Step-by-Step introduction to Simulating Dynamic and Equilibrium Behavior on the example of alanine zwitterions salvation.

This Lab further explores HyperChem's molecular mechanics functionality, and demonstrates how to use molecular dynamics with HyperChem.
Using the AMBER force field you will optimize an alanine zwitterions in both isolation and solution to determine the effect of solvent on the optimal structure. You will also perform molecular dynamics in solution to simulate the behavior of this species in biological systems

This Lab has 5 sections:
In section 1, you will create an optimized alanine zwitterion.
In section 2, you will use a molecular solvent model with periodic boundary conditions to solvate the zwitterion.
In section 3, you will learn how to superpose molecular structures on each other to visually compare the isolated molecule and the solvated molecule.
In section 4, you will use molecular dynamics to anneal the system to obtain a lower energy minimum.
In section 5, you will use Langevin dynamics to simulate the presence of a solvent during annealing, and Monte Carlo to sample configurations from a Boltzmann-weighted distribution.
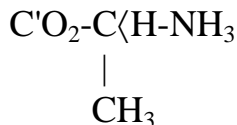Advanced exercise- playback dynamics

<u>Section 1</u>

Creating the Isolated Alanine Zwitterion and measuring it properties
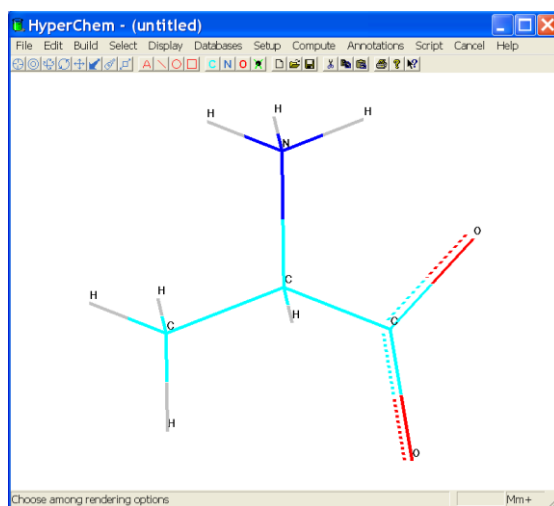
a. Sketching the Alanine Zwitterion
Although you could easily use the HyperChem amino acid library to display alanine, as a practice exercise you will build it from scratch, using the chemical formula: $C'O_2\text{-}C \langle H\text{-}NH_3$
                                      |
                                      CH_3

Before drawing**:**
Turn on Allow Arbitrary Valence and Explicit hydrogens in Built menu
Turn off Show Aromatic Rings as Circles in the Display menu.

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b. Assigning Atomic Charges

The next step is to place charges on some atoms to approximately represent the charge distribution in the zwitterion.

In this exercise, you make a simple approximation of a charge of **+1.0** on the nitrogen atom and charges of –0.5 on the oxygens (why?). In order to do this you need to assign nonzero values for the charges on these three atoms.

To assign atomic charges:

1. Get into selection mode and set the select level to atoms.
2. Select the nitrogen atom.
3. Choose Set Charge on the Build menu and assign a charge of +1.
4. R-click in an empty area to clear the selection.
5. Select both oxygen atoms and assign a charge of **–0.5**.
This sets a charge of **–0.5** for each of the oxygen atoms.
6. R-click in an empty area to deselect the atoms.

c. Choosing the Force Field

The next step is to choose a force field. You should choose a force field before you invoke the Model Builder because the Model Builder assigns atom types to each atom according to the force field that you specify. Alternatively, you could explicitly assign atom types any time by using Calculate Types on the Build menu.

To choose the force field:

1. Select Molecular Mechanics on the Setup menu.
The Molecular Mechanics Force Field dialog box opens.

2. Select **AMBER**, then L-click on Options.
The Force Field Options dialog box opens.
3. Use the following default values, then choose OK.
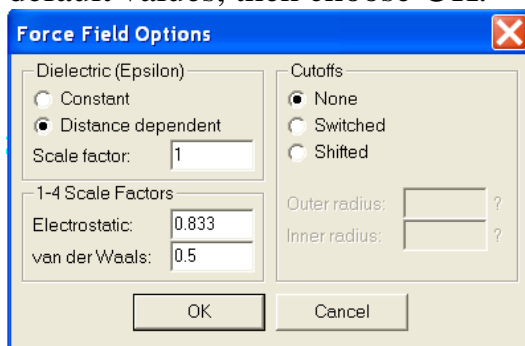
d. Building, Exploring and calculating the alanine zwitterion properties
1. Using the Model Builder build and display a first approximation of the alanine zwitterion.
2. Rotate and translate the structure to look at its conformation.
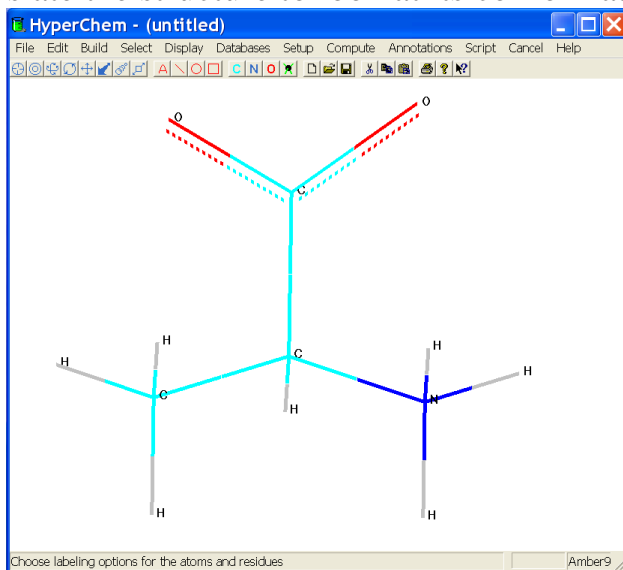
3. Open the Labels dialog box from the Display menu and choose Chirality for atoms. If the central carbon is labelled R rather than S, then switch to the drawing tool, hold down the [Shift] key and click on the central carbon.
You can use [Shift]+L-click with the drawing tool to rotate two neighbors, thus changing chirality.
You can also draw wedges to specify conformation or chirality.
4. Measure and report main geometry parameters (the planar O-C'-O angle, the O-C'-C⟨-N torsion angle, and the bound lengths).
5. Save the structure as ala_vac.hin.

