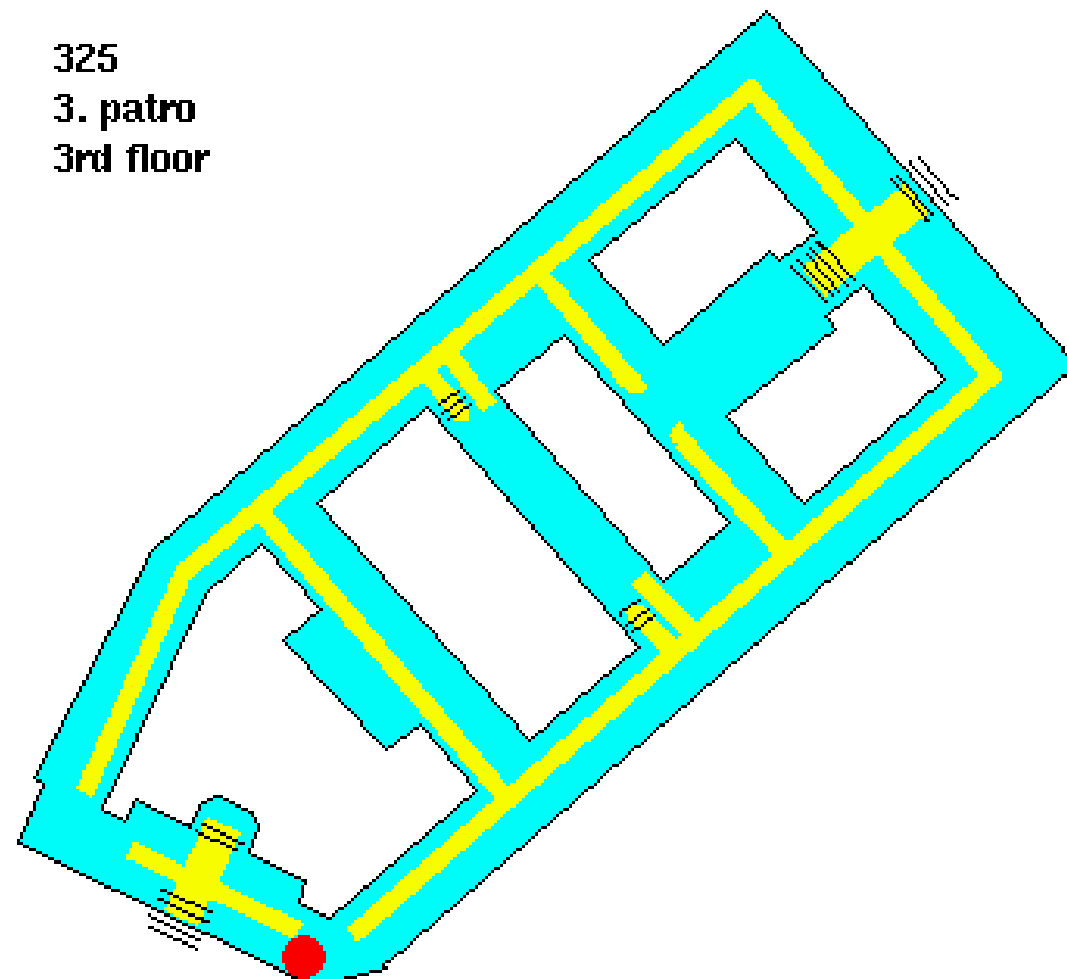


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Google: Kolafa Molecular modeling and simulation
Kolafa Molekulární modelování a simulace



- ? *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
- *Coarsened-grained models*: meso/nanoscale scale
element = polyatomic group
(surfactant = head + tail, polymer = [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

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

*optionally: auxiliary interaction centers (sites), bigger groups (-CH₃)

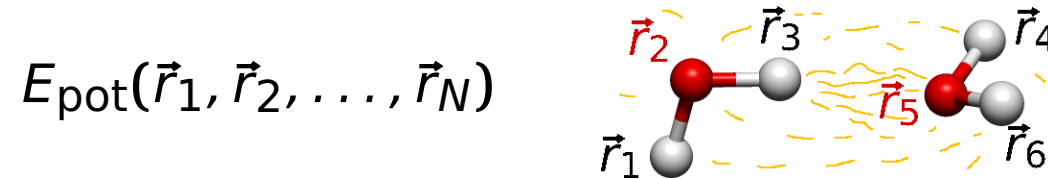
Potential Energy Surface (PES)

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

Potential energy surface (PES):

energy as a function of positions of all nuclei

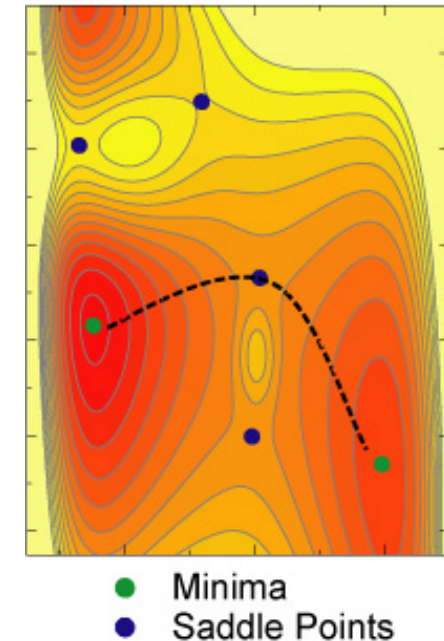
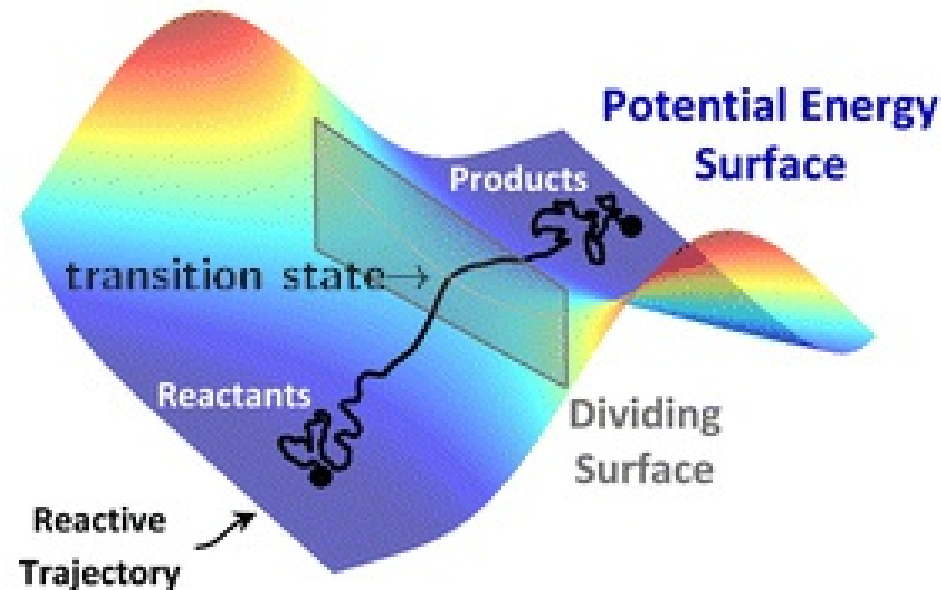
for me (show/SPCEdimer.sh):
- change cfg
- click [info]



Chemical example:

reaction coordinate

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



- from quantum calculations (Schrödinger equation: *ab initio*, DFT)
- approximated by a formula (“force field”, “potential”, “model”, ...)
force field: $E_{\text{pot}} = \text{sum of many terms}$
term = function form + parameters for atoms/groups
- combination: QM/MM methods (**q**uantum **m**echanics/**m**olecular **m**echanics)

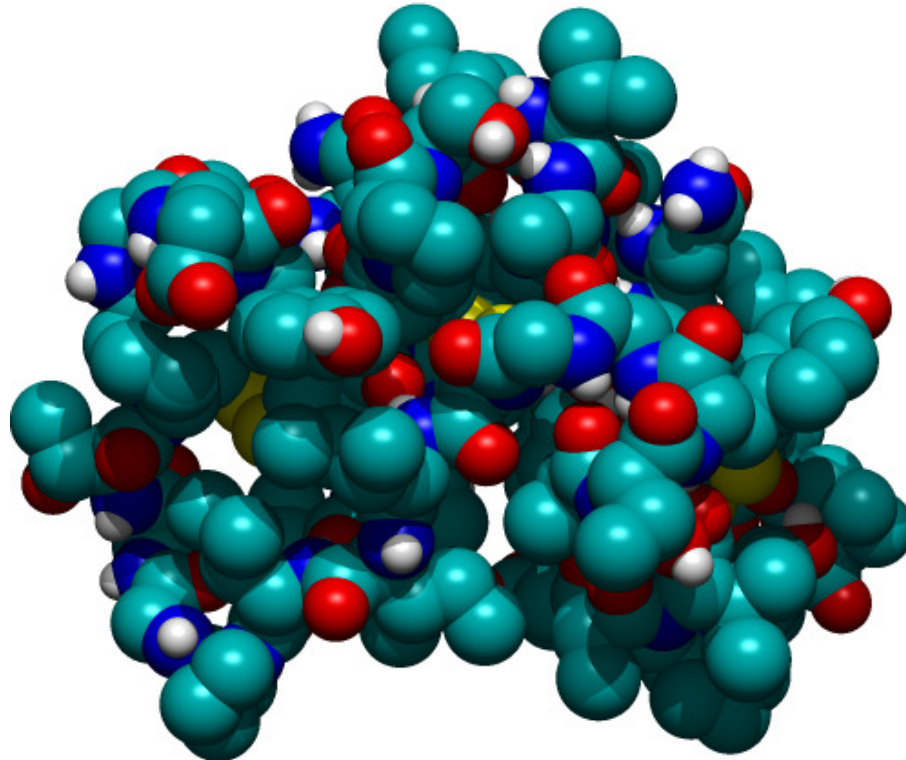
PES and modeling in chemistry

- 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

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), hydrophilic/hydrophobic
- QSAR (**Q**uantitative **S**tructure–**A**ctivity **R**elationship) descriptors



