Introduction:
Learning molecular energy functions

CS/CME/Biophys/BMI 371

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A typical molecular mechanics force field

$$U = \sum_{\text{bonds}} k_b \left(b - b_0\right)^2$$

Bond lengths ("Stretch")

$$+ \sum_{\text{angles}} k_\theta \left(\theta - \theta_0\right)^2$$

Bond angles ("Bend")

$$+ \sum_{\text{torsions}} \sum_{n} k_{\phi,n} \left[1 + \cos\left(n\phi - \phi_n\right)\right]$$

Torsional/dihedral angles

Bonded terms

$$+ \sum_{i} \sum_{j>i} \frac{q_i q_j}{r_{ij}}$$

Electrostatic

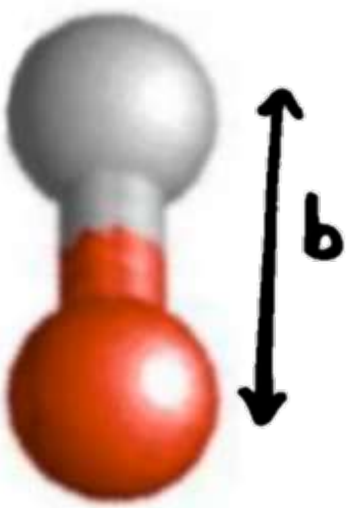
$$+ \sum_{i} \sum_{j>i} \frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^{6}}$$