e. Performing a Single Point Calculation
Now, perform a single point calculation to compute the energy. Report the Energy value, the gradient and the geometry.
The large energy and gradient indicate that the model-built structure is far from optimal. The principal strain is due to the C-N and C-O distances.

f. Optimizing the Isolated Molecule
1. Perform geometry optimization, using following parameters in the Molecular Mechanics Optimization dialog box:
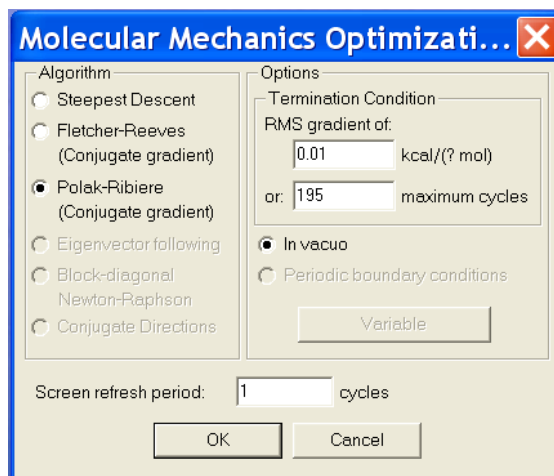
2. What are the optimal geometry, energy, gradient?
Report all the calculated values.
Which parameters changed the most?
Later in this lesson, you use the N-C⟨-C'-O angle to demonstrate molecular dynamics features of HyperChem, so save this angle as a named selection.
3. With the angle still selected, choose Name Selection on the Select menu.
 •Select Other, enter **ncco**, then choose OK (you may choose the second NCCO torsion and save it as nooc_2).
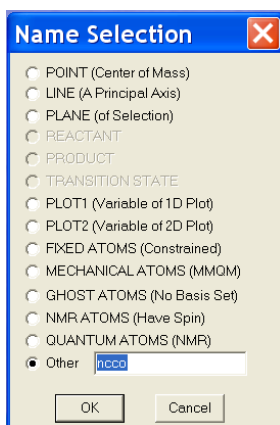
4. Save the optimized isolated alanine structure as ala_vac_opt.hin file so that you can compare it with the solvated structure you create next.

Section 2

Solvating the Structure

HyperChem lets you place a molecular system in a box of water molecules with periodic boundary conditions to simulate behavior in aqueous solution, as in a biological system. In this part of the project, you solvate the alanine zwitterions you created in such model water.

a. Before you continue, follow these steps:

1. Remove labels from the display by using the default settings in the Labels dialog box.
2. Choose Periodic Box on the Setup menu to open the Periodic Box Options dialog box.
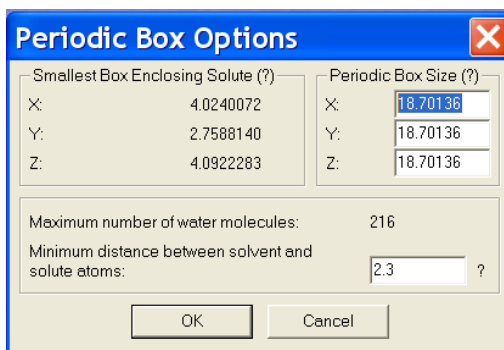
b. Setting up Periodic Boundary Conditions

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To solvate a system with HyperChem you specify a rectangular box or cube of equilibrated water molecules. You define the dimensions of the box, place the solute in the center, and define the minimum distance between the solvent and solute atoms. HyperChem eliminates all water molecules with atoms that come closer to a solute atom than the specified distance.

Specifying the Periodic Box Size
There are several factors to consider when you define the size of the periodic box. Most importantly, it must be large enough to accommodate the solute. To take care of that look up the parameter Smallest box enclosing solute (this box is called the reference cube), appears automatically in the Periodic Box Options dialog box.
In addition, the solute should not see its image in the next box. Box dimensions at least twice the largest solute dimension avoid solute-solute interactions when using the default cutoffs. A smaller box can be used if the cutoff radius that controls the range of the solute potential is made smaller. (so that the largest solute dimension plus the cutoff radius and range is less than the smallest box dimension). The standard reference cube of water is formed from an equilibrated cube of 18.70136Å and its nearest images, so you shouldn't use dimensions larger than 56.10408Å. Dimensions that are multiples of 18.70136Å minimize initial bad contacts.

To choose the periodic box size:
1. Specify a box size of 12.0 by 10.0 by 12.0 Ångstroms, as shown in the following illustration.
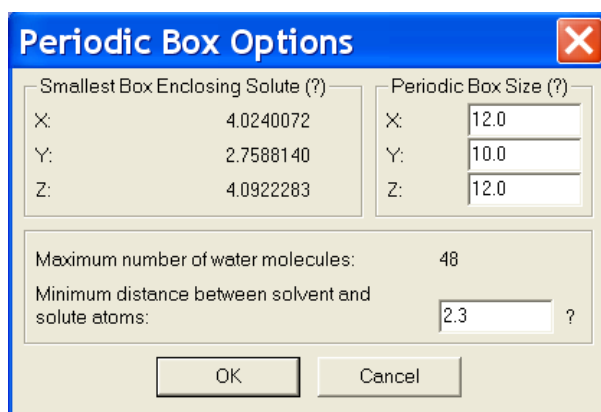
2. Choose OK.
This places the structure in the center of the box surrounded by 40 water molecules.