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

- 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)

● 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

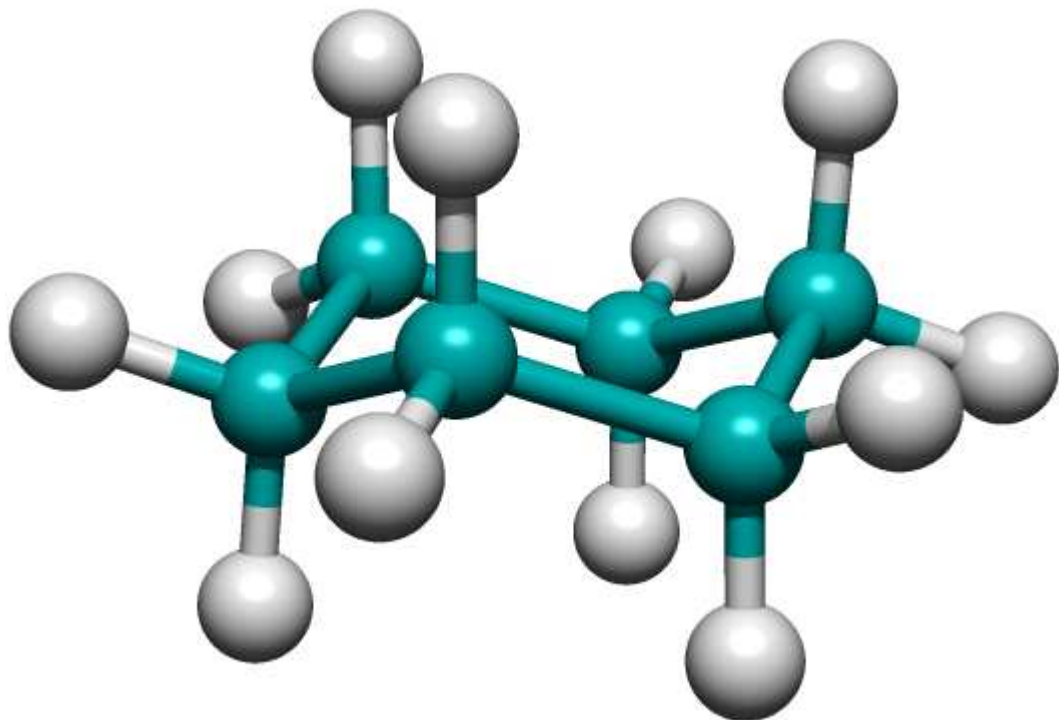
● Nanoobjects:

- micelles, polymers, self-assembly (coarse-grained models, lattices)

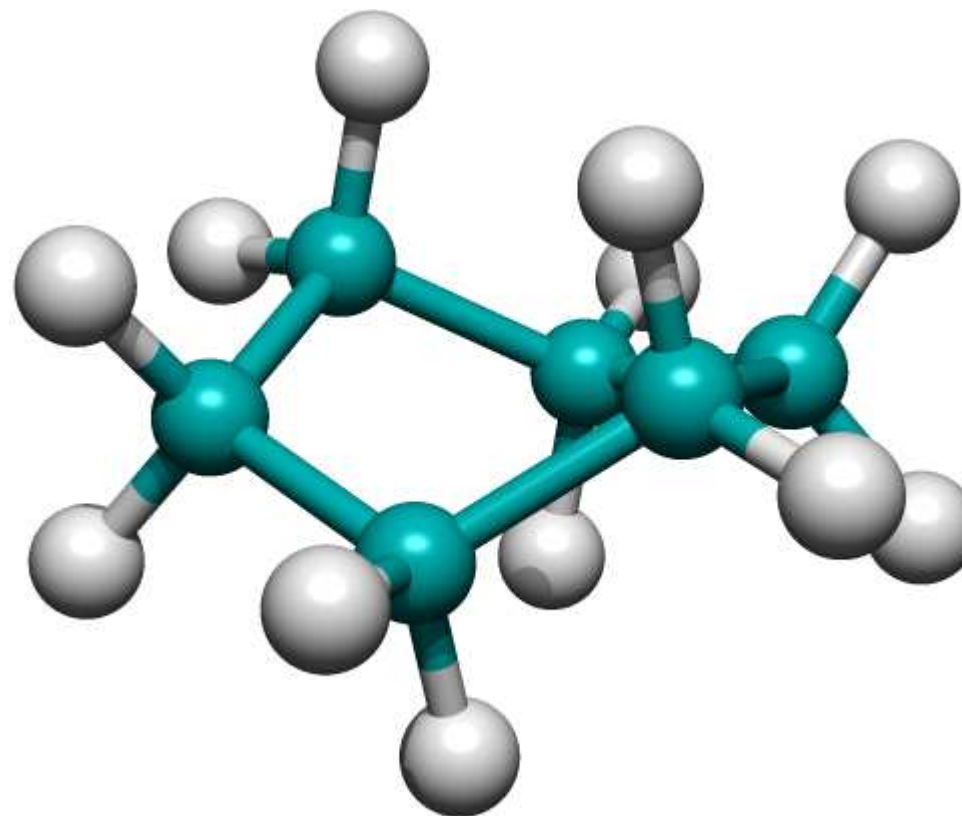
● Similar methods can be used for:

- granular materials, optimization, spreading of epidemics, active matter, agent-based models, evo-devo (evolutionary developmental biology)...

Structure optimization (example of molecular mechanics)



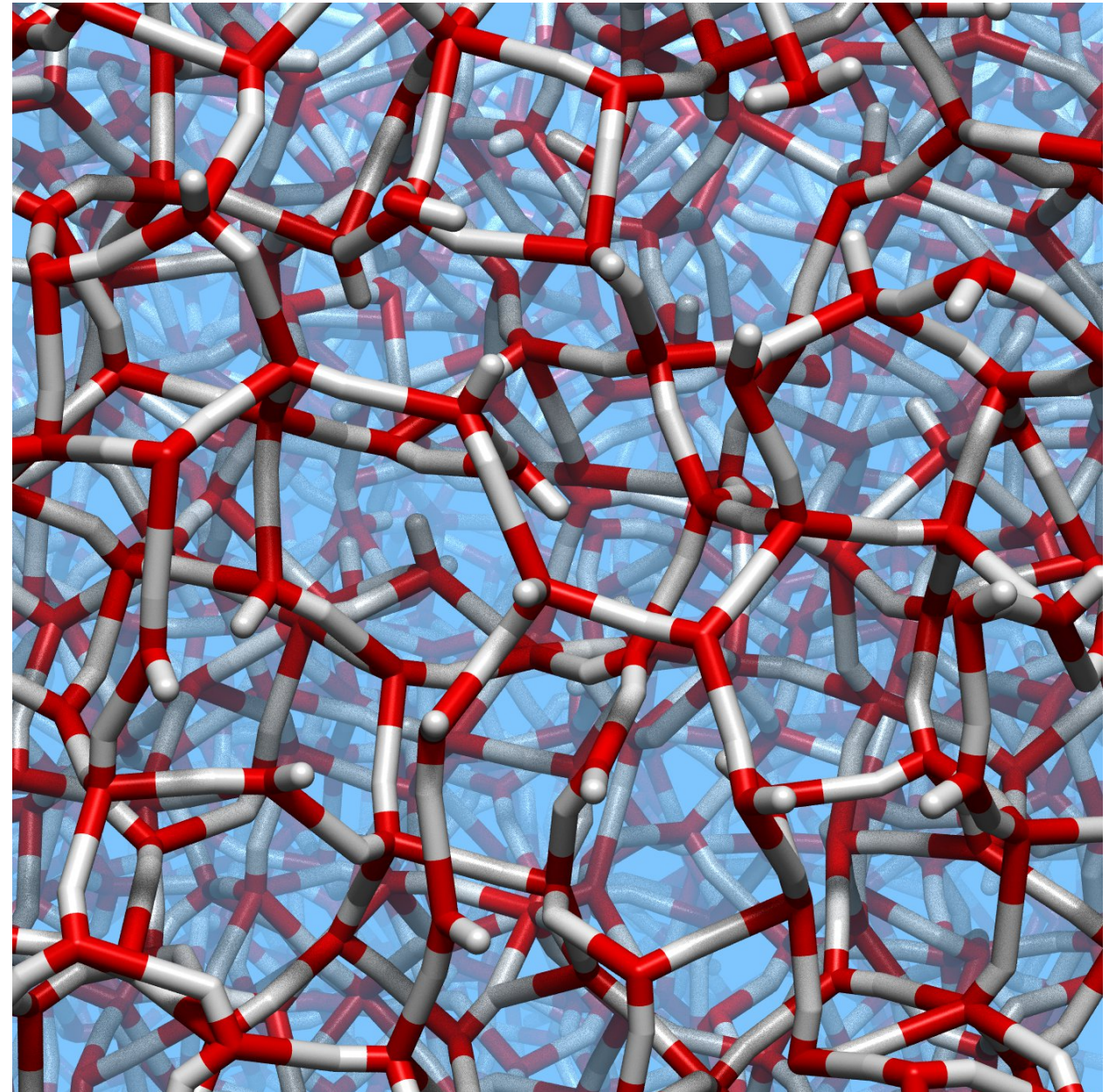
chair
experiment: 28 kJ/mol
model: 26 kJ/mol



