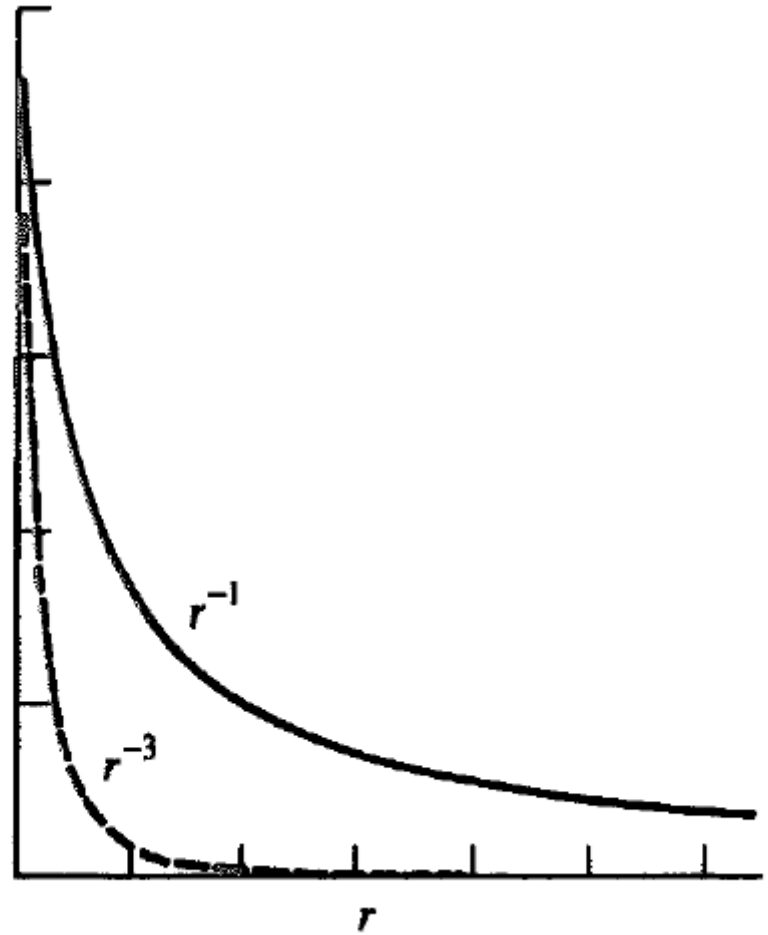
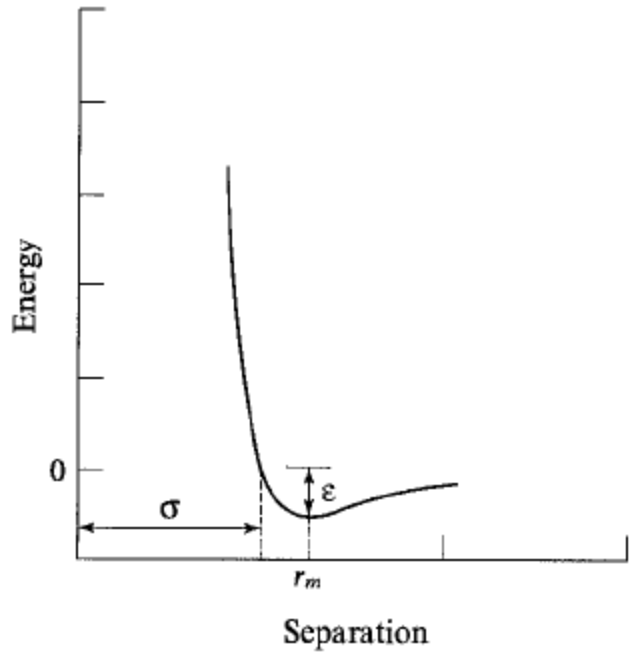
$$\mathcal{V}(\mathbf{r}^N) = \sum_{\text{bonds}} \frac{k_i}{2}(l_i - l_{i,0})^2 + \sum_{\text{angles}} \frac{k_i}{2}(\theta_i - \theta_{i,0})^2 + \sum_{\text{torsions}} \frac{V_n}{2}(1 + \cos(n\omega - \gamma))$$
$$+ \sum_{i=1}^{N} \sum_{j=i+1}^{N} \left(4\varepsilon_{ij} \left[\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^{6} \right] + \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}} \right)$$

Electrostatics

$$\mathscr{V} = \sum_{i=1}^{N_A} \sum_{j=1}^{N_B} \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}$$

