

## CHAPTER 5

### DETAILS OF CALCULATIONS

#### 5.1 Geometry of Molecules

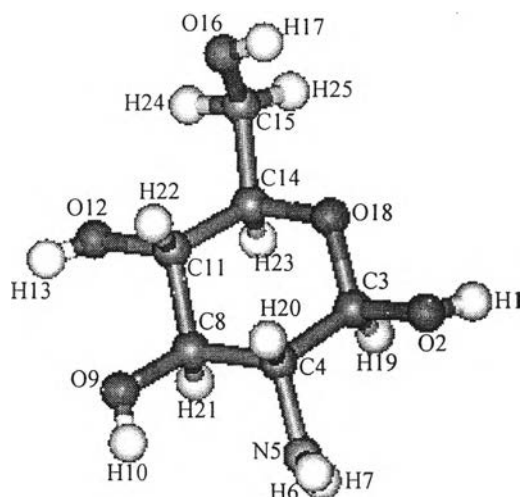
The experimental values for gas phase of water, with an O-H distance of 0.957 Å and an H-O-H angle of 104.5°, have been used [47] and kept constant throughout the calculations. Its Cartesian coordinates were shown in Table 5.1. A unit of the chitosan's geometry which taken from literature [48], has been used to represent glucosamine molecule. To obtain optimal orientation of the O-H groups, the following dihedral angles, H1-O2-C3-C4, C4-C8-O9-H10, C8-C11-O12-H13, and C14-C15-O16-H17 (see Figure 5.1), have been optimized using *ab initio* calculations with DZ basis set [49]. The obtained Cartesian coordinates and the corresponding bond lengths and bond angles were summarized in Table 5.2 – 5.5. The atomic net charges obtained from the Mulliken population analysis which are used in the Coulombic term in the pair potential was also given in Table 5.2. We found that these values are not significantly difference from those obtained from the Natural Population Analysis (NPA) [50].

**Table 5.1** Cartesian coordinates of water molecule (in Angstroms).

Atom	X	Y	Z
O	0.00000	0.00000	0.00000
H	0.00000	0.75669	0.58589
H	0.00000	-0.75669	0.58589

**Table 5.2** Cartesian coordinates (in Angstroms) obtained from the experiment and atomic net charges (in a.u.) of glucosamine molecule obtained from *ab initio* calculations using DZ basis set.

Atom	X	Y	Z	Atomic Charge
H1	-0.531	3.149	0.450	0.306
O2	0.003	2.568	0.819	-0.489
C3	0.000	1.433	0.001	0.248
C4	1.278	0.670	0.345	0.016
N5	2.443	1.448	-0.009	-0.597
H6	2.902	1.760	0.705	0.257
H7	2.417	1.772	-0.854	0.233
C8	1.287	-0.699	-0.345	0.119
O9	2.407	-1.469	0.083	-0.499
H10	3.104	-1.104	-0.024	0.271
C11	0.000	-1.433	-0.001	0.153
O12	-0.037	-2.665	-0.748	-0.542
H13	0.521	-3.234	-0.656	0.282
C14	-1.206	-0.571	-0.396	0.243
C15	-2.564	-1.184	-0.121	-0.056
O16	-2.758	-1.575	1.231	-0.547
H17	-2.893	-0.989	1.895	0.331
O18	-1.151	0.684	0.310	-0.485
H19	-0.052	1.796	-0.897	0.088
H20	1.381	0.504	1.373	0.148
H21	1.351	-0.576	-1.397	0.072
H22	0.063	-1.740	1.010	0.120
H23	-1.095	-0.379	-1.439	0.077
H24	-2.542	-1.995	-0.781	0.149
H25	-3.237	-0.608	-0.734	0.104



**Figure 5.1** Structure of glucosamine with atomic numbering

**Table 5.3** Bond distances of glucosamine molecule (in Angstroms).

H1-O2	0.871	O9-H10	0.792
O2-C3	1.398	C11-C14	1.534
C3-C4	1.529	C11-O2	1.440
C3-O18	1.407	C11-H22	1.059
C3-H19	0.970	O12-H13	0.802
C4-C8	1.534	C14-C15	1.515
C4-N5	1.443	C14-O18	1.443
C4-H20	1.045	C14-H23	1.065
N5-H6	0.905	C15-O16	1.420
N5-H7	0.905	C15-H24	1.046
C8-C11	1.522	C15-H25	1.077
C8-O9	1.425	O16-H17	0.896
C8-H21	1.060		

