

Chapter 4

Interaction function and force fields

To accommodate the potential functions used in some popular force fields (see 4.10), GROMACS offers a choice of functions, both for non-bonded interaction and for dihedral interactions. They are described in the appropriate subsections.

The potential functions can be subdivided into three parts

1. *Non-bonded*: Lennard-Jones or Buckingham, and Coulomb or modified Coulomb. The non-bonded interactions are computed on the basis of a neighbor list (a list of non-bonded atoms within a certain radius), in which exclusions are already removed.
2. *Bonded*: covalent bond-stretching, angle-bending, improper dihedrals, and proper dihedrals. These are computed on the basis of fixed lists.
3. *Restraints*: position restraints, angle restraints, distance restraints, orientation restraints and dihedral restraints, all based on fixed lists.

4.1 Non-bonded interactions

Non-bonded interactions in GROMACS are pair-additive and centro-symmetric:

$$V(\mathbf{r}_1, \dots, \mathbf{r}_N) = \sum_{i < j} V_{ij}(\mathbf{r}_{ij}); \quad (4.1)$$

$$\mathbf{F}_i = - \sum_j \frac{dV_{ij}(r_{ij})}{dr_{ij}} \frac{\mathbf{r}_{ij}}{r_{ij}} = -\mathbf{F}_j \quad (4.2)$$

The non-bonded interactions contain a repulsion term, a dispersion term, and a Coulomb term. The repulsion and dispersion term are combined in either the Lennard-Jones (or 6-12 interaction), or the Buckingham (or exp-6 potential). In addition, (partially) charged atoms act through the Coulomb term.

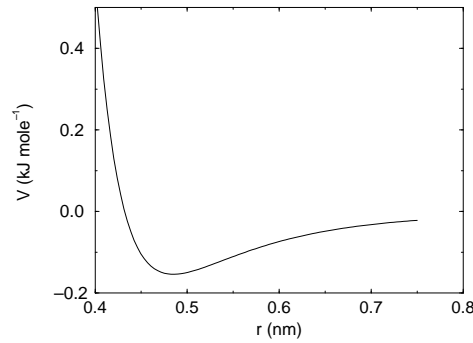


Figure 4.1: The Lennard-Jones interaction.

4.1.1 The Lennard-Jones interaction

The Lennard-Jones potential V_{LJ} between two atoms equals:

$$V_{LJ}(r_{ij}) = \frac{C_{ij}^{(12)}}{r_{ij}^{12}} - \frac{C_{ij}^{(6)}}{r_{ij}^6} \quad (4.3)$$

See also Fig. 4.1 The parameters $C_{ij}^{(12)}$ and $C_{ij}^{(6)}$ depend on pairs of *atom types*; consequently they are taken from a matrix of LJ-parameters. In the Verlet cut-off scheme, the potential is shifted by a constant such that it is zero at the cut-off distance.

The force derived from this potential is:

$$\mathbf{F}_i(\mathbf{r}_{ij}) = \left(12 \frac{C_{ij}^{(12)}}{r_{ij}^{13}} - 6 \frac{C_{ij}^{(6)}}{r_{ij}^7} \right) \frac{\mathbf{r}_{ij}}{r_{ij}} \quad (4.4)$$

The LJ potential may also be written in the following form:

$$V_{LJ}(r_{ij}) = 4\epsilon_{ij} \left(\left(\frac{\sigma_{ij}}{r_{ij}} \right)^{12} - \left(\frac{\sigma_{ij}}{r_{ij}} \right)^6 \right) \quad (4.5)$$

In constructing the parameter matrix for the non-bonded LJ-parameters, two types of combination rules can be used within GROMACS, only geometric averages (type 1 in the input section of the force-field file):

$$\begin{aligned} C_{ij}^{(6)} &= \left(C_{ii}^{(6)} C_{jj}^{(6)} \right)^{1/2} \\ C_{ij}^{(12)} &= \left(C_{ii}^{(12)} C_{jj}^{(12)} \right)^{1/2} \end{aligned} \quad (4.6)$$

or, alternatively the Lorentz-Berthelot rules can be used. An arithmetic average is used to calculate σ_{ij} , while a geometric average is used to calculate ϵ_{ij} (type 2):

$$\begin{aligned} \sigma_{ij} &= \frac{1}{2}(\sigma_{ii} + \sigma_{jj}) \\ \epsilon_{ij} &= (\epsilon_{ii} \epsilon_{jj})^{1/2} \end{aligned} \quad (4.7)$$

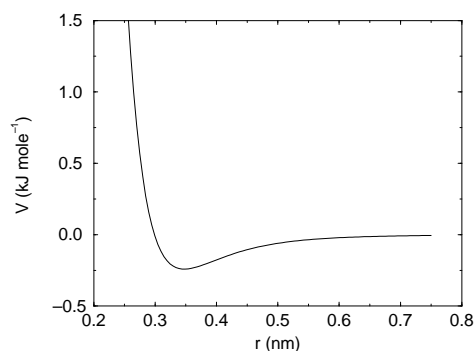


Figure 4.2: The Buckingham interaction.

finally an geometric average for both parameters can be used (type 3):

$$\begin{aligned}\sigma_{ij} &= (\sigma_{ii} \sigma_{jj})^{1/2} \\ \epsilon_{ij} &= (\epsilon_{ii} \epsilon_{jj})^{1/2}\end{aligned}\quad (4.8)$$

This last rule is used by the OPLS force field.

4.1.2 Buckingham potential

The Buckingham potential has a more flexible and realistic repulsion term than the Lennard-Jones interaction, but is also more expensive to compute. The potential form is:

$$V_{bh}(r_{ij}) = A_{ij} \exp(-B_{ij}r_{ij}) - \frac{C_{ij}}{r_{ij}^6} \quad (4.9)$$

See also Fig. 4.2. The force derived from this is:

$$\mathbf{F}_i(r_{ij}) = \left[A_{ij} B_{ij} \exp(-B_{ij}r_{ij}) - 6 \frac{C_{ij}}{r_{ij}^7} \right] \frac{\mathbf{r}_{ij}}{r_{ij}} \quad (4.10)$$

4.1.3 Coulomb interaction

The Coulomb interaction between two charge particles is given by:

$$V_c(r_{ij}) = f \frac{q_i q_j}{\epsilon_r r_{ij}} \quad (4.11)$$

See also Fig. 4.3, where $f = \frac{1}{4\pi\epsilon_0} = 138.935\,485$ (see chapter 2)

The force derived from this potential is:

$$\mathbf{F}_i(r_{ij}) = f \frac{q_i q_j}{\epsilon_r r_{ij}^2} \frac{\mathbf{r}_{ij}}{r_{ij}} \quad (4.12)$$

