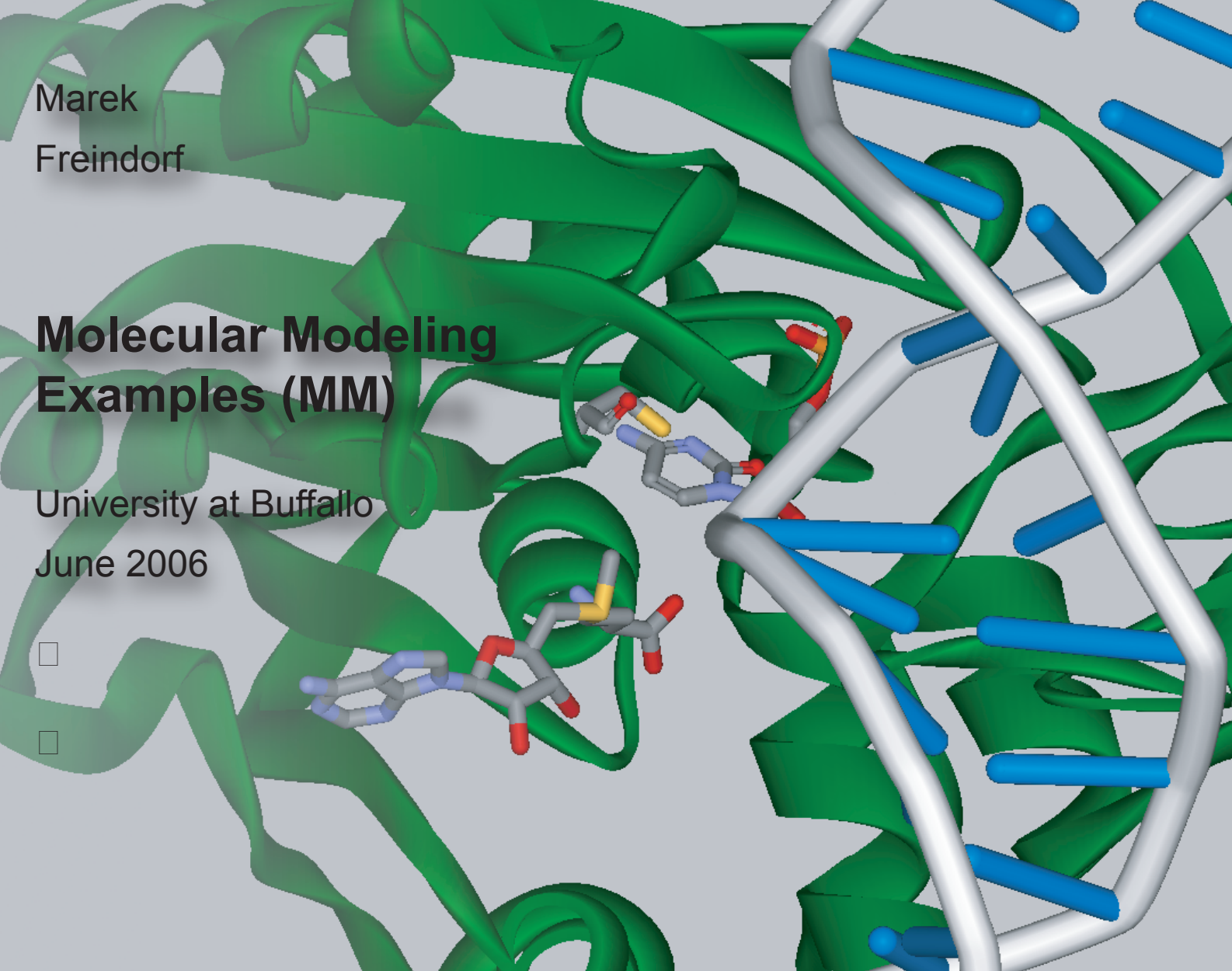
Marek
Freindorf

Molecular Modeling Examples (MM)

University at Buffallo

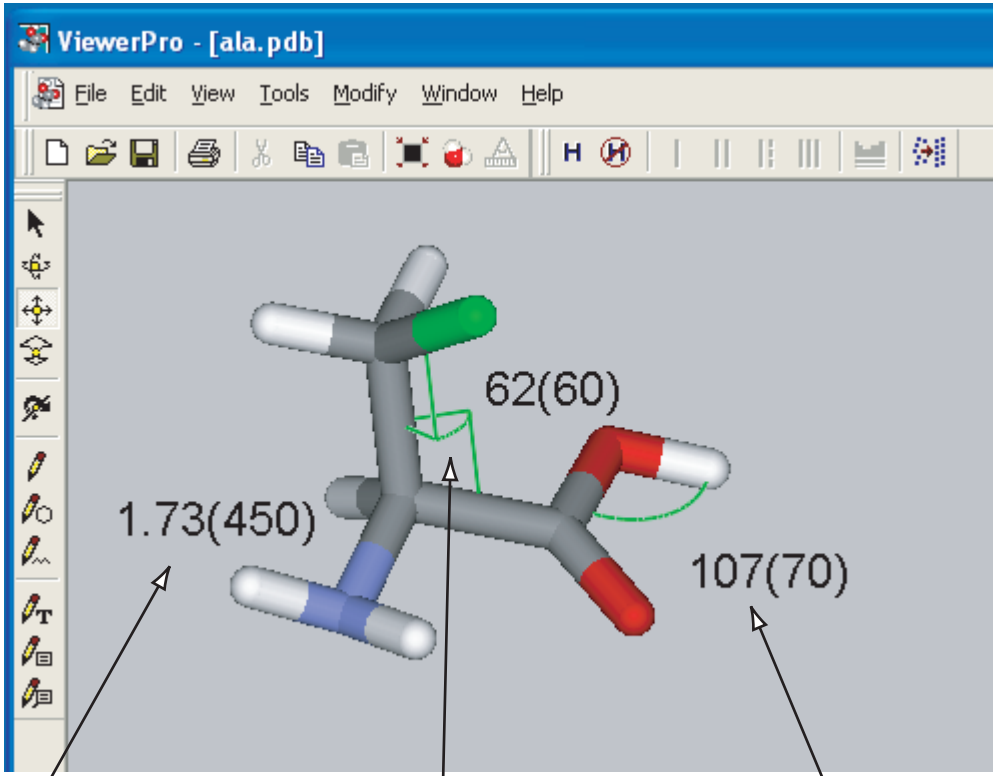
June 2006



MM parameters

Bonded parameters are related to bonding interactions between atoms

- Stretching
- Bending
- Torsion



Distance (force constant)

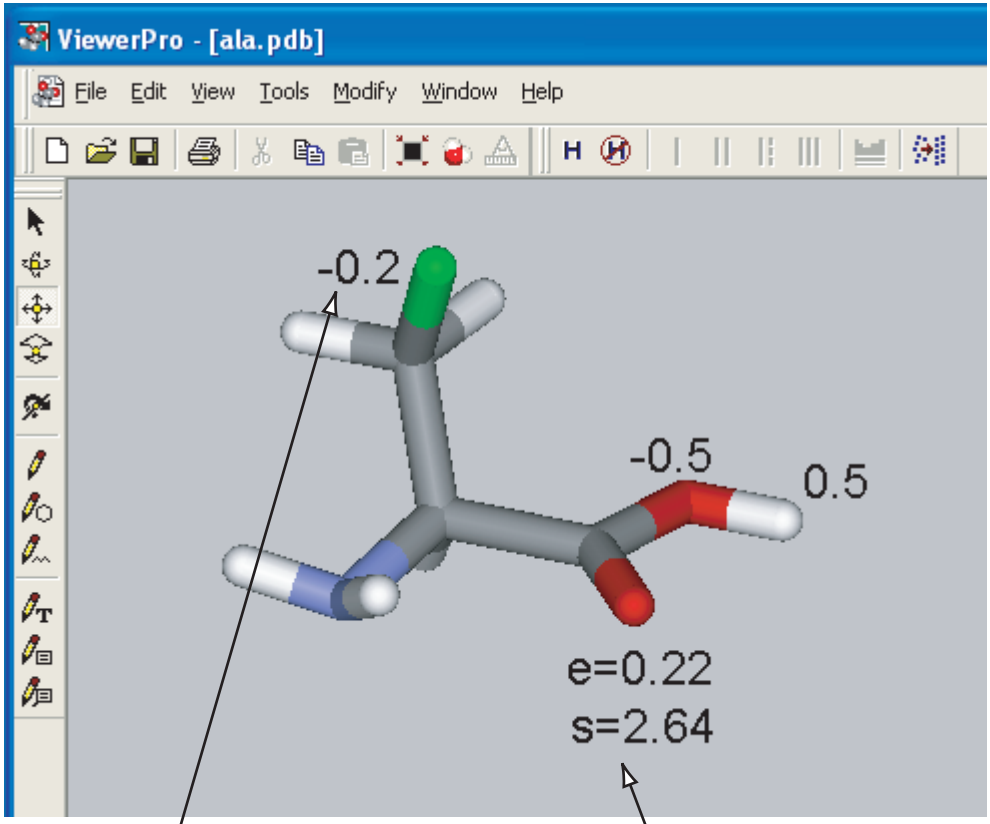
Torsion (force constant)

Angle (force constant)

MM parameters

Non-bonded parameters are related to non-bonding interactions between atoms:

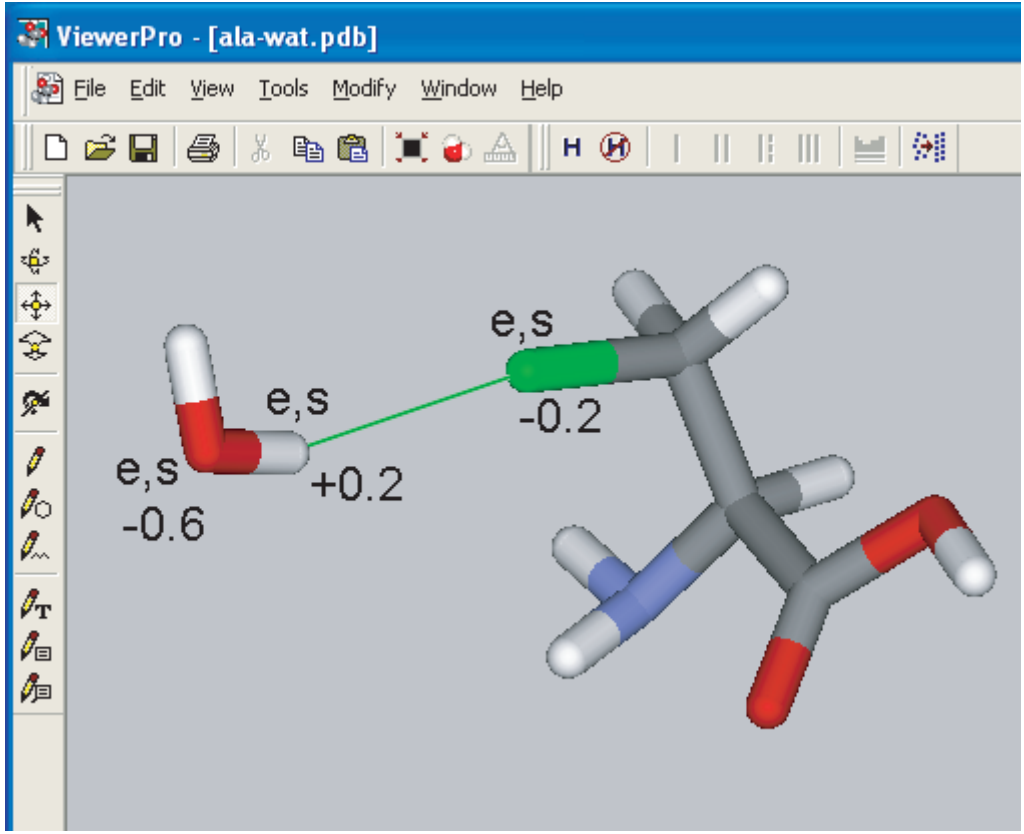
- Electrostatic
- Steric



MM parameters

Hydrogen bonding interactions are combination of

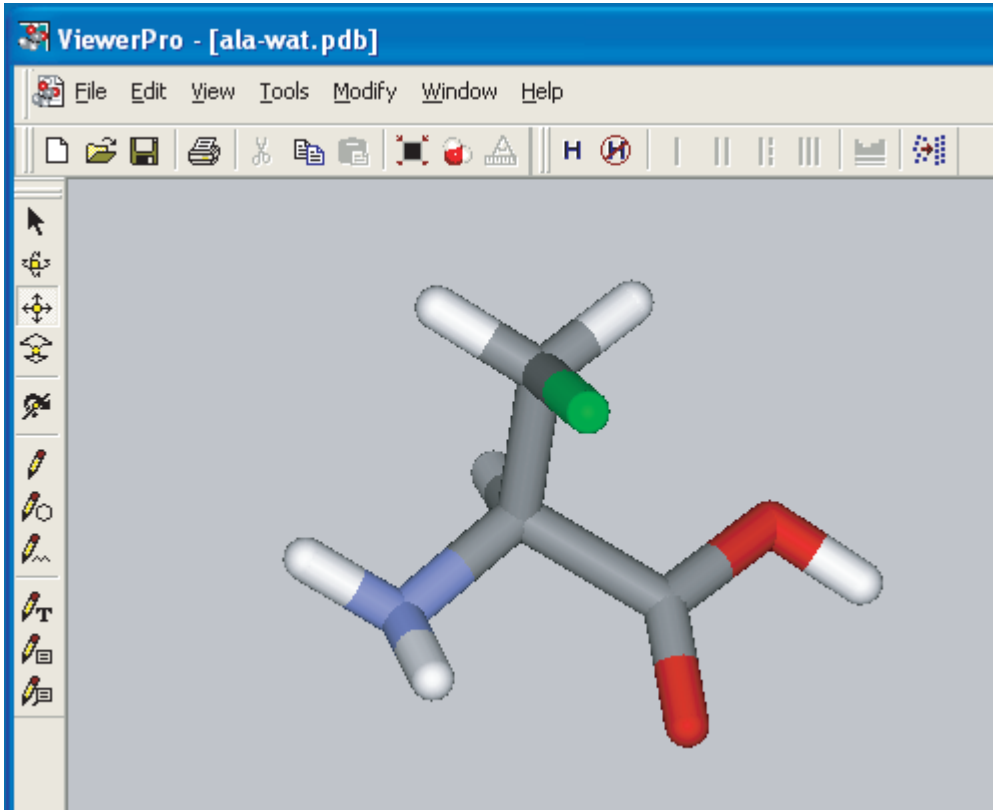
- Electrostatic
- Steric



MM parameters

Three methods
of evaluation
MM parameters

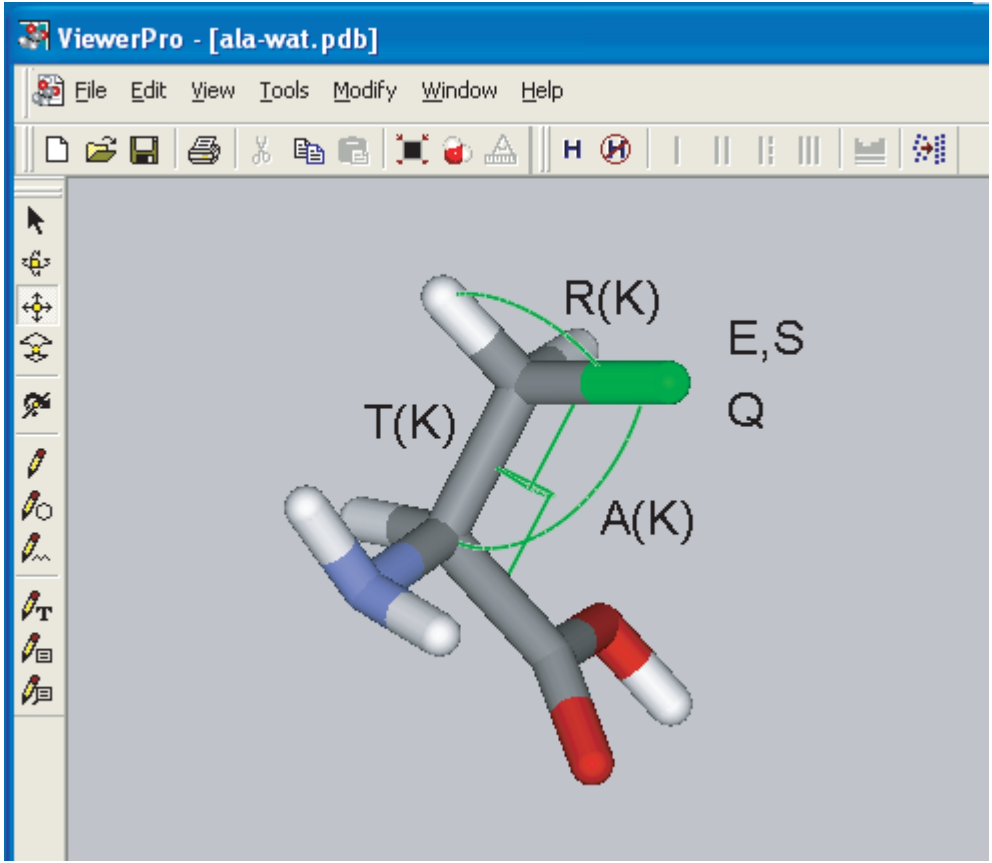
- QM calculations
- Experiment
- Analogy



MM parameters (Chloro-alanine)

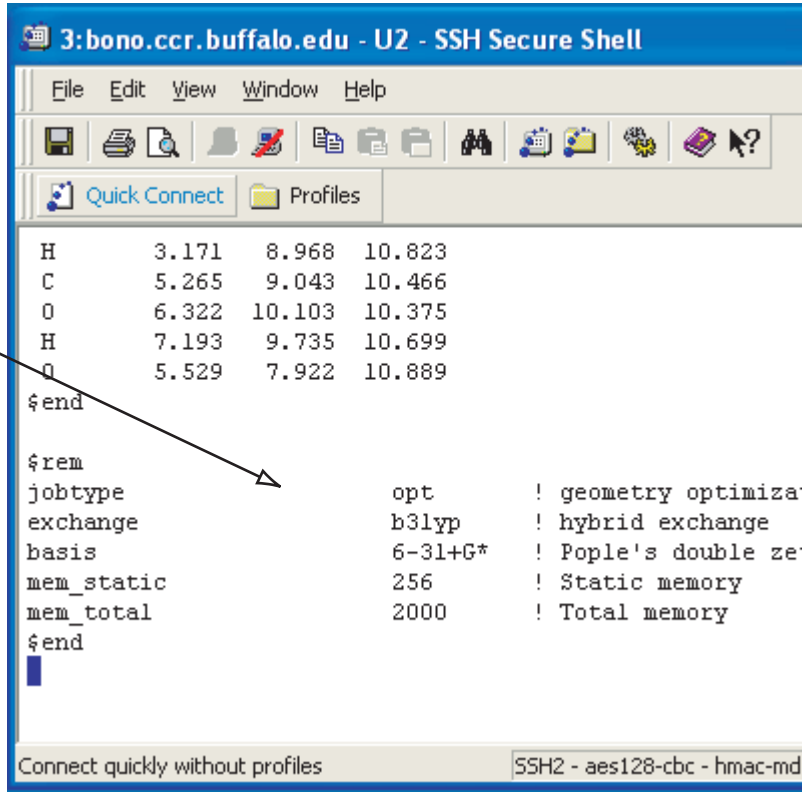
New atom

- Distances (Cons.)
- Angles (Const.)
- Torsions (Const.)
- Charge
- Van der Waals



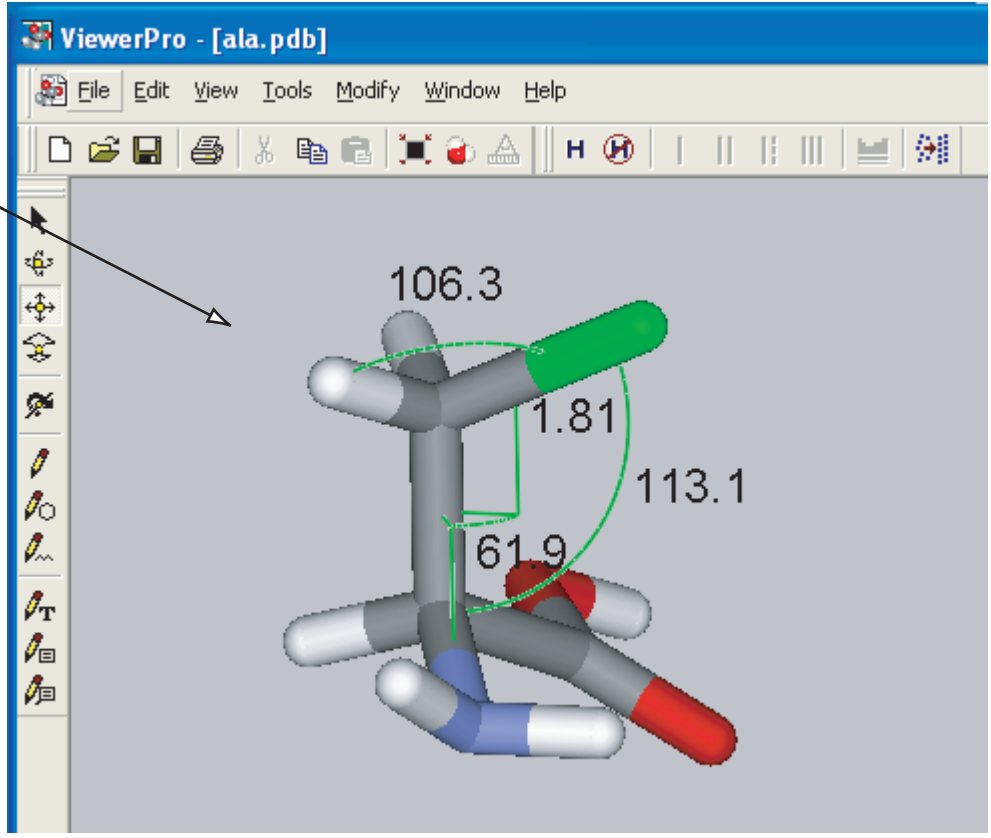
MM parameters (Chloro-alanine)

QM geometry optimization of the molecule in the gas phase



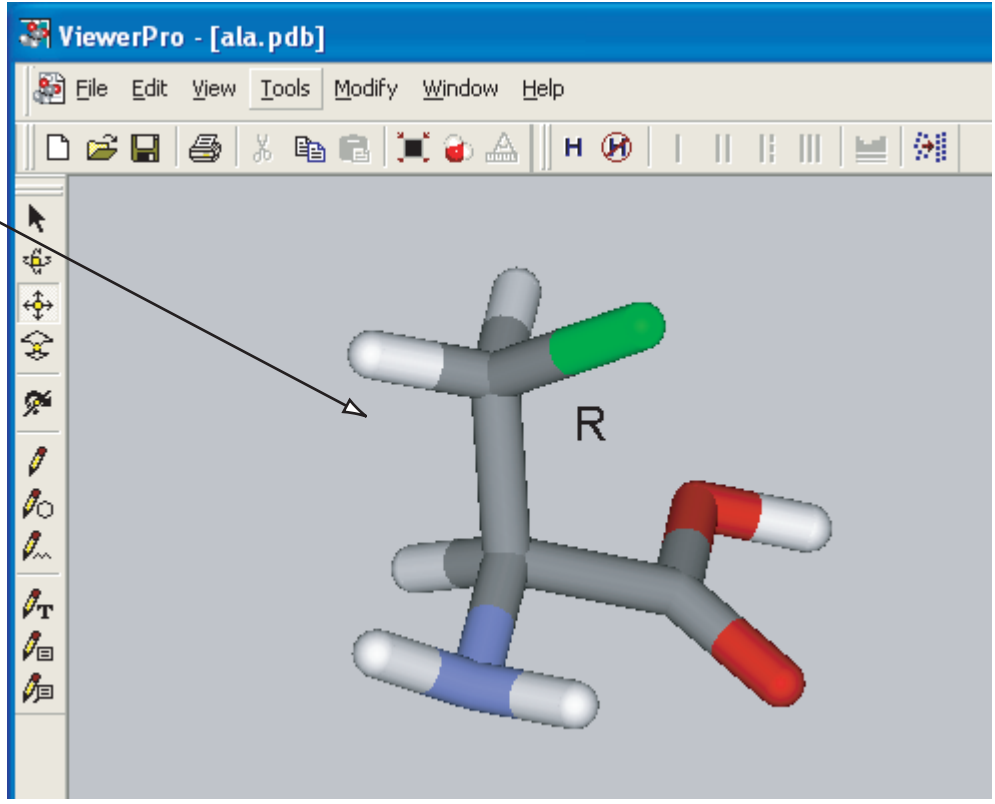
MM parameters (Chloro-alanine)

Results of the calculations



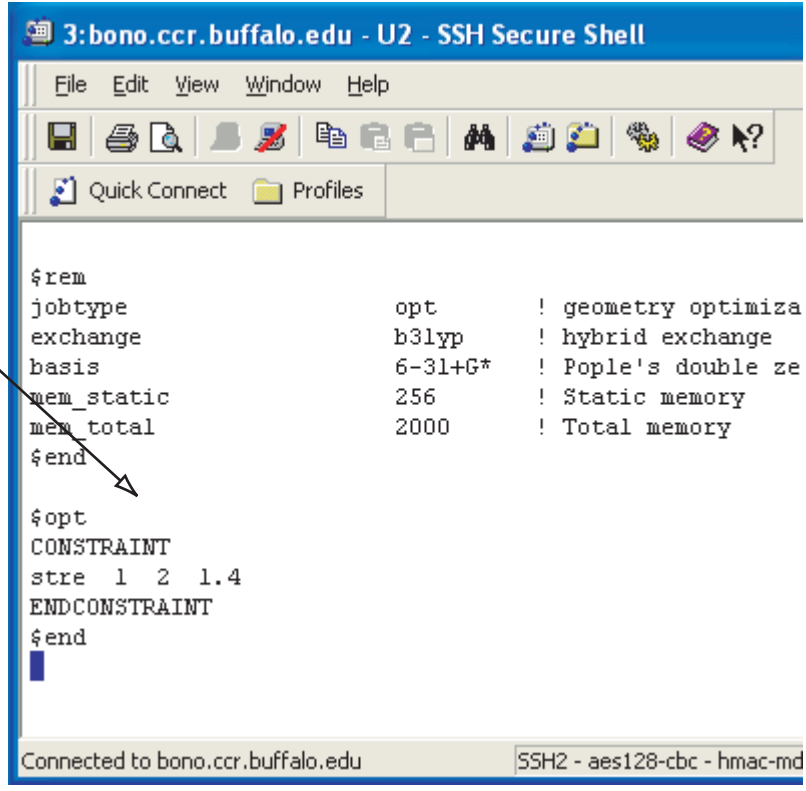
MM parameters (Chloro-alanine)

Calculations of the optimal geometry with a fixed interatomic distance



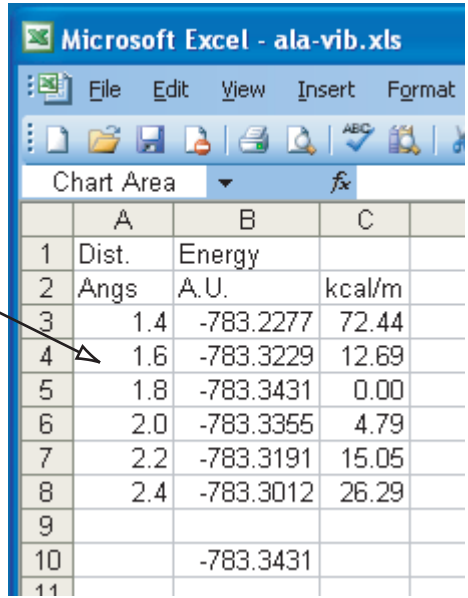
MM parameters (Chloro-alanine)

Constrined interatomic distance



MM parameters (Chloro-alanine)

Results of the calculations



Microsoft Excel - ala-vib.xls

File Edit View Insert Format

Chart Area

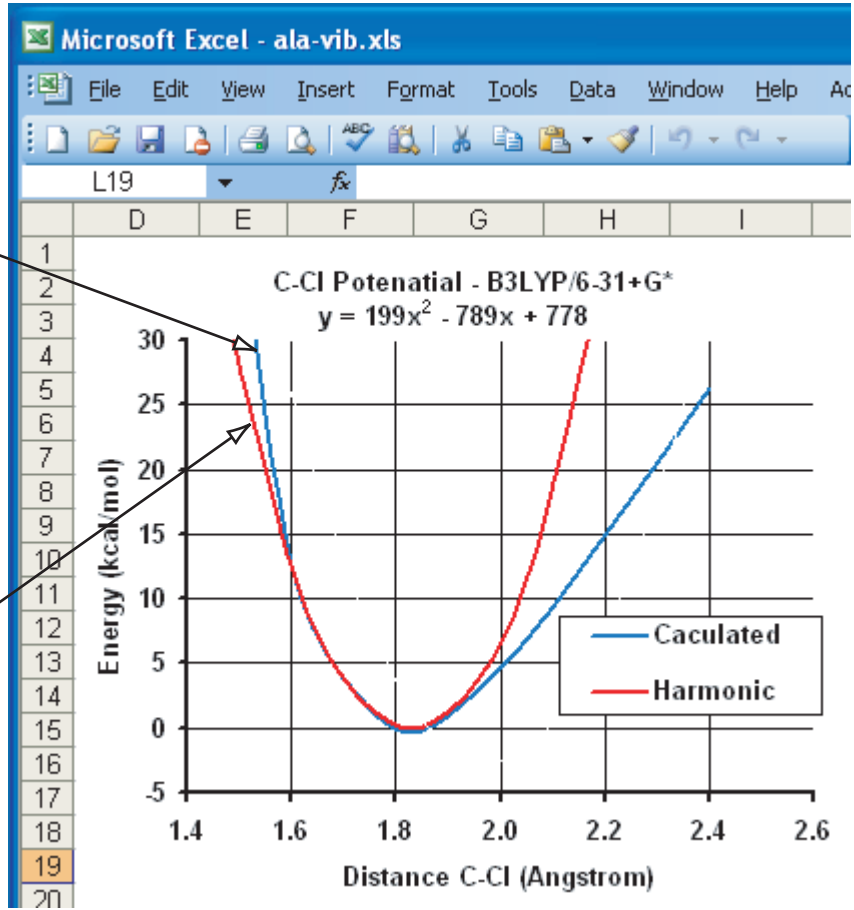
	A	B	C
1	Dist.	Energy	
2	Angs	A.U.	kcal/m
3	1.4	-783.2277	72.44
4	1.6	-783.3229	12.69
5	1.8	-783.3431	0.00
6	2.0	-783.3355	4.79
7	2.2	-783.3191	15.05
8	2.4	-783.3012	26.29
9			
10		-783.3431	

MM parameters (Chloro-alanine)

Potential energy surface of the C-Cl stretching

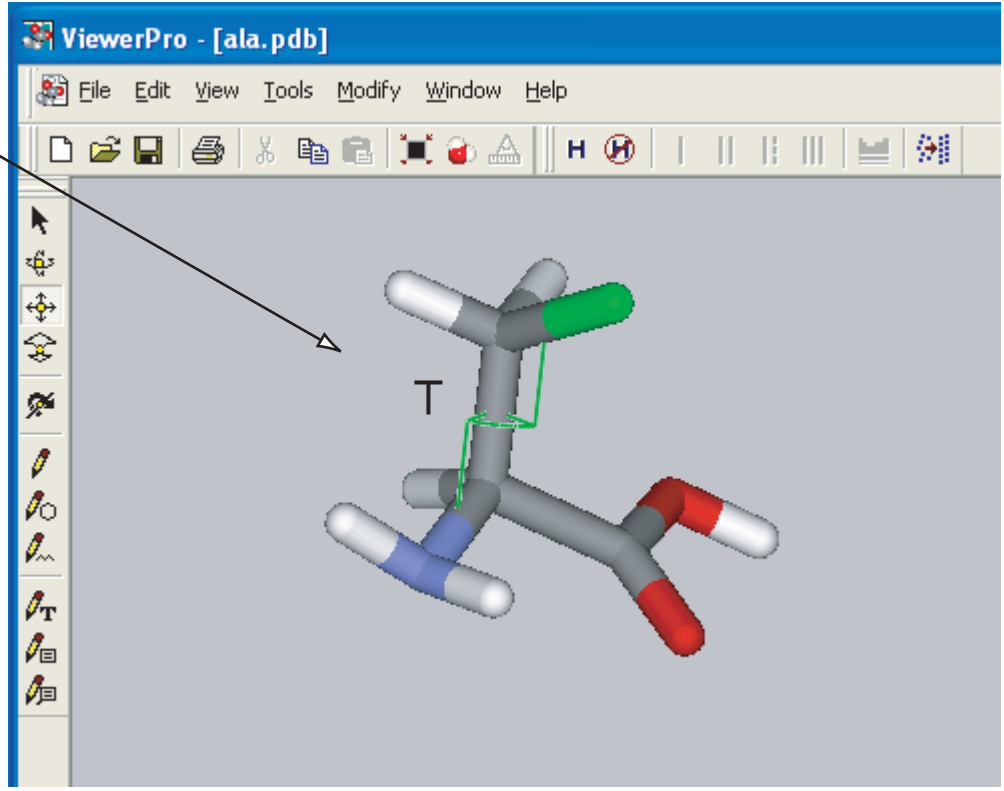
Harmonic approximation:

$$E = \frac{1}{2} K (q - q_0)^2$$



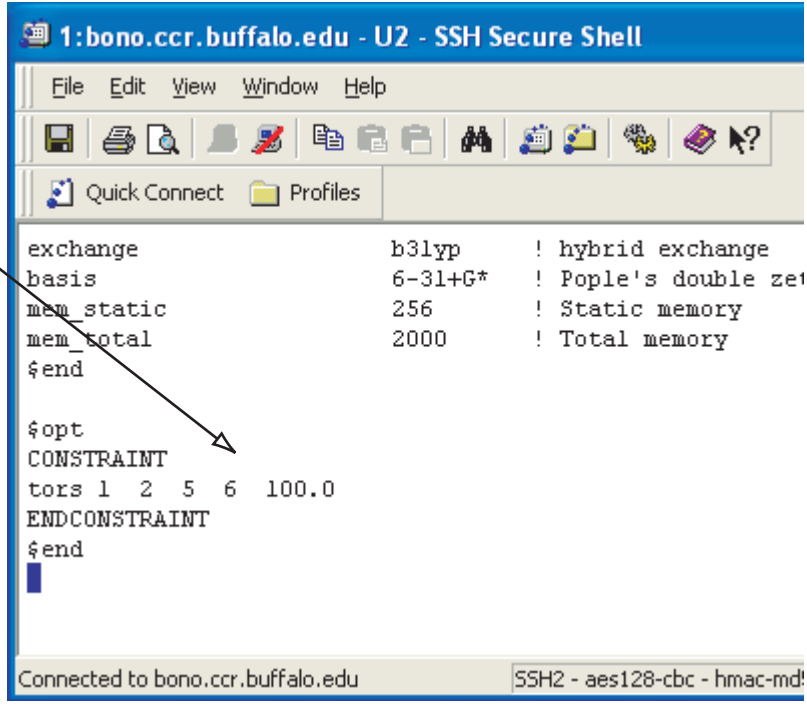
MM parameters (Chloro-alanine)

Geometry optimization with a constrined torsion angle



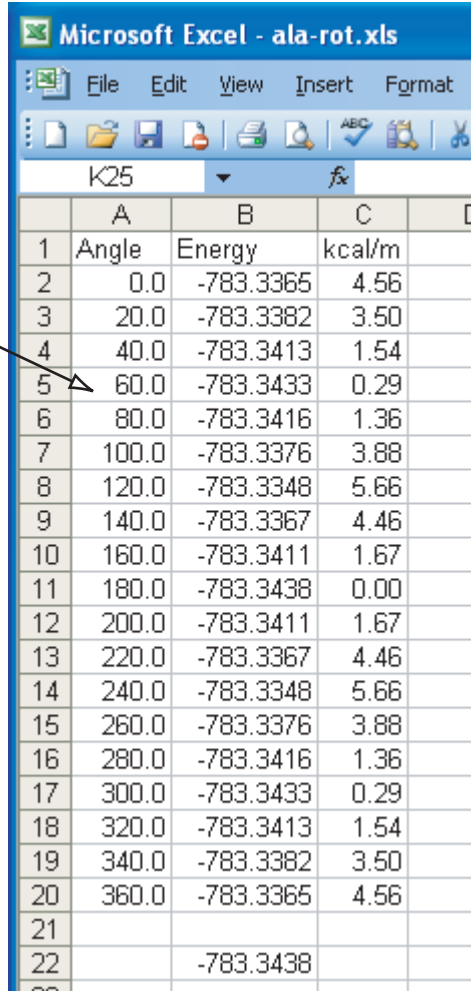
MM parameters (Chloro-alanine)

Geometry optimization with a constrined torsion angle



MM parameters (Chloro-alanine)

