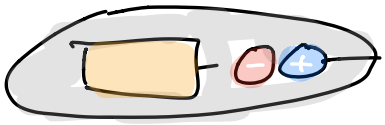
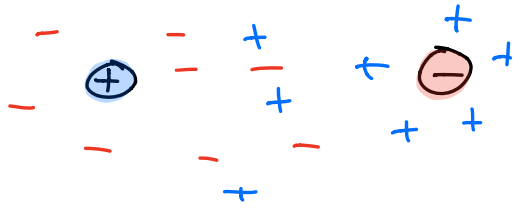
10/30/19 : SAMPLING METHODS

LEFT OFF WITH $\Delta G_{RIGID} = \Delta G_{HASA} + \Delta G_{COULOMB} + \Delta G_{VDW} + \ldots$



SALT-DEPENDENCE OF $\Delta G_{COULOMB}$:

DEBYE-HÜCKLE THEORY.



- IONS TEND TO BRING IN A MOBILE CLOUD OF OPPOSITELY CHARGED IONS
- AT LONG DISTANCES, NO EFFECT
- ATTENUATES ELECTROSTATICS.

$$U_{COUL}(I) = U_{COUL} \cdot e^{-r_{ij}/K}$$

$$K = \gamma \sqrt{\frac{\varepsilon \cdot T}{I}}$$

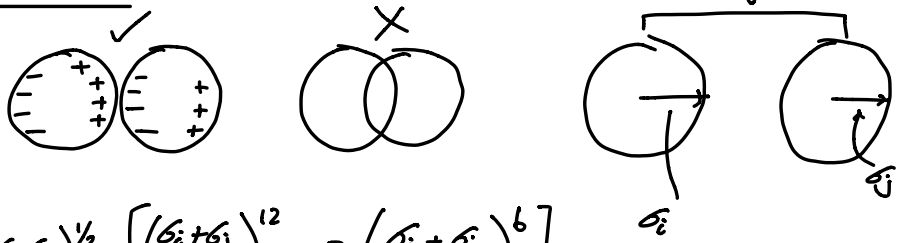
UNITS!

DIELECTRIC CONSTANT

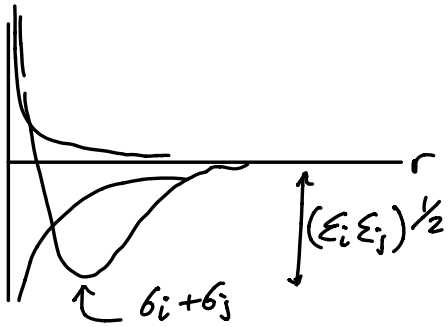
TEMPERATURE

IONIC STRENGTH

VAN DER WAALS



$$U_{VDW} = (\varepsilon_i \varepsilon_j)^{1/2} \cdot \left[\left(\frac{\sigma_i + \sigma_j}{2 r_{ij}} \right)^{12} - 2 \left(\frac{\sigma_i + \sigma_j}{2 r_{ij}} \right)^{6} \right]$$



PARAMETERIZE TO REPRODUCE QUANTUM CALCULATIONS.

HBOND:

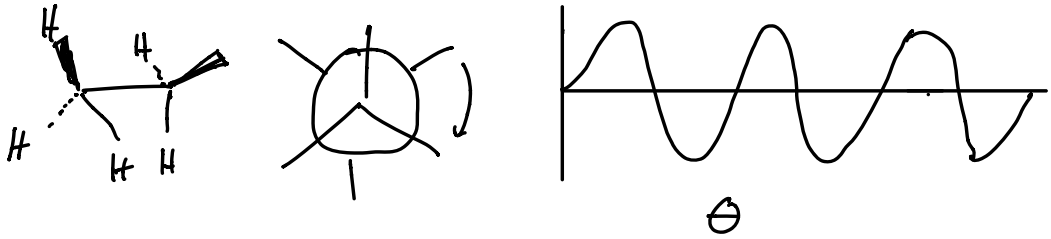
$$U_{HBOND} = a\left(\frac{q_A \cdot q_H}{r^2}\cos(\theta) + b\,c^{r}\right)$$

(PARTIAL CHARGE)

a, b, c CONSTANTS

SO: $\Delta G_{BIND} = \Delta G_{ASA(NONPOLAR)} + \Delta G_{COULOMB} + \Delta G_{LBOLS} + \Delta G_{HBOND} + \Delta G_{VDW}$

SAMPLING METHODS



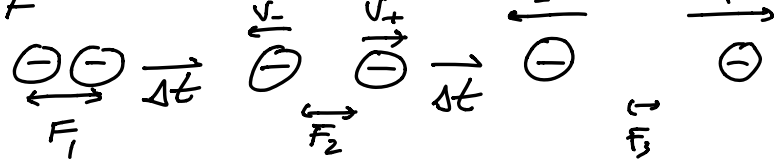
HOW DO YOU SAMPLE THIS?