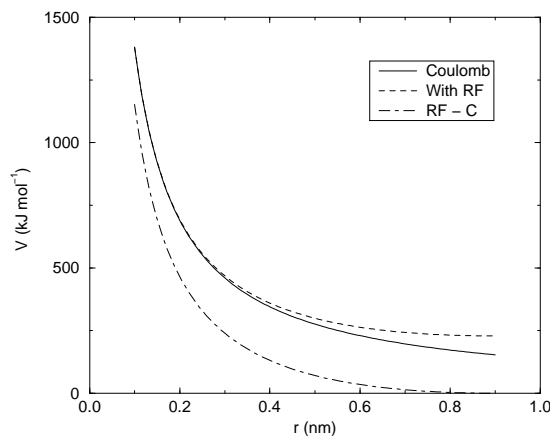


Figure 4.3: The Coulomb interaction (for particles with equal signed charge) with and without reaction field. In the latter case ε_r was 1, ε_{rf} was 78, and r_c was 0.9 nm. The dot-dashed line is the same as the dashed line, except for a constant.

A plain Coulomb interaction should only be used without cut-off or when all pairs fall within the cut-off, since there is an abrupt, large change in the force at the cut-off. In case you do want to use a cut-off, the potential can be shifted by a constant to make the potential the integral of the force. With the group cut-off scheme, this shift is only applied to non-excluded pairs. With the Verlet cut-off scheme, the shift is also applied to excluded pairs and self interactions, which makes the potential equivalent to a reaction field with $\varepsilon_{rf} = 1$ (see below).

In GROMACS the relative dielectric constant ε_r may be set in the input for `grompp`.

4.1.4 Coulomb interaction with reaction field

The Coulomb interaction can be modified for homogeneous systems by assuming a constant dielectric environment beyond the cut-off r_c with a dielectric constant of ε_{rf} . The interaction then reads:

$$V_{crf} = f \frac{q_i q_j}{\varepsilon_r r_{ij}} \left[1 + \frac{\varepsilon_{rf} - \varepsilon_r}{2\varepsilon_{rf} + \varepsilon_r} \frac{r_{ij}^3}{r_c^3} \right] - f \frac{q_i q_j}{\varepsilon_r r_c} \frac{3\varepsilon_{rf}}{2\varepsilon_{rf} + \varepsilon_r} \quad (4.13)$$

in which the constant expression on the right makes the potential zero at the cut-off r_c . For charged cut-off spheres this corresponds to neutralization with a homogeneous background charge. We can rewrite eqn. 4.13 for simplicity as

$$V_{crf} = f \frac{q_i q_j}{\varepsilon_r} \left[\frac{1}{r_{ij}} + k_{rf} r_{ij}^2 - c_{rf} \right] \quad (4.14)$$

with

$$k_{rf} = \frac{1}{r_c^3} \frac{\varepsilon_{rf} - \varepsilon_r}{(2\varepsilon_{rf} + \varepsilon_r)} \quad (4.15)$$

$$c_{rf} = \frac{1}{r_c} + k_{rf} r_c^2 = \frac{1}{r_c} \frac{3\varepsilon_{rf}}{(2\varepsilon_{rf} + \varepsilon_r)} \quad (4.16)$$

For large ε_{rf} the k_{rf} goes to $r_c^{-3}/2$, while for $\varepsilon_{rf} = \varepsilon_r$ the correction vanishes. In Fig. 4.3 the modified interaction is plotted, and it is clear that the derivative with respect to r_{ij} ($=$ -force) goes to zero at the cut-off distance. The force derived from this potential reads:

$$\mathbf{F}_i(\mathbf{r}_{ij}) = f \frac{q_i q_j}{\varepsilon_r} \left[\frac{1}{r_{ij}^2} - 2k_{rf} r_{ij} \right] \frac{\mathbf{r}_{ij}}{r_{ij}} \quad (4.17)$$

The reaction-field correction should also be applied to all excluded atoms pairs, including self pairs, in which case the normal Coulomb term in eqns. 4.13 and 4.17 is absent.

Tironi *et al.* have introduced a generalized reaction field in which the dielectric continuum beyond the cut-off r_c also has an ionic strength I [75]. In this case we can rewrite the constants k_{rf} and c_{rf} using the inverse Debye screening length κ :

$$\kappa^2 = \frac{2I F^2}{\varepsilon_0 \varepsilon_{rf} R T} = \frac{F^2}{\varepsilon_0 \varepsilon_{rf} R T} \sum_{i=1}^K c_i z_i^2 \quad (4.18)$$

$$k_{rf} = \frac{1}{r_c^3} \frac{(\varepsilon_{rf} - \varepsilon_r)(1 + \kappa r_c) + \frac{1}{2} \varepsilon_{rf} (\kappa r_c)^2}{(2\varepsilon_{rf} + \varepsilon_r)(1 + \kappa r_c) + \varepsilon_{rf} (\kappa r_c)^2} \quad (4.19)$$

$$c_{rf} = \frac{1}{r_c} \frac{3\varepsilon_{rf}(1 + \kappa r_c + \frac{1}{2}(\kappa r_c)^2)}{(2\varepsilon_{rf} + \varepsilon_r)(1 + \kappa r_c) + \varepsilon_{rf} (\kappa r_c)^2} \quad (4.20)$$

where F is Faraday's constant, R is the ideal gas constant, T the absolute temperature, c_i the molar concentration for species i and z_i the charge number of species i where we have K different species. In the limit of zero ionic strength ($\kappa = 0$) eqns. 4.19 and 4.20 reduce to the simple forms of eqns. 4.15 and 4.16 respectively.

4.1.5 Modified non-bonded interactions

In GROMACS, the non-bonded potentials can be modified by a shift function. The purpose of this is to replace the truncated forces by forces that are continuous and have continuous derivatives at the cut-off radius. With such forces the timestep integration produces much smaller errors and there are no such complications as creating charges from dipoles by the truncation procedure. In fact, by using shifted forces there is no need for charge groups in the construction of neighbor lists. However, the shift function produces a considerable modification of the Coulomb potential. Unless the “missing” long-range potential is properly calculated and added (through the use of PPPM, Ewald, or PME), the effect of such modifications must be carefully evaluated. The modification of the Lennard-Jones dispersion and repulsion is only minor, but it does remove the noise caused by cut-off effects.

