Chapter 14
Molecular Mechanics

Classical molecular mechanics simulations have become a very valuable tool for the investigation of atomic and molecular systems [97, 115, 157, 212, 225], mainly in the area of materials science and molecular biophysics. Based on the Born-Oppenheimer separation which assumes that the electrons move much faster than the nuclei, nuclear motion is described quantum mechanically by the Hamiltonian

$$H = \left[T^{Nuc} + U\left(\mathbf{r}_j^{Nuc}\right)\right]. \tag{14.1}$$

Molecular mechanics uses the corresponding classical energy function

$$T^{Nuc} + U\left(\mathbf{r}_j^{Nuc}\right) = \sum_j \frac{(p_j^{Nuc})^2}{2m_j} + U\left(\mathbf{r}_j^{Nuc}\right) \tag{14.2}$$

which treats the atoms as mass points interacting by classical forces

$$\mathbf{F}_i = -\operatorname{grad}_{\mathbf{r}_i} U\left(\mathbf{r}_j^{Nuc}\right). \tag{14.3}$$

Stable structures, i.e. local minima of the potential energy can be found by the methods discussed in Chap. 6. Small amplitude motions around an equilibrium geometry are described by a harmonic normal mode analysis. Molecular dynamics (MD) simulations solve the classical equations of motion

$$m_i \frac{\mathrm{d}^2\mathbf{r}_i}{\mathrm{d}t^2} = \mathbf{F}_i = -\operatorname{grad}_{\mathbf{r}_i} U \tag{14.4}$$

numerically.

The potential energy function $U(\mathbf{r}_j^{Nuc})$ can be calculated with simplified quantum methods for not too large systems [50, 152]. Classical MD simulations for larger molecules use empirical force fields, which approximate the potential energy surface of the electronic ground state. They are able to describe structural and conformational changes but not chemical reactions which usually involve more than one electronic state. Among the most popular classical force fields are AMBER [63], CHARMM [163] and GROMOS [58, 262].

In this chapter we discuss the most important interaction terms, which are conveniently expressed in internal coordinates, i.e. bond lengths, bond angles and dihedral angles. We derive expressions for the gradients of the force field with respect

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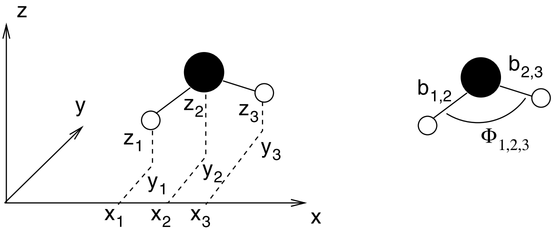

Fig. 14.1 (Molecular coordinates) Cartesian coordinates (*left*) are used to solve the equations of motion whereas the potential energy is more conveniently formulated in internal coordinates (*right*)

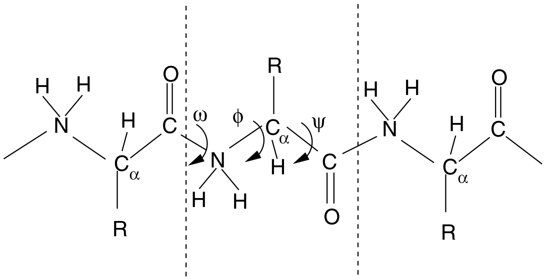

Fig. 14.2 (Conformation of a protein) The relative orientation of two successive protein residues can be described by three angles (Ψ, Φ, ω)

to Cartesian coordinates. In a computer experiment we simulate a glycine dipeptide and demonstrate the principles of energy minimization, normal mode analysis and dynamics simulation.

14.1 Atomic Coordinates

The most natural coordinates for the simulation of molecules are the Cartesian coordinates (Fig. 14.1) of the atoms,

$$\mathbf{r}_i = (x_i, y_i, z_i) \tag{14.5}$$

which can be collected into a $3N$-dimensional vector

$$(\xi_1, \xi_2 \cdots \xi_{3N}) = (x_1, y_1, z_1, x_2 \cdots x_N, y_N, z_N). \tag{14.6}$$

The second derivatives of the Cartesian coordinates appear directly in the equations of motion (14.4)

$$m_r \ddot{\xi}_r = F_r \quad r = 1 \cdots 3N. \tag{14.7}$$

Cartesian coordinates have no direct relation to the structural properties of molecules. For instance a protein is a long chain of atoms (the so called backbone) with additional side groups (Fig. 14.2).

The protein structure can be described more intuitively with the help of atomic distances and angles. Internal coordinates are (Fig. 14.3) distances between two bonded atoms (bond lengths)

$$b_{ij} = |\mathbf{r}_{ij}| = |\mathbf{r}_i - \mathbf{r}_j|, \tag{14.8}$$

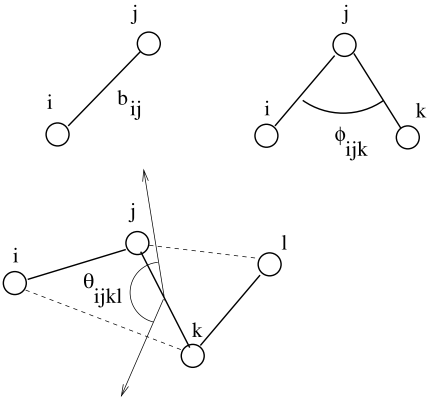

Fig. 14.3 (Internal coordinates) The structure of a molecule can be described by bond lengths, bond angles and dihedral angles

