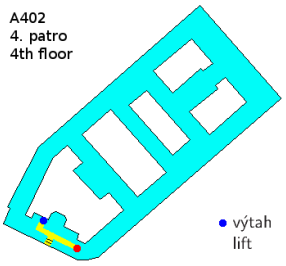
Info

Jiří Kolafa
Department of Physical Chemistry
University of Chemistry and Technology, Prague
Technická 5 (building A)
room 402
http://www.mapy.cz/s/98vC
jiri.kolafa@vscht.cz
220 444 257



Google: Kolafa Molecular modeling and simulation
Kolafa Molekulární modelování a simulace

Elements of modeling

- ? *elementary particles* + *gravity*, GUT, dark energy, . . .
- *known elementary particles*: Standard model, atomic nuclei,. . .
- *Nuclei* + *electrons* + *photons*: QED, accurate spectroscopy
- *Nuclei* + *electrons*: Schrödinger equation – small molecules, spectra, gas-phase equilibria, chemical kinetic, photochemistry . . .
- *Atoms** – classical (or quantum) atomistic modeling
- *implicit solvent*: continuum + random forces
- *Coarse-grained models*: meso/nanoscopic scale
  element = polyatomic group
  (surfactant = head + tail, polymer = $[\text{bead}]_n$. . .)
- *Microscopic scale* (dispersions, granular materials)
- *Continuum*: partial differential equations – heat, weather models, neutrons in A-bomb, statics in civil engineering
- *gravity*: spacetime – black holes, gravitational waves

see DOI: 10.1017/S0033583515000256 for time- and size-scales of simulation techniques

multiscale modeling: QM/MM (enzymes etc.) . . .

*optionally: auxiliary interaction centers (sites), bigger groups (-CH_3)

Potential Energy Surface (PES)

Nuclei are much heavier than electrons ⇒ electron motion is much faster (Born–Oppenheimer **approximation**)

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for me (show/SPCEdimer.sh):
- change cfg
- click [info]
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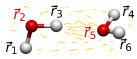
Potential energy surface (PES):

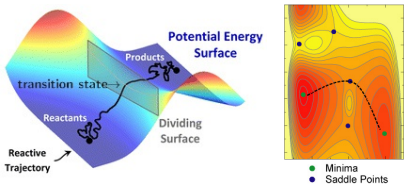
energy as a function of positions of all nuclei

$$E_{\text{pot}}(\vec{r}_1, \vec{r}_2, \ldots, \vec{r}_N)$$



Chemical example:
reaction coordinate

A reaction proceeds over (near to) a saddle point (transition state)



credits: http://www.ucl.ac.uk/~ucecmst/publications.html, http://theory.cm.utexas.edu/henkelman/research/ltd/

How to obtain PES?

- from quantum calculations (Schrödinger equation: *ab initio*, DFT) – expensive
- via neural network trained on quantum data – medium cost
- approximated by a formula (“force field”, “potential”, “model”, . . .) – cheap
  force field: E_{pot} = sum of many terms
  term = function form + parameters for atoms/groups
- combination: QM/MM methods (**q**uantum **m**echanics/**m**olecular **m**echanics)

PES and modeling in chemistry

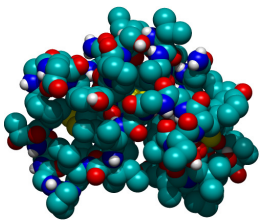
- using classical mechanics:
  – static calculations: minimum of energy, potential around a molecule
  – time development of system (**m**olecular **d**ynamics, MD);
  with *ab initio* PES = AIMD (demanding!)
  thermodynamic variables by sampling (**M**onte **C**arlo, MC)
- using quantum mechanics to nuclei:
  – path integral methods (PI MC, PI MD); with AIMD extremely demanding
  – classical mechanics + quantum corrections

combination force field + classical mechanics = “**m**olecular **m**echanics” (MM); strictly speaking does not include MC and MD

Molecular mechanics: static approach

We use PES, usually described by a force field

- Energy minimization ($T = 0$)
  “molecular mechanics”, “structure optimization”
- Refinement – more accurate structure (from diffraction data)
- Biochemistry: molecular shape (lock and key), hydrophillic/hydrophobic
- QSAR (**Q**uantitative **S**tructure–**A**ctivity **R**elationship) descriptors



. . . but what about **motion**?

