**Drug Design Package Software**

**with In Silico Drug Discovery**

# *MolDesk Basic*

# *Ver.1.1.100*

**Manual**

IMSBIO Co., Ltd.

Contents

# 1. Operating environment

This application works in the following environments.

## OS

- Windows 11 / 10
- Linux（64bit）
- macOS 10.11 or later

- Supported MAC Hardware Specs：MacBook Air (11-inch, Early 2014) or higher.
  Apple silicon version works with Rosetta 2.

# 2. install

## 2.1. Windows

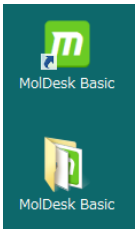
### 2.1.1. Install MolDesk Basic

Double-click the following startup file to start the installation.

| environment | Installer to use |
|---|---|
| Windows 64bit | moldesk_basic_64_setup_1.1.100.exe |

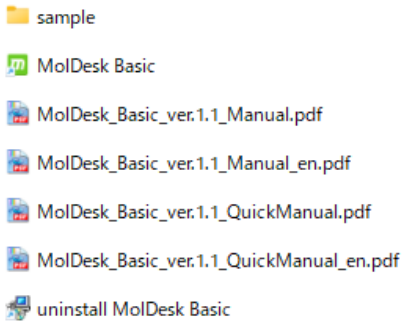
- When installing on Windows, "Windows SmartScreen stopped launching unrecognited apps. ***" may appear. In that case, you can install it by selecting "More information" and selecting the "Run" button.

- If you have an older version of MolDesk installed, uninstall the old version and then install the new version.




After the installation is complete, the MolDesk Basic startup icon and MolDesk Basic folder are created on the desktop.

The MolDesk Basic folder contains the following files and folders:




Sample input files
MolDesk Basic start icon
Manual (Japanese)
Manual (English)
Quick manual (Japanese)
Quick manual (English)
Uninstall icon

#### 2.1.2. Uninstall MolDesk Basic

Double-click the uninstall icon to run it, or in the control panel, click Uninstall in the Windows standard way from Programs and Features.

### 2.2. Linux

#### 2.2.1. Install MolDesk Basic

MolDesk_Basic_Deploy Linux64_1.1.100.tar.gz to any area, double-click the following boot file: MolDesk starts.

| environment | Startup file |
|---|---|
| Linux 64bit | MolDesk_Basic_Linux64 / MolDesk |

- If you have an older version of MolDesk installed, uninstall the old version and then install the new version.

- If your Linux desktop environment is Unity, MolDesk will not work properly due to Unity glitches. If you use MolDesk, change your desktop **environment to GNOME.**

#### 2.2.2. Uninstall MolDesk Basic

Deletes the folder that you MolDesk_Basic_Linux64 deployed during installation.
If you want to keep project information, be careful not to delete the saved project files.

## 2.3. Mac

### 2.3.1. Install MolDesk Basic

Run theinstaller (MolDesk_Basic_Mac_1.1.100.pkg) and follow the instructions in the wizard to install it.

- When the installer starts, "~ can not be opened because the developer is unconfirmed. If you see a warning to that effect, right-click on the installer file and select "Open" in the context menu to run it.

Two things are installed: Installation destination can be changed

| Installation | Default installation location |
|---|---|
| “MolDeskBasic.app” (execution file) | /Applications |
| MolDesk Basic folder (manual , sample data set) | /Library |

### 2.3.2. Uninstall MolDesk Basic

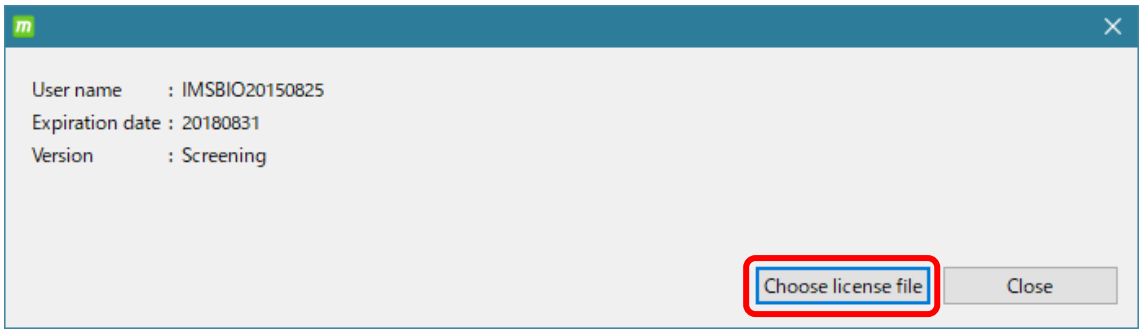
Drag and drop the installed files/folders into the Trash, or right-click and select "Put in Trash" in the context menu to delete them.

# 3. Activation

## 3.1. Enter license file

After you install it, MolDesk is disabled and will be available after activation. Here are the activation steps:

Select the [Help] - [Activate License] menu to display the following dialog:




[Choose license file] to load the license file.