There is *no* fundamental difference between a switch function (which multiplies the potential with a function) and a shift function (which adds a function to the force or potential) [76]. The switch function is a special case of the shift function, which we apply to the *force function* $F(r)$, related to the electrostatic or van der Waals force acting on particle i by particle j as:

$$\mathbf{F}_i = cF(r_{ij}) \frac{\mathbf{r}_{ij}}{r_{ij}} \quad (4.21)$$

For pure Coulomb or Lennard-Jones interactions $F(r) = F_\alpha(r) = r^{-(\alpha+1)}$. The shifted force $F_s(r)$ can generally be written as:

$$\begin{aligned} F_s(r) &= F_\alpha(r) & r < r_1 \\ F_s(r) &= F_\alpha(r) + S(r) & r_1 \leq r < r_c \\ F_s(r) &= 0 & r_c \leq r \end{aligned} \quad (4.22)$$

When $r_1 = 0$ this is a traditional shift function, otherwise it acts as a switch function. The corresponding shifted coulomb potential then reads:

$$V_s(r_{ij}) = f\Phi_s(r_{ij})q_iq_j \quad (4.23)$$

where $\Phi(r)$ is the potential function

$$\Phi_s(r) = \int_r^\infty F_s(x) dx \quad (4.24)$$

The GROMACS shift function should be smooth at the boundaries, therefore the following boundary conditions are imposed on the shift function:

$$\begin{aligned} S(r_1) &= 0 \\ S'(r_1) &= 0 \\ S(r_c) &= -F_\alpha(r_c) \\ S'(r_c) &= -F'_\alpha(r_c) \end{aligned} \quad (4.25)$$

A 3^{rd} degree polynomial of the form

$$S(r) = A(r - r_1)^2 + B(r - r_1)^3 \quad (4.26)$$

fulfills these requirements. The constants A and B are given by the boundary condition at r_c :

$$\begin{aligned} A &= -\frac{(\alpha + 4)r_c - (\alpha + 1)r_1}{r_c^{\alpha+2} (r_c - r_1)^2} \\ B &= \frac{(\alpha + 3)r_c - (\alpha + 1)r_1}{r_c^{\alpha+2} (r_c - r_1)^3} \end{aligned} \quad (4.27)$$

Thus the total force function is:

$$F_s(r) = \frac{\alpha}{r^{\alpha+1}} + A(r - r_1)^2 + B(r - r_1)^3 \quad (4.28)$$

and the potential function reads:

$$\Phi(r) = \frac{1}{r^\alpha} - \frac{A}{3}(r - r_1)^3 - \frac{B}{4}(r - r_1)^4 - C \quad (4.29)$$

where

$$C = \frac{1}{r_c^\alpha} - \frac{A}{3}(r_c - r_1)^3 - \frac{B}{4}(r_c - r_1)^4 \quad (4.30)$$

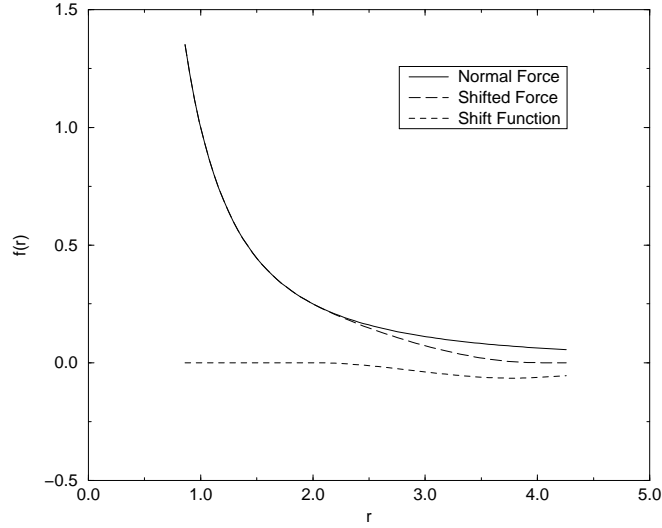


Figure 4.4: The Coulomb Force, Shifted Force and Shift Function $S(r)$, using $r_1 = 2$ and $r_c = 4$.

When $r_1 = 0$, the modified Coulomb force function is

$$F_s(r) = \frac{1}{r^2} - \frac{5r^2}{r_c^4} + \frac{4r^3}{r_c^5} \quad (4.31)$$

which is identical to the function recommended to be used as a short-range function in conjunction with a Poisson solver for the long-range part [77]. The modified Coulomb potential function is:

$$\Phi(r) = \frac{1}{r} - \frac{5}{3r_c} + \frac{5r^3}{3r_c^4} - \frac{r^4}{r_c^5} \quad (4.32)$$

See also Fig. 4.4.

4.1.6 Modified short-range interactions with Ewald summation

When Ewald summation or particle-mesh Ewald is used to calculate the long-range interactions, the short-range Coulomb potential must also be modified, similar to the switch function above. In this case the short range potential is given by:

$$V(r) = f \frac{\text{erfc}(\beta r_{ij})}{r_{ij}} q_i q_j, \quad (4.33)$$

where β is a parameter that determines the relative weight between the direct space sum and the reciprocal space sum and $\text{erfc}(x)$ is the complementary error function. For further details on long-range electrostatics, see sec. 4.8.

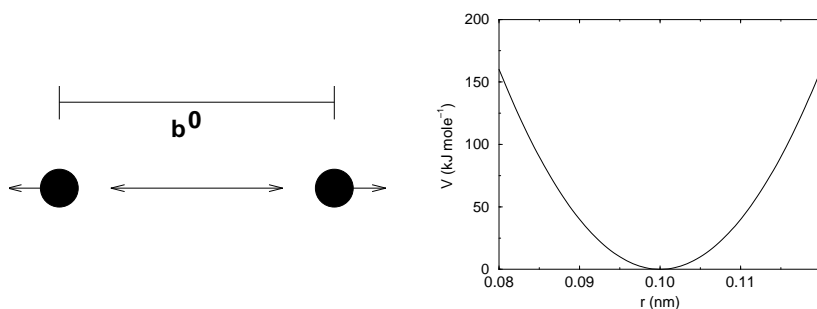


Figure 4.5: Principle of bond stretching (left), and the bond stretching potential (right).

4.2 Bonded interactions

Bonded interactions are based on a fixed list of atoms. They are not exclusively pair interactions, but include 3- and 4-body interactions as well. There are *bond stretching* (2-body), *bond angle* (3-body), and *dihedral angle* (4-body) interactions. A special type of dihedral interaction (called *improper dihedral*) is used to force atoms to remain in a plane or to prevent transition to a configuration of opposite chirality (a mirror image).

