Empirical force fields (potential functions)

Problem: Reduce the ab initio potential energy surface among the atoms

\[ U(\{R_i\}) = \sum_{i>j} \frac{z_i z_j e^2}{|R_i - R_j|} + E_e(\{R_i\}) \]

To a classical many-body interaction in the form

\[ U(\{R_i\}) = \sum_{i>j} U_2(R_i, R_j) + \sum_{i>j>k} U_3(R_i, R_j, R_k) + \ldots \]

Such a program has been tried for water but so far it has failed to produce a classical potential that works. In a strongly interacting systems, it is difficult to describe the collective effects by summing up the many-body terms.

Practical solution: Truncate the series at the two-body level and assume (hope!) that the effects of higher order terms can be absorbed in \( U_2 \) by reparametrizing it.
Interaction of two atoms at a distance $R$ can be decomposed into 4 pieces:

1. Coulomb potential ($1/R$)

2. Induced polarization ($1/R^2$)

3. Dispersion (van der Waals) ($1/R^6$)

4. Short range repulsion ($e^{-R/a}$)

The first two can be described using classical electromagnetism:

1. Coulomb potential:
   \[ U_{\text{Coul}} = \frac{q_i q_j}{R}, \quad R = |\mathbf{R}_i - \mathbf{R}_j| \]

2. Induced polarization:
   \[ \delta \mathbf{p}_i = \alpha_i \mathbf{E}_i \]

Dipole field:
\[ \mathbf{E}_{\text{pol}} = \frac{1}{R^3} [3(\delta \mathbf{p} \cdot \mathbf{R})\mathbf{R} - \delta \mathbf{p}] \]

Total polarization int.:
\[ U_{\text{pol}} = -\frac{1}{2} \sum_i \alpha_i \mathbf{E}_i \cdot \mathbf{E}_i^{(0)} \] (Initial and final E fields in iteration)
The last two interactions are quantum mechanical in origin. Dispersion is a dipole-dipole interaction that arises from quantum fluctuations (electronic excitations to non-spherical states)

\[ U_{\text{disp}} = -\frac{3\hbar \omega \alpha^2}{4R^6} \]

Short range repulsion arises from Pauli exclusion principle (electron clouds of two atoms avoid each other), so it is proportional to the electron density

\[ U_{\text{sr}} = Ae^{-R/a} \]

The two interactions are combined using a 12-6 Lennard-Jones (LJ) potential

\[ U_{\text{LJ}} = 4\varepsilon \left[ (\sigma/R)^{12} - (\sigma/R)^6 \right] \]

Here \( \varepsilon \) corresponds to the depth of the potential at the minimum; \( 2^{1/6}\sigma \)

Combination rules for different atoms: \( \varepsilon_{ij} = \sqrt{\varepsilon_i \varepsilon_j} \) \( \sigma_{ij} = (\sigma_i + \sigma_j)/2 \)
\[ \varepsilon = \frac{1}{4} kT, \quad \sigma = 3 \AA \]

12-6 Lennard-Jones potential (U is in kT, r in Å)
Because the polarization interaction is many-body and requires iterations, it has been neglected in current generations of force fields. The non-bonded interactions are thus represented by the Coulomb and 12-6 LJ potentials.

**Popular water models (rigid)**

<table>
<thead>
<tr>
<th>Model</th>
<th>$R_{O-H}$ (Å)</th>
<th>$\theta_{HOH}$</th>
<th>$q_H$ (e)</th>
<th>$\varepsilon$ (kT)</th>
<th>$\sigma$ (Å)</th>
<th>$\mu$ (D)</th>
<th>$\varepsilon$ (T=298 C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SPC</td>
<td>1.0</td>
<td>109.5</td>
<td>0.410</td>
<td>0.262</td>
<td>3.166</td>
<td>2.27</td>
<td>65±5</td>
</tr>
<tr>
<td>TIP3P</td>
<td>0.957</td>
<td>104.5</td>
<td>0.417</td>
<td>0.257</td>
<td>3.151</td>
<td>2.35</td>
<td>97±7</td>
</tr>
<tr>
<td>Exp.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1.85 80</td>
</tr>
</tbody>
</table>

SPC: simple point charge
TIP3P: transferable intermolecular potential with 3 points
There are hundreds of water models in the market, some explicitly including polarization interaction. But as yet there is no model that can describe all the properties of water successfully. SPC and TIP3P have been quite successful in simulation of biomolecules, and have become industry standards.

