

Practical Issues in Using Force Fields

Computational Bottlenecks

- The evaluation of U_{local} , with n atoms: each atom type is involved in $x_i < k$ bonds, so it takes $O(kn) = O(n)$ - *linear*
- Conversely, the evaluation of $U_{nonlocal}$ takes $O(n^2)$ - *quadratic*
- To reduce computational cost, three techniques have been developed:
 - Spherical cutoff
 - Particle-mesh Ewald method (PME)
 - Multipole schemes

Hofstadter's law:
It always takes longer than you expect,
even when you take into account Hofstadter's law
(D.R. Hofstadter, in *Gödel, Escher, Bach*, 1979)

Spherical Cutoff


- Cutoff radius **b**: For $r > b$, always $U=0$
- Each atom, within a distance **b**, has at least other $x_i < k$ atoms, so the evaluation of $U_{nonlocal}$ takes $O(kn)=O(n)$ - *linear*
- Cutoff can be used either for *energy* or *force* functions
 - **Truncation**: U unaltered for $r < b$, 0 for $r > b$
 - **Switching**: for r in $[a, b]$, U goes to 0
 - **Shift**: U gradually changes for each $r < b$
- Usually, in Å, $[a, b] \approx [8, 12]$ or $[a, b] \approx [11, 15]$
- Choice criteria:
 - Short-range energies/forces possibly kept unaltered
 - Energies altered gradually (avoid spurious minima)
 - Cutoff must avoid spurious large forces around b
 - Energy should be conserved...

General Cutoff Formulation

- The general modification can be expressed as follows:

$$U_{non-bonded} = \sum_{ij} w_{ij} \mathbf{S}(\mathbf{r}_{ij}) [(-A_{ij}/r_{ij}^6 + B_{ij}/r_{ij}^{12}) + q_i q_j / r_{ij}]$$

(between atoms i and j)



- w_{ij} are weights ($0 \leq w_{ij} \leq 1$) possibly used to exclude bonded or bond/angle terms, etc.
- Depending on the particular $S(r)$, different approximations apply.

- **Truncation** function $S(r)$:

$$S(r) = \begin{cases} 1 & r < b \\ 0 & r \geq b \end{cases}$$

Potential Switch

$$U_{non-bonded} = \sum_{ij} w_{ij} \textcolor{red}{S}(\textcolor{red}{r}_{ij}) [(-A_{ij}/r_{ij}^6 + B_{ij}/r_{ij}^{12}) + q_i q_j / r_{ij}]$$

- In $S(r)$, the polynomial degree must be sufficiently high to assure that energy and its gradient are continuous functions.
- **Potential Switch** function $S(r)$ (example):

$$S(r) = \begin{cases} 1 & r < a \\ 1 + y(r)^2(2r-3) & a \leq r < b \\ 0 & r > b \end{cases}$$

with

$$y(r) = (r^2 - a^2)/(b^2 - a^2)$$

- Region $[a,b]$ is known as the **switching buffer region**

Shift Functions

$$U_{non-bonded} = \sum_{ij} w_{ij} \textcolor{red}{S}(\textcolor{red}{r}_{ij}) [(-A_{ij}/r_{ij}^6 + B_{ij}/r_{ij}^{12}) + q_i q_j / r_{ij}]$$

- Shift functions avoid abrupt changes in forces, but lead to underestimates of short-range forces.
- **Potential Shift** functions $S(r)$ (example):

$$S_1(r) = \left[1 - \left(\frac{r}{b} \right)^2 \right]^2 \quad \text{for } r \leq b$$

or

$$S_2(r) = \left[1 - \frac{r}{b} \right]^2 \quad \text{for } r \leq b$$

- Previous functions are usually applied to electrostatic potential.

"Additive" Shift

$$U_{Van\ der\ Waals} = \sum_{ij} w_{ij} [(-A_{ij}/r_{ij}^6 + B_{ij}/r_{ij}^{12}) + \textcolor{red}{S(r_{ij})}]$$

- The Van der Waals potential is usually shifted to zero by an additive term (e.g. in CHARMM)
- **Additive Shift** function $S(r)$ (example):

$$\bar{U}_{vdw}(r) = \begin{cases} \sum_{i,j} w_{ij} \left[\left(-\frac{A_{ij}}{r_{ij}^6} + \frac{B_{ij}}{r_{ij}^{12}} \right) + S_{ij}(r) \right] & \text{for } r \leq b \\ 0 & \text{for } r > b \end{cases}$$

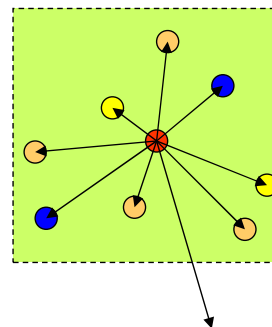
with

$$S_{ij}(r) = C_{ij}r_{ij}^6 + D_{ij}$$

Constants C and D are chosen so that both potential and force are 0 at b.

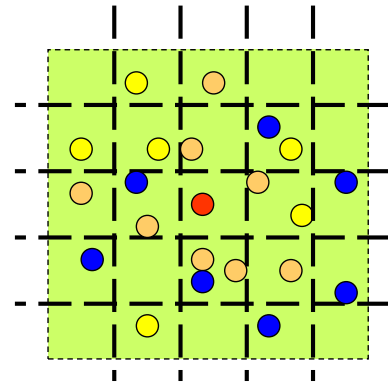
Interaction Computation

- The computation of interactions could consider all possible pairs but, if cutoff is adopted, data must be properly organized to exploit the trick.
Possible methods:
- Cell subdivision
- Neighbor list



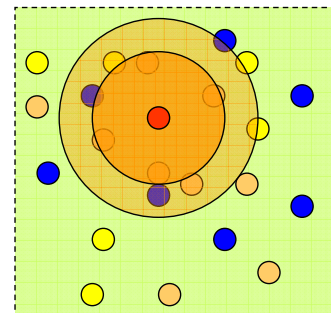
Cell Subdivision

- In “cell subdivision” the whole system is subdivided in a lattice of boxes whose edge is greater than the cutoff radius.
- Interactions can be checked only among adjacent cells.
- Data of each atom is kept in the list corresponding to the current hosting box
- As an atom enters a different cell, its data must be moved to another list



Neighbor List

- For each atom, we can keep a list of other atoms within a radius $b + \Delta r$
- The method success depends on the fact that such list remains valid over several timesteps (about 10-20) because of $\Delta r \dots$
- The decision to refresh the lists depends on the monitored maximum velocity at each step



QSAR: What's This?

- QSAR stands for Quantitative Structure-Activity Relationships
- QSAR is a catch-all term in Chemistry that refers to (computational) methods aimed at obtaining quantitative results on chemical activity from molecular structure information
- 3D-QSAR is the application of force-fields calculations to achieve typical QSAR goals