4.2.1 Bond stretching

Harmonic potential

The bond stretching between two covalently bonded atoms i and j is represented by a harmonic potential:

$$V_b(r_{ij}) = \frac{1}{2} k_{ij}^b (r_{ij} - b_{ij})^2 \quad (4.34)$$

See also Fig. 4.5, with the force given by:

$$\mathbf{F}_i(\mathbf{r}_{ij}) = k_{ij}^b (r_{ij} - b_{ij}) \frac{\mathbf{r}_{ij}}{r_{ij}} \quad (4.35)$$

Fourth power potential

In the GROMOS-96 force field [78], the covalent bond potential is, for reasons of computational efficiency, written as:

$$V_b(r_{ij}) = \frac{1}{4} k_{ij}^b (r_{ij}^2 - b_{ij}^2)^2 \quad (4.36)$$

The corresponding force is:

$$\mathbf{F}_i(\mathbf{r}_{ij}) = k_{ij}^b (r_{ij}^2 - b_{ij}^2) \mathbf{r}_{ij} \quad (4.37)$$

The force constants for this form of the potential are related to the usual harmonic force constant $k^{b,\text{harm}}$ (sec. 4.2.1) as

$$2k^b b_{ij}^2 = k^{b,\text{harm}} \quad (4.38)$$

The force constants are mostly derived from the harmonic ones used in GROMOS-87 [79]. Although this form is computationally more efficient (because no square root has to be evaluated), it is conceptually more complex. One particular disadvantage is that since the form is not harmonic, the average energy of a single bond is not equal to $\frac{1}{2}kT$ as it is for the normal harmonic potential.

4.2.2 Morse potential bond stretching

For some systems that require an anharmonic bond stretching potential, the Morse potential [80] between two atoms i and j is available in GROMACS. This potential differs from the harmonic potential in that it has an asymmetric potential well and a zero force at infinite distance. The functional form is:

$$V_{\text{morse}}(r_{ij}) = D_{ij}[1 - \exp(-\beta_{ij}(r_{ij} - b_{ij}))]^2, \quad (4.39)$$

See also Fig. 4.6, and the corresponding force is:

$$\mathbf{F}_{\text{morse}}(\mathbf{r}_{ij}) = 2D_{ij}\beta_{ij}r_{ij} \exp(-\beta_{ij}(r_{ij} - b_{ij})) * [1 - \exp(-\beta_{ij}(r_{ij} - b_{ij}))] \frac{\mathbf{r}_{ij}}{r_{ij}}, \quad (4.40)$$

where D_{ij} is the depth of the well in kJ/mol, β_{ij} defines the steepness of the well (in nm^{-1}), and b_{ij} is the equilibrium distance in nm. The steepness parameter β_{ij} can be expressed in terms of the reduced mass of the atoms i and j , the fundamental vibration frequency ω_{ij} and the well depth D_{ij} :

$$\beta_{ij} = \omega_{ij} \sqrt{\frac{\mu_{ij}}{2D_{ij}}} \quad (4.41)$$

and because $\omega = \sqrt{k/\mu}$, one can rewrite β_{ij} in terms of the harmonic force constant k_{ij} :

$$\beta_{ij} = \sqrt{\frac{k_{ij}}{2D_{ij}}} \quad (4.42)$$

For small deviations $(r_{ij} - b_{ij})$, one can approximate the exp-term to first-order using a Taylor expansion:

$$\exp(-x) \approx 1 - x \quad (4.43)$$

and substituting eqn. 4.42 and eqn. 4.43 in the functional form:

$$\begin{aligned} V_{\text{morse}}(r_{ij}) &= D_{ij}[1 - \exp(-\beta_{ij}(r_{ij} - b_{ij}))]^2 \\ &= D_{ij}[1 - (1 - \sqrt{\frac{k_{ij}}{2D_{ij}}}(r_{ij} - b_{ij}))]^2 \\ &= \frac{1}{2}k_{ij}(r_{ij} - b_{ij})^2 \end{aligned} \quad (4.44)$$

we recover the harmonic bond stretching potential.

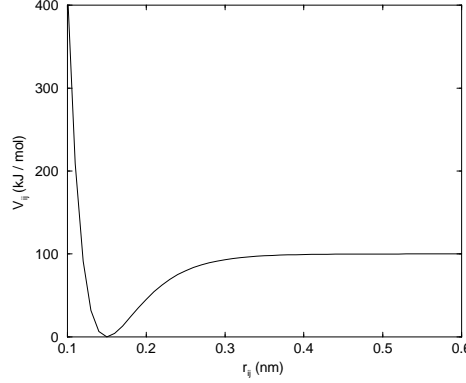


Figure 4.6: The Morse potential well, with bond length 0.15 nm.

4.2.3 Cubic bond stretching potential

Another anharmonic bond stretching potential that is slightly simpler than the Morse potential adds a cubic term in the distance to the simple harmonic form:

$$V_b(r_{ij}) = k_{ij}^b(r_{ij} - b_{ij})^2 + k_{ij}^b k_{ij}^{cub}(r_{ij} - b_{ij})^3 \quad (4.45)$$

A flexible water model (based on the SPC water model [81]) including a cubic bond stretching potential for the O-H bond was developed by Ferguson [82]. This model was found to yield a reasonable infrared spectrum. The Ferguson water model is available in the GROMACS library (`flexwat-ferguson.itp`). It should be noted that the potential is asymmetric: overstretching leads to infinitely low energies. The integration timestep is therefore limited to 1 fs.

The force corresponding to this potential is:

$$\mathbf{F}_i(\mathbf{r}_{ij}) = 2k_{ij}^b(r_{ij} - b_{ij}) \frac{\mathbf{r}_{ij}}{r_{ij}} + 3k_{ij}^b k_{ij}^{cub}(r_{ij} - b_{ij})^2 \frac{\mathbf{r}_{ij}}{r_{ij}} \quad (4.46)$$

4.2.4 FENE bond stretching potential

In coarse-grained polymer simulations the beads are often connected by a FENE (finitely extensible nonlinear elastic) potential [83]:

$$V_{\text{FENE}}(r_{ij}) = -\frac{1}{2}k_{ij}^b b_{ij}^2 \log\left(1 - \frac{r_{ij}^2}{b_{ij}^2}\right) \quad (4.47)$$

The potential looks complicated, but the expression for the force is simpler:

$$\mathbf{F}_{\text{FENE}}(\mathbf{r}_{ij}) = -k_{ij}^b \left(1 - \frac{r_{ij}^2}{b_{ij}^2}\right)^{-1} \mathbf{r}_{ij} \quad (4.48)$$

At short distances the potential asymptotically goes to a harmonic potential with force constant k^b , while it diverges at distance b .