However, the mean field description of the polarization interaction is bound to break in certain situations:
1. Ion channels
2. Interfaces
3. Divalent ions

To deal with these, we need polarizable force fields. Grafting point polarizabilities on atoms and fitting the model to data has not worked well. Ab initio methods are needed to make further progress.
Covalent bonds

In molecules, atoms are bonded together with covalent bonds, which arise from sharing of electrons in partially occupied orbitals. If the bonds are very strong, the molecule can be treated as rigid as in water molecule. In a classical representation, partial charges are assigned to the atoms in order to account for the dipole moment. In most large molecules, however, the structure is quite flexible and this must be taken into account for a proper description of the molecules. This is literally done by replacing the bonds by springs.
Interaction of two H atoms in the ground (1s) state can be described using Linear Combinations of Atomic Orbitals (LCAO)

\[ \psi = c_1 \phi_A (1s) + c_2 \phi_B (1s) \]

From symmetry, two solutions with lowest and highest energies are:

\[ \psi = \frac{1}{\sqrt{2}} [\phi_A (1s) \pm \phi_B (1s)] \]

- Symmetric
  - Anti-symmetric

\[ \psi_{\text{g}} \]
\[ \psi_{\text{u}} \]
The R dependence of the potential energy is approximately given by the Morse potential

\[ U_{\text{Morse}} = D_e \left(1 - e^{-\alpha(R - R_0)}\right)^2 \]

Where

- \( D_e \): dissociation energy
- \( R_e \): equilibrium bond distance

\[ \alpha = \sqrt{k / 2D_e} \]

Controls the width of the potential

Classical representation:

\[ U_{\text{bond}} = \frac{1}{2} k (R - R_0)^2 \]
Electronic wave functions for the 1s, 2s and 2p states in H atom

H₂ molecule:

Bond is region of constructive interference (higher e⁻ probability)

Anti-bonding region of destructive interference (low e⁻ probability)
In carbon, 4 electrons (in 2s and 2p) occupy 4 hybridized \( \text{sp}^3 \) orbitals

\[
\psi_1 = \frac{1}{2} \left[ \varphi_s + \varphi_{px} + \varphi_{py} + \varphi_{px} \right]
\]

\[
\psi_2 = \frac{1}{2} \left[ \varphi_s + \varphi_{px} - \varphi_{py} - \varphi_{px} \right]
\]

\[
\psi_3 = \frac{1}{2} \left[ \varphi_s - \varphi_{px} + \varphi_{py} - \varphi_{px} \right]
\]

\[
\psi_4 = \frac{1}{2} \left[ \varphi_s - \varphi_{px} - \varphi_{py} + \varphi_{px} \right]
\]

Tetrahedral structure of \( \text{sp}^3 \)

Thus carbon needs 4 bonds to have a stable configuration.

Nitrogen has an extra electron, so needs 3 bonds.

Oxygen has 2 extra electrons, so needs 2 bonds.
For a complete description of flexibility, we need, besides bond stretching, bending and torsion. The former can be described with a harmonic form:

\[ U_{\text{bend}} = \frac{1}{2} k_\theta (\theta_{ijk} - \theta_0)^2 \]

While the latter is represented with a periodic function

\[ U_{\text{torsion}} = k_\varphi \cos(n\varphi - \varphi_0) \]

This set of bonding interactions is a good approximation for most covalent bonds in polymers and biomolecules (proteins, lipids, etc.)