Note: Because the orientations of the water molecules in the box are not symmetrical, you may end up with fewer than 40 water molecules after the ones that are too close to your structure are deleted. If this happens, the results that you get from calculations may not be quite the same as those given in this lesson. This will depend on how your structure is oriented before you solvate it.

c. Displaying the Solvated System
1. Choose Rendering on the Display menu.
2. Turn on Perspective in the Vector and Line Options dialog box
3. Set the select level to Molecules.
4. Select a bond or atom of the alanine molecule, and rotate the whole system to look like this:
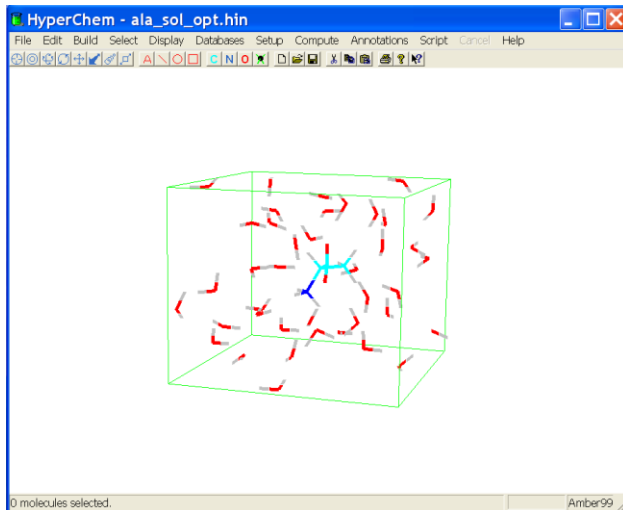
d. Adjusting Cutoffs and Dielectric Options
When you use periodic boundary conditions, you need to check the options for cutoffs and dielectric in the Force Field Options dialog box.

To check the options for cutoffs and dielectric:
1. Choose Molecular Mechanics on the Setup menu.
2. Choose Options to open the Force Field Options dialog box.
3. Look at the Cutoffs options at the right of the dialog box.
When you choose the Periodic box menu option, HyperChem automatically changes the options for cutoffs to Inner and Outer options, which are more appropriate for the solvated system with the nearest-image periodic boundary conditions. The Outer cutoff is set to one-half of the smallest box

dimension, and the Inner cutoff is set to 4Å less to ensure that there are no discontinuities in the potential surface.

4. Now look at options for Dielectric, which are at the top of the dialog box. When you use explicit solvent, you should use a constant dielectric.
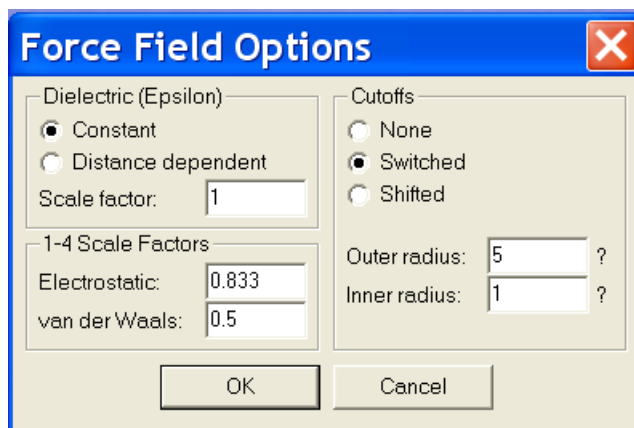
5. Select Constant instead of Distance dependent.

Note: The dielectric constant is not automatically changed because the new setting is stored in the chem.ini file.

6. Choose OK to close the Force Field Options dialog box.

7. Choose OK to close the Molecular Mechanics Force Field dialog box.

The Force Field Options dialog box should look like:

e. Optimizing the Solvated Molecule

The next step is to optimize the solvated system using the chosen periodic boundary conditions. Since the alanine molecule was set in its optimum (isolated state) geometry, the optimization primarily relaxes the solvent, but also, to some extent, the alanine is changed. Changes in alanine reflect the differences between the structures of a single isolated alanine molecule and the same molecule in solution.

To optimize the molecule in solution:

1. Get into selection mode and R-click in an empty area to deselect the alanine. When there is an active selection, an optimization is performed on the selection only. Therefore if you started the optimization with alanine selected, only the position of the alanine atoms is allowed to change and the water molecules are constrained. To optimize the complete system and allow reorganization of the solvent structure in the presence of alanine, you must clear the selection.

2. Using Geometry Optimization on the Compute menu, start the optimization of the solvated alanine, including the water molecules. (Set the

Molecular Mechanics Optimization parameters as in step 1.). If the calculation hasn't converged, increase the number of maximum cycles in the Molecular Mechanics diagonal box to 800 and perform the calculation again.
3. When the calculation finishes, <u>report</u> the energy and gradient values, which appear on the status line.

The optimized structure for the solvated system might only be a local minimum. In a system with many degrees of freedom, such as this one, there might be many minima and it can be very difficult to locate the global minimum. When there are enough degrees of freedom, it is possible that any single static conformation is insignificant, and that only a statistical treatment of many low-energy conformations is appropriate.
4. Save the structure as ala_sol_opt.hin.