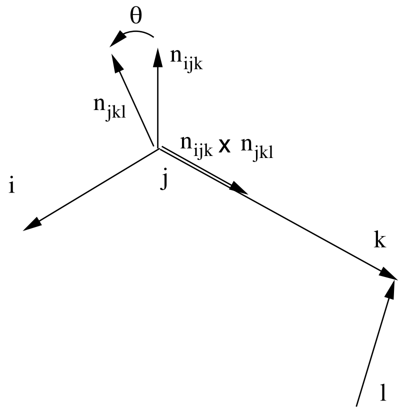

Fig. 14.4 Dihedral angle

angles between two bonds (bond angles)

$$\phi_{ijk} = \arccos\left(\frac{\mathbf{r}_{ij}\mathbf{r}_{kj}}{|\mathbf{r}_{ij}||\mathbf{r}_{kj}|}\right) \tag{14.9}$$

and dihedral angles which describe the planarity and torsions of the molecule. A dihedral angle (Fig. 14.4) is the angle between two planes which are defined by three bonds

$$\theta_{ijkl} = \operatorname{sign}(\theta_{ijkl}) \arccos(\mathbf{n}_{ijk}\mathbf{n}_{jkl}) \tag{14.10}$$

$$\mathbf{n}_{ijk} = \frac{\mathbf{r}_{ij} \times \mathbf{r}_{kj}}{|\mathbf{r}_{ij} \times \mathbf{r}_{kj}|} \qquad \mathbf{n}_{jkl} = \frac{\mathbf{r}_{kj} \times \mathbf{r}_{kl}}{|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|} \tag{14.11}$$

where the conventional sign of the dihedral angle [136] is determined by

$$\operatorname{sign}\theta_{ijkl} = \operatorname{sign}\big(\mathbf{r}_{kj}(\mathbf{n}_{ijk} \times \mathbf{n}_{jkl})\big). \tag{14.12}$$

Internal coordinates are very convenient for the formulation of a force field. On the other hand, the kinetic energy (14.2) becomes complicated if expressed in internal coordinates. Therefore both kinds of coordinates are used in molecular dynamics

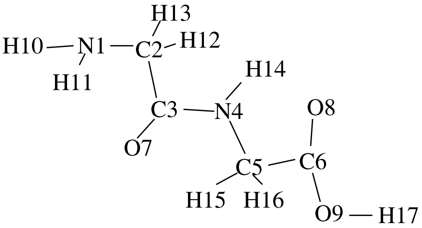

Fig. 14.5 (Glycine dipeptide model) The glycine dipeptide is the simplest model for a peptide. It is simulated in Problem 14.1. Optimized internal coordinates are shown in Table 14.1

calculations. The internal coordinates are usually arranged in Z-matrix form. Each line corresponds to one atom i and shows its position relative to three atoms j, k, l in terms of the bond length b_{ij}, the bond angle ϕ_{ijk} and the dihedral angle θ_{ijkl} (Fig. 14.5 and Table 14.1).

14.2 Force Fields

Classical force fields are usually constructed as an additive combination of many interaction terms. Generally these can be divided into intramolecular contributions

Table 14.1 (Z-matrix) The optimized values of the internal coordinates from Problem 14.1 are shown in Z-matrix form. Except for the first three atoms the position of atom i is given by its distance b_{ij} to atom j, the bond angle ϕ_{ijk} and the dihedral angle θ_{ijkl}

Number i	Label	j	k	l	Bond length (Å) b_{ij}	Bond angle ϕ_{ijk}	Dihedral θ_{ijkl}
1	N1						
2	C2	1			1.45		
3	C3	2	1		1.53	108.6	
4	N4	3	2	1	1.35	115.0	160.7
5	C5	4	3	2	1.44	122.3	−152.3
6	C6	5	4	3	1.51	108.7	−153.1
7	O7	3	2	1	1.23	121.4	−26.3
8	O8	6	5	4	1.21	124.4	123.7
9	O9	6	5	4	1.34	111.5	−56.5
10	H10	1	2	3	1.02	108.7	−67.6
11	H11	1	2	3	1.02	108.7	49.3
12	H12	2	3	4	1.10	109.4	−76.8
13	H13	2	3	4	1.10	109.4	38.3
14	H14	4	3	2	1.02	123.1	27.5
15	H15	5	4	3	1.10	111.2	−32.5
16	H16	5	4	3	1.10	111.1	86.3
17	H17	9	6	5	0.97	106.9	−147.4

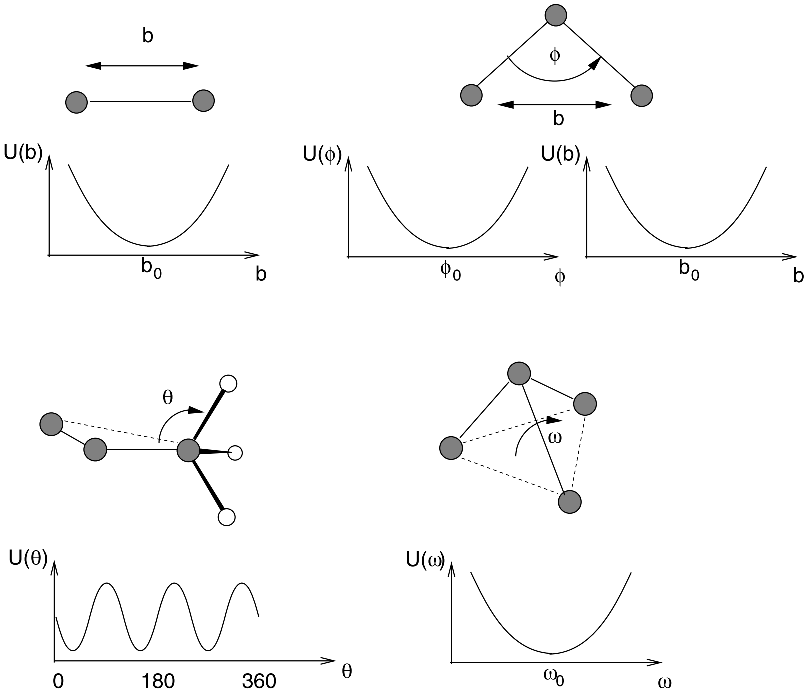

Fig. 14.6 Intramolecular forces

U_{bonded} which determine the configuration and motion of a single molecule and intermolecular contributions $U_{non\text{-}bonded}$ describing interactions between different atoms or molecules

$$U = U_{bonded} + U_{non\text{-}bonded}. \tag{14.13}$$

14.2.1 Intramolecular Forces

The most important intramolecular forces depend on the deviation of bond lengths, bond angles and dihedral angles from their equilibrium values. For simplicity a sum of independent terms is used as for the CHARMM force field [39, 40, 163]

$$U_{intra} = \sum U_{ij}^{bond} + \sum U_{ijk}^{angle} + \sum U_{ijk}^{UB} + \sum U_{ijkl}^{dihedral} + \sum U_{ijkl}^{improper}. \tag{14.14}$$