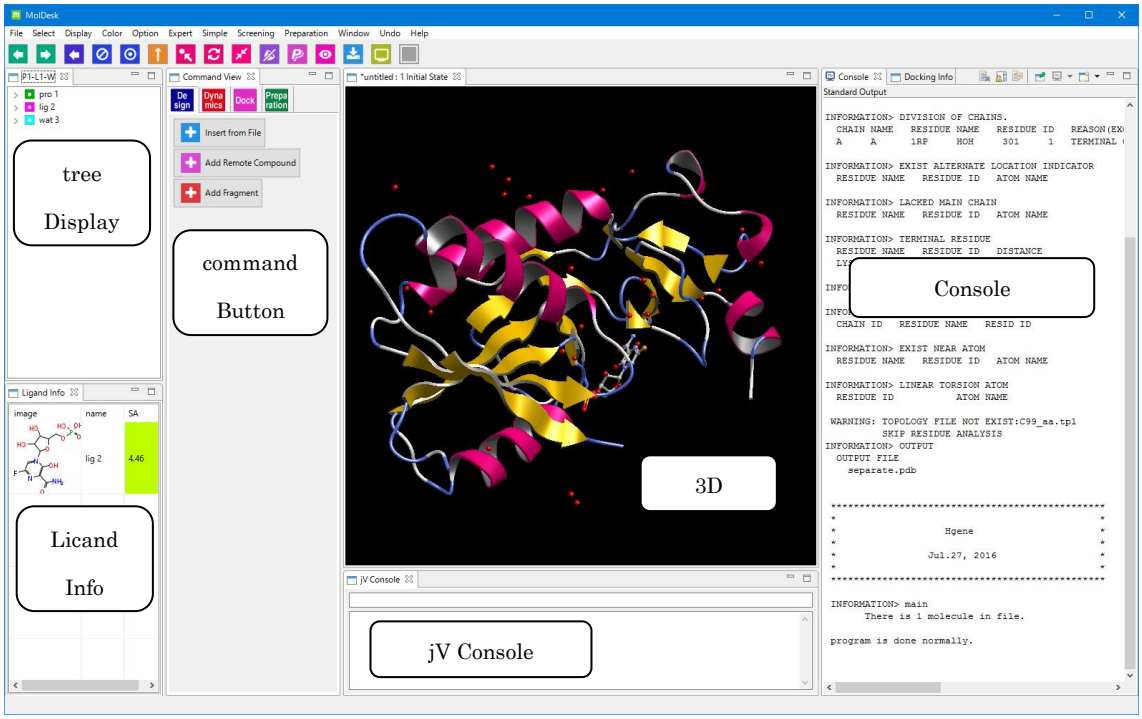
When the load is complete, you will see the following:

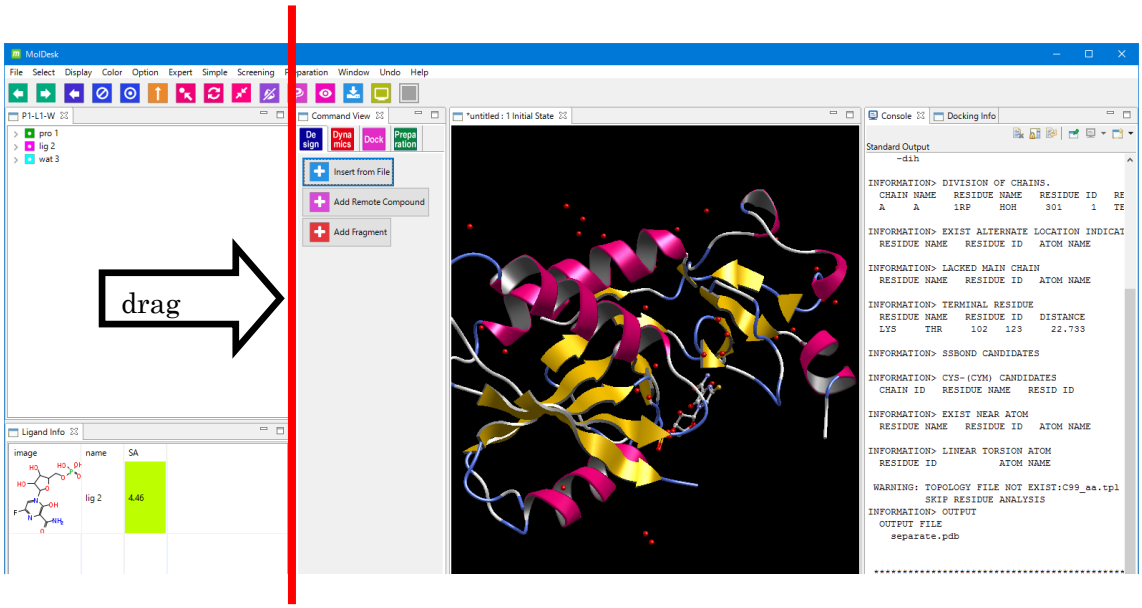
[User name] ： Display user name, license information, etc. filled in the license file
[Expiration date] ： View license expiration dates, for perpetual licenses, "-"
[Version] ： Displayed as “Basic” for MolDesk Basic license
Displayed as “Screening” for MolDesk Secreening license