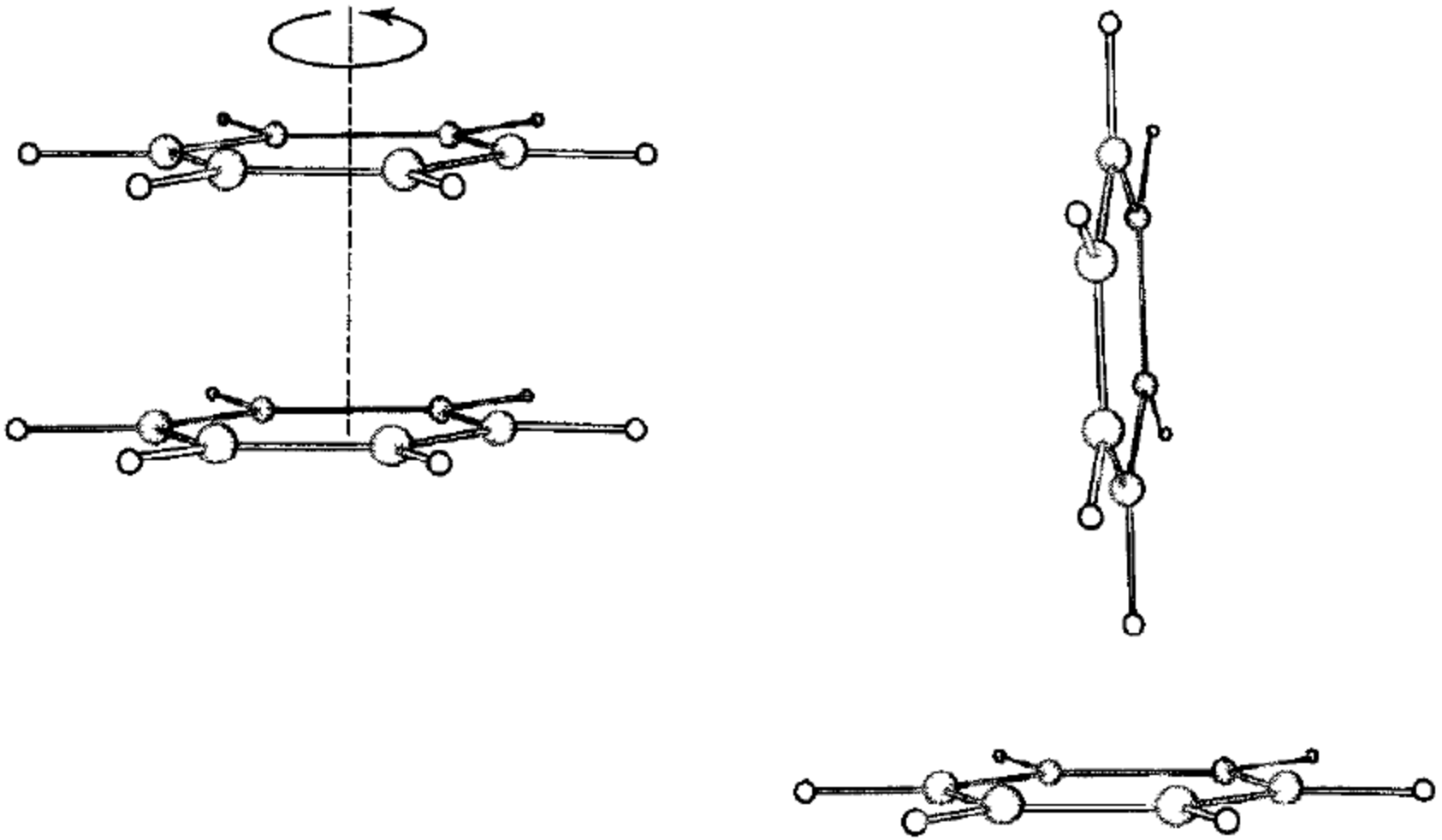


van der Waals



$$+\sum_{i=1}^{N}\sum_{j=i+1}^{N}\left(4\varepsilon_{ij}\left[\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{12}-\left(\frac{\sigma_{ij}}{r_{ij}}\right)^{6}\right]\right.$$

