**2. Prepare ligands**

***2.1 Download compounds***

This module is used to automatically download compound structure files (*.sdf*) for docking from the PubChem database. The 3D conformations of these compounds have been optimized for energy minimization, which are appropriate as the initial conformations for docking. A compound index file (*.xlsx* or .*xls*) containing all the SMILES or CID number of the compounds to download is required. The format of the index file is the same as that in module 1.1. **Note that SMILES and CID number cannot be filled in the same index file.** **Each cell can only be filled with one SMILES or CID number. Don’t fill in any other content, such as line number, title, and so on.**

1. Click "Select a compound index file" to select the *Excel* file containing SMILES or CID number of the compounds to download.
2. Click "Choose saving directory" to set the directory where the compound structure files will be saved.
3. Select the download mode: By compound CID or SMILES.
4. Click "Begin to download" and wait……

After the download task is complete, you can click "View download failure list" to see which compounds were not downloaded successfully (Blank content means that all the compounds were downloaded successfully).

***2.2 Prepare docking ligands***

This module is used to prepare original compound structure files and convert them into the *pdbqt* format which can be recognized by Vina and its derivatives.

1. Click "Choose ligands directory" to set where the compound structure files are located (e.g. the saving directory in module 2.1). **Note that all the files in *sdf, mol2,* or *mol* format in this directory will be considered as docking ligands**.

In another case, such as virtual screening, all compound structures are saved in a single compound library file. Click "or a compound library file" to select this file (*sdf*, *mol2*, or *mol*). This compound library will be split into single structure files first. You can find them in the “*split\_database*” folder in the saving directory. Then, these single compounds will be prepared and converted into *pdbqt* format.

1. Click "Choose saving directory" to set the directory where the docking ligands will be saved.
2. (Optional) Correct the protonation state of ligands. (Usually at pH=7.4 or 7.0. The pH in human body fluid is about 7.35~7.45)
3. (Optional) Randomize the ligand’s initial pose to avoid structure clashes. (It’s recommended to check this option if the compound structures have not been minimized. It’s also necessary to check this option when the 2D structures are used instead of 3D structures, although this is not recommended because some complex 2D structures cannot be converted to 3D conformations correctly by OpenBabel.)
4. Click "Begin to prepare" and wait……

**For some complex ligands, such as natural ingredients and polycyclic compounds, OpenBabel may not convert them correctly or not sense correct bonds (there is no information for bonds in the *pdbqt* format file). It is recommended to check the converted *pdbqt* format file with visualization software (e.g. PyMol) to make sure the compounds have been prepared as expected**.

**2. 准备配体**

***2.1下载化合物结构***

该模块用于自动地、批量化地从PubChem数据库下载对接所需化合物结构(*.sdf*)。这些化合物的3D构象已经过能量最小化，适宜作为对接的初始结构。一个包含所有要下载的化合物的SMILES或CID号的索引文件是必须的，格式为*.xlsx*或*.xls*。该索引文件与模块1.1中使用的类似。**注意SMILES和CID号不能在同一个索引文件中填写。每个单元格只能填写一个SMILES或CID号。不要填写任何其他内容，如行号、标题等。**

1. 点击“选择化合物索引文件”，选择含有要下载的化合物SMILES或CID号的*Excel*文件。
2. 点击“选择保存路径”，设定化合物结构文件的保存位置。
3. 选择下载方式：通过CID号或者SMILES下载。
4. 点击“开始下载”并等待……

下载全部完成后，可以点击“查看下载失败列表”来查看哪些化合物下载失败了，显示空白说明全部下载成功。

***2.2准备对接配体***

该模块用于准备原始化合物结构文件并将其转化为Vina及其系列软件能够识别的*pdbqt*格式。

1. 点击“选择配体所在路径”，设置化合物结构文件所在位置(例如模块2.1中使用的结构保存路径)。**注意该目录下的所有*sdf, mol2*和*mol*格式文件都会被视为对接配体。**

在另一种情况下，如虚拟筛选，所有的化合物结构被保存在一个单一化合物库文件中。此时点击 "分割单一化合物库"来选择这个文件(*sdf*, *mol2*,或*mol*)。这个化合物库将首先被分割成单个结构文件。可以在保存目录中的 "*split\_database* "文件夹中找到它们。然后，这些结构文件将被准备并转化为*pdbqt*格式。

1. 点击“选择保存路径”设定准备后的对接配体保存位置。
2. (可选的) 修正配体的质子化状态。(通常pH设定为7.4或7.0，参考人体体液的pH约为7.35~7.45)
3. (可选的) 随机化配体初始构象以避免结构冲突。(如果化合物的结构没有被事先能量最小化，建议勾选此选项。如果使用的是2D结构而不是3D结构，也有必要勾选这个选项，不过不建议使用2D结构，因为有些复杂的2D结构无法被OpenBabel正确地转换为3D构象)
4. 点击“开始转化”并等待……

**对于一些复杂的配体，如天然成分或多环化合物，OpenBabel可能无法正确识别，或者无法正确感知化学键(因为*pdbqt*格式文件中没有化学键的信息)。建议通过可视化软件(如PyMol)检查转换后的*pdbqt*格式文件，以确保化合物被正确准备了。**