FORECASTER Suite 2019

SPLASH'EM

Tutorial

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I. What will be Covered in this Tutorial

In this example, you will learn how to use SPLASH'EM, a modified version of PREPARE that is used for **adding water molecules** to **RNA** and **DNA** structures. If you'd like more familiarity with PREPARE, we suggest trying the **docking tutorial** first.

The interface is identical to that of PREPARE, but under the hood, the SPLASH'EM algorithms are entirely different. They place water molecules in the highly charged environment within nucleic acid structures.

SPLASH'EM can be integrated into a workflow for docking small molecules to RNA or DNA

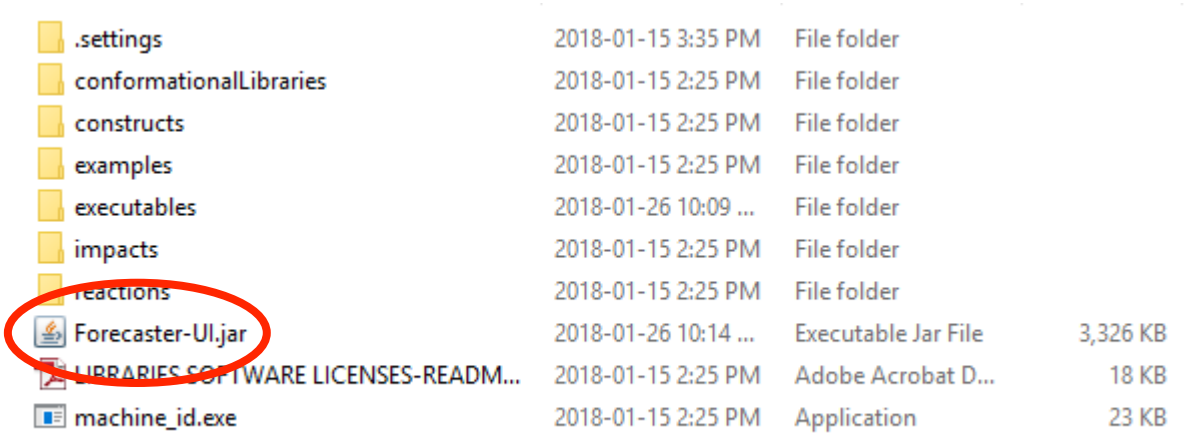
How long will the tutorial take? The tutorial itself is run at your own pace. The workflows take a minute or two to complete, depending on your computing hardware. A standard laptop should handle the experiment in under a minute.

II. Running FORECASTER with the User Interface

The user interface (UI) can be started by double clicking on the `Forecaster-UI.jar` file in the `Forecaster` folder. This will open the main window.

Under Linux and Mac OSX, it is recommended to launch it from a terminal window by typing the command below. Make sure that you are located in the folder where this jar file is.

```
Forecaster@Linux/Forecaster:~$ java -jar Forecaster-UI.jar
```



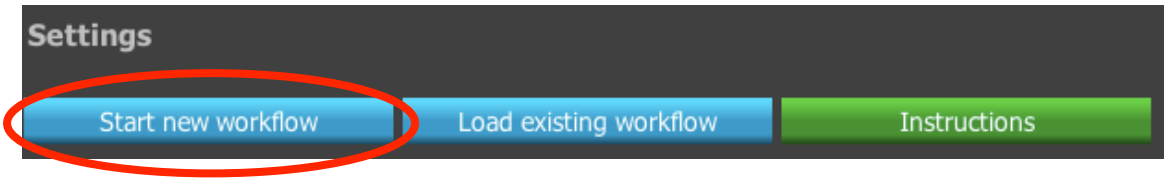
The first step is to set the working directory. Click **Browse**, under **Working Directory**. You will be prompted to navigate to the folder where you will save various files while working with FORECASTER. For this tutorial, go to “examples” and then to “NA-Water”.

All the necessary files will be written there. The molecules can be drawn using the FORECASTER sketcher and the molecule/reaction files will be written there as well. If you are planning to run calculation from an external library (e.g., a catalog of chemicals, a file from the ZINC database,…), a copy should be in your working directory.

A workflow with SPLASH’EM is accessed by scrolling down to **Modular Workflows** and click on **Start Forecasting**.

III. Creating a SPLASH'EM workflow

You can create a SPLASH'EM workflow by clicking on **Start new workflow**



The workflow builder will appear. You can click on **Options and Glossary** to learn more about the functionality of our modular workflows.