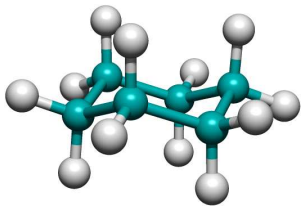
Molecular simulations

- molecular dynamics (MD)
  - time development of a system composed of many molecules
  - instantaneous forces acting on atoms cause their motion
- Monte Carlo (MC); more precisely: Metropolis method and its variants
  - a sequence of configurations of the system is generated using random numbers
  - an attempt is made to move a molecule (randomly with a certain distribution)
  - this trial move is accepted or rejected so that its probability is the same as in reality
- kinetic Monte Carlo
  - the simulated process is divided into elementary events
    (e.g., adsorption of an atom on a growing crystal, catalytical reaction)
  - the event to happen is chosen according to a known probability
- quantum simulations – MD, MC
- Las Vegas algorithms – deterministic result (random pivot, search for minimum)

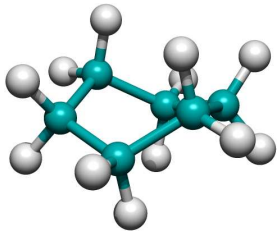
What can be studied

- Liquids:
  - how structure affects properties (anomalies of water), solutions
  - phase equilibria, solubility
  - surfaces, interfaces, surfactants
- Solids:
  - crystal structure, materials (defects)
  - adsorption (zeolites)
- Biochemistry:
  - proteins, nucleic acids, ion channels, lipid membranes
- Nanoobjects:
  - micelles, polymers, self-assembly (coarse-grained models, lattices)
- Similar methods can be used for:
  - granular materials, optimization, spreading of epidemics, active matter, agent-based models, evo-devo (evolutionary developmental biology). . .

Structure optimization (example of molecular mechanics)



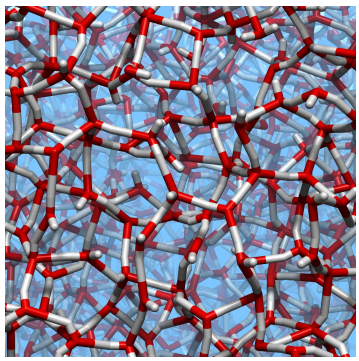
chair
experiment: 28 kJ/mol
model: 26 kJ/mol



twist (skew) boat
experiment: 45 kJ/mol
model: 53 kJ/mol

Liquid water (example of equilibrium molecular dynamics)

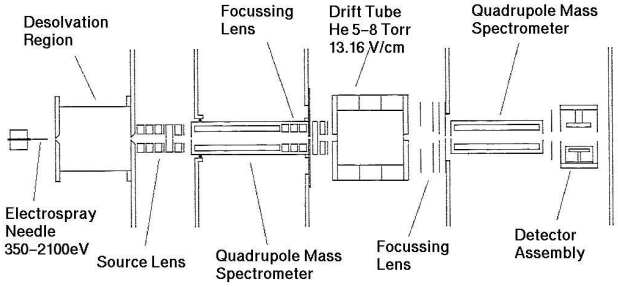
- 10000 molecules
- 300 K
- periodic in x, y
- adhesive pad
- nonadhesive lid



More movies: https://vesmir.cz/cz/on-line-clanky/2014/07/struktura-anomalie-vody.html