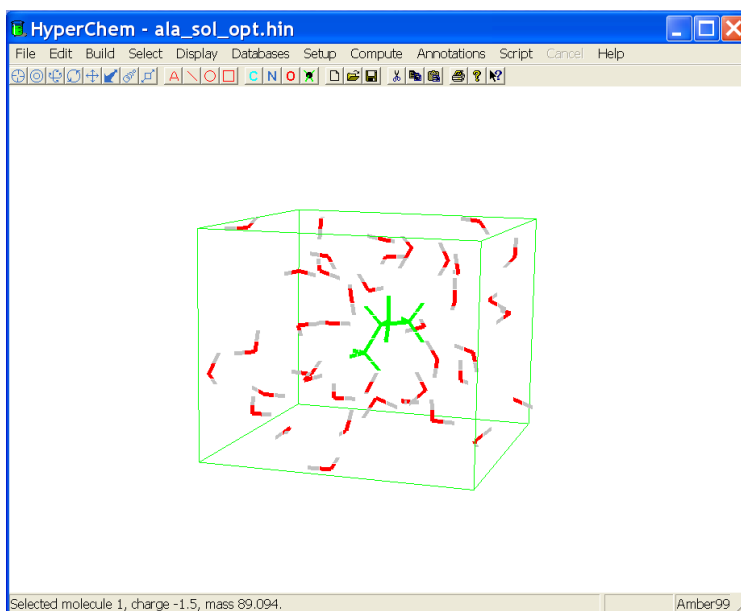# **Section 3**

Superposition
The system currently displayed is a minimized structure for the alanine zwitterion in water. It is instructive to compare the structure with the corresponding isolated optimized structure. Instead of comparing the molecules by measuring individual structural properties, you use HyperChem's superposition feature to visually compare the two structures by superimposing.

Deleting the Water Molecules
Before superposing, delete the water molecules from the isolated structure.

a. To delete the water molecules:
1. Get into selection mode and set the select level to Molecules.
2. L-click on the alanine. This selects the alanine.

3. Choose Complement Selection from the Selection menu. This selects only the water molecules.

4. Choose Clear on the Edit menu.

5. If a dialog box appears asking if you want to delete the selected atoms, choose Yes.

6. Choose Show Periodic box in Display menu so that it is not set and only the alanine molecule is shown.

7. Save the file as ala_sol_opt_NoSol.hin .

Measure and report the geometry parameters, the energy, and the gradient.

b. Merging the Two Systems
The next step is to merge this structure with the isolated structure.
Before you merge the two systems, you should select the current system so that you can distinguish it on the workspace after the merge.

To merge the two systems:
1. Select the alanine.

2. Choose Name Selection on the Select menu and save the selection as **solvated**. This makes it convenient for you to display this selection later if you want to recover it.

3. Choose Merge on the File menu and open ala-gas.hin. Both the isolated and the solvated structures should now be on screen. The solvated structure should still be selected.
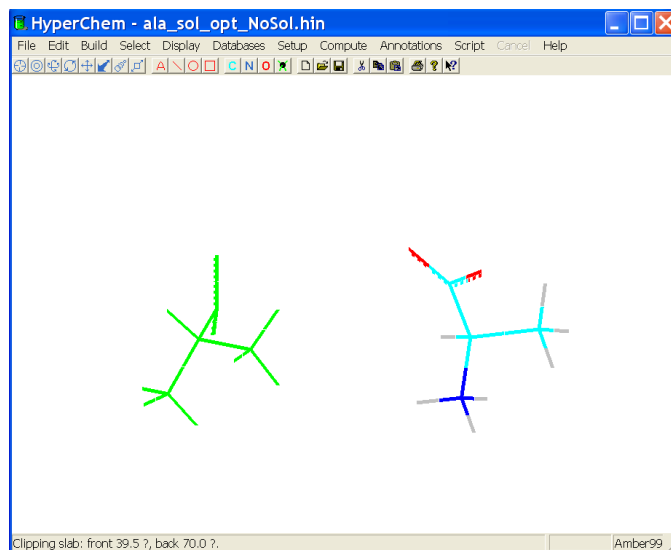
Merge lets you combine the current system and another system that has been stored in a file. This union becomes the current system.

4. If necessary, use the Translation tool with the right mouse button until both structures are in full view. At this point, use labels and color to differentiate the molecules.

5. Color the selected solvated structure (Display->Color Atoms) yellow and label the molecule by symbol.

Note: If Thick line is not being used as the Selection option in the Preferences dialog box, the solvated structure does not appear yellow until it is deselected.

6. Choose Complement Selection on the Select menu. The solvated system is deselected and the isolated alanine is selected.

7. Color the selected isolated alanine violet and label it by symbol.

8. R-click in an empty area to deselect the isolated alanine.

c. Superposing Molecules

When a system includes at least two molecules, as in this example, HyperChem can superpose the molecules. Superposition is based on the selection of three non-collinear atoms in each molecule. To begin, the first selected atoms of each molecule are made coincident. Next, the bonds between the first and second selected atoms of each molecule are made collinear. Finally, the third selected atoms of each molecule are put in the same plane.

To perform the superposition:

1. Get into selection mode, set the select level to atoms and turn Multiple Selections on.

2. L-drag the N-C ⟨ -C 'bond angle of each molecule. You might have to rotate the structures to do this.
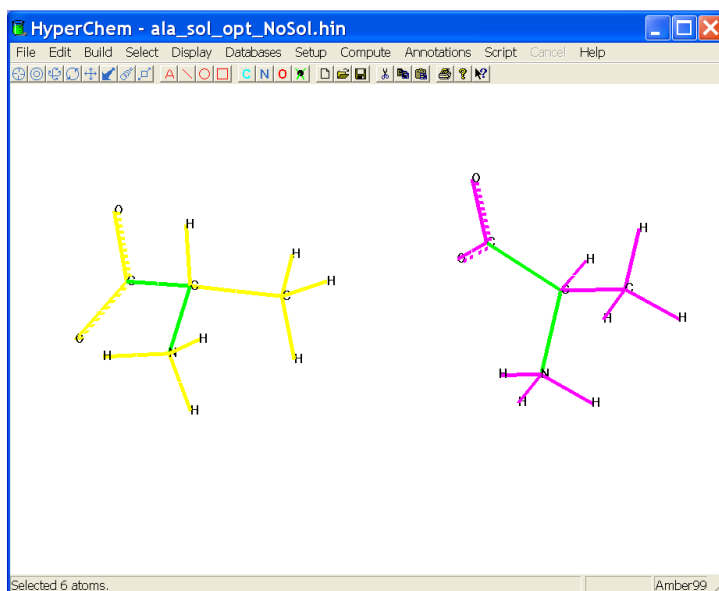
3. Choose Overlay on the Display menu.
4. R-click in an empty area to clear the selection.
5. Press the space bar to center the superposed structures in the workspace. The current system should now look similar to this:
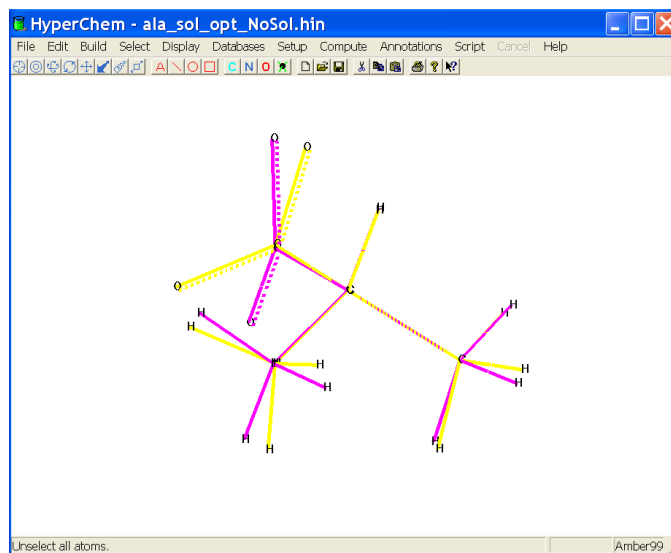
6. Choose Save As on the File menu and save the superposed molecules as ala-sup.hin. What is the effect of the solvent on the optimized geometry?

Which parameters can be compared between the two structures? and which cannot?

# Section 4

Molecular Dynamics
Here you use molecular dynamics to anneal the system to obtain a lower energy minimum. You must first retrieve the solvated alanine zwitterion system to perform molecular dynamics with it.

a. To retrieve the solvated system:
1. Open the file ala_sol_opt.hin.
2. If necessary, turn on Show Periodic Box to display the periodic box you defined earlier.
3. If necessary, remove labels from the display.

b. To set up the dynamics simulation:
1. Choose Molecular Dynamics on the Compute menu.
The Molecular Dynamics Options dialog box lets you set the options for a molecular dynamics calculation. Take a moment to look at the options.
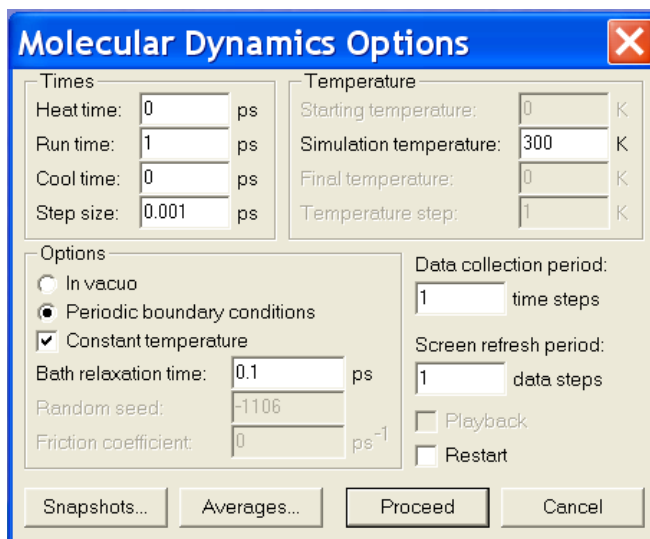
A dynamics run for simulated annealing has three optional phases: heat, run, and cool.

In the *heat phase* the system is brought to the desired temperature by rescaling the velocities. The starting temperature is used to set initial

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velocities, then, rescaling of velocities is done gradually, with temperature increments, until simulation temperature is reached. This is the start of the *run phase,* a standard run that can be done at constant temperature (by occasionally rescaling velocities) or constant energy.

The final *cooling phase* the temperature is brought down by rescaling of velocities at temperature increments until the desired final temperature is reached. (The cooling phase is required for stimulated annealing, not done here)

2. Set the Heat time to 0.1 picoseconds.

3. Set the Temperature step to 30K.

Because the gradient is very small in the starting system (corresponding to a near-zero temperature),a short heat time of 0.1 picoseconds is used to raise the temperature from a starting temperature of 100 K to the simulation temperature of 300K incrementing by a temperature step of 30K.

4. Set the Run time to 0.5 picoseconds.

The temperatures are used here to set up initial atom velocities or to adjust atom velocities. This kinetic energy might be converted into potential energy during simulation, causing the calculated temperature to drop. If the temperature eventually rises (as it does in this example),it means that potential energy is being converted into kinetic energy as the system moves to a more stable conformation.

5. Make sure the Periodic boundary conditions option is on. This option is automatically turned on by HyperChem when periodic boundary conditions are used, but it can be overridden by selecting In vacuo.

6. Set the Step Size to 0.0005 picoseconds.

7. Set the Data Collection period to 4.

For systems such as this that have explicit hydrogen atoms, a 0.5 fs step size is appropriate for accurately integrating the hydrogen stretching motion. You can update the screen at any number of time steps to display real-time molecular dynamics.