Results of the calculations



Microsoft Excel - ala-rot.xls

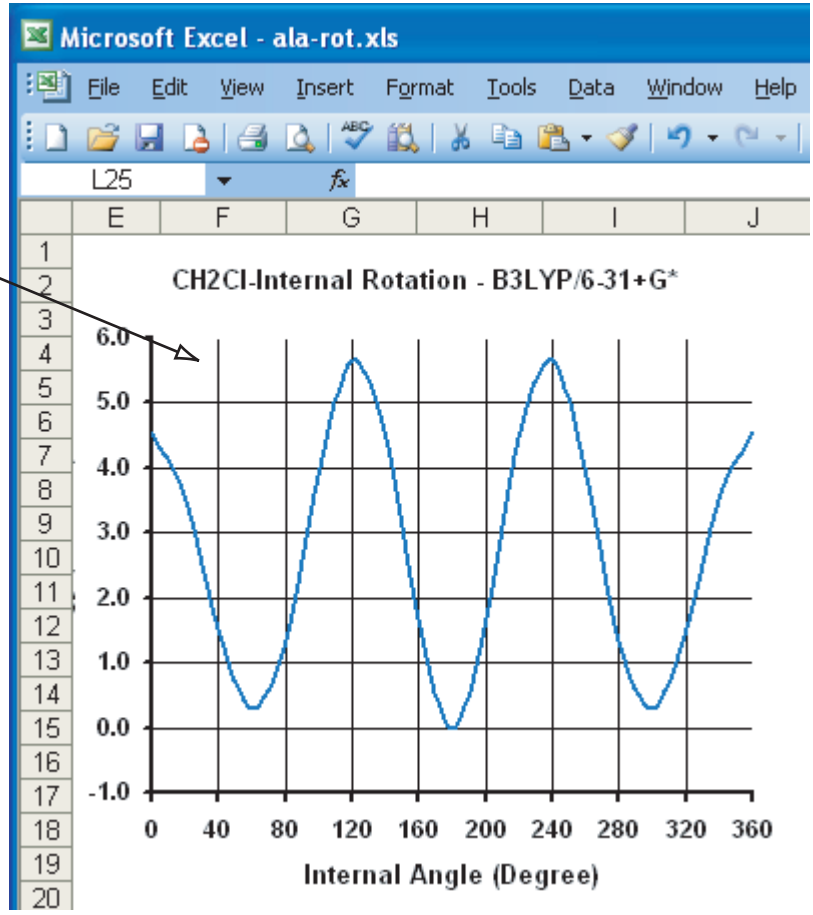
File Edit View Insert Format

K25

	A	B	C
1	Angle	Energy	kcal/m
2	0.0	-783.3365	4.56
3	20.0	-783.3382	3.50
4	40.0	-783.3413	1.54
5	60.0	-783.3433	0.29
6	80.0	-783.3416	1.36
7	100.0	-783.3376	3.88
8	120.0	-783.3348	5.66
9	140.0	-783.3367	4.46
10	160.0	-783.3411	1.67
11	180.0	-783.3438	0.00
12	200.0	-783.3411	1.67
13	220.0	-783.3367	4.46
14	240.0	-783.3348	5.66
15	260.0	-783.3376	3.88
16	280.0	-783.3416	1.36
17	300.0	-783.3433	0.29
18	320.0	-783.3413	1.54
19	340.0	-783.3382	3.50
20	360.0	-783.3365	4.56
21			
22		-783.3438	

MM parameters (Chloro-alanine)

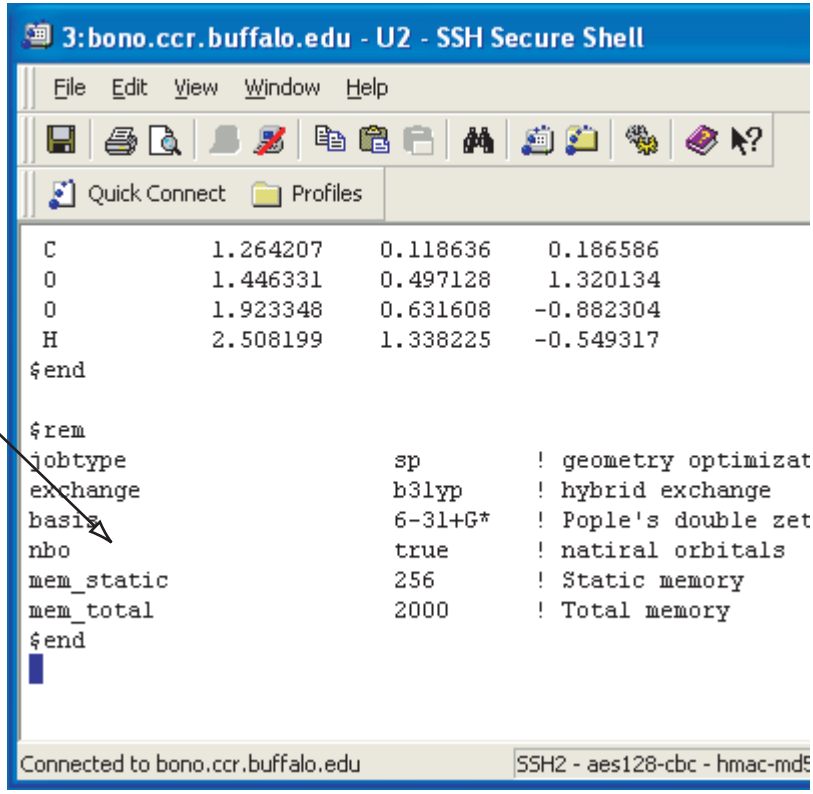
Potential energy surface of the internal rotation



- Angle at the minimum
- Energy at the maximum
- Number of maxima

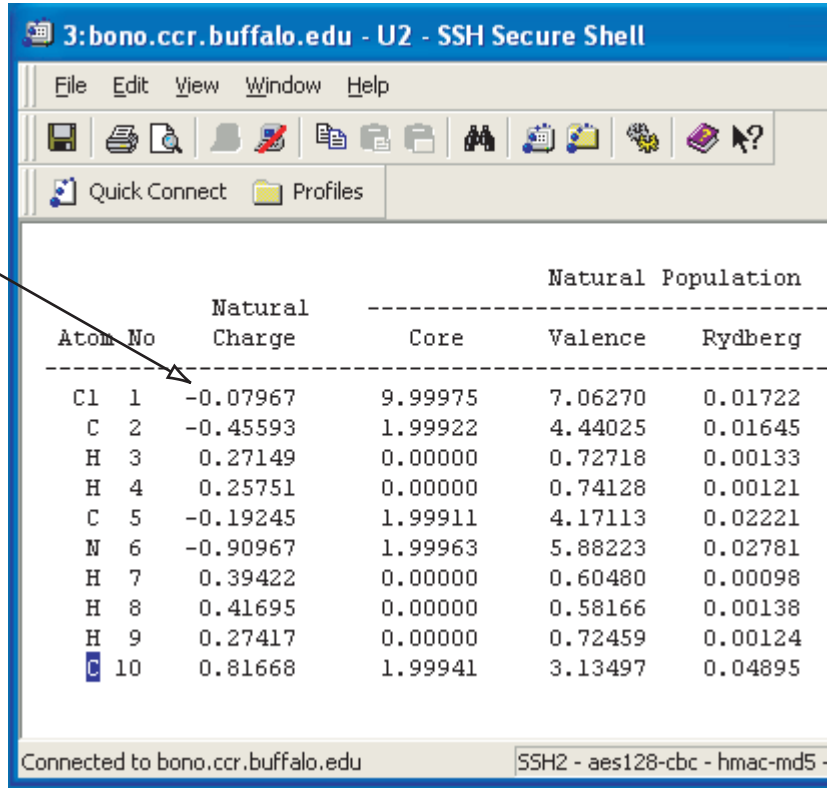
MM parameters (Chloro-alanine)

Calculations of natural orbitals



MM parameters (Chloro-alanine)

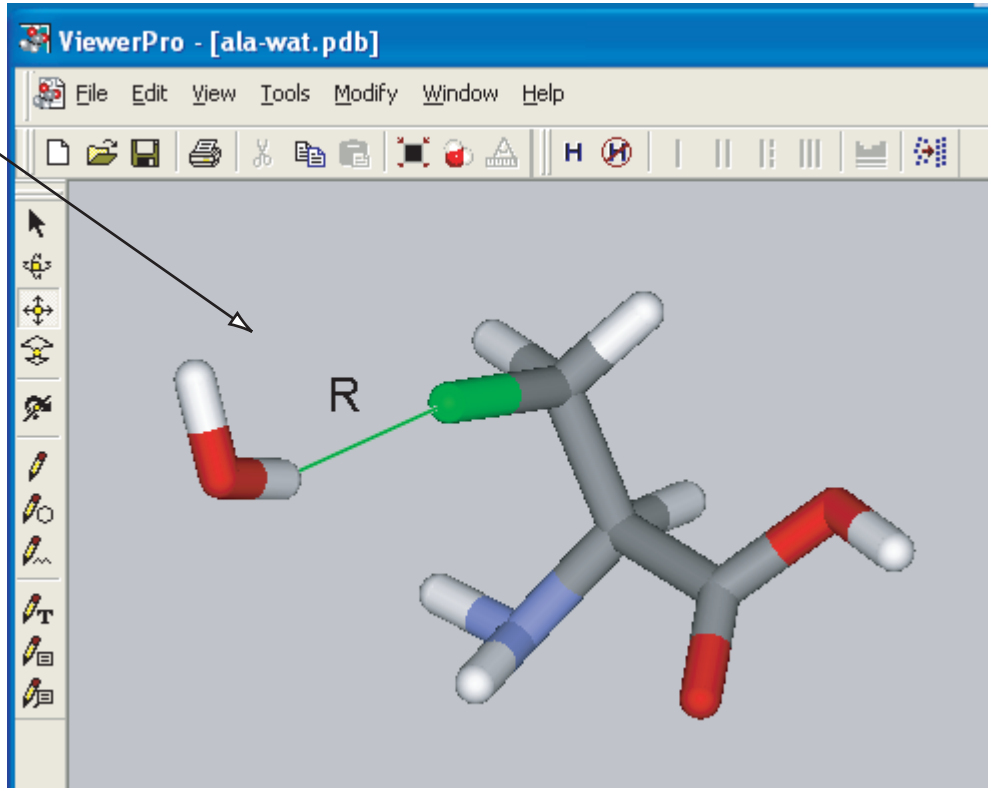
Atomic charges calculated using natural orbitals



Atom	No	Natural Charge	Natural Population: Core	Valence	Rydberg
Cl	1	-0.07967	9.99975	7.06270	0.01722
C	2	-0.45593	1.99922	4.44025	0.01645
H	3	0.27149	0.00000	0.72718	0.00133
H	4	0.25751	0.00000	0.74128	0.00121
C	5	-0.19245	1.99911	4.17113	0.02221
N	6	-0.90967	1.99963	5.88223	0.02781
H	7	0.39422	0.00000	0.60480	0.00098
H	8	0.41695	0.00000	0.58166	0.00138
H	9	0.27417	0.00000	0.72459	0.00124
O	10	0.81668	1.99941	3.13497	0.04895

MM parameters (Chloro-alanine)

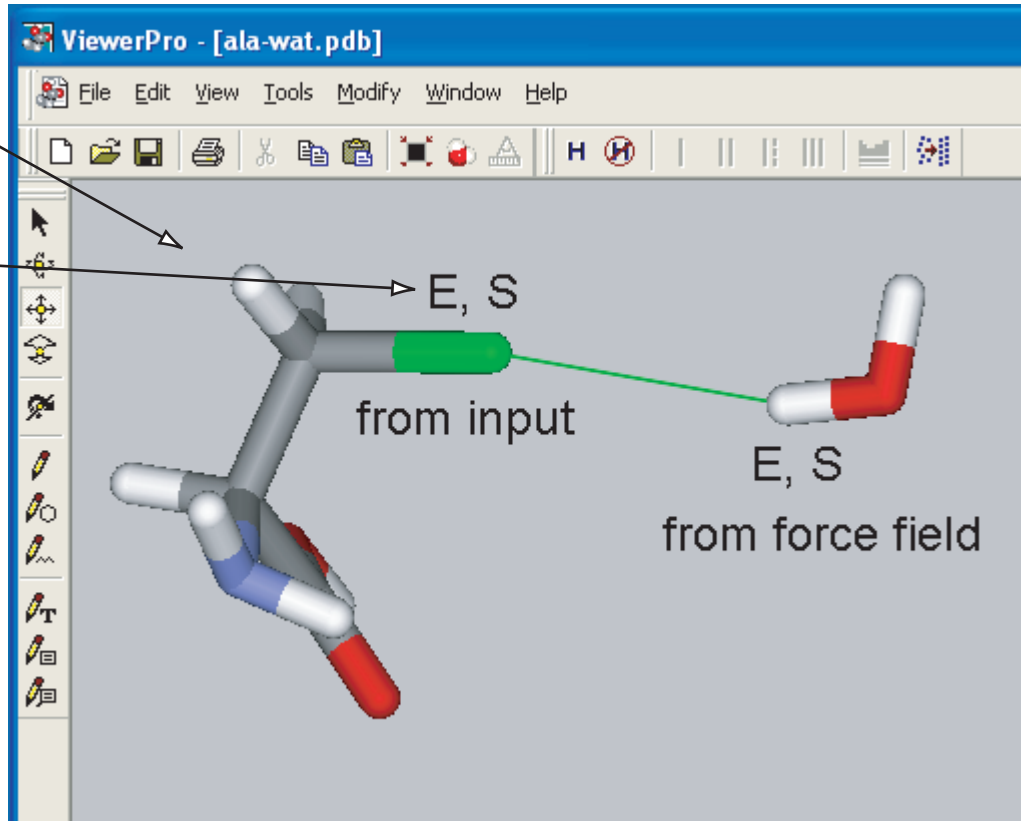
QM calculations of a dimer with a water molecule



MM parameters (Chloro-alanine)

Geometry optimization using the MM method

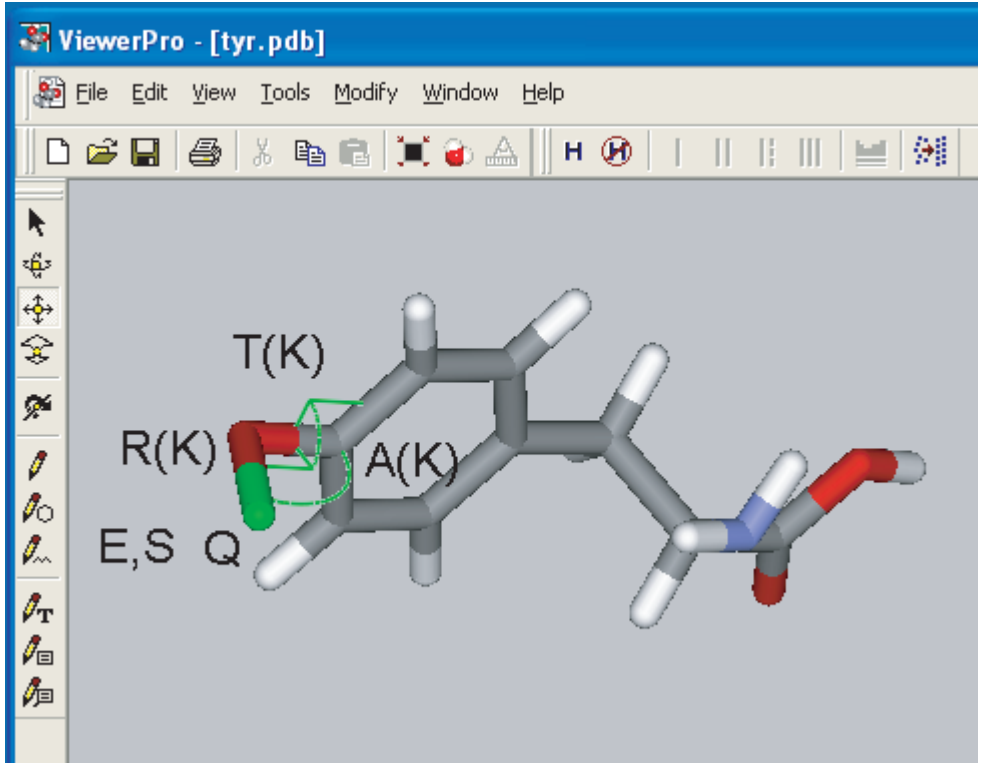
E and S parameters for Chlorine are modified in order to have the same geometry of the dimer as from the QM calculations



MM parameters (Chloro-tyrosine)

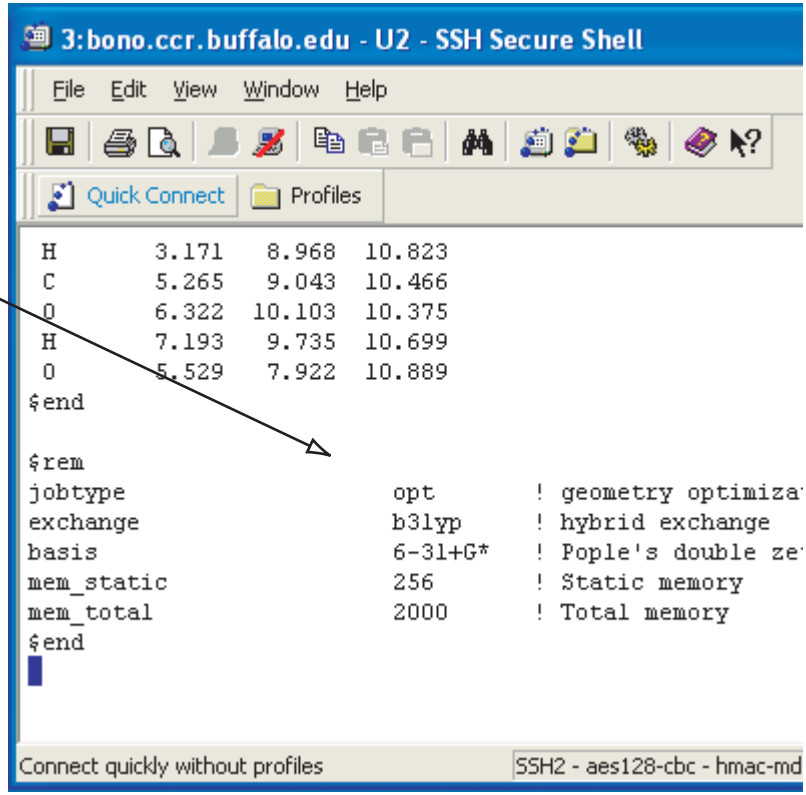
New atom

- Distance (Cons.)
- Angle (Const.)
- Torsion (Const.)
- Charge
- Van der Waals



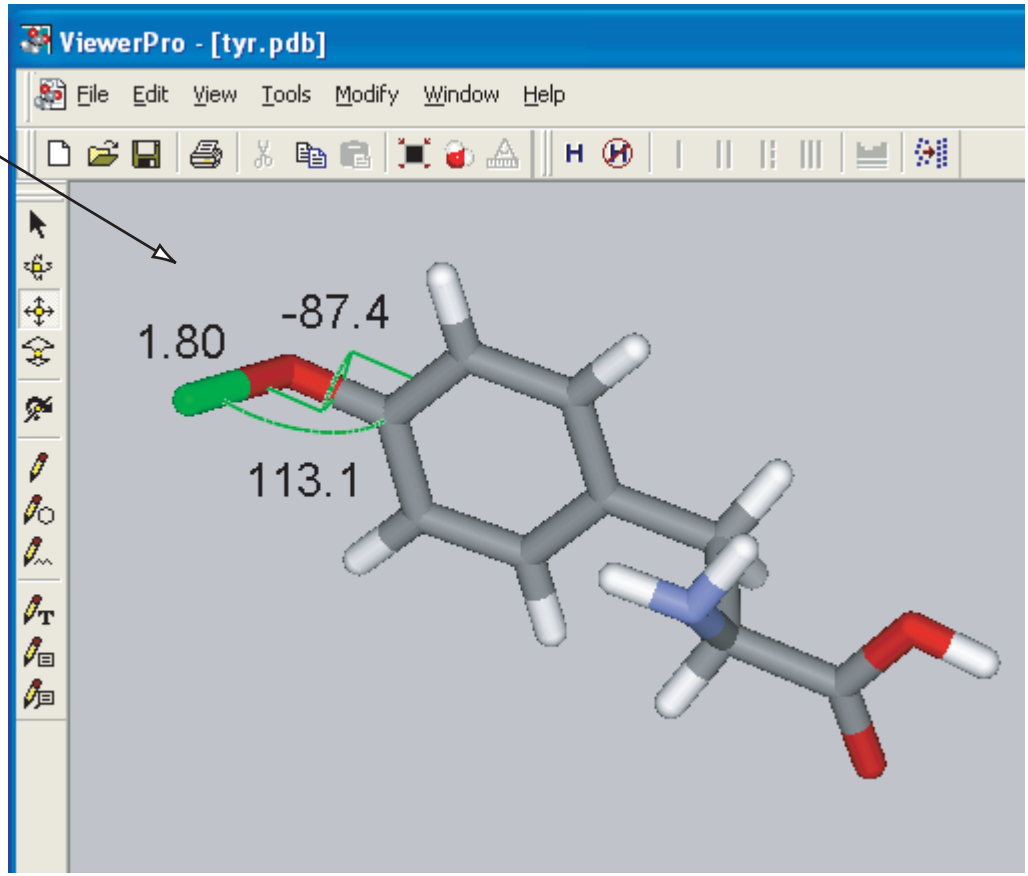
MM parameters (Chloro-tyrosine)

QM geometry optimization of the molecule in the gas phase



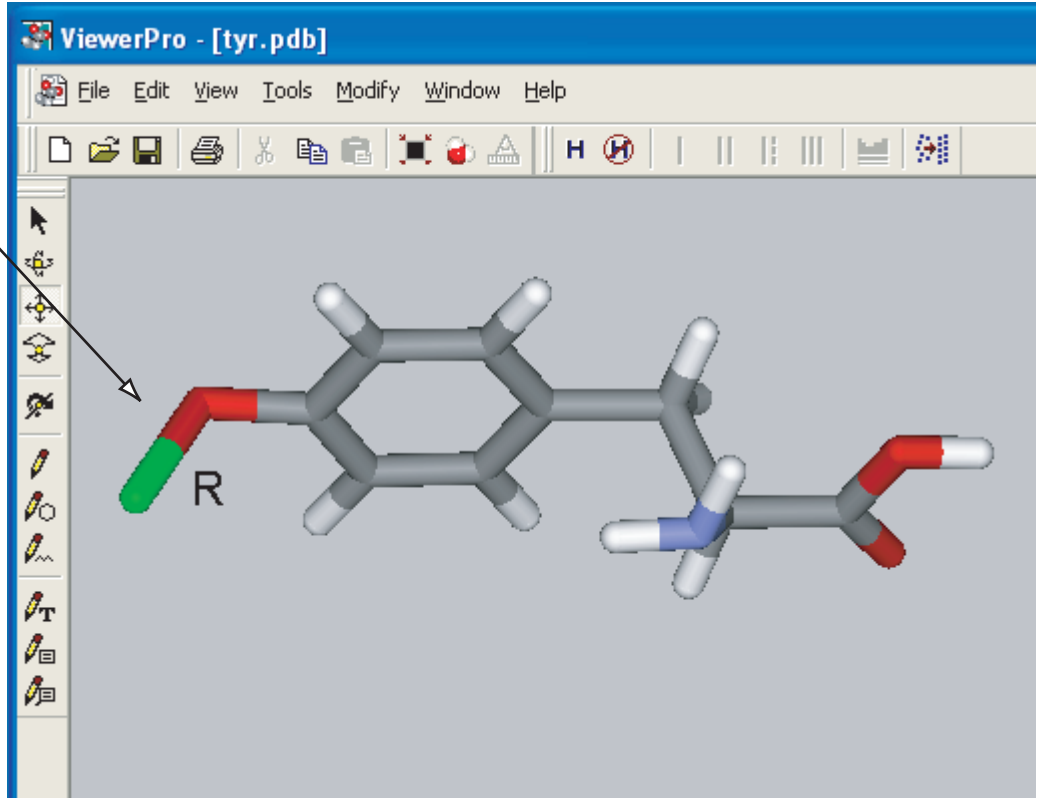
MM parameters (Chloro-tyrosine)

Results of the calculations



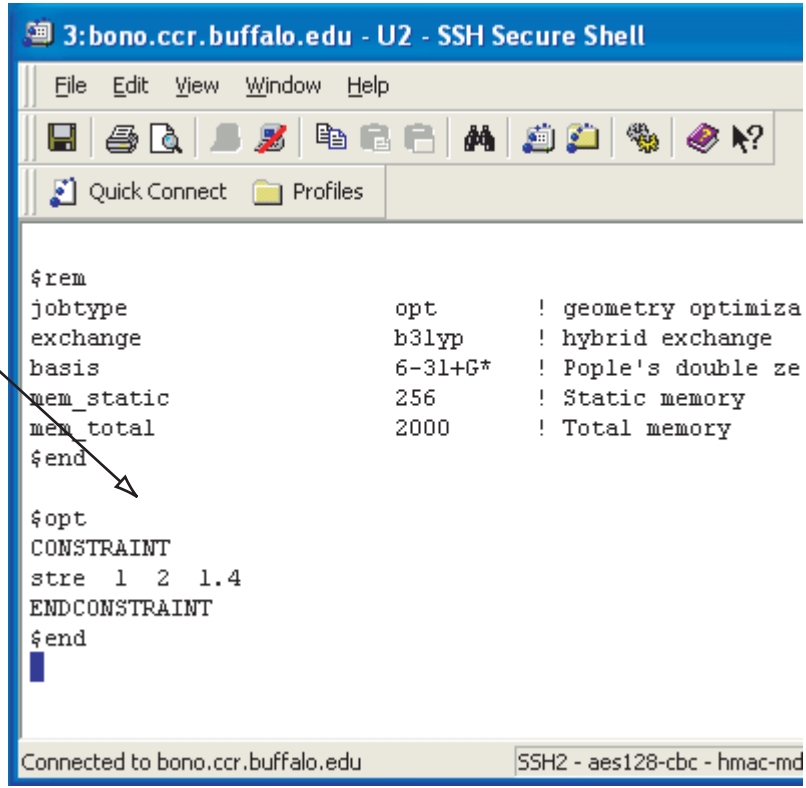
MM parameters (Chloro-tyrosine)

Calculations of the optimal geometry with a fixed interatomic distance



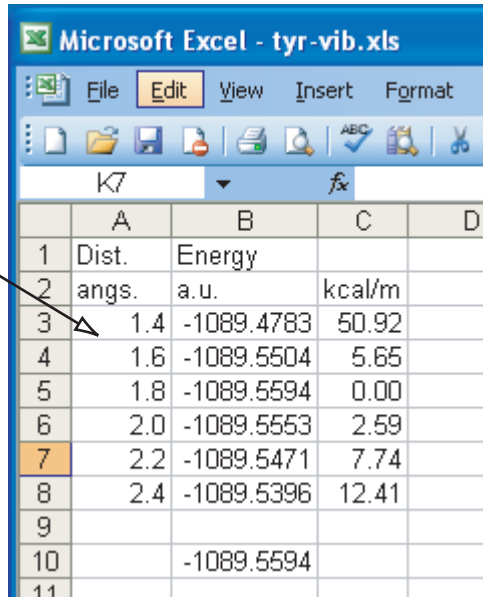
MM parameters (Chloro-tyrosine)

Constrined interatomic distance



MM parameters (Chloro-tyrosine)

Results of the calculations



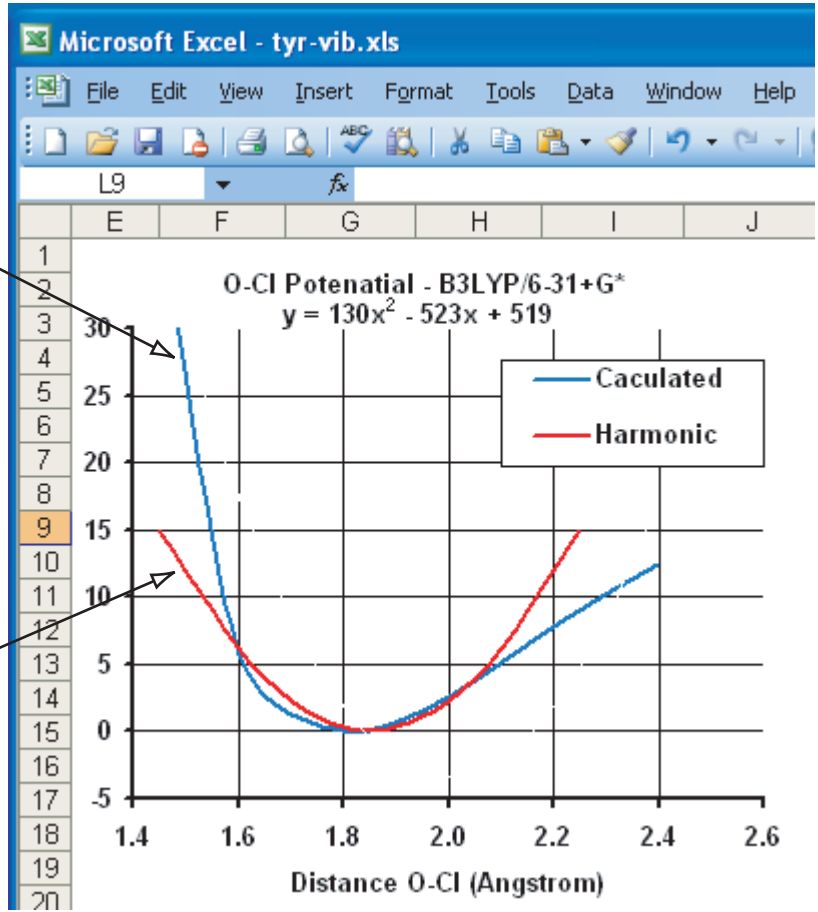
	A	B	C	D
1	Dist.	Energy		
2	angs.	a.u.	kcal/m	
3	1.4	-1089.4783	50.92	
4	1.6	-1089.5504	5.65	
5	1.8	-1089.5594	0.00	
6	2.0	-1089.5553	2.59	
7	2.2	-1089.5471	7.74	
8	2.4	-1089.5396	12.41	
9				
10		-1089.5594		
11				

MM parameters (Chloro-tyrosine)

Potential energy surface of the O-Cl stretching

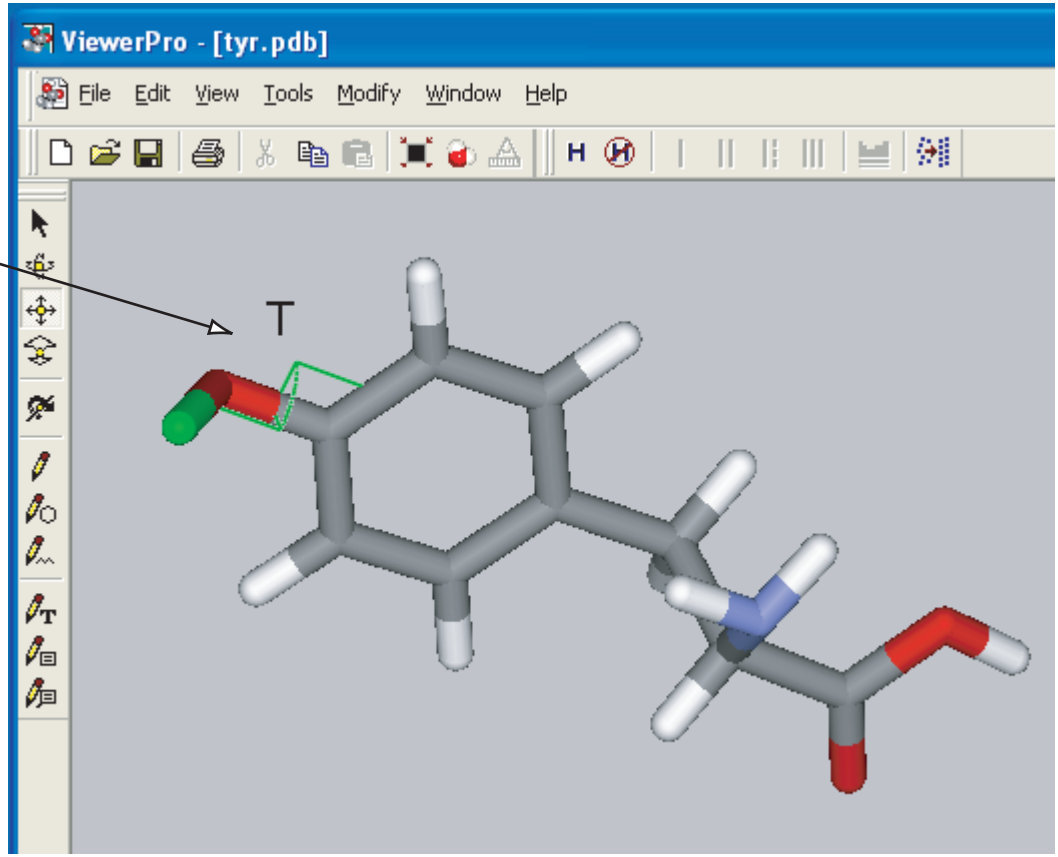
Harmonic approximation:

$$E = \frac{1}{2} K (q - q_0)^2$$



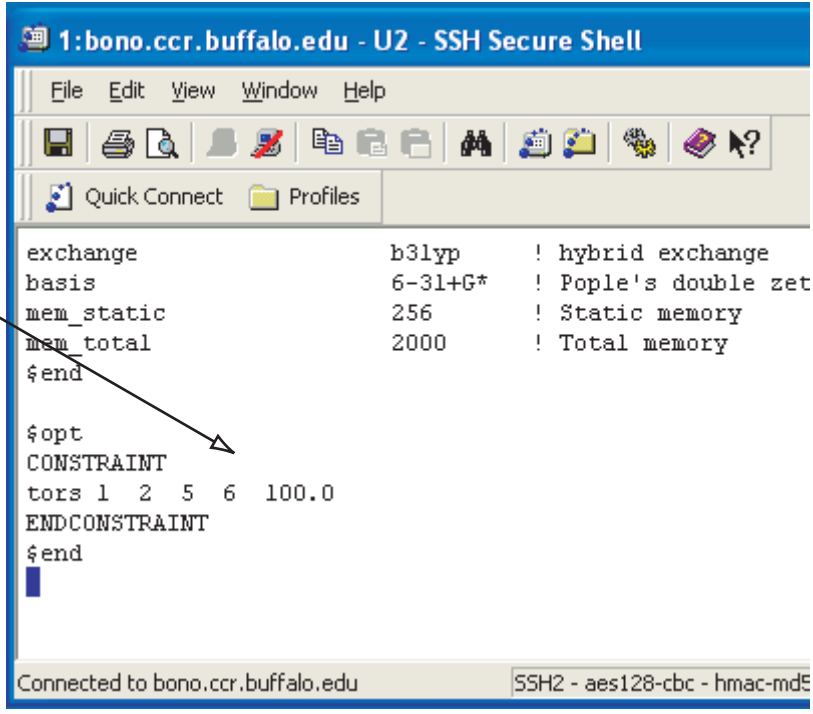
MM parameters (Chloro-tyrosine)

Geometry optimization with a constrined torsion angle



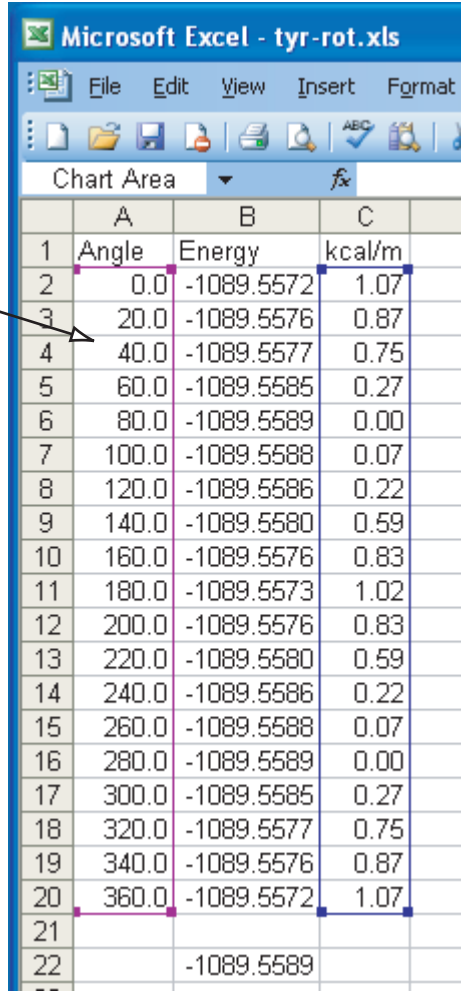
MM parameters (Chloro-tyrosine)

Geometry optimization with a constrined torsion angle



MM parameters (Chloro-tyrosine)

Results of the calculations



Microsoft Excel - tyr-rot.xls

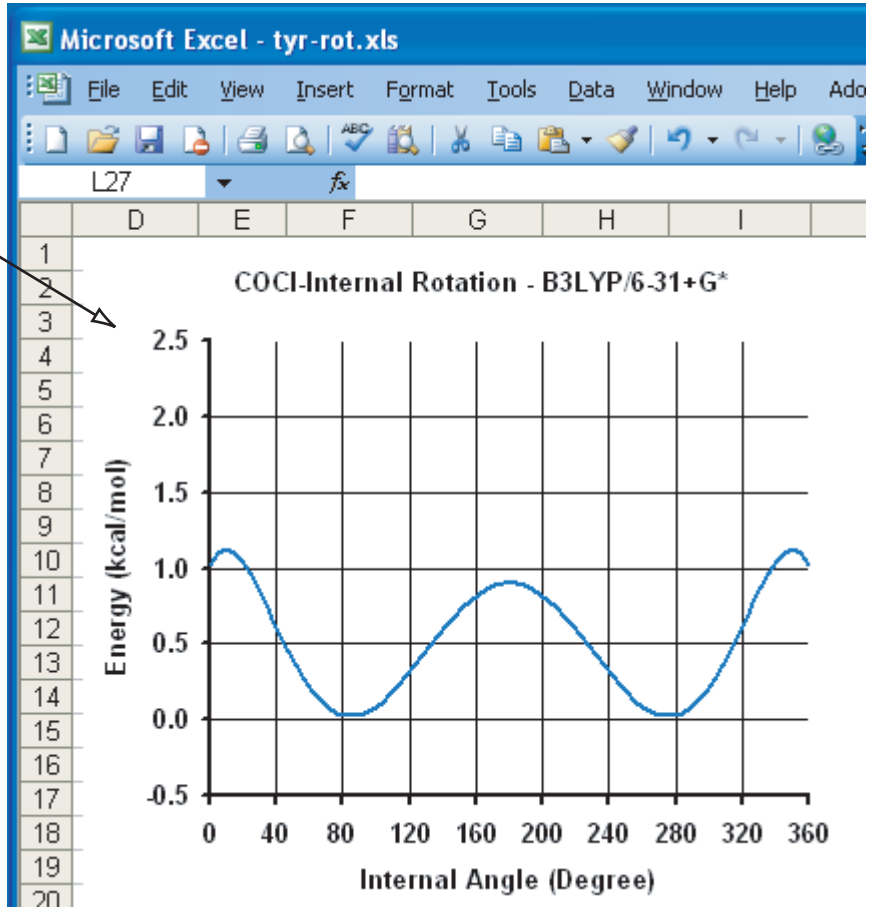
File Edit View Insert Format

Chart Area

	A	B	C
1	Angle	Energy	kcal/m
2	0.0	-1089.5572	1.07
3	20.0	-1089.5576	0.87
4	40.0	-1089.5577	0.75
5	60.0	-1089.5585	0.27
6	80.0	-1089.5589	0.00
7	100.0	-1089.5588	0.07
8	120.0	-1089.5586	0.22
9	140.0	-1089.5580	0.59
10	160.0	-1089.5576	0.83
11	180.0	-1089.5573	1.02
12	200.0	-1089.5576	0.83
13	220.0	-1089.5580	0.59
14	240.0	-1089.5586	0.22
15	260.0	-1089.5588	0.07
16	280.0	-1089.5589	0.00
17	300.0	-1089.5585	0.27
18	320.0	-1089.5577	0.75
19	340.0	-1089.5576	0.87
20	360.0	-1089.5572	1.07
21			
22		-1089.5589	