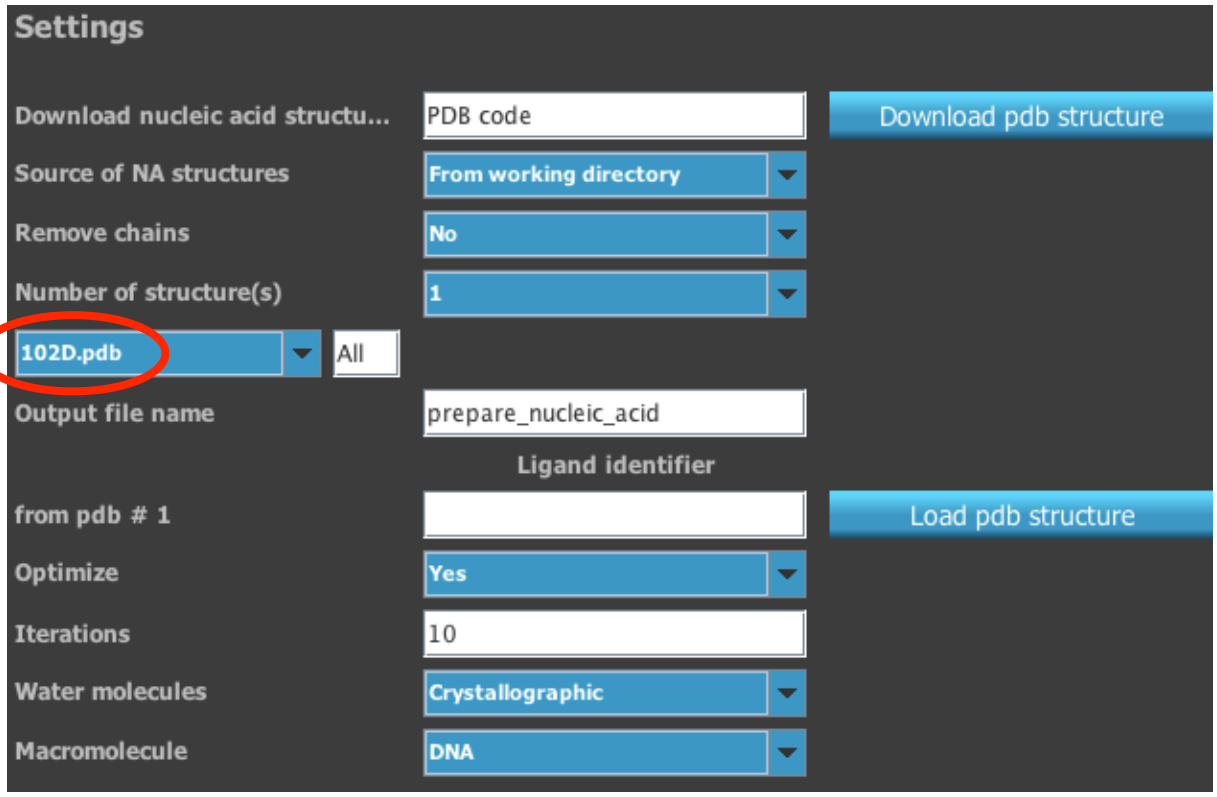
From the dropdown menu, you will scroll to and click on **SPLASH'EM**. Then click on **Confirm**. You should see the SPLASH'EM box turn blue like this:

Now you are set to **finalize this workflow** since we will only be running SPLASH'EM. See our tutorial on modular workflows to learn how else you might want to create a more complex workflow.

IV. Running SPLASH'EM

Clicking on the gear icon will open the parameters section for SPLASH'EM.

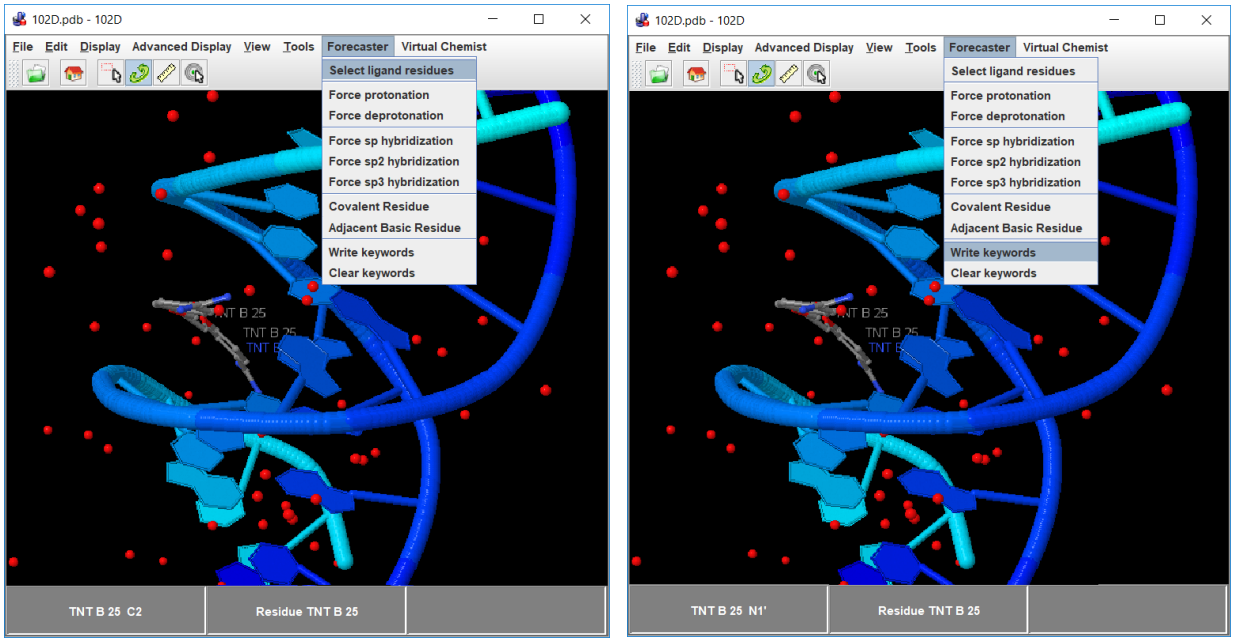
Since the `102D.pdb` file is already in the working directory, there is no need to download the file from the PDB site and it should be already listed in the nucleic acid structure menu.



