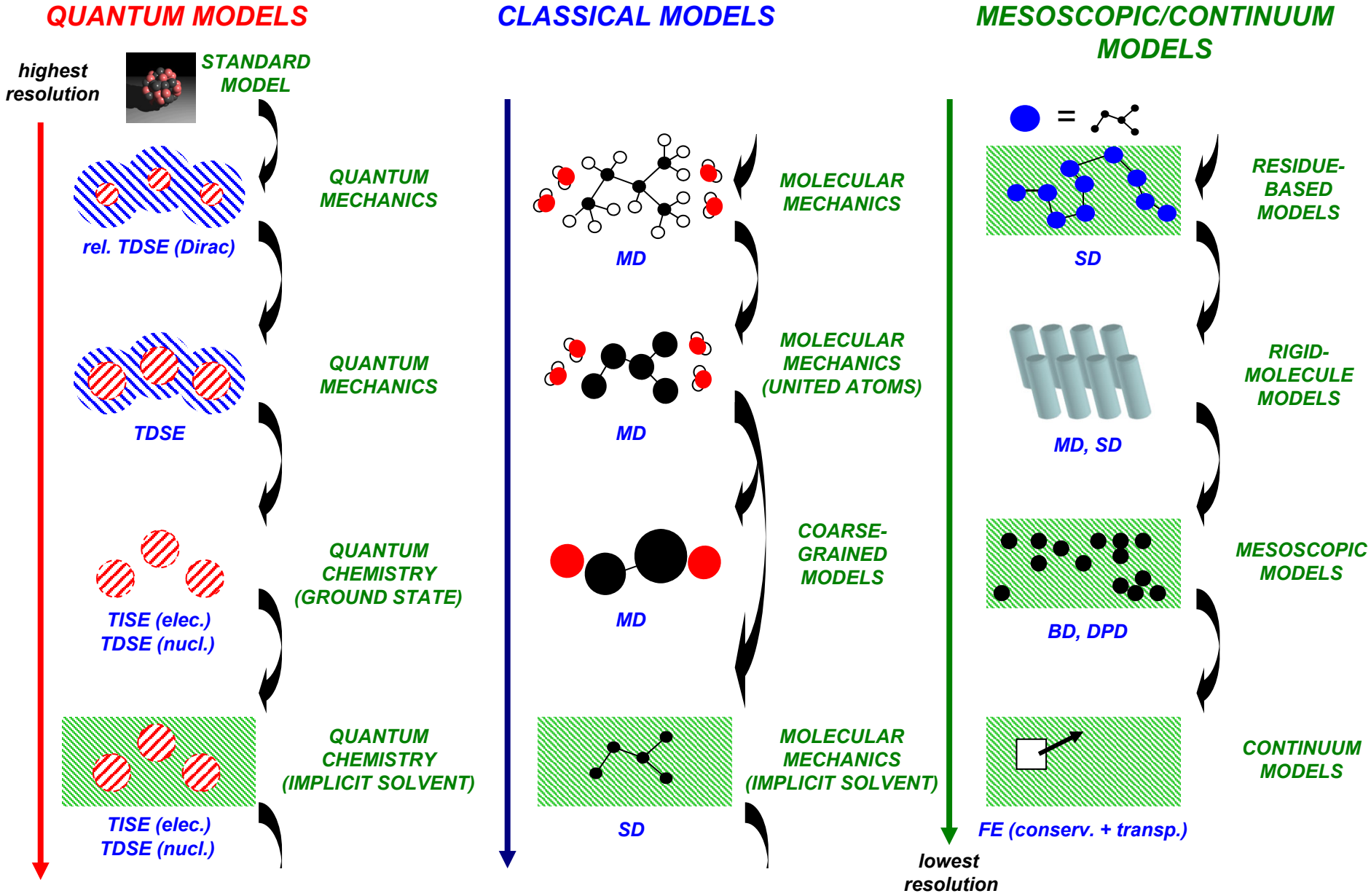
*Simulation can **complement** experiment when:*

- approximate simulations reduce the number of experiments to be performed or/and increase their likelihood of success
  e.g. ***modeling in industry***
  drug design, protein engineering
- a simulation reproducing an experiment provides additional **insight**
  e.g. ***modeling in academia***
  quantum chemistry, molecular simulations

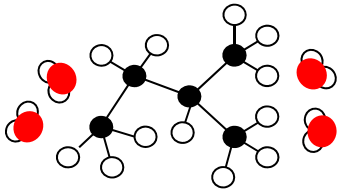
e.g. experimentally inaccessible resolution in time/space/energy