MM parameters (Chloro-tyrosine)

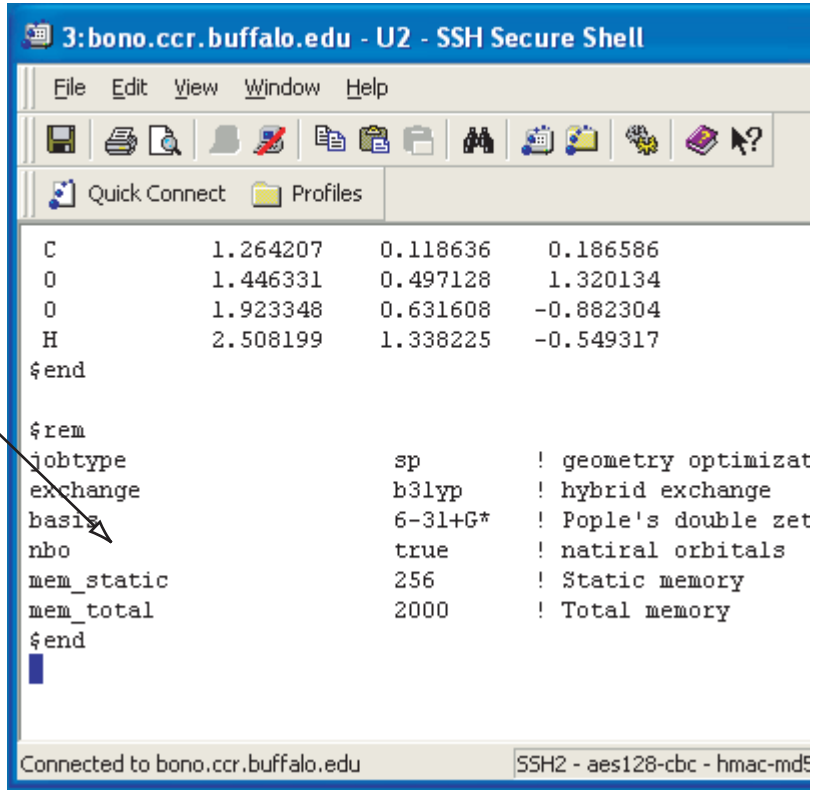
Potential energy surface of the internal rotation



- Angle at the minimum
- Energy at the maximum
- Number of maxima

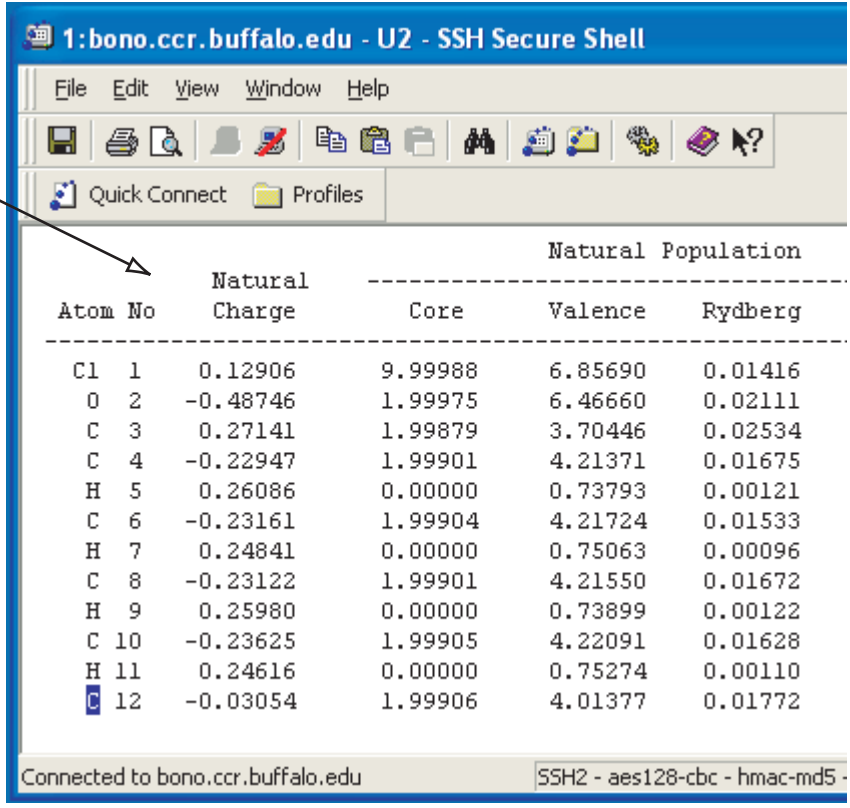
MM parameters (Chloro-tyrosine)

Calculations of natural orbitals



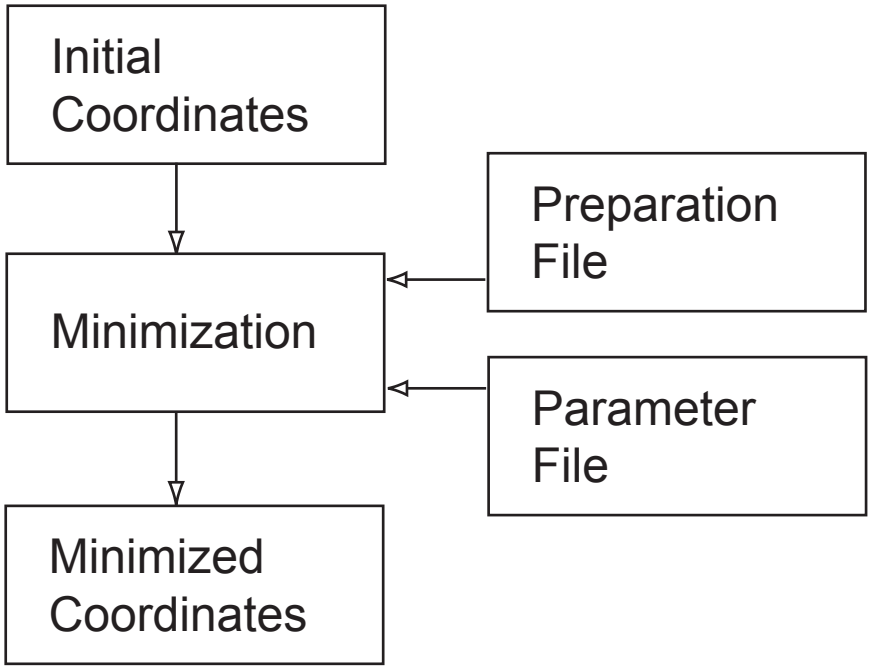
MM parameters (Chloro-tyrosine)

Atomic charges calculated using natural orbitals



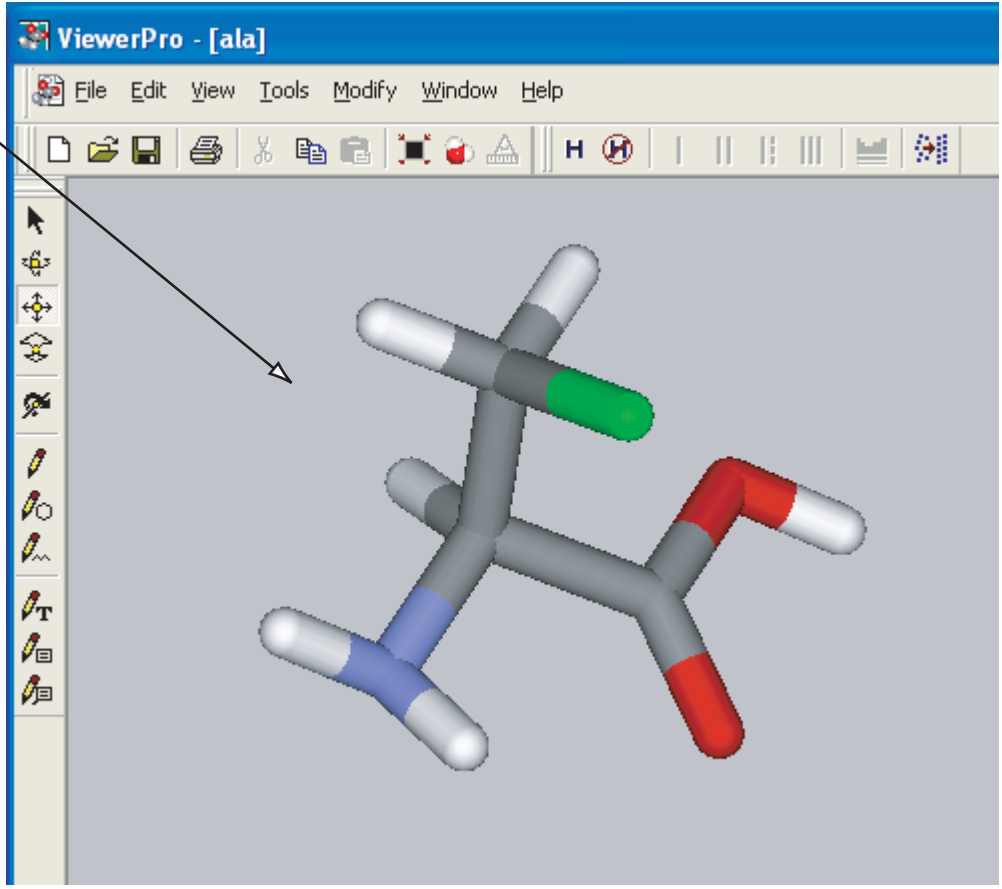
MM minimization of amino acids and base pairs

MM minimization requires two files: preparation and parameters files for each molecule (amino acid)



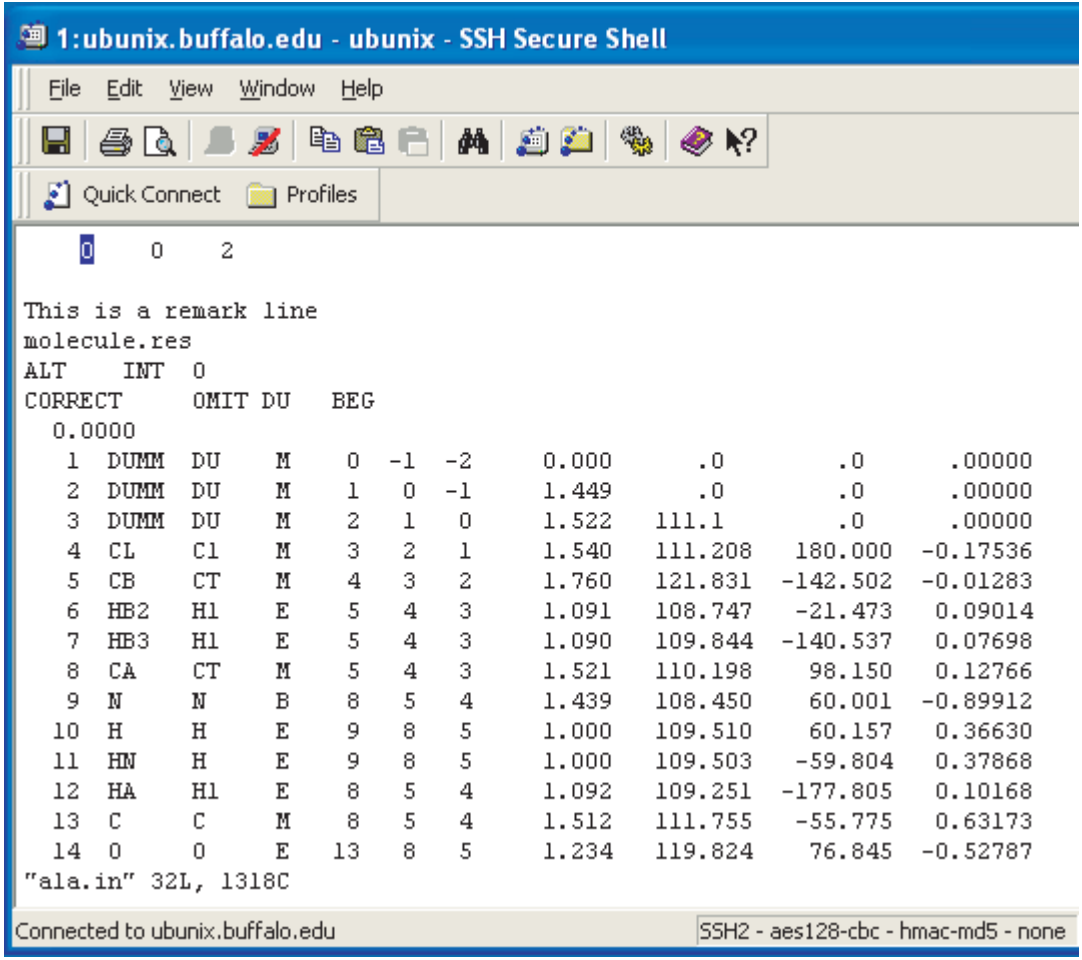
MM minimization of Chloro-alanine

Chloro-alanine



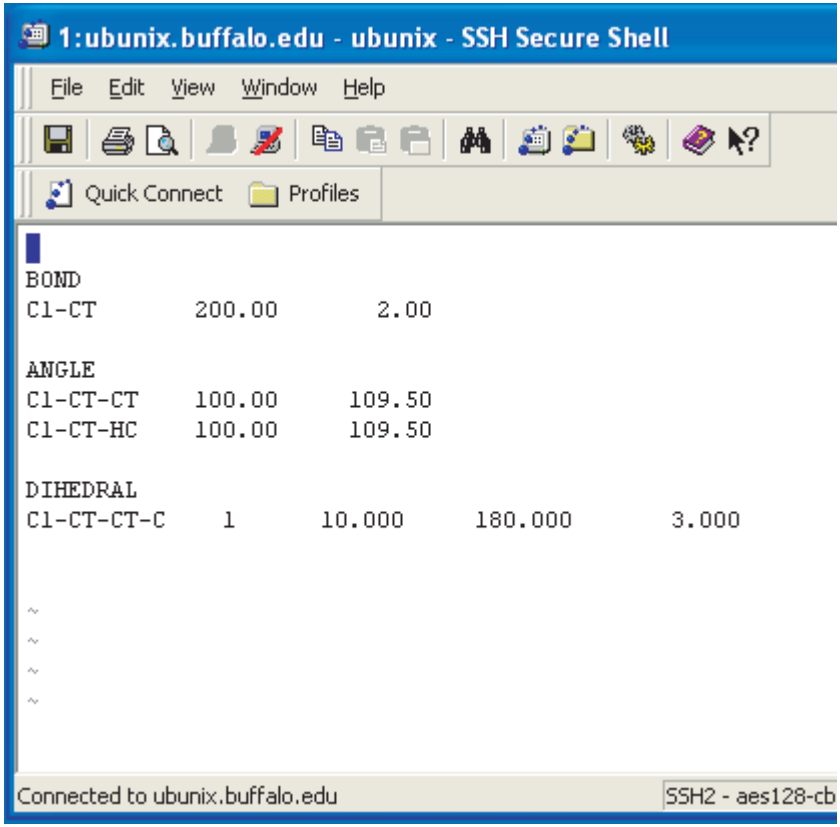
MM minimization of Chloro-alanine

Preparation file of Chloro-alanine



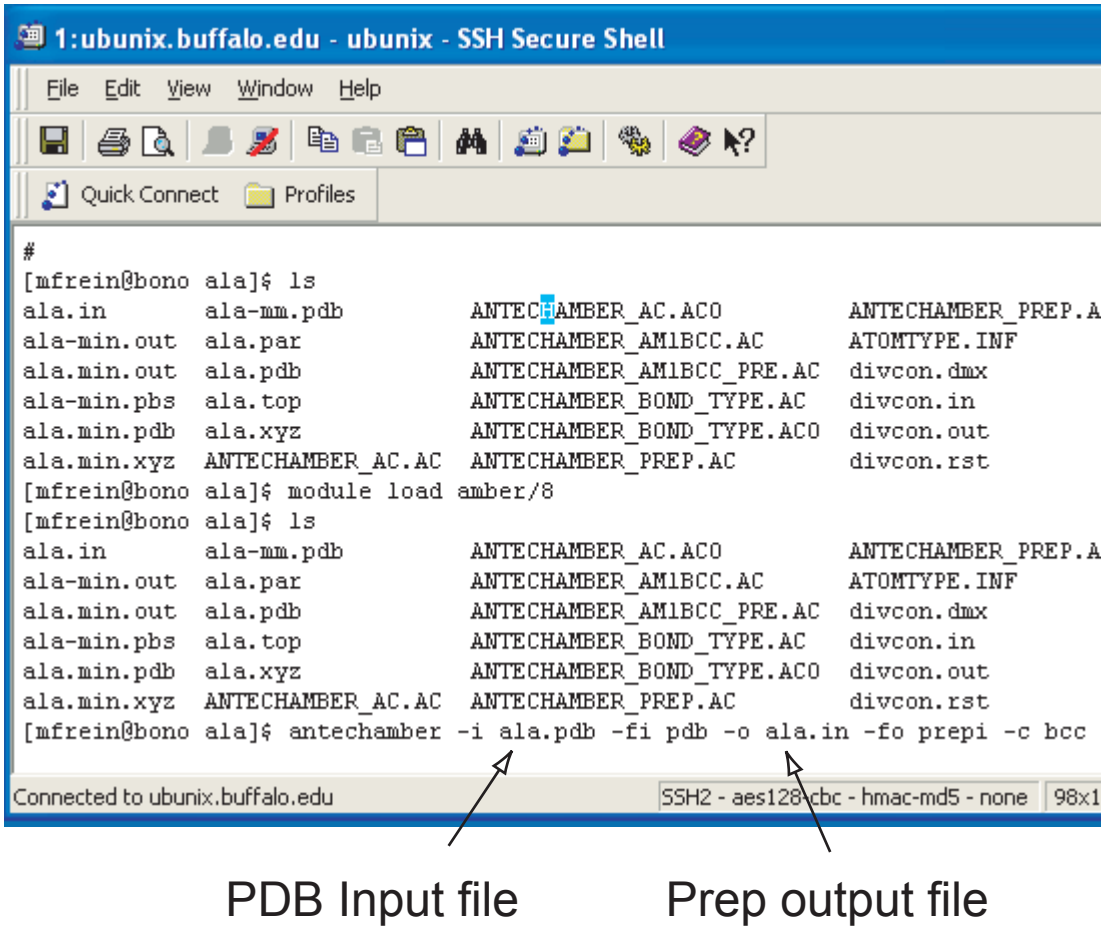
MM minimization of Chloro-alanine

Parameter file of Chloro-alanine



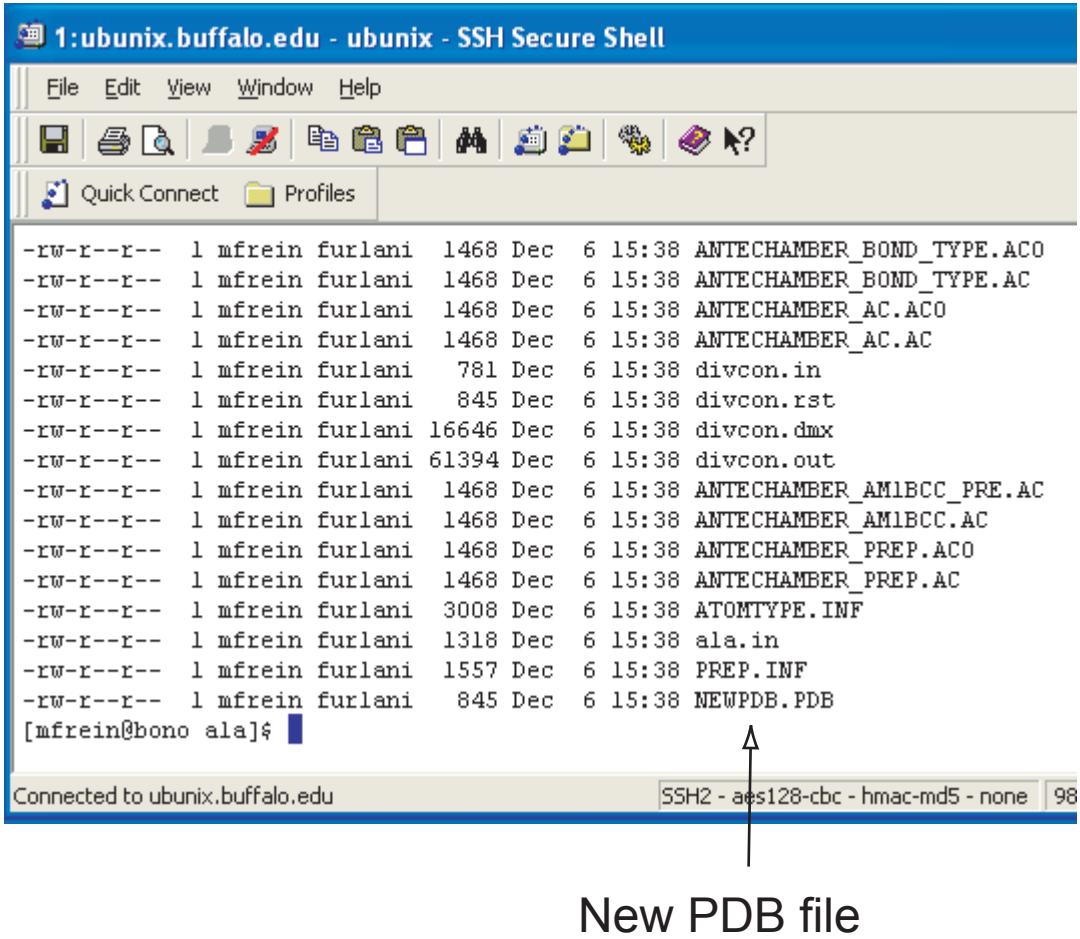
MM minimization of Chloro-alanine

Antechamber program generating the preparation file for Chloro-alanine



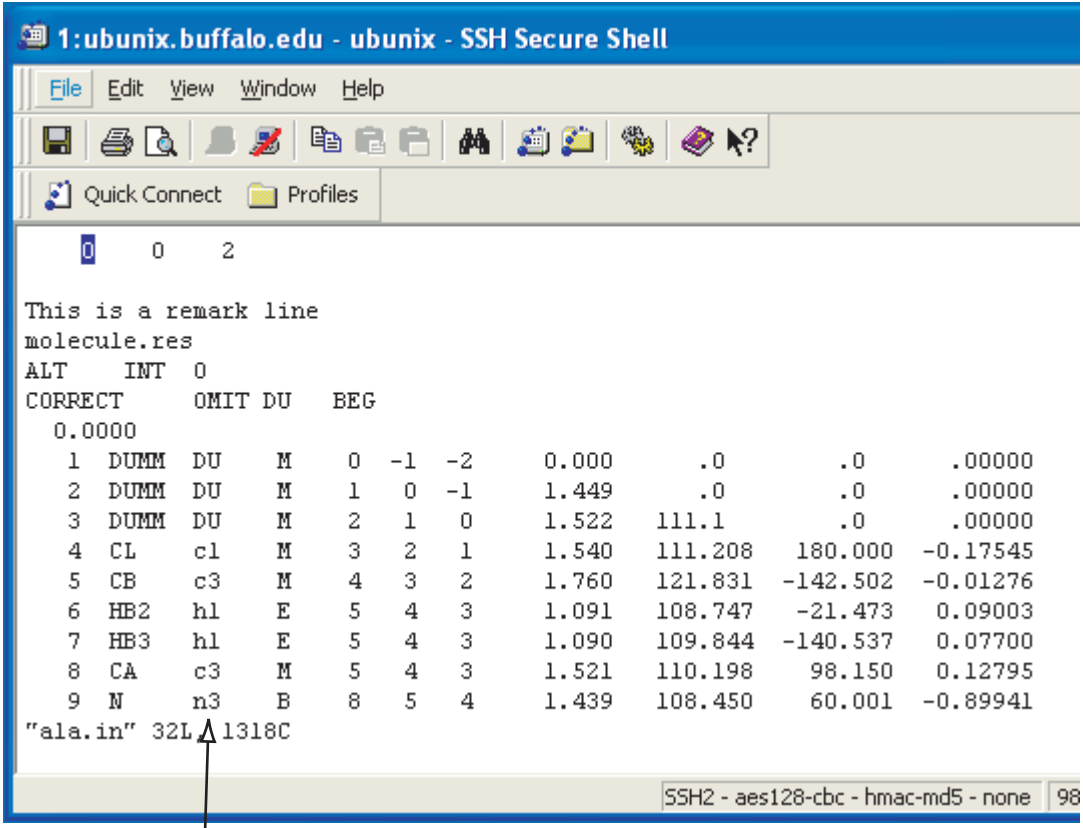
MM minimization of Chloro-alanine

Antechamber program generating the preparation file for Chloro-alanine



MM minimization of Chloro-alanine

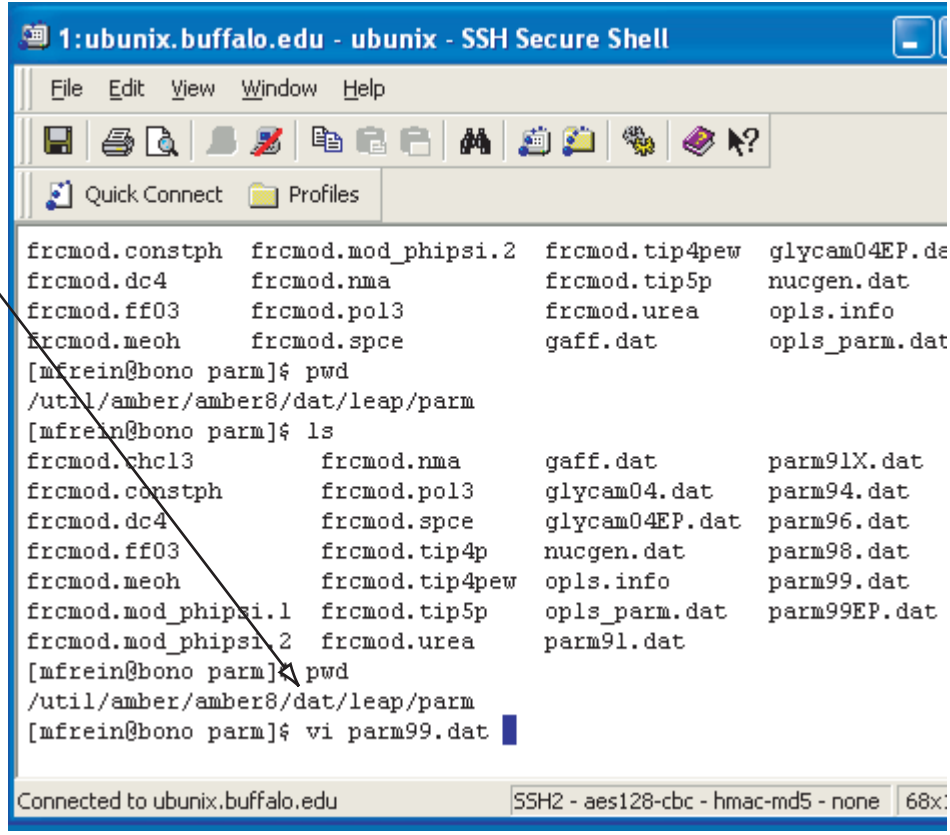
The preparation file for Chloro-alanine



The atomic types should be corrected

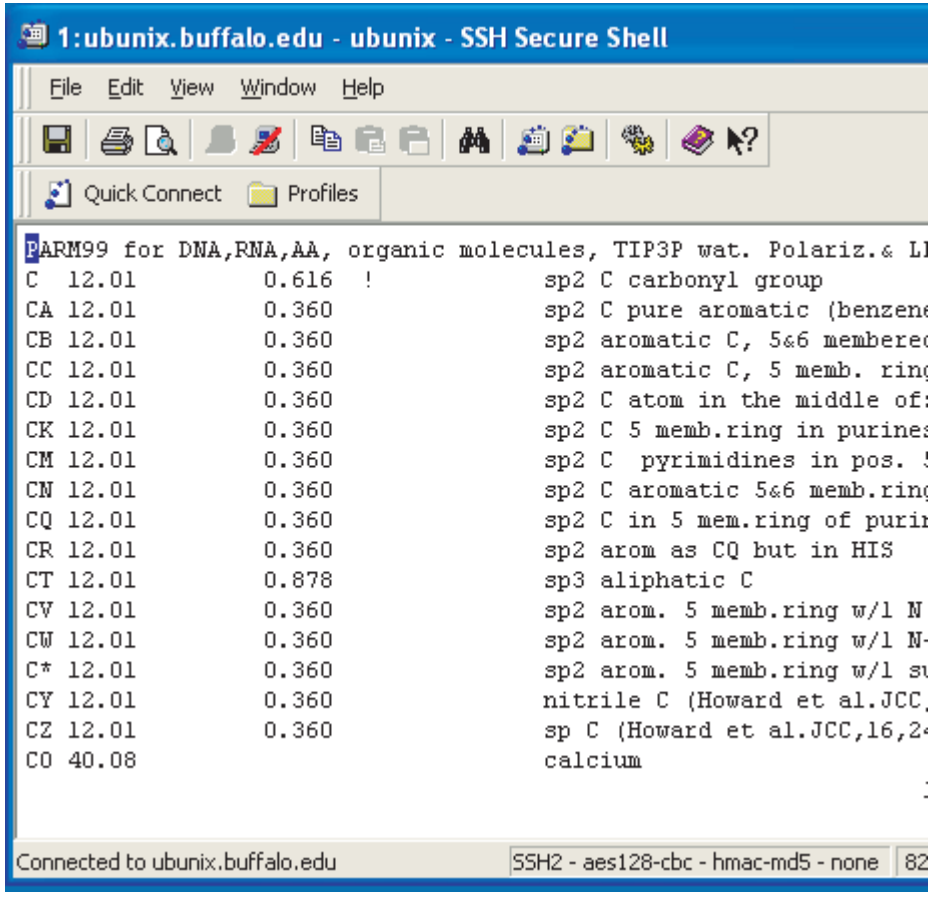
MM minimization of Chloro-alanine

The home directory of the AMBER program



MM minimization of Chloro-alanine

The Parm99 file

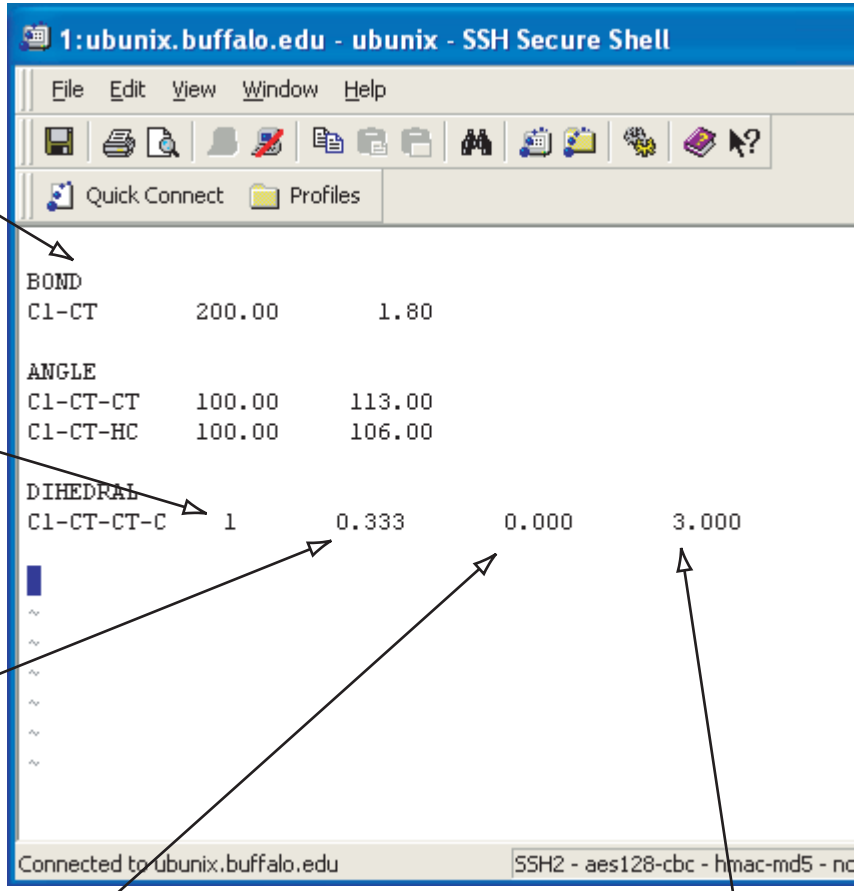


MM minimization of Chloro-alanine

The parameter file for Chloro-alanine

Should be 1 for a particular torsion

The maximum energy divided by 2 and by number of torsions involved in this bond

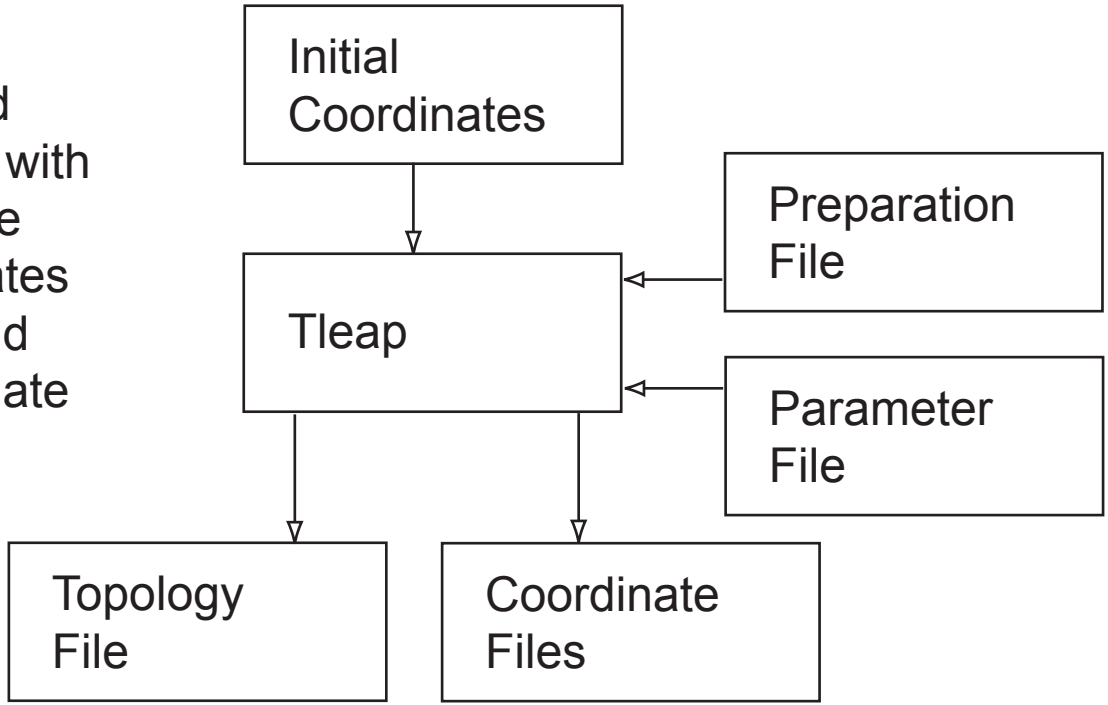


Should be 0 if the Maximum is at 0 degree

Should be 180 if the Minimum is at 0 degree

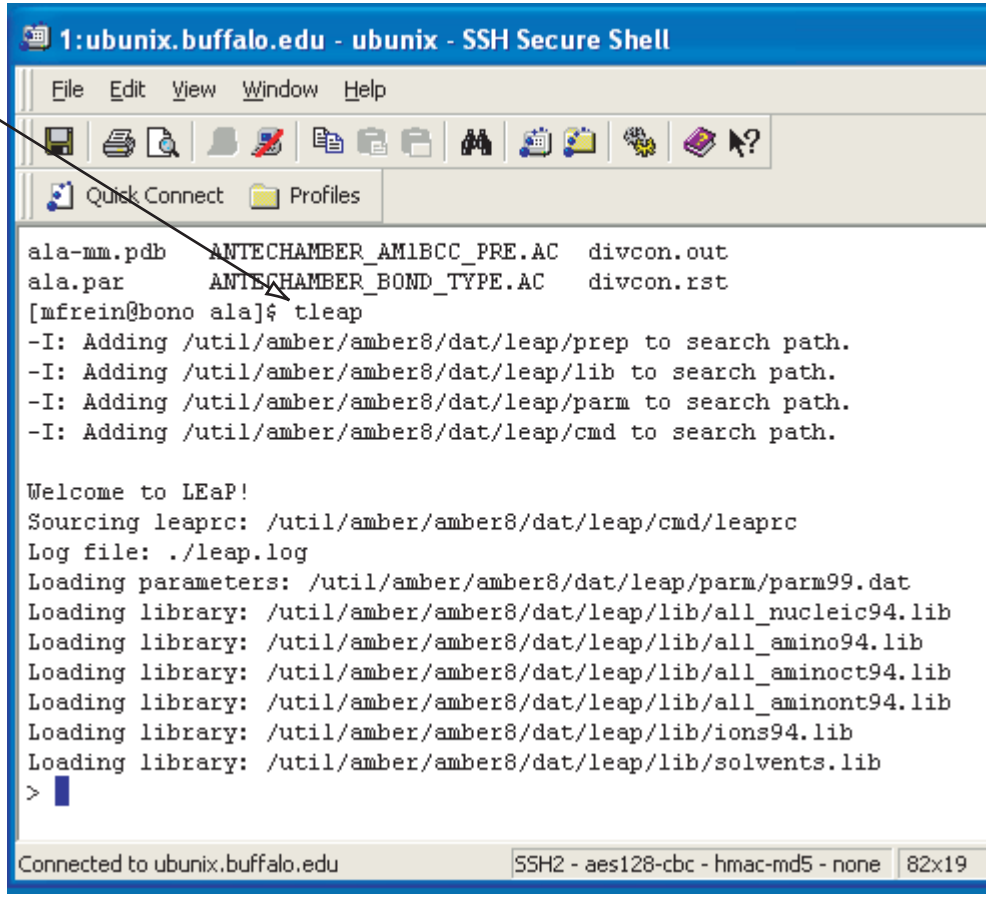
Number of maxima

Tleap program links the preparation and parameter files with initial coordinate file, and generates the topology and starting coordinate files