**Table 5.4** Bond angles of glucosamine molecule (in degree).

H1-O2-C3	107.06	C8-O9-H10	113.62
O2-C3-C4	105.71	O9-C8-H21	108.32
O2-C3-O18	107.72	O9-C8-C11	109.61
O2-C3-H19	103.86	C11-C8-H21	109.37
C3-C4-C8	110.36	C11-C14-O18	109.43
C3-C4-N5	110.51	C11-C14-C15	115.52
C3-C4-H20	112.47	C11-C14-H23	105.77
C3-O18-C14	112.73	C11-O12-H13	121.91
C4-C3-O18	111.66	O12-C11-H22	104.52
C4-C3-H19	116.15	O12-C11-C14	109.01
C4-N5-H6	113.58	C14-C11-H22	117.15
C4-N5-H7	113.55	C14-C15-O16	113.98
C4-C8-C11	108.93	C14-C15-H24	100.35
C4-C8-O9	110.50	C14-C15-H25	103.87
C4-C8-H21	110.10	C15-C14-H23	110.14
N5-C4-C8	111.44	C15-C14-O18	107.24
N5-C4-H20	104.47	C15-O16-H17	123.09
C8-C4-H20	107.45	O16-C15-H24	112.88
C8-C11-C14	109.59	O16-C15-H25	127.24
C8-C11-O12	108.45	O18-C14-H23	108.59
C8-C11-H22	107.75	O18-C3-H19	110.96

**Table 5.5** Dihedral angles of glucosamine molecule (in degree) obtained from the experiment and from *ab initio* calculation using DZ basis set (\*).

H1-O2-C3-C4 *	159.47	N5-C4-C8-C11	-176.57
O2-C3-C4-N5	-64.41	C8-C4-C3-O18	55.00
O2-C3-C4-C8	171.87	C8-C4-N5-H6	-127.13
O2-C3-O18-C14	-175.20	C8-C4-N5-H7	73.23
O2-C3-C4-O18	116.87	C8-C11-O12-H13 *	61.25
C3-C4-N5-H6	109.78	C8-C11-C14-O18	-59.35
C3-C4-N5-H7	-49.86	C8-C11-C14-C15	179.54
C3-C4-C8-O9	-173.85	C8-C11-C14-O12	118.55
C3-C4-C8-C11	-53.39	O9-C8-C11-O12	-64.06
C3-C4-C8-N5	123.18	O9-C8-C11-C14	177.04
C3-O18-C14-C11	61.47	C11-C14-C15-O16	55.34
C3-O18-C14-C15	-172.52	C11-C14-C15-H24	-65.58
C4-C8-O9-H10 *	-55.66	C11-C14-C15-H25	-162.29
C4-C8-C11-C14	56.04	C11-C14-C15-O18	122.28
C4-C8-C11-O12	174.93	O12-C11-C14-O18	-177.90
C4-C8-C11-O9	-121.01	O12-C11-C14-C15	60.99
C4-C3-O18-C14	-59.55	C14-C15-O16-H17 *	73.63
C4-N5-H6-H7	-155.81	C14-C15-H24-H25	-104.88
N5-C4-C3-O18	178.71	O16-C15-H24-H25	133.42
N5-C4-C8-O9	62.98	O16-C15-C14-O18	-66.95

## 5.2 Selection of the Suitable Basis Set for the SCF Calculations

To obtain reliable results for the molecular orbital calculations, one must compromise between computational effort and accuracy. However, the models have to be chosen so as to preserve as closely as possible the chemical and physical integrity of the whole system.