Molecular modeling/simulation in (bio)chemistry

Levels of modeling, resolution and degrees of freedom

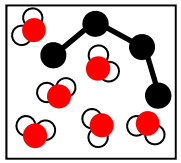


A one-slide crash course in Molecular Dynamics (MD) simulation

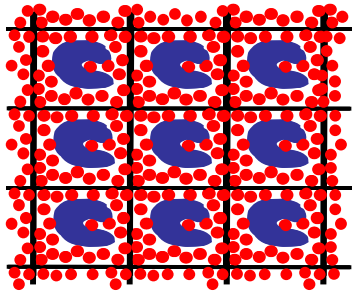


ATOMS
(solute & solvent)

degrees of freedom

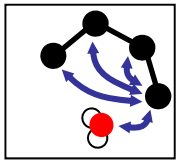


boundary conditions

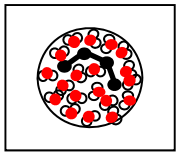


PERIODIC
BOUNDARY CONDITIONS

+ EVTL. BAROSTAT
OR/AND THERMOSTAT



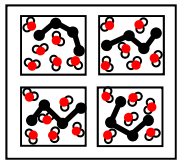
MOLECULAR MODEL



interaction

Classical potential energy function or "force field"

$$\mathcal{U} = \mathcal{U}(\boldsymbol{r})$$



generation of configurations

Classical equations of motion (Newton)

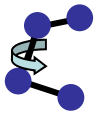
$$\mathcal{H}(\boldsymbol{r},\boldsymbol{p}) = \mathcal{U}(\boldsymbol{r}) + \mathcal{K}(\boldsymbol{p})$$

$$\boldsymbol{F} = -\nabla\mathcal{U}(\boldsymbol{r}) \quad \mathcal{K} = (1/2)\,\boldsymbol{p}^T \underline{\boldsymbol{M}}^{-1}\boldsymbol{p}$$

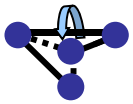
Covalent terms

bond stretching

bond-angle bending

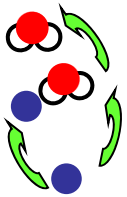


torsional dihedral

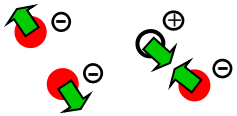


improper dihedral

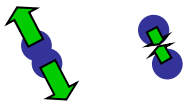
Non-bonded terms



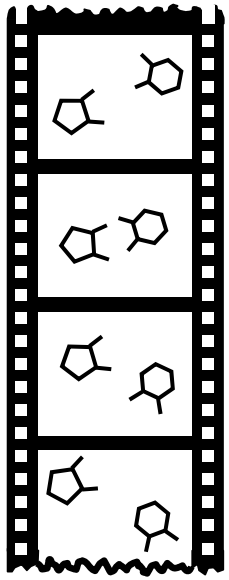
all atom pairs in the system



electrostatic interactions



van der Waals interactions



$$\boldsymbol{a} = \underline{\boldsymbol{M}}^{-1}\boldsymbol{F}$$

$$\Delta\boldsymbol{v} = \boldsymbol{a}\,\Delta t$$

$$\Delta\boldsymbol{x} = \boldsymbol{v}\,\Delta t$$

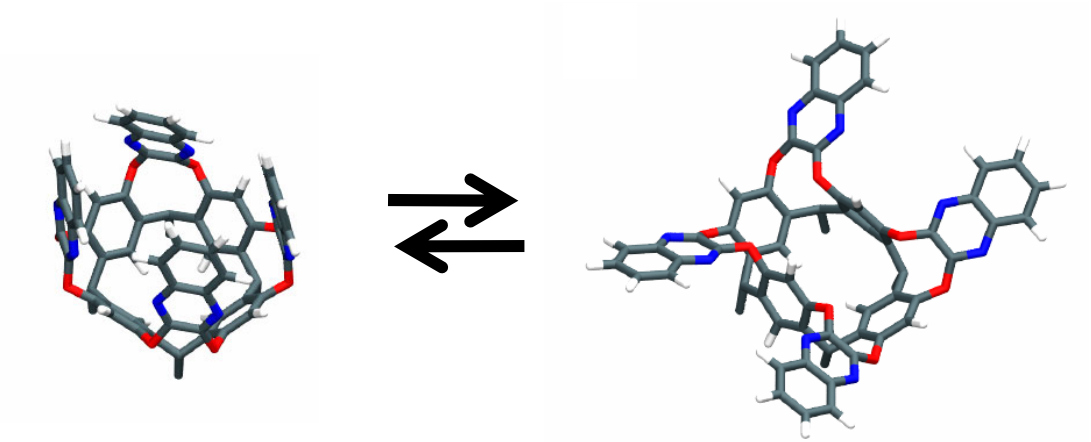
time t { *coordinate*, *velocity*, *force* }

time (t+Δt)