The forces are derived from potential functions which are in the simplest case approximated by harmonic oscillator parabolas (Fig. 14.6), like the bond stretching energy

$$U_{ij}^{bond} = \frac{1}{2} k_{ij} \left(b_{ij} - b_{ij}^{0} \right)^2 \tag{14.15}$$

Table 14.2 (Atom types of the glycine dipeptide) Atom types for glycine oligopeptides according to Bautista and Seminario [15]. The atoms are classified by element and bonding environment. Atoms of the same atom type are considered equivalent

Atom type	Atoms
C	C3,
C_1	C2, C5
C_2	C6
N	N4
N_2	N1
O	O7
O_1	O9
O_2	O8
H	H14
H_1	H12, H13, H15, H16
H_2	H17
H_3	H10, H11

angle bending terms

$$U_{ijk}^{angle} = \frac{1}{2} k_{ijk} \left(\phi_{ijk} - \phi_{ijk}^0 \right)^2 \tag{14.16}$$

together with the Urey-Bradly correction

$$U_{ijk}^{UB} = \frac{1}{2} k_{ijk} \left(b_{ik} - b_{ik}^0 \right)^2 \tag{14.17}$$

and “improper dihedral” terms which are used to keep planarity

$$U_{ijkl}^{improper} = \frac{1}{2} k_{ijkl} \left(\theta_{ijkl} - \theta_{ijkl}^0 \right)^2. \tag{14.18}$$

Torsional energy contributions are often described by a cosine function[1]

$$U_{ijkl}^{dihedral} = k_{ijkl} \left(1 - \cos\left(m\theta_{ijkl} - \theta_{ijkl}^0 \right) \right) \tag{14.19}$$

where $m = 1, 2, 3, 4, 6$ describes the symmetry. For instance $m = 3$ for the three equivalent hydrogen atoms of a methyl group. In most cases the phase shift $\theta_{ijkl}^0 = 0$ or $\theta_{ijkl}^0 = \pi$. Then the dihedral potential can be expanded as a polynomial of $\cos\theta$, for instance

$$m = 1: \quad U_{ijkl}^{dihedral} = k(1 \pm \cos\theta_{ijkl}) \tag{14.20}$$

$$m = 2: \quad U_{ijkl}^{dihedral} = k \pm k\left(1 - 2(\cos\theta_{ijkl})^2\right) \tag{14.21}$$

$$m = 3: \quad U_{ijkl}^{dihedral} = k\left(1 \pm 3\cos\theta_{ijkl} \mp 4(\cos\theta_{ijkl})^3\right). \tag{14.22}$$

For more general θ_{ijkl}^0 the torsional potential can be written as a polynomial of $\cos\theta_{ijkl}$ and $\sin\theta_{ijkl}$.

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[1] Some force-fields like Desmond [33] or UFF [213] use a more general sum $k \sum_{m=0}^{M} c_m \cos(m\theta - \theta^0)$.

Table 14.3 (Bond stretching parameters) Equilibrium bond lengths (Å) and force constants (kcal mol^{-1} Å^{-2}) for the glycine dipeptide from [15]

Bond type	b^0	k	Bonds
$r_{\mathrm{C,N}}$	1.346	1296.3	C3-N4
$r_{\mathrm{C1,N}}$	1.438	935.5	N4-C5
$r_{\mathrm{C1,N2}}$	1.452	887.7	N1-C2
$r_{\mathrm{C2,C1}}$	1.510	818.9	C5-C6
$r_{\mathrm{C,C1}}$	1.528	767.9	C2-C3
$r_{\mathrm{C2,O2}}$	1.211	2154.5	C6-O8
$r_{\mathrm{C,O}}$	1.229	1945.7	C3-O7
$r_{\mathrm{C2,O1}}$	1.339	1162.1	C6-O9
$r_{\mathrm{N,H}}$	1.016	1132.4	N4-H14
$r_{\mathrm{N2,H3}}$	1.020	1104.5	N1-H10, N1-H11
$r_{\mathrm{C1,H1}}$	1.098	900.0	C2-H12, C2-H13, C5-H15, C5-H16
$r_{\mathrm{O1,H2}}$	0.974	1214.6	O9-H17

The atoms are classified by element and bonding environment. Atoms of the same atom type are considered equivalent and the parameters transferable (for an example see Tables 14.2, 14.3, 14.4).

14.2.2 Intermolecular Interactions

Interactions between non-bonded atoms

$$U_{non\text{-}bonded} = U^{Coul} + U^{vdW} \tag{14.23}$$

include the Coulomb interaction and the weak attractive van der Waals forces which are usually combined with a repulsive force at short distances to account for the Pauli principle. Very often a sum of pairwise Lennard-Jones potentials is used (Fig. 14.7) [3]

$$U^{vdw} = \sum_{A\neq B} \sum_{i\in A, j\in B} U^{vdw}_{i,j} = \sum_{A\neq B} \sum_{ij} 4\varepsilon_{ij} \left(\frac{\sigma_{ij}^{12}}{r_{ij}^{12}} - \frac{\sigma_{ij}^{6}}{r_{ij}^{6}} \right). \tag{14.24}$$