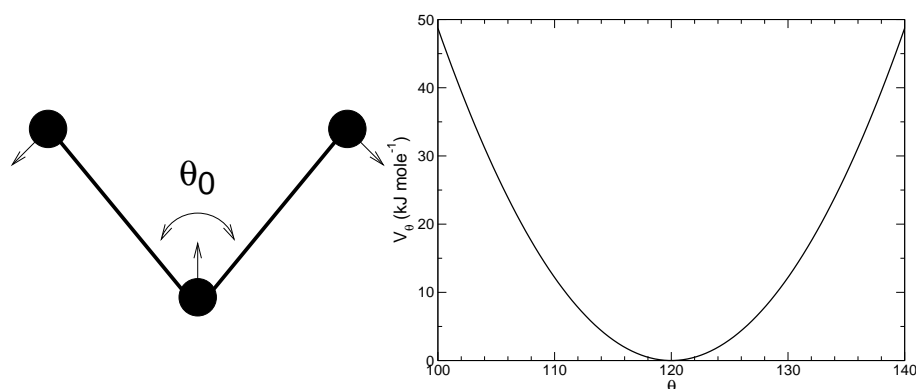


Figure 4.7: Principle of angle vibration (left) and the bond angle potential (right).

4.2.5 Harmonic angle potential

The bond-angle vibration between a triplet of atoms $i - j - k$ is also represented by a harmonic potential on the angle θ_{ijk}

$$V_a(\theta_{ijk}) = \frac{1}{2} k_{ijk}^{\theta} (\theta_{ijk} - \theta_{ijk}^0)^2 \quad (4.49)$$

As the bond-angle vibration is represented by a harmonic potential, the form is the same as the bond stretching (Fig. 4.5).

The force equations are given by the chain rule:

$$\begin{aligned} \mathbf{F}_i &= - \frac{dV_a(\theta_{ijk})}{d\mathbf{r}_i} \\ \mathbf{F}_k &= - \frac{dV_a(\theta_{ijk})}{d\mathbf{r}_k} \quad \text{where} \quad \theta_{ijk} = \arccos \frac{(\mathbf{r}_{ij} \cdot \mathbf{r}_{kj})}{r_{ij} r_{kj}} \\ \mathbf{F}_j &= -\mathbf{F}_i - \mathbf{F}_k \end{aligned} \quad (4.50)$$

The numbering i, j, k is in sequence of covalently bonded atoms. Atom j is in the middle; atoms i and k are at the ends (see Fig. 4.7). **Note** that in the input in topology files, angles are given in degrees and force constants in kJ/mol/rad^2 .

4.2.6 Cosine based angle potential

In the GROMOS-96 force field a simplified function is used to represent angle vibrations:

$$V_a(\theta_{ijk}) = \frac{1}{2} k_{ijk}^{\theta} \left(\cos(\theta_{ijk}) - \cos(\theta_{ijk}^0) \right)^2 \quad (4.51)$$

where

$$\cos(\theta_{ijk}) = \frac{\mathbf{r}_{ij} \cdot \mathbf{r}_{kj}}{r_{ij} r_{kj}} \quad (4.52)$$

The corresponding force can be derived by partial differentiation with respect to the atomic positions. The force constants in this function are related to the force constants in the harmonic form $k_{ijk}^{\theta, \text{harm}}$ (4.2.5) by:

$$k^{\theta} \sin^2(\theta_{ijk}^0) = k^{\theta, \text{harm}} \quad (4.53)$$

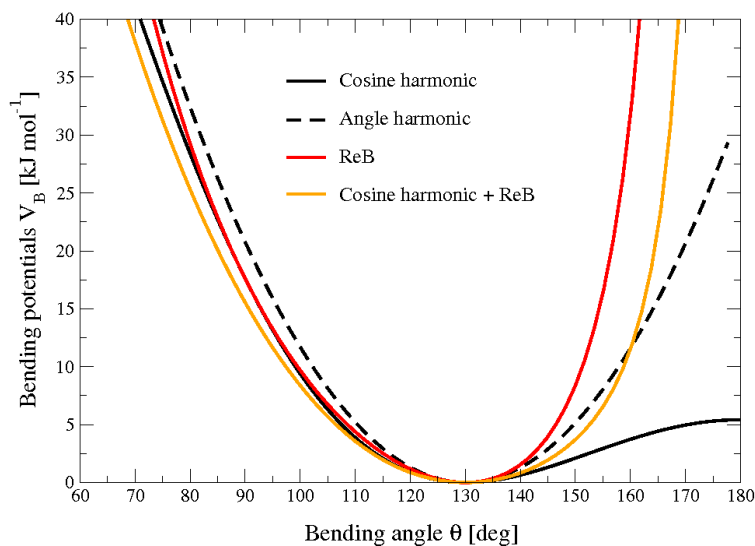


Figure 4.8: Bending angle potentials: cosine harmonic (solid black line), angle harmonic (dashed black line) and restricted bending (red) with the same bending constant $k_\theta = 85 \text{ kJ mol}^{-1}$ and equilibrium angle $\theta_0 = 130^\circ$. The orange line represents the sum of a cosine harmonic ($k = 50 \text{ kJ mol}^{-1}$) with a restricted bending ($k = 25 \text{ kJ mol}^{-1}$) potential, both with $\theta_0 = 130^\circ$.

In the GROMOS-96 manual there is a much more complicated conversion formula which is temperature dependent. The formulas are equivalent at 0 K and the differences at 300 K are on the order of 0.1 to 0.2%. **Note** that in the input in topology files, angles are given in degrees and force constants in kJ/mol.

4.2.7 Restricted bending potential

The restricted bending (ReB) potential [84] prevents the bending angle θ from reaching the 180° value. In this way, the numerical instabilities due to the calculation of the torsion angle and potential are eliminated when performing coarse-grained molecular dynamics simulations.

To systematically hinder the bending angles from reaching the 180° value, the bending potential 4.51 is divided by a $\sin^2 \theta$ factor:

$$V_{\text{ReB}}(\theta_i) = \frac{1}{2} k_\theta \frac{(\cos \theta_i - \cos \theta_0)^2}{\sin^2 \theta_i}. \quad (4.54)$$

Figure Fig. 4.8 shows the comparison between the ReB potential, 4.54, and the standard one 4.51. The wall of the ReB potential is very repulsive in the region close to 180° and, as a result, the bending angles are kept within a safe interval, far from instabilities. The power 2 of $\sin \theta_i$ in the denominator has been chosen to guarantee this behavior and allows an elegant differentiation:

$$F_{\text{ReB}}(\theta_i) = \frac{2k_\theta}{\sin^4 \theta_i} (\cos \theta_i - \cos \theta_0) (1 - \cos \theta_i \cos \theta_0) \frac{\partial \cos \theta_i}{\partial \vec{r}_k}. \quad (4.55)$$

Due to its construction, the restricted bending potential cannot be used for equilibrium θ_0 values too close to 0° or 180° (from experience, at least 10° difference is recommended). It is very important that, in the starting configuration, all the bending angles have to be in the safe interval to avoid initial instabilities. This bending potential can be used in combination with any form of torsion potential. It will always prevent three consecutive particles from becoming collinear and, as a result, any torsion potential will remain free of singularities. It can be also added to a standard bending potential to affect the angle around 180° , but to keep its original form around the minimum (see the orange curve in Fig. 4.8).