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

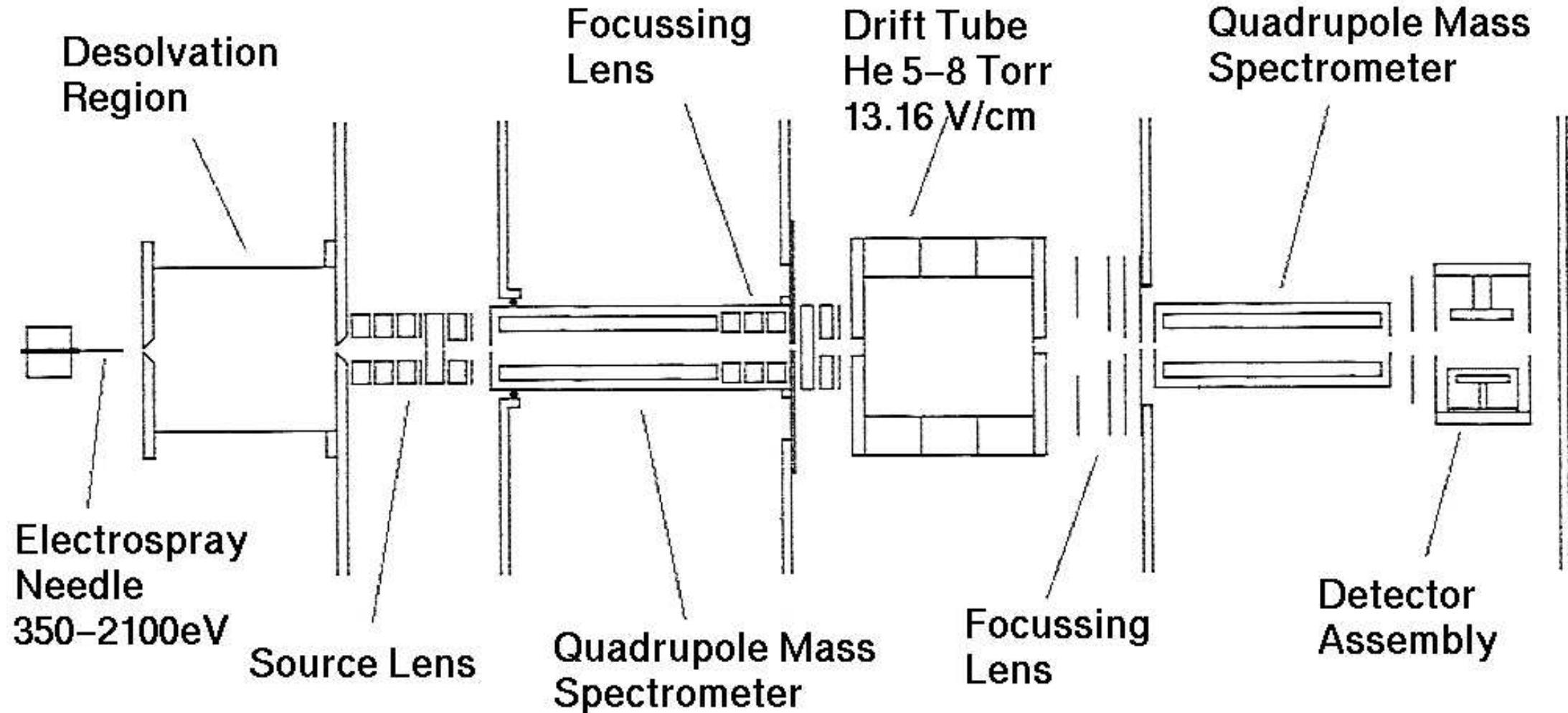
Liquid water (example of equilibrium molecular dynamics)

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



Electrospray of Cytochrome C

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

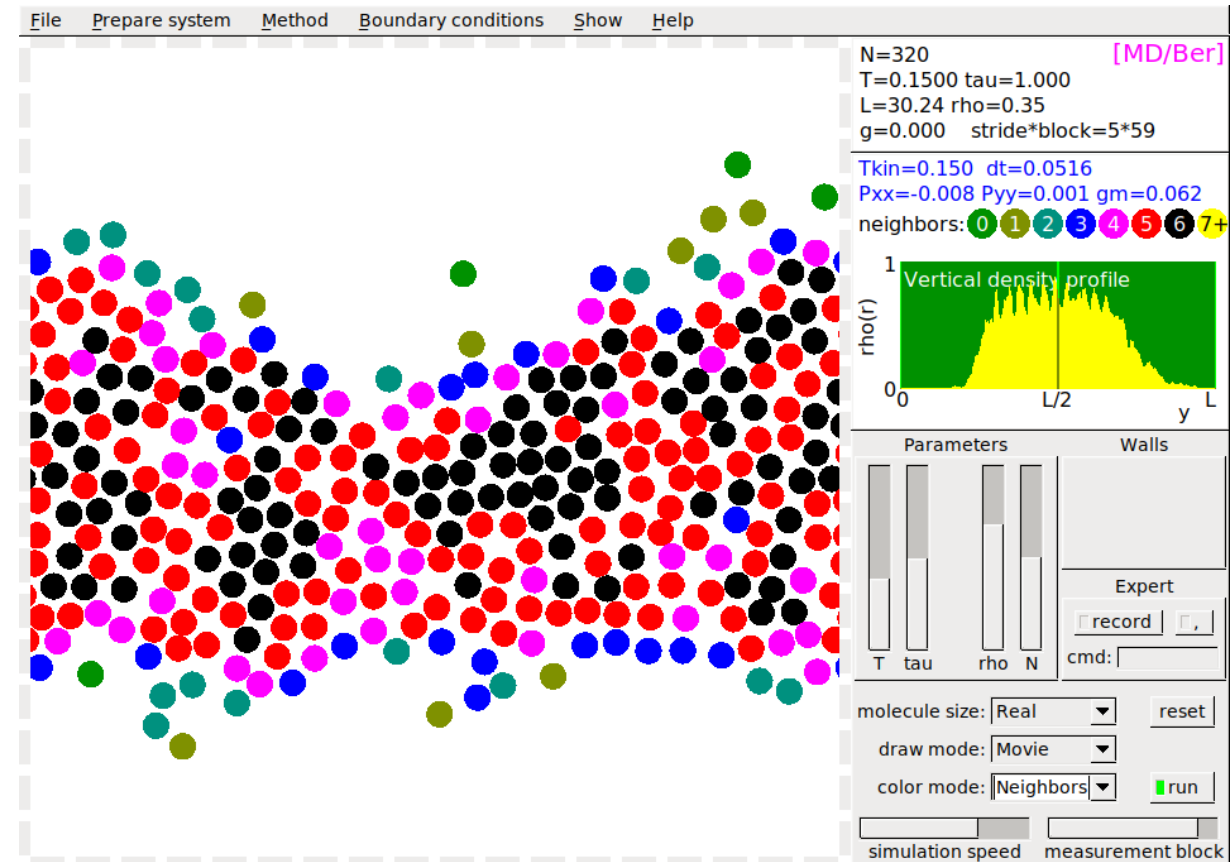


Features:

- 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
- capillary action
- gas in a gravitational field
- vapor-liquid equilibrium
- nucleation

