

Discovery Studio 2.0

Tutorials
Version 1.0

Note. Some tutorials require data files that can be downloaded here:
<http://www.accelrys.com/doc/life/dstudio/20/tutorials/tutorialdata.zip>.

Save the zip file to your computer and then extract the contents to a folder. We recommend that you add this folder to the Files Explorer as a top-level or 'root' folder. To do this, navigate to the folder, right-click the folder, and choose the Add Root Node... command from the context menu. Next, on the dialog, enter a display name for the root folder (e.g., Tutorial Data) and click the OK button. The tutorial data files will then be readily accessible at the top-level of the Files Explorer.

Simulation of a small peptide with restraints (protein simulation) tutorial

Purpose: Build a small peptide and run the Standard Dynamics Cascade protocol with distance and dihedral restraints.

Required functionality and modules: Discovery Studio Visualizer client and CHARMM.

Required data files: none.

Time: 20 minutes.

Background

CHARMM is designed to simulate molecular systems and provides capabilities to analyze such simulations. CHARMM requires atomic coordinates and forcefield parameters, including partial charges, as input. Discovery Studio provides these inputs, allowing you to simulate and analyze molecular systems using CHARMM. In this tutorial, an input molecule is built using the Protein Builder, forcefield parameters and partial atomic charges are assigned to the system, a molecular dynamics calculation is carried out, and the resulting dynamics trajectory is animated.

Introduction

Build a small peptide and run the Standard Dynamics Cascade protocol with distance and dihedral restraints.

1. To build enkephalin in a new 3D Window

From the menu bar, choose **File | New | 3D Window**.

This opens a new 3D Window.

In the Tools Explorer, choose **Protein Modeling** from the dropdown list.

This opens the Protein Modeling tool panels.

In the Tools Explorer, in the Build and Edit Protein tool panel, in the *Choose Build Action* tools group and choose **Create/Grow Chain** from the dropdown list.

In the *Choose Amino Acid* tools group, click the following commands (in the indicated order): **Tyr, Gly, Gly, Phe, Met**.

This builds a met-enkephalin. As each residue is clicked, that residue is added to in the 3D Window. The *Choose Conformation* setting on the tool panel specifies the conformation.

2. To assign forcefield parameters

In the Tools Explorer, choose **Simulations** from the dropdown list.

This opens the Simulations tool panels.

In the Forcefield tool panel, choose **CHARMm** from the dropdown list. Click **Apply Forcefield**.

This selects the CHARMM all-atom forcefield for this calculation and then assigns the CHARMM all-atom forcefield parameterization to your system. A message that the molecule is typed is displayed in the *Status* group (*Molecule typed with CHARMM*).

3. To define a distance monitor

In the Hierarchy View, expand **Molecule** and then expand **chain A**.

Next, expand **TYR1** and expand **Met5**.

In *TYR1*, click **N** to select the atom. Next, press and hold the **CTRL** key, and in *MET5*, click **C** to select the atom.

This selects the terminal ammonium nitrogen (the N in the NH_3^+ group of Tyr) and the carboxylate carbon (C in the COO^- group in Met).

From the menu bar, choose **Structure | Monitor | Distance**.

A green line connecting the selected atoms is created, indicating that the distance between the atoms is monitored.

4. To set up a distance restraint

Reselect the atoms in the Hierarchy that you selected from the previous step.

In the Tools Explorer, in the Constraints tool panel, click **Create Distance Restraint**.

A *DistanceRestraint* entry is added to the Hierarchy View and to the Data Table.

5. To modify the distance parameters of the distance restraint

In the Data Table View, click the **DistanceRestraint** tab, scroll to the **ThresholdMaximum** column, and enter **17.0 Å** for the value. Next, scroll to the **ThresholdMinimum** column and enter **16.0 Å** for the value.

This will allow the N and C atoms to move without penalty within a distance of 16 Å to 17 Å. Blue, ball-shaped objects are displayed on the two selected atoms.

6. To set up a dihedral restraint

In the Hierarchy View, expand **Gly2** and **Gly3**.

In *Gly2*, click **C** to select the atom. Next, press and hold down the **CTRL** key, and in *Gly3*, click **N**, **CA**, and **C** to select the atoms.

This selects four atoms in the middle of the peptide chain defining the Phi angle in the second Gly residue of the enkephalin molecule.

In the Tools Explorer, in the Constraint tool panel, click **Create Dihedral Restraint**.

Blue, ball-shaped graphical objects are displayed on the four selected atoms. A *DihedralRestraint* entry is added to the Hierarchy View and to the Data Table View. By default, the dihedral restraint value is the current angle.

7. To modify the dihedral restraint value

In the Data Table View, click the **DihedralRestraint** tab, scroll to the **Force Constant** column and enter **500** for the value.

Scroll to the **Periodicity** column and enter **3** for the value.

Scroll to the **Reference Angle** column and enter **-57** for the value.

If the *Periodicity* is set to **0**, the constraint is assumed to be a planar constraint (pseudo-dihedral constraint). A *Periodicity* of **3** means that a 360° rotation has three energy minima (every 120° starting from the *Reference Angle*).

8. To open the Standard Dynamics Cascade protocol

In the Protocols Explorer, expand the **Simulation** folder and double-click the **Standard Dynamics Cascade** protocol.

This opens the parameters in the Parameters Explorer.

9. To disable the distance and dihedral restraints during the production stage

In the Parameters Explorer, expand the **Production** parameter group and click the **Constraints** parameter.

This displays a listbox of constraints.

In the listbox, uncheck the **Dihedral** and **Distance** restraints.

This removes the restraints from the production stage of the cascade.

10. To run the Standard Dynamics Cascade

The default value for the *Steps* parameters in the *Equilibration* and the *Production* parameter groups is **1000** steps. In most cases, the *Equilibration* and *Production* steps will need to be much longer. The default value for the *Save Results Frequency* parameter in the *Production* parameter group is set to **100** steps. This could be changed to save only once every 1,000 or 10,000 steps. Remember, all frames from the Production phase are saved in the final MSV file, which can lead to an extremely large file.

On the Protocols toolbar, click the **Run**  button and wait for the job to complete.

The job should take about three minutes on a single processor Pentium 4, 2Gb RAM, 2.8GHz machine.

The Job Completed dialog displays when the job is complete.

From the menu bar, choose **Window | Close All**.

11. To inspect the results from your minimization and dynamics calculation

In the Jobs Explorer, double-click the completed job.

This opens the Report.htm file in an Html Window.

Browse through the report to inspect the results from various stages of the simulation cascade.

12. To animate frames from the simulation

In the Html Window, in the *Output Files* section, click the **Molecule.msv** link.

This opens the final structure.

From the menu bar, choose **Structure | Animation | Play**.

Frames from the enkephalin molecule production dynamics trajectory are displayed in the 3D Window in sequence.

In this short (1 picosecond) animation, you will see that the distance between the amino and carboxylic acid groups diminishes during the production stage of the simulation because the distance restraint is disabled. Molecular dynamics calculations such as this allow you to explore the time dependent conformational characteristics of molecular structures.

This is the end of the tutorial.

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