Electrospray of Cytochrome C

- Electrospray: spray of charged aerosol
- Cross section is determined



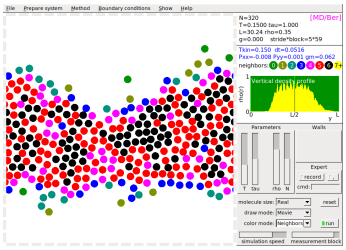
Yi Mao, J. Woenckhaus, J. Kolafa, M. A. Ratner, M. F. Jarrold: *J. Am. Chem. Soc.* **121**, 2712–2721 (1999)

SIMOLANT

simolant 11/25 s00/3

Features:

- 2D “atoms” with a Lennard-Jones type potential (8–4)
- repulsive/attractive walls, gravity
- MC and MD
- constant energy and thermostat



Phenomena:

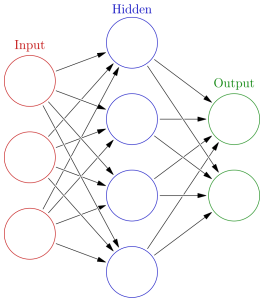
- condensation of vapor
- freezing of a droplet
- crystal defects
- capilary action
- gas in a gravitational field
- vapor-liquid equilibrium
- nucleation

Install SIMOLANT: http://old.vscht.cz/fch/software/simolant/index-en.html

Artificial neural networks

16/25 s00/3

- several layers
- discrete or continuous signal
- usually →, rarely with feedback
- nonlinear activation function (sigmoid)
- weights for input mixing are adjustable



learning = determining the weights using a training set (optimization)

Self-assembly (primitive example)

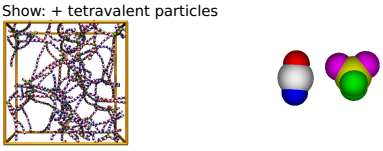
show/janus.sh 12/25 s00/3

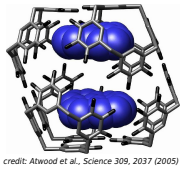
Supramolecular chemistry: assembling molecules using noncovalent forces (van der Waals, hydrogen bonds) to higher structural elements

- Show: bivalent particles in a solution ≈ “Janus particles”

credit: wikipedie, www.nasa.gov/mission_pages/cassini

- Show: + tetravalent particles



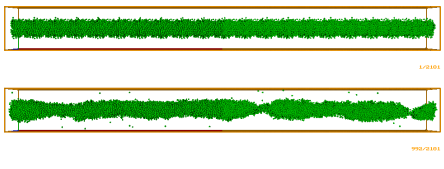


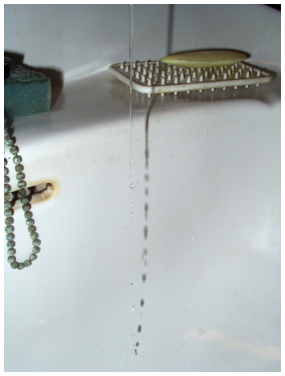
credit: Atwood et al., Science 309, 2037 (2005)

(Plateau-)Rayleigh instability

../simul/rayleigh/show.sh 17/25 s00/3

A stream of water splits into droplets. Instability for $kr < 1$ (for perturbation $\propto \sin(kz)$), max. instability for $kr = \ln 2$.



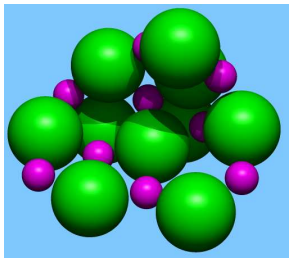


NB: “$\propto$” = “is proportional to”

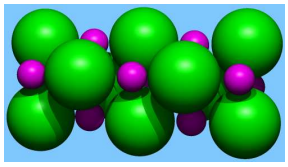
How to get energy minimum (simulated annealing)

uvodsim/min.sh 13/25 s00/3

Minimum energy of (a model of) $Na_{10}Cl_{10}$ cluster



fast cooling (quenching)