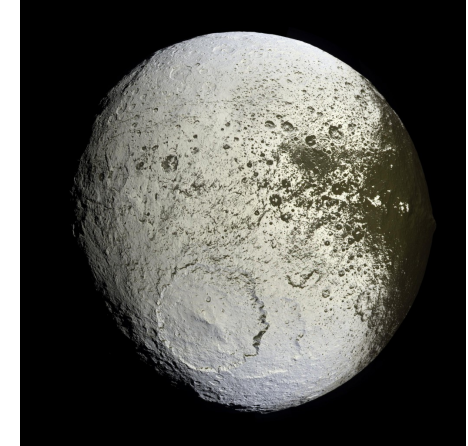
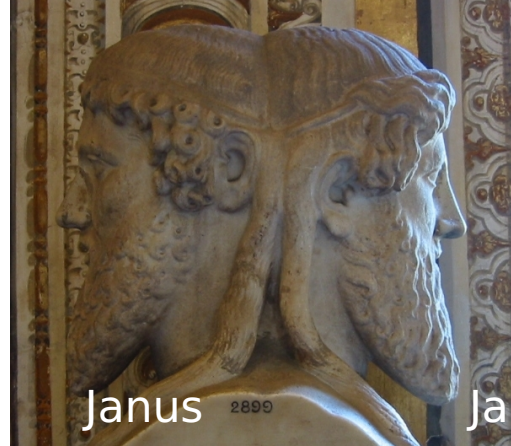
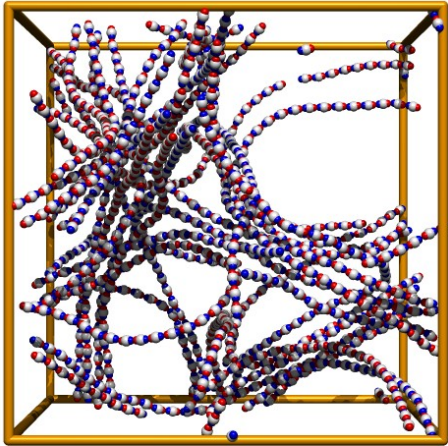


Install SIMOLANT: <http://old.vscht.cz/fch/software/simolant/index-en.html>

Self-assembly (primitive example)

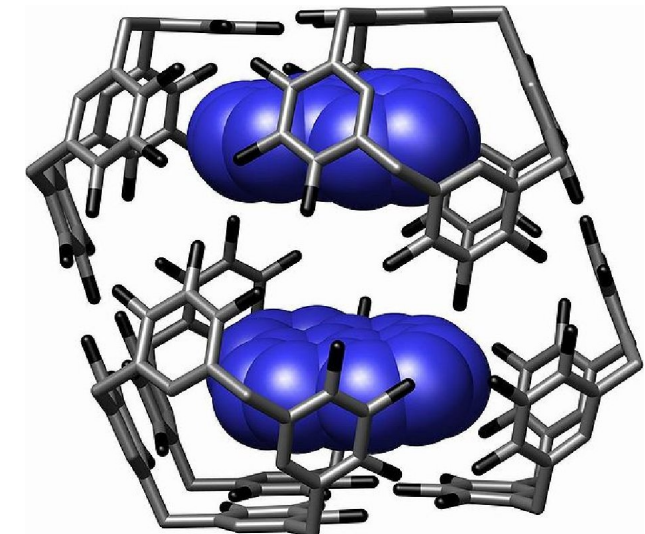
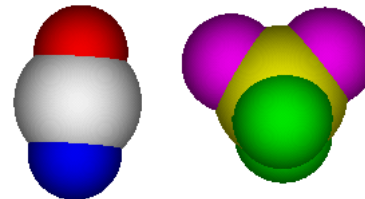
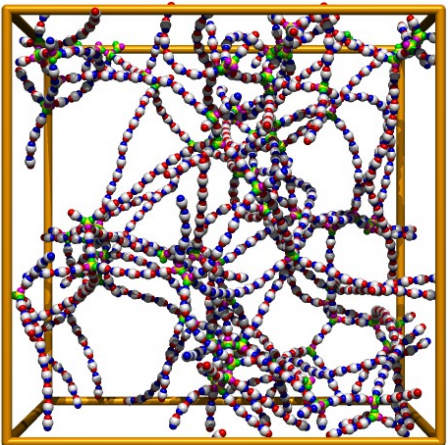
Supramolecular chemistry: assembling molecules using noncovalent forces (van der Waals, hydrogen bonds) to higher structural elements

● Show: bivalent particles in a solution \approx “Janus particles”



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

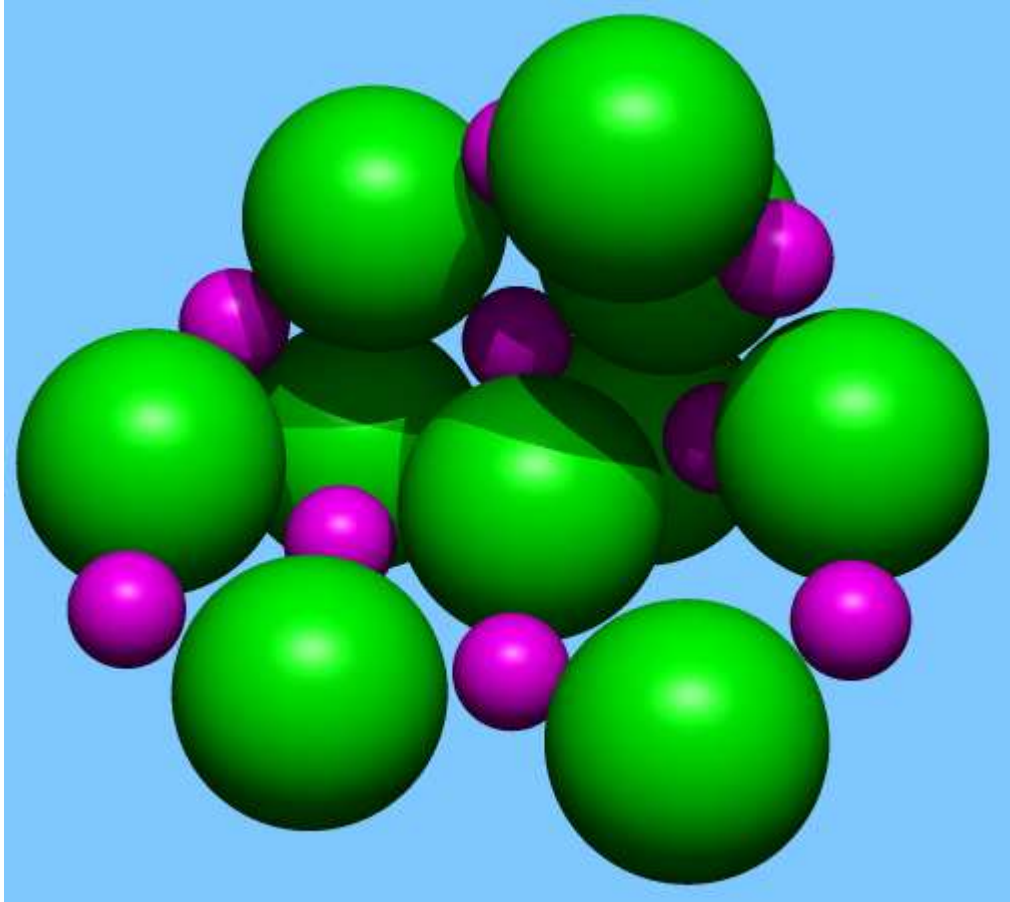
● Show: + tetratetraivalent particles



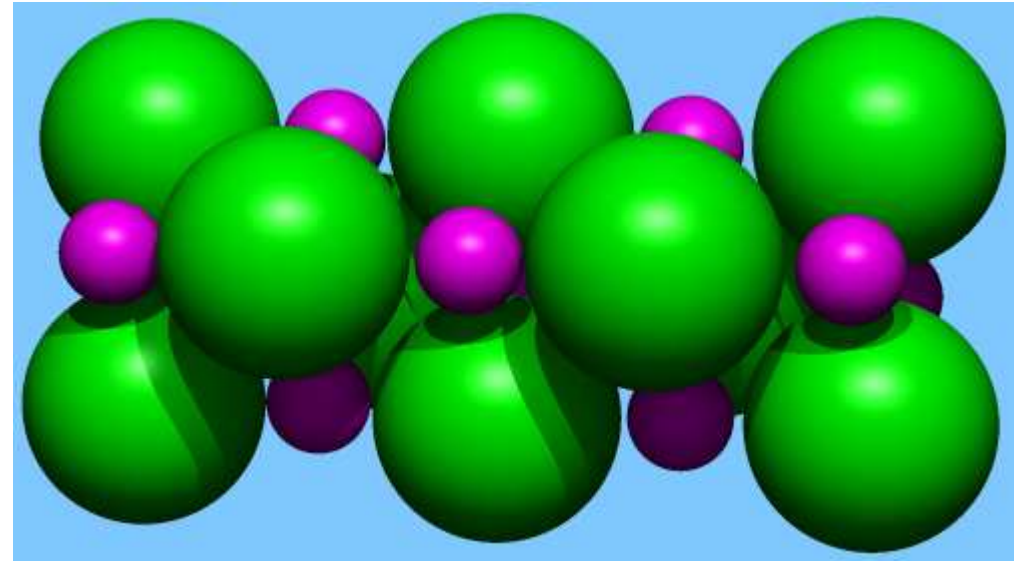
credit: Atwood et al., *Science* 309, 2037 (2005)

