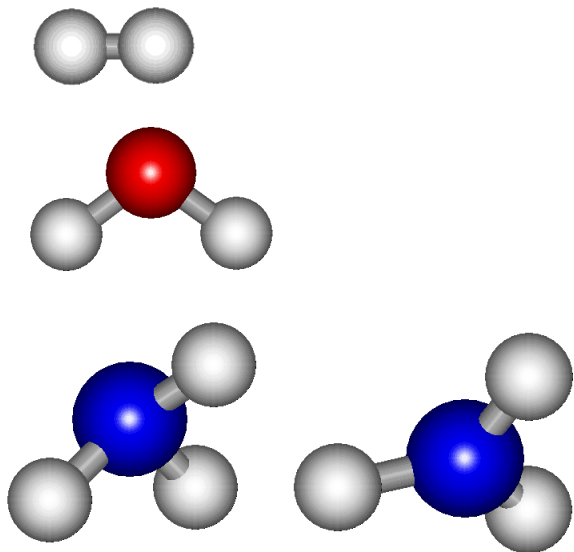


Molecular Dynamics, Langevin Dynamics, and Monte Carlo

Computational Chemistry lab

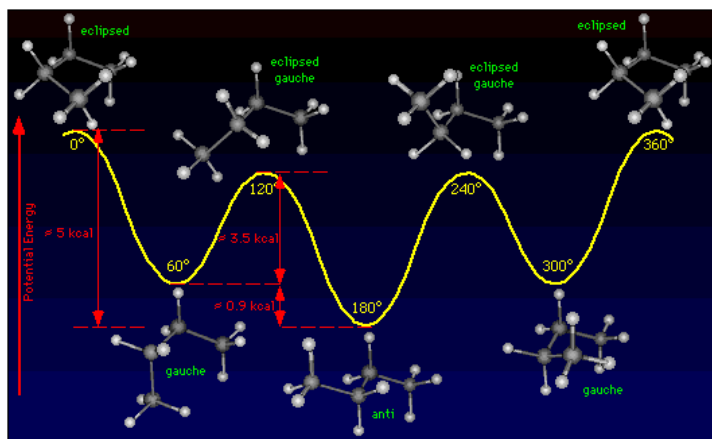
2021



- One configuration is known for H₂
- One configuration is known for H₂O
- The planar and pyramidal configurations are known for NH₃

The number of local minima typically goes exponentially with the number of variables (degrees of freedom). **Combinatorial Explosion Problem**

Possible Conformations (3^n) for linear alkanes CH₃(CH₂)_{n+1}CH₃



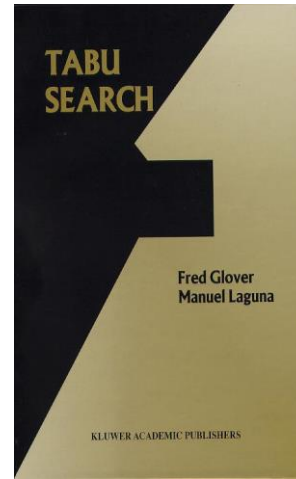
$n = 1$	3
$n = 2$	9
$n = 5$	243
$n = 10$	59,049
$n = 15$	14,348,907

