



Introduction to Molecular Dynamics

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History of Protein Motion

- Proteins were anticipated (in 1950s) to be the molecules of inheritance.
- In 1958, John Kendrew and associates successfully determined the structure of myoglobin.
- John Kendrew shared the 1962 Nobel Prize in chemistry with Max Perutz for his characterization of Myoglobin.
- The structure was scrutinized until recently (2000).
 - Access to the embedded heme group was hindered.
 - Crystal structure shattered upon exposure to air.
 - Should have much more affinity to CO than O₂.



Brownian Motion

- In 1827 the botanist Robert Brown observed the motion of plant spores floating in water and moving randomly.
- The explanation for this was already thought to be the random motion of molecules "hitting" the spores.
- The first satisfactory theoretical treatment of the Brownian motion was made by Albert Einstein in 1905.
- Einstein's theory enabled significant statistical predictions about the motion of particles that are randomly distributed in a fluid.
- Stock market behavior.



Why the Blue Sky? Tyndall Effect

- In 1859, John Tyndall passed a beam of white light through a clear container of water in which small, invisible particles were suspended.
- From the side it looked blue, but directly it looked orange.
- Molecules in the air (O, N, C, Ar) exhibit Brownian motion.
- Brownian motion scatters blue light.
- This means that white sunlight has its blue components scattered to the side while its red components keep traveling straight. White sunlight bathes the atmosphere of the earth. The sky is blue because molecules in the air scatter blue to your eyes more than they scatter red.



Maxwell-Boltzmann Distribution

- Potential energy of an object with mass m raised to the height of h :

$$E = m \cdot g \cdot h$$

- In the presence of gravitational field the concentration of gas molecules is not the same at various points of the space.
- Likelihood of finding a molecule in height h is dictated by the M-B distribution.

$$f(h) = e^{\left(\frac{-mgh}{kT}\right)}$$

- k is the Boltzman constant (1.380×10^{-23} J/K)
- T is temperature in degrees of Kelvin

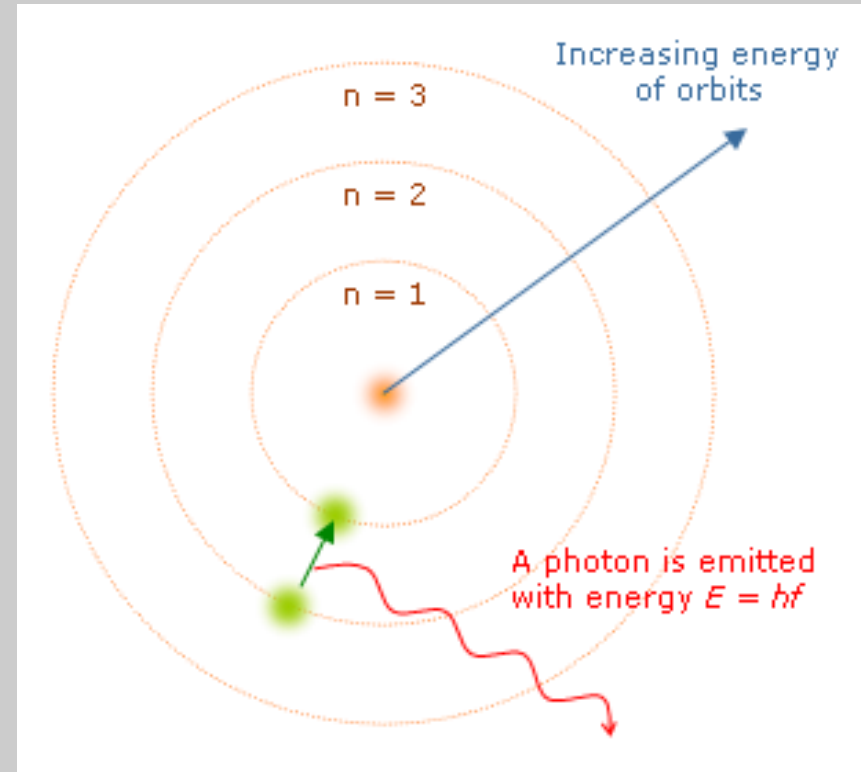




Discrete Energy States

- Bohr atomic model
 - Electrons can exist in discrete orbits.
- Total number of entities in energy level i is dictated by MB-distribution:

$$\frac{N_i}{N} = \frac{e^{\left(-E_i/kT\right)}}{\sum_j e^{\left(-E_j/kT\right)}}$$