How to get energy minimum (simulated annealing)

Minimum energy of (a model of) $\text{Na}_{10}\text{Cl}_{10}$ cluster



fast cooling (quenching)



slow cooling (annealing)

Optimization by simulated annealing

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

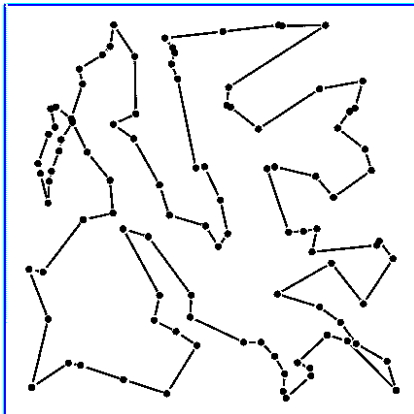
- Configuration changes $A_i \rightarrow A_j$
- Metropolis MC simulation while decreasing “temperature” T

Example: Traveling salesman problem

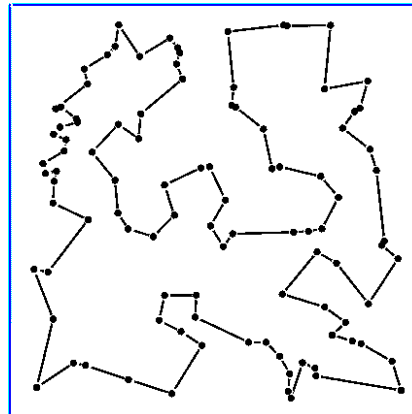
- 100 cities randomly in square 1×1
- Configuration = sequence of cities
- U = path length
- Configuration change = interchange of 2 randomly chosen cities

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

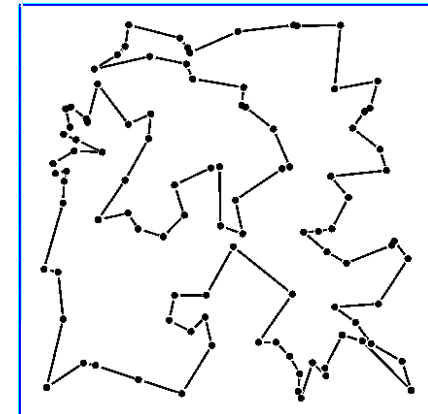
“greedy”
(Metropolis $T = 0$)
 $l = 8.5778$



simulated
annealing
 $l = 7.6663$



genetic
algorithm
 $l = 8.1817$



Genetic algorithms (evolutionary programming)

+ 15/23
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)

Application:

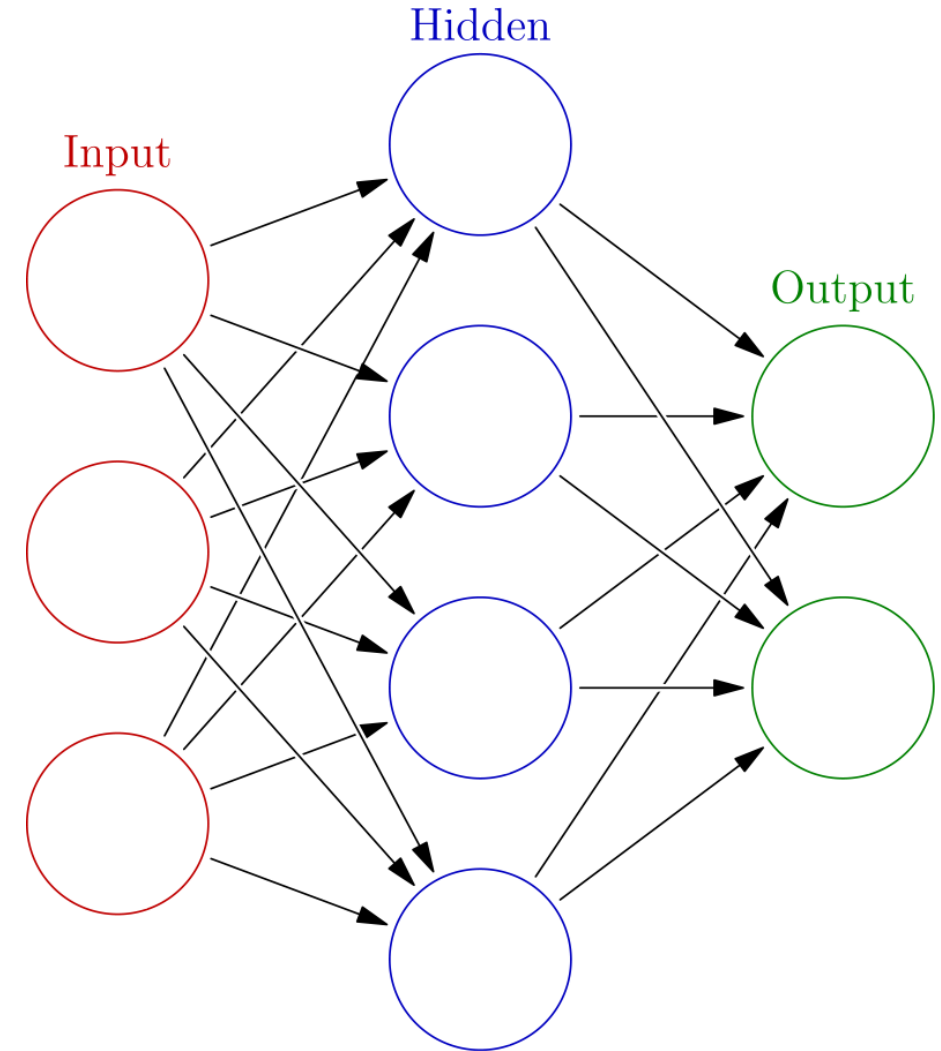
- logistics, economy, control of processes
- biochemistry – protein folding
- electronics – circuit design, antenna shape
- algorithm design

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

Artificial neural networks

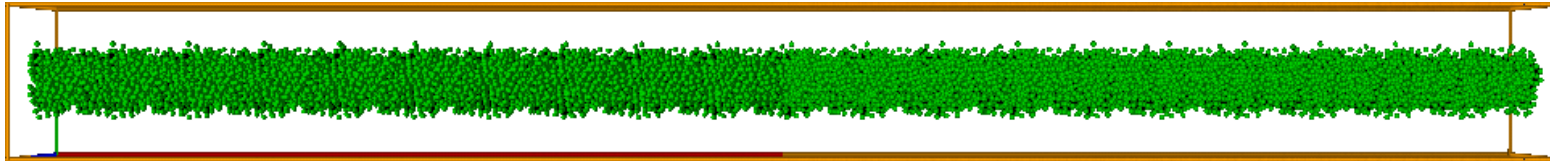
- several layers
- discrete or continuous signal
- usually \rightarrow , rarely with feedback
- nonlinear activation function (sigmoid)
- weights for input mixing are adjustable

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

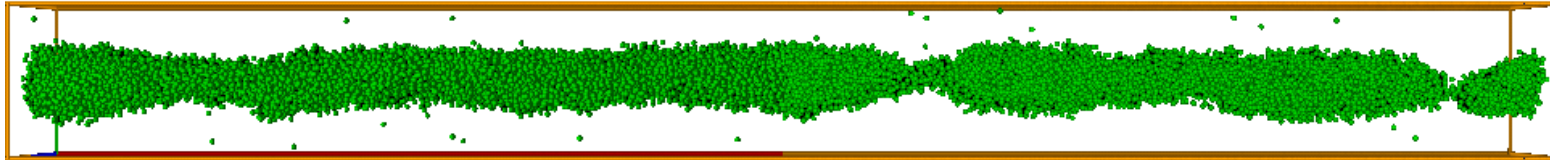


(Plateau-)Rayleigh instability

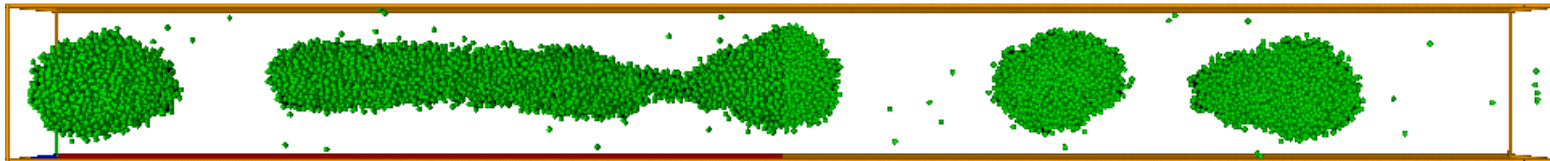
A stream of water splits into droplets. Instability for $kr < 1$ (for perturbation $\propto \sin(kz)$), max. instability for $kr = \ln 2$.