8. Turn Constant Temperature off.

9. The settings in the dialog box should look like this:
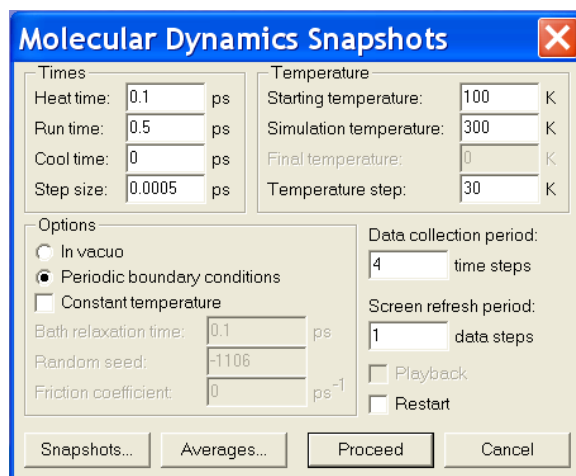
c. Setting up Playback Dynamics

The next step is to set up playback dynamics. Playback dynamics is convenient because it saves the trajectory – a sequence of configurations at successive time points so you can analyze the time evolution later.

Molecular dynamics simulates the evolution of a system over time, producing a trajectory of atomic positions and velocities. These calculations can be very time consuming, and for statistically meaningful results, long simulation times corresponding to many thousands of time steps might be required.

Often you'll want to save the calculated trajectory for later play-back or analysis, rather than having to repeat the simulation.

To set up playback dynamics:

1. Choose Snapshots at the bottom of the Molecular Dynamics
Options dialog box.

The Molecular Dynamics Snapshots dialog box opens.

2. Enter **ala_MD_run** as the filename.

HyperChem generates two files with the prefix ala-run.

One file, ala-run.hin, is a HIN file that contains a snapshot entry.

Another file, ala-run.snp, is a binary file containing atomic coordinates and velocities.

3. Use a Snapshot period of 1 data step.

4. Choose OK to return to the Molecular Dynamics Options dialog box.

NOTE: To playback a trajectory that has been stored in a snapshot file you must first read the appropriate HIN file unless you have already saved snapshots with the current system. When reading the HIN file a warning will be issued that the attached SNP file is only valid if the molecular system in the HIN file is not edited in any way.

That is, the attached *.snp trajectory applies only to the molecular system as it is currently constituted. Any editing of the molecular system such as deleting an atom, etc. will gray the playback option, making it inaccessible. It is possible, however, to change the view of the system, define new named selections, etc. as long as its atomic information is not altered.

**d. Setting up Averaging from Molecular Dynamics**
Molecular dynamics is often used to obtain macroscopic information by sampling a microscopic simulation over a long period of time.
It is also useful to track energetic and geometric quantities as the simulation proceeds to see if the system has stabilized enough for sampling to be statistically valid or not.
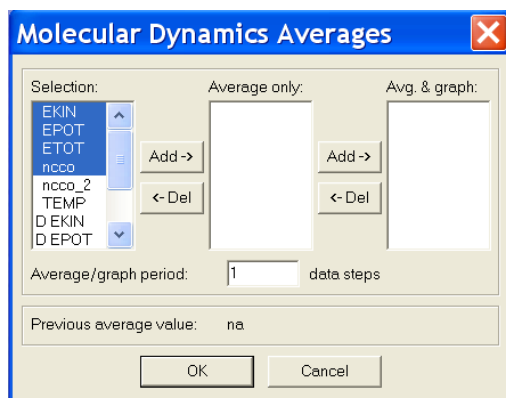**Note:** When you start the Averaging function, HyperChem creates a file with the extension *.csv* in the current working directory.
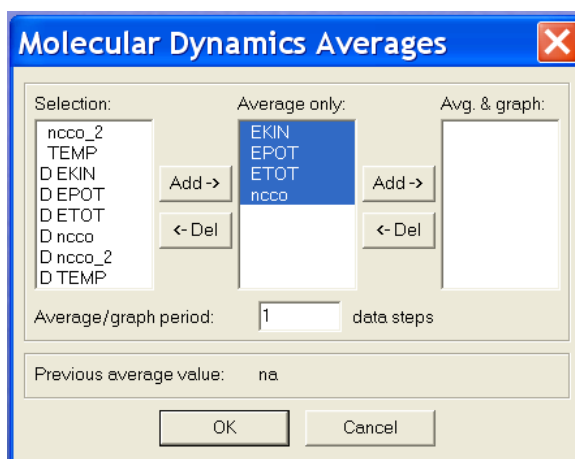
To set up averaging:
1. Choose Averages to open the Molecular Dynamics Averages dialog box.
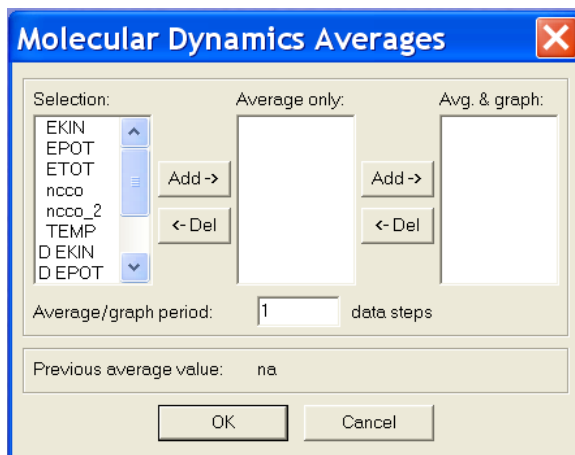
2. L-click on EKIN, EPOT, ETOT, and ncco in the Selection box, then L-click on Add to move them to the Average only box.

3. L-click on EKIN, EPOT, ETOT, and ncco in the Average only box, then L-click on Add to move them to the Avg.&graph box.

This specifies a plot of total energy, potential energy, kinetic energy, and the N-C⟨-C'-O torsion angle you saved as a named selection earlier.