(1) EXHAUSTIVE SAMPLE. NOT FEASIBLE FOR PROTEINS. WAY TOO MANY DEGREES OF FREEDOM.

(2) RANDOMLY TRY CONFORMATIONS. END UP TRYING LOTS OF TERRIBLE, IMPROBABLE CONFORMATIONS.

(3) LET SAMPLE OVER TIME.

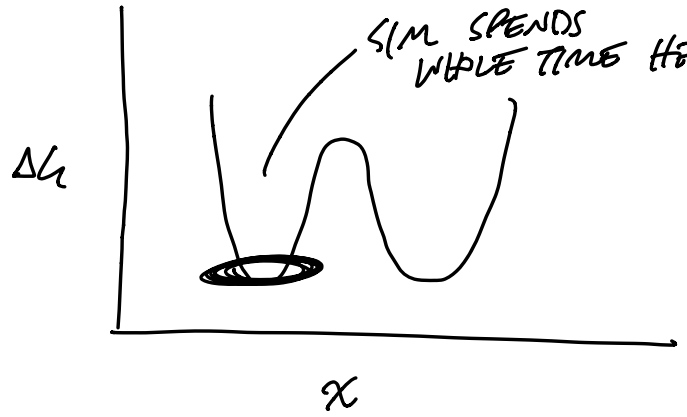
$$\frac{dU}{dx} = F$$



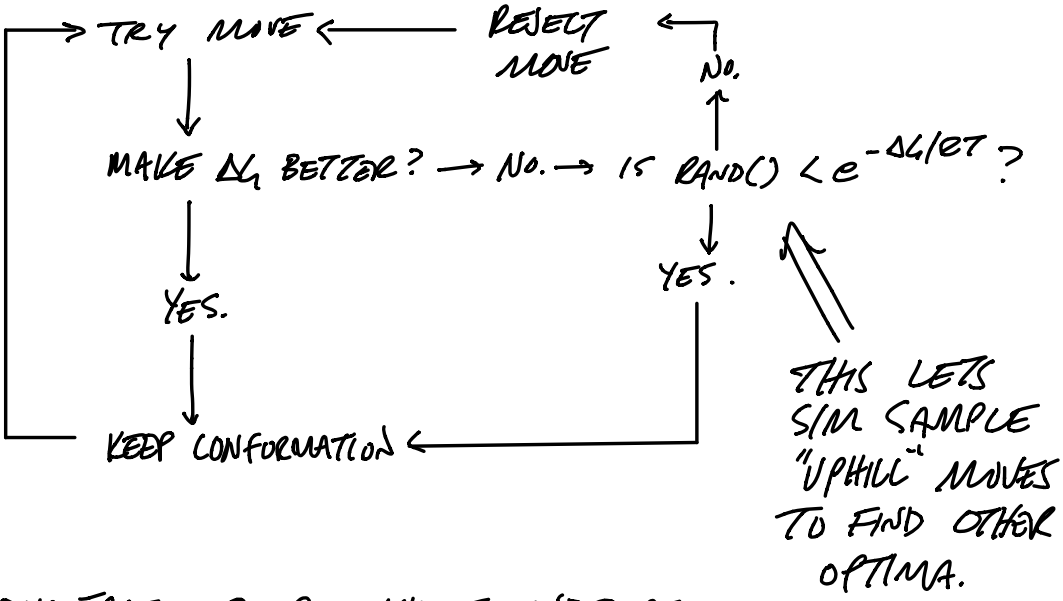
THIS IS A STANDARD MOLECULAR DYNAMICS SIMULATION.

ADVANTAGES: - CAN SEE PROCESSES OCCUR
- DON'T WASTE TIME SAMPLING TERRIBLE CONFORMATIONS.

DISADVANTAGES: - SPEND A TON OF TIME SAMPLING SAME STATES OVER AND OVER.
- CAN END UP NOT SAMPLING WHOLE SPACE.



(4) MONTE CARLO METHODS:



ADVANTAGES: - SAMPLE WHOLE LANDSCAPE
- DOES CONVERGE
- CAN MAKE HIGHLY PARALLEL

DISADVANTAGES: - NO "TIME" CONCEPT
- CAN STILL TAKE A LONG TIME TO CONVERGE.