# 4. manual

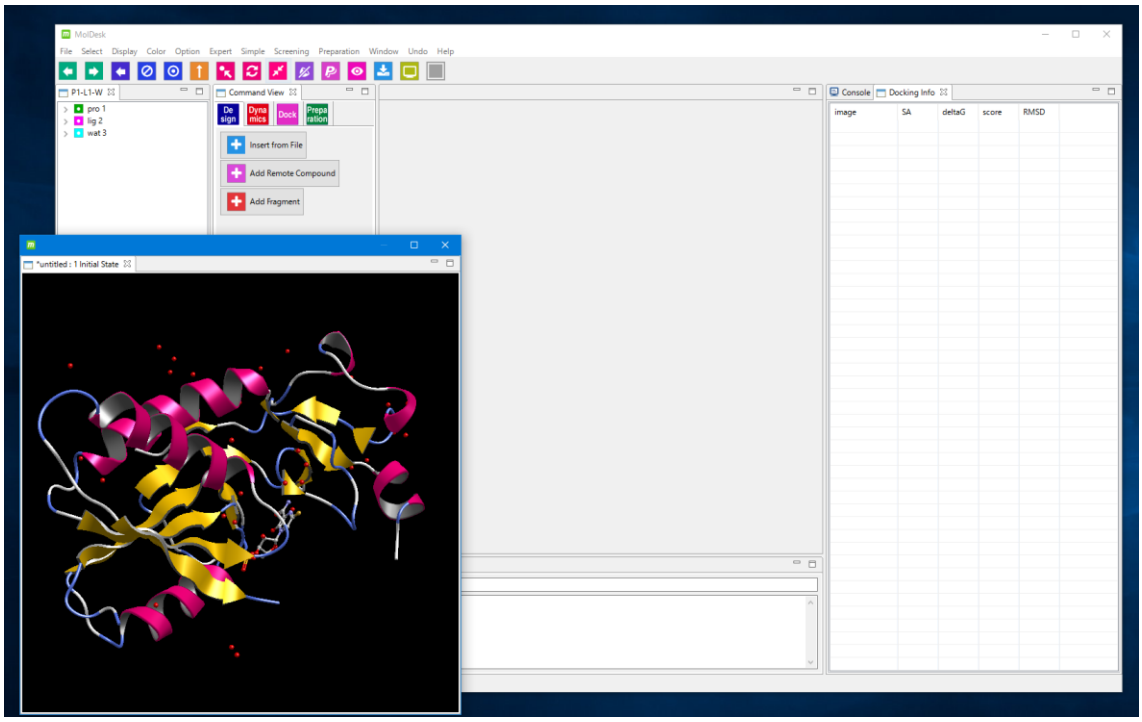
## 4.1. Screen configuration

The MolDesk Basic screen consists of multiple tabs.




You can change the width of each area by dragging it over the tab boundary.




You can also drag the tab outside the main screen to make it appear larger.

To close a tab, click × on the tab.

To open a closed tab, run the following menu:
[Window] - [Tree View]
[Window] - [Command View]
[Window] - [Console]
[Window] - [jV Console]
[Window] - [MD Analysis]
[Window] - [Ligand Info]
[Window] - [MolGate] (currently not available)

[Show All View]  to restore all closed tabs.

**Once changed, the layout is saved and retained the next time it starts.**

※ **If you want to** reset the screendisplay, run [Reset All View] and restart it. At this time, please note that the various preference values set by the user in [Help] - [Preference] will also return to the default values.

## 4.2. List of command buttons

The command buttons on the command button screen are shown below. For those with a detailed description, the section corresponding to the description was shown.

[Design] - Other

| Command button | explanation | Display conditions |
|---|---|---|
| [Copy] | copy | Molecules, chains, afterastes, When the atom is selected |
| [Insert From File] | 4.4.3 | Always visible |
| [Add Remote Compound] | 4.4.3 | Always visible |
| [Add Fragment] | 4.4.3 | Always visible |
| [Delete Molecule] | deletion | Molecules, chains, afterastes, When the atom is selected |
| [Add Hydrogens] | 4.27.2 | Molecules, chains, afterastes, When the atom is selected |
| [Delete Hydrogens] | 4.27.2 | Molecules, chains, afterastes, When the atom is selected |
| [Cap with ACE and NME] | 4.27.1 | When a protein is selected |
| [Create S-S Bond] | 4.27.3 | When a protein is selected |
| [Break S-S Bond] | 4.27.3 | When a protein is selected |
| [Delete Residue without Calpha] | 4.27.4 | When a protein is selected |
| [Mutate Residue] | 4.27.5 | When a protein is selected |
| [Delete] | 4.24.8 | Molecules, chains, afterastes, When the atom is selected |
| [Move] | 4.24.16 | Molecules, chains, afterastes, When the atom is selected |

[Design] - Ligand

| Command button | explanation | Display conditions |
|---|---|---|
| [Copy] | copy | Molecules, chains, afterastes, When the atom is selected |
| [Insert From File] | 4.4.3 | Always visible |
| [Add Remote Compound] | 4.4.3 | Always visible |
| [Add Fragment] | 4.4.3 | Always visible |
| [Delete Molecule] | deletion | Molecules, chains, afterastes, When the atom is selected |
| [Add Hydrogens] | 4.27.2 | Molecules, chains, afterastes, When the atom is selected |
| [Delete Hydrogens] | 4.27.2 | Molecules, chains, afterastes, When the atom is selected |
| [Partial Charge] | 4.24.10 | When the compound is selected |
| [Clean Geometry] | 4.24.11 | When the compound is selected |
| [Delete] | 4.24.8 | Molecules, chains, afterastes, When the atom is selected |
| [Move] | 4.24.16 | Molecules, chains, afterastes, When the atom is selected |
| [Extract Atom] | 4.24.12 | When the atom is selected |
| [Connect Fragment] | 4.24.6 | When the atom is selected |
| [Change Element] | 4.24.7 | When the atom is selected |
| [Delta G] | Structural optimization | When the compound is selected |

[Design] - Lig2

| Command button | explanation | Display conditions |
|---|---|---|
| [Torsion] | 4.24.14 | 2 When atoms are selected |
| [Change Bond Order] | 4.24.9 | When two atoms are selected |
| [Delete Bond] | 4.24.15 | When two atoms are selected |
| [Insert Element] | 4.24.13 | When two atoms are selected |