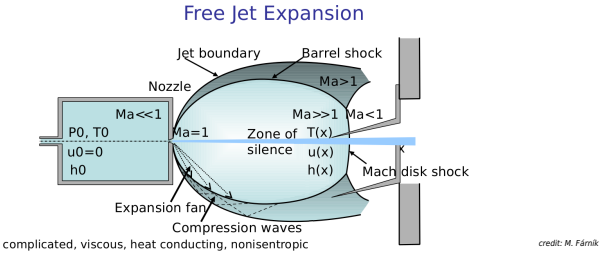
slow cooling (annealing)

Nucleation at supersonic expansion

show/supexp.sh 18/25 s00/3

Water vapor (about 150 °C and 5 bar) expands through a small (100 μm) nozzle to a vacuum. It cools adiabatically below freezing point.

Motivation: stratospheric physical chemistry.



Question: what is the shape and structure of ice clusters?

J. Klíma, J. Kolafa: *J. Chem. Theory Comput.* **14**, 2332–2340 (2018)

Optimization by simulated annealing

uvodsim/salesman.sh 100 14/25 s00/3

We are looking for the **global minimum** of function $U(A_i)$ (with many local minima)

- Configuration changes $A_i \to A_j$
- Metropolis MC simulation while decreasing “temperature” T

Example: Traveling salesman problem

- 100 cities randomly in square 1 × 1
- Configuration = sequence of cities
- U = path length
- Configuration change = interchange of 2 randomly chosen cities

```
for me (uvodsim/salesman.sh):
- random start
- numerical results in the console
```

“greedy” (Metropolis $T = 0$) $l = 8.5778$

simulated annealing $l = 7.6663$

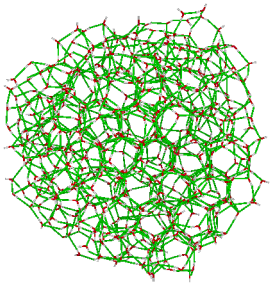
genetic algorithm $l = 8.1817$

Melting of nanoparticles

show/kroupa.sh 19/25 s00/3

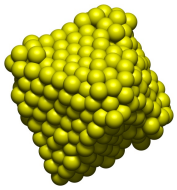
Ice

- hail of 600 water molecules (ice Ih)
- gradual heating
- simulation time = 5 ns
- this model of water melts at 250 K



Gold

- nanocrystal of 489 gold atoms
- gradual heating
- simulation time = 77 ps



the melting point of nanoparticles is lower than in the bulk

Genetic algorithms (evolutionary programming)

15/25 s00/3

The function to maximize is called here “fitness”

- configuration → individual → genom = chromosome = list of alleles (“column of numbers”)
- initial (e.g., random) population
- next generation:
  - kill the least fit individuals
  - copying (parthenogenesis) with a mutation
  - breeding from two parents with crossover

Numbers are coded by a Gray code (consecutive integers differ by one bit)

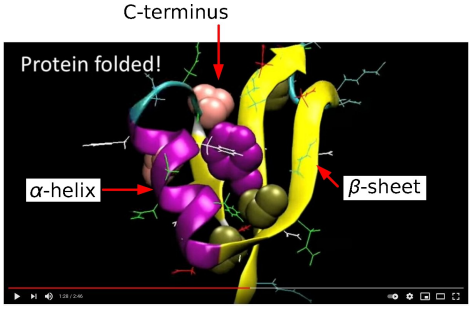
0	0000
1	0001
2	0011
3	0010
4	0110
5	0111
6	0101
7	0100
8	1100
9	1101
10	1111
11	1110
12	1010
13	1011
14	1001
15	1000

Application:

– logistics, economy, control of processes
– biochemistry – protein folding
– electronics – circuit design, antenna shape
– algorithm design