$\Delta t \sim$ fs

Example 1: Free-energy calculations (David Hahn)

- **Resorcin[4]arenes** molecules: synthetic "cavitands"



Closed ("vase") *Open ("kite")*

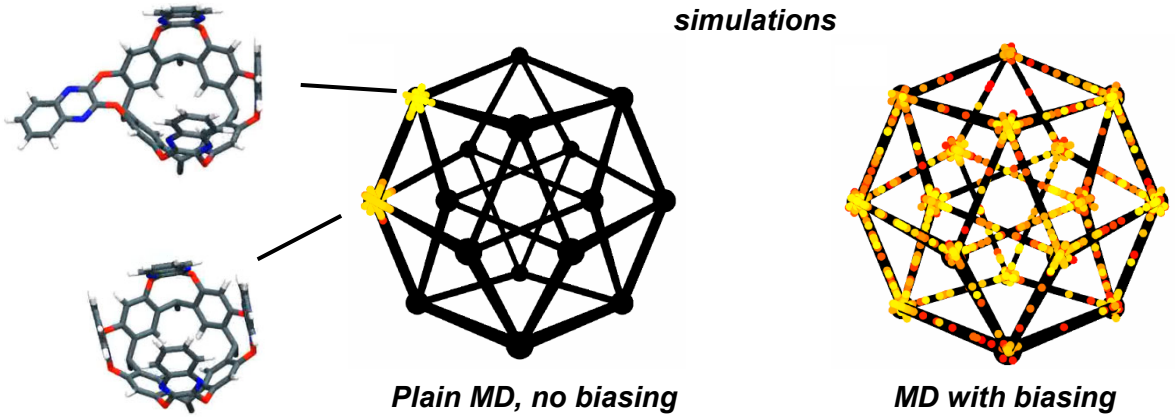
Can be used to trap/release molecules (→molecular "machines")

Equilibrium on the millisecond timescale (→ still too long to simulate)

Mechanism unknown (concerted [all at once], or asynchronous [flaps in sequence] ?)

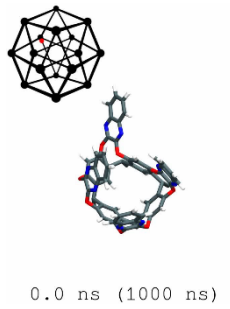
- Biased MD simulation dramatically **enhances the sampling**, so that the relative free energies of all states can be calculated

1 microsecond simulations

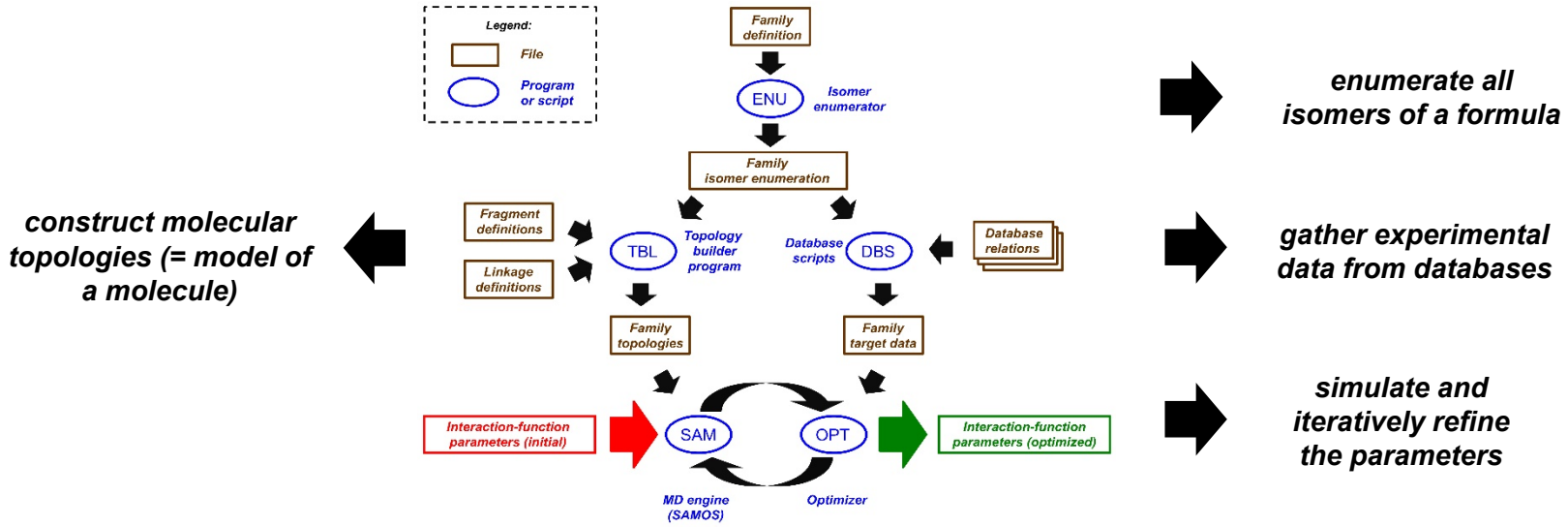


Plain MD, no biasing (only one flaps open)