The charge distribution of a molecular system can be described by a set of multipoles at the position of the nuclei, the bond centers and further positions (lone pairs for example). Such distributed multipoles can be calculated quantum chemically for not too large molecules. In the simplest models only partial charges are taken into account giving the Coulomb energy as a sum of atom-atom interactions

$$U^{Coul} = \sum_{A\neq B} \sum_{i\in A, j\in B} \frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}}. \tag{14.25}$$

Table 14.4 (Bond angle parameters) Equilibrium bond angles (deg) and force constants (kcal mol^{-1} rad^{-2}) for the glycine dipeptide from [15]

Angle type	ϕ^0	k	Angles
$\phi_{\mathrm{N,C,C1}}$	115.0	160.0	C2-C3-N4
$\phi_{\mathrm{C1,N,C}}$	122.3	160.1	C3-N4-C5
$\phi_{\mathrm{C1,C2,O1}}$	111.5	156.0	C5-C6-O9
$\phi_{\mathrm{C1,C2,O2}}$	124.4	123.8	C5-C6-O8
$\phi_{\mathrm{C1,C,O}}$	121.4	127.5	C2-C3-O7
$\phi_{\mathrm{O2,C2,O1}}$	124.1	146.5	O8-C6-O9
$\phi_{\mathrm{N,C,O}}$	123.2	132.7	N4-C3-O7
$\phi_{\mathrm{C,C1,H1}}$	110.1	74.6	H12-C2-C3, H13-C2-C3
$\phi_{\mathrm{C2,C1,H1}}$	109.4	69.6	H16-C5-C6, H15-C5-C6
$\phi_{\mathrm{C,N,H}}$	123.1	72.0	C3-N4-H14
$\phi_{\mathrm{C1,N,H}}$	114.6	68.3	C5-N4-H14
$\phi_{\mathrm{C1,N2,H3}}$	108.7	71.7	H10-N1-C2, H11-N1-C2
$\phi_{\mathrm{H1,C1,H1}}$	106.6	48.3	H13-C2-H12, H15-C5-H16
$\phi_{\mathrm{H3,N2,H3}}$	107.7	45.2	H10-N1-H11
$\phi_{\mathrm{C,C1,N2}}$	109.0	139.8	N1-C2-C3
$\phi_{\mathrm{C2,C1,N}}$	108.6	129.0	N4-C5-C6
$\phi_{\mathrm{C2,O1,H2}}$	106.9	72.0	H17-O9-C6
$\phi_{\mathrm{N,C1,H1}}$	111.1	73.3	H15-C5-N4, H16-C5-N4
$\phi_{\mathrm{N2,C1,H1}}$	112.6	80.1	H13-C2-N1, H12-C2-N1

More sophisticated force fields include higher charge multipoles and polarization effects.

14.3 Gradients

The equations of motion are usually solved in Cartesian coordinates and the gradients of the potential are needed in Cartesian coordinates. Since the potential depends only on relative position vectors $\mathbf{r}_{ij}$, the gradient with respect to a certain atom position $\mathbf{r}_k$ can be calculated from

$$\mathrm{grad}_{\mathbf{r}_k} = \sum_{i<j} (\delta_{ik} - \delta_{jk})\, \mathrm{grad}_{\mathbf{r}_{ij}} . \tag{14.26}$$

Therefore it is sufficient to calculate gradients with respect to the difference vectors. Numerically efficient methods to calculate first and second derivatives of many force field terms are given in [156, 259, 260]. The simplest potential terms depend only on the distance of two atoms. For instance bond stretching terms, Lennard-Jones and Coulomb energies have the form

$$U_{ij} = U(r_{ij}) = U\left(|\mathbf{r}_{ij}|\right) \tag{14.27}$$

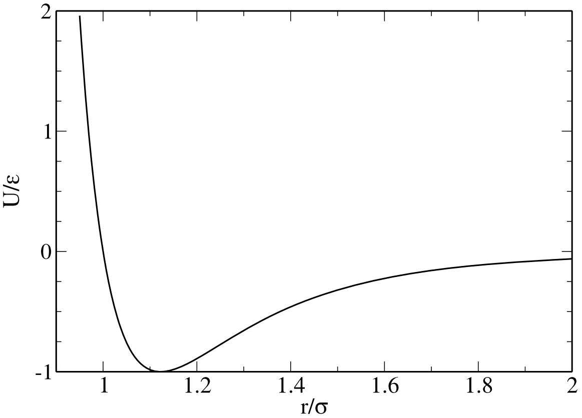

Fig. 14.7 (Lennard-Jones potential) The 6–12 potential (14.24) has its minimum at $r_{\min} = \sqrt[6]{2}\sigma \approx 1.12\sigma$ with $U_{\min} = -\epsilon$

where the gradient is

$$\operatorname{grad}_{\mathbf{r}_{ij}} U_{ij} = \frac{\Delta U}{\Delta r}\frac{\mathbf{r}_{ij}}{|\mathbf{r}_{ij}|}. \tag{14.28}$$

The most important gradients of this kind are

$$\operatorname{grad}_{\mathbf{r}_{ij}} U_{i,j}^{bond} = k\big(r_{ij} - b^0\big)\frac{\mathbf{r}_{ij}}{r_{ij}} = k\left(1 - \frac{b^0}{r_{ij}}\right)\mathbf{r}_{ij} \tag{14.29}$$

$$\operatorname{grad}_{\mathbf{r}_{ij}} U_{i,j}^{vdw} = 24\varepsilon_{ij}\left(-2\frac{\sigma_{ij}^{12}}{r_{ij}^{14}} + \frac{\sigma_{ij}^{6}}{r_{ij}^{8}}\right)\mathbf{r}_{ij} \tag{14.30}$$

$$\operatorname{grad}_{\mathbf{r}_{ij}} U_{ij}^{Coul} = -\frac{q_i q_j}{4\pi\varepsilon_0 r_{ij}^3}\mathbf{r}_{ij}. \tag{14.31}$$