Global minimization

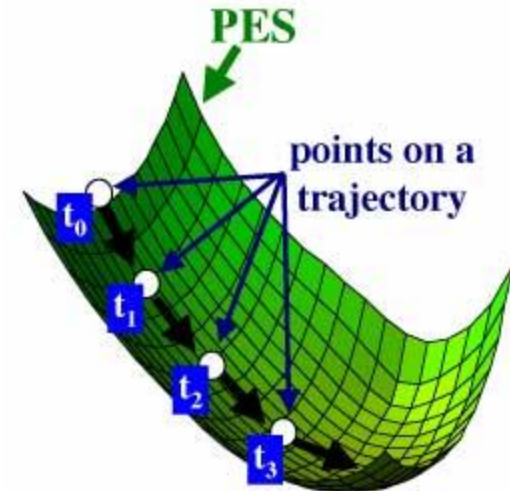
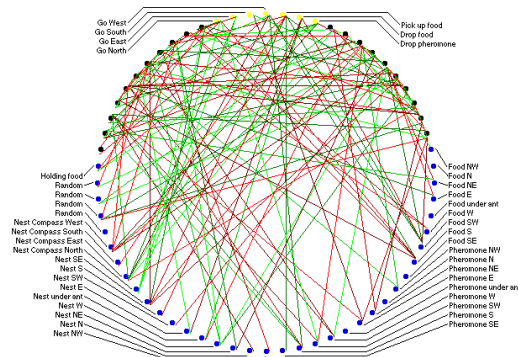
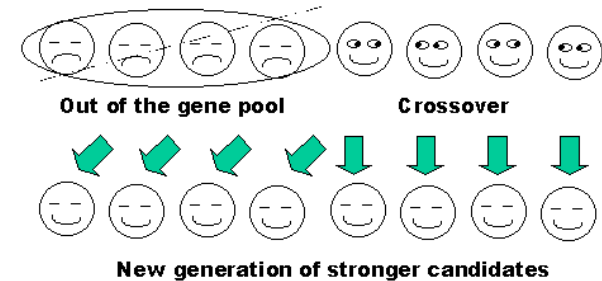
- **"building up" the structure:** combining a large molecule from preoptimized fragments (protein from preoptimized aminoacids)
- **conformational sampling:** take various starting points for local minimization (simulation of nature)
- **None of these are guaranteed to find the global minimum!**