[Dynamics]

| Command button | explanation | Display conditions |
|---|---|---|
| [Insert From File] | 4.4.3 | Always visible |
| [Delete Molecule] | deletion | Molecules, chains, afterastes, When the atom is selected |
| [Add Hydrogens] | 4.27.2 | Molecules, chains, afterastes, When the atom is selected |
| [Partial Charge] | 4.24.10 | When the compound is selected |
| [Delete] | 4.24.8 | Molecules, chains, afterastes, When the atom is selected |
| [Solvate] | 4.29.2 | Always visible |
| [Global Minimize] | 4.29.3 | Always visible |
| [Global Dynamics] | 4.29.5 | Always visible |
| [Auto Minimize] | 4.32.1 | Always visible |
| [Auto Solvate and Minimize] | 4.32.2 | Always visible |
| [Auto Dynamics] | 4.32.3 | Always visible |
| [Auto Solvate and Dynamics] | 4.32.4 | Always visible |

| | | |
|---|---|---|
| [Build Membrane] | 4.30 | When a protein is selected. |
| [Solvate Membrane] | 4.30 | After [Build Membrane] is executed |

[Dock]

| Command button | explanation | Display conditions |
|---|---|---|
| [Insert fFrom File] | 4.4.3 | Always visible |
| [Delete Molecule] | deletion | Molecules, chains, afterastes, When the atom is selected |
| [Add Hydrogens] | 4.27.2 | Molecules, chains, afterastes, When the atom is selected |
| [Partial Charge] | 4.24.10 | When the compound is selected |
| [Delete] | 4.24.8 | Molecules, chains, afterastes, When the atom is selected |
| [Make Pocket] | 4.18.3 | Always visible |
| [Find Pocket] | 4.20.2 | Always visible |
| [Select Receptor Molecule] | Receptor selection | Always visible |
| [Docking] | 4.18.5 | Always visible |
| [Docking NMR] | 4.22.4 | Always visible |
| [Auto Docking] | 4.17.2 | Always visible |

[Screening]

| Command button | explanation | Display conditions |
|---|---|---|
| [Insert From File] | 4.4.3 | Always visible |
| [Delete Molecule] | deletion | Molecules, chains, afterastes, When the atom is selected |
| [Add Hydrogens] | 4.27.2 | Molecules, chains, afterastes, When the atom is selected |

| | | |
|---|---|---|
| [Partial Charge] | 4.24.10 | When the compound is selected |
| [Delete] | 4.24.8 | Molecules, chains, afterastes, When the atom is selected |
| [Make Pocket] | 4.18.3 | Always visible |
| [Find Pocket] | 4.20.2 | Always visible |
| [Select Receptor Molecule] | Receptor selection | Always visible |
| [MTS / Docking score ranking] | MolDesk Screening Features of(not available with MolDesk Basic) | Always visible |
| [ML-MTS] | | Always visible |
| [ML-DSI] | | Always visible |
| [MVO Screening] | | Always visible |
| [Topology Graph Similarity] | | Always visible |
| [Substructure Search] | | Always visible |
| [Predict Activity] | | Always visible |

[Preparation]

| Command button | explanation | Display conditions |
|---|---|---|
| [Delete Molecule] | deletion | Molecules, chains, afterastes, When the atom is selected |
| [Add Hydrogens] | 4.27.2 | Molecules, chains, afterastes, When the atom is selected |
| [Partial Charge] | 4.24.10 | When the compound is selected |
| [Delete] | 4.24.8 | Molecules, chains, afterastes, When the atom is selected |
| [Convert to 3D Mol2] | 4.25.1 | Always visible |
| [Make DB for Screening] | MolDesk Screening features (not available with MolDesk Basic) | Always visible |
| [Remake DB for Screening] | | Always visible |
| [Make DB to predict Activity] | | Always visible |

## 4.3. project

MolDesk processes data on a project-by-project basis.
As ageneral rule, oneproject is created for each file that you enter, such as [File] -[Open Manual File].

The projectis a [Help] – [Preference] – [8. Other] directory set in Default Project Directory
MoldeskProject00000
MoldeskProject00001
MoldeskProject00002
・・・
created as .

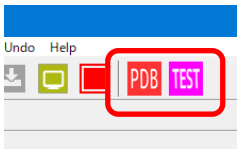
The Default Project Directory directory above is set to the system's default tmp directory immediately after installation, and is different for Windows, Linux, and MAC,so where is it stored?

[Help] - [Preference] - [8. Other]

Please check with .

If the user changes the Default Project Directory in [Help]-[Preference]-[8. Other], the screen prompting you to save the project will disappear when the program ends.
It is recommended that you change to a directory (folder) with sufficient disk space.

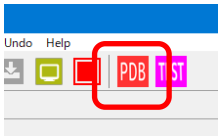
## 4.4. Create project



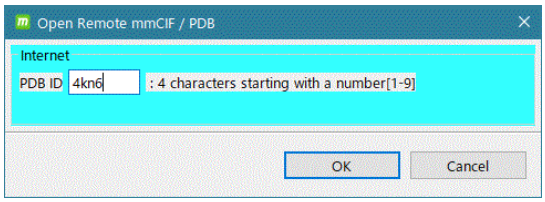

If you are connected to the Internet,
Click the [PDB] [TEST] button on the top page.