The gradient of the harmonic bond angle potential is

$$\operatorname{grad}_{\mathbf{r}} U_{i,j,k}^{angle} = k\big(\phi_{ijk} - \phi^0\big)\operatorname{grad}_{\mathbf{r}} \phi_{ijk} \tag{14.32}$$

where the gradient of the angle can be calculated from the gradient of its cosine

$$\begin{aligned}\operatorname{grad}_{\mathbf{r}_{ij}} \phi_{ijk} &= -\frac{1}{\sin\phi_{ijk}}\operatorname{grad}_{\mathbf{r}_{ij}} \cos\phi_{ijk} = -\frac{1}{\sin\phi_{ijk}}\left(\frac{\mathbf{r}_{kj}}{|\mathbf{r}_{ij}||\mathbf{r}_{kj}|} - \frac{\mathbf{r}_{ij}\mathbf{r}_{kj}}{|\mathbf{r}_{ij}|^3|\mathbf{r}_{kj}|}\mathbf{r}_{ij}\right) \\ &= -\frac{1}{\sin\phi_{ijk}}\left(\frac{\mathbf{r}_{kj}}{|\mathbf{r}_{ij}||\mathbf{r}_{kj}|} - \frac{\cos\phi_{ijk}}{|\mathbf{r}_{ij}|^2}\mathbf{r}_{ij}\right)\end{aligned} \tag{14.33}$$

$$\operatorname{grad}_{\mathbf{r}_{kj}} \phi_{ijk} = -\frac{1}{\sin\phi_{ijk}}\left(\frac{\mathbf{r}_{ij}}{|\mathbf{r}_{ij}||\mathbf{r}_{kj}|} - \frac{\cos\phi_{ijk}}{|\mathbf{r}_{kj}|^2}\mathbf{r}_{kj}\right). \tag{14.34}$$

In principle, the sine function in the denominator could lead to numerical problems which can be avoided by treating angles close to 0 or π separately or using a function of $\cos\phi_{ijk}$ like the trigonometric potential

$$U_{ijk}^{angle} = \frac{1}{2}k_{ijk}\big(\cos\phi_{ijk} - \cos\phi_{ijk}^0\big)^2 \tag{14.35}$$

instead [5, 213, 224]. Alternatively, the gradient of ϕ can be brought to a form which is free of singularities by expressing the sine in the denominator by a cosine [59]

$$\begin{aligned}\operatorname{grad}_{\mathbf{r}_{ij}} \phi_{ijk} &= -\frac{1}{\sqrt{r_{ij}^2 r_{kj}^2 (1-\cos^2\phi_{ijk})}}\left(\mathbf{r}_{kj} - \frac{\mathbf{r}_{ij}\mathbf{r}_{kj}}{r_{ij}^2}\mathbf{r}_{ij}\right)\\ &= -\frac{r_{ij}^2\mathbf{r}_{kj} - (\mathbf{r}_{ij}\mathbf{r}_{kj})\mathbf{r}_{ij}}{r_{ij}\sqrt{(r_{ij}^2\mathbf{r}_{kj} - (\mathbf{r}_{ij}\mathbf{r}_{kj})\mathbf{r}_{ij})^2}}\\ &= -\frac{1}{r_{ij}}\frac{\mathbf{r}_{ij}\times(\mathbf{r}_{kj}\times\mathbf{r}_{ij})}{|\mathbf{r}_{ij}\times(\mathbf{r}_{kj}\times\mathbf{r}_{ij})|}\end{aligned} \tag{14.36}$$

and similarly

$$\operatorname{grad}_{\mathbf{r}_{kj}} \phi_{ijk} = -\frac{1}{r_{kj}}\frac{\mathbf{r}_{kj}\times(\mathbf{r}_{ij}\times\mathbf{r}_{kj})}{|\mathbf{r}_{kj}\times(\mathbf{r}_{ij}\times\mathbf{r}_{kj})|}. \tag{14.37}$$

Gradients of the dihedral potential are most easily calculated for $\theta_{ijkl}^0 = 0$ or π. In that case, the dihedral potential is a polynomial of $\cos\theta_{ijkl}$ only (14.20)–(14.22) and

$$\operatorname{grad}_{\mathbf{r}} U_{ijkl}^{dihedral} = \frac{\mathrm{d}U_{ijkl}^{dihedral}}{\mathrm{d}\cos\theta_{ijkl}} \operatorname{grad}_{\mathbf{r}} \cos\theta_{ijkl} \tag{14.38}$$

whereas in the general case $0 < \theta_{ijkl} < \pi$ application of the chain rule gives

$$\operatorname{grad} U_{ijkl}^{dihedral} = mk_{ijkl}\sin\bigl(m\bigl(\theta_{ijkl}-\theta^0\bigr)\bigr)\operatorname{grad}\theta_{ijkl}. \tag{14.39}$$

If this is evaluated with the help of

$$\operatorname{grad}\theta_{ijkl} = -\frac{1}{\sin\theta_{ijkl}}\operatorname{grad}\cos\theta_{ijkl} \tag{14.40}$$

singularities appear for $\theta = 0$ and π. The same is the case for the gradients of the harmonic improper potential

$$\operatorname{grad} U_{ijkl}^{improper} = k\bigl(\theta_{ijkl}-\theta_{ijkl}^0\bigr)\operatorname{grad}\theta_{ijkl}. \tag{14.41}$$

Again, one possibility which has been often used, is to treat angles close to 0 or π separately [39]. However, the gradient of the angle θ_{ijkl} can be calculated directly, which is much more efficient [19].