1/2101



992/2101



1366/2101



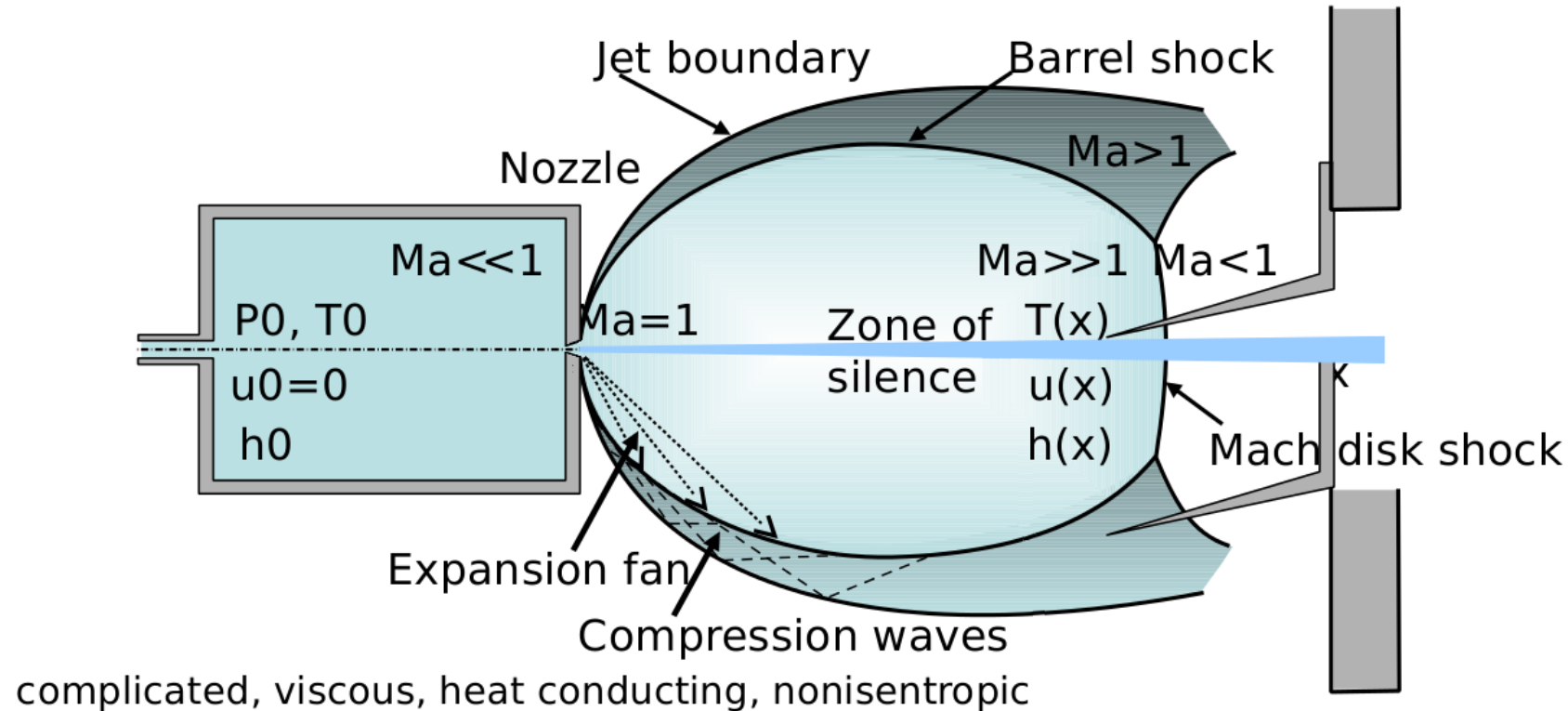
NB: “ \propto ” = “is proportional to”

Nucleation at supersonic expansion

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.

Free Jet Expansion



credit: M. Fárník

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

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

Melting of nanoparticles

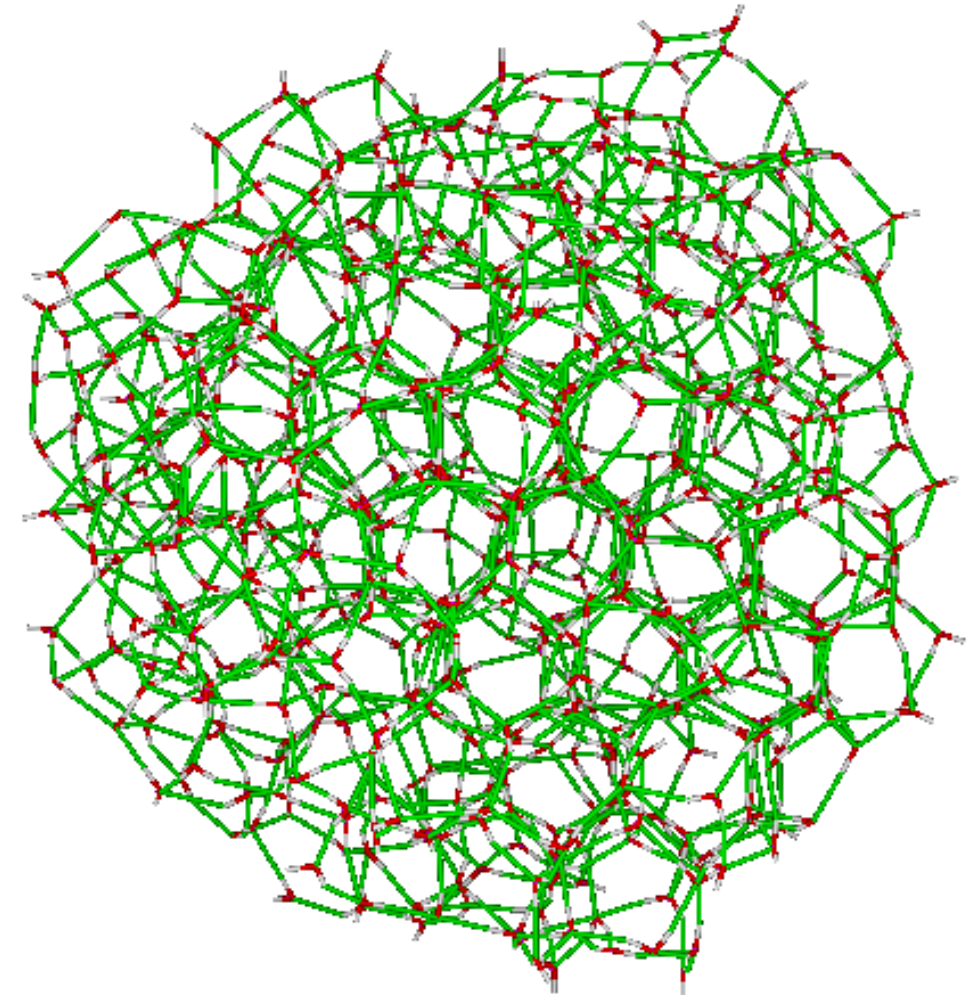
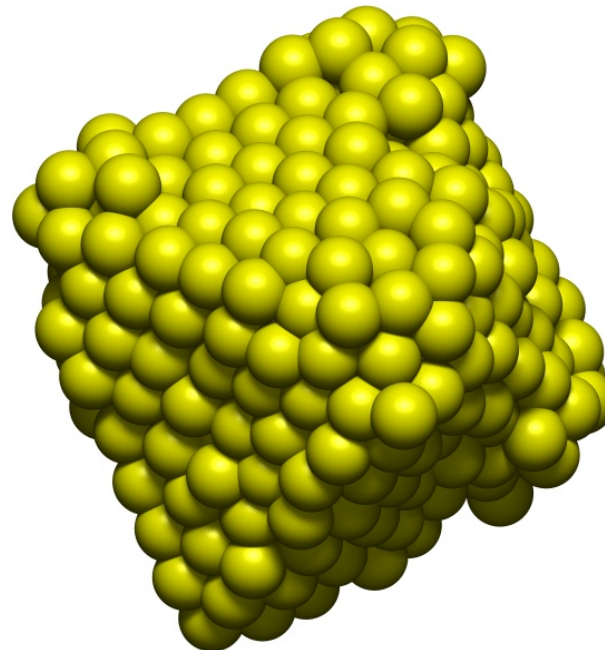
Ice