MM minimization of Chloro-alanine

Tleap program

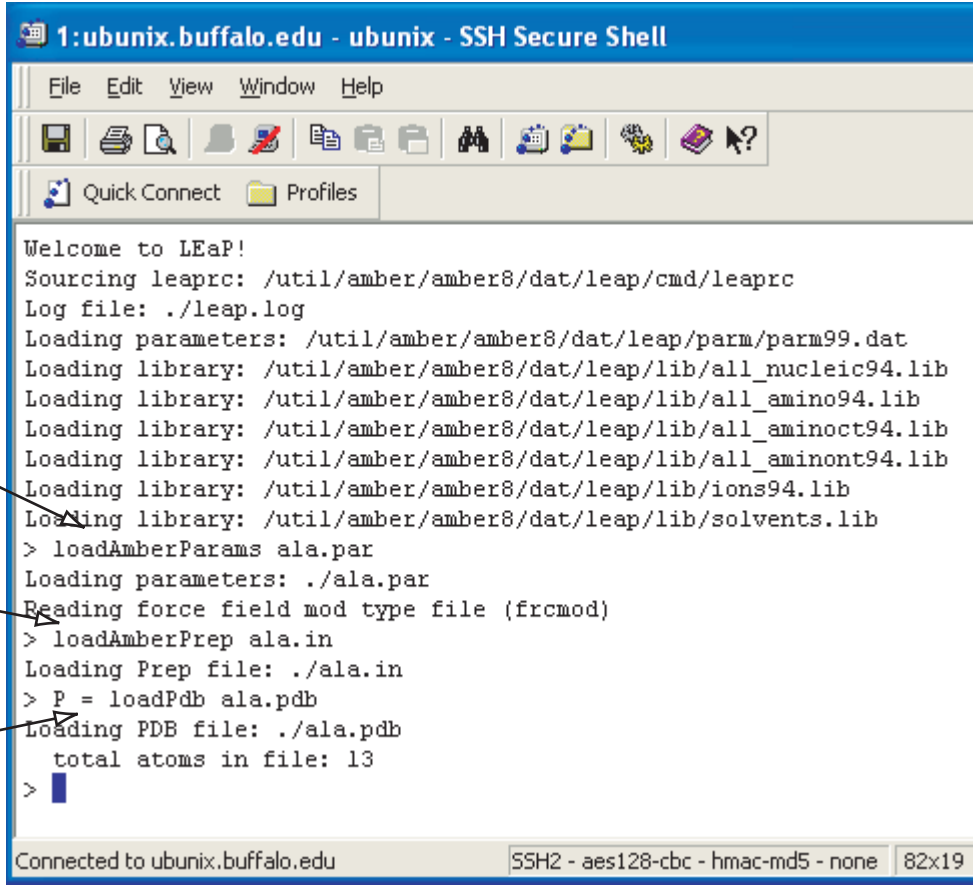


MM minimization of Chloro-alanine

Loading parameter file

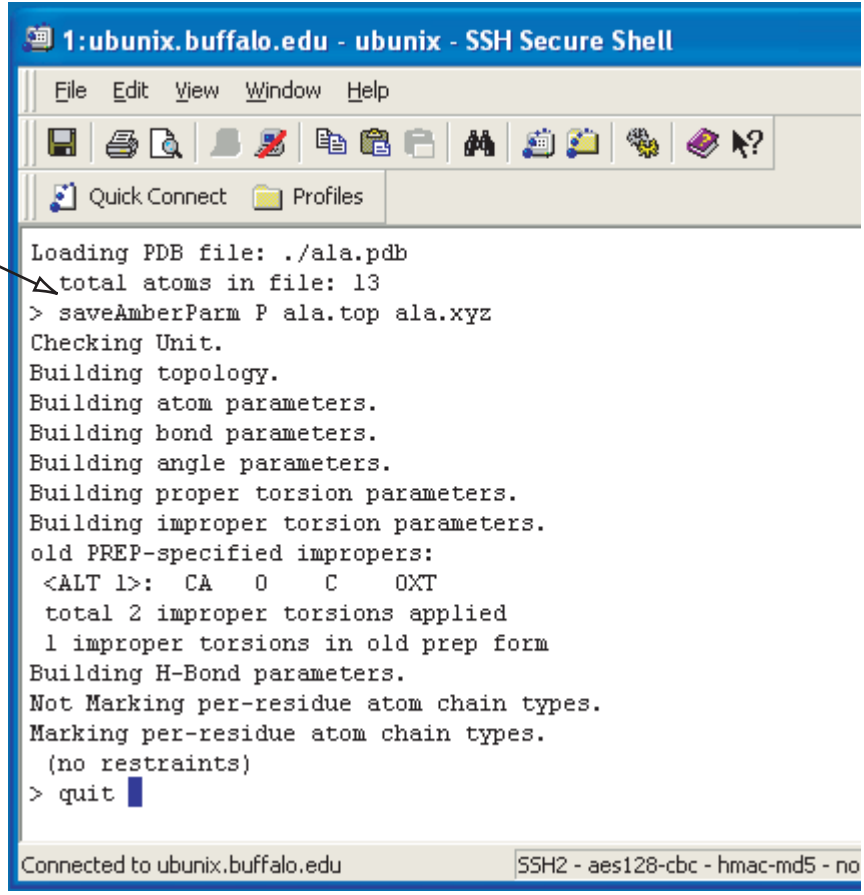
Loading preparation file

Loading coordinate file



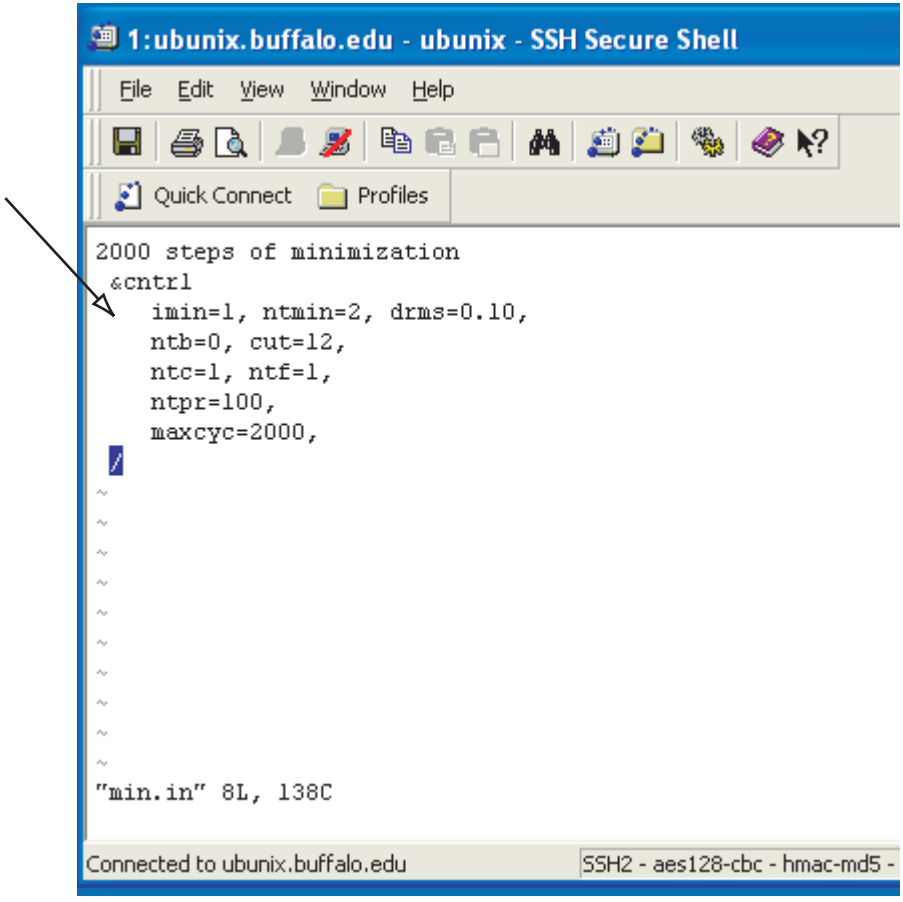
MM minimization of Chloro-alanine

Generating and saving the topology and initial coordinate files



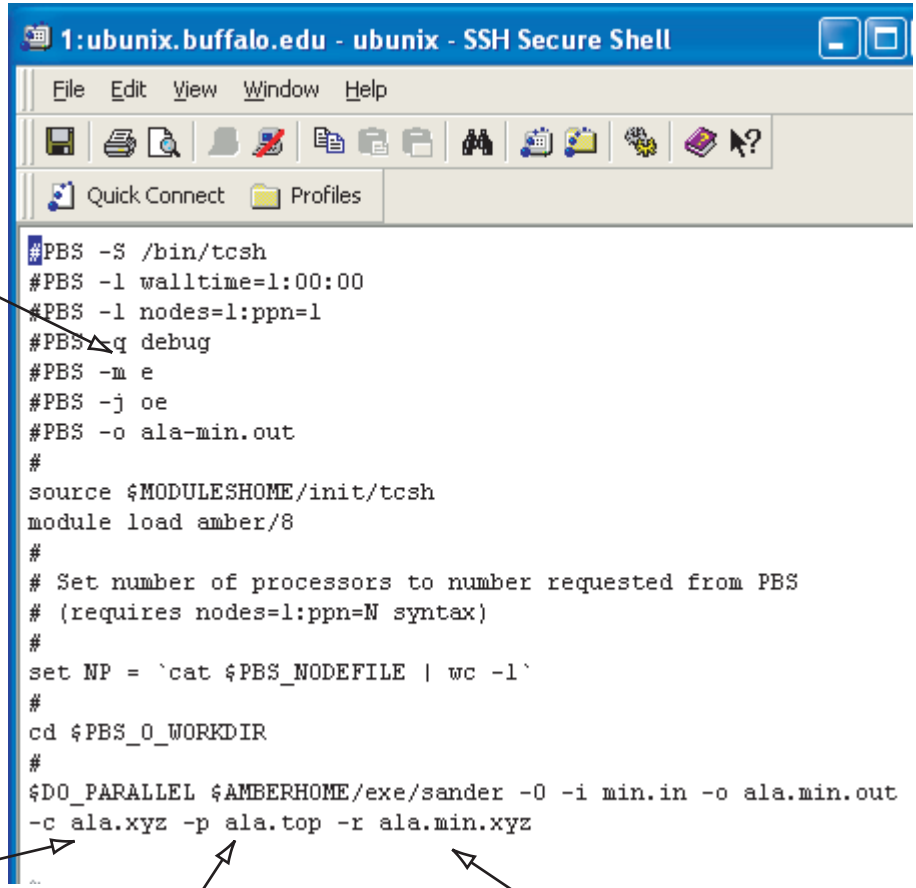
MM minimization of Chloro-alanine

Generating and saving by hand technical details of minimization



MM minimization of Chloro-alanine

Generating and saving by hand technical details of running the minimization



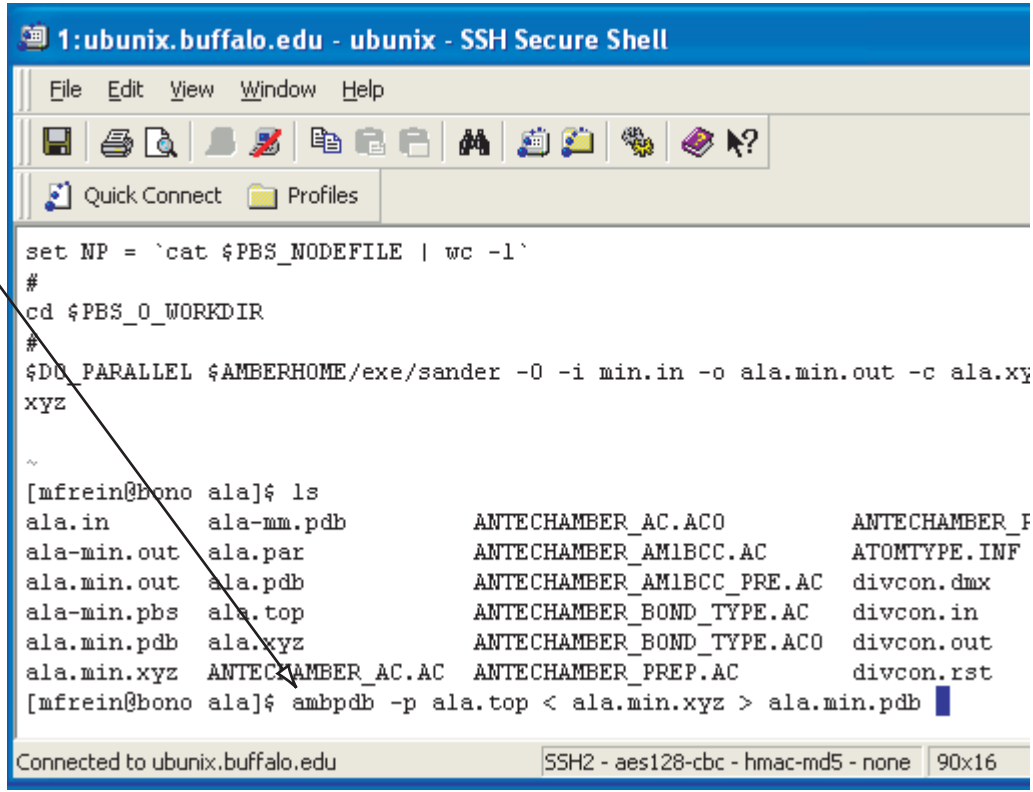
Initial coordinate file

Topology file

Minimized coordinate file

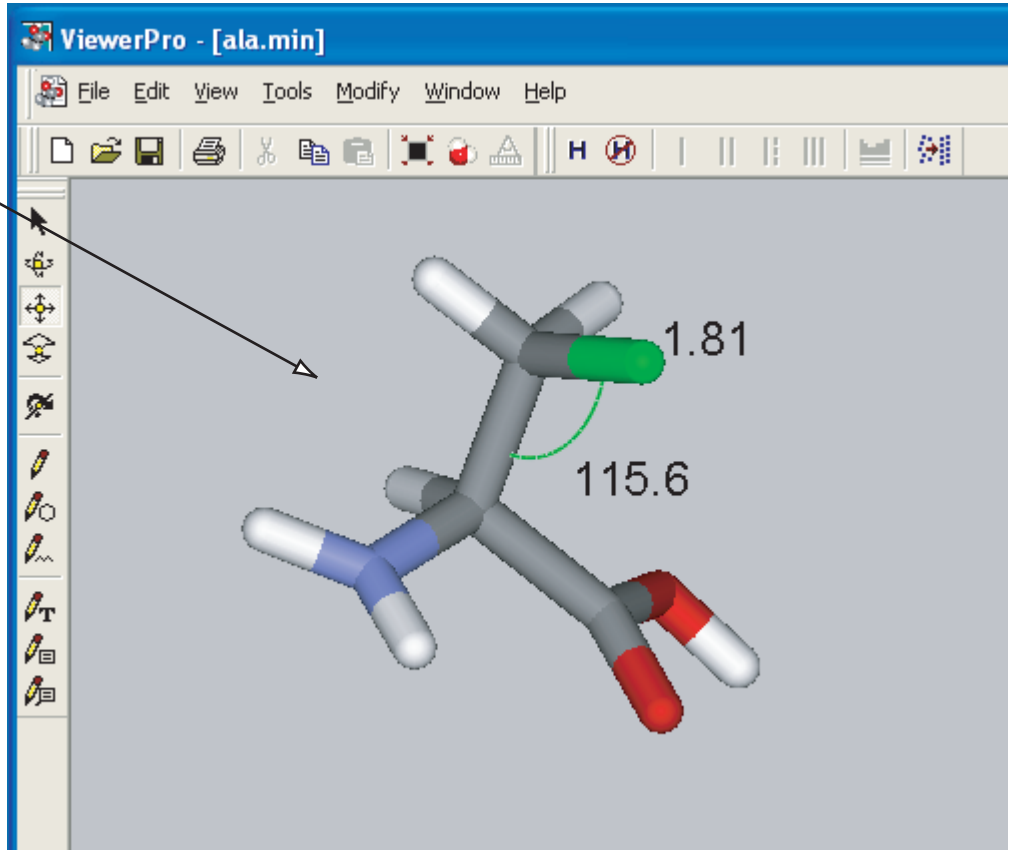
MM minimization of Chloro-alanine

Transforming the coordinate file into a PDB file



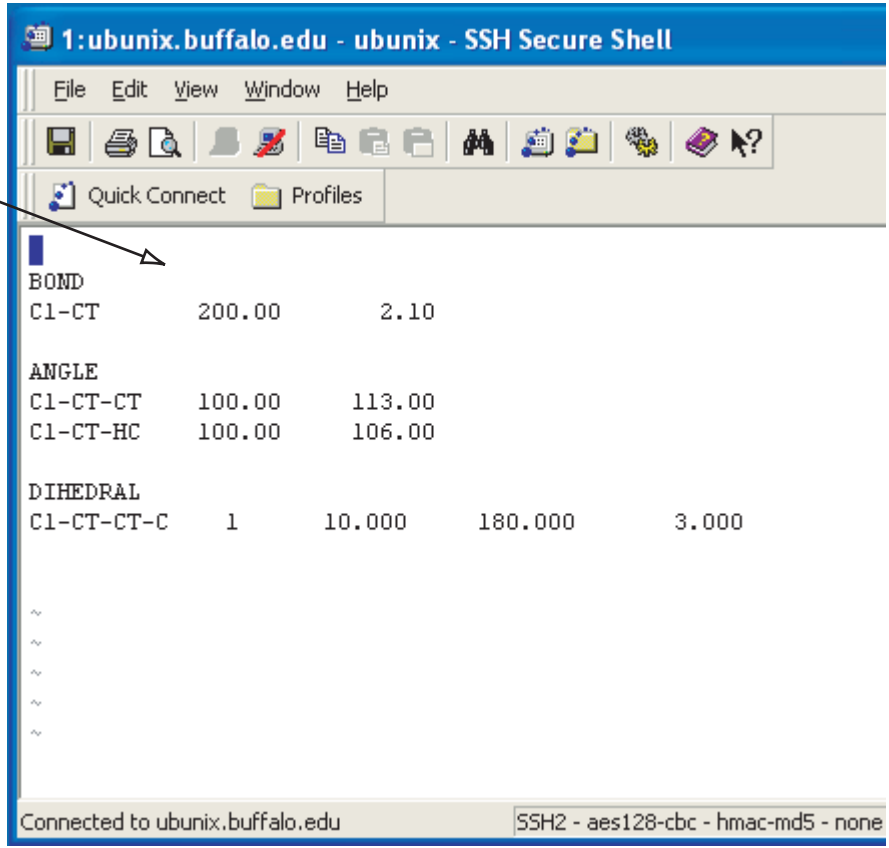
MM minimization of Chloro-alanine

Optimal geometry of Chloro-alanine after MM minimization



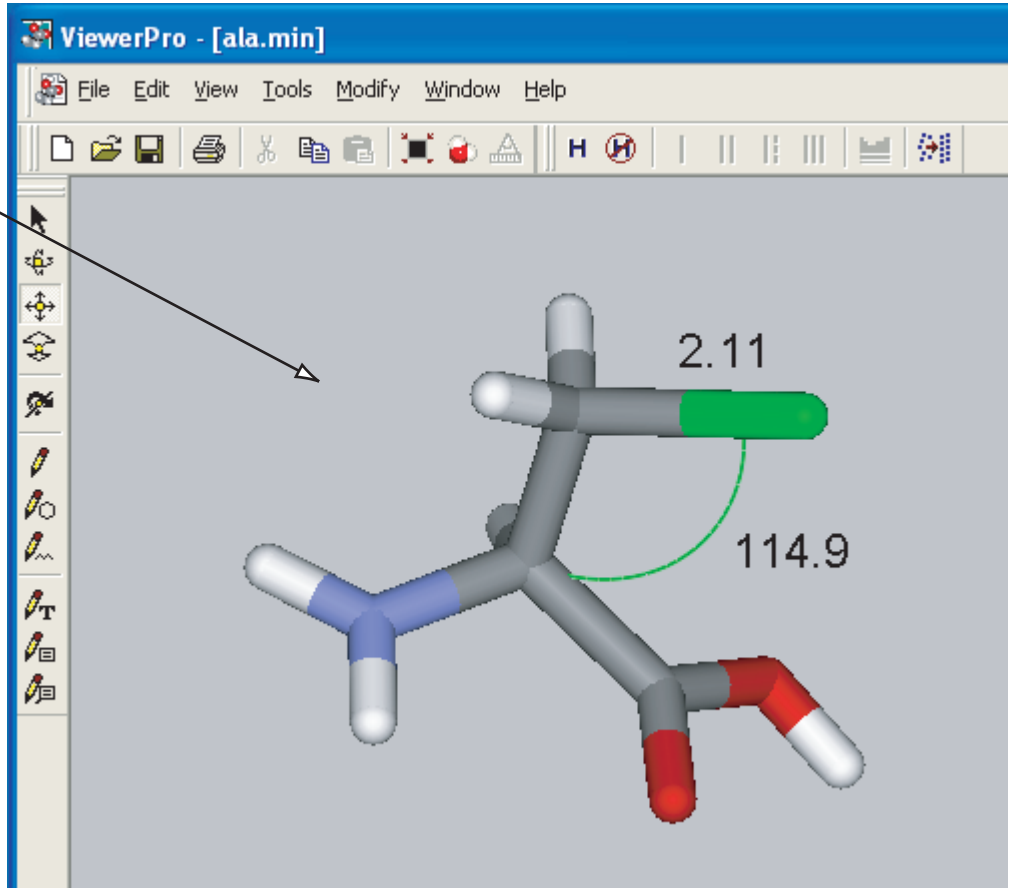
MM minimization of Chloro-alanine

Modified parameter file of Chloro-alanine



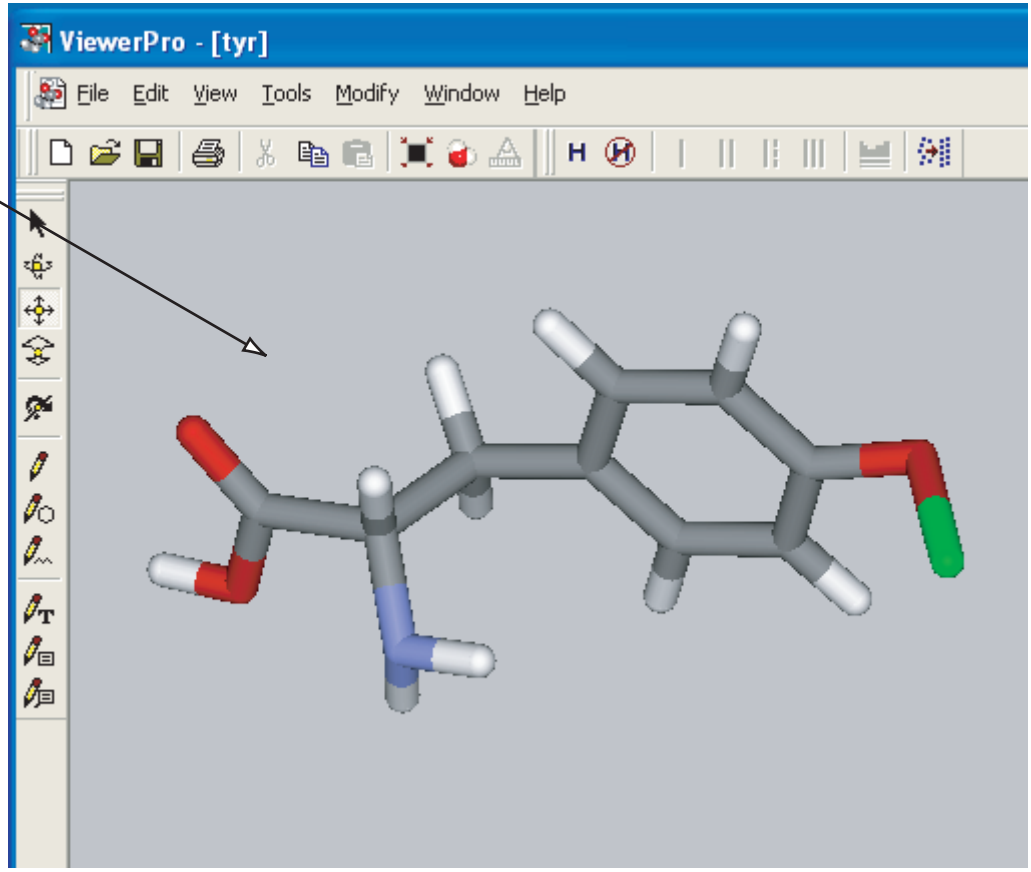
MM minimization of Chloro-alanine

Optimal structure of Chloro-alanine after parameter modification



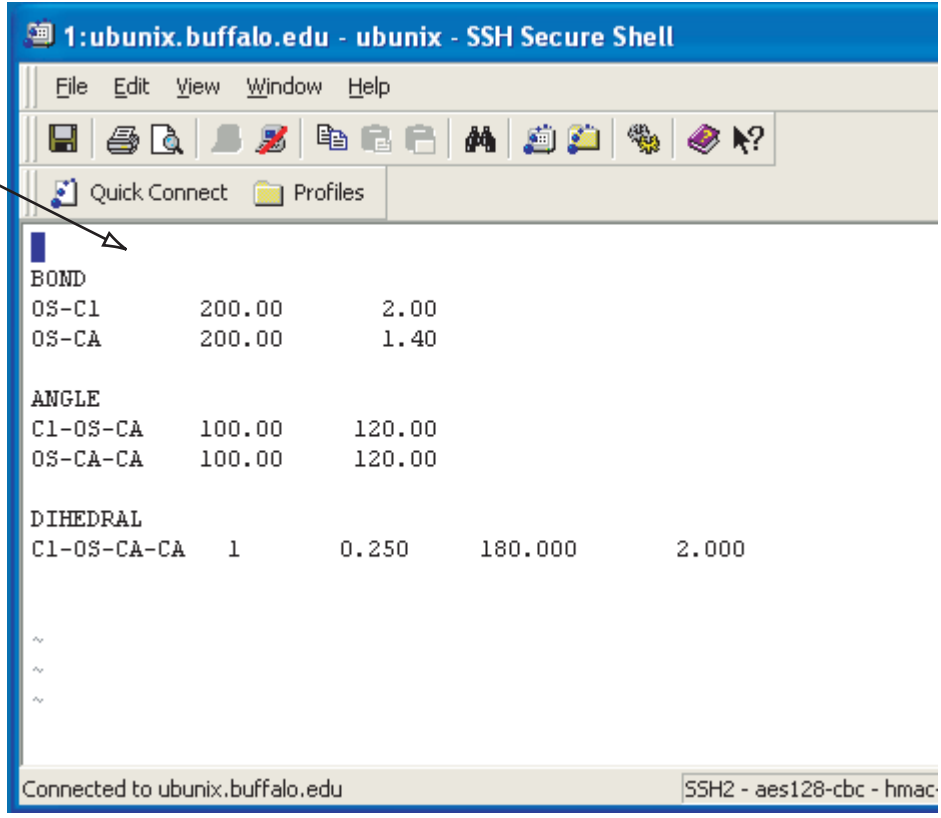
MM minimization of Chloro-tyrosine

Optimal structure of Chloro-tyrosine after QM calculations



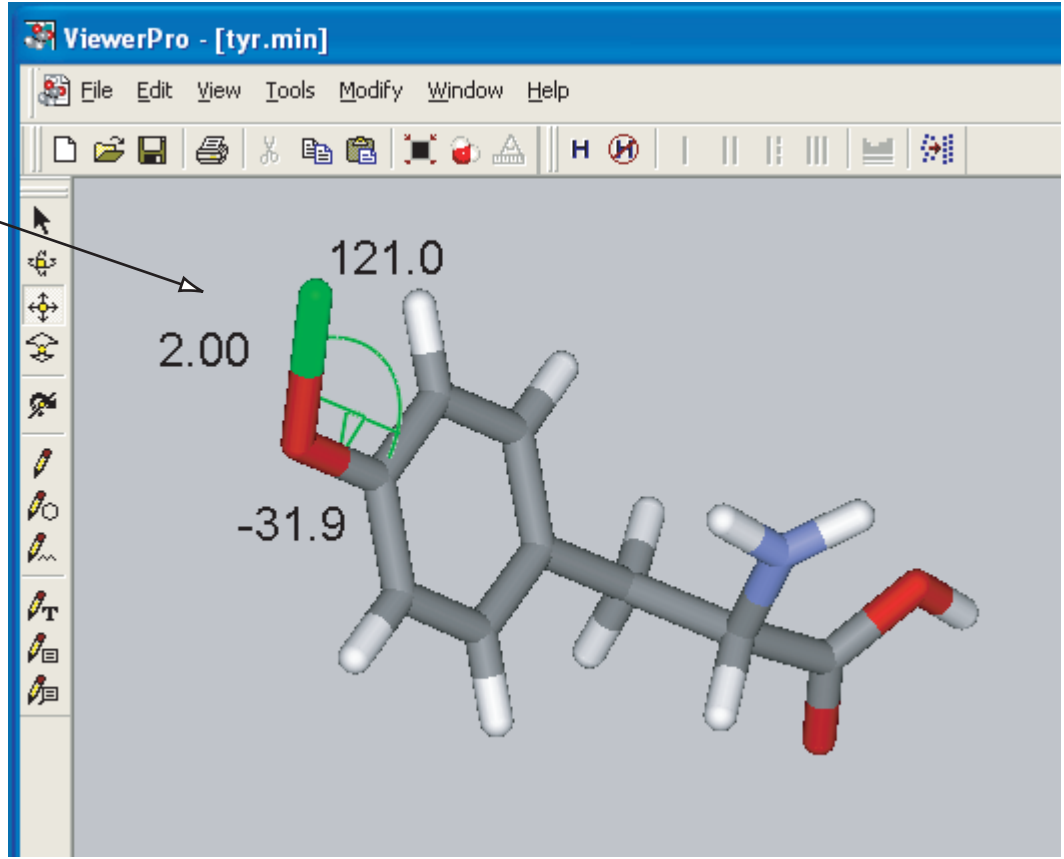
MM minimization of Chloro-tyrosine

The parameter file of Chloro-tyrosine



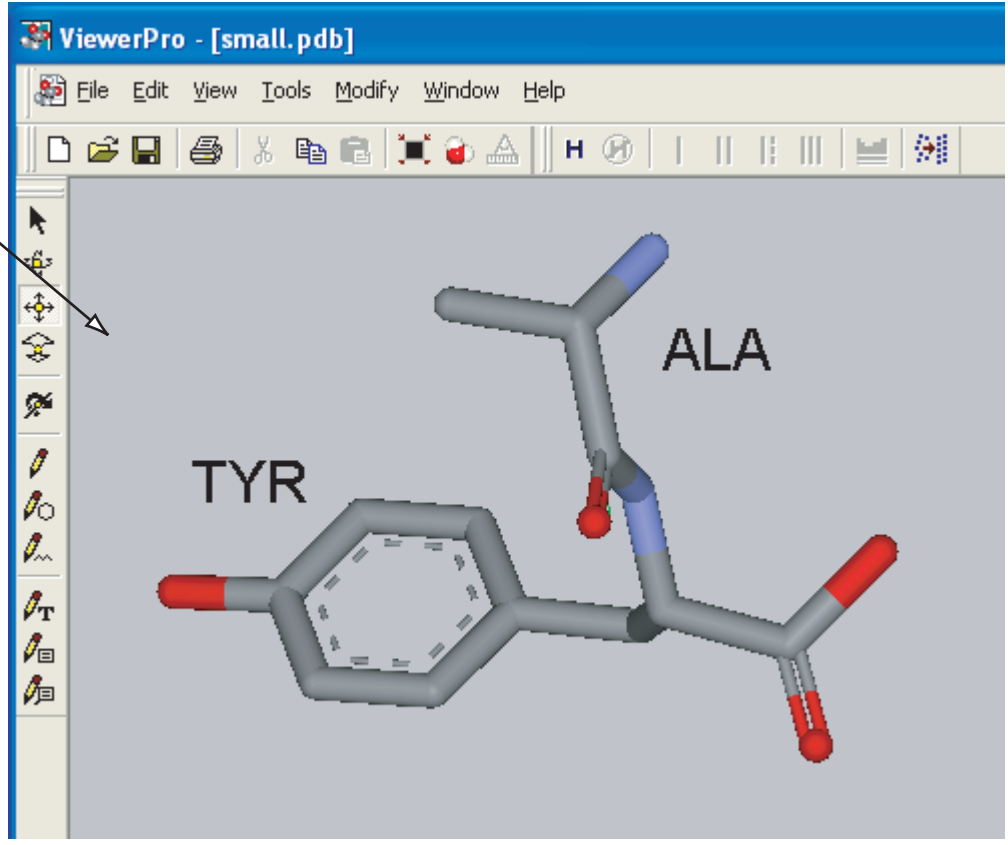
MM minimization of Chloro-tyrosine

The optimal geometry of Chloro-tyrosine after modified MM minimization



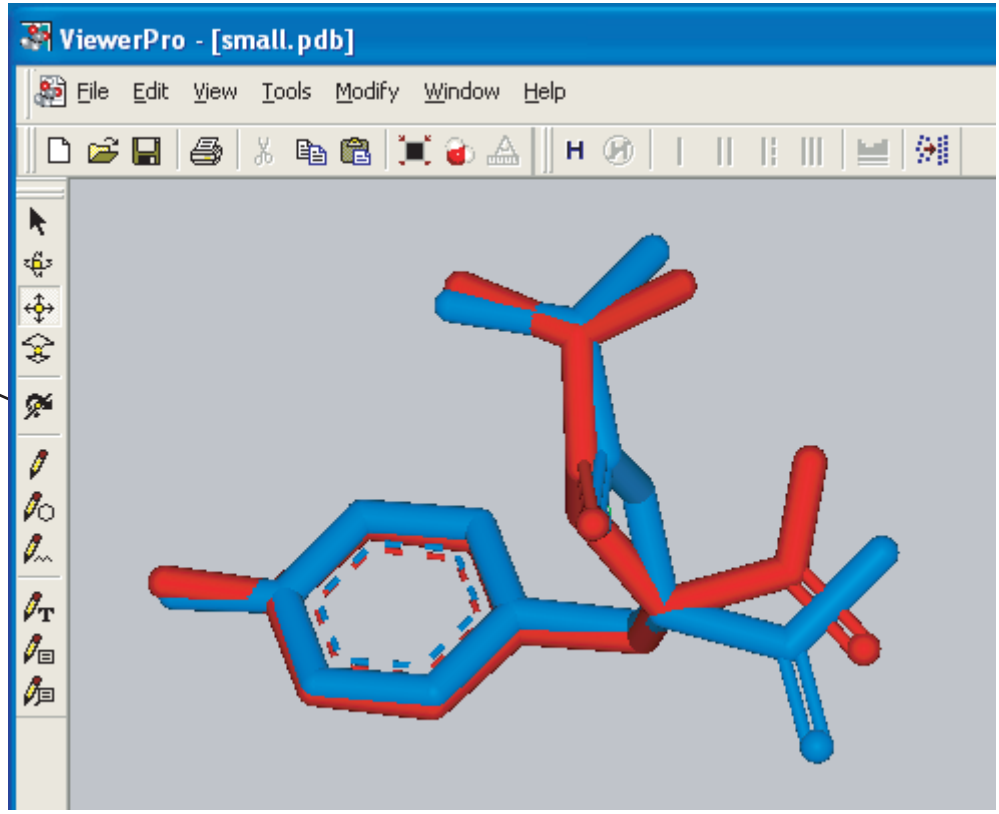
MM minimization of a small peptide

The initial geometry of ALA-TYR peptide



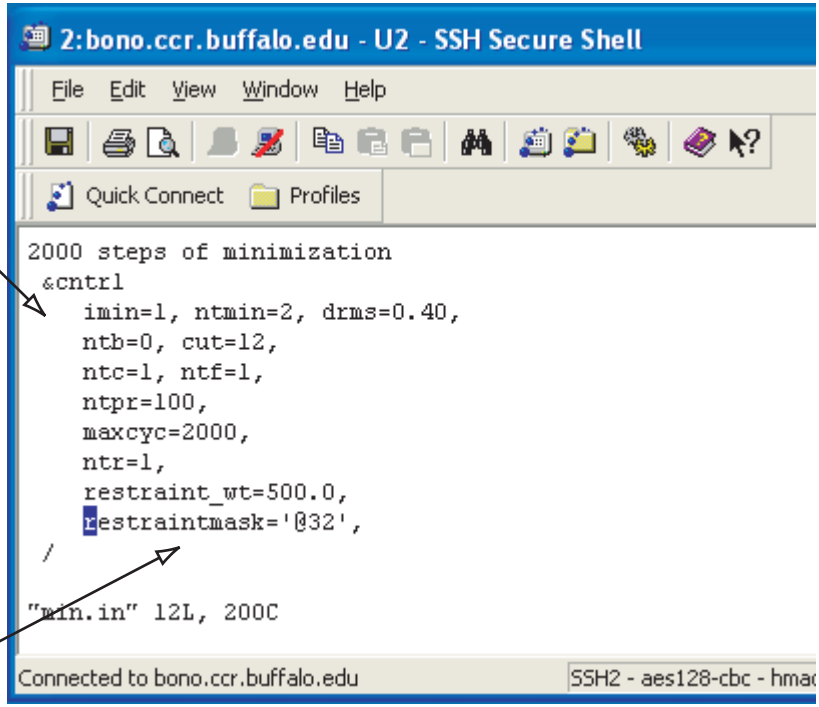
MM minimization of a small peptide

The minimized structure of the peptide (red) compared with the initial structure of this molecule (blue)