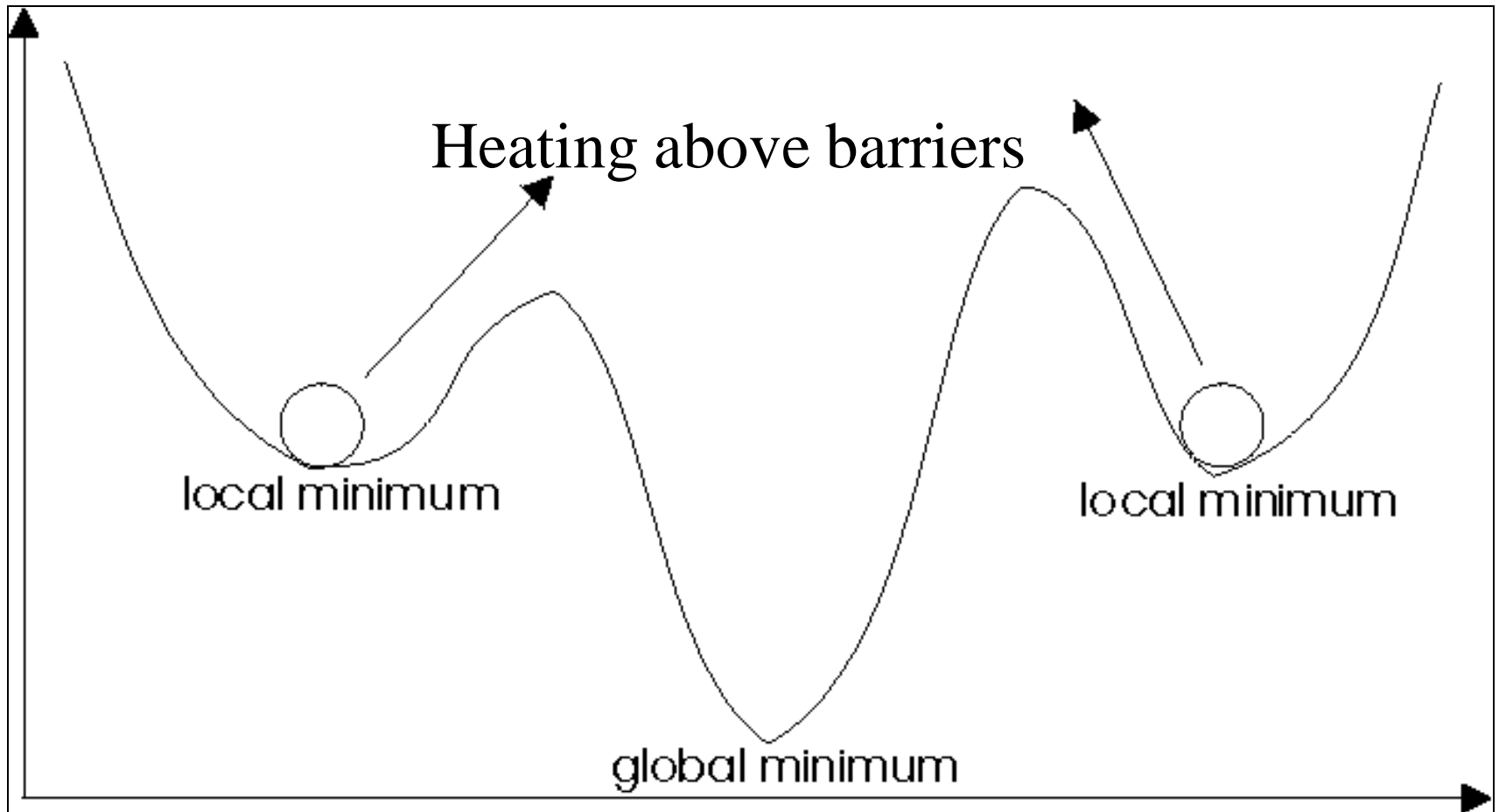
Global Minimum- conformational sampling

- Molecular Dynamics
- Monte Carlo
- Simulated Annealing
- Tabu search
- Genetic Algorithms
- Ant Colony Optimizations
- Diffusion Methods
- Distance Geometry Methods



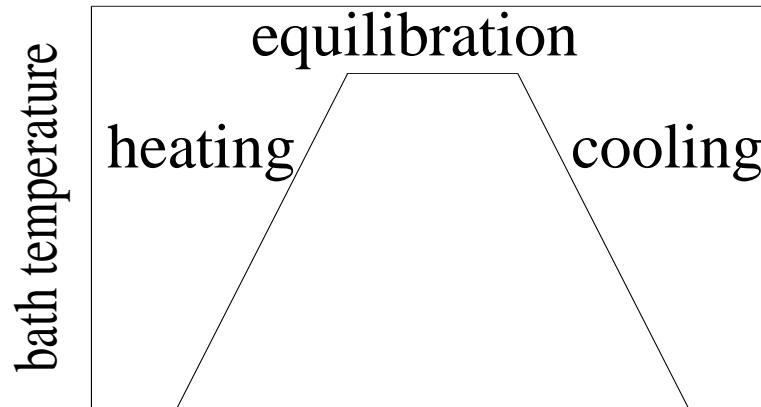
Genetic Optimization





- System overcomes barriers at sufficiently high temperature T_0
- Equilibrium (Boltzmann) distribution $P(\mathbf{R}) \sim \exp(-E(\mathbf{R})/(k_B T_0))$
- Higher probability to find the system near the global minimum

Molecular Dynamics



Equilibration no "constant temperature"

-free dynamics with constant total energy

Solve equations of motion : $\frac{d}{dt} \mathbf{v}_j = -\frac{1}{m_j} \nabla_j E(R)$

The molecular system explicitly includes the solvent molecules.