4.2.8 Urey-Bradley potential

The Urey-Bradley bond-angle vibration between a triplet of atoms $i - j - k$ is represented by a harmonic potential on the angle θ_{ijk} and a harmonic correction term on the distance between the atoms i and k . Although this can be easily written as a simple sum of two terms, it is convenient to have it as a single entry in the topology file and in the output as a separate energy term. It is used mainly in the CHARMM force field [85]. The energy is given by:

$$V_a(\theta_{ijk}) = \frac{1}{2}k_{ijk}^\theta(\theta_{ijk} - \theta_{ijk}^0)^2 + \frac{1}{2}k_{ijk}^{UB}(r_{ik} - r_{ik}^0)^2 \quad (4.56)$$

The force equations can be deduced from sections 4.2.1 and 4.2.5.

4.2.9 Bond-Bond cross term

The bond-bond cross term for three particles i, j, k forming bonds $i - j$ and $k - j$ is given by [86]:

$$V_{rr'} = k_{rr'} (|\mathbf{r}_i - \mathbf{r}_j| - r_{1e}) (|\mathbf{r}_k - \mathbf{r}_j| - r_{2e}) \quad (4.57)$$

where $k_{rr'}$ is the force constant, and r_{1e} and r_{2e} are the equilibrium bond lengths of the $i - j$ and $k - j$ bonds respectively. The force associated with this potential on particle i is:

$$\mathbf{F}_i = -k_{rr'} (|\mathbf{r}_k - \mathbf{r}_j| - r_{2e}) \frac{\mathbf{r}_i - \mathbf{r}_j}{|\mathbf{r}_i - \mathbf{r}_j|} \quad (4.58)$$

The force on atom k can be obtained by swapping i and k in the above equation. Finally, the force on atom j follows from the fact that the sum of internal forces should be zero: $\mathbf{F}_j = -\mathbf{F}_i - \mathbf{F}_k$.

4.2.10 Bond-Angle cross term

The bond-angle cross term for three particles i, j, k forming bonds $i - j$ and $k - j$ is given by [86]:

$$V_{r\theta} = k_{r\theta} (|\mathbf{r}_i - \mathbf{r}_k| - r_{3e}) (|\mathbf{r}_i - \mathbf{r}_j| - r_{1e} + |\mathbf{r}_k - \mathbf{r}_j| - r_{2e}) \quad (4.59)$$

where $k_{r\theta}$ is the force constant, r_{3e} is the $i - k$ distance, and the other constants are the same as in Equation 4.57. The force associated with the potential on atom i is:

$$\mathbf{F}_i = -k_{r\theta} \left[(|\mathbf{r}_i - \mathbf{r}_k| - r_{3e}) \frac{\mathbf{r}_i - \mathbf{r}_j}{|\mathbf{r}_i - \mathbf{r}_j|} + (|\mathbf{r}_i - \mathbf{r}_j| - r_{1e} + |\mathbf{r}_k - \mathbf{r}_j| - r_{2e}) \frac{\mathbf{r}_i - \mathbf{r}_k}{|\mathbf{r}_i - \mathbf{r}_k|} \right] \quad (4.60)$$

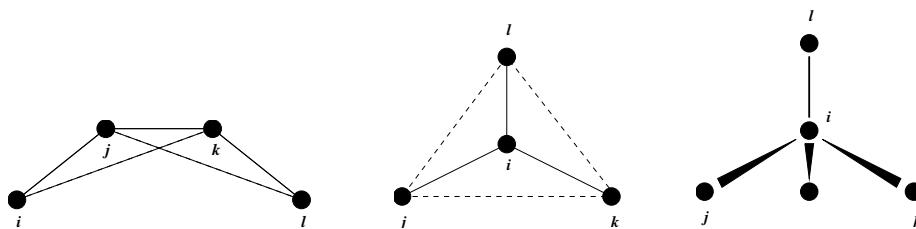


Figure 4.9: Principle of improper dihedral angles. Out of plane bending for rings (left), substituents of rings (middle), out of tetrahedral (right). The improper dihedral angle ξ is defined as the angle between planes (i,j,k) and (j,k,l) in all cases.

4.2.11 Quartic angle potential

For special purposes there is an angle potential that uses a fourth order polynomial:

$$V_q(\theta_{ijk}) = \sum_{n=0}^5 C_n (\theta_{ijk} - \theta_{ijk}^0)^n \quad (4.61)$$

4.2.12 Improper dihedrals

Improper dihedrals are meant to keep planar groups (*e.g.* aromatic rings) planar, or to prevent molecules from flipping over to their mirror images, see Fig. 4.9.

Improper dihedrals: harmonic type

The simplest improper dihedral potential is a harmonic potential; it is plotted in Fig. 4.10.

$$V_{id}(\xi_{ijkl}) = \frac{1}{2} k_{\xi} (\xi_{ijkl} - \xi_0)^2 \quad (4.62)$$

Since the potential is harmonic it is discontinuous, but since the discontinuity is chosen at 180° distance from ξ_0 this will never cause problems. **Note** that in the input in topology files, angles are given in degrees and force constants in kJ/mol/rad².

Improper dihedrals: periodic type

This potential is identical to the periodic proper dihedral (see below). There is a separate dihedral type for this (type 4) only to be able to distinguish improper from proper dihedrals in the parameter section and the output.

4.2.13 Proper dihedrals

For the normal dihedral interaction there is a choice of either the GROMOS periodic function or a function based on expansion in powers of $\cos \phi$ (the so-called Ryckaert-Bellemans potential). This choice has consequences for the inclusion of special interactions between the first and the fourth

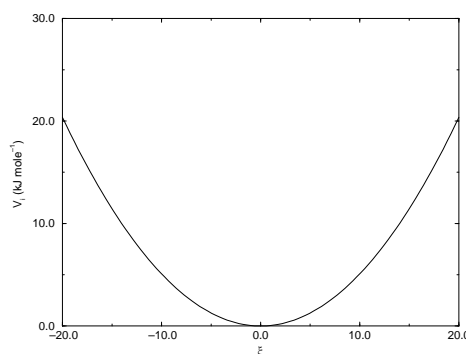


Figure 4.10: Improper dihedral potential.

atom of the dihedral quadruple. With the periodic GROMOS potential a special 1-4 LJ-interaction must be included; with the Ryckaert-Bellemans potential *for alkanes* the 1-4 interactions must be excluded from the non-bonded list. **Note:** Ryckaert-Bellemans potentials are also used in *e.g.* the OPLS force field in combination with 1-4 interactions. You should therefore not modify topologies generated by `pdb2gmx` in this case.