MM minimization of a small peptide

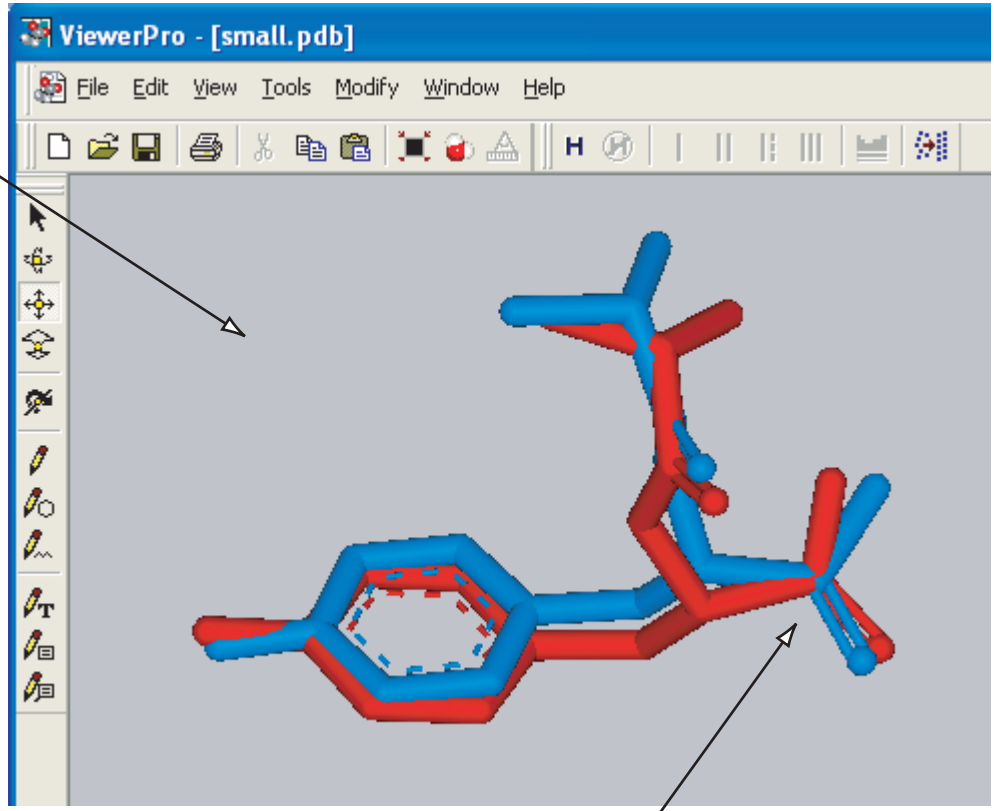
The input file of minimization with absolute constrins



The position of the atom 32 is constrined

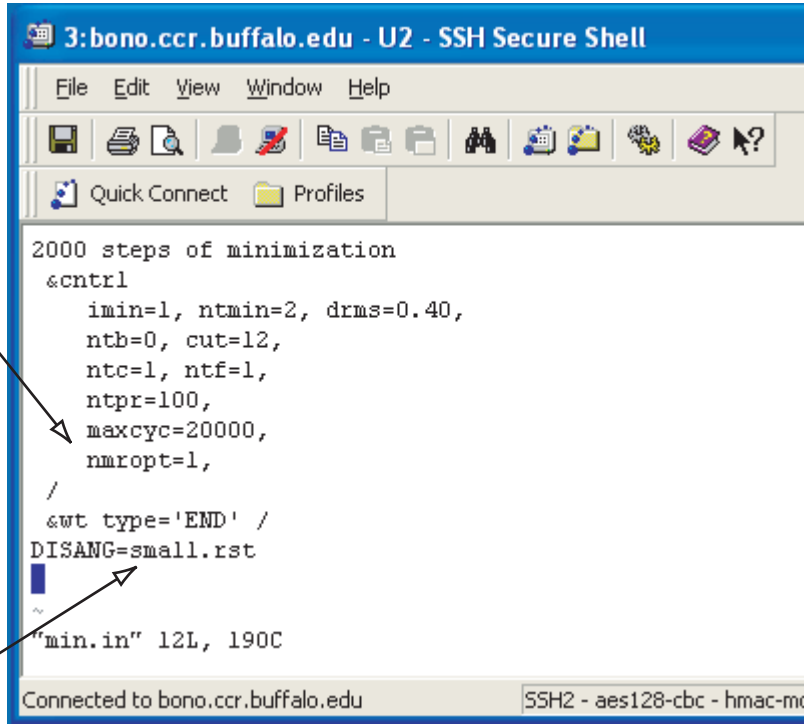
MM minimization of a small peptide

The initial (blue) and final (red) geometry of the peptide after minimization with a constrined position of the carbon atom



MM minimization of a small peptide

The input file of minimization with relative constrins



The file with constrins

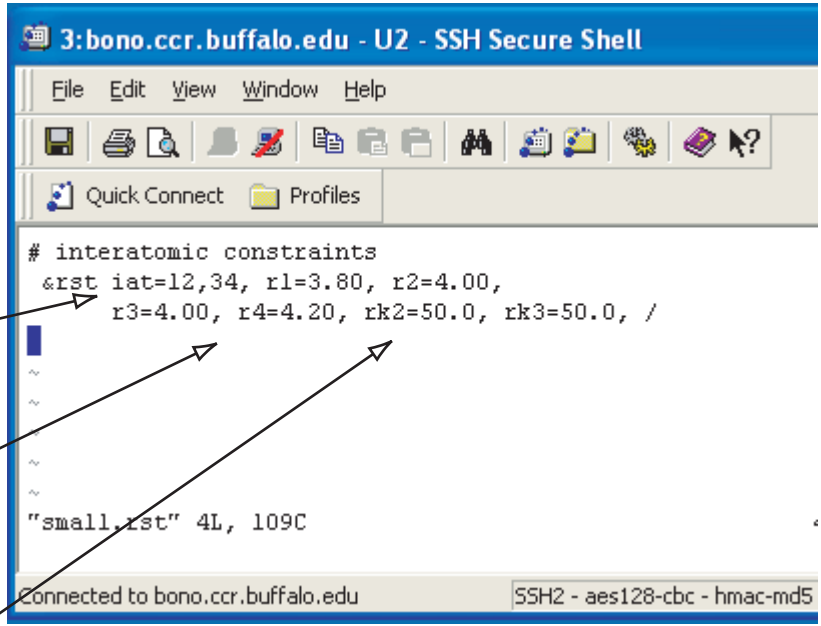
MM minimization of a small peptide

The constrains file

The atoms to be constrined

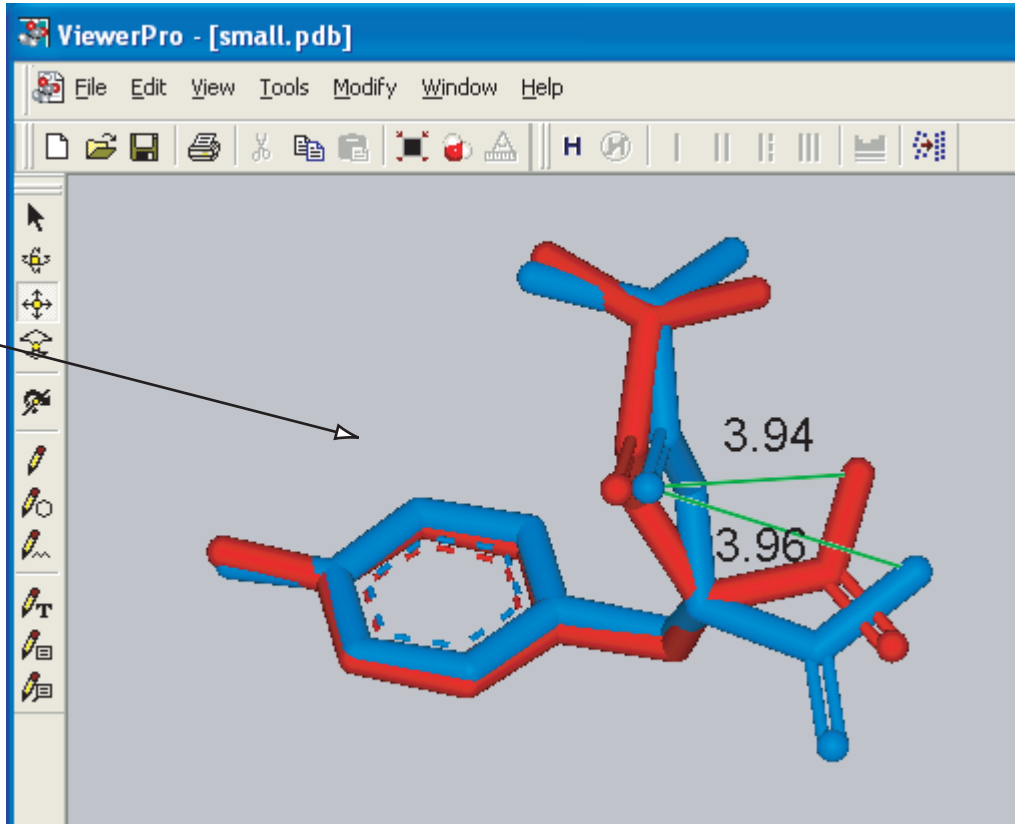
The shape of the potential

The potential force constants



MM minimization of a small peptide

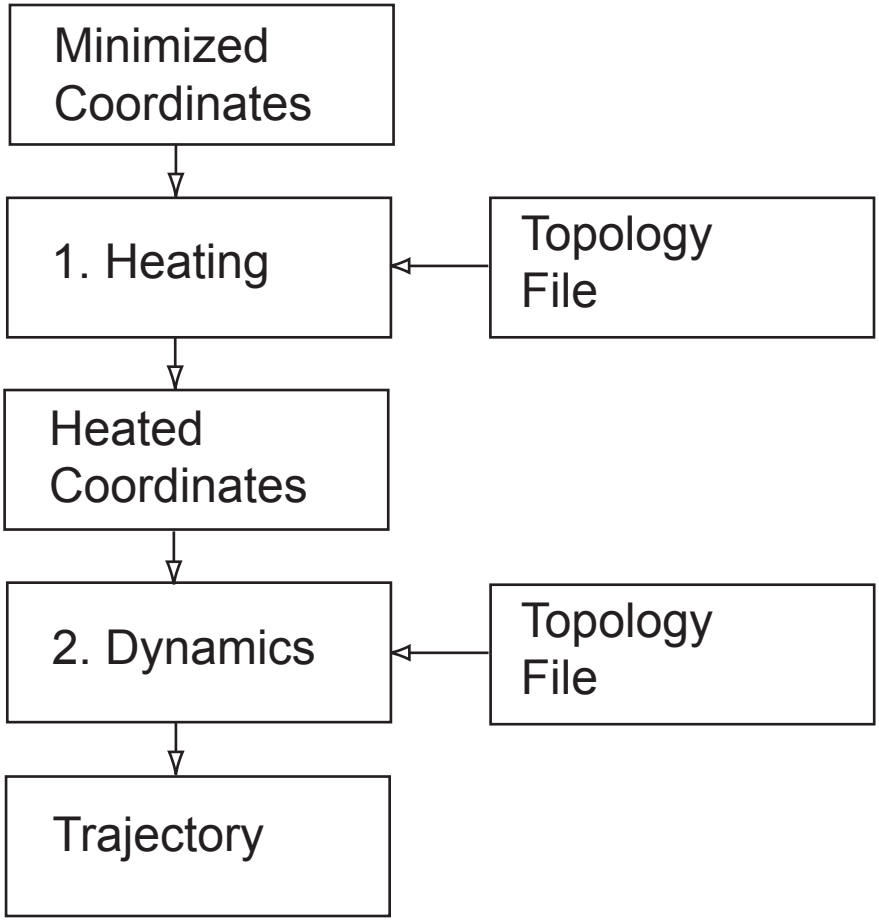
The initial (blue) and the final (red) geometry of the peptide, minimized with the interatomic constrain



MM dynamics of small proteins and nucleic acids

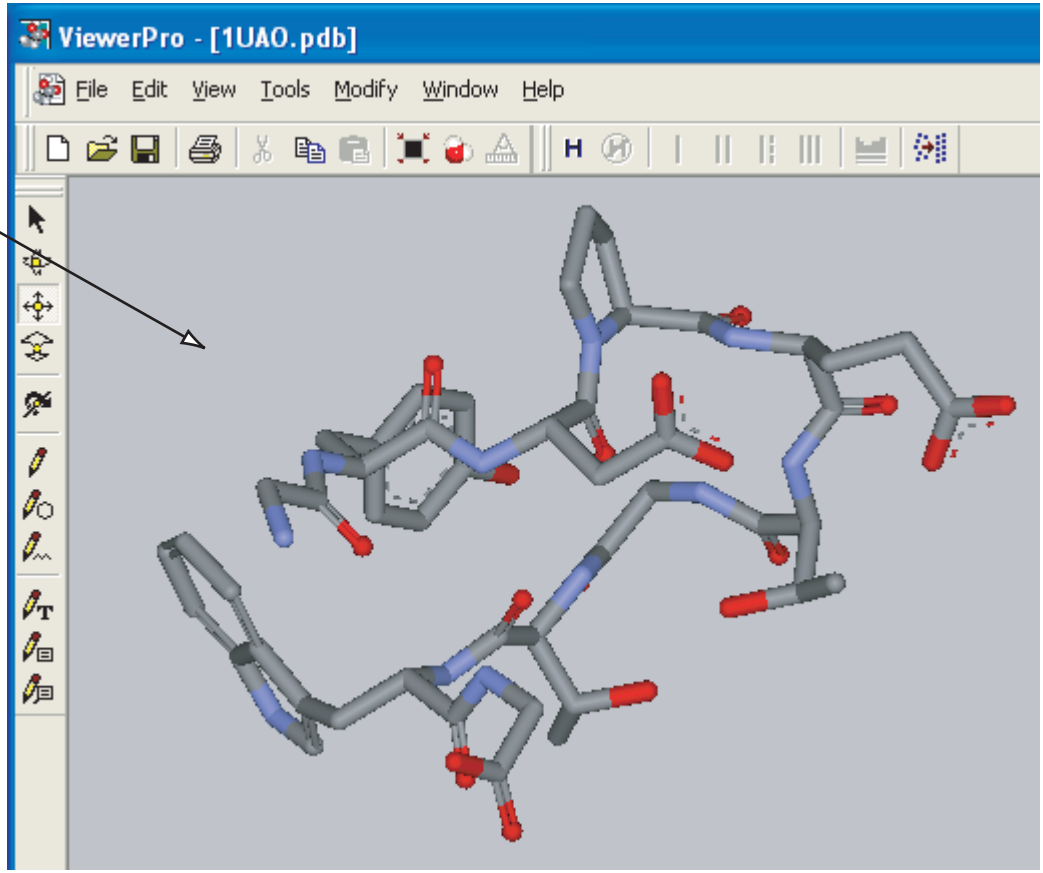
MM dynamics has two steps: heating and real dynamics

Each step requires two files the topology file and the initial coordinates file



MM dynamics of Chignolin

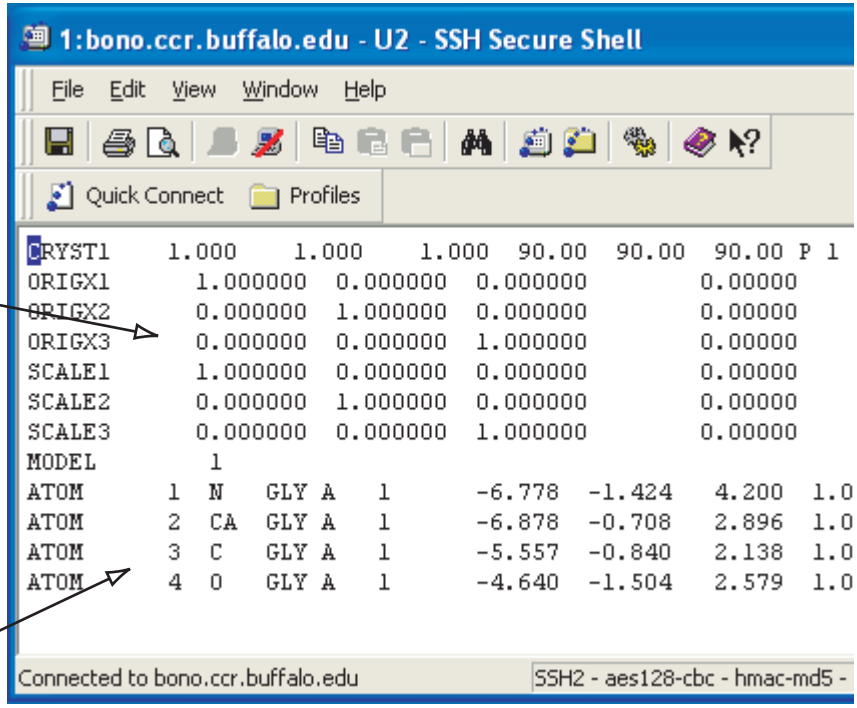
Experimental PDB structure of Chignolin



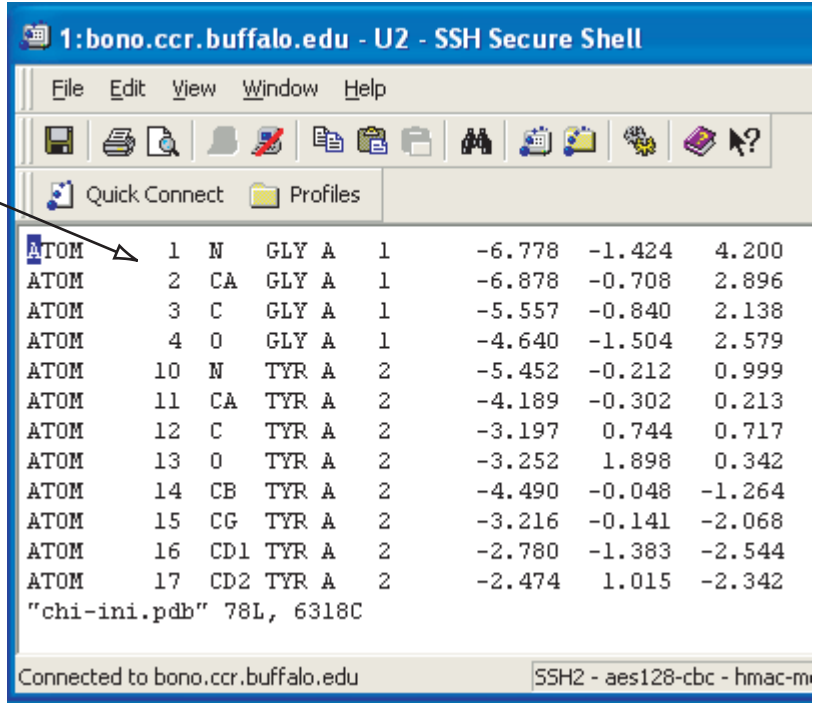
The PDB file of Chignolin

Technical details of experiment

Atomic coordinates



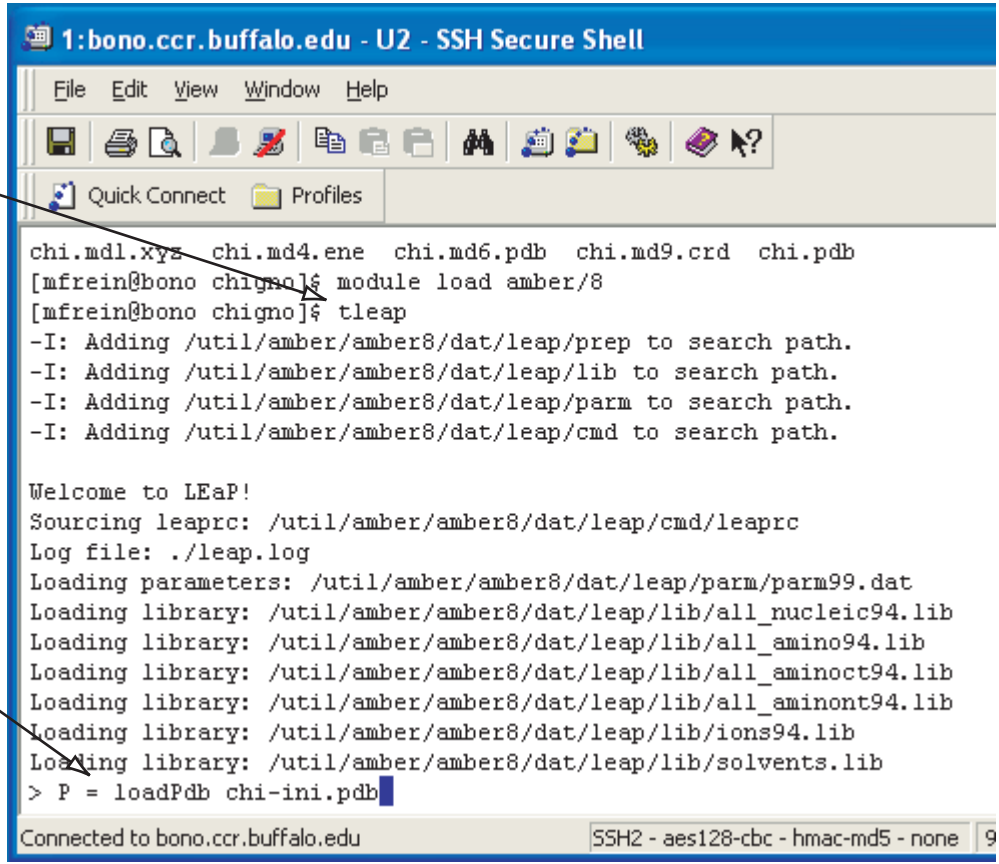
The initial coordinates in a PDB format



MM dynamics of Chignolin

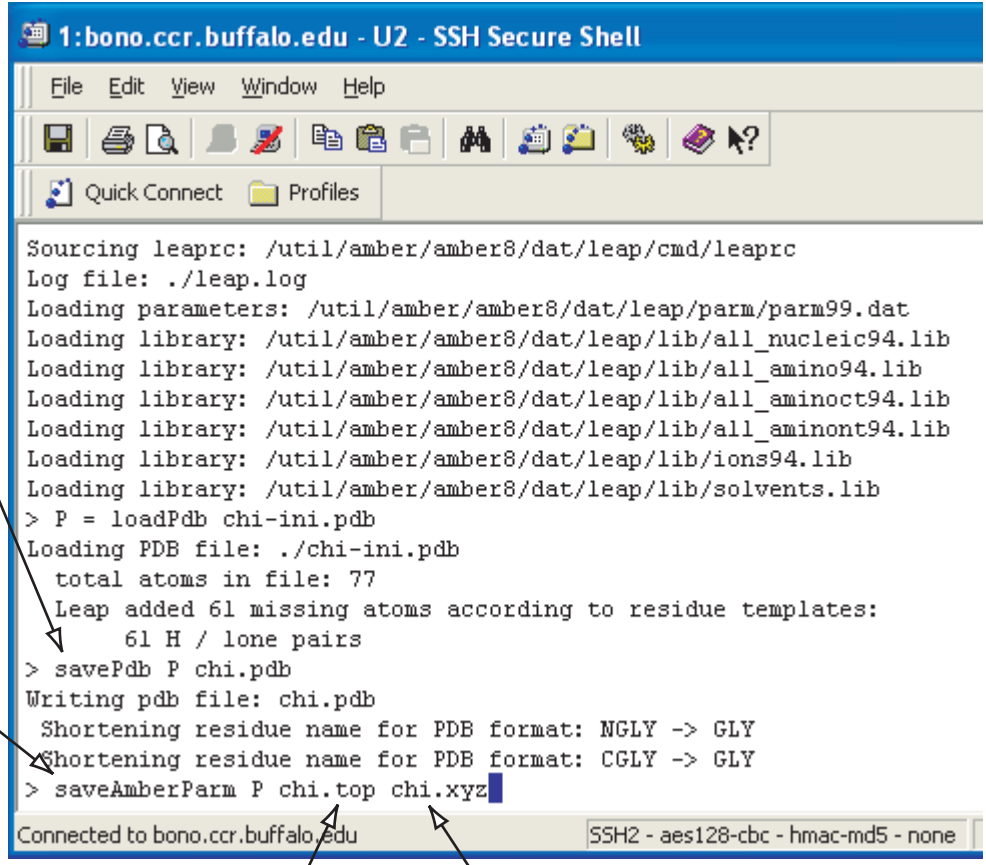
The Tlep program generating topology and coordinates files

Loading the initial coordinates



Saving the initial PDB files (with hydrogens)

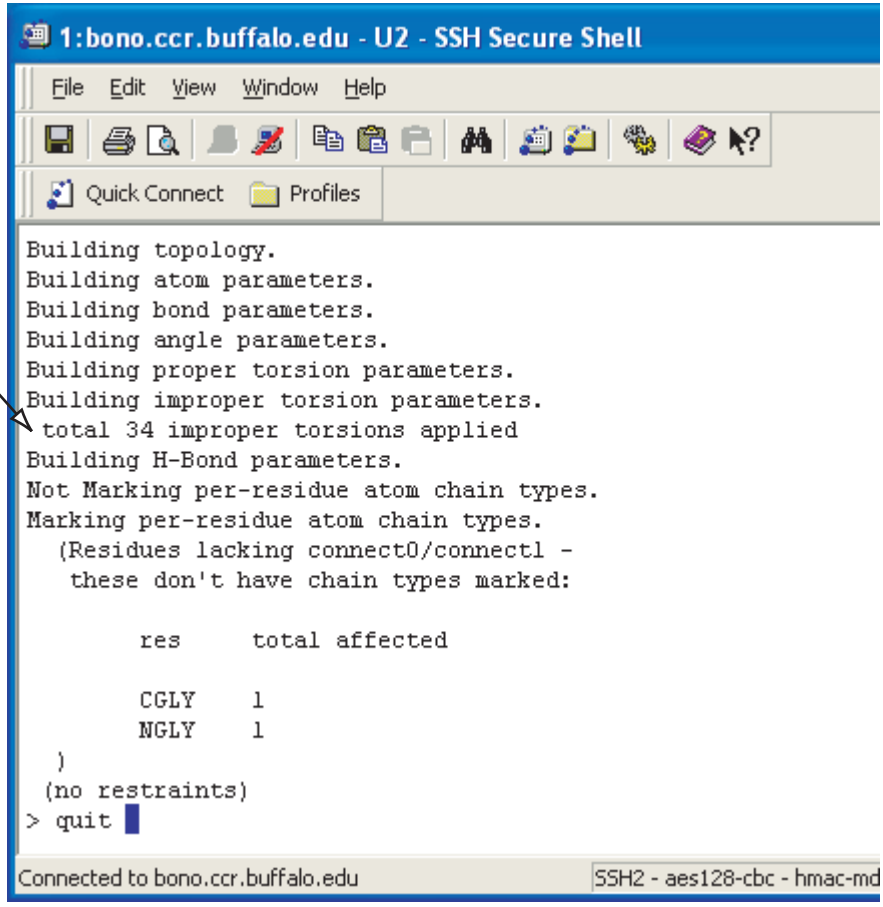
Saving the topology and coordinates files



