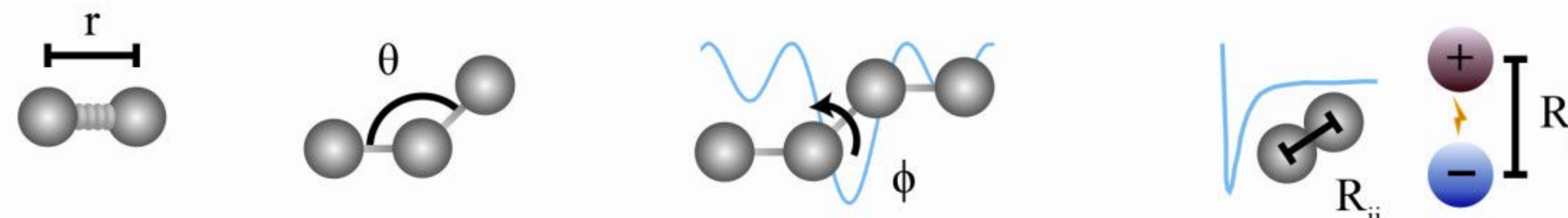


Scoring is based on molecular mechanics

$$E_{total} = \underbrace{\sum_{bonds} K_r (r - r_{eq})^2 + \sum_{angles} K_\theta (\theta - \theta_{eq})^2 + \sum_{dihedrals} \frac{V_n}{2} [1 + \cos(n\phi - \gamma)]}_{\text{Bonded}} + \underbrace{\sum_{i < j} \left[\frac{A_{ij}}{R_{ij}^{12}} - \frac{B_{ij}}{R_{ij}^6} + \frac{q_i q_j}{\epsilon R_{ij}} \right]}_{\text{Non-bonded}}$$


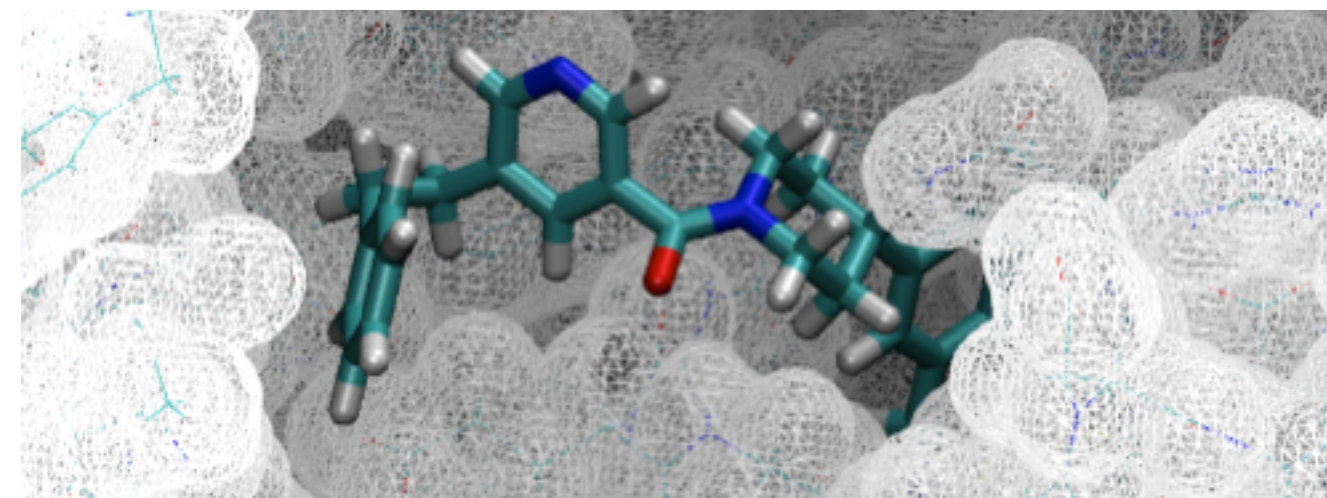
From Figure 3 of
Durant and McCammon, 2011

