

Working with Forcefield tools

Required functionality and modules: Discovery Studio Client.

Required data files: 1hho.pdb and 2hho.pdb

Time: 15 minutes

Introduction

In molecular mechanics simulations, an essential step is to first assign a forcefield to the input molecule. For novice users, the CHARMM forcefield with automatic parameter estimation can be used to automatically assign complete forcefield parameters for almost any type of molecule. However, advanced users may find it desirable to modify and define their own forcefield parameters for certain residues. In addition, some other forcefields, such as charmm19 or charmm27, do not have automatic parameter estimation capability built in, so you must create new residue and atom types for systems other than common biomolecular monomers. For these forcefields, non-standard residues may not be assigned forcefield parameters successfully, and manual customization of the residues is necessary to ensure complete forcefield assignment of the molecule. In Discovery Studio, you can use Forcefield tools to help the customization of residues during the forcefield assignment process.

In this tutorial, you will learn how to apply the charmm27 forcefield to proteins containing HEME residues, which cannot be typed automatically by charmm27. The following tasks are covered:

- [Applying charmm27 to a protein that contains a HEME residue](#)
- [Customizing the HEME residue](#)
- [Adding the customized HEME residue template to the charmm27 forcefield](#)

Applying charmm27 to a protein that contains a HEME residue

From the **Files Explorer**, open **Samples | Tutorials | Simulation | 1hho.pdb**.

This opens the protein 1hho in the Molecule Window. The protein has an amino acid chain and a chain containing the HEME residue.

In the **Tools Explorer**, select the **Simulation** layout from the dropdown list.

This opens a set of Simulation tool panels, which contain tools to prepare a structure for simulation jobs.

Open the **Simulate Structures** tool panel.

From the **Forcefield** list, choose **charmm27**.

Click **Apply Forcefield**

This applies charmm27 forcefield to the 1hho protein.

After the typing is finished, the *Forcefield Status* tool panel displays "1hho is not fully typed with 1hho-charmm27". This is because the charmm27 forcefield does not have a residue template for the HEME residue.

Click **More...**

This brings up a Forcefield Window that details why 1hho cannot be fully typed with the charmm27 forcefield.

The Forcefield Window has two tabs: *Residues* and *Atoms*. The *Residues* tab lists all residues that cannot be typed by the standard residue template. For example, HEM143 is listed with a status of "No matching template" because it does not match any residue template of the charmm27 forcefield.

Click the **Atoms** tab.

The *Atoms* tab in the Forcefield Window lists all the atoms that do not have forcefield type assigned. There are four atoms (NA, NB, NC, and ND) with a status of "Missing". Their forcefield type is unknown and listed as "?" in the table, as charmm27 forcefield failed to find an appropriate forcefield type for them.

Customizing the HEME residue

Now you can modify the HEME residue so it can be completely typed by charmm27 for use in simulation jobs. Begin by hiding everything except the HEME residue.

Tip. You can drag the tab of the Forcefield Window to the right side of the application to display the Molecule Window

and the Forcefield Window side-by-side

Click on the 1hho molecule window tab. Press **CTRL+H** to open the Hierarchy View.

Expand the second **chain A** and select the **HEM143** residue under the chain.

Right-click the Hierarchy View and choose **Show Only**.

Now only the HEME residue is shown in the Molecule Window.

Expand the **HEM143** residue and select the **NA, NB, NC, and ND** atoms.

These are the four atoms in the Atoms tab of the Forcefield Window that do not have a forcefield type.

Open the **Simulate Structures** tool panel.

From the **Forcefield Customization** group click **Modify Atom Type**.

This opens the Choose a Forcefield Type dialog. This dialog allows you to either assign an existing or new forcefield type to the selected atoms.

Choose **NPH** as the Forcefield type for the four atoms, and then click **OK**.

In the Choose a Forcefield Type dialog, the Description field for type NPH is "heme pyrrole N", which matches the chemical environment for the four nitrogen atoms.

Alternatively, you may also define a new atom type by filling in the *Type* and *Description* fields.

Note. If you think the assigned atom type is incorrect, or you want to use your own parameters, you can choose a different forcefield type or define a new atom type for any atoms in the molecule.

Now all atoms have been assigned an assigned forcefield type, the *Forcefield* tool will automatically calculate the forcefield parameters needed for the molecule, and update the Forcefield Window with any missing or estimated parameters that are not in the original forcefield.

The *Forcefield Status* tool panel now shows "1hho typed with 1hho-charmm27" since all atoms have forcefield type assigned, and all parameters are either provided or estimated by the charmm27 forcefield.

In the Forcefield Window, each of the four atoms in the *Atoms* tab now have the forcefield type as **NPH**. Notice that the Forcefield Window now has a few more tabs. In the *Bonds*, *Angles*, *Torsions*, and *Improper* tabs, estimated parameters associated with the HEME residue are listed. You can either accept these estimated parameters as is, or modify them appropriately based on other sources, such as accurate quantum mechanical calculations.

Once all parameters are acceptable, you can use the 1hho protein with charmm27 forcefield as input to Simulation protocols such as Minimization, or Standard Dynamics Cascade.

Adding the customized HEME residue template to the charmm27 forcefield

Once you have modified the HEME residue, you can also add it as part of your own forcefield library, so you do not have to manually assign the missing atom types each time when applying the charmm27 forcefield to HEME containing proteins.

In the **hierarchy view** of the typed 1hho protein, select the **HEM143** residue.

From the **Tools Explorer**, click the **Add Residue Template** tool in the Forcefield Customization group.

This adds the HEME residue template along with any estimated parameters to your forcefield library. You can now use the template to type any other HEME containing proteins by charmm27 forcefield in the future.

You can check the residue template file (HEM143.rtf) and parameter file (HEM143.prm) for the HEME residue under your user's forcefield folder. The folder is stored in:

```
<Settings Folder>/Forcefield/charmm27
```

Note. For details about locations of folders in different operating systems, see [Installation folders](#).

Note. If you are an advanced user who is familiar with the CHARMM file format, you can manually modify the RTF files under your Forcefield folder. You can also copy any new RTF and PRM files that are compatible with the corresponding forcefield to this folder. Any residue templates and parameter files placed under this folder will be used by the Forcefield engine after restarting the application. Be aware that a residue template will only be matched if the atom labels, order, and bonds of the residue are exactly the same as the RTF file.

From the **Files Explorer**, open **Samples | Tutorials | Simulation | 2hhb.pdb**.

From the **Tools Explorer**, click **Apply Forcefield** to apply the charmm27 forcefield.

The *Forcefield Status* now displays "2hhb typed with 2hhb-charmm27".

Click **More...**

Although the HEME residue cannot be typed by the original charmm27 forcefield, the *Residues* tab in the Forcefield Window now shows that four HEM residues all match the custom template because HEME has been added to the charmm27 forcefield's residue template library in the previous step.

Further information

[Working with forcefields](#)

[Forcefield Window](#)

[Choose a Forcefield Type dialog](#)