Proper dihedrals: periodic type

Proper dihedral angles are defined according to the IUPAC/IUB convention, where ϕ is the angle between the ijk and the jkl planes, with **zero** corresponding to the *cis* configuration (i and l on the same side). There are two dihedral function types in GROMACS topology files. There is the standard type 1 which behaves like any other bonded interactions. For certain force fields, type 9 is useful. Type 9 allows multiple potential functions to be applied automatically to a single dihedral in the `[dihedral]` section when multiple parameters are defined for the same atomtypes in the `[dihedraltypes]` section.

$$V_d(\phi_{ijkl}) = k_\phi(1 + \cos(n\phi - \phi_s)) \quad (4.63)$$

Proper dihedrals: Ryckaert-Bellemans function

For alkanes, the following proper dihedral potential is often used (see Fig. 4.12):

$$V_{rb}(\phi_{ijkl}) = \sum_{n=0}^5 C_n (\cos(\psi))^n, \quad (4.64)$$

where $\psi = \phi - 180^\circ$.

Note: A conversion from one convention to another can be achieved by multiplying every coefficient C_n by $(-1)^n$.

An example of constants for C is given in Table 4.1.

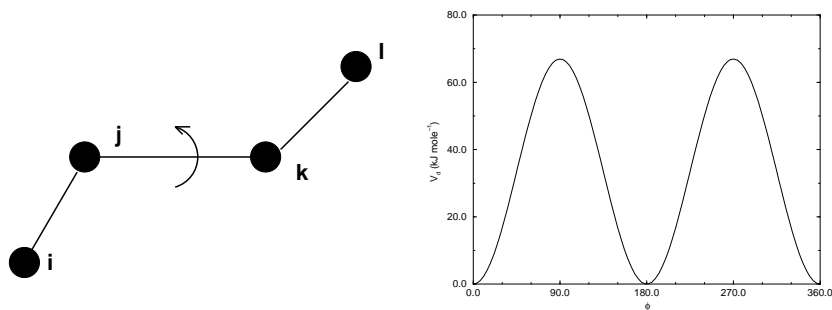


Figure 4.11: Principle of proper dihedral angle (left, in *trans* form) and the dihedral angle potential (right).

C_0	9.28	C_2	-13.12	C_4	26.24
C_1	12.16	C_3	-3.06	C_5	-31.5

Table 4.1: Constants for Ryckaert-Bellemans potential (kJ mol^{-1}).

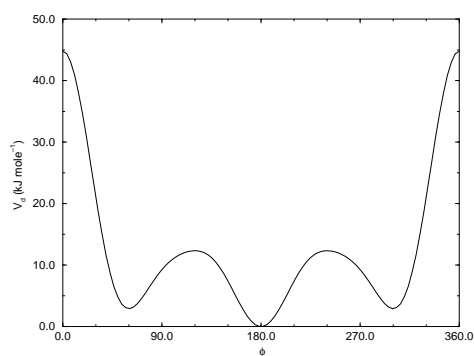


Figure 4.12: Ryckaert-Bellemans dihedral potential.

(**Note:** The use of this potential implies exclusion of LJ interactions between the first and the last atom of the dihedral, and ψ is defined according to the “polymer convention” ($\psi_{trans} = 0$).)

The RB dihedral function can also be used to include Fourier dihedrals (see below):

$$V_{rb}(\phi_{ijkl}) = \frac{1}{2} [F_1(1 + \cos(\phi)) + F_2(1 - \cos(2\phi)) + F_3(1 + \cos(3\phi)) + F_4(1 - \cos(4\phi))] \quad (4.65)$$

Because of the equalities $\cos(2\phi) = 2\cos^2(\phi) - 1$, $\cos(3\phi) = 4\cos^3(\phi) - 3\cos(\phi)$ and $\cos(4\phi) = 8\cos^4(\phi) - 8\cos^2(\phi) + 1$ one can translate the OPLS parameters to Ryckaert-Bellemans parameters as follows:

$$\begin{aligned} C_0 &= F_2 + \frac{1}{2}(F_1 + F_3) \\ C_1 &= \frac{1}{2}(-F_1 + 3F_3) \\ C_2 &= -F_2 + 4F_4 \\ C_3 &= -2F_3 \\ C_4 &= -4F_4 \\ C_5 &= 0 \end{aligned} \quad (4.66)$$

with OPLS parameters in protein convention and RB parameters in polymer convention (this yields a minus sign for the odd powers of $\cos(\phi)$).

Note: Mind the conversion from kcal mol^{-1} for literature OPLS and RB parameters to kJ mol^{-1} in GROMACS.

Proper dihedrals: Fourier function

The OPLS potential function is given as the first three or four [87] cosine terms of a Fourier series. In GROMACS the four term function is implemented:

$$V_F(\phi_{ijkl}) = \frac{1}{2} [C_1(1 + \cos(\phi)) + C_2(1 - \cos(2\phi)) + C_3(1 + \cos(3\phi)) + C_4(1 + \cos(4\phi))] , \quad (4.67)$$

Internally, GROMACS uses the Ryckaert-Bellemans code to compute Fourier dihedrals (see above), because this is more efficient.

Note: Mind the conversion from kcal mol^{-1} for literature OPLS parameters to kJ mol^{-1} in GROMACS.

Proper dihedrals: Restricted torsion potential

In a manner very similar to the restricted bending potential (see 4.2.7), a restricted torsion/dihedral potential is introduced:

$$V_{\text{ReT}}(\phi_i) = \frac{1}{2} k_\phi \frac{(\cos \phi_i - \cos \phi_0)^2}{\sin^2 \phi_i} \quad (4.68)$$

with the advantages of being a function of $\cos \phi$ (no problems taking the derivative of $\sin \phi$) and of keeping the torsion angle at only one minimum value. In this case, the factor $\sin^2 \phi$ does not allow the dihedral angle to move from the $[-180^\circ:0]$ to $[0:180^\circ]$ interval, i.e. it cannot have maxima both at $-\phi_0$ and $+\phi_0$ maxima, but only one of them. For this reason, all the dihedral

angles of the starting configuration should have their values in the desired angles interval and the equilibrium ϕ_0 value should not be too close to the interval limits (as for the restricted bending potential, described in 4.2.7, at least 10° difference is recommended).

Proper dihedrals: Combined bending-torsion potential

When the four particles forming the dihedral angle become collinear (this situation will never happen in atomistic simulations, but it can occur in coarse-grained simulations) the calculation of the torsion angle and potential leads to numerical instabilities. One way to avoid this is to use the restricted bending potential (see 4.2.7) that prevents the dihedral from reaching the 180° value.