AMBER interaction energies

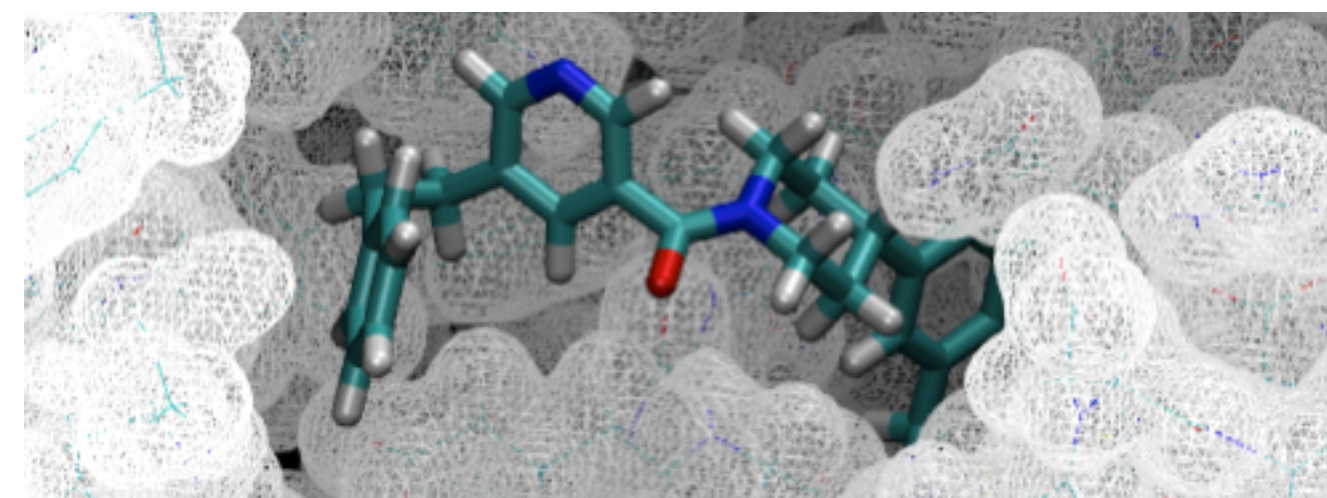
$$E = \sum_{i=1}^{lig} \sum_{j=1}^{rec} \left[\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^6} + 332.0 \frac{q_i q_j}{Dr_{ij}} \right],$$

$$A_{ij} = \sqrt{A_{ii}} \sqrt{A_{jj}} \quad \text{and} \quad B_{ij} = \sqrt{B_{ii}} \sqrt{B_{jj}},$$

[Meng, Shoichet, and Kuntz, 1992]

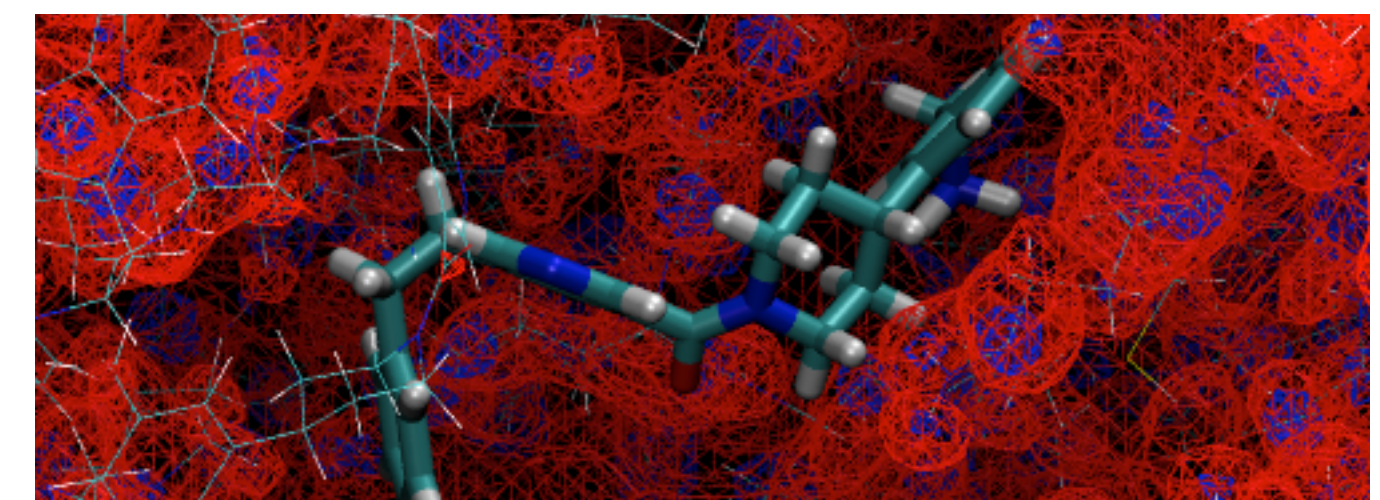


LJ repulsive



LJ attractive

Nonbonded interactions are often
interpolated from precomputed grids



Electrostatic

$E(x)$ is often rugged, requiring special optimization

This principle can be understood considering climbing a mountain peak. For minimization, flip everything upside down.