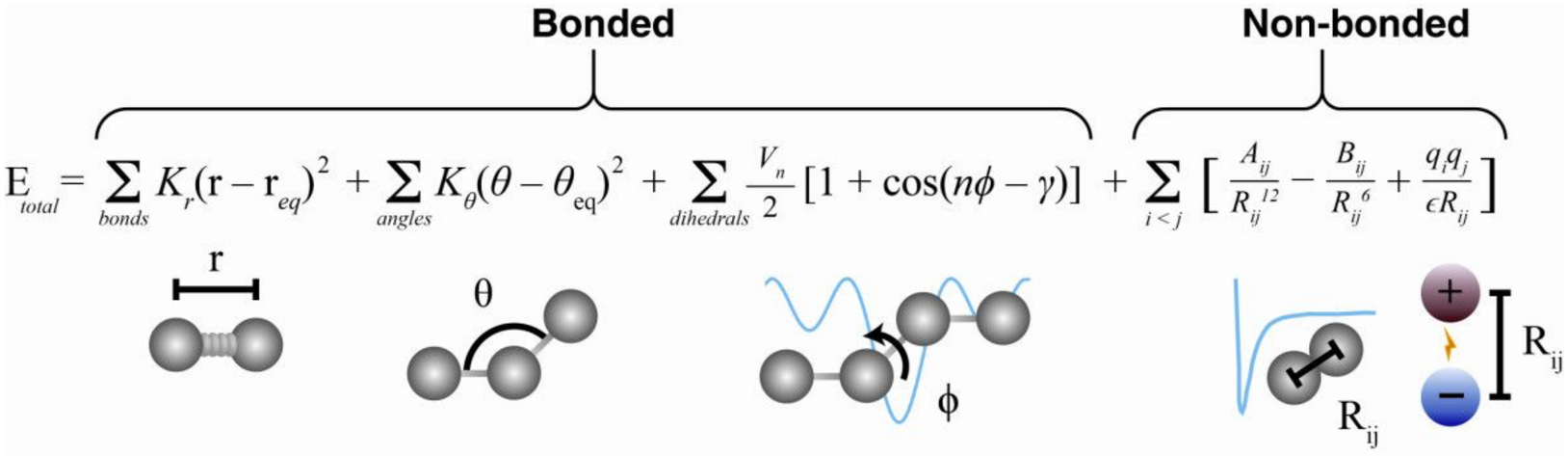
How does docking work?

- Docking is optimization of a scoring function, E(x)
  - E can be the total potential energy or interaction energy
    - can be entirely physics-based or partly knowledge-based
    - physics-based are usually molecular mechanics energies
  - x is a vector describing the molecular coordinates
- Optimization algorithms include
  - anchor-and-grow in UCSF DOCK, the original docking program
  - genetic algorithm in AutoDock, the most popular docking program
  - Fast fourier transform, especially for fragment and protein-protein docking

Scoring is based on molecular mechanics



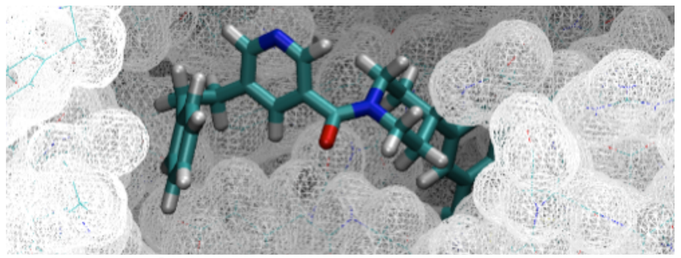
From Figure 3 of
Durant and McCammon, 2011

AMBER interaction energies

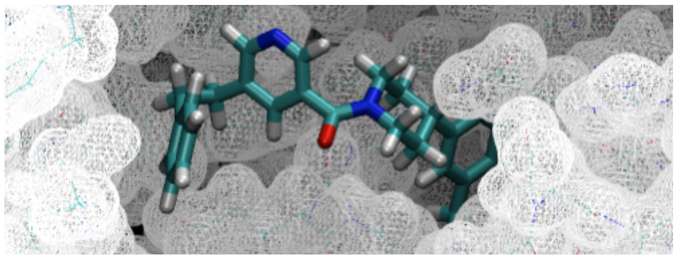
$$E = \sum_{i=1}^{lig} \sum_{j=1}^{rec} \left[\frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{6}} + 332.0 \frac{q_i q_j}{D r_{ij}} \right],$$

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

[Meng, Shoichet, and Kuntz, 1992]

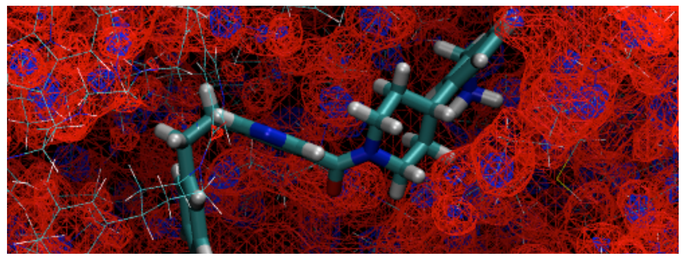


LJ repulsive



LJ attractive

Nonbonded interactions are often interpolated from precomputed grids



Electrostatic