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

Gold

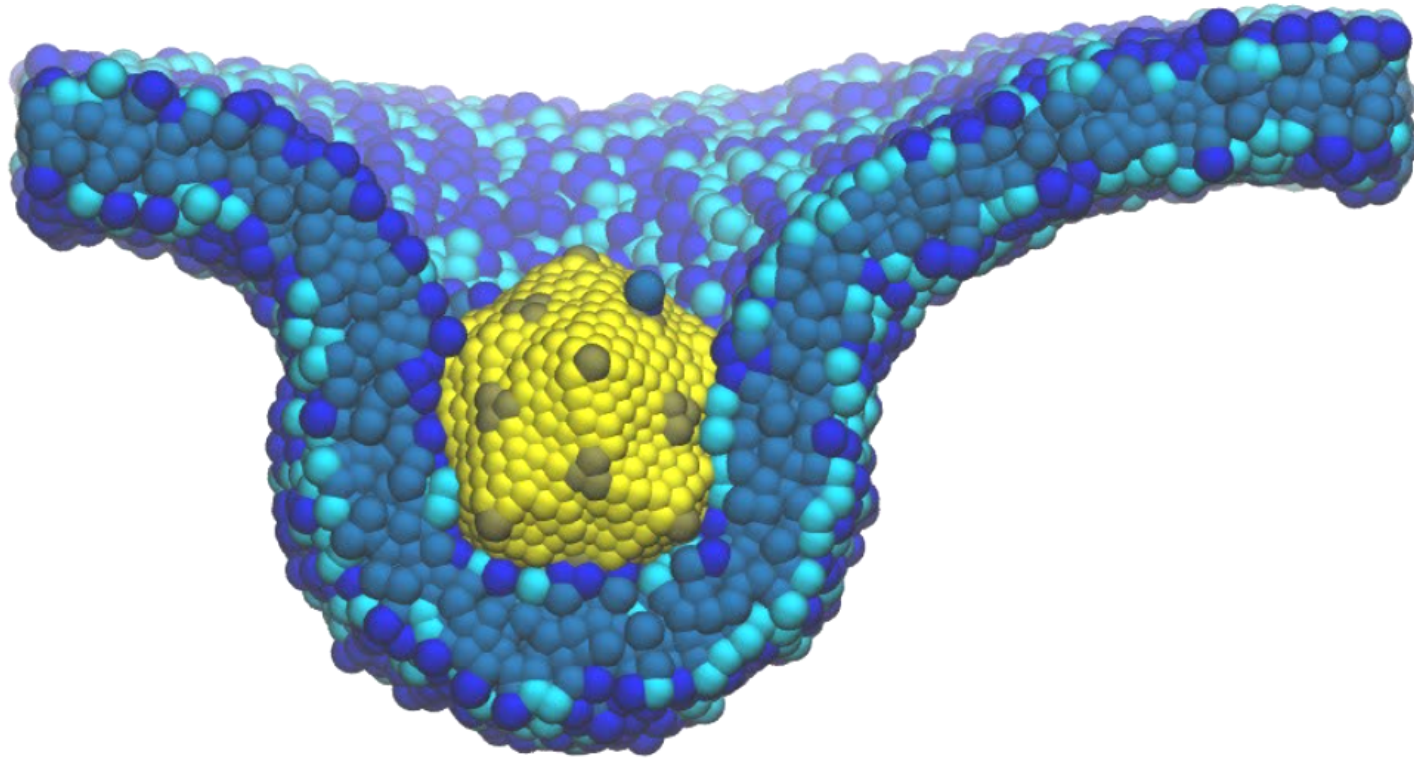
- nanocrystal of 489 gold atoms
- gradual heating
- simulation time = 77 ps

the melting point
of nanoparticles
is lower than in the bulk

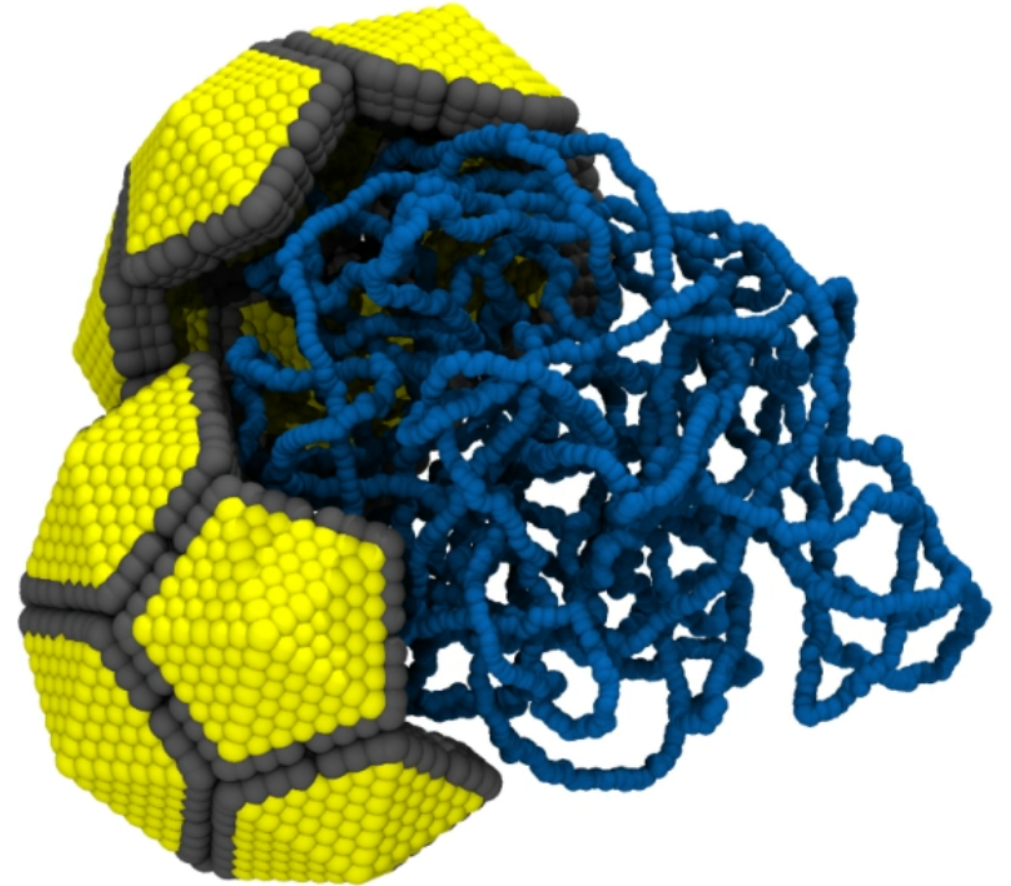


Coarse-grained simulations

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



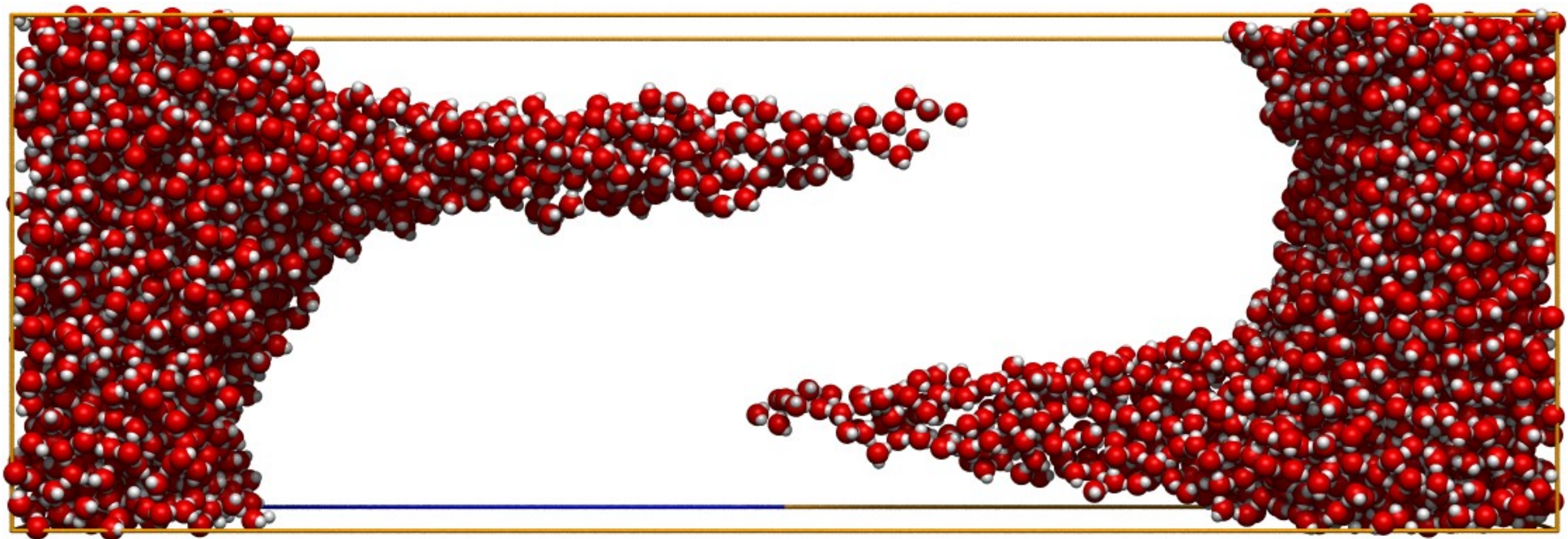
endocytosis



release of RNA from the capsid

Electrospinning

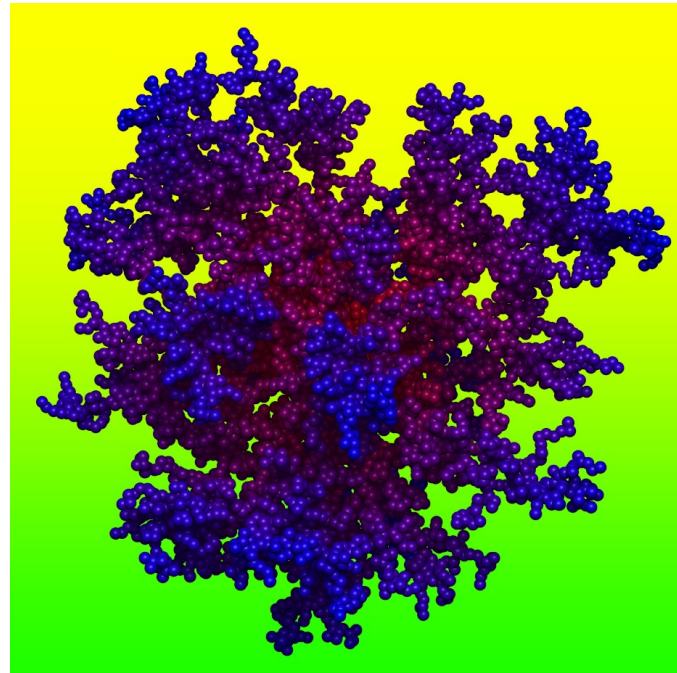
- 5000 SPC/E water molecules, field 1.5 V/nm, simulation time 135 ps
- electrospinning starts by the “Taylor cone”
- the tip elongates and produces a jet stabilized by electric field