HyperChem generates a file named ala-run.csv (or chem.csv if playback dynamics is not set up), which records the quantities being averaged in a format that can be easily read by plotting or spreadsheet programs for analysis.

e. Proceeding with Dynamics
1. Choose OK to return to the Molecular Dynamics Options dialog box, then choose Proceed to start dynamics.
A graph titled Molecular Dynamics Results opens on the work-space.
2. Move the graph so that you can watch the simulation.
While the calculation is running, you can change the view of the system by using the rotation, translation, zoom, and clip tools. You can also use applications in other windows, but this can slow down the simulation.

3. As the simulation continues, choose Rescale to rescale the values being plotted.

Once the heating phase is finished, (when energy is being added) the total energy remains constant, and the kinetic energy mirrors the potential energy.

Caution: You cannot recover the plot if you L-click on Done. To recover the plot, you must use replay dynamics.

In the early part of the run after heating, the potential energy and temperature should be fairly stable, but then the system temperature rises. The potential energy during the run eventually drops significantly. The molecular dynamics at room temperature lets the system surmount energy barriers on the potential surface and find regions of lower potential energy that would not be reached by a minimization algorithm.

4. When the dynamics run has completed, plot the averages graph and report the total energy.
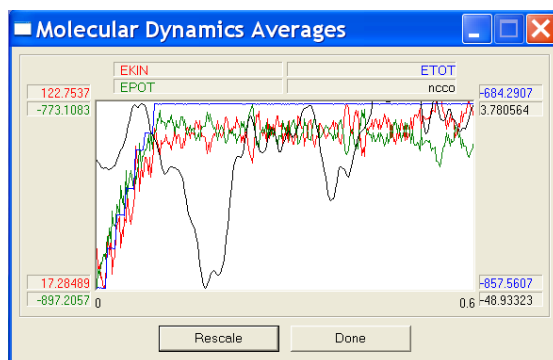
5. Clear the window and reload the starting structure (ala_sol_opt.hin).

Run MD using the same parameters, this time choose in the Molecular Dynamics Averages Selection EKIN, EPOT, ETOT and TEMP.

6. Plot the averages graph.

7. Compare with the previous graph. Are the total energy and temperature conserved? Discuss the nature of the simulation.

8. according to the ncco torsion curve, has the simulation converged?

f. Reoptimizing the New Structure

1. Now that the dynamics run is finished, you can optimize the structure to determine a new local minimum using Geometry Optimization on the Compute menu. (Set the Molecular Mechanics Optimization parameters as in section 1.)

After the optimization finishes, the status line shows a structure that can have lower energy than the solvated local minimum found earlier.

2. Report the energy and gradient.

3. Delete the water molecules

4. Measure and report the geometry parameters.

The results demonstrate that molecular dynamics can be used to reach thermodynamically favored conformations separated from the starting conformation by energy barriers. Thus molecular dynamics can be used to explore conformational space.

Such sampling should begin once the system has been equilibrated, often judged by kinetic and potential energies fluctuating about consistent values for a long period of simulation.

Section 5

Langevin and Monte Carlo Simulations

In this section you use Langevin and Monte Carlo simulation methods to further explore conformations of the alanine zwitterion system. The Langevin Dynamics method simulates the motion of molecules subjected to random collisions and frictional forces and can be used to model solvated systems without explicitly including solvent molecules. It provides information on the time evolution of the molecular system. The Monte Carlo method is used to simulate equilibrium properties.
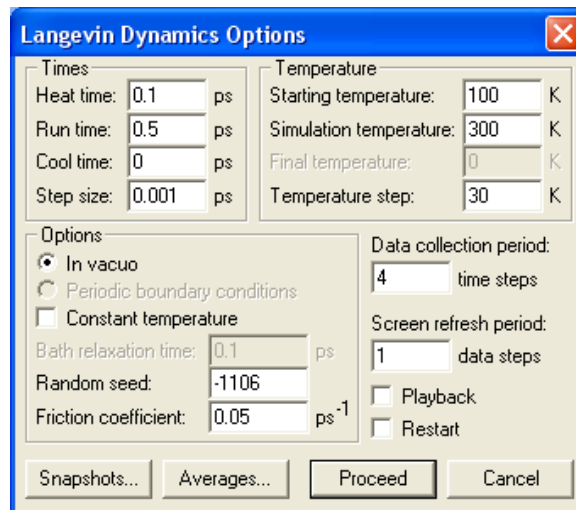

Part 1: Langevin Dynamics

A Langevin Dynamics simulation is set up in much the same way as a Molecular Dynamics simulation, with small differences due to the addition of the friction coefficient.

1. Retrieve the gas phase alanine zwitterion, which you saved as ala_vac_opt.hin, adjust Force Field Options for vacuum as in section 1.

2. Choose Langevin Dynamics on the Compute menu and set the Langevin Dynamics Options as the Molecular Dynamics Options in the preceding Exercise.

3. Set the Friction coefficient to **0.05** ps -1.

When the friction coefficient is set to zero, HyperChem performs regular molecular dynamics, and one should use a time step that is appropriate for that method. With larger values of the friction coefficient, motions that occur over a short time are less important and larger time steps can be used.

4. Set the Step size to **0.001** picoseconds.

The settings in the dialog box should look like this:

Langevin Dynamics Options

Times
Heat time: 0.1 ps
Run time: 0.5 ps
Cool time: 0 ps
Step size: 0.001 ps

Temperature
Starting temperature: 100 K
Simulation temperature: 300 K
Final temperature: 0 K
Temperature step: 30 K

Options
⦿ In vacuo
○ Periodic boundary conditions
☐ Constant temperature
Bath relaxation time: 0.1 ps
Random seed: -1106
Friction coefficient: 0.05 ps^{-1}

Data collection period:
4 time steps

Screen refresh period:
1 data steps

☐ Playback
☐ Restart

Snapshots... Averages... Proceed Cancel

5. Set up **Averages** (select EKIN, EPOT, ETOT and TEMP) and **Snapshots** as in the preceding exercise.

6. Choose **Proceed** to start the Langevin Dynamics simulation.

7. Plot the averages graphs and report the total energy.

8. clear the window and reload the starting structure (ala_opt_vac.hin).
Setup LD using the same parameters with a different seed number.
Set the Averages (select EKIN, EPOT, ETOT and TEMP).