Equilibration with "constant temperature", heating and cooling – constant temperature dynamics

Constant Temperature Molecular Dynamics

Solve equations of motion : $\frac{d}{dt} \mathbf{v}_j = -\frac{1}{m_j} \nabla_j E(R) + \frac{\mathbf{v}_j}{2\tau} \left(\frac{T_0}{T} - 1 \right)$

Berendsen temperature coupling changes the total energy

\mathbf{R}_j – atomic coordinates, $\mathbf{v}_j = \frac{d}{dt} \mathbf{R}_j$ – atomic velocities

$$T = \frac{3}{2k_B N} \sum_{j=1}^N \frac{\mathbf{v}_j^2}{m_j} \text{ – temperature}$$

T_0 – bath temperature, τ – bath relaxation time

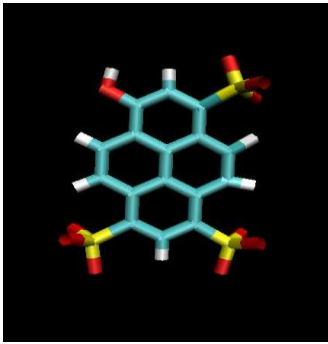
Scaling the velocities

$$\mathbf{v} \leftarrow \mathbf{v} \sqrt{\left(\frac{T_0}{T} - 1 \right) \frac{\Delta t}{\tau} + 1}, \Delta t \text{ - time step size}$$

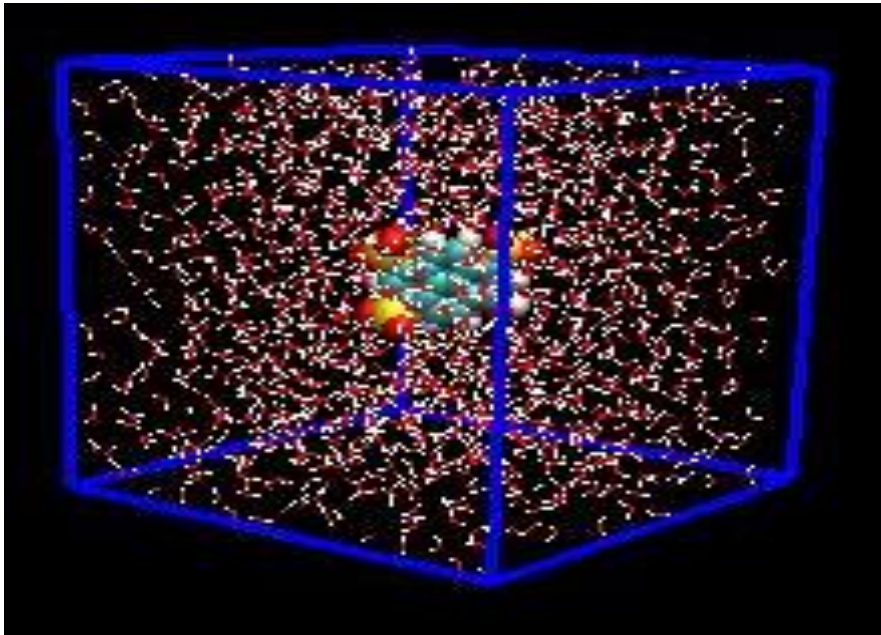
Always used during heating and cooling phases