Van der Waals

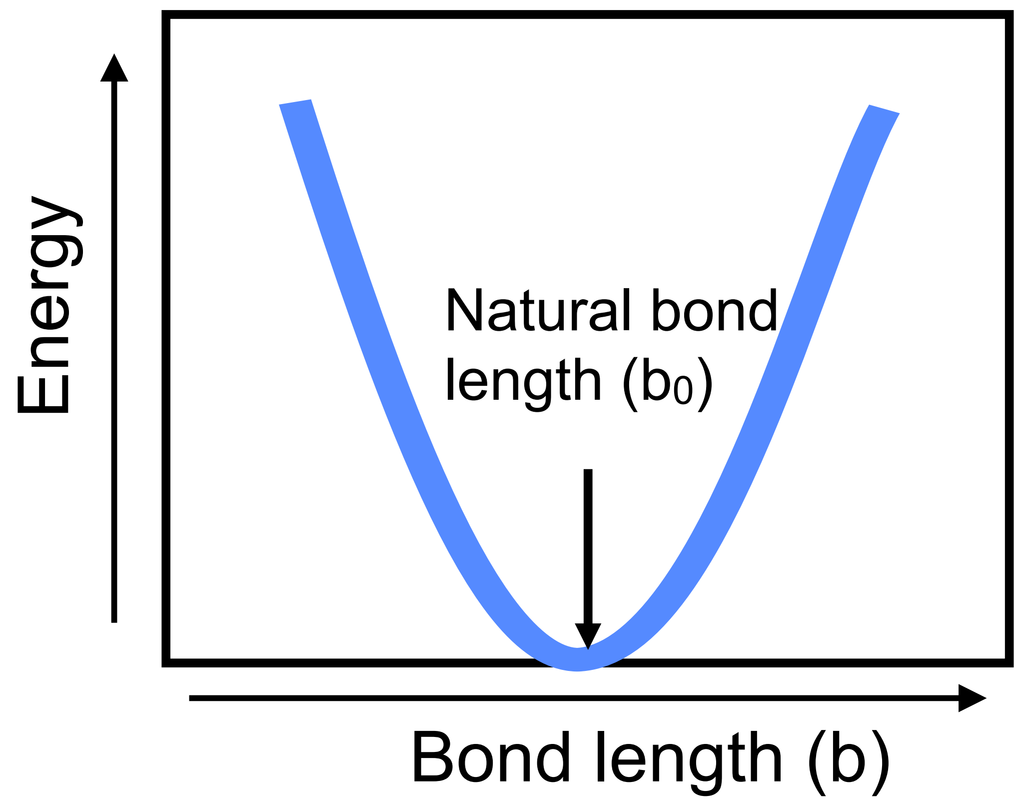
Non-bonded terms

Example: Bond length stretching

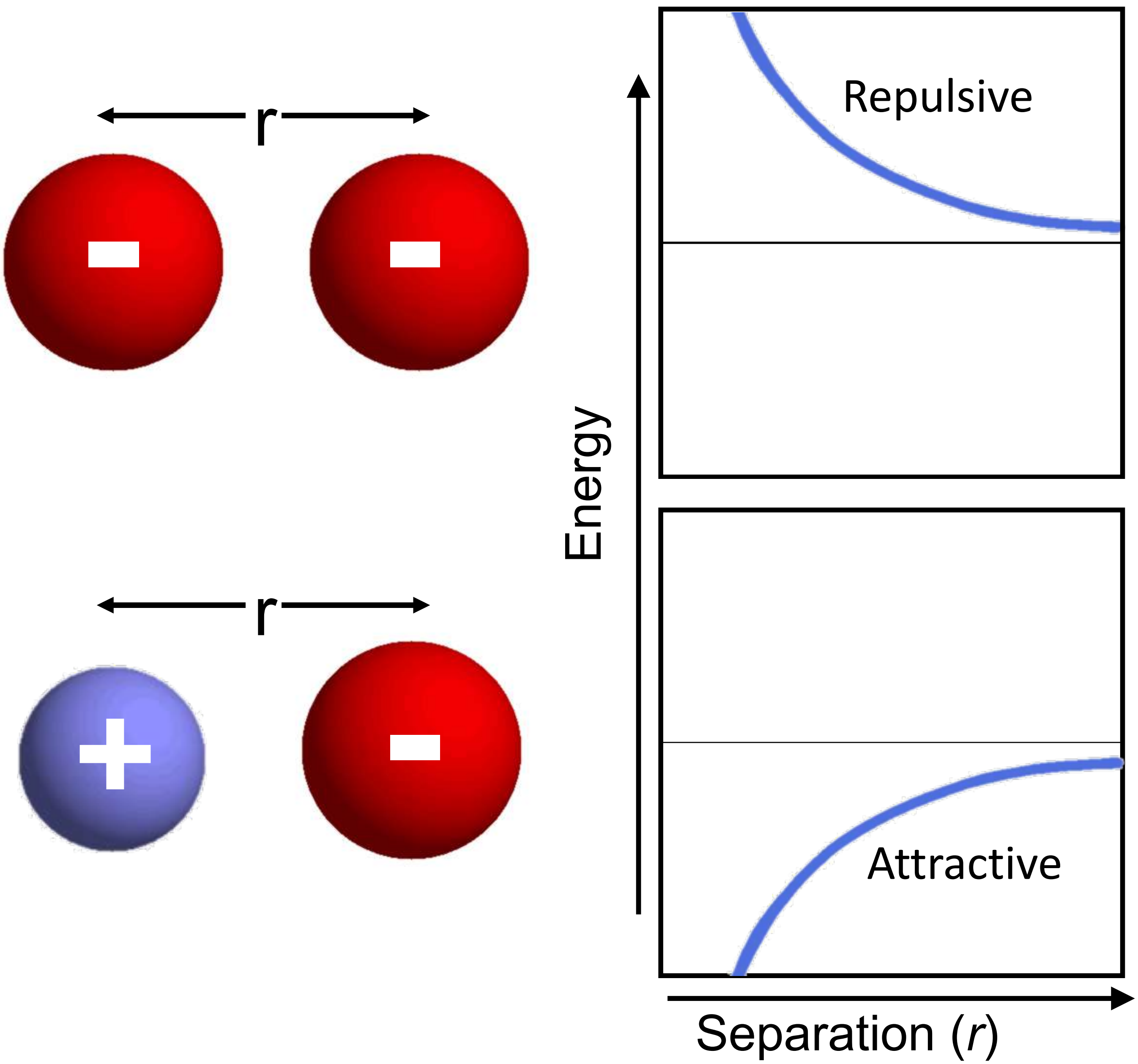
- A bonded pair of atoms is effectively connected by a spring with some preferred (natural) length. Stretching or compressing it requires energy.



$$U(b) = k_b\left(b - b_0\right)^2$$



Example: Electrostatics interaction



- Like charges repel. Opposite charges attract.
- Each atom carries some "partial charge" (may be a fraction of an elementary charge), which depends on which atoms it's connected to

$$U(r) = \frac{q_i q_j}{r}$$

where q_i and q_j are partial charges on atoms i and j

Could we learn an energy function (force field)

- What if instead of writing the force field as a sum of terms each of which makes physical sensewe represent it as a large neural network?
  - We can then train that network on the results of many quantum chemistry computations
- Researchers have been working on this for over a decade, but it’s picked up steam in the last couple year
- One of Tuesday’s papers (Smith et al.) reports a substantial step in this direction

Two related ideas

- Another paper (Faber et al.) explores prediction of chemical properties of small molecules by machine learning
  – Learning is again based on quantum chemistry results, but there's no force field involved
- A third paper (Park et al.) discusses improvement of the Rosetta all-atom force field by fitting to a wider variety of data types

Background material

- Introduction to energy functions (force fields) from CS/CME/BioE/Biophys/BMI 279:
  - http://web.stanford.edu/class/cs279/lectures/lecture3.pdf
- Discussion of the Rosetta force fields from CS/CME/BioE/Biophys/BMI 279:
  - http://web.stanford.edu/class/cs279/lectures/lecture5.pdf