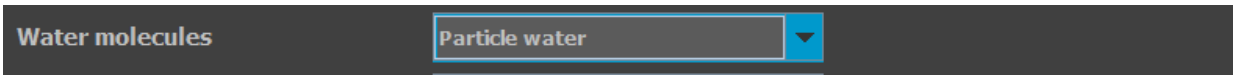
The ligand residue(s) must be identified in order to define the active site and extract the ligands from the nucleic acid/ligand complexes. To automatically identify the ligand residues, click the **Load pdb structure** button and a 3D viewer will open with the nucleic acid loaded.

Within this 3D viewer, the ligand is selected by clicking any ligand atom. The lower left box will then show the name of the selected ligand atom (TNT B 25 C2 in our case). If the correct ligand residue is selected, clicking **Select ligand residues** in the **Forecaster** menu will save the residue in the lower middle box (Residue TNT B 25). When the ligand is made of more than one residue, all of the residues must be listed.

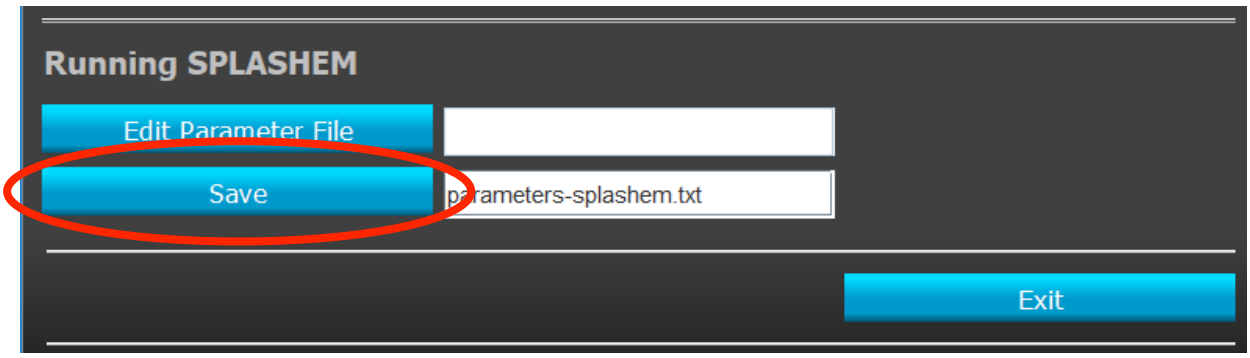
Clicking on **Write keywords** will automatically save the information back to the SPLASH'EM menu. The 3D viewer can then be closed to return to the parameters section.



Here we want SPLASH'EM to place the water molecules, thus **particle water** should be selected from the **water molecules** dropdown menu.



Once all the parameters are set, click the **Save** button. Clicking the **Exit** button will close the SPLASH'EM parameters section and return to the main workflow.



A green check should now appear in the SPLASH'EM box indicating that this box is now configured.

The workflow can be executed by clicking the **Run workflow** button. The program runs in a terminal and once the calculations are complete, the terminal window will close. Do not close the terminal window manually unless you want to stop the execution of the workflow (cannot be resumed).

V. Result Analysis

SPLASH'EM takes a nucleic acid-ligand complex in pdb format and will create the 102D_pro.mol2 and 102D_lig.mol2 files, while the `prepare_nucleic_acid.out` file contains the output information (printing display is dependent on operating system).

```
|-----------------------------------------------------------------------------|
| SUCCESSFUL COMPLETION                                                       |
| Program now closing.                                                        |
| Carefully reading the output file is recommended!                           |
|-----------------------------------------------------------------------------|
|-----------------------------------------------------------------------------|
| The program will now exit.                                                  |
| Reading the .out and .log files is recommended                              |
|-----------------------------------------------------------------------------|
| Reports of any bug and suggestions for improvement are more than welcome    |
| info@molecularforecaster.com                                                |
logout
Saving session...
...copying shared history...
...saving history...truncating history files...
...completed.

[Process completed]
```

The 102D_pro.mol2 file can now be used for docking small molecules to this nucleic acid structure or any other purpose.