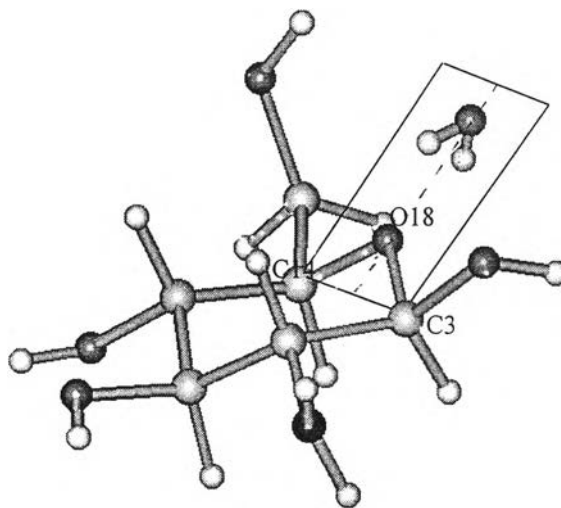
To seek for such goal, SCF calculations have been performed for the glucosamine-water complex in the configuration given in Figure 5.2. The STO-3G, 3-21G, 6-31G, DZ (double zeta), DZP (double zeta plus polarization) and cc-pVTZ (correlation consistent polarized valence triple zeta) basis sets have been used. Moreover, in order to estimate the possible influence of basis set superposition error, additional calculations have been made including the Boys-Bernardi counterpoise correction [44].

The STO-3G, in which each Slater type function contains 3 primitives, is  $(6s3p/3s)/[2s1p/1s]$  as in ref. [51-53]. It means that the 6s and 3p primitives for C, N and O atoms are contracted to 2s and 1p, respectively. For the hydrogen atom, 3s are contracted to 1s.

For the split-valence basis sets, 3-21G [54-55] and 6-31G [56], the corresponding contractions are  $(6s3p/3s)/[3s2p/2s]$  and  $(10s4p/4s)/[3s2p/2s]$ , respectively.

The Dunning's double zeta quality of the form  $(9s5p/4s)/[4s2p/2s]$  and  $(9s5p1d/4s1p)/[4s2p1d/2s1p]$  which corresponding notations are DZ and DZP have been taken from references [49] and [57], respectively.

The largest basis set which is taken into consideration is the triple zeta quality, cc-pVTZ. The corresponding contraction is (10s5p2d1f/5s2p1d)/[4s3p2d1f/3s2p1d] [58]. The exponents of the functions, together with their coefficients, are summarized in the Appendix (I).



**Figure 5.2** Glucosamine-water configurations for investigating suitable basis sets; O atom of water molecule lie in C3-C14-O18 plane which perpendicular with the plane of H-O-H of water molecule .

### 5.3 Development of Intermolecular Potential Function

The simulated system requires 2 types of intermolecular potential function, namely water-water and glucosamine-water potential functions. The first function was taken from literature [59] while the second one was developed newly using *ab initio* data points.

The MCY potential ( $\Delta E$  in kcal.mol<sup>-1</sup>,  $r$  in Å) for water-water has the following form,

$$\begin{aligned}
\Delta E(W, W) = & \frac{Q^2}{4\pi\epsilon_0} \left[ \left( \frac{1}{r_{13}} + \frac{1}{r_{23}} + \frac{1}{r_{14}} + \frac{1}{r_{24}} \right) + \frac{4}{r_{78}} - 2 \left( \frac{1}{r_{18}} + \frac{1}{r_{28}} + \frac{1}{r_{37}} + \frac{1}{r_{47}} \right) \right] \\
& + a_1 \exp(-b_1 r_{56}) \\
& + a_2 [\exp(-b_2 r_{13}) + \exp(-b_2 r_{14}) + \exp(-b_2 r_{23}) + \exp(-b_2 r_{24})] \\
& + a_3 [\exp(-b_3 r_{16}) + \exp(-b_3 r_{26}) + \exp(-b_3 r_{35}) + \exp(-b_3 r_{45})] \\
& - a_4 [\exp(-b_4 r_{16}) + \exp(-b_4 r_{26}) + \exp(-b_4 r_{35}) + \exp(-b_4 r_{45})] \quad (5.1)
\end{aligned}$$