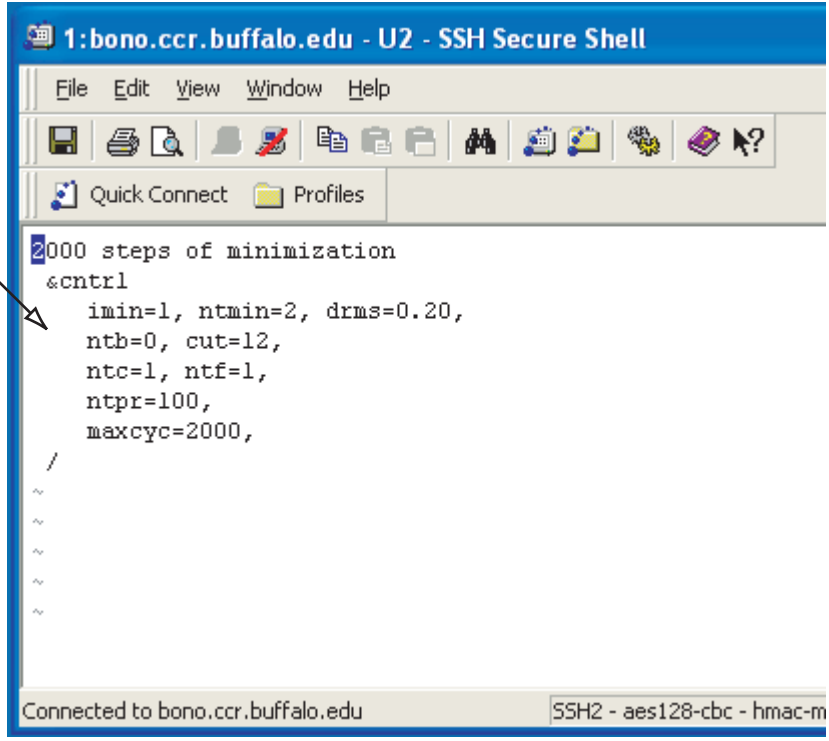
Topology file

Coordinates file

Building the topology and parameter data



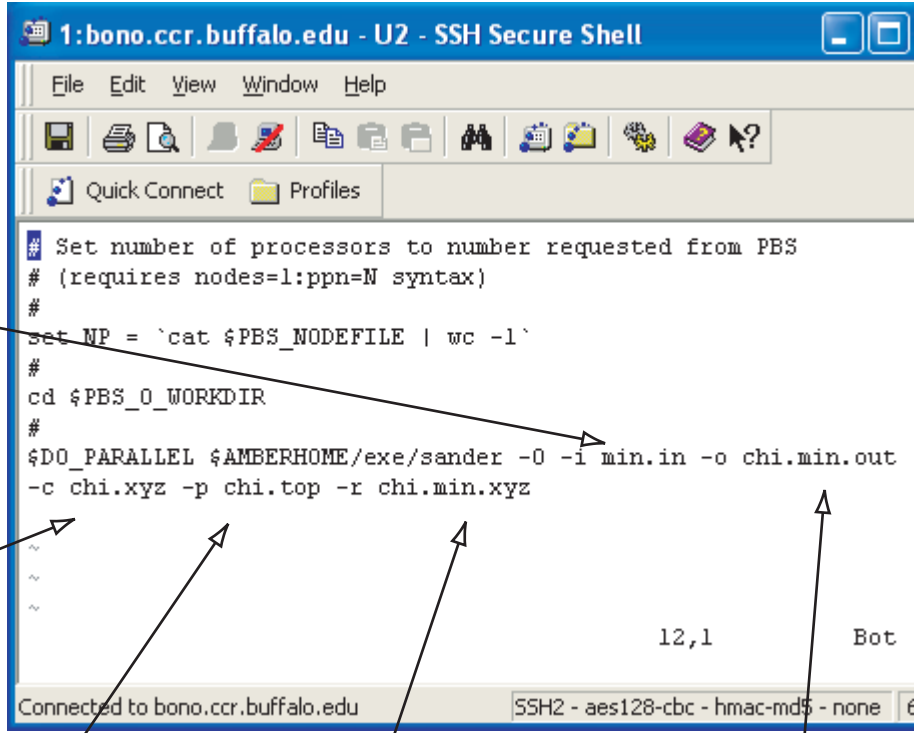
Technical details of minimization



Technical details of running minimization

Input file of minimization

Initial coordinates



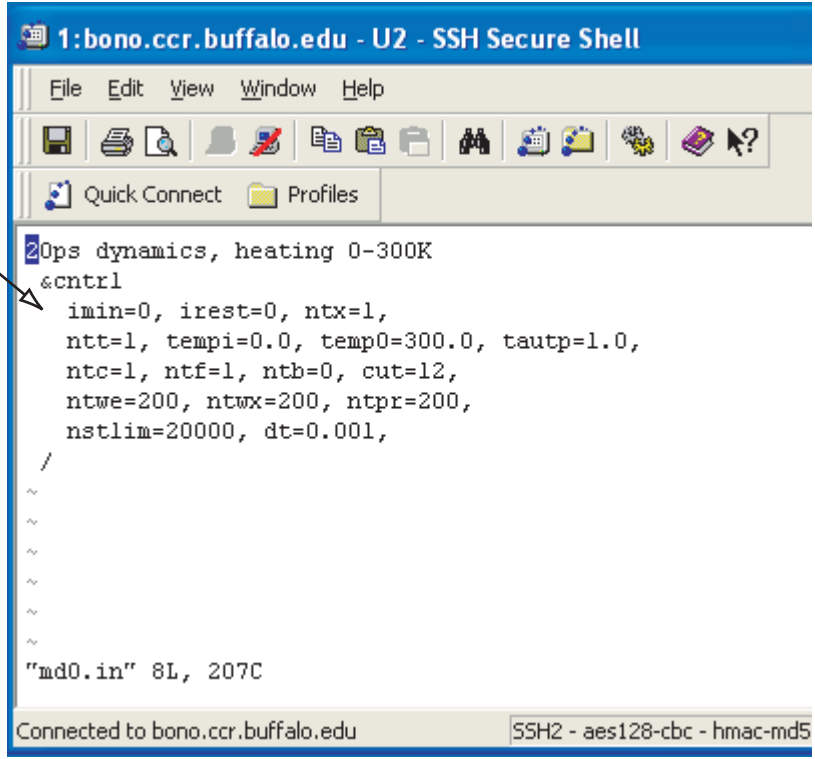
Topology file

Minimized coordinates

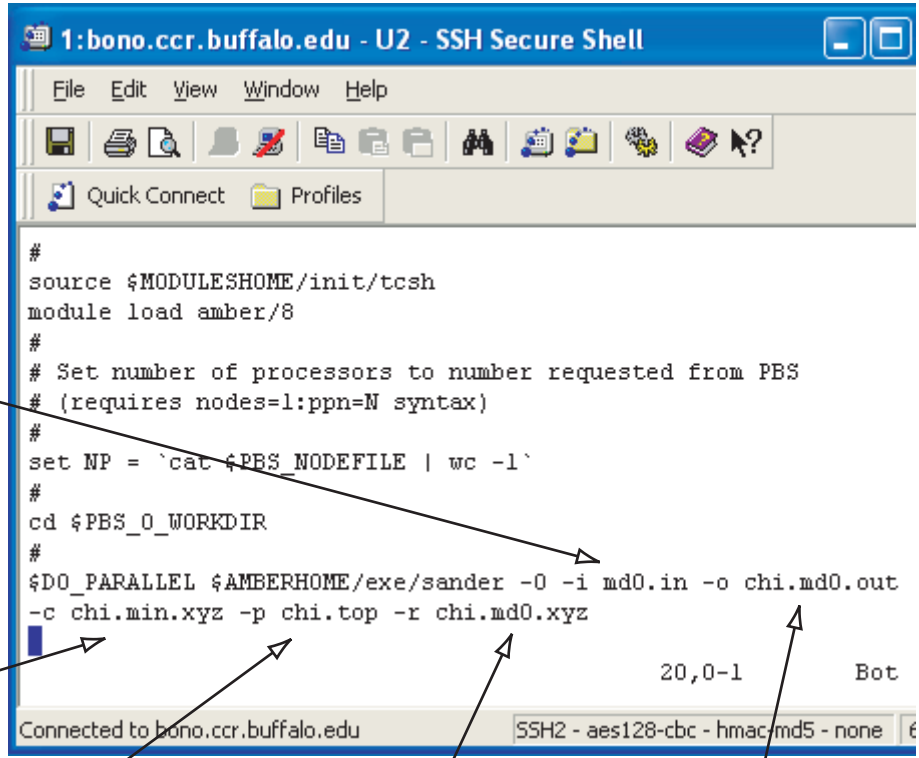
Output file of minimization

MM dynamics of Chignolin

Technical details
of heating



Technical details of running heating



Input file of heating

Initial coordianates

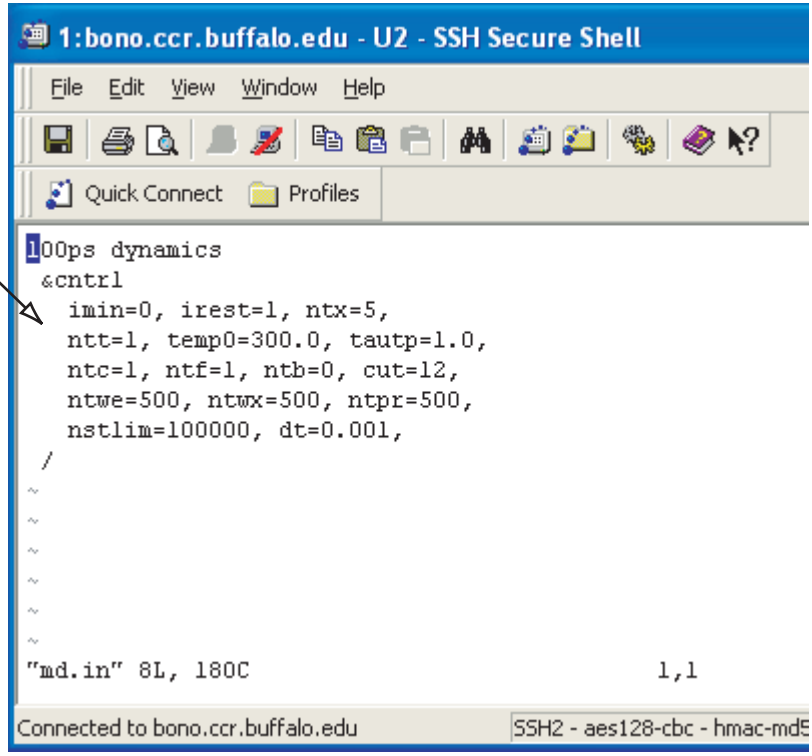
Topology file

Heated coordianates

Output file of heating

MM dynamics of Chignolin

Technical details
of dynamics



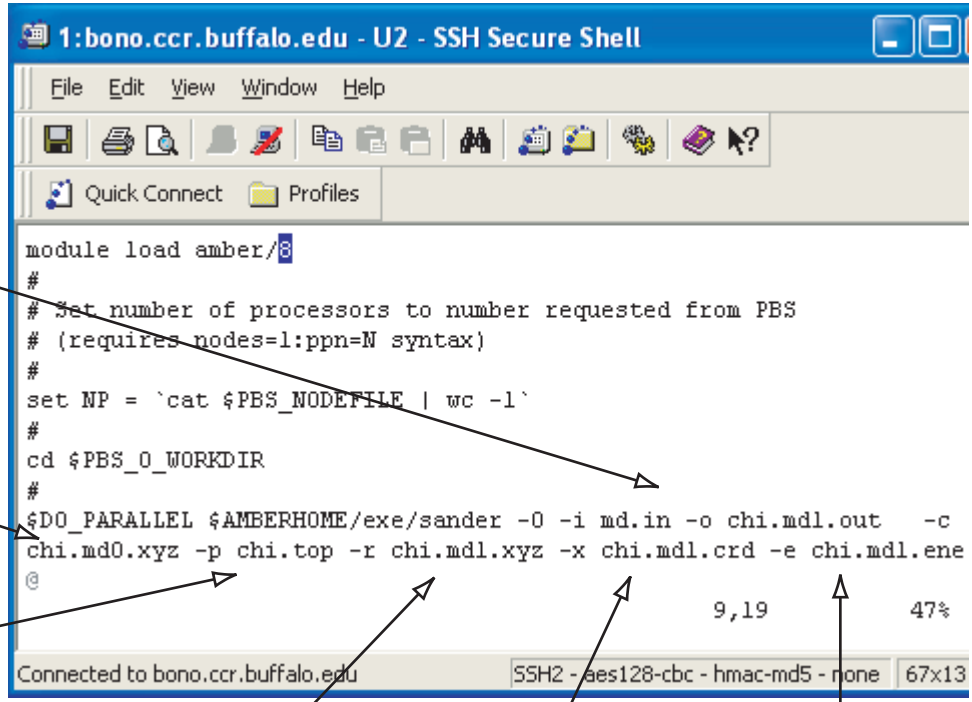
MM dynamics of Chignolin

Technical details of running dynamics

Input and output files of dynamics

Initial coordinates

Topology file



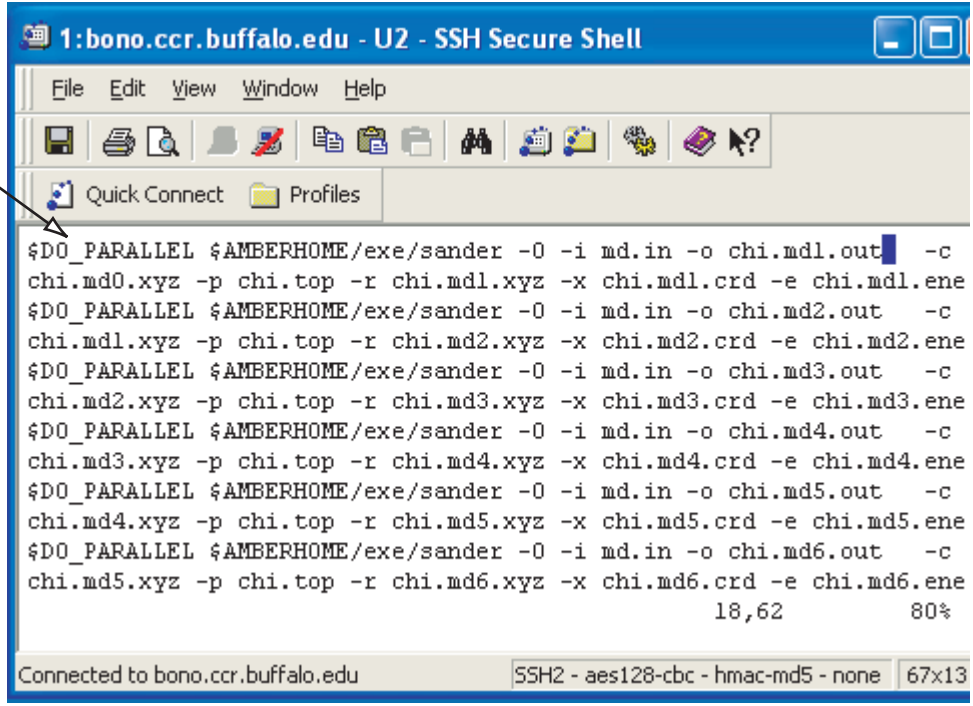
Final coordinates

Complete trajectory

Energy components

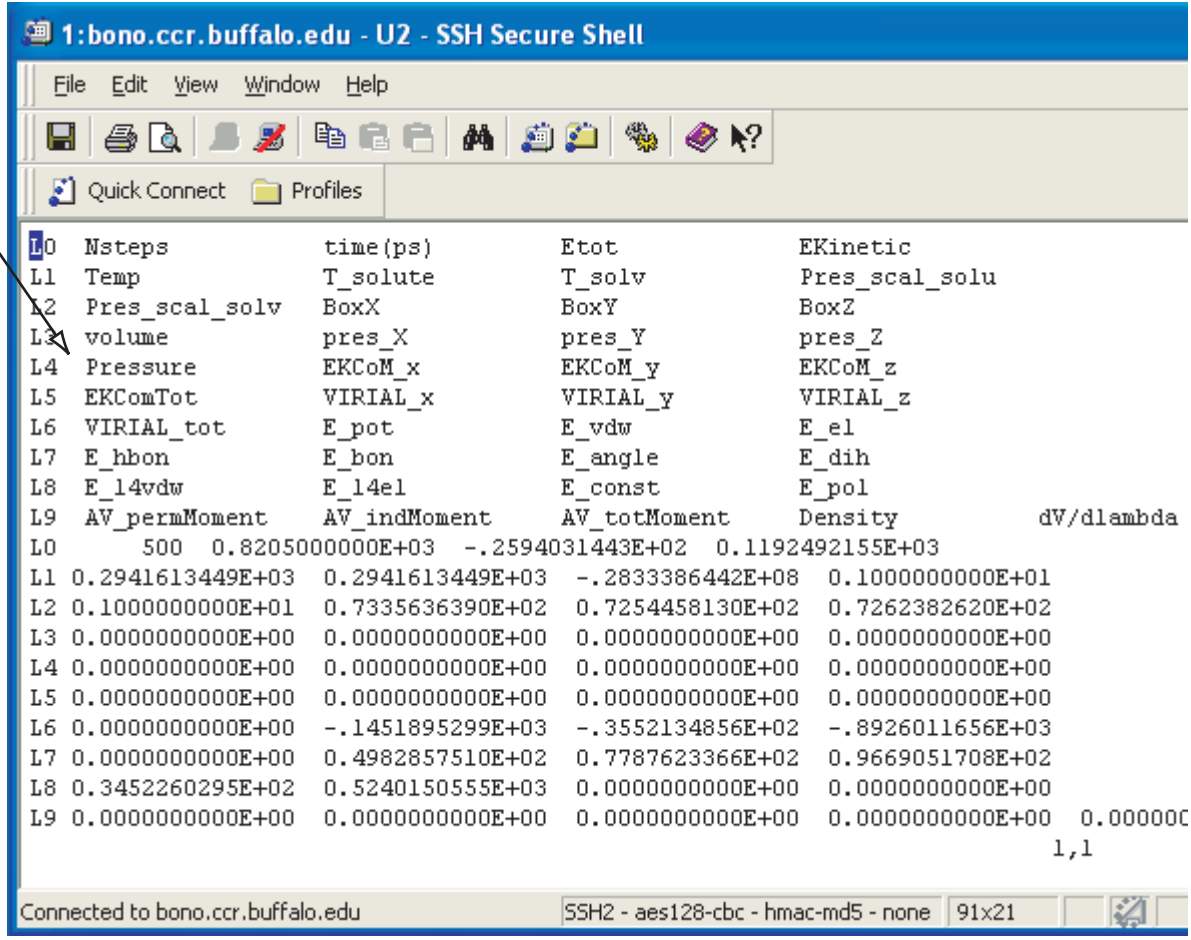
MM dynamics of Chignolin

Technical details of running several steps of the same dynamics



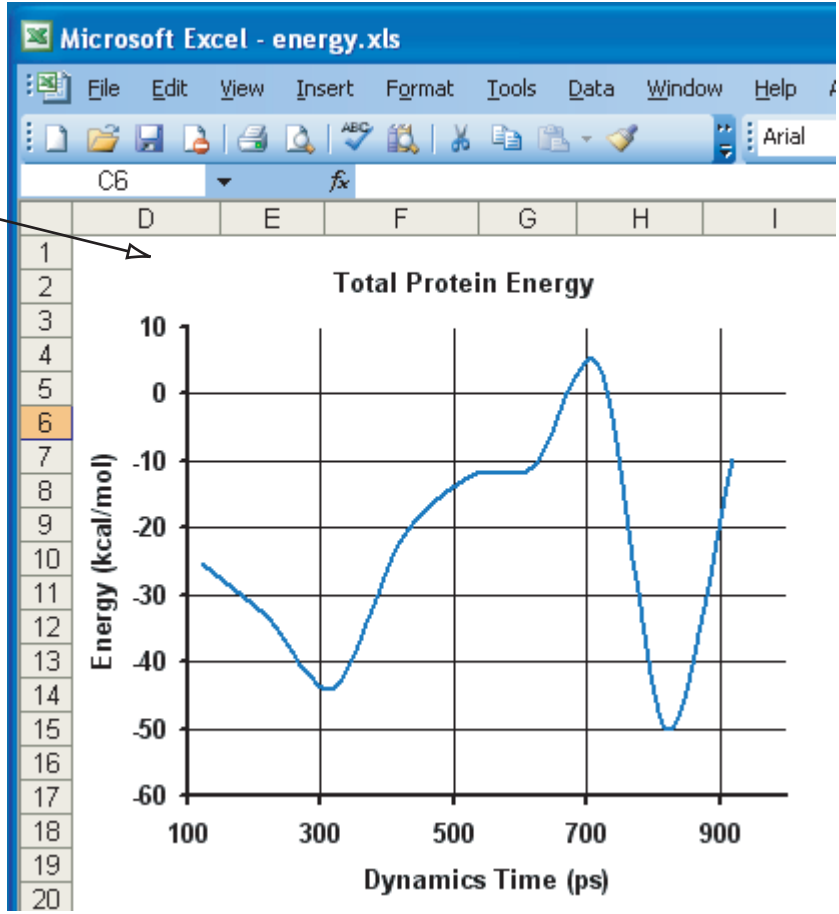
MM dynamics of Chignolin

Energy components after 820ps



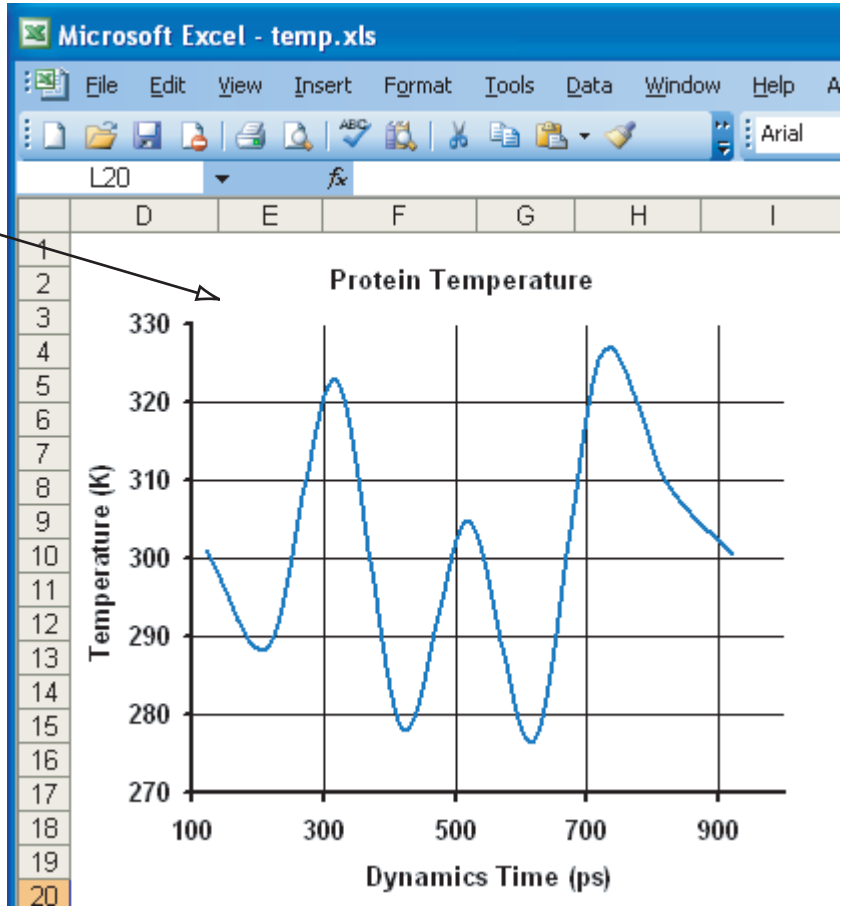
MM dynamics of Chignolin

Total energy of the protein as a function of dynamics time



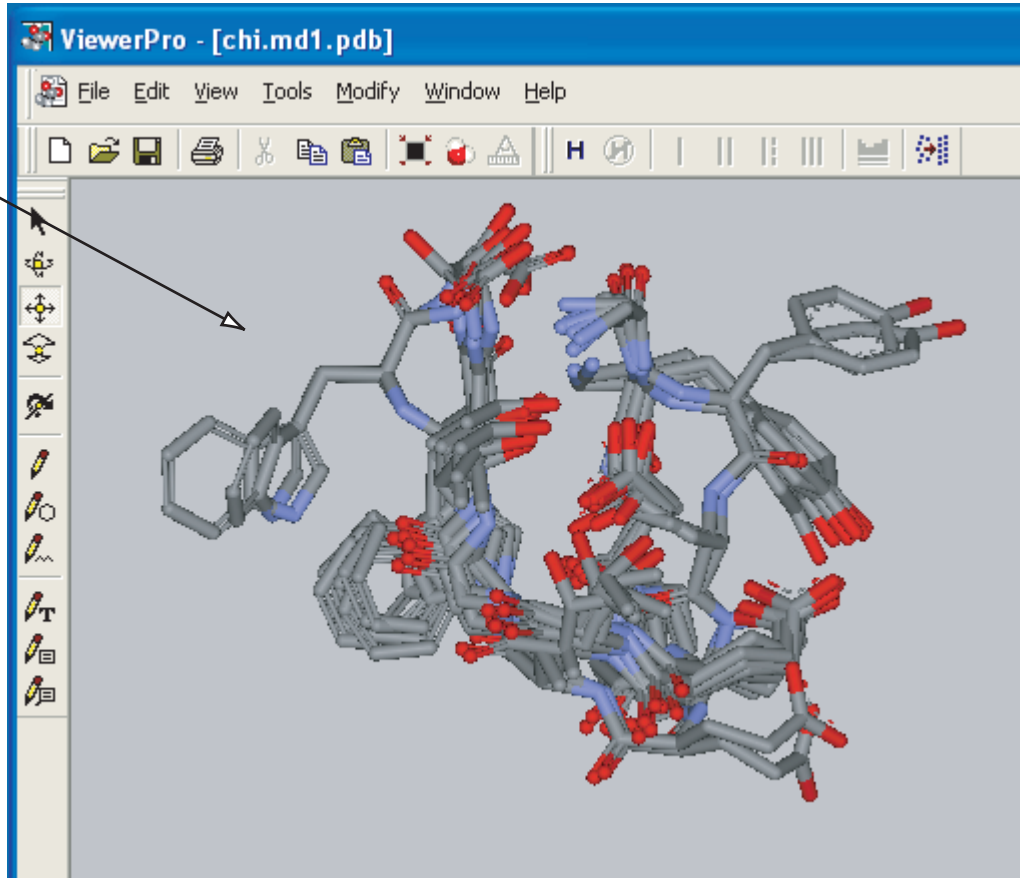
MM dynamics of Chignolin

Temperature of the protein as a function of dynamics time



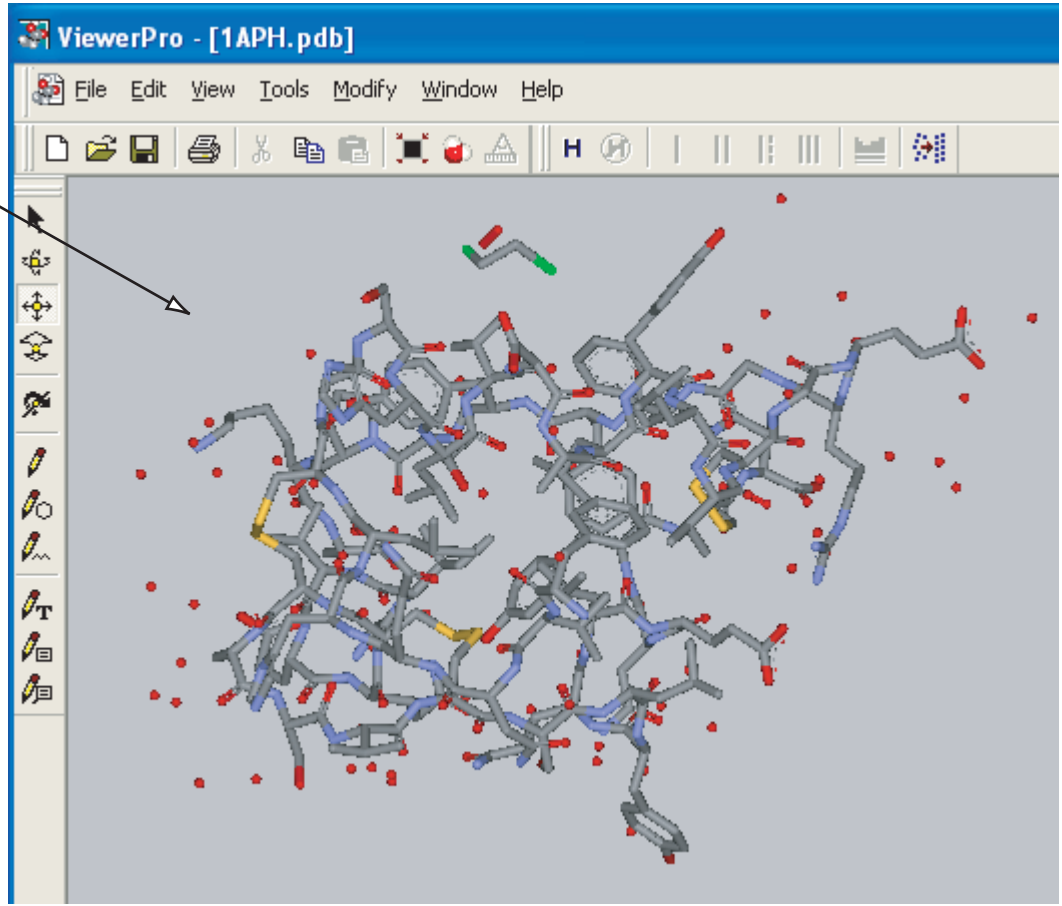
MM dynamics of Chignolin

Superposition of 10 protein structures obtained from 1ns dynamics



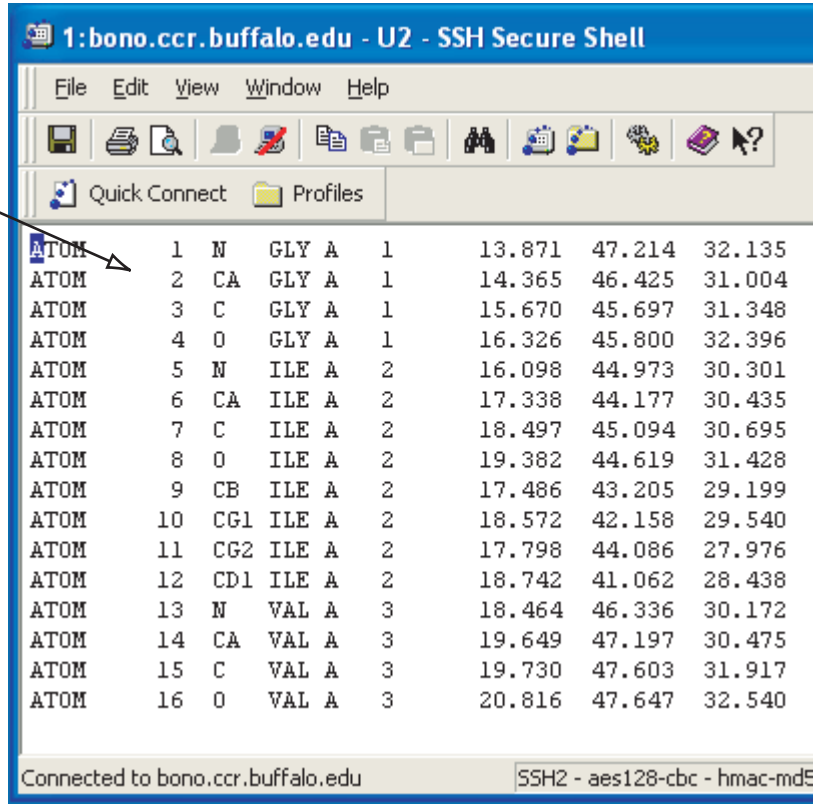
MM dynamics of Insulin

Experimental PDB structure of Insulin



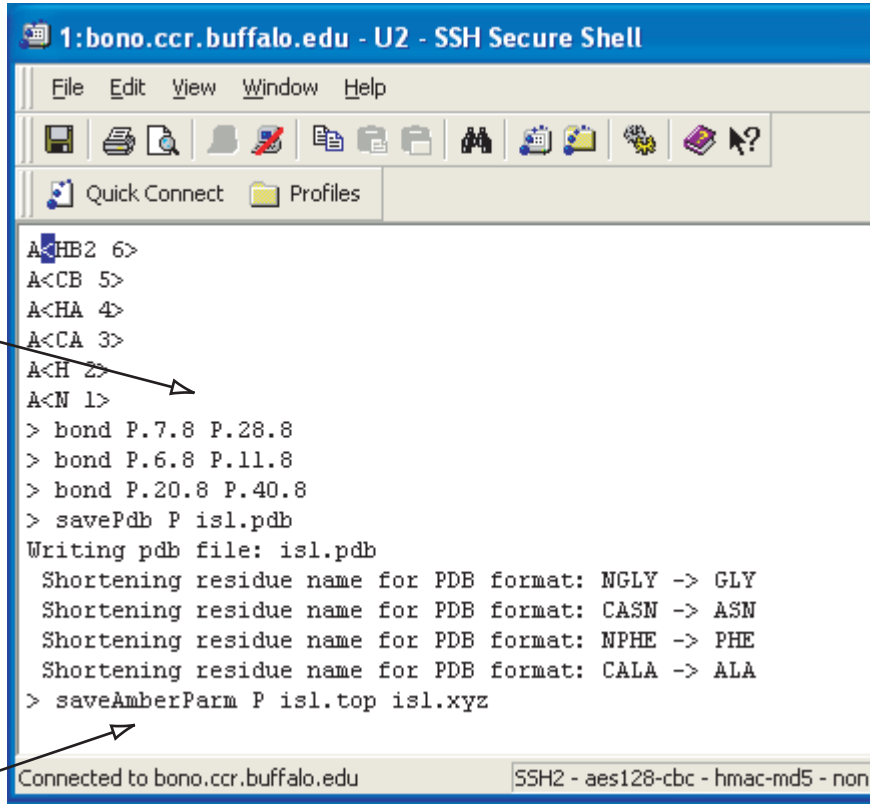
MM dynamics of Insulin

Modified PDB file of insulin
(no crystalographic water molecules)



Bonding cysteine amino acids in the tlep program

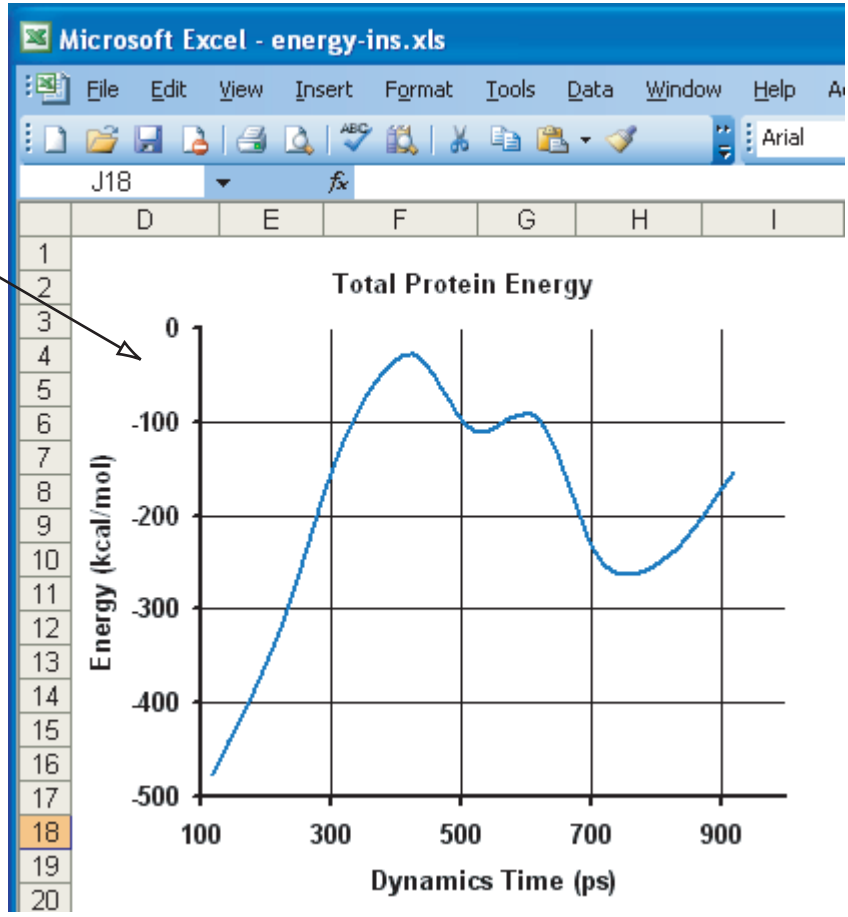
- Unit name
- Residue number
- Atom number



Saving the topology and coordinates files with sulfur bridges

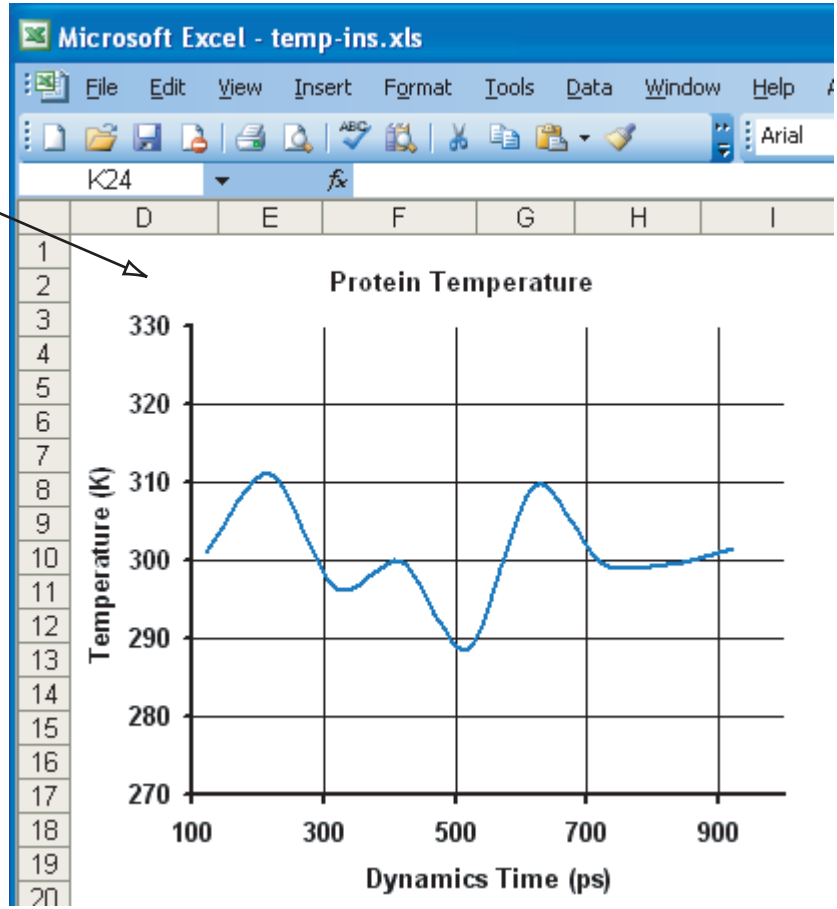
MM dynamics of Insulin

The total energy of the protein as a function of dynamics time



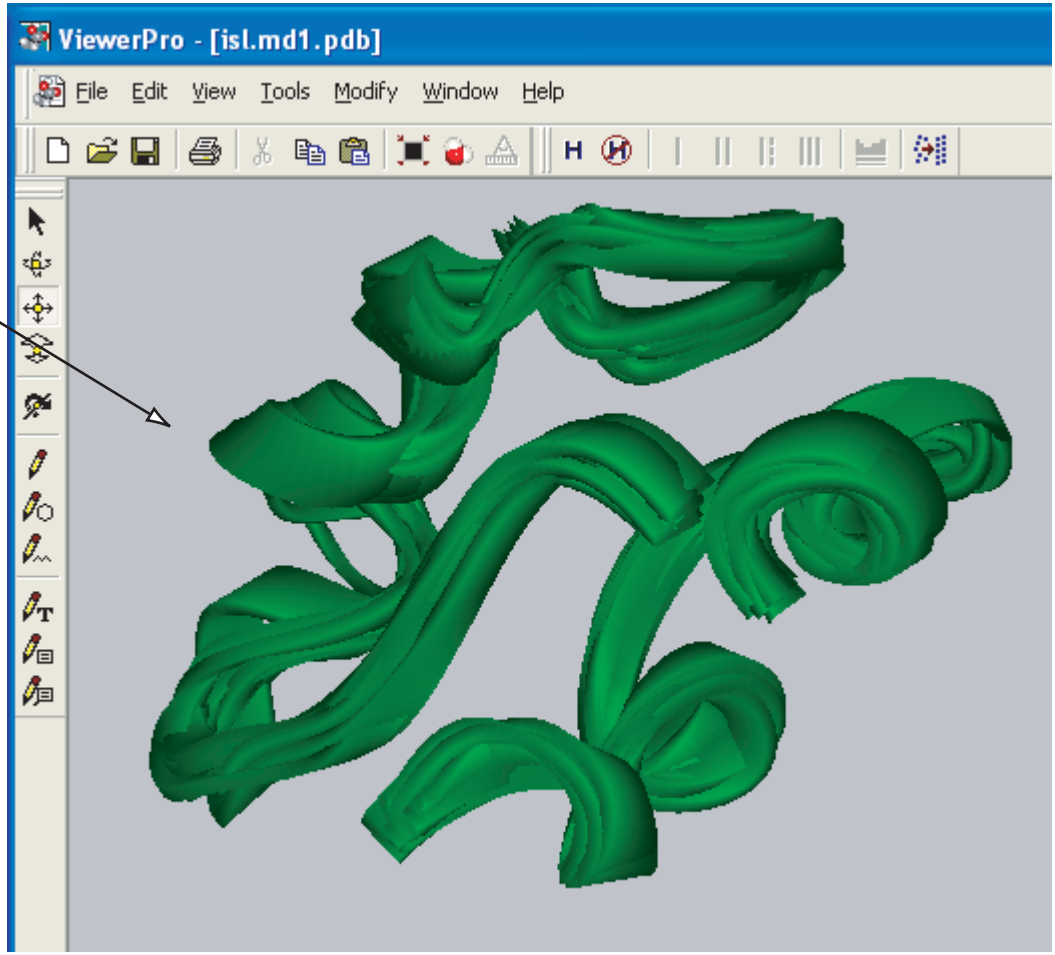
MM dynamics of Insulin

Temperature of the protein as a function of dynamics time

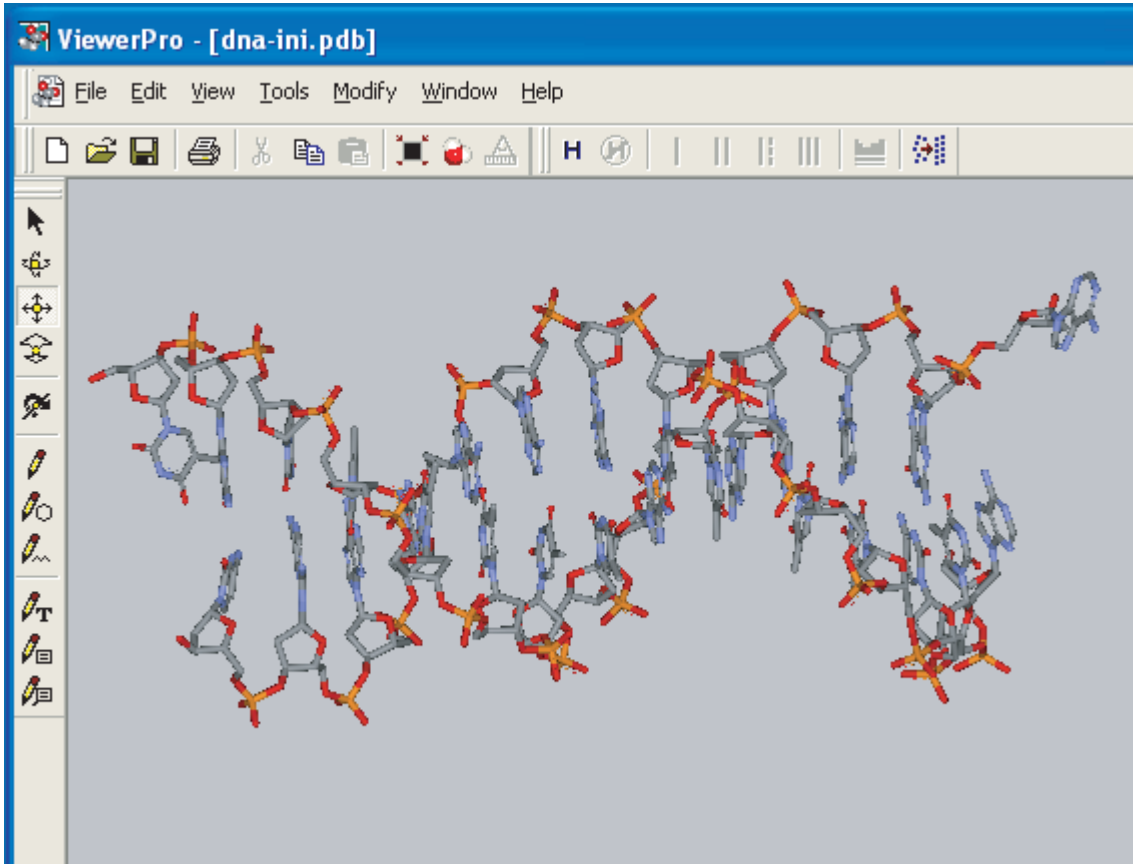


MM dynamics of Insulin

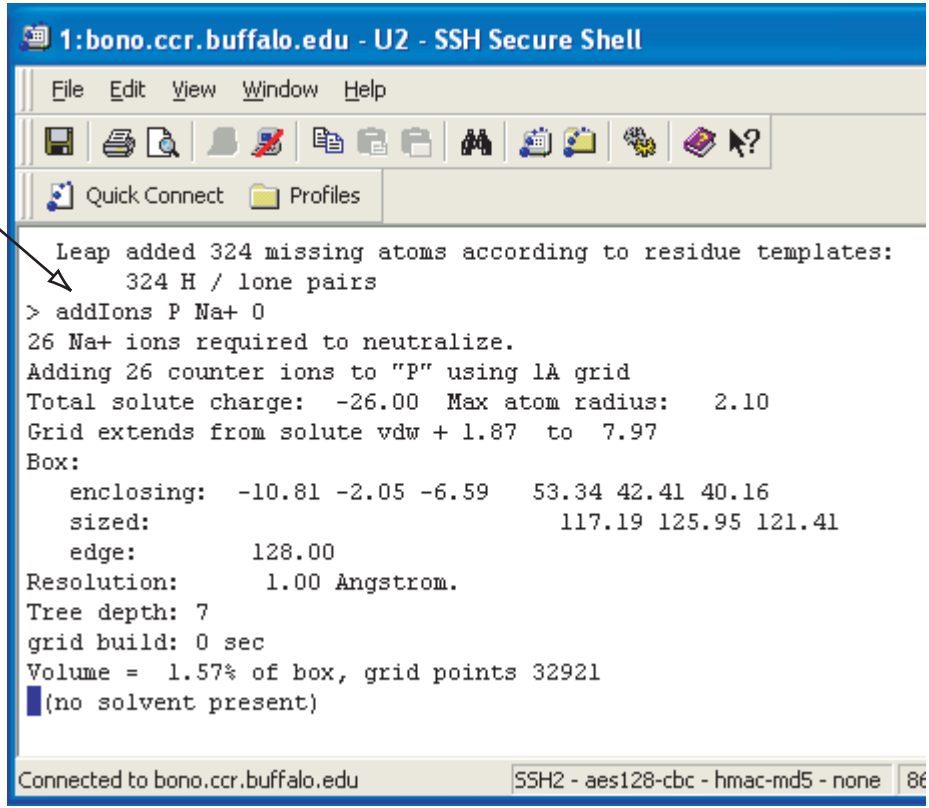
Superposition of 10 protein structures obtained from 1ns dynamics



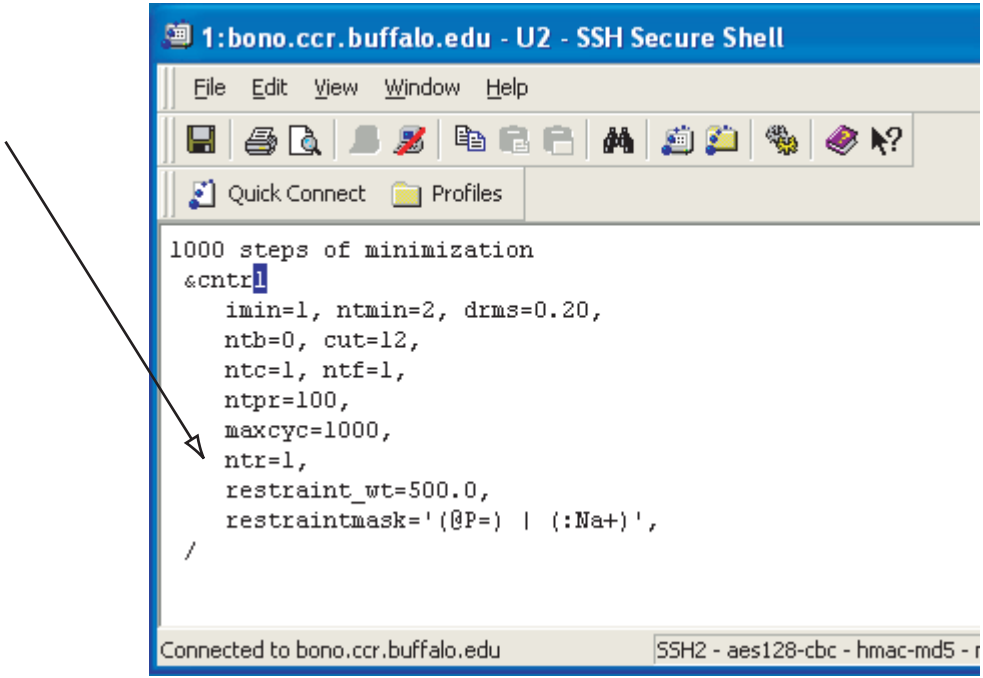
Experimental PDB structure of a small DNA