The following functions are available for each.
[PDB] ：Enter molecules with PDB ID by user
[TEST] ：Enter any PDB ID molecules

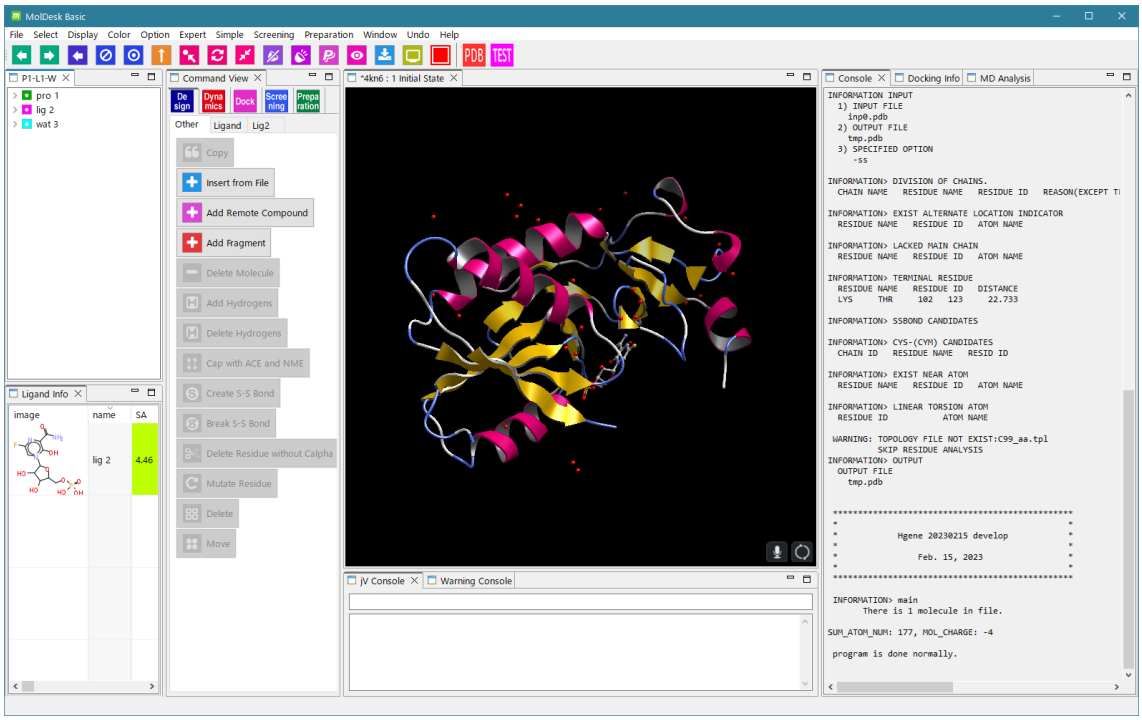
### 4.4.1. [PDB]




Click the [PDB] button on the top page, and the following PDB ID entry screen will appear.



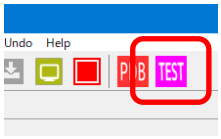

Example:Load PDB ID 4kn6
Download mmCIF and PDB files via the internet. Import the mmCIF file and create a new project.



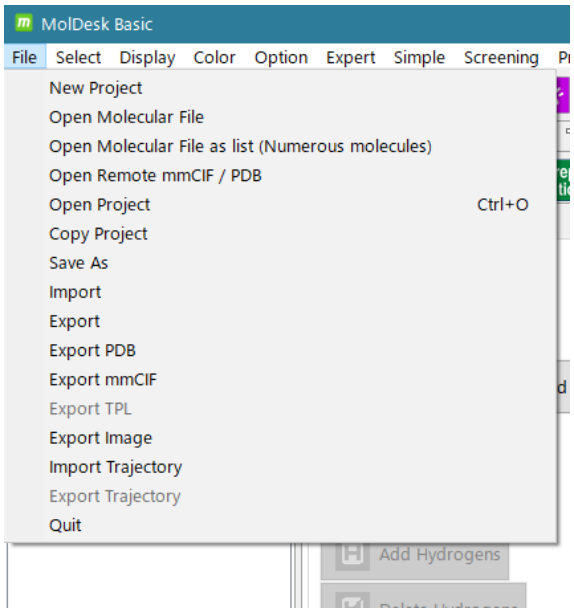

※ If you enter a protein, it generates an S-S bond by default.

※ The [PDB] button on the top page has the same function as [File] - [Open Remote mmCIF / PDB].

### 4.4.2. [TEST]




Click the [TEST] button on the top page to download an mmCIF file and a PDB file of any PDB ID via the Internet.
Load the mmCIF file and create a new project.




The [File] menu contains various project creation functions.

[File] - [New Project]
[File] - [Open Molecular File]
[File] - [Open Molecular File as list (Numerous Molecules)]
[File] - [Open Remote mmCIF / PDB]
[File] - [Open Project]
[File] - [Import]
[File] - [Import Trajectory]

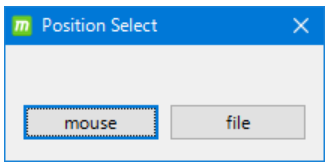
### 4.4.3. [File] - [New Project]

Create a new empty project.
After you create the project, load the molecule in one of the following ways:


[Insert From File] : Reads a molecule with a file.

The file formats that can be read are sdf / mol / mol2 / pdb / mmCIF / SMILES.

The Position Select dialog appears after selecting the file in the file selector.

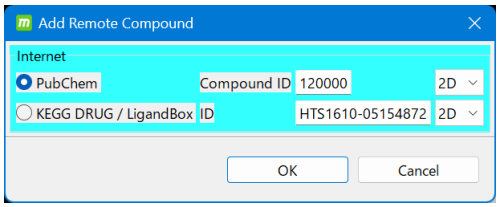



[mouse] : Enter compoundat mouse click point on 3D screen
[file] : Enter compound in the coordinates of the compound file

※ If you select a PDB file who has a file name of point.pdb in the file selector, load it as the point file to use in the docking calculation. A point file is a collection of probe points in a pocket.