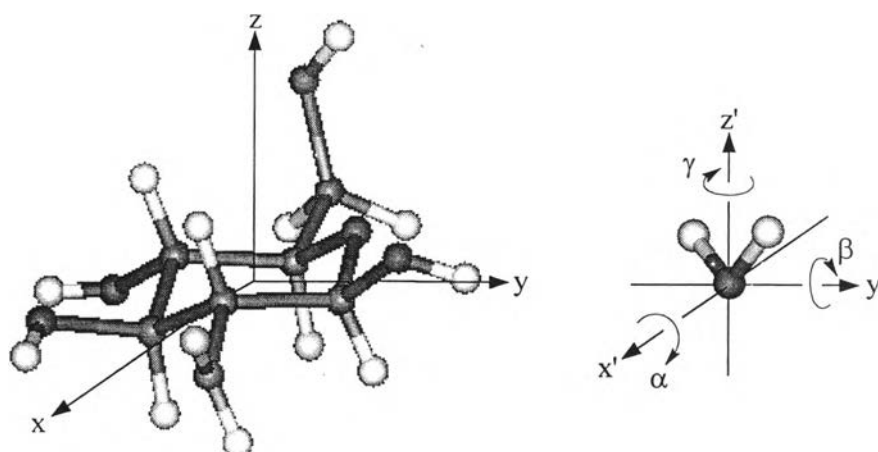
where  $Q$  is a positive charge situated on each hydrogen atom and  $a_1 - a_4$  and  $b_1 - b_4$  are fitting parameters. The hydrogen atoms are labeled 1 – 4 and the oxygen atoms are labeled 5 and 6. The labels 7 and 8 refer to point charges of  $-2Q$  situated along the axis of the dipole-moment vector. The fitting parameters are summarized in Appendix (II).

To develop the glucosamine-water potential, general procedure consists of four consecutive steps:

*a) selection of representative geometries of the pairs, glucosamine-water*

The pair geometries were selected with special regard to chemically representative conformations and molecular symmetry. The center of glucosamine molecule was placed at the origin of Cartesian coordinate and the water molecule was placed at numerous positions within  $0^\circ \leq \alpha < 360^\circ$ ,  $0^\circ \leq \beta < 360^\circ$ ,  $0^\circ \leq \gamma < 180^\circ$  and  $2.0 \leq r \leq 10.0$  Å, when  $r$  is distance between the center of glucosamine molecule and the oxygen atom of water molecule. Here,  $\alpha$ ,  $\beta$  and  $\gamma$  denote rotational angles around x, y and z-axis, respectively (Figure 5.3). With this consideration 4,300 configurations of the water molecule have been generated. A non-symmetric geometry of glucosamine molecule,  $C_1$ , leads to such high number of configurations. Both molecules were treated as rigid throughout the calculations.





**Figure 5.3** Definition of the glucosamine-water configuration.

*b) performance of the SCF calculations*

The interaction energy  $\Delta E_{\text{SCF}}$  between glucosamine (L) and water (W) is determined as the difference of the supersystem energy ( $E_{\text{LW}}$ ) and sum of the subsystem energies ( $E_{\text{L}}, E_{\text{W}}$ )

$$\Delta E_{\text{SCF}} (\text{kcal.mol}^{-1}) = [E_{\text{LW}} - (E_{\text{L}} + E_{\text{W}})] \times 627.5 \quad (5.2)$$

where  $E_{\text{LW}}, E_{\text{L}}$  and  $E_{\text{W}}$  are total energy calculated (in atomic units) using suitable basis which is examined in section 5.2.

The interaction energy yielded from this expression is quite simple. However, some difficulties are encountered in the numerical treatment.

c) fitting of the computed interaction energies to a functional form

In this study, the Lennard-Jones 12-6 potential, consisting of attractive and repulsive parts and the Coulombic term, has been used to describe the interaction between the atom pairs. The Mulliken population analysis from the *ab initio* calculations of the separated subsystems was used to get a first estimation of the fractional atomic charges,  $q_i$ . Therefore, a trial potential function was set up as

$$\Delta E(L, W) = \sum_{i=1}^{25} \sum_{j=1}^3 \left( -\frac{A_{ij}}{r_{ij}^6} + \frac{B_{ij}}{r_{ij}^{12}} + \frac{q_i q_j}{r_{ij}} \right) \quad (5.3)$$

where 25 and 3 denote numbers of atoms of glucosamine and water molecules, respectively.  $A_{ij}$  and  $B_{ij}$  are fitting parameters and  $r_{ij}$  is the distance between an atom  $i$  and  $j$ .

Due to the difference of the atomic net charges (see Table 5.2), carbon, oxygen and hydrogen atoms of glucosamine were classified into 2, 4 and 5 groups, respectively, as exhibited in Table 5.6.

The fitting procedure, which was *linear least square fit*, was performed starting from an initial guess for the parameters, based on 4,300 energy points, and iterating until the standard deviation was minimized, whereby constancy of the fitting parameters was reached. To improve the quality of the fit, especially in the most important configurations (which correspond to the lowest SCF energy points), additional weight factors were introduced, and very repulsive configurations were also excluded from the process.