9.Plot the averages graphs.

10. Compare to the previous graph. Has the simulation terminated with same energy values? Is it a deterministic or a stochastic run?

11. Do you observe both the EKIN and the TEMP curves? Why? What is the temperature curve equal to?

Note: In order for the temperature of a system to be defined, the system must be in thermodynamic equilibrium. When two systems are in thermal equilibrium and the net heat transferred between them is zero, they have the same temperature

12. (bonus) Were the energy and temperature conserved? Which ensemble is it (NVT, NVE, ...)? Explain.

13. Reoptimize the structure, report the energy and gradient, measure and report the geometry parameters.

As with the Molecular Dynamics technique, heating and cooling phases may also be added to a Langevin dynamics simulation.

14. Compare the energy and geometry to that of the starting structure (ala_opt_vac.hin).

Equilibration of the system is not crucial for locating additional low-energy structures, but it is important when comparing simulated values with experimental properties.

Part 2: Monte Carlo Simulation

The Monte Carlo method samples configurations from a Boltzmann-weighted distribution at a given temperature. At elevated temperatures, this technique may be used to move the molecular system of interest across potential energy barriers. In this exercise we employ the Monte Carlo method followed by geometry optimization as an additional conformational search technique.

a. To set up the Monte Carlo simulation:

1. First retrieve the solvated alanine zwitterion system, which was saved as ala_sol_opt.hin, adjust Cutoffs and Dielectric Options for solution as in section 2.

2. Choose Monte Carlo on the Compute menu.

The Monte Carlo Options dialog box allows you to set up the Monte Carlo simulation parameters. In this example we will run a constant temperature simulation with 1000 steps. For some systems, it may be useful to add optional heat and cool phases.

3. Set the Run Steps to **1000**.Set Heat and Cool steps to **0**.

4. Set the maximum step size, Max Delta, to **0.05** Å.

This sets the maximum trial atomic displacement. If it is too small only limited sampling of new configurations will occur.
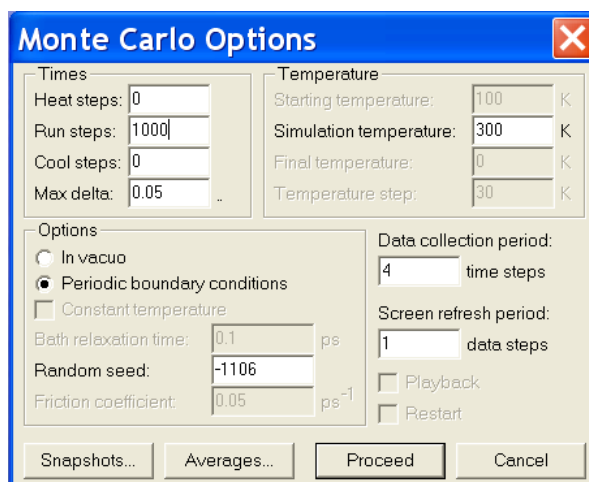
If it is too large, unphysical configurations may be generated.

This reduces the efficiency of the simulation.

5. Set the Simulation Temperature to **300**K.

6. Make sure that Periodic boundary conditions is on.

7. Set the Data Collection period to **4** steps.

b. Setting up Monte Carlo Playback

Set up a snapshot file, if desired.

Playback of the Monte Carlo "trajectory" is set up in the same way as Dynamics playback. As with Dynamics, analysis of the simulation may be conveniently carried out at playback. For example, you can stop the playback at the point in a simulation where the potential energy falls, and save the structure at that point. You can also change the graphing and averaging selections before playing back a run.

c. Setting up Averaging from Monte Carlo

Set up Averages and Graphing as desired.

The Monte Carlo Averages setup is identical to Molecular Dynamics Averages setup. There is an additional parameter that you can monitor in Monte Carlo:the acceptance ratio. It appears as ACCR on the list of possible selections in the Monte Carlo Averages dialog box; DACCR, the rms deviation of ACCR from its mean, appears also. The acceptance ratio is a running average of the ratio of the number of accepted moves to attempted moves. Optimal values are close to 0.5.Varying the step size can have a large effect on the acceptance ratio.

1. Choose Proceed to start the Monte Carlo simulation.

2. Choose Monte Carlo on the Compute menu, open the Monte Carlo Averages dialog box. Average values may be conveniently retrieved by L-click on one of the properties previously selected for averaging; the average value is reported just below.

3. Report the average total energy (ETOT).

4. Was the energy conserved? Why?

5. Reoptimize the structure, report the energy and gradient

6. Delete the water molecules, measure <u>and report</u> the geometry parameters.
7. Adjust Force Field Options for vacuum as in step 1. Reoptimize the structure, <u>report</u> the energy and gradient, measure <u>and report</u> the geometry parameters.

Summarized you results:
1. Tabulate the energy and geometry parameters of all the minimized structure (sections 1-5). Compare between the structures. Which comparisons are valid?
2. How many local minima did you find for the gas phase and how many for solution?
3. What is the main difference between the optimal geometries?
4. What are the differences between the methods being used in this lab?
5. What is the significance of the temperature in all the above methods?

Advanced Exercises
1. Follow these steps to view playback dynamics:
•Open the file ala_MD_run.hin.
•Open the Molecular Dynamics Options dialog box and choose Playback (at the bottom to the right). Choose Snapshots to determine which part of the simulation to replay.
•Choose Proceed to start playback dynamics.
The simulation will playback substantially faster then the initial dynamics calculation.
2. Create named selections for two, three, or four atoms, and use playback dynamics to plot the values.