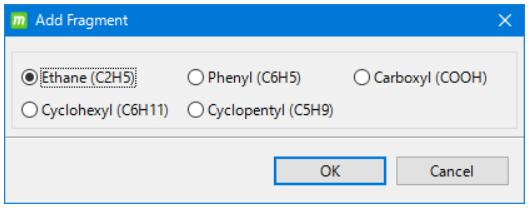

[Add Remote Compound] : Reads molecules over the Internet.

PubChem Compound ID or KEGG DRUG / LigandBox ID Enter one. You can choose 2D or 3D.




An example of an ID number to enter is:
For PubChem, for example,120000.
For LigandBox, for example,HTS1610-05154872.


[Add Fragment] : Enter the specified molecular species as the initial structure.




There are five types of molecules that can be selected.
After selecting the molecular species, [Position Select]
Dialog (in the above [Insert From File] See description) is displayed.

### 4.4.4. [File] - [Open Molecular File]

Load the specified file to create a new project.

There are six file formats that can be entered:PDB / mmCIF / Sybyl Mol2 / MDL SDF / MDL MOL / SMILES.

| file | File extension |
|---|---|
| PDB | . pdb / . ent |
| mmCIF | . cif |
| Sybyl Mol2 | .mol2 / .sm2 / . SM2 / .ml2 |
| MDL SDF | . sdf |
| MDL MOL | .mol / .mdl |
| SMILES | . smi / . SMI / .smiles / . SMILES |

- The file extension must be as shown in the table. If the extensions are different, change the extension before entering them.

- If the entered file is a mol2 file, automatic charge calculation is not performed at the time of input because the charge information in the file is used. For compounds that

do not have charge information, perform charge calculations accordingly.

- The format of the SMILES file that you canenter is a text file that has a description in the form of one molecule, single molecule per line. It is also possible to input multiple molecules.

※ If you enter a protein, it generates anS-S bond by default.

When you load the file, the structure of the molecule is displayed on the 3D screen.

The project name is not yet attached at this time.
When saving the project name with "5.6.1 [File]-[Save As]" described later, save it with the project name.

### 4.4.5. [File] - [Open Molecular File as list (Numerous Molecules)]

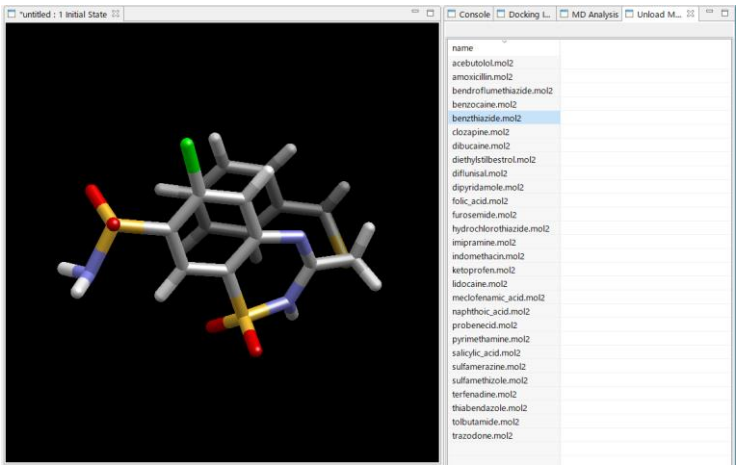
Fast loading of files containing more than 10,000 molecules. It can be used as a molecular viewer for files with large numbers of molecules.
Because a large number of molecules are loaded as lists, no new projects are created when loaded.

There are four file formats that can be entered:PDB / Sybyl Mol2 / MDL SDF / MDL MOL.

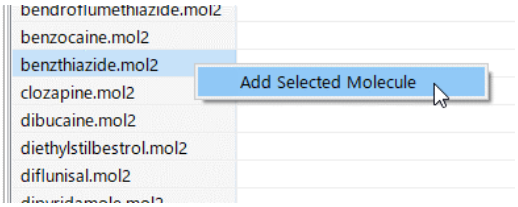
| file | File extension |
|---|---|
| PDB | . pdb |
| Sybyl Mol2 | .mol2 |
| MDL SDF | . sdf |
| MDL MOL | .mol |

- The file extension must be as shown in the table. If the extensions are different, change the extension before entering them.

Example of loading MolDesk Basic -> sample -> mol2 -> multi28.mol2.
This file contains only 28 molecules, but reads it as a list as follows:

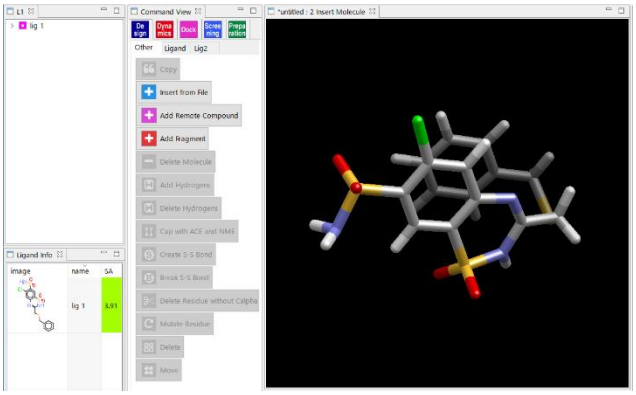


Click the name of the molecule in the list to display the molecule in 3D




Right-click the molecular name ofthe list to display the [Add Selected Molecular] menu. Clicking on it allows you to take the molecule as a project and adds the molecules that you have taken into the tree display.

This is the first time a project is created.



* Before the molecules are taken in in the [Add Selected Molecular] menu, the project is not generated simply by displaying the molecules.