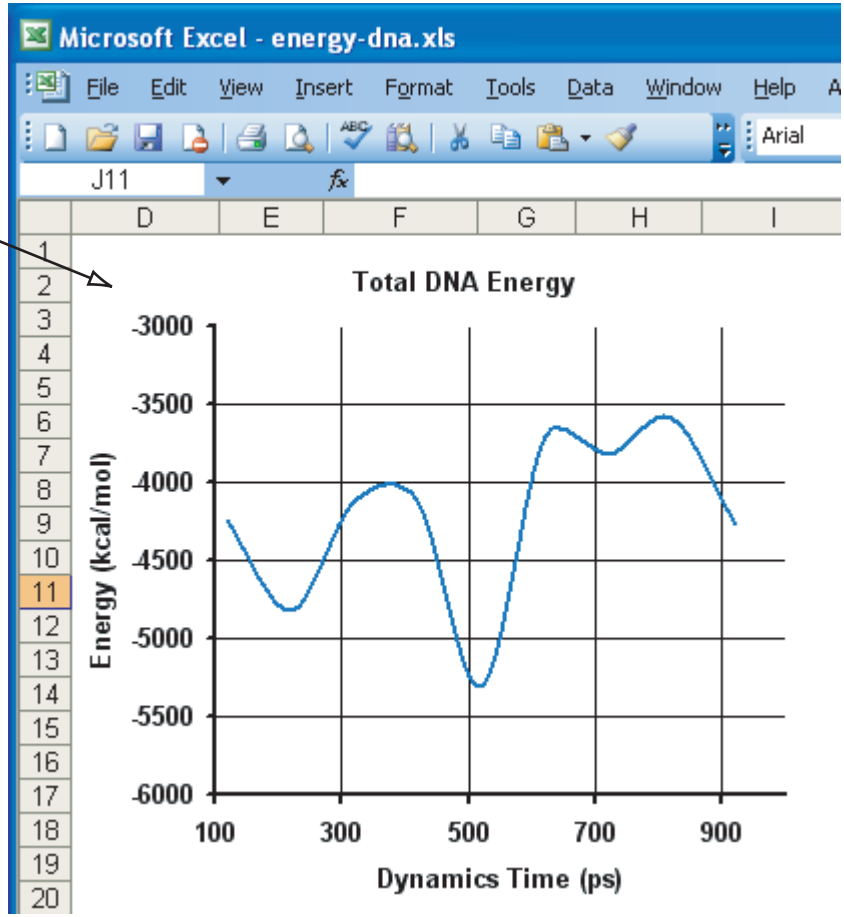
Adding sodium cations to neutralize the nucleic acid, in the tleap program



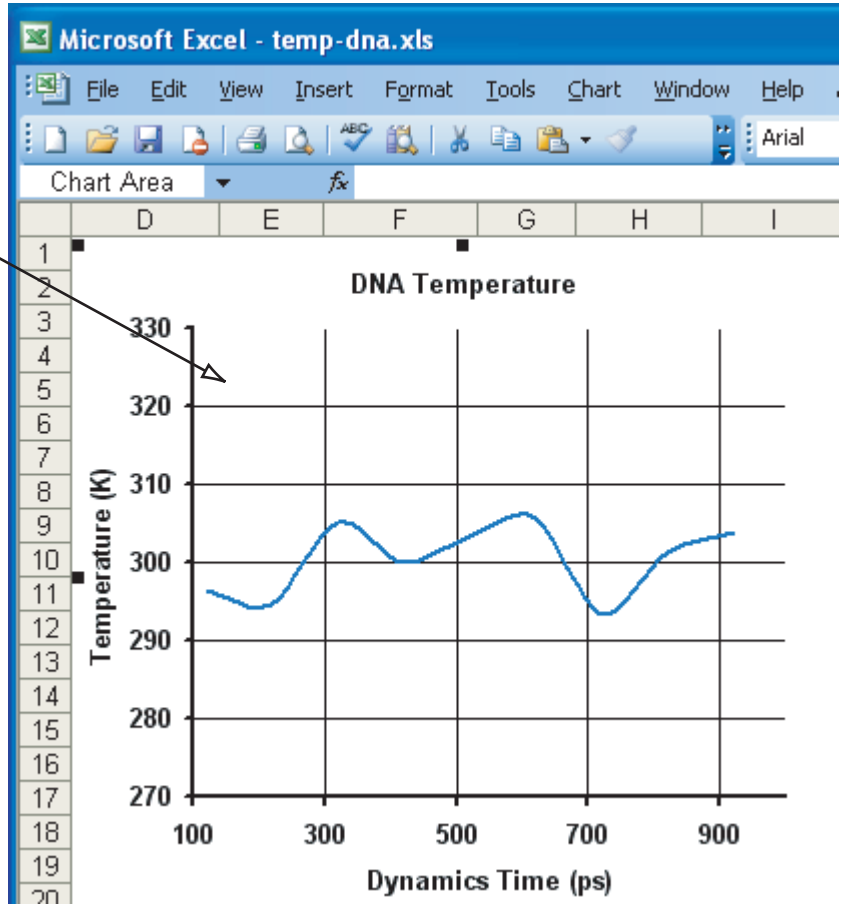
Minimization with constrained positions of phosphorus and sodium atoms



Total DNA energy as a function of dynamics time

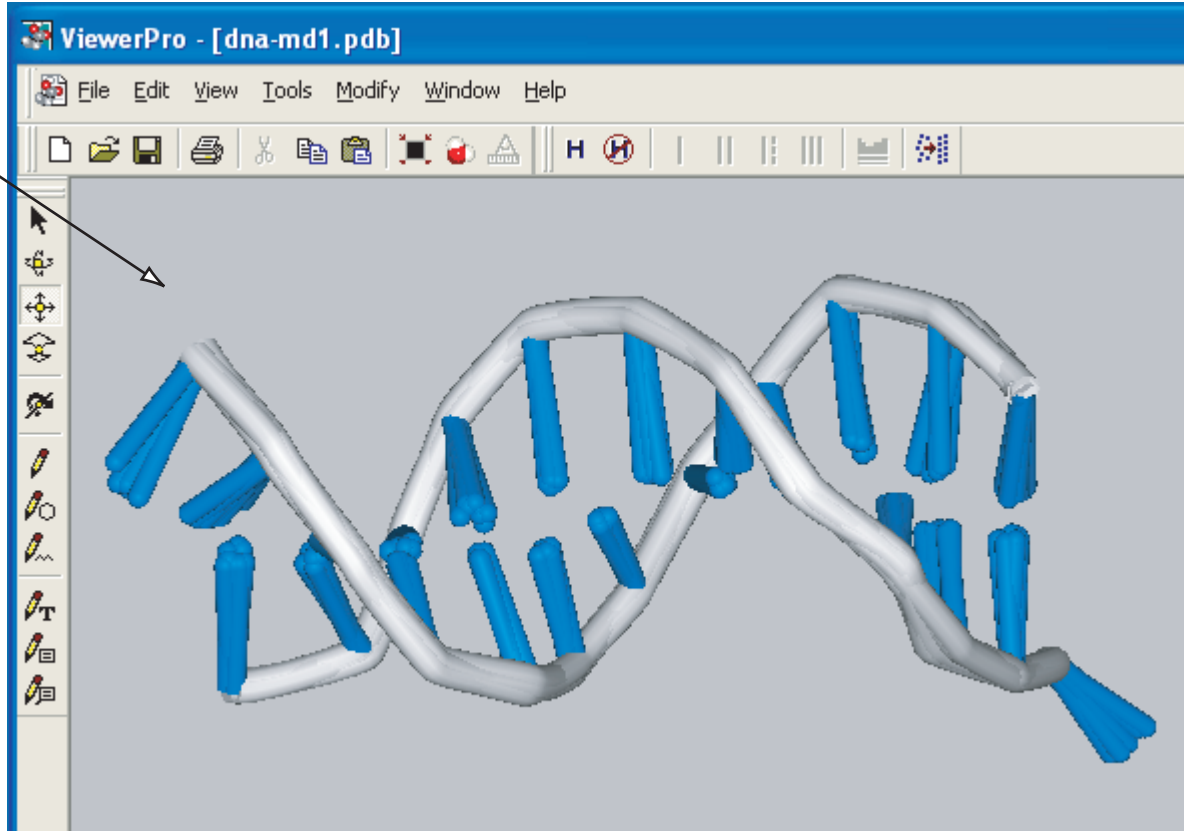


DNA temperature as a function of dynamics time



MM dynamics of DNA

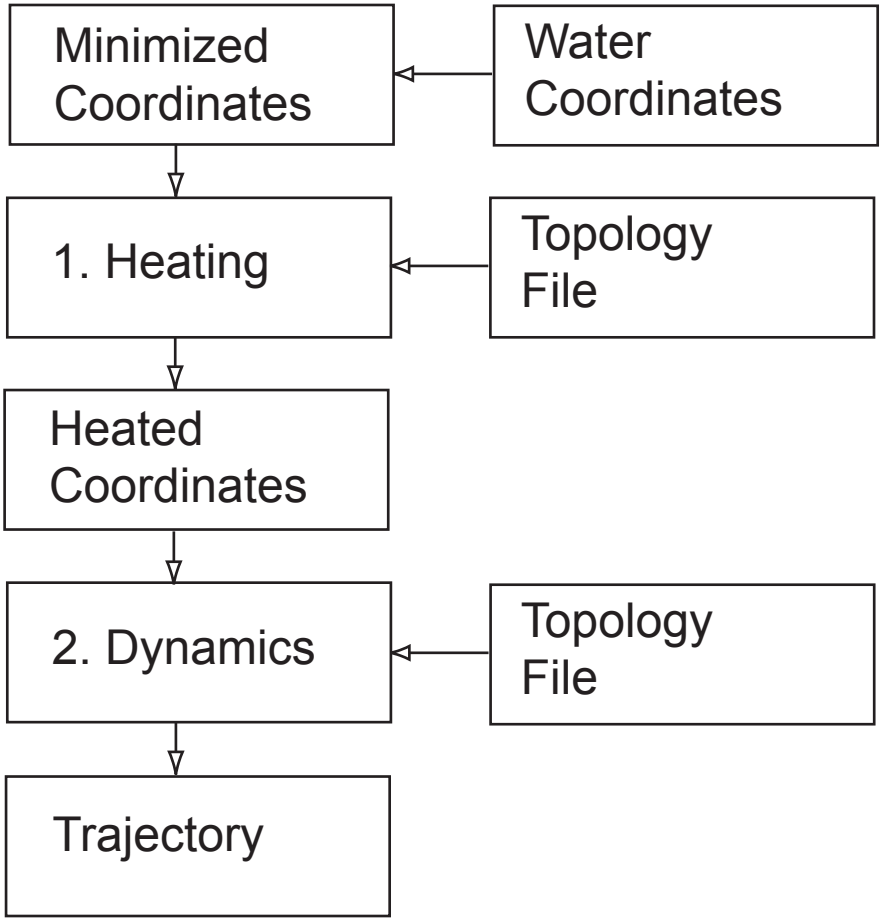
Superposition of 10 DNA structures after 1ns dynamics temperature



MM dynamics in water solution

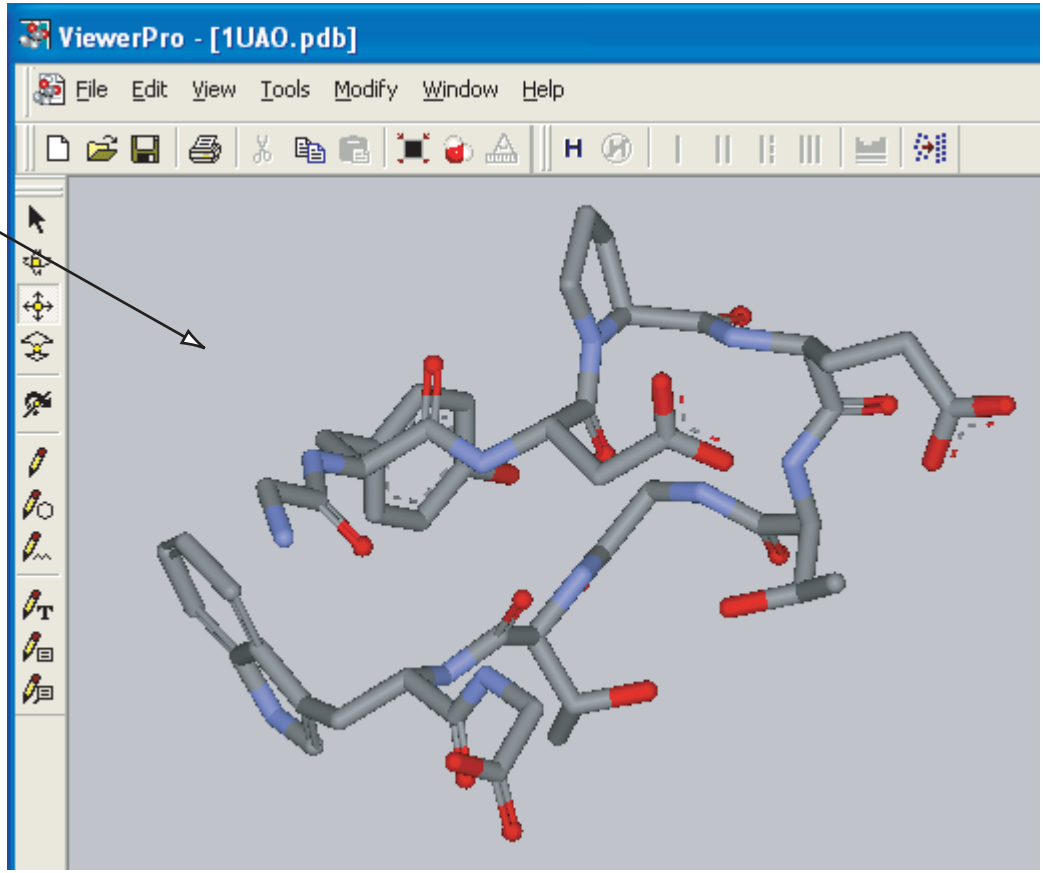
MM dynamics in water solution can be performed using implicit or explicit water molecules

MM dynamics with explicit water molecules used a TIP3P water model



MM dynamics of Chignolin in a sphere of water

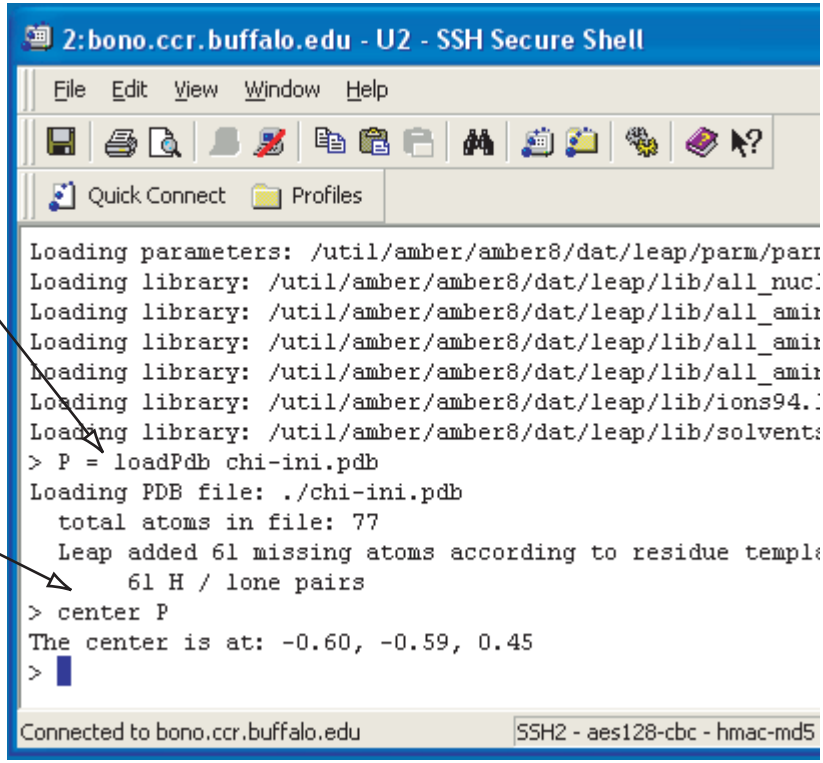
Experimental PDB structure of Chignolin



MM dynamics of Chignolin in a sphere of water

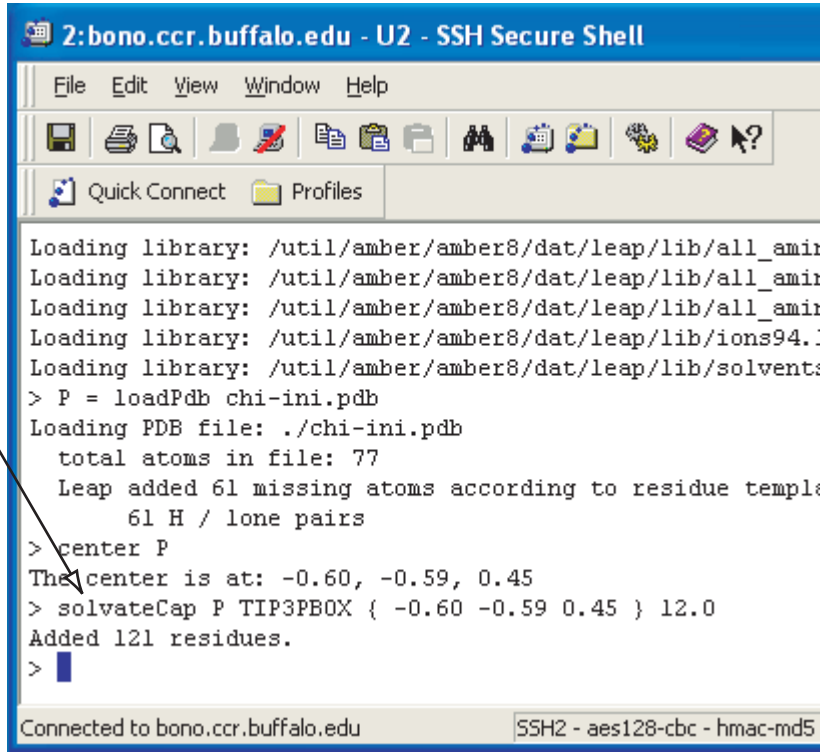
Loading the initial PDB file of the protein

Finding the center of the protein



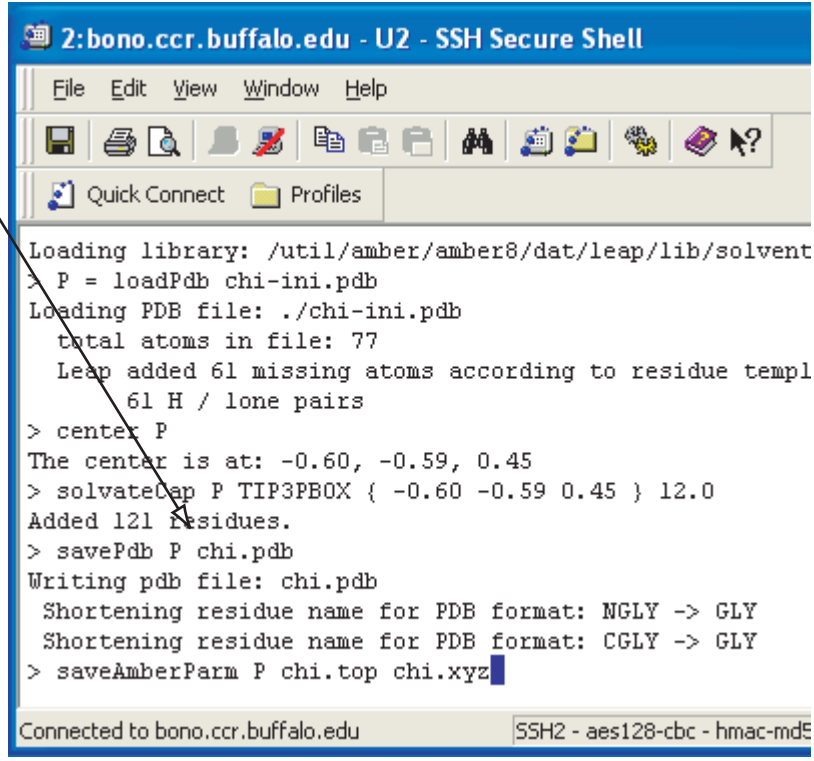
MM dynamics of Chignolin in a sphere of water

Solwating the protein by a sphere of explicit water molecules, of a radius 12A

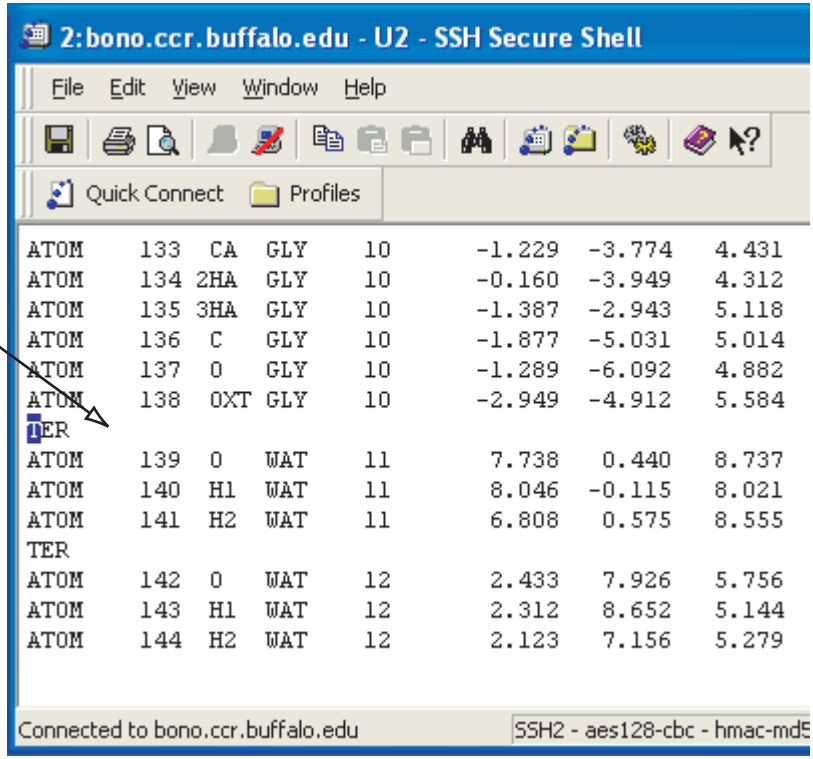


MM dynamics of Chignolin in a sphere of water

Saving the PDB, the topology and the initial coordinates files

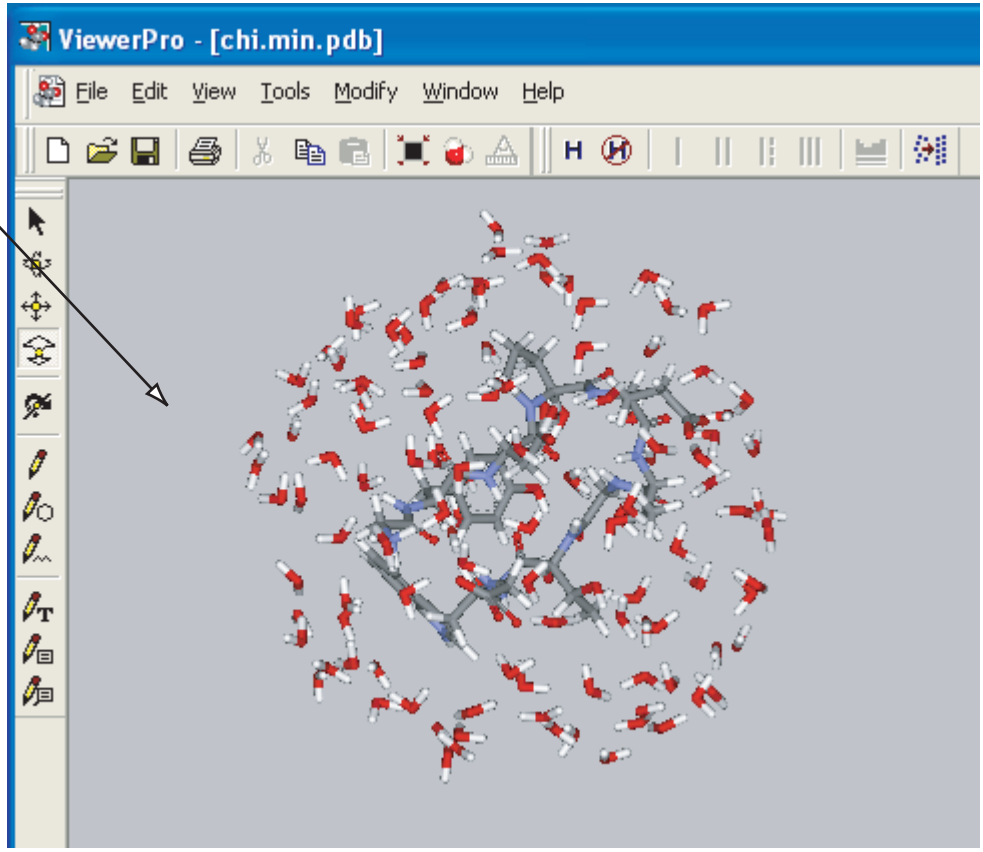


The coordinates of TIP3P water molecules in the PDB file



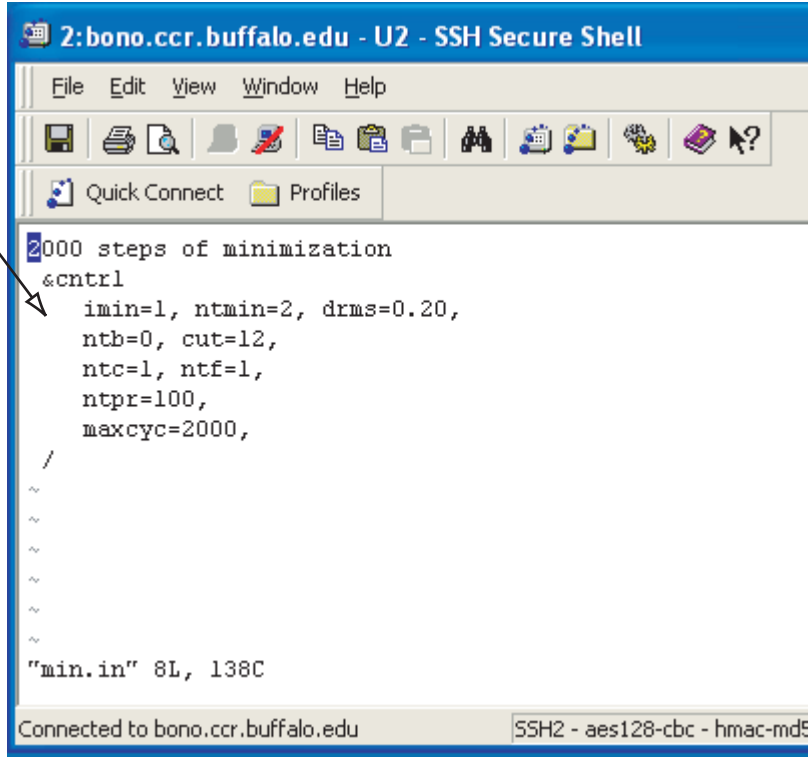
MM dynamics of Chignolin in a sphere of water

Chignolin protein surrounded by water molecules



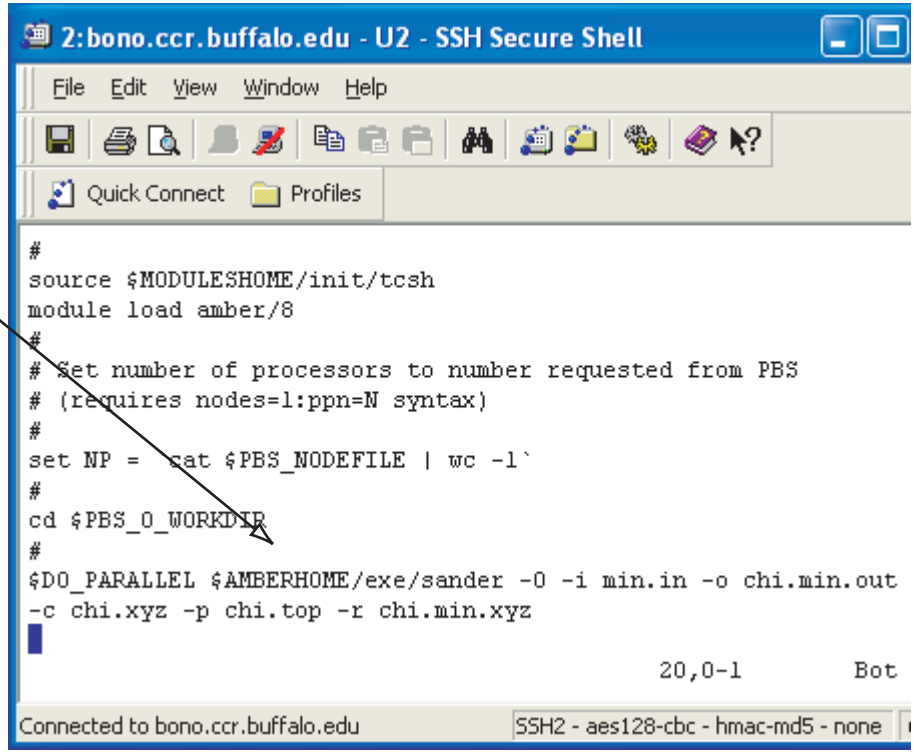
MM dynamics of Chignolin in a sphere of water

Technical details of minimization



MM dynamics of Chignolin in a sphere of water

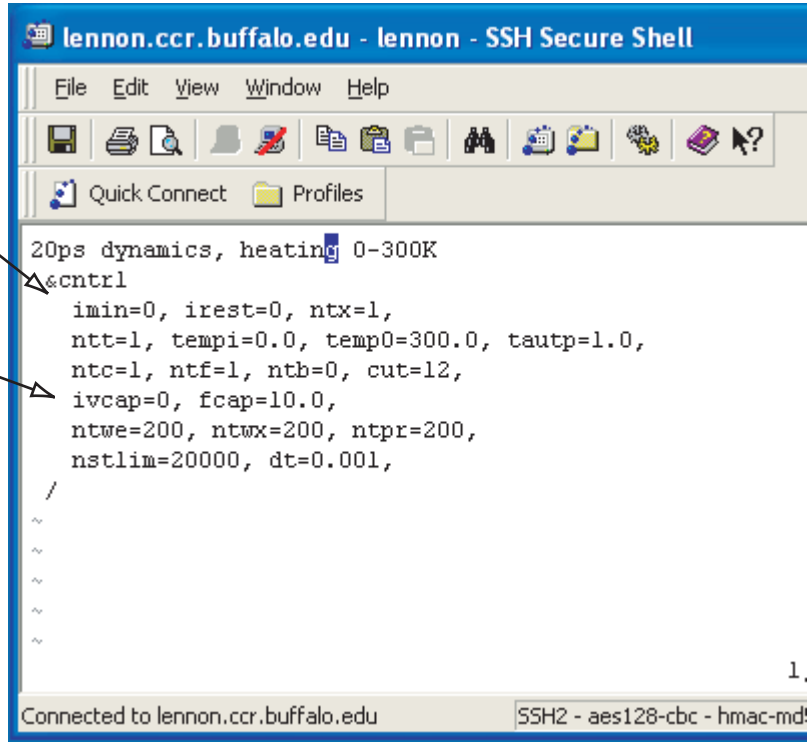
Technical details of running minimization



MM dynamics of Chignolin in a sphere of water

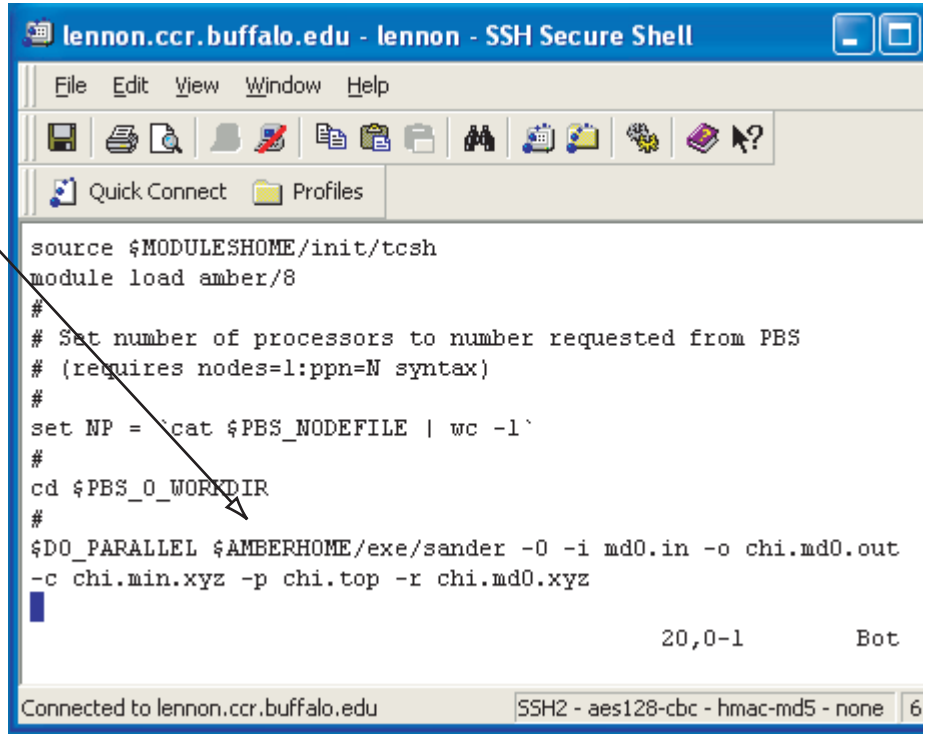
Technical details of heating

Parameters of the water sphere



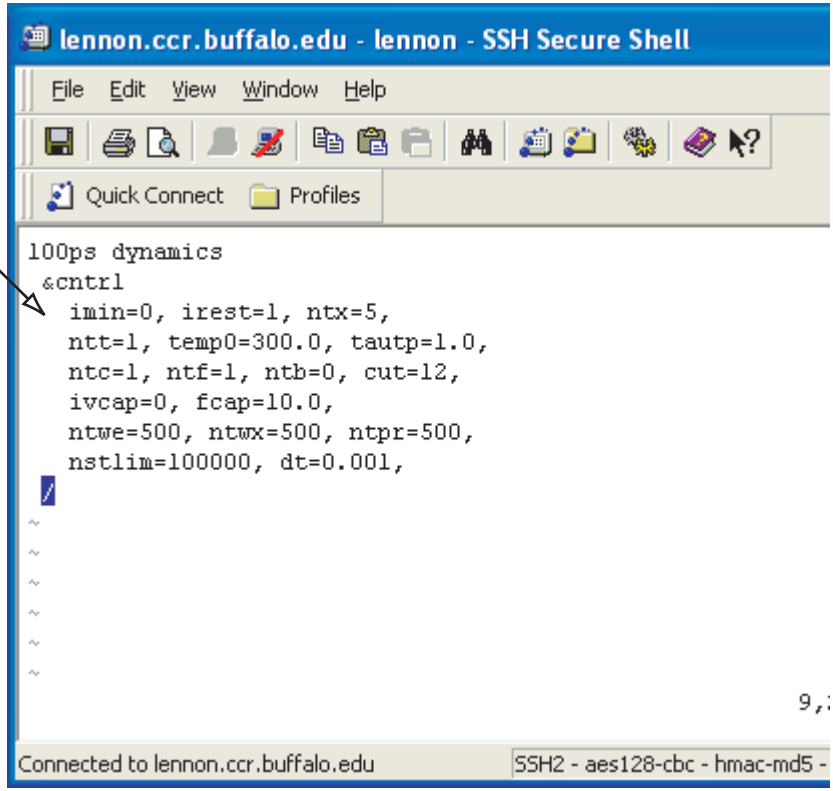
MM dynamics of Chignolin in a sphere of water

Technical details of running heating



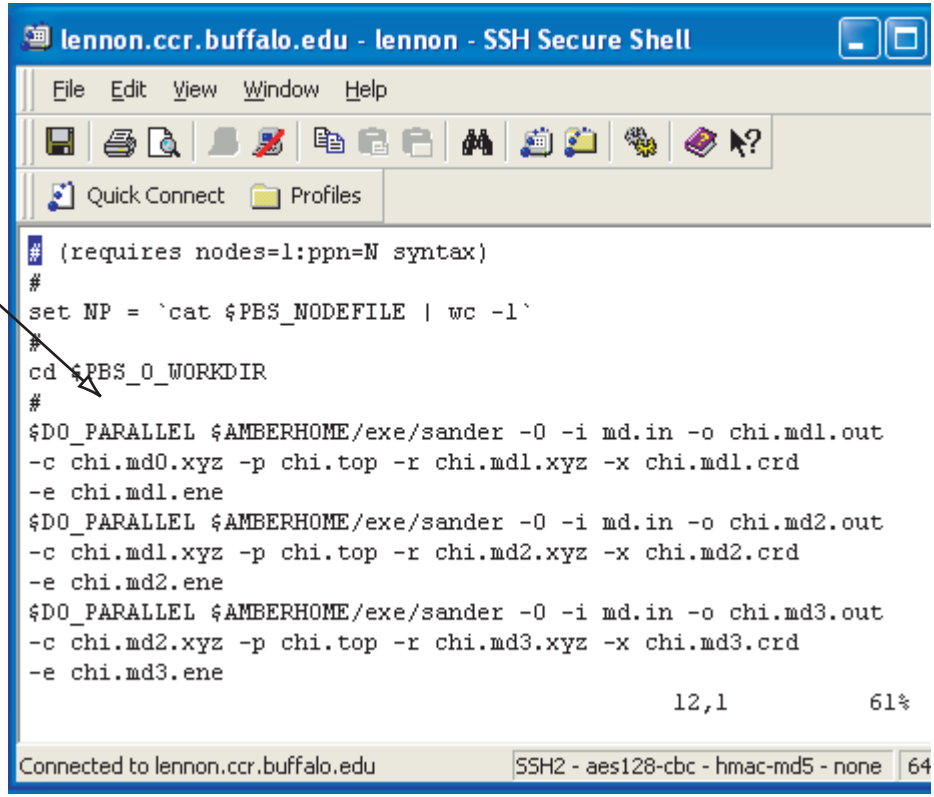
MM dynamics of Chignolin in a sphere of water