Dendrimers by diffusion-limited aggregation

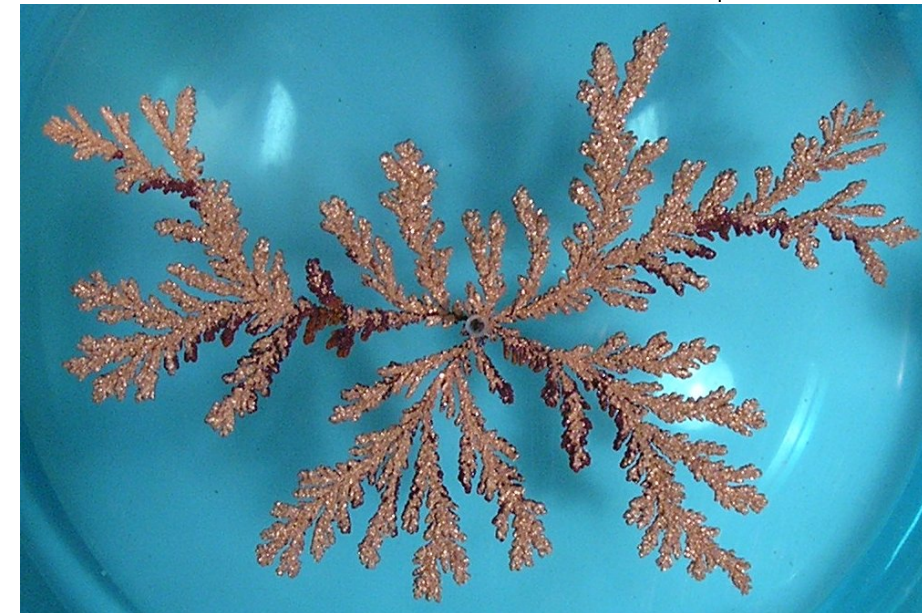
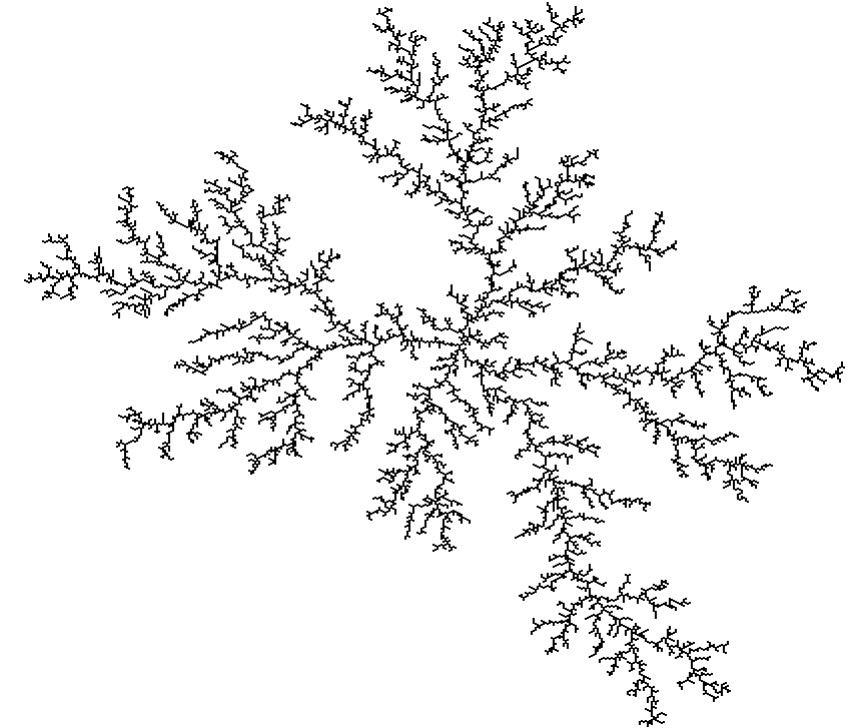
Fractals:

- 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: $D = 2.97$

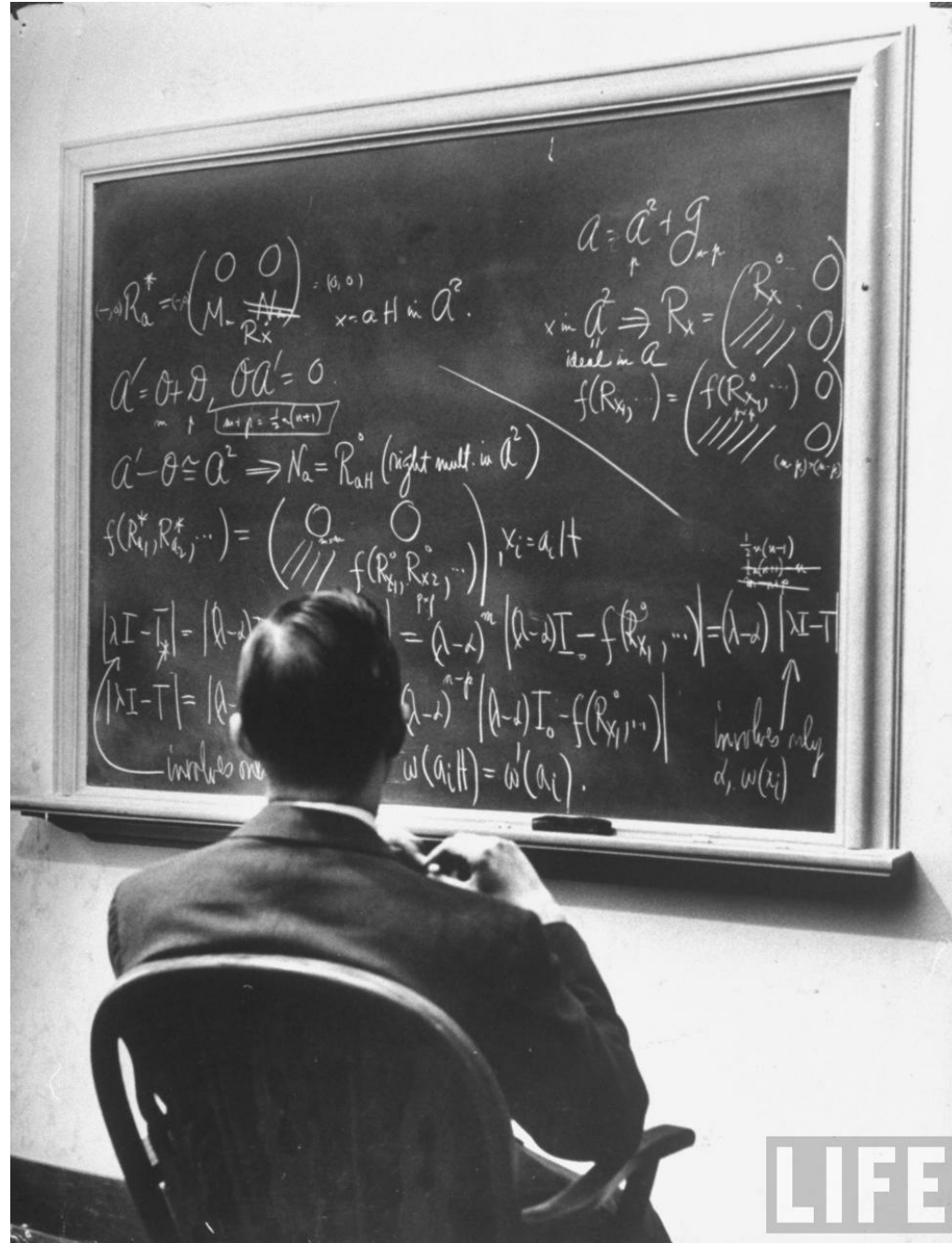


copper electrodeposition →

credit: Wikipedia



End of introduction – real lecture ahead...



LIFE