During equilibration – only if "constant temperature" selected

Simulation in a finite box



The simulating molecule

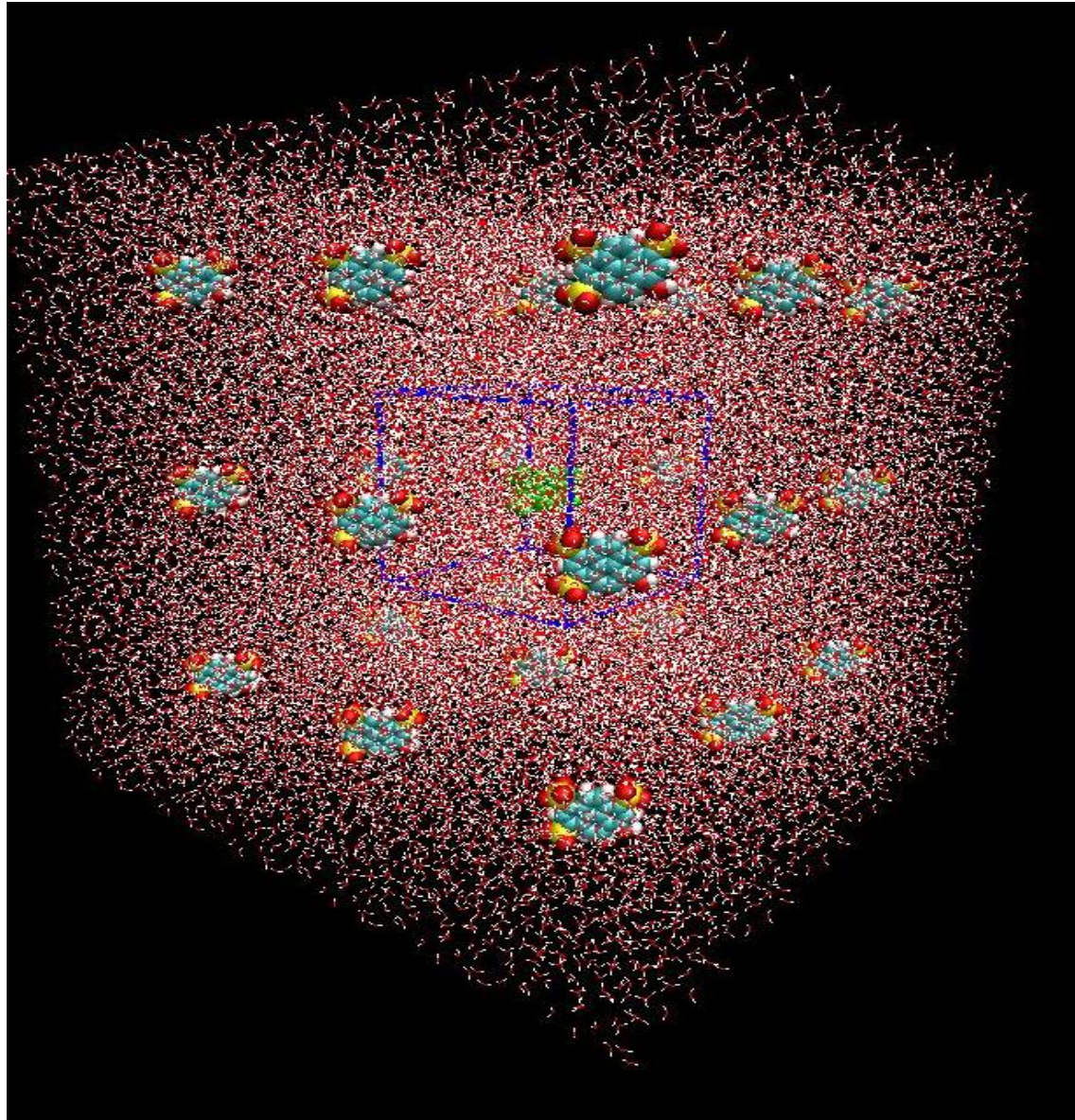


The molecule in a solvent

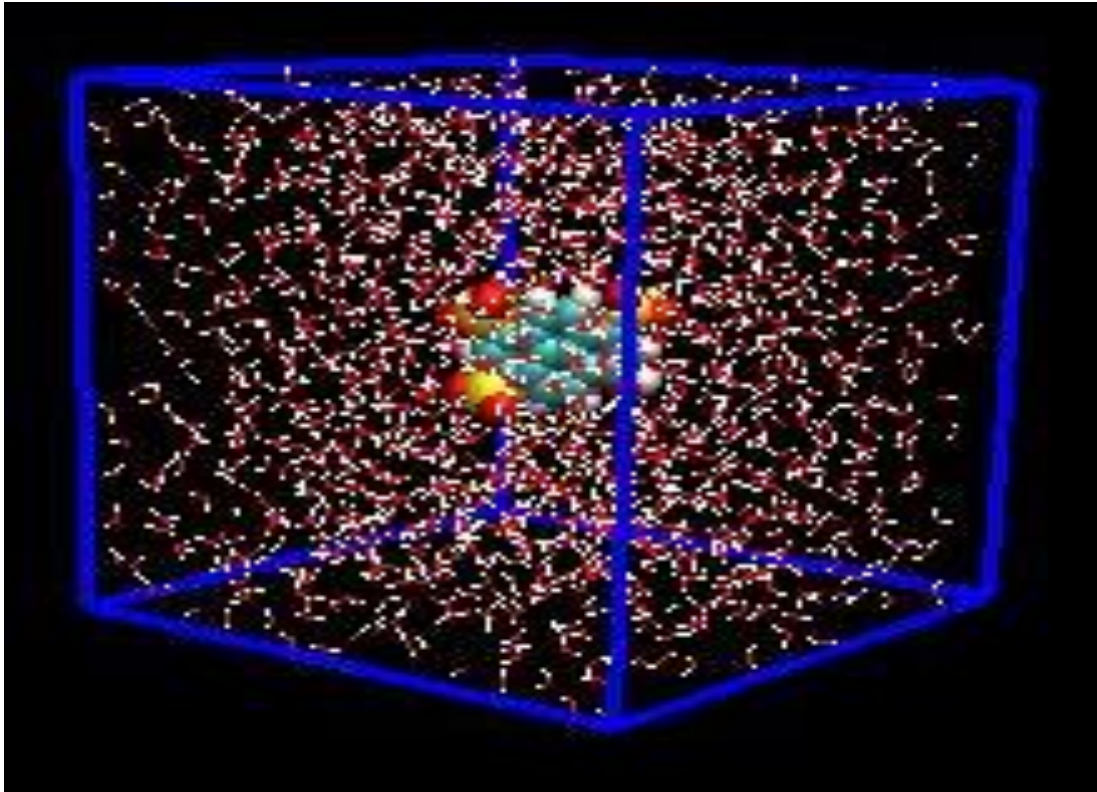
Problem at the boundaries:

- need forces to keep molecules from escaping
- different forces then in the center (solvent on one side, vacuum on another side)
- small number of solvent molecules, compared to Avogadro

Periodic Boundary Conditions



Set the box size



Solute should not see its image in the next box

The largest solute dimension plus the interaction range (or cutoff radius) should be less than the smallest box dimension

Langevin Dynamics

Implicitly simulates the effect of molecular collisions in real solvents

No equations of motion for solvent molecules