Technical details of dynamics



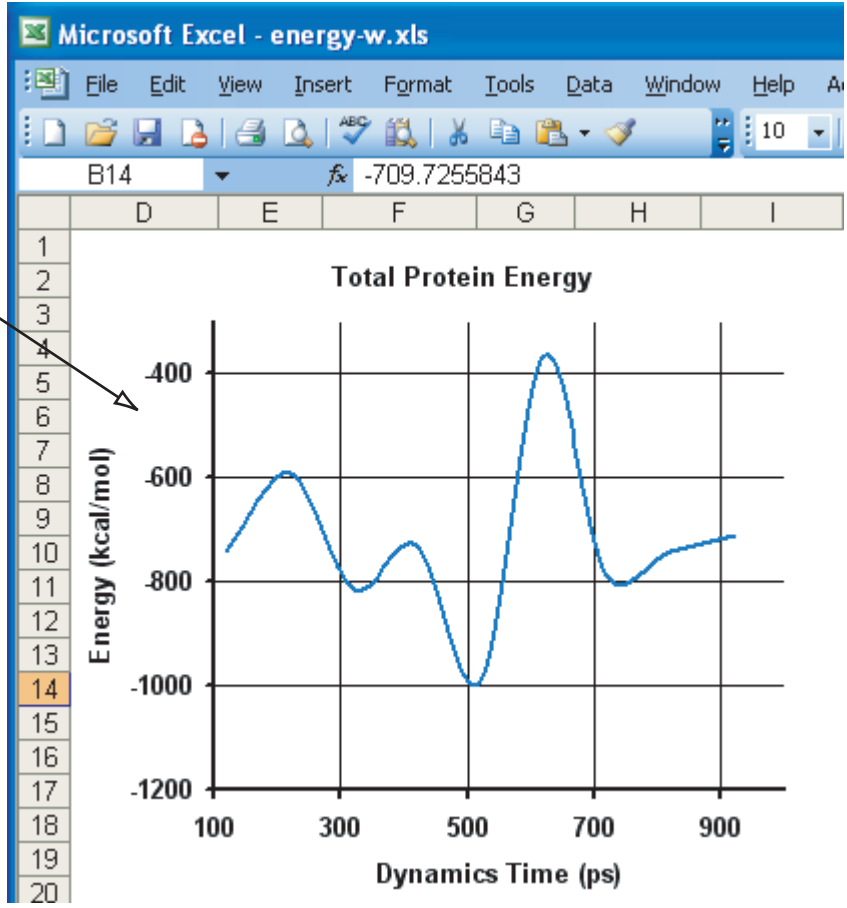
MM dynamics of Chignolin in a sphere of water

Technical details of running dynamics



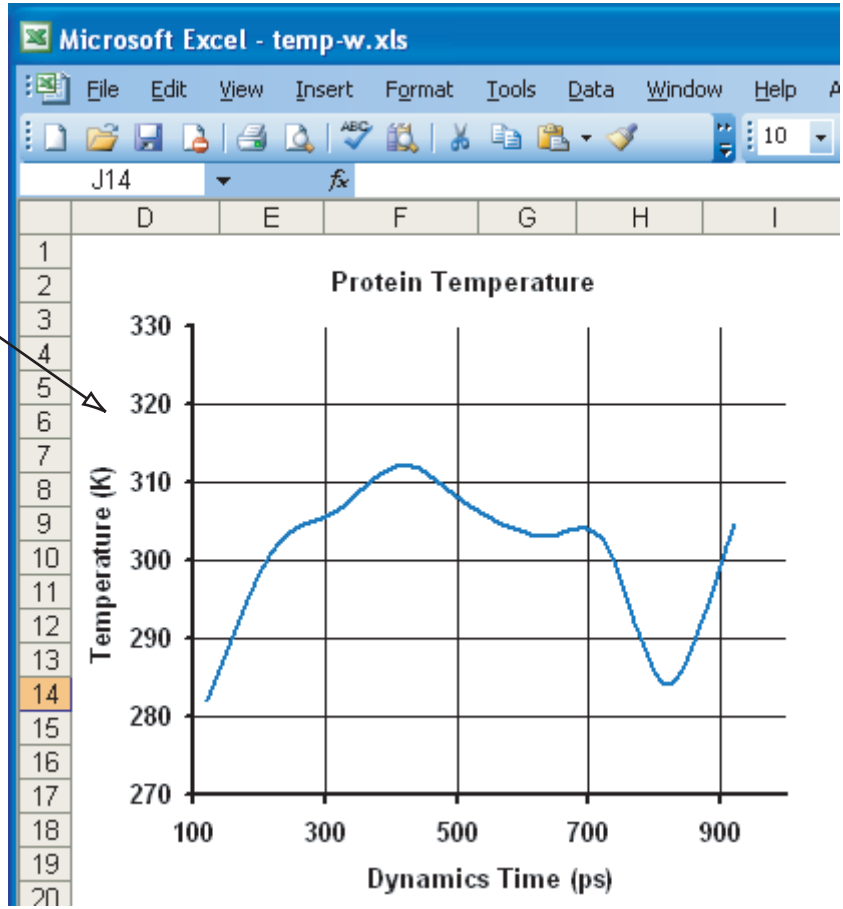
MM dynamics of Chignolin in a sphere of water

Total energy of the protein after dynamics in water solution



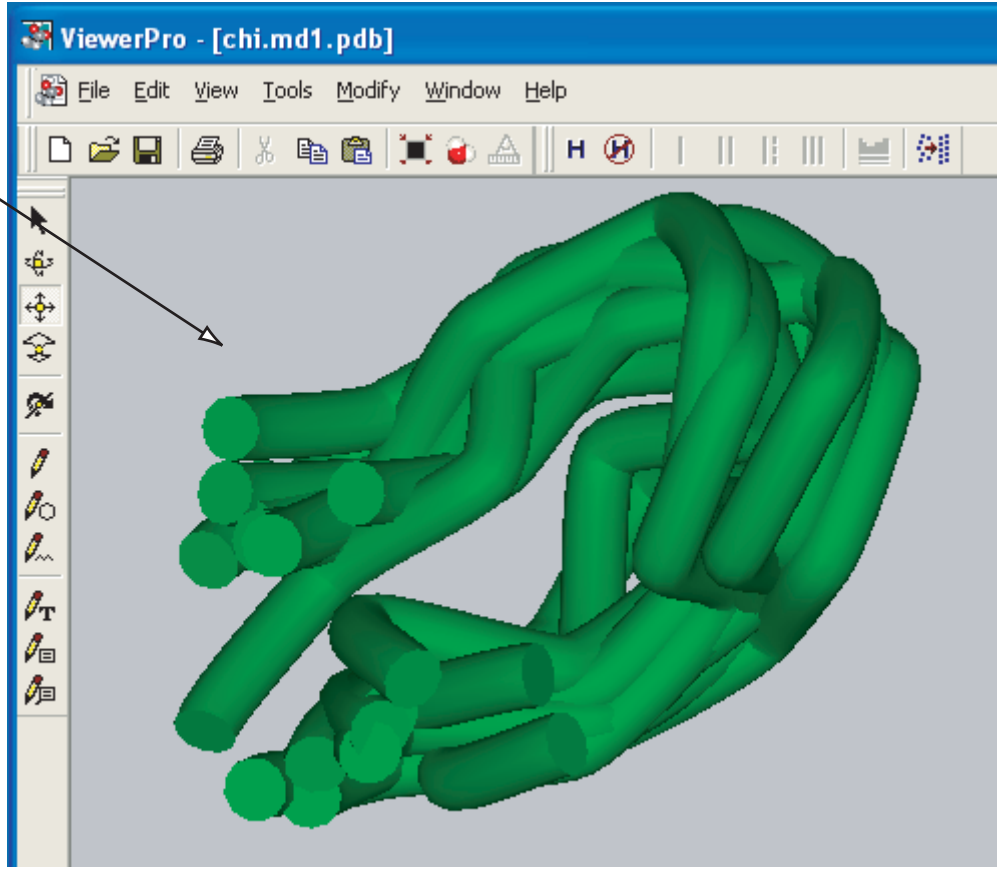
MM dynamics of Chignolin in a sphere of water

Temperature of the protein after dynamics in water solution



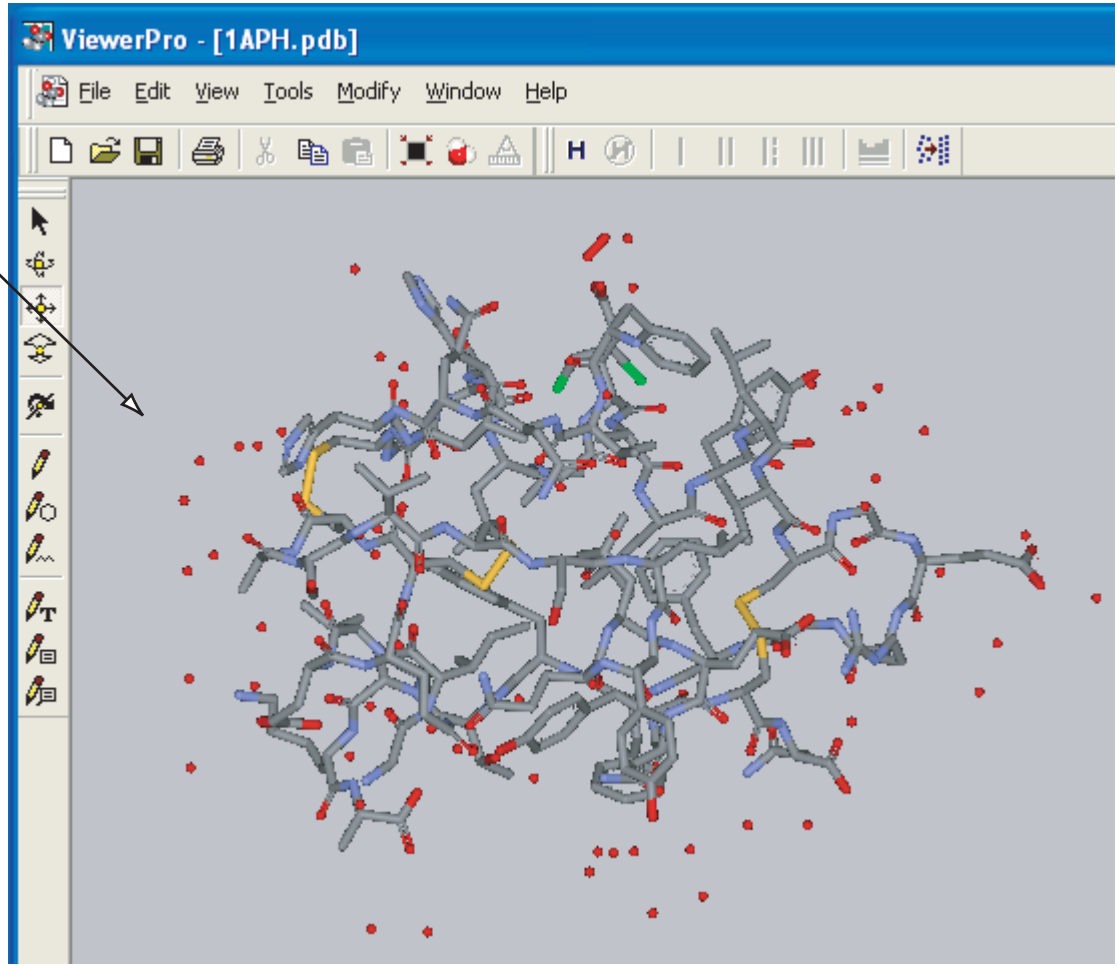
MM dynamics of Chignolin in a sphere of water

Superposition of 9 protein structure obtained from MD in water solution



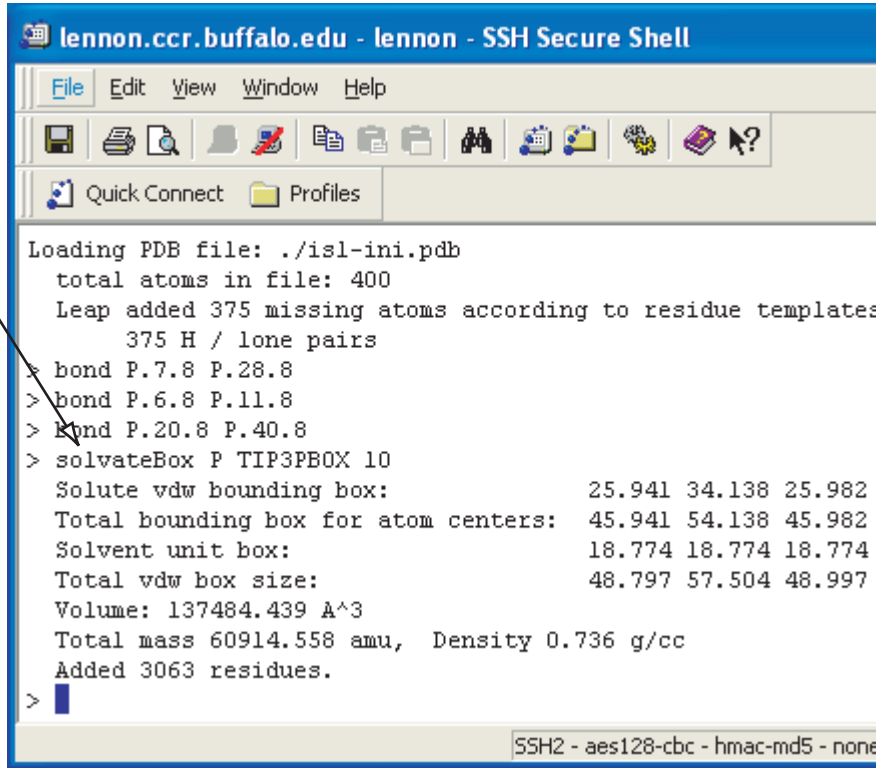
MM dynamics of Insulin in a periodic box of water

Experimental PDB file of Insuline



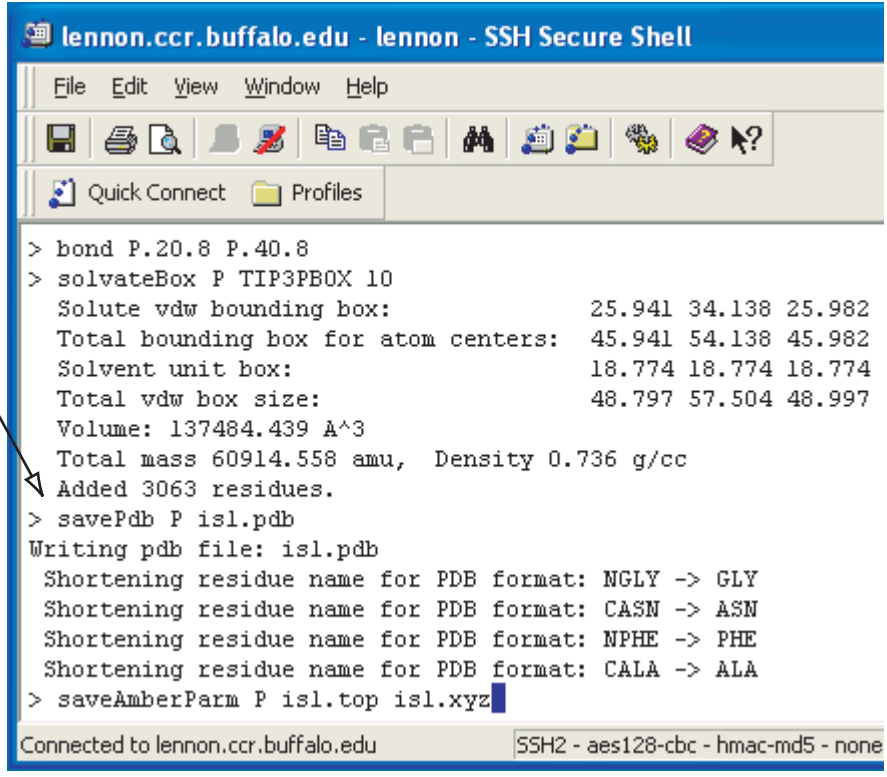
MM dynamics of Insulin in a periodic box of water

Solvating the protein by a box of explicit water molecules



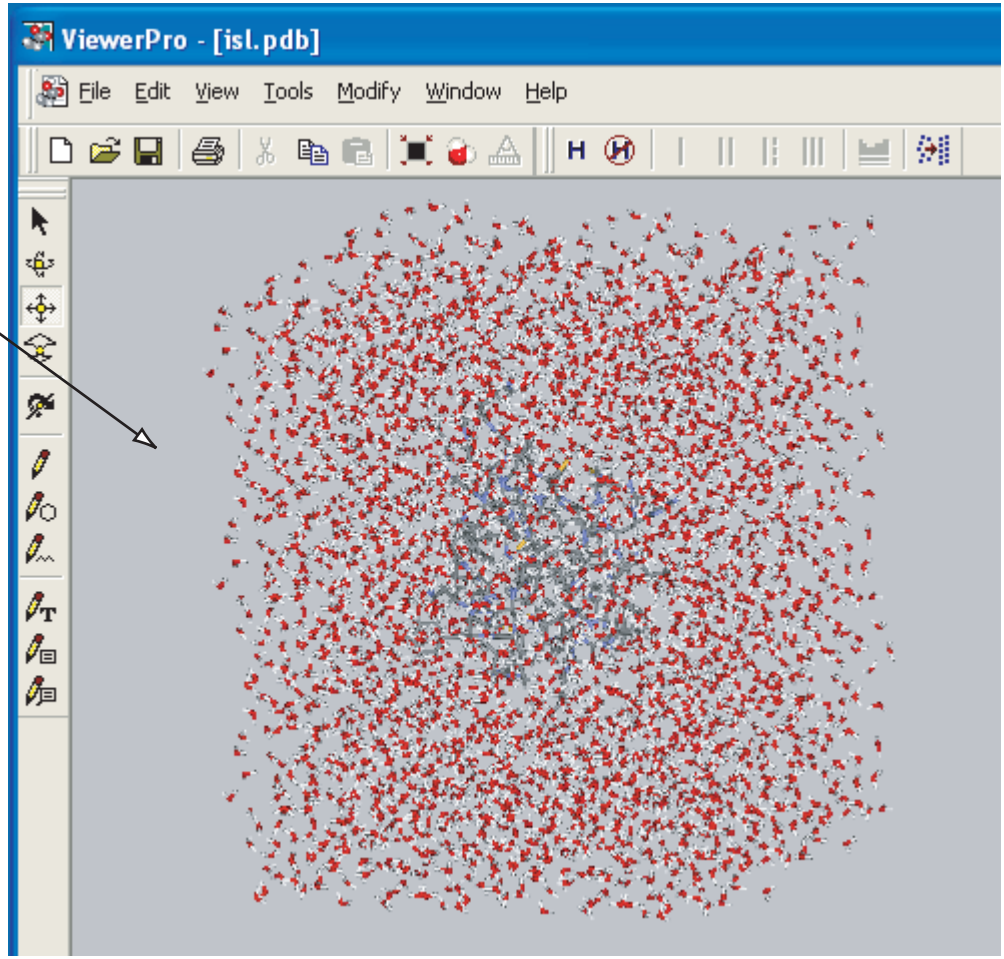
MM dynamics of Insulin in a periodic box of water

Saving the PDB, topology and coordinates files



MM dynamics of Insulin in a periodic box of water

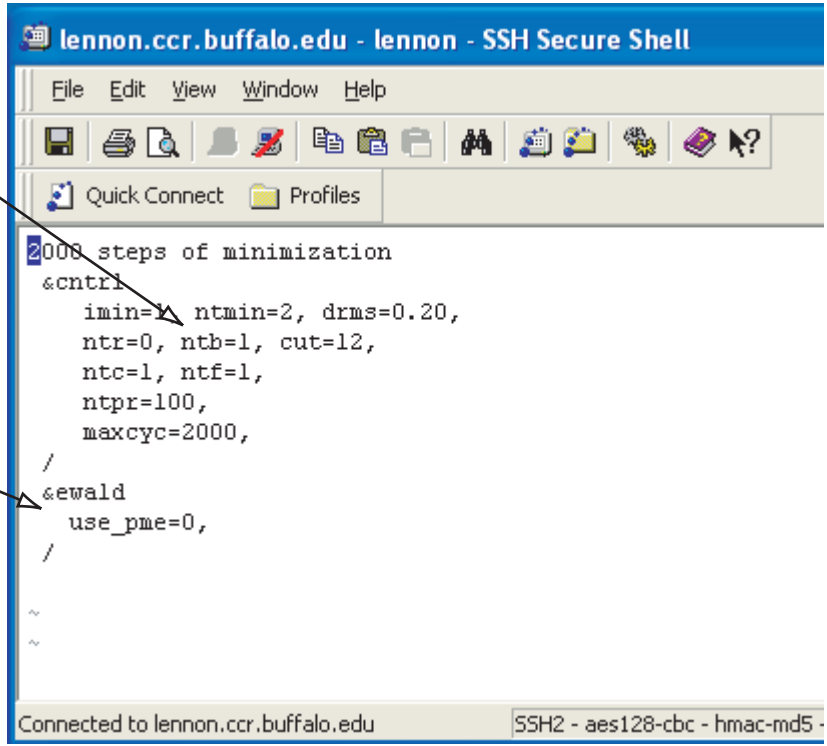
The PDB file of the protein in a preiodic box of explicit water molecules



MM dynamics of Insulin in a periodic box of water

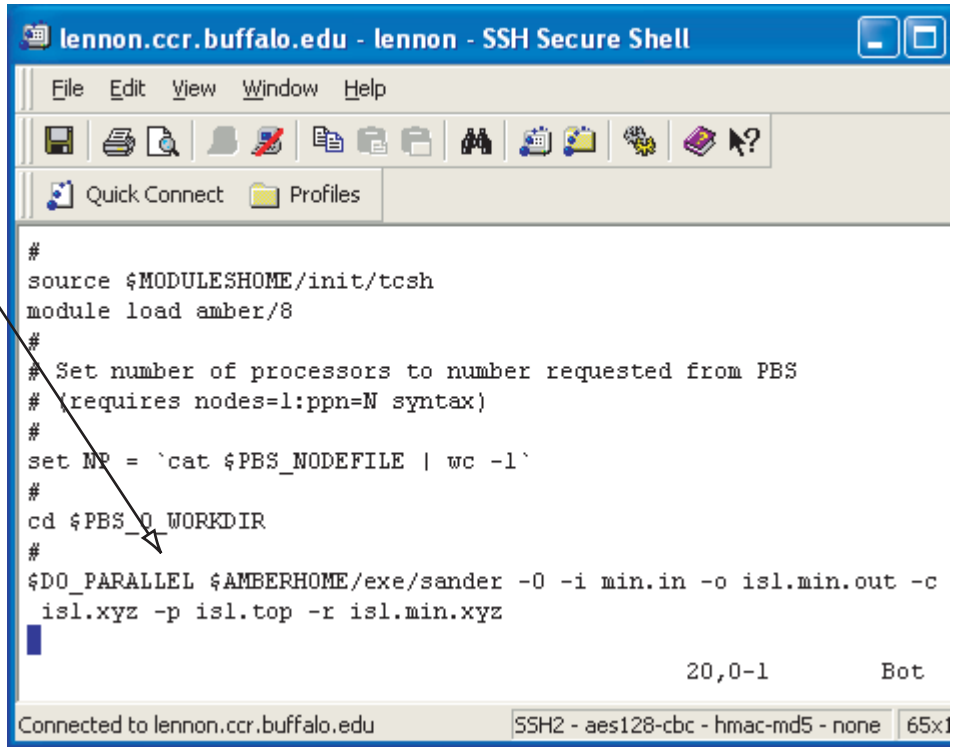
Technical details of minimization in constance volume

We are not using the Particle Mesh Ewald method



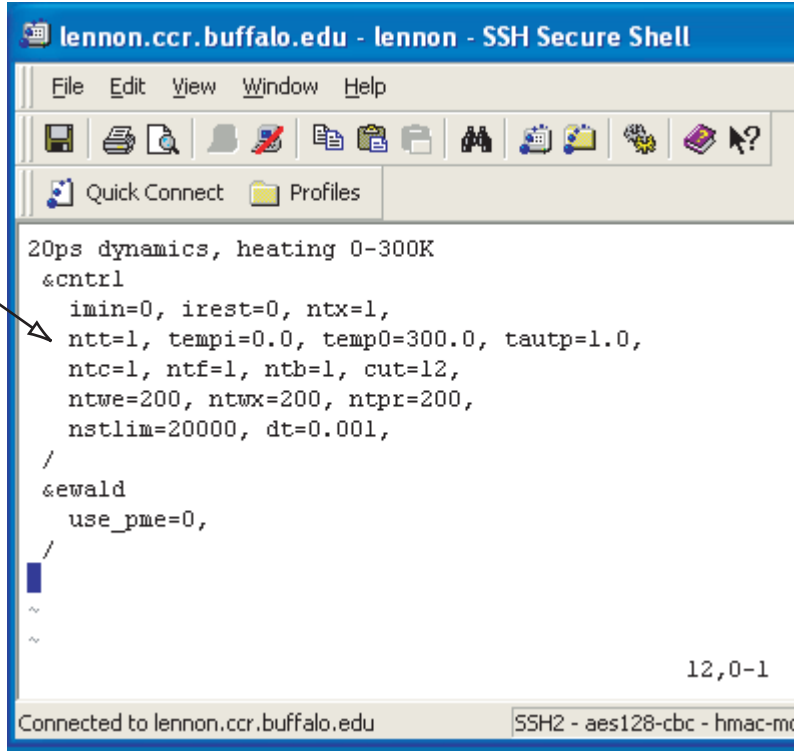
MM dynamics of Insulin in a periodic box of water

Technical details of running minimization



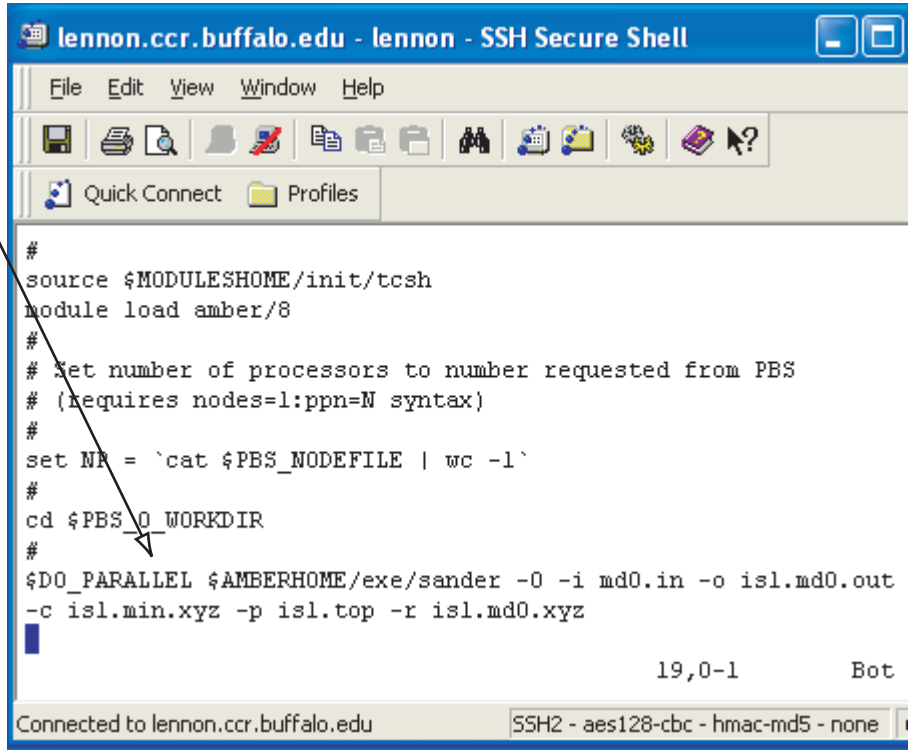
MM dynamics of Insulin in a periodic box of water

Technical details of heating in constance volume



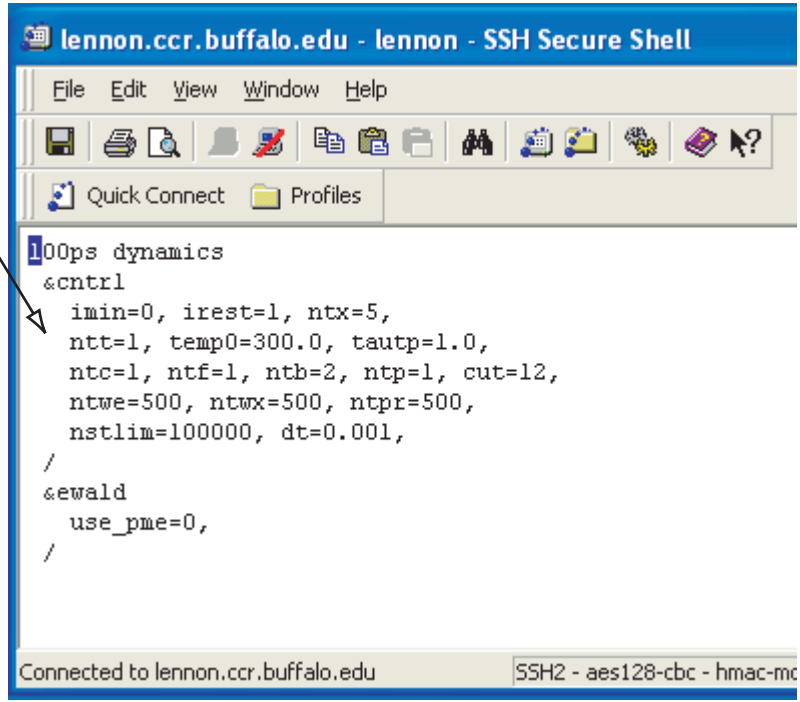
MM dynamics of Insulin in a periodic box of water

Technical details of running heating



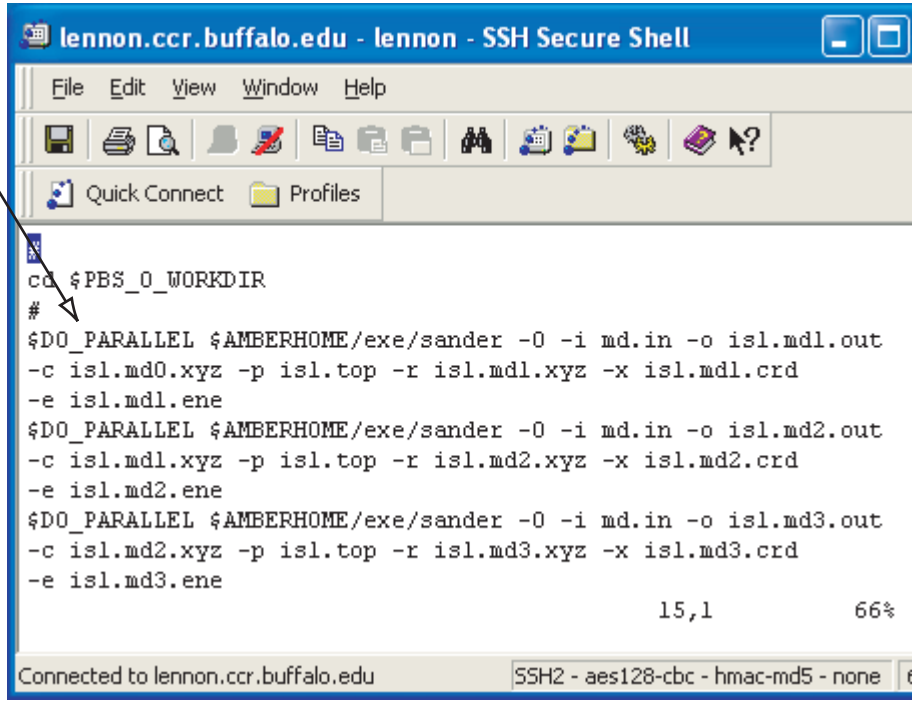
MM dynamics of Insulin in a periodic box of water

Technical details of dynamics in constant pressure



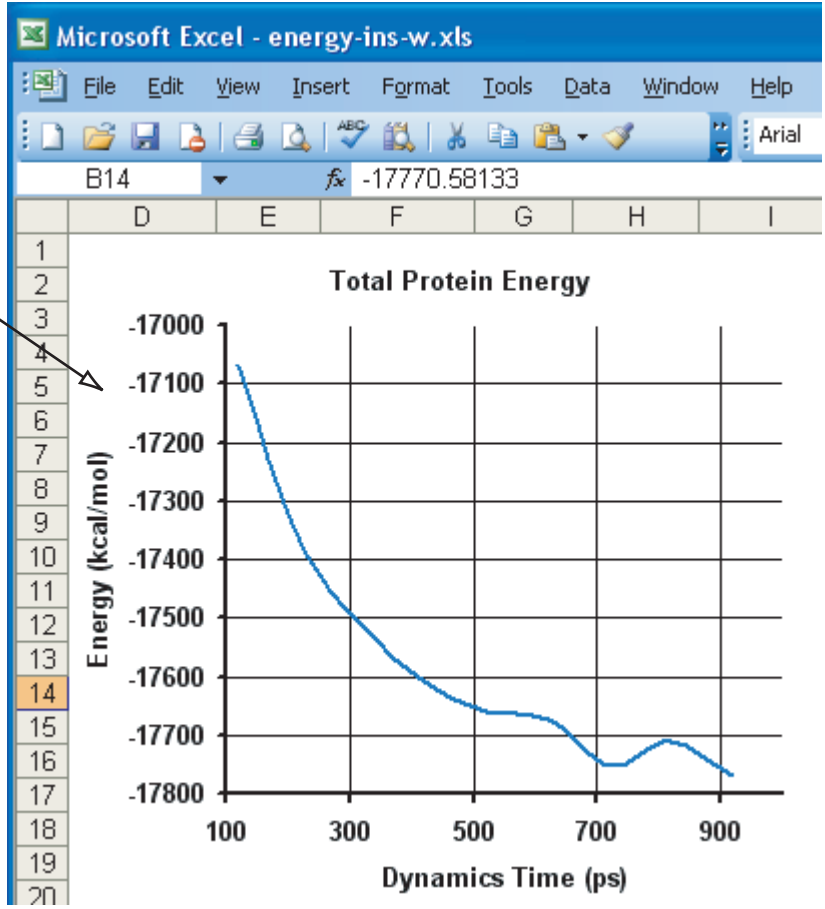
MM dynamics of Insulin in a periodic box of water

Technical details of running dynamics



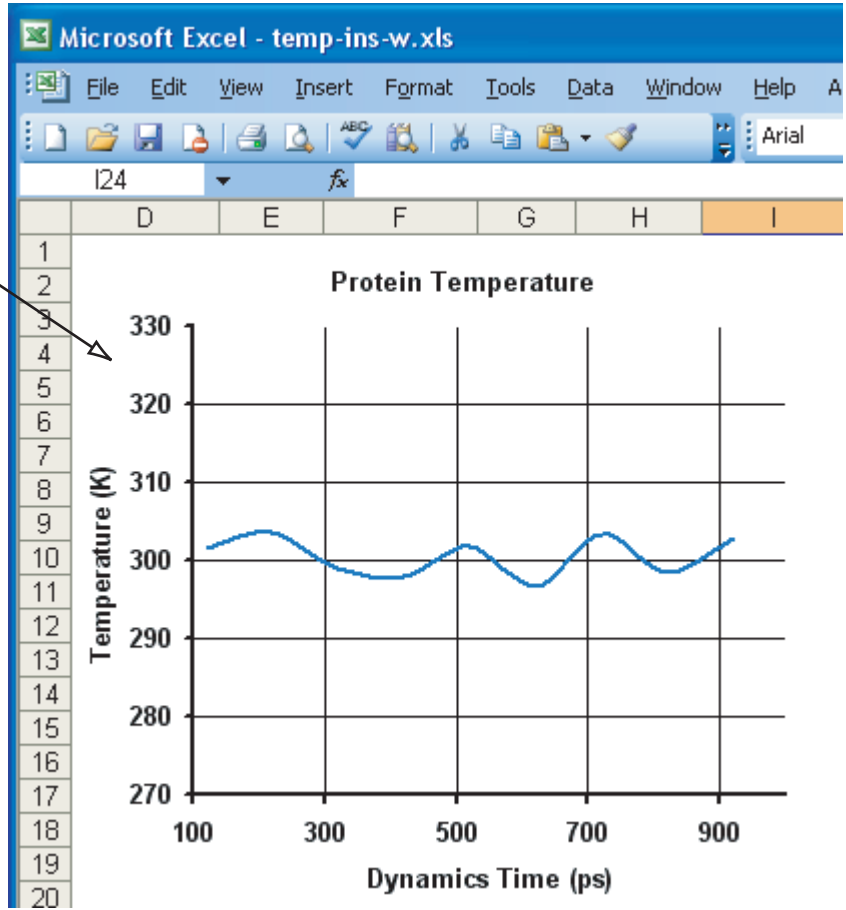
MM dynamics of Insulin in a periodic box of water

The energy of the protein after 1ns dynamics in water solution



MM dynamics of Insulin in a periodic box of water

The temperature of the protein after 1ns dynamics in water solution



MM dynamics of Insulin in a periodic box of water

Superposition of 9 protein snapshots after 1ns dynamics in water solution