Protein folding on the millisecond timescale

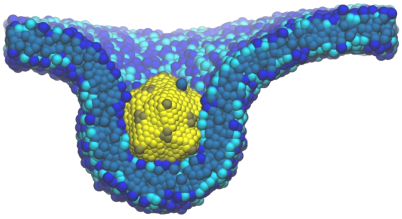
firefox https://www.youtube.com/watch?v=gFcp2Xpd29I 20/25 s00/3



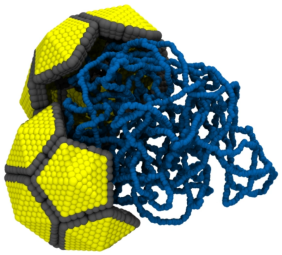
Credit: Pande Lab Science, https://pubs.acs.org/doi/abs/10.1021/ja9090353

Coarse-grained simulations

- Coarse-grained model, Langevin thermostat (random forces)
- Water not shown



endocytosis



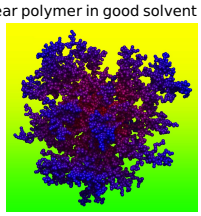
release of RNA from the capsid

Courtesy: © Robert Vácha (CEITEC)

Dendrimers by diffusion-limited aggregation

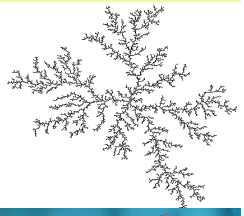
Fractals:

- Trajectory of Brownian motion = random walk = linear polymer in θ-solvent: $D = 2$
- Self-avoiding random walk = linear polymer in good solvent (in 3D): $D = 1.7$
- Dendrimer in 2D: $D = 1.7$
- Dendrimer in 3D: $D = 2.5$
- Broccoli: $D = 2.66$
- Lung surface: $D = 2.97$



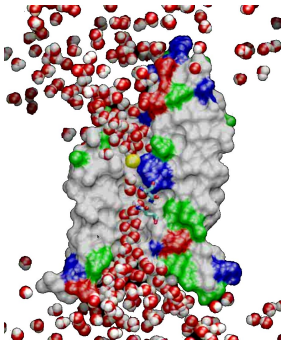
copper electrodeposition →

credit: Wikipedia

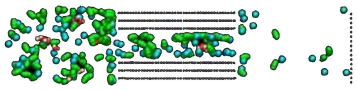


Pores

diffusion of water through aquaporine channel

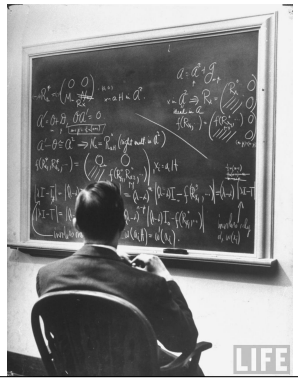


diffusion of water vapor, nitrogen, and carbon dioxide through a carbon nanotube



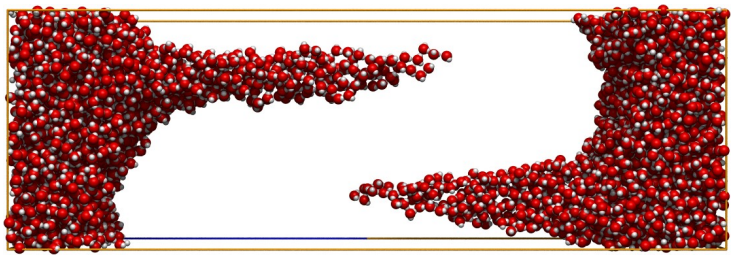
Courtesy: Pál Jedlovszky

End of introduction – real lecture ahead. . .



Electrospinning

- 5000 SPC/E water molecules, field 1.5 V/nm, simulation time 135 ps
- electrospinning starts by the “Taylor cone”
- the tip elongates and produces a jet stabilized by electric field



Jan Jirsák, Filip Moučka, Ivo Nezbeda: *Ind. Eng. Chem. Res.* **53**, 8257–8264 (2014)