The gradient of the cosine follows from application of the product rule

$$\operatorname{grad}\cos\theta = \operatorname{grad}\left(\frac{\mathbf{r}_{ij}\times\mathbf{r}_{kj}}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|}\frac{\mathbf{r}_{kj}\times\mathbf{r}_{kl}}{|\mathbf{r}_{kj}\times\mathbf{r}_{kl}|}\right). \tag{14.42}$$

First we derive the differentiation rule

$$\begin{aligned}\operatorname{grad}_{\mathbf{a}}\bigl[(\mathbf{a}\times\mathbf{b})(\mathbf{c}\times\mathbf{d})\bigr] &= \operatorname{grad}_{\mathbf{a}}\bigl[(\mathbf{ac})(\mathbf{bd}) - (\mathbf{ad})(\mathbf{bc})\bigr]\\ &= \mathbf{c}(\mathbf{bd}) - \mathbf{d}(\mathbf{bc}) = \mathbf{b}\times(\mathbf{c}\times\mathbf{d})\end{aligned} \tag{14.43}$$

which helps us to find

$$\mathrm{grad}_{r_{ij}}(\mathbf{r}_{ij}\times\mathbf{r}_{kj})(\mathbf{r}_{kj}\times\mathbf{r}_{kl}) = \mathbf{r}_{kj}\times(\mathbf{r}_{kj}\times\mathbf{r}_{kl}) \tag{14.44}$$

$$\mathrm{grad}_{r_{kl}}(\mathbf{r}_{ij}\times\mathbf{r}_{kj})(\mathbf{r}_{kj}\times\mathbf{r}_{kl}) = \mathbf{r}_{kj}\times(\mathbf{r}_{kj}\times\mathbf{r}_{ij}) \tag{14.45}$$

$$\mathrm{grad}_{r_{kj}}(\mathbf{r}_{ij}\times\mathbf{r}_{kj})(\mathbf{r}_{kj}\times\mathbf{r}_{kl}) = \mathbf{r}_{kl}\times(\mathbf{r}_{ij}\times\mathbf{r}_{kj}) + \mathbf{r}_{ij}\times(\mathbf{r}_{kl}\times\mathbf{r}_{kj}) \tag{14.46}$$

and

$$\mathrm{grad}_{r_{ij}}\frac{1}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|} = -\frac{\mathbf{r}_{kj}\times(\mathbf{r}_{ij}\times\mathbf{r}_{kj})}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|^3} \tag{14.47}$$

$$\mathrm{grad}_{r_{kj}}\frac{1}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|} = -\frac{\mathbf{r}_{ij}\times(\mathbf{r}_{kj}\times\mathbf{r}_{ij})}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|^3} \tag{14.48}$$

$$\mathrm{grad}_{r_{kj}}\frac{1}{|\mathbf{r}_{kj}\times\mathbf{r}_{kl}|} = -\frac{\mathbf{r}_{kl}\times(\mathbf{r}_{kj}\times\mathbf{r}_{kl})}{|\mathbf{r}_{kj}\times\mathbf{r}_{kl}|^3} \tag{14.49}$$

$$\mathrm{grad}_{r_{kl}}\frac{1}{|\mathbf{r}_{kj}\times\mathbf{r}_{kl}|} = -\frac{\mathbf{r}_{kj}\times(\mathbf{r}_{kl}\times\mathbf{r}_{kj})}{|\mathbf{r}_{kj}\times\mathbf{r}_{kl}|^3}. \tag{14.50}$$

Finally we collect terms to obtain the gradients of the cosine [59]

$$\begin{aligned}
\mathrm{grad}_{\mathbf{r}_{ij}}\cos\theta_{ijkl} &= \frac{\mathbf{r}_{kj}\times(\mathbf{r}_{kj}\times\mathbf{r}_{kl})}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}||\mathbf{r}_{kj}\times\mathbf{r}_{kl}|} - \frac{\mathbf{r}_{kj}\times(\mathbf{r}_{ij}\times\mathbf{r}_{kj})}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|^2}\cos\theta_{ijkl} \\
&= \frac{\mathbf{r}_{kj}}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|}\times(\mathbf{n}_{jkl} - \mathbf{n}_{ijk}\cos\theta) \\
&= \frac{\mathbf{r}_{kj}}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|}\times\big(\mathbf{n}_{jkl} - \mathbf{n}_{ijk}(\mathbf{n}_{jkl}\mathbf{n}_{ijk})\big) \\
&= \frac{\mathbf{r}_{kj}}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|}\times\big(\mathbf{n}_{ijk}\times(\mathbf{n}_{jkl}\times\mathbf{n}_{ijk})\big) \\
&= \frac{\mathbf{r}_{kj}}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|}\times\left(\mathbf{n}_{ijk}\times\frac{1}{r_{kj}}(-\mathbf{r}_{kj})\sin\theta\right) \\
&= \frac{\sin\theta}{r_{kj}}\frac{\mathbf{r}_{kj}}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|}\times\big(\mathbf{n}_{ijk}\times(-\mathbf{r}_{kj})\big) \\
&= \frac{\sin\theta}{r_{kj}}\frac{1}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|}\big(-\mathbf{n}_{ijk}r_{kj}^2\big) \\
&= -r_{kj}\sin\theta\frac{\mathbf{n}_{ijk}}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}|}
\end{aligned} \tag{14.51}$$

$$\begin{aligned}
\mathrm{grad}_{\mathbf{r}_{kl}}\cos\theta_{ijkl} &= \frac{\mathbf{r}_{kj}\times(\mathbf{r}_{kj}\times\mathbf{r}_{ij})}{|\mathbf{r}_{ij}\times\mathbf{r}_{kj}||\mathbf{r}_{kj}\times\mathbf{r}_{kl}|} - \frac{\mathbf{r}_{kj}\times(\mathbf{r}_{kl}\times\mathbf{r}_{kj})}{|\mathbf{r}_{kj}\times\mathbf{r}_{kl}|^2}\cos\theta_{ijkl} \\
&= \frac{\mathbf{r}_{kj}}{|\mathbf{r}_{kj}\times\mathbf{r}_{kl}|}\times(-\mathbf{n}_{ijk} + \mathbf{n}_{jkl}\cos\theta) \\
&= \frac{\mathbf{r}_{kj}}{|\mathbf{r}_{kj}\times\mathbf{r}_{kl}|}\times\big(-\mathbf{n}_{ijk} + \mathbf{n}_{jkl}(\mathbf{n}_{ijk}\mathbf{n}_{jkl})\big) \\
&= -\frac{\mathbf{r}_{kj}}{|\mathbf{r}_{kj}\times\mathbf{r}_{kl}|}\times\big(\mathbf{n}_{jkl}\times(\mathbf{n}_{ijk}\times\mathbf{n}_{jkl})\big)
\end{aligned}$$

