

## 2.1: History and Fundamental Assumptions

$$U(r_{AB}) = \frac{1}{2} k_{AB} (r_{AB} - r_{AB,eq})^2$$

Vibrational potential energy  
using Hooke's Law & Taylor expansion

## 2.2: Potential Energy Functional Forms

### 2.2.1: Bond Stretching

$$U(r_{AB}) = \frac{1}{2} [k_{AB} + k_{AB}^{(3)} (r_{AB} - r_{AB,eq})] (r_{AB} - r_{AB,eq})^2$$

<sup>(3)</sup> represents cubic term vs quadratic

Bad b/c diverges to  $-\infty$  w/ increasing bond length

Addition of next term helps

$$U(r_{AB}) = \frac{1}{2} [k_{AB} + k_{AB}^{(3)} (r_{AB} - r_{AB,eq}) + k_{AB}^{(4)} (r_{AB} - r_{AB,eq})^2] (r_{AB} - r_{AB,eq})^2$$

$$U(r_{AB}) = D_{AB} [1 - e^{-\alpha_{AB}(r_{AB} - r_{AB,eq})}]^2$$

Morse function  $D_{AB}$ : dissociation energy  
 $\alpha_{AB}$ : fitting constant

$$U(r_{AB}) = D_{AB} \left[ \alpha_{AB}^2 - \alpha_{AB}^3 (r_{AB} - r_{AB,eq}) + \frac{7}{12} \alpha_{AB}^4 (r_{AB} - r_{AB,eq})^2 \right] (r_{AB} - r_{AB,eq})^2$$

Morse function +  
Taylor Expansion

$$k_{AB} = 2\alpha_{AB}^2 D_{AB}$$

relation between parameters in Morse function

## 2.2.2: Valence Angle Bonding

$$U(\theta_{ABC}) = \frac{1}{2} [k_{ABC} + k_{ABC}^{(1)} (\theta_{ABC} - \theta_{ABC,eq}) + k_{ABC}^{(2)} (\theta_{ABC} - \theta_{ABC,eq})^2 + \dots] (\theta_{ABC} - \theta_{ABC,eq})^2$$

Force field for angle strain energy

## 2.2.3: Torsions

Torsional angle  $\rightarrow$  dihedral angle

$$U(\omega_{ABCD}) = \frac{1}{2} \sum_{\{j\}_{ABCD}} V_{j,ABCD} [1 + (-1)^{j+1} \cos(j\omega_{ABCD} + \psi_{j,ABCD})] \quad \text{Torsional potential energy}$$

$$U(\theta_{ABC}) = \sum_{\{j\}_{ABC}} k_{j,ABC}^{\text{Fourier}} [1 + \cos(j\theta_{ABC} + \psi)] , \quad k_{j,ABC}^{\text{Fourier}} = \frac{2k_{ABC}^{\text{harmonic}}}{j^2}$$

inorganic SHAPES force field to compute angle bending energy.

## 2.2.4: van der Waals Interactions

$$F_a = -\frac{\partial U}{\partial q}$$

$$U(r_{AB}) = \frac{a_{AB}}{r_{AB}^{12}} - \frac{b_{AB}}{r_{AB}^6} \quad \text{Lennard-Jones potential}$$

$$r_{AB} = \sqrt{(x_A - x_B)^2 + (y_A - y_B)^2 + (z_A - z_B)^2}$$

$$U(r_{AB}) = 4\varepsilon_{AB} \left[ \left( \frac{\sigma_{AB}}{r_{AB}} \right)^{12} - \left( \frac{\sigma_{AB}}{r_{AB}} \right)^6 \right] \quad \text{typical Lennard-Jones}$$

$$\frac{dU(r_{AB})}{dr_{AB}} = \frac{4\varepsilon_{AB}}{r_{AB}} \left[ -12 \left( \frac{\sigma_{AB}}{r_{AB}} \right)^{12} + 6 \left( \frac{\sigma_{AB}}{r_{AB}} \right)^6 \right] \quad \text{differentiate}$$

$$r_{AB}^* = 2^{1/6} \sigma_{AB}$$

$$U(r_{AB}) = \varepsilon_{AB} \left[ \frac{6}{\beta_{AB} - 6} \exp\left(\beta_{AB} \frac{1 - r_{AB}}{r_{AB}^*}\right) - \frac{\beta_{AB}}{\beta_{AB} - 6} \left( \frac{r_{AB}^*}{r_{AB}} \right)^6 \right]$$

better equation

## 2.2.5: Electrostatic Interactions

$$U_{AB} = M^{(A)} V^{(B)} \rightarrow U_{AB} = \frac{q_A q_B}{\epsilon_{AB} r_{AB}}$$

$$U_{AB/CD} = \frac{\mu_A \mu_B \mu_C \mu_D}{\epsilon_{AB/CD} r_{AB/CD}^3} (\cos \chi_{AB/CD} - 3 \cos \alpha_{AB} \cos \alpha_{CD}) \quad \text{dipole moment}$$

$$\epsilon_{AB} = \begin{cases} \infty & \text{if A \& B are 1,2- or 1,3-related} \\ 3.0 & \text{if A \& B are 1,4-related} \\ 1.5 & \text{otherwise} \end{cases}$$

$$U(r_{XH}) = \frac{a_{XH}^I}{r_{XH}^{12}} - \frac{b_{XH}^I}{r_{XH}^{10}} \quad \text{hydrogen bonding energy}$$

## 2.2.6: Cross Terms and Additional Non-Bonded Terms

$$U(q) = U(q_{eq}) + \sum_{i=1}^{3N-6} (q_i - q_{i,eq}) \left. \frac{\partial U}{\partial q_i} \right|_{q=q_{eq}}$$

$$+ \frac{1}{2!} \sum_{i=1}^{3N-6} \sum_{j=1}^{3N-6} (q_i - q_{i,eq})(q_j - q_{j,eq}) \left. \frac{\partial^2 U}{\partial q_i \partial q_j} \right|_{q=q_{eq}} + \dots$$

$$U(r_{AB}, \theta_{ABC}) = \frac{1}{2} k_{AB,ABC} (r_{AB} - r_{AB,eq}) (\theta_{ABC} - \theta_{ABC,eq}) \quad \text{including energy terms make force field more complete.}$$

$$U(r_{BC}, \omega_{ABCD}) = \frac{1}{2} k_{BC,ABCD} (r_{BC} - r_{BC,eq}) [1 + \cos(j\omega + \psi)] \quad \text{stretch-torsion coupling}$$

## 2.2.7: Parameterization Strategies

$$\chi = \left[ \sum_i^{\text{observables}} \sum_j^{\text{occurrences}} \frac{(\text{calc}_{i,j} - \text{expt}_{i,j})^2}{w_i^2} \right]^{1/2} \quad \text{example of a "penalty function"}$$

$$\sigma_{AB} = \sigma_A + \sigma_B$$

&

Simplify scope of the problem

$$\epsilon_{AB} = (\epsilon_A \epsilon_B)^{1/2}$$

## 2.3 : Force - field Energies and Thermodynamics

Strain energies for two different molecules cannot be meaningfully compared unless the zero of energy is identical

ex. ethanol vs dimethyl ether

both have formula  $C_2H_6O$  but do not have same  $\Delta H_f$

ethanol has a force field of 2  $sp^3$  carbons, 1  $sp^3$  oxygen, 5 C-H, and 1 O-H

dimethyl ether has a force field of 2  $sp^3$  carbons, 1  $sp^3$  oxygen, and 6 C-H

Some atom types, energetic comparisons are limited to conformers / isomers that can be formed without change to atom type,

## 2.4 : Geometry Optimization

### 2.4.1: Optimization Algorithms

$$g(q) = \begin{bmatrix} \frac{\partial U}{\partial q_1} \\ \frac{\partial U}{\partial q_2} \\ \vdots \\ \frac{\partial U}{\partial q_n} \end{bmatrix} \quad \begin{array}{l} \text{gradient vector} \\ q: n\text{-dimensional coordinate vector} \\ n = 3N - 6 \text{ if using internal coordinates} \\ n = 3N \text{ if using cartesian coordinates.} \end{array}$$

$$\frac{\partial U}{\partial x_A} = \sum_{\substack{i \text{ bonded} \\ \text{to } A}} \frac{\partial U}{\partial r_{Ai}} \frac{\partial r_{Ai}}{\partial x_A} \quad \frac{\partial U}{\partial r_{Ai}} = \frac{1}{2} \left[ 2k_{Ai} + 3k_{Ai}^{(3)} (r_{Ai} - r_{Ai,eq}) + 4k_{Ai}^{(4)} (r_{Ai} - r_{Ai,eq})^2 \right] (r_{Ai} - r_{Ai,eq})$$

bond stretching terms

$$\frac{\partial r_{Ai}}{\partial x_A} = \frac{(x_A - x_i)}{\sqrt{(x_A - x_i)^2 + (y_A - y_i)^2 + (z_A - z_i)^2}}$$

$$U(q^{(k+1)}) = U(q^{(k)}) + (q^{(k+1)} - q^{(k)})^T g^{(k)} + \frac{1}{2} (q^{(k+1)} - q^{(k)})^T H^{(k)} (q^{(k+1)} - q^{(k)})$$

Force-field energy  
Taylor expanded and  
rewritten as matrices.

↓ a lot of math

$$q^{(k+1)} = q^{(k)} - (H^{(k)})^{-1} g^{(k)}$$

describes location of stationary points

## 2.4.2: Optimization Aspects Specific to Force Fields

- Force fields usually have a cut-off range for van der Waals energies
- cut-offs can pose a problem for optimizers.
- electrostatic interactions diverge with  $r^{-1}$
- reactive processes like transition states are a problem
  - 1) • define new atom types and parameters for bond-making/breaking.
    - define force field where transition state is minima.
  - 2) • compute same energy irrespective of whether the atomic connectivity is that of reactant or that of product.
  - 3) • Mixing force-field representation of the bulk of molecule with a QM representation.

## 2.5: Menagerie of Modern Force Fields

### 2.5.1: Available Force Fields

There are a lot

### 2.5.2: Validation

Validation: testing the utility of a force field for molecules

- 1) How do I pick the best force field for my problem?
  - 2) How will I know whether I can trust the results?
- individual problems tend to have highly tailored force fields.
  - experimental measurements carry error.

### 3: Simulations of Molecular Ensembles

#### 3.1: Relationship Between MM Optima and Real Systems.

- Zero-point vibrational effects dictate, even at 0K, a molecule can have a range of different structures.
- "stiff" molecules have well-defined PES energy well.
- "loose" molecules (polyethylene glycol) call for structures to be time-dependent

#### 3.2: Phase Space and Trajectories

$$X' = (x_1, y_1, z_1, p_{x,1}, p_{y,1}, p_{z,1}, x_2, y_2, z_2, p_{x,2}, p_{y,2}, p_{z,2}, \dots)$$

$$Q = (x_1, y_1, z_1, x_2, y_2, z_2, \dots) \quad P = (p_{x,1}, p_{y,1}, p_{z,1}, p_{x,2}, p_{y,2}, p_{z,2}, \dots)$$

$$X = (Q, P) \quad \text{phase space}$$

##### 3.2.1: Properties as Ensemble Averages

$$\langle A \rangle = \iint A(q, p) P(q, p) dq dp \quad \text{average value of } A$$

$$P(q, p) = Q^{-1} e^{-E(q, p)/k_B T} \quad \text{probability of being at a particular phase point.}$$

$$Q = \iint e^{-E(q, p)/k_B T} dq dp \quad \text{system partition function.}$$

##### 3.2.2: Properties as Time Averages of Trajectories

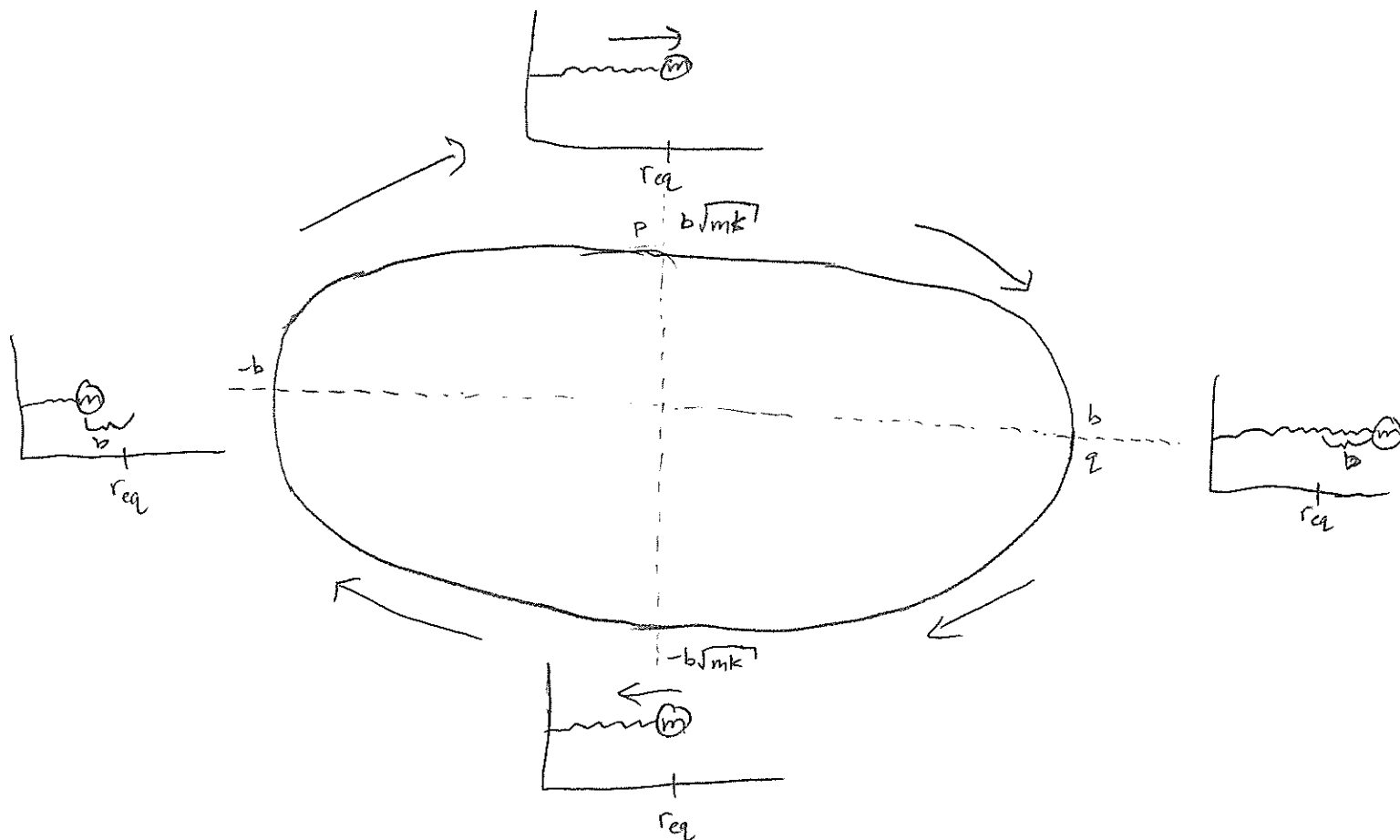
$$\langle A \rangle = \frac{1}{M} \sum_i^M A(t_i) \quad M = \# \text{ of times the property is sampled.}$$

$$\langle A \rangle = \lim_{t \rightarrow \infty} \frac{1}{t} \int_{t_0}^{t_0+t} A(\tau) d\tau \quad \text{indefinite trajectory}$$

### 3.3: Molecular Dynamics

- A phase point determines the location of the next phase point
- The forward trajectory is determined by the initial phase point.

#### 3.3.1: Harmonic Oscillator Trajectories



phase-space trajectory for 1D harmonic oscillator

$$q(t_2) = q(t_1) + \int_{t_1}^{t_2} \frac{p(t)}{m} dt$$

relationship between two positions

$$p(t_2) = p(t_1) + m \int_{t_1}^{t_2} a(t) dt$$

relationship between two momentum vectors.

$$q(t) = b \cos\left(\sqrt{\frac{k}{m}} t\right)$$

$$p(t) = -b\sqrt{mk} \sin\left(\sqrt{\frac{k}{m}} t\right)$$

position  
and  
momentum

after applying boundary conditions,

### 3.3.2: Non-analytical Systems

$$q(t+\Delta t) = q(t) + \frac{p(t)}{m} \Delta t \quad \Delta t \rightarrow 0$$

$$p(t+\Delta t) = p(t) + m a(t) \Delta t$$

$$T(t) = \frac{1}{(3N-n)k_B} \sum_{i=1}^N \frac{|p_i(t)|^2}{m_i}$$

### 3.3.3: Practical Issues in Propagation

$$q(t+\Delta t) = 2q(t) - q(t-\Delta t) + a(t)(\Delta t)^2 \quad \text{subsequent positions are determined by current position.}$$

↓ math magic

$$q(t+\Delta t) = q(t) + v(t+\frac{1}{2}\Delta t) \Delta t \quad \text{do same for velocity } v(t+\frac{1}{2}\Delta t) = v(t-\frac{1}{2}\Delta t) + a(t) \Delta t$$

$$|r_{ij}|^2 - d_{ij}^2 = 0 \quad \text{"freezing" bond lengths to eliminate degrees of freedom.}$$

$$r_i(t+\Delta t) = r_i^o(t+\Delta t) + \Delta r_i(t) \quad \text{use of Verlet algorithm by taking unconstrained steps}$$

### 3.3.4: Stochastic Dynamics

$$a(t) = -\zeta p(t) + \frac{1}{m} [F_{\text{intra}}(t) + F_{\text{continuum}}(t)]$$

$$r(t) = r(t_0) + \frac{1}{\zeta} \int_{t_0}^t [F_{\text{intra}}(\tau) + F_{\text{continuum}}(\tau)] d\tau$$