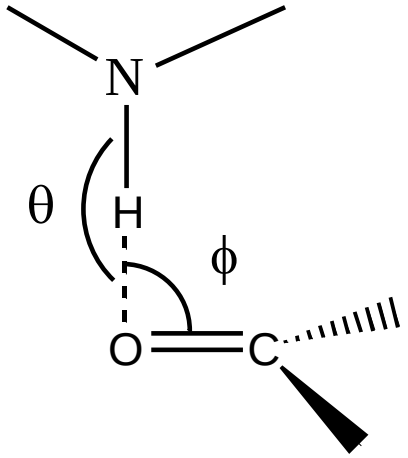
Aromatic Pi-Pi Interactions



Face-to-face (left) and T-shaped (right) orientations of the benzene dimer

Hydrogen bonding

$$E_{HB} = D_0\left[5\left(\frac{R_0}{R}\right)^{12} - 6\left(\frac{R_0}{R}\right)^{10}\right]F(\theta)$$



sp³ donor – sp³ acceptor	$F = \cos^2\theta\cos^2(\phi - 109.5)$	
	$\theta > 90°,\ \phi - 109.5° < 90°$	(3)
sp³ donor – sp² acceptor	$F = \cos^2\theta\cos^2\phi$	(4)
	$\phi > 90°$	
sp² donor – sp³ acceptor	$F = \cos^4\theta$	(5)
sp² donor – sp² acceptor	$F = \cos^2\theta\cos^2(\max[\phi,\varphi])$.	(6)

Energy functions for protein design

D Benjamin Gordon*, Shannon A Marshall* and Stephen L Mayo†

Current Opinion in Structural Biology 1999, 9:509–513

Water Models

Simple Point Charge

	SPC	SPC/E	TIP3P	BF	TIP4P	ST2
r(OH), Å	1.0	1.0	0.9572	0.96	0.9572	1.0
HOH, deg	109.47	109.47	104.52	105.7	104.52	109.47
$A \times 10^{-3}$, kcal Å^{12}/mol	629.4	629.4	582.0	560.4	600.0	238.7
C, kcal Å^{6}/mol	625.5	625.5	595.0	837.0	610.0	268.9
q(O)	−0.82	−0.8472	−0.834	0.0	0.0	0.0
q(H)	0.41	0.4238	0.417	0.49	0.52	0.2375
q(M)	0.0	0.0	0.0	−0.98	−1.04	−0 2375
r(OM), Å	0.0	0.0	0.0	0.15	0.15	0.8

An ensemble is a collection of all possible systems which have different microscopic states but have an identical macroscopic or thermodynamic state.

- Microcanonical ensemble (NVE) : The thermodynamic state characterized by a fixed number of atoms, N, a fixed volume, V, and a fixed energy, E. This corresponds to an isolated system.
- Canonical Ensemble (NVT): This is a collection of all systems whose thermodynamic state is characterized by a fixed number of atoms, N, a fixed volume, V, and a fixed temperature, T.
- Isobaric-Isothermal Ensemble (NPT): This ensemble is characterized by a fixed number of atoms, N, a fixed pressure, P, and a fixed temperature, T.
- Grand canonical Ensemble (μVT): The thermodynamic state for this ensemble is characterized by a fixed chemical potential, μ, a fixed volume, V, and a fixed temperature, T.

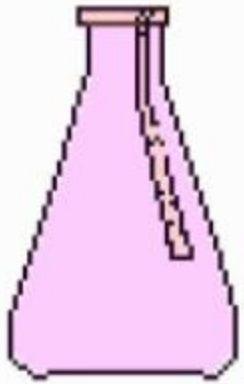
Temperature and Pressure Coupling

Berendsen Thermostat and Barostat

$$\frac{dT}{dt} = \frac{T_0 - T}{\tau}$$

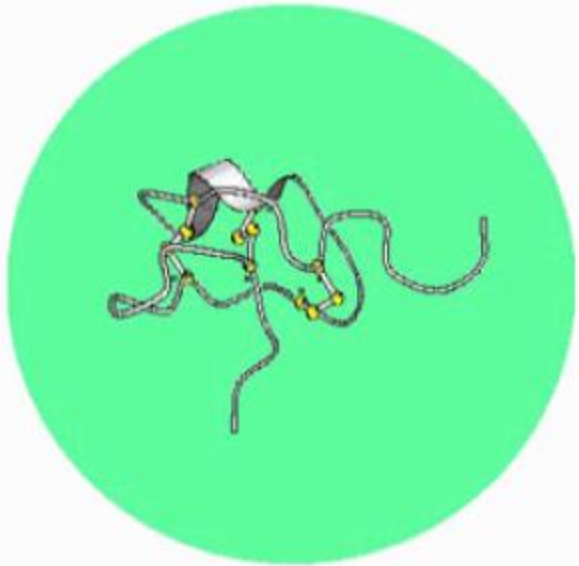
$$\left.\frac{dP}{dt}\right|_{\text{bath}} = \frac{P_0 - P}{\tau_P}$$

Experiment



Macroscopic

Molecular Simulation



Microscopic

The **Ergodic hypothesis** states

$$\langle A \rangle_{ensemble} = \langle A \rangle_{time}$$

Ensemble average = Time average