$$
\begin{aligned}
&= -\frac{\mathbf{r}_{kj}}{|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|} \times \left(\mathbf{n}_{jkl} \times \left(\frac{\mathbf{r}_{kj}}{r_{kj}} \sin\theta\right)\right) \\
&= -\frac{\sin\theta}{r_{kj}|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|} \mathbf{r}_{kj} \times (\mathbf{n}_{jkl} \times \mathbf{r}_{kj}) \\
&= -\frac{r_{kj}\sin\theta}{|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|} \mathbf{n}_{jkl}
\end{aligned}
\tag{14.52}
$$

$$
\begin{aligned}
&\operatorname{grad}_{\mathbf{r}_{kj}} \cos\theta_{ijkl} \\
&= \frac{\mathbf{r}_{kl} \times (\mathbf{r}_{ij} \times \mathbf{r}_{kj}) + \mathbf{r}_{ij} \times (\mathbf{r}_{kl} \times \mathbf{r}_{kj})}{|\mathbf{r}_{ij} \times \mathbf{r}_{kj}||\mathbf{r}_{kj} \times \mathbf{r}_{kl}|} \\
&\quad - \frac{\mathbf{r}_{ij} \times (\mathbf{r}_{kj} \times \mathbf{r}_{ij})}{|\mathbf{r}_{ij} \times \mathbf{r}_{kj}|^2} \cos\theta - \frac{\mathbf{r}_{kl} \times (\mathbf{r}_{kj} \times \mathbf{r}_{kl})}{|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|^2} \cos\theta \\
&= \frac{\mathbf{r}_{ij}}{|\mathbf{r}_{ij} \times \mathbf{r}_{kj}|} \times (-\mathbf{n}_{jkl} + \mathbf{n}_{ijk}\cos\theta) + \frac{\mathbf{r}_{kl}}{|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|} \times (\mathbf{n}_{ijk} - \mathbf{n}_{jkl}\cos\theta) \\
&= -\frac{\mathbf{r}_{ij}}{|\mathbf{r}_{ij} \times \mathbf{r}_{kj}|} \times \big(\mathbf{n}_{ijk} \times (\mathbf{n}_{jkl} \times \mathbf{n}_{ijk})\big) + \frac{\mathbf{r}_{kl}}{|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|}\big(\mathbf{n}_{jkl} \times (\mathbf{n}_{ijk} \times \mathbf{n}_{jkl})\big) \\
&= \frac{\mathbf{r}_{ij}}{|\mathbf{r}_{ij} \times \mathbf{r}_{kj}|} \times \left(\mathbf{n}_{ijk} \times \left(\frac{\mathbf{r}_{kj}}{r_{kj}} \sin\theta\right)\right) + \frac{\mathbf{r}_{kl}}{|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|}\left(\mathbf{n}_{jkl} \times \left(\frac{\mathbf{r}_{kj}}{r_{kj}} \sin\theta\right)\right) \\
&= \frac{\sin\theta}{r_{kj}} \frac{1}{|\mathbf{r}_{ij} \times \mathbf{r}_{kj}|} \mathbf{r}_{ij} \times (\mathbf{n}_{ijk} \times \mathbf{r}_{kj}) + \frac{\sin\theta}{r_{kj}} \frac{1}{|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|} \mathbf{r}_{kl} \times (\mathbf{n}_{jkl} \times \mathbf{r}_{kj}) \\
&= \frac{\sin\theta}{r_{kj}} \frac{\mathbf{n}_{ijk}(\mathbf{r}_{ij}\mathbf{r}_{kj})}{|\mathbf{r}_{ij} \times \mathbf{r}_{kj}|} + \frac{\sin\theta}{r_{kj}} \frac{\mathbf{n}_{jkl}(\mathbf{r}_{kl}\mathbf{r}_{kj})}{|\mathbf{r}_{kj} \times \mathbf{r}_{kl}|} \\
&= -\frac{\mathbf{r}_{ij}\mathbf{r}_{kj}}{r_{kj}^2} \operatorname{grad}_{ij} \cos\theta - \frac{\mathbf{r}_{kl}\mathbf{r}_{kj}}{r_{kj}^2} \operatorname{grad}_{kl} \cos\theta.
\end{aligned}
\tag{14.53}
$$

14.4 Normal Mode Analysis

The nuclear motion around an equilibrium configuration can be approximately described as the combination of independent harmonic normal modes. Equilibrium configurations can be found with the methods discussed in Sect. 6.2. The convergence is usually rather slow (Fig. 14.8) except for the full Newton-Raphson method, which needs the calculation and inversion of the Hessian matrix.

14.4.1 Harmonic Approximation

At an equilibrium configuration

$$\xi_i = \xi_i^{eq} \tag{14.54}$$

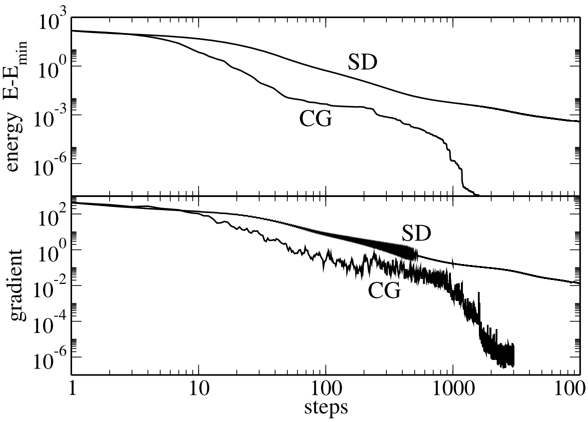

Fig. 14.8 (Convergence of energy and gradient) The energy of the glycine dipeptide is minimized with the methods of steepest descent and conjugate gradients

the gradient of the potential energy vanishes. For small deviations from the equilibrium

$$\zeta_i = \xi_i - \xi_i^{eq} \tag{14.55}$$

approximation by a truncated Taylor series gives

$$U(\zeta_1 \cdots \zeta_{3N}) = U_0 + \frac{1}{2}\sum_{i,j} \frac{\partial^2 U}{\partial \zeta_i \partial \zeta_j} \zeta_i \zeta_j + \cdots \approx U_0 + \frac{1}{2}\sum_{i,j} H_{i,j} \zeta_i \zeta_j \tag{14.56}$$

and the equations of motion are approximately

$$m_i \ddot{\zeta}_i = -\frac{\partial}{\partial \zeta_i} U = -\sum_j H_{i,j} \zeta_j. \tag{14.57}$$

Assuming periodic oscillations

$$\zeta_i = \zeta_i^0 \mathrm{e}^{\mathrm{i}\omega t} \tag{14.58}$$

we have

$$m_i \omega^2 \zeta_i^0 = \sum_j H_{ij} \zeta_j^0. \tag{14.59}$$

If mass weighted coordinates are used, defined as

$$\tau_i = \sqrt{m_i}\zeta_i \tag{14.60}$$

this becomes an ordinary eigenvalue problem

$$\omega^2 \tau_i^0 = \sum_j \frac{H_{ij}}{\sqrt{m_i m_j}} \tau_j^0. \tag{14.61}$$

The eigenvectors $\mathbf{u}_r$ of the symmetric matrix

$$\tilde{H}_{ij} = \frac{H_{ij}}{\sqrt{m_i m_j}} \tag{14.62}$$

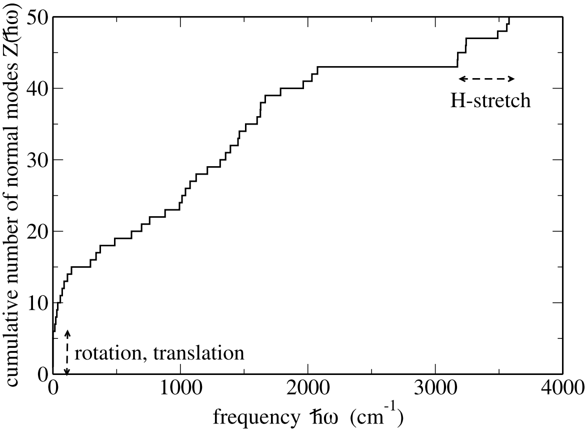

Fig. 14.9 (Normal mode distribution for the dipeptide model) The cumulative distribution (Sect. 8.1.2) of normal mode frequencies is shown for the glycine dipeptide. Translations and rotations of the molecule correspond to the lowest 6 frequencies which are close to zero. The highest frequencies between 3100 cm^{-1} and 3600 cm^{-1} correspond to the stretching modes of the 8 hydrogen atoms

are the solutions of

$$\sum_j \tilde{H}_{ij} u_{jr} = \lambda_r u_{ir} \tag{14.63}$$

and satisfy (14.61)

$$\omega^2 u_{ir} = \sum \tilde{H}_{ij} u_{jr} = \lambda_r u_{ir} \tag{14.64}$$

with normal mode frequencies

$$\omega_r = \sqrt{\lambda_r}. \tag{14.65}$$

Finally, the Cartesian coordinates are linear combinations of all normal modes

$$\zeta_i = \sum_r C_r \frac{u_{ir}}{\sqrt{m_i}} \mathrm{e}^{\mathrm{i}\omega_r t}. \tag{14.66}$$

In a true local energy minimum the Hessian matrix H_{ij} is positive definite and all frequencies are real valued. The six lowest frequencies are close to zero and correspond to translations and rotations of the whole system (Fig. 14.9).

14.5 Problems

Problem 14.1 (Simulation of a glycine dipeptide) In this computer experiment a glycine dipeptide (Fig. 14.5) is simulated. Parameters for bond stretching (Table 14.3) and bond angle (Table 14.4) terms have been derived from quantum calculations by Bautista and Seminario [15].

- Torsional potential terms (Table 14.5) can be added to make the structure more rigid. This is especially important for the O9-H17, N4-H14 and N1-H10 bonds, which rotate almost freely without torsional potentials.

Table 14.5 (Torsional potential terms) Torsional potential terms $V_{ijkl} = k_{ijkl}(1 - \cos(\theta_{ijkl} - \theta^0_{ijkl}))$, which can be added to the forcefield. Minimum angles are from the optimized structure without torsional terms (14.1). The barrier height of $2k_{ijkl} = 2$ kcal/mol is only a guessed value

i	j	k	l	θ^0_{ijkl}	k_{ijkl}	Backbone
10	1	2	3	−67.6	1.0	
14	4	3	2	27.5	1.0	
17	9	6	5	−147.4	1.0	
4	3	2	1	160.7	1.0	Ψ
5	4	3	2	−152.3	1.0	ω
6	5	4	3	−153.1	1.0	Φ
8	6	5	4	123.7	1.0	
9	6	5	4	−56.5	1.0	
15	5	4	3	−32.5	1.0	
16	5	4	3	86.3	1.0	
7	3	2	1	−26.3	1.0	

- The energy can be minimized with the methods of steepest descent or conjugate gradients.
- A normal mode analysis can be performed (the Hessian matrix is calculated by numerical differentiation). The r-th normal mode can be visualized by modulating the coordinates periodically according to

$$\xi_i = \xi_i^{eq} + C_r \frac{u_{ir}}{\sqrt{m_i}} \cos \omega_r t. \tag{14.67}$$

- The motion of the atoms can be simulated with the Verlet method. You can stretch the O9-H17 or N4-H14 bond and observe, how the excitation spreads over the molecule.