## 4.5. Load project

Describes the following two menus for loading projects:

[File] - [Open Project]

[File] - [Import]

### 4.5.1. [File] - [Open Project]

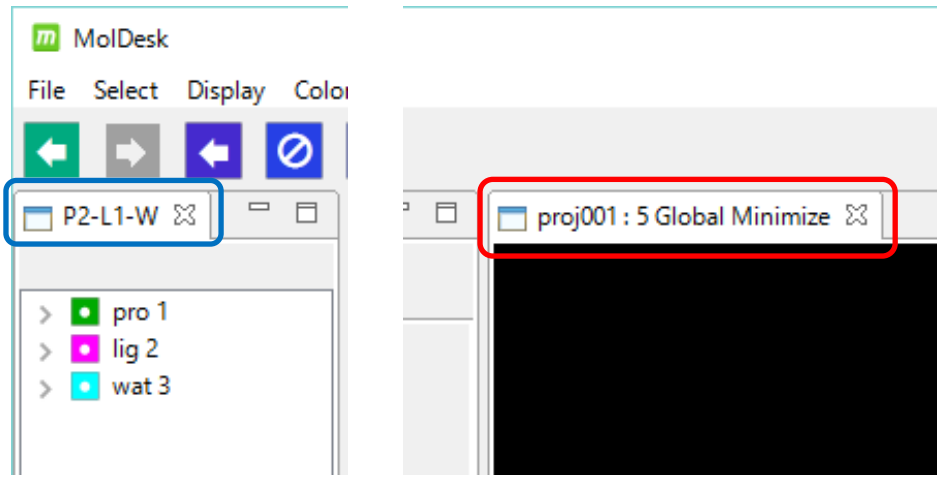
Projects previouslysaved in [File] - [Save As] ,
Or, it is in the directory set in Default Project Directory of [Help]-[Preference]-[8. Other].
MoldeskProject00000
MoldeskProject00001
MoldeskProject00002
・・・
Open.

[Select project directory] In the dialog, select a folder for an existing project (including the original and work folders directly below),and then click [OK].

The tab name of the tree display screen(P2- L1-W in the blue framebelow) indicates the number of proteins and compounds. P indicates protein chain, L indicates compound, W indicates crystalline water,and M indicates metal ions.
On the tree display screen, shows proteins, compounds, water, glycan, and metals and ions.

※ Glycans are represented as **SNFG** in the initial display of the 3D screen.
※ **Glycans will change their display to compounds when the tplgeneX/tplgeneL programs, which are myPresto's force field generation programs, are run when MD calculations, docking calculations, etc. are run.** The current version does not support force fields for glycans such as GLYCAM force field, and this is because the compounds are processed with the same force field.

The last command you interacted with can be found in thetab name of the 3D screen(proj001: 5 GlobalMinimum).
The tab name indicates [**Project Name: History Number Execution Command Name**] .




### 4.5.2. [File] - [Import]

Open a project that you previouslysaved in [File] - [Export].

The difference between [File]-[Save As] and [File]-[Export] is whether the saved file is compressed. Use [File]-[Import] to import the file saved by [File]-[Export].

| How to save | Saved files | If you want to load again |
|---|---|---|
| [File] - [Save As] | Not compressed | [File] - [Open] |
| [File] - [Export] | Zipped into 1 file | [File] - [Import] |

Run [File] - [Import], select the file and click [Open].

In the [Select project directory] dialog, select [Create New Folder] and enter the folder name. This folder name will be the new project name.

The folder you created stores all the data for the imported project.

## 4.6. Save project

Describes the following three menus for saving projects:

[File] - [Save As]

[File] - [Copy Project]

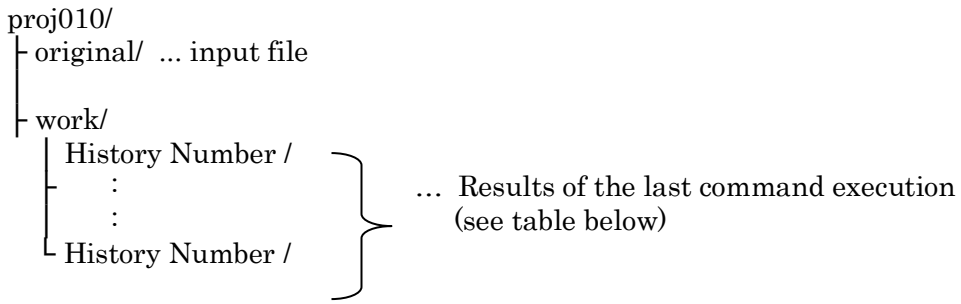
[File] - [Export]

### 4.6.1. [File] - [Save As]

Save the system you are displaying with the project name. The history of the command is also saved.

Run [File] -[Save As], select
[Create New Folder] or [New Folder]
Or, from the right-click menu, select [New] - [Folder]
in the [Make PROJECT directory] dialog, and enter the folder name. This folder name will be the new project name.

In the folder you created, all data (including command history) of the system being displayed is saved.
The contents are as follows.