**Table 5.6** Group of atoms of glucosamine molecule (see Figure 5.1) classified by atomic net charges.

Group	Atom	Averaged charge (in a.u.)
C <sup>1</sup>	C3, C4, C8, C11, C14	0.156
C <sup>2</sup>	C15	-0.056
N	N5	-0.597
O <sup>1</sup>	O2, O9	-0.494
O <sup>2</sup>	O12	-0.542
O <sup>3</sup>	O16	-0.547
O <sup>4</sup>	O18	-0.485
H <sup>1</sup>	H19, H20, H21, H22, H23, H24, H25	0.108
H <sup>2</sup>	H6, H7	0.245
H <sup>3</sup>	H1, H10	0.289
H <sup>4</sup>	H13	0.282
H <sup>5</sup>	H17	0.331

*d) testing the quality of the function*

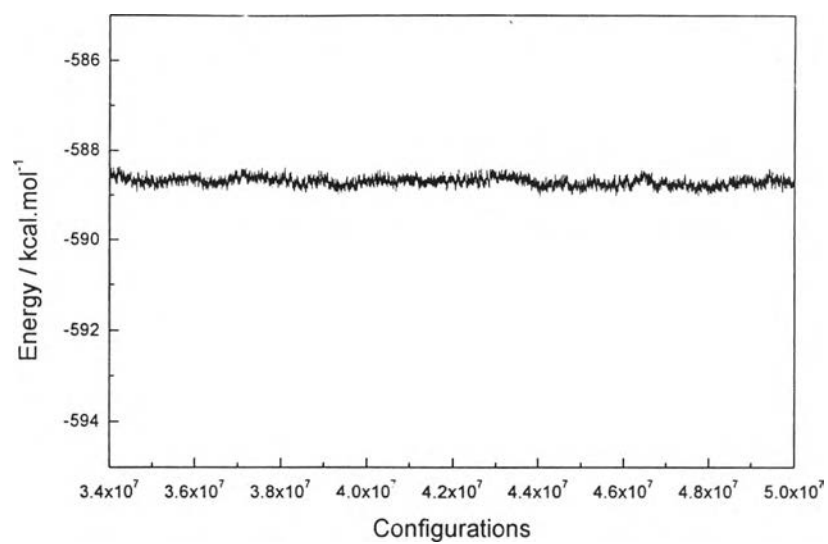
Quality of the function which plays directly role on the reliability of the simulation results is normally judged by statistical (standard deviation, residuals etc.) and the values and positions of the energy minima at the chemically important configurations. The later one is graphically represented between the fitted energies versus their quantum mechanically calculated values. In this study, the 370 glucosamine-water configurations, which different from the first 4,300 configurations, were generated. The 370 energy points were calculated using both SCF method and the pair potential which is yielded from the first 4.300 data set and

named  $\Delta E_{\text{SCF}}$  and  $\Delta E_{\text{FIT}}$ , respectively. Afterwards, the  $\Delta E_{\text{SCF}}$  and  $\Delta E_{\text{FIT}}$  370 data points were compared.

#### 5.4 Monte Carlo Simulation

Monte Carlo simulation has been carried out for a glucosamine molecule in aqueous solution. The system contains 202 rigid particles, including one glucosamine molecule, which fixed at the center of the cube, and 201 water molecules. An experiment density of  $1 \text{ g.cm}^{-3}$  at 298 K of water, plus additional space occupied by the glucosamine molecule estimated as  $76 \text{ \AA}^3$ , yielded a periodic cubic volume of side length  $18.26 \text{ \AA}$ . A spherical cut-off of the site-site interaction potentials was applied at half of this length. The starting configuration of water molecules was randomly generated. The Metropolis sampling algorithm [2] was applied. The MCY potential [59] was employed to describe water-water interactions while the newly developed potential was used for the glucosamine-water interactions.

Equilibrium was reached after  $3.4 \times 10^7$  configurations. Further  $1.6 \times 10^7$  configurations were generated and every 500 of them was stored for subsequent analysis. Energy profile at equilibration of the glucosamine-water simulation is plotted in Figure 5.4.



**Figure 5.4** Energy profile at equilibration of the glucosamine-water simulation .