Another way is to disregard any effects of the dihedral becoming ill-defined, keeping the dihedral force and potential calculation continuous in entire angle range by coupling the torsion potential (in a cosine form) with the bending potentials of the adjacent bending angles in a unique expression:

$$V_{\text{CBT}}(\theta_{i-1}, \theta_i, \phi_i) = k_\phi \sin^3 \theta_{i-1} \sin^3 \theta_i \sum_{n=0}^4 a_n \cos^n \phi_i. \quad (4.69)$$

This combined bending-torsion (CBT) potential has been proposed by [88] for polymer melt simulations and is extensively described in [84].

This potential has two main advantages:

- it does not only depend on the dihedral angle ϕ_i (between the $i - 2$, $i - 1$, i and $i + 1$ beads) but also on the bending angles θ_{i-1} and θ_i defined from three adjacent beads ($i - 2$, $i - 1$ and i , and $i - 1$, i and $i + 1$, respectively). The two $\sin^3 \theta$ pre-factors, tentatively suggested by [89] and theoretically discussed by [90], cancel the torsion potential and force when either of the two bending angles approaches the value of 180° .
- its dependence on ϕ_i is expressed through a polynomial in $\cos \phi_i$ that avoids the singularities in $\phi = 0^\circ$ or 180° in calculating the torsional force.

These two properties make the CBT potential well-behaved for MD simulations with weak constraints on the bending angles or even for steered / non-equilibrium MD in which the bending and torsion angles suffer major modifications. When using the CBT potential, the bending potentials for the adjacent θ_{i-1} and θ_i may have any form. It is also possible to leave out the two angle bending terms (θ_{i-1} and θ_i) completely. Fig. 4.13 illustrates the difference between a torsion potential with and without the $\sin^3 \theta$ factors (blue and gray curves, respectively). Additionally, the derivative of V_{CBT} with respect to the Cartesian variables is straightforward:

$$\frac{\partial V_{\text{CBT}}(\theta_{i-1}, \theta_i, \phi_i)}{\partial \vec{r}_l} = \frac{\partial V_{\text{CBT}}}{\partial \theta_{i-1}} \frac{\partial \theta_{i-1}}{\partial \vec{r}_l} + \frac{\partial V_{\text{CBT}}}{\partial \theta_i} \frac{\partial \theta_i}{\partial \vec{r}_l} + \frac{\partial V_{\text{CBT}}}{\partial \phi_i} \frac{\partial \phi_i}{\partial \vec{r}_l} \quad (4.70)$$

The CBT is based on a cosine form without multiplicity, so it can only be symmetrical around 0° . To obtain an asymmetrical dihedral angle distribution (e.g. only one maximum in $[-180^\circ:180^\circ]$ interval), a standard torsion potential such as harmonic angle or periodic cosine potentials should be used instead of a CBT potential. However, these two forms have the inconveniences of the force derivation ($1/\sin \phi$) and of the alignment of beads (θ_i or $\theta_{i-1} = 0^\circ, 180^\circ$). Coupling such non- $\cos \phi$ potentials with $\sin^3 \theta$ factors does not improve simulation stability since there are cases

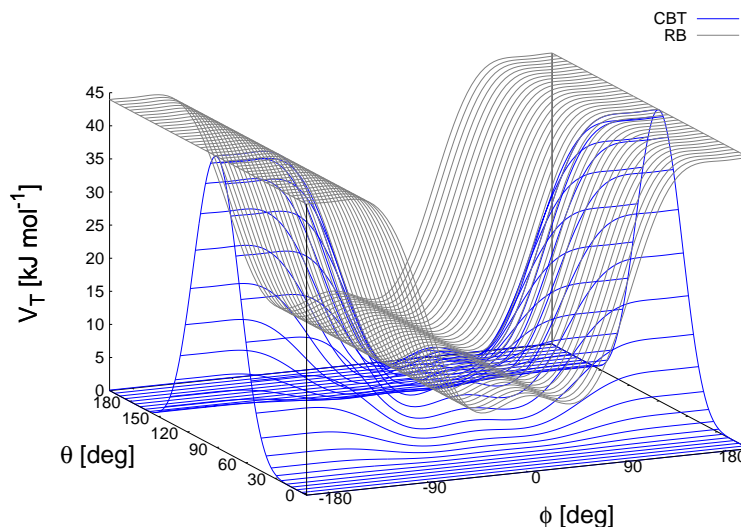


Figure 4.13: Blue: surface plot of the combined bending-torsion potential (4.69 with $k = 10$ kJ mol^{-1} , $a_0 = 2.41$, $a_1 = -2.95$, $a_2 = 0.36$, $a_3 = 1.33$) when, for simplicity, the bending angles behave the same ($\theta_1 = \theta_2 = \theta$). Gray: the same torsion potential without the $\sin^3 \theta$ terms (Ryckaert-Bellemans type). ϕ is the dihedral angle.

in which θ and ϕ are simultaneously 180° . The integration at this step would be possible (due to the cancelling of the torsion potential) but the next step would be singular (θ is not 180° and ϕ is very close to 180°).

4.2.14 Tabulated bonded interaction functions

For full flexibility, any functional shape can be used for bonds, angles and dihedrals through user-supplied tabulated functions. The functional shapes are:

$$V_b(r_{ij}) = k f_n^b(r_{ij}) \quad (4.71)$$

$$V_a(\theta_{ijk}) = k f_n^a(\theta_{ijk}) \quad (4.72)$$

$$V_d(\phi_{ijkl}) = k f_n^d(\phi_{ijkl}) \quad (4.73)$$

where k is a force constant in units of energy and f is a cubic spline function; for details see 6.10.1. For each interaction, the force constant k and the table number n are specified in the topology. There are two different types of bonds, one that generates exclusions (type 8) and one that does not (type 9). For details see Table 5.5. The table files are supplied to the `mdrun` program. After the table file name an underscore, the letter “b” for bonds, “a” for angles or “d” for dihedrals and the table number are appended. For example, for a bond with $n = 0$ (and using the default table file name) the table is read from the file `table_b0.xvg`. Multiple tables can be supplied simply by using different values of n , and are applied to the appropriate bonds, as specified in the topology (Table 5.5). The format for the table files is three columns with x , $f(x)$, $-f'(x)$, where x should be uniformly-spaced. Requirements for entries in the topology are given in Table 5.5. The setup of the tables is as follows:

bonds: x is the distance in nm. For distances beyond the table length, `mdrun` will quit with an error message.

angles: x is the angle in degrees. The table should go from 0 up to and including 180 degrees; the derivative is taken in degrees.

dihedrals: x is the dihedral angle in degrees. The table should go from -180 up to and including 180 degrees; the IUPAC/IUB convention is used, *i.e.* zero is cis, the derivative is taken in degrees.