The solvent is modeled by the average interaction

$$\frac{d}{dt} \mathbf{v}_j = -\frac{1}{m_j} \nabla_j E(R) - \gamma \mathbf{v}_j + \frac{\mathbf{F}_j}{m_j}$$

γ - friction coefficient of the solvent, \mathbf{F}_j - random force

No energy conservation

Stochastic method

(Molecular dynamics---deterministic method)

Both molecular and Langevin dynamics

---classical equations of motion

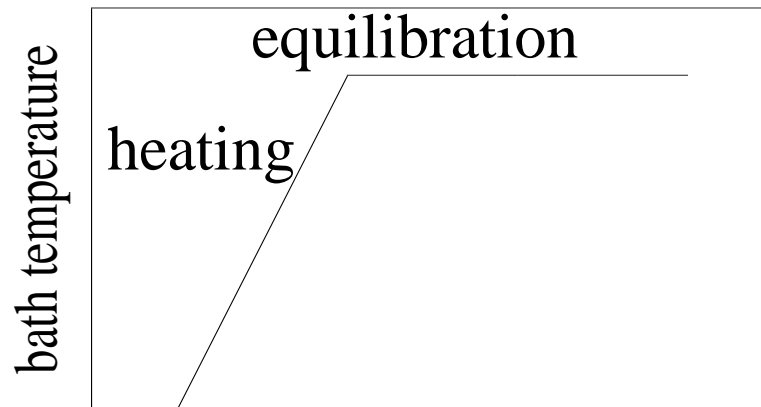
Monte Carlo

-no equations of motion

1. One atom is randomly "kicked"
2. The energy change $\Delta E = E_{\text{new}} - E_{\text{old}}$ is calculated
3. If $\Delta E < 0$ the new configuration is accepted
4. If $\Delta E > 0$ the new configuration is accepted with probability $\exp(-\Delta E / (k_B T_0))$
5. Next atom is randomly "kicked"

Stochastic method

The molecular dynamics, Langevin, and Monte Carlo methods lead to *equilibrium* averaged distribution in the limits of *infinite* time or number of steps



Molecular dynamics vs. Monte-Carlo

MD

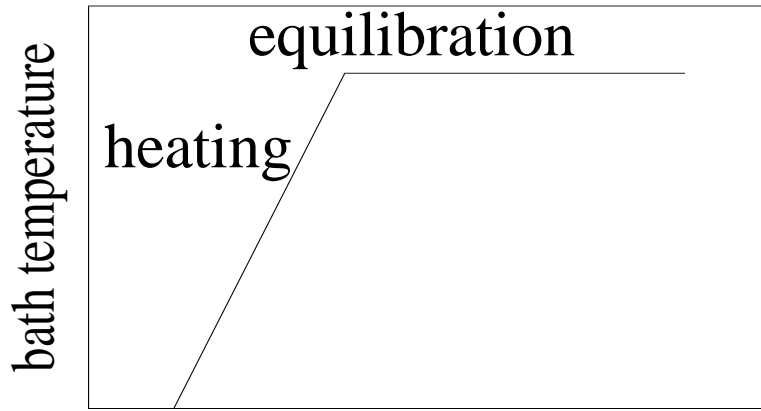
- + simulates the physical evolution of configurations
- tends to only sample the region close to the starting condition and can become trapped in energy wells
- only classical simulation

MC

- no time dimension and atomic velocities - not suitable for time-dependent phenomena or momentum-dependent properties
- + can tunnel between energetically separated regions, giving a better coverage
- + both classical and quantum simulation

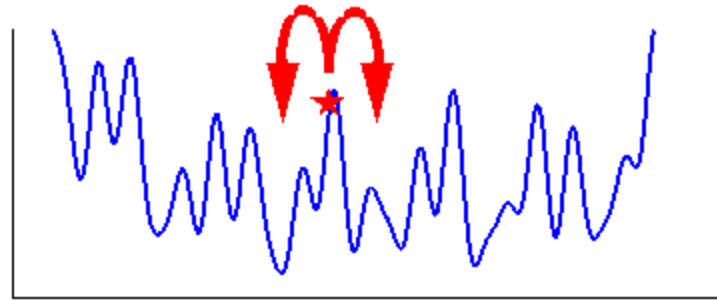
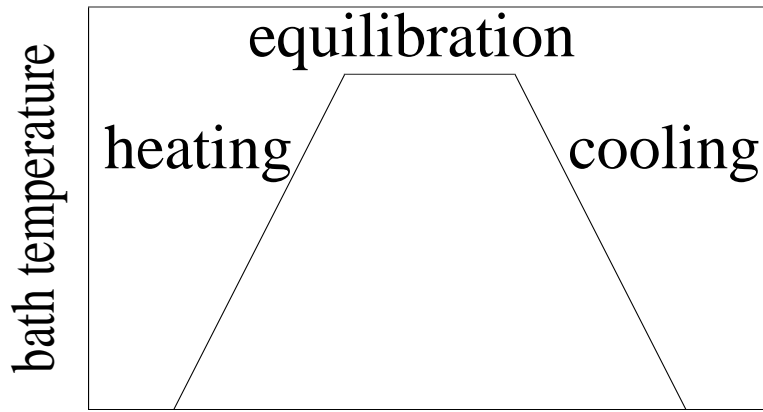
Simulated annealing

If a slow cooling is applied to a liquid, this liquid freezes naturally to a state of minimum energy.



Simulated annealing

If a slow cooling is applied to a liquid, this liquid freezes naturally to a state of minimum energy.



- Is guaranteed to find the global minimum if the equilibration is *infinitely* long and the cooling is *infinitely* slow.
- Either Molecular-Dynamics or Monte-Carlo simulation can be used.