MD with biasing (all states are visited)



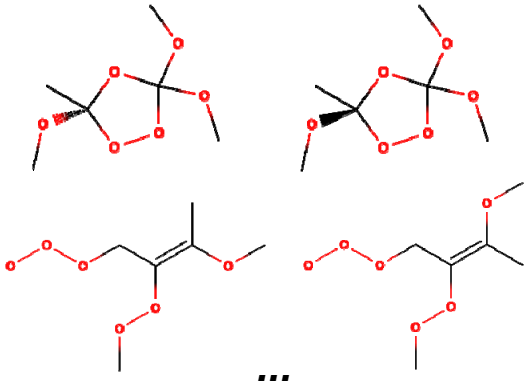
Example 2: Automated Force Field Parametrization (Salomé Rieder / Marina Pereira)



- Enumerator (ENU)

A C++ program to enumerate all constitutional and stereoisomers (SMILES strings) of a chemical formula based on graph theory

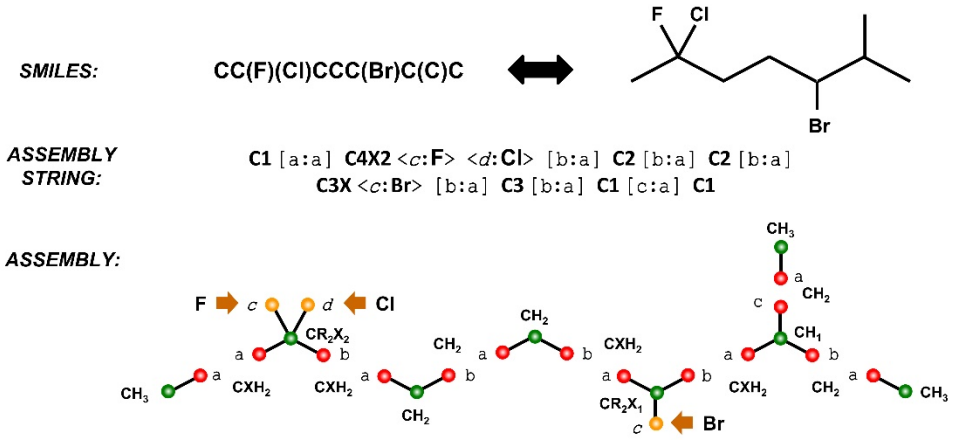
Example: 1'160'337 isomers of $C_6H_{12}O_6$ in 7s



- Topology builder (TBL)

A C++ program to construct the topology of an isomer (SMILES strings) by assembly of fragments

Example: assembly of a haloalkane



Vertiefungsgebiet Chemie: Vorlesungen

incorrect on the slides of the video (sorry)

Bachelor Studium

Vorlesung	*SWS*	*Semester*	*Departement*	*KP*
- Classical Simulation of (Bio)Molecular Systems (formerly CSCBP)	**4G**	HS	CHAB *Hünenberger*	7
- Quantenchemie (German!)	3G	FS	CHAB *Reiher*	6

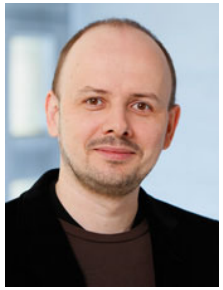
Master Studium

Vorlesung	*SWS*	*Semester*	*Departement*	*KP*
- Classical Simulation of (Bio)Molecular Systems (formerly CSCBP)	3G	HS	CHAB *Hünenberger*	7
- Quantenchemie (German!)	3G	FS	CHAB *Reiher*	6
- Advanced Quantum Chemistry	3G	HS	CHAB *Reiher*	**7**
- Computer Applications: Finite Elements in Solids and Structures	2V 2U	FS	MATL *Gusev*	4
- Seminar for Chemistry in CSE	2S	HS/FS	RW *Hünenberger/Reiher*	4

Contact:

Prof. Philippe Hünenberger

(phil@igc.phys.chem.ethz.ch)



Prof. Markus Reiher

(markus.reiher@phys.chem.ethz.ch)

Prof. Sereina Riniker

(sriniker@ethz.ch)