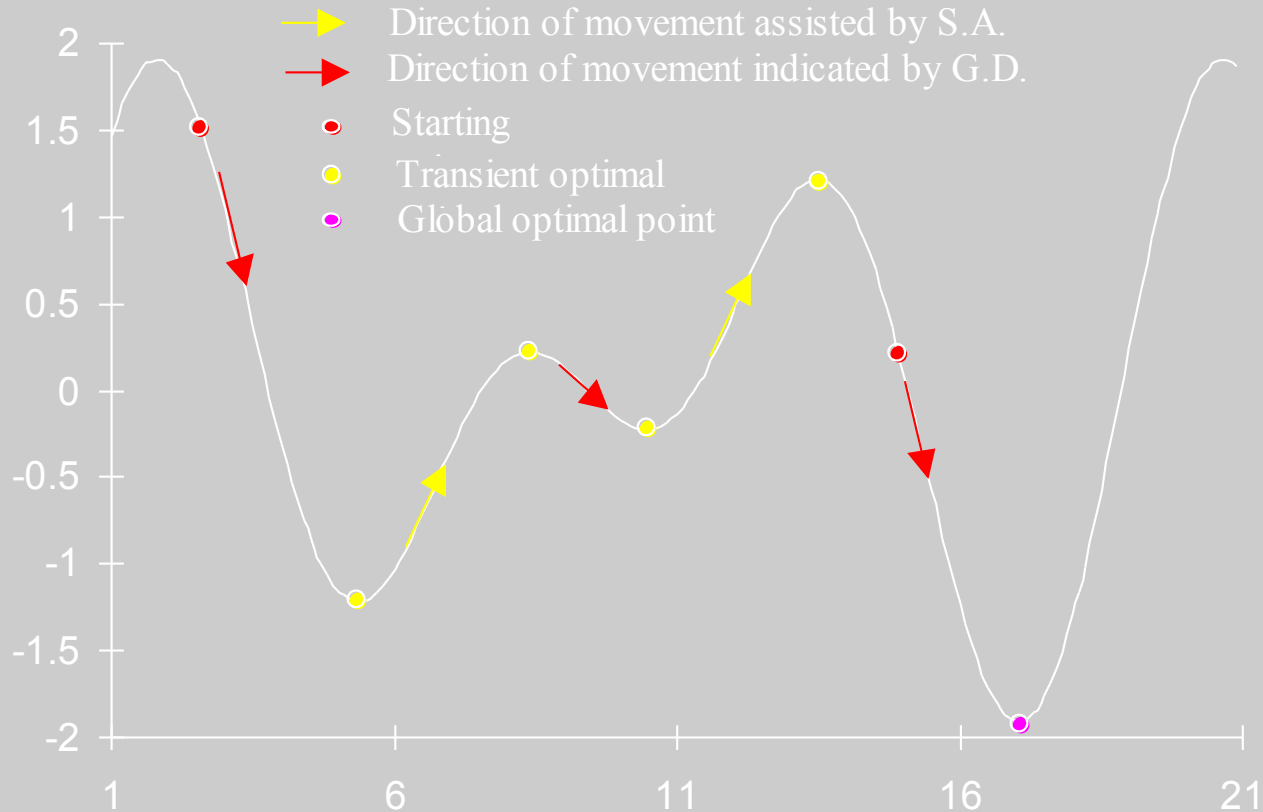
Metropolis Monte Carlo (SA)

- Start at S_0 , E_0 and T_0
- Loop 1: Make a transition to S_1 , E_1
- Accept S_1 as the new state if $E_1 < E_0$
- If $E_1 > E_0$ then
- Accept S_1 as the new state with a probability of:
$$p_a = e^{\left(\frac{-(E_1 - E_0)}{kT}\right)}$$
- Reject S_1 as the new state with a probability of:
$$p_r = e^{\left(\frac{-(E_1 - E_0)}{kT}\right)}$$
- Repeat Loop 1 N times:
- Reduce temperature and repeat loop 1



Contribution of Simulated Annealing

Simulated annealing helps to escape from the local minima.





MD Simulation with XPLOR-NIH

- Initial velocities can be assigned to each atom
 - Using uniformly random velocities
 - Maxwell:
 - Xplor statement:
 - set seed=432324368 end
 - vector do (vx=maxwell(4000.)) (all)
 - vector do (vy=maxwell(4000.)) (all)
 - vector do (vz=maxwell(4000.)) (all)
 - Perform MD:
 - dynamics verlet
 - nstep=1000 timestep=0.001 iasvel=current
 - firsttemperature=300 nprint=25 end

$$\left(\frac{m_i}{2\pi k_B T_i} \right)^{\frac{3}{2}} e^{\left(\frac{-3m_i \delta^2}{2k_B T_i} \right)}$$



SA with XPLOR-NIH

- Temperature needs to reduce over time.
 - Define the following two terms
 - First temperature.
 - Bath temperature.
 - Temperature can be coupled to the bath temperature and reduce over time.
1. set seed=432324368 end
 2. vector do (vx=maxwell(4000.)) (all)
 3. vector do (vy=maxwell(4000.)) (all)
 4. vector do (vz=maxwell(4000.)) (all)

 1. evaluate (\$1=4000)
 2. while (\$1 > 300.0) loop main
 3. dynamics verlet timestep=0.0005
 4. nstep=50 iasvel=current nprint=5
 5. iprfrq=0 tcoupling=true tbath=\$1 end
 6. evaluate (\$1=\$1-25)
 7. end loop main