The files in the history number folder are as follows:

| File name | | explanation |
|---|---|---|
| common | all.pdb | pdb containing molecules throughout the system |
| | inp*.pdb or pro1.pdb,lig2.pdb etc | pdb of each molecule(minutes of molecules) |
| | inp*.mol2 or lig2.mol2, etc | Mol2 for each compound (compound only) |
| | *.tpl, etc | Tpl file for each molecule (when the command is created) |
| | log.txt | command standard output log file (Ascii) |
| cosgene minimize relation | 00_min.inp | [Global minimize] and Clean Geometry Cosgene Energy Desculation Calculation Configuration File |
| | Pro.tpl | cosgene tpl file |
| | cap.bc | Cosgene Cap water boundary condition setting file |
| | Position.res | Cosgene location constraint file |
| cosgene md relation | 00_md.inp | [Global Dynamics] Run-time cosgene MD calculation configuration file |
| | Pro.pdb | Cosgene PDB file |
| | Pro.tpl | cosgene tpl file |
| | cap.bc | Cosgene Cap water boundary condition setting file |
| | Position.res | Cosgene user-specified atomic position constraint file |

| | | |
|---|---|---|
| | md.shk | COSgene SHAKE configuration file |
| | md.rst | Restart file for cosgene MD calculations |
| | md.ene | Cosgene Energy Output File (ASCII) |
| | md.cor | Cosgene coordinate output file (binary) |
| | md.vel | Cosgene speed output file (Ascii) |
| GROMACS minimize relations | min.mdp | GROMACS energy minimization calculation configuration file |
| | Pro.pdb | PDB file (output of gmx mdrun) |
| | Pro.top | top file (Ascii) |
| | *.itp / convTpl_nb.itp | Include file of top file, positional constraints / convTpl_nb.itp is atomtype. (Ascii) |
| | min.gro | gro file (Ascii) |
| | min.cpt | cpt file (binary) |
| | min.edr | edr file (binary) |
| | min.log | log file (Ascii) |
| | min.tpr | tpr file (binary, output of gmx grompp) |
| | min.trr | trr file (binary) |
| | *.xvg | gmx energy analysis results file (Ascii) |
| GROMACS md relations | md.mdp | Configuration file for GROMACS MD calculation |
| | Pro.pdb | PDB file (output of mdrun) |
| | Pro.top | top file (Ascii) |
| | *.itp / convTpl_nb.itp | Include file of top file, positional constraints / convTpl_nb.itp is atomtype. (Ascii) |
| | md.gro | gro file (Ascii) |
| | md.cpt | cpt file (binary) |
| | md.edr | edr file (binary) |
| | md.log | log file (Ascii) |
| | md.tpr | tpr file (binary, output of gmx grompp) |
| | md.trr | trr file (binary) |
| | md.xtc / md_noPBC.xtc | Trajectory files before / after PBC correction |
| | *.xvg / *.xpm / proj3d.gro | Trajectory analysis result file (Ascii) |
| sievgene relation | 00_dock.inp | [Docking] Setup file for docking calculations for sievgene at run time |
| | Pro.pdb (= docking.pdb) | [Docking] Of sievgene docking calculations at run time Input pdb file |
| | Pro.tpl (= docking.tpl) | [Docking] Of sievgene docking calculations at run time Input tpl file |
| | point.pdb | [Docking] Of sievgene docking calculations at run time Input point pdb file |
| | grid.file | Sievgene grid file (binary) |
| | output.mol2 | [Docking] Of sievgene docking calculations at run time Output mol2 file |
| | output.score | [Docking] Of sievgene docking calculations at run time Output score result file |

**Note that if you specify an existing folder without [Create a new folder], the following folders and files will be printed directly under the folder:**

original folder

work folder
cif and pdb files downloaded via internet

### 4.6.2. [File] - [Copy Project]

Duplicate the displayed project. The command history is also saved.
The operation procedure is the same as [File]-[Save As]. The source project remains intact.

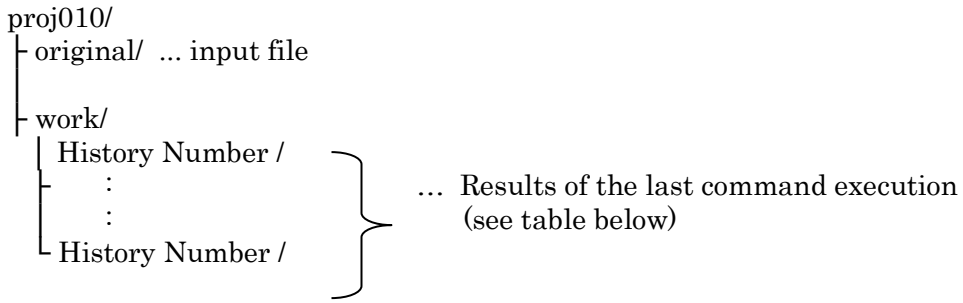
### 4.6.3. [File] - [Export]

Output the system you are displaying to a zip file with the project name.
The history of the command is not output.

This menu moves the execution environment including the configuration file to linux machine, etc.
It is assumed that it is an application to make high-speed calculation.

When you execute [File]-[Export], a dialog for entering the file name is displayed.
Save it with a name. This will be the project name.

The contents of the zip file output by [File] - [Export] are as follows.




If you want to check the contents of the file, please extract the zip compressed file with the decompression software, u nzip command, etc.

**If you deployed a** zip-compressed[File] - [Import]file -[File] - [Open Project]
Must be loaded.

## 4.7. System-wide PDB file output

### 4.7.1. [File] - [Export PDB]

Outputs a PDB file containing all the molecules of the system you are displaying.

However, in order to make it easier to take over to the docking calculation on another calculation server, the PDB file containing only the receptor is output in the following cases.

- You are creating a probepoint (point.pdb) for the docking pocket.
- If you are performing docking calculations
- Delta G (manual docking calculation)

## 4.8. System-wide mmCIF file output

### 4.8.1. [File] - [Export mmCIF]

Outputs an mmCIF file containing all the molecules of the system you are displaying.
However, it outputs a receptor-only mmCIF file in the following cases:

- You are creating a probepoint (point.pdb) for the docking pocket.
- If you are performing docking calculations
- Delta G (manual docking calculation)

## 4.9. System-wide TPL file output

### 4.9.1. [File] - [Export TPL]

Outputs a TPL file containing all the molecules of the displayed system.
You need to run [Global Minimