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Chapter 2 - Molecular Mechanics

★ 2.1 History + Fundamental Assumptions

Hooke's Law for a spring
force constant

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

A heterodiatomic molecule represents the simplest case for vibrational spectroscopy

★ 2.2.1 Bond Stretching

Practical solutions to bond stretching is to include the Taylor expansion

$$U_{\text{CAB}} = \frac{1}{2} [k_{\text{AB}} + k^3_{\text{AB}} (r_{\text{AB}} - r_{\text{AB,eq}})] (r_{\text{AB}} - r_{\text{AB,eq}})^2$$

This diverges to $-\infty$, lowest energy w/ ~~now~~ have dissociated bonds. To fix this, more terms were added

$$U_{\text{CAB}} = \frac{1}{2} [k_{\text{AB}} + k^3_{\text{AB}} (r_{\text{AB}} - r_{\text{AB,eq}}) + k^5_{\text{AB}} (r_{\text{AB}} - r_{\text{AB,eq}})^2] (r_{\text{AB}} - r_{\text{AB,eq}})^2$$

Morse + Taylor together is

$$U_{\text{CAB}} = D_{\text{AB}} \left[e^{-2\alpha_{\text{AB}} (r_{\text{AB}} - r_{\text{AB,eq}})} + \frac{7}{12} \alpha^2_{\text{AB}} (r_{\text{AB}} - r_{\text{AB,eq}})^2 \right] (r_{\text{AB}} - r_{\text{AB,eq}})^2$$

★ 2.2.2 Valence Angle Bending

Vibrational spec. reveals that energy associated w/ bond angles are modeled well by polynomial expansions. The force field function for angle strain energy is

$$U(\theta_{ABC}) = \frac{1}{2} [K_{ABC} + K_{ABC}^{(2)} (\theta_{ABC} - \theta_{ABC,eq}) + K_{ABC}^{(3)} (\theta_{ABC} - \theta_{ABC,eq})^2 + \dots]$$

↑
Valence angle

★ 2.2.3 Torsions

Torsional angle is the dihedral angle

$$U(\omega_{ABCD}) = \frac{1}{2} \sum_{j \in \{ABCD\}} V_{j,ABCD} [1 + (-1)^{j+1} \cos(j\omega_{ABCD} + \gamma_{j,ABCD})]$$

Torsional potential energy. phase energy

$$U(\theta_{ABC}) = \sum_{j,ABC} K_{j,ABC}^{\text{Fourier}} [1 + \cos(j\theta_{ABC} + \gamma)]$$

for inorganic shapes

★ 2.2.4 van der Waals Interactions

The best equation for this, where \downarrow potential energy $U=0$ and by differentiation, is the Lennard-Jones

$$\frac{dU(r_{AB})}{dr_{AB}} = \frac{4\epsilon_{AB}}{r_{AB}} \left[-12 \left(\frac{6_{AB}}{r_{AB}} \right)^{12} + 6 \left(\frac{6_{AB}}{r_{AB}} \right)^6 \right]$$

↑ constants

From here, we can find the Lennard-Jones potential as

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

★ 2.2.5 Electrostatic Interactions

Classical electrostatic energy of interaction

$$U_{AB} = \overset{\substack{\uparrow \\ \text{ordered vector} \\ \text{of multiple} \\ \text{moments}}}{M^{(A)}} \cdot \overset{\substack{\leftarrow \\ \text{ordered row vector} \\ \text{of electrical potentials}}}{V^{(B)}}$$

Taking into account ~~interaction~~ van der Waals

$$U_{AB} = \frac{\epsilon_{AB} q_A q_B}{\epsilon_{AB} r_{AB}}$$

When thinking about dipole moments, we get

$$U_{AB}/CD = \frac{\epsilon_{AB} q_A q_B}{\epsilon_{AB} CD^3} \cos \chi_{AB/CD} - 3 \cos \alpha_{AB} \cos \alpha_{CD}$$

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

★ 2.2.6 Cross Terms + Additional Non-bonded Terms

Stretch-stretch terms can be useful in modeling systems characterized by π conjugation. Stretch-torsion coupling can be useful in systems eclipsing interactions w/ high strain. Coupling \downarrow

$$U_{r_{BC}, \omega_{ABCO}} = \frac{1}{2} K_{BC, ABCO} (r_{BC} - r_{BC, eq}) [1 + \cos(j\omega + \psi)]$$

\downarrow phase angle
 \uparrow periodicity of torsional term

★ 2.2.7 Parameterization Strategies

The goal of parameterization is to develop a model that has high, ~~pre~~ reproducible results.

$$Z = \left[\sum_i^{\text{observable}} \sum_j^{\text{parameters}} \frac{(calc_{ij} - exp_{ij})^2}{w_i^2} \right]^{1/2}$$

\uparrow
 might include bond lengths, angles, etc.

★ 2.3 Force-Field Energies + Thermodynamics

Strain energies for two different molecules cannot be meaningfully compared unless the zero of energy is identical! To find the H_f of a compound, we must find the H_f of each hypothetical + unstrained atom type. Energetic comparisons are necessarily limited to conformers, or other isomers that can be formed w/o any change in atom type

★ 2.4 Geometry Optimization

Real molecules vibrate thermally about equilibrium structures, finding minimum energy structures is key in describing equilibrium constants

★ 2.4.1 Optimizing Algorithms

At a given point in the multidimensional case, we want to move in the direction of the greatest downward slope in the energy in respect to all the coordinates. This is the opposite of the gradient vector

$$g(q) = \begin{bmatrix} \frac{\partial U}{\partial q_1} \\ \frac{\partial U}{\partial q_2} \\ \frac{\partial U}{\partial q_3} \\ \vdots \\ \frac{\partial U}{\partial q_n} \end{bmatrix}$$

$g(q)$ is the negative of the gradient vector.
n-dimensional coordinate vector
3N

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

reference point
"Hessian" matrix

Force Field energy
Taylor expanded
matrices

★ 2.4.2 Optimization Aspects Specific to Force Fields

- Force fields has cut-off ranges for van der Waals energies. These cut^{ts} offs poses a problem for optimizers.
- Electrostatic interacts diverge w/ r^{-1}
- To handle reactive processes
 - Define a new atom type + ~~parameters~~ parameters to make/break bonds
 - Compute the same energy regardless of if the atomic connectivity is of the reactant or product
 - Mixing force-field representation of the molecule w/ a QM representation

★ 2.5 Menagerie of Modern Force Fields

★ 2.5.1 Available Force Fields

Table 2.1 has alphabetic listing of active forcefields we use today. Watch out for confusing nomenclature

★ 2.5.2 Validation

Validation is the process of testing the utility of a force field for molecules other than those that were parameterized. When looking for a force field, it is highly likely it will not have all the possible parameters for the specific research you do. QM values will take the place of experimental data

Chapter 3 - Simulations of Molecular Ensembles

★ 3.1 Relationship Between MM Optima and Real Systems

The zero point vibrational effects dictate that a molecule is capable of having a range of different structures. Molecules that are "stiff" have well-defined PES energy while "loose" molecules call for structures that are time dependent.

★ 3.2 Phase Space & Trajectories

The $6N$ -dimensional space defined by these coordinates is called the "phase space" of the system. At any given time, the system occupies one point in phase space.

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

$$X = (q, p)$$

★ 3.2.1 Properties as Ensemble Averages

The average value of a property A at equilibrium for a system at constant T, V , & # of particles can be written as

$$\langle A \rangle = \iint A(q, p) \overset{\substack{\text{probability of being at a particular phase point} \\ \downarrow}}{P(q, p)} dq dp$$

System partition function ~~can~~

$$Q = \iint e^{-E(q, p)/k_B T} dq dp$$

★ 3.2.2 Properties as Time Averages of Trajectories

In a reasonable system, its energy-conserving evolution over time seems likely to sample relevant regions of phase space

$$\langle A \rangle = \frac{1}{M} \sum_i^M A(t_i)$$

↑
of times
the property was
sampled

When sampling continuously, the equation becomes

$$\langle A \rangle = \lim_{T \rightarrow \infty} \frac{1}{T} \int_0^T A(t) dt$$

★ 3.3 Molecular Dynamics

Phase point determines the location of the next phase point in the absence of outside force acting upon the system.

Single phase points completely determines full trajectory, this is why phase points cannot cross themselves

★ 3.3.1 Harmonic Oscillator

After passing through equilibrium, the magnitude of the momentum begins to decrease until the ball returns to the same point in phase space from where it began.

The relationship between 2 positions → $q(t_2) = q(t_1) + \int_{t_1}^{t_2} \frac{p(t)}{m} dt$

The relationship between 2 vectors → $p(t_2) = p(t_1) + m \int_{t_1}^{t_2} a(t) dt$

★ 3.3.2 Non-analytical Systems

If we approximate past equations as Euler's, w/ the exact limit of $\Delta t \rightarrow 0$, we are offered a way of simulating a phase space trajectory.

$$\begin{aligned} \cancel{q(t)} \quad q(t + \Delta t) &= q(t) + \frac{p(t)}{m} \Delta t \\ p(t + \Delta t) &= p(t) + m a(t) \Delta t \end{aligned}$$

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

\uparrow
 # of constrained degrees

★ 3.3.3 Practical Issues in Propagation

Sophisticated integration schemes have been developed for propagating trajectories. One such way was created by Verlet, which considers the sum of the Taylor expansions to steps Δt

$$q(t + \Delta t) \approx 2q(t) - q(t - \Delta t) + a(t)(\Delta t)^2$$

This can lead to the use of Verlet algorithm by taking steps -

$$r_i(t + \Delta t) = r_i^0(t + \Delta t) + \Delta r_i(t)$$

★ 3.3.4 Stochastic Dynamics

Significant computational savings can be made by modeling the larger system stochastically.

Langevin dynamics of motion -

$$a(t) = -\overset{\substack{\text{friction} \\ \text{coefficient}}}{\gamma} p(t) + \frac{1}{m} [F_{\text{intra}}(t) + F_{\text{ext}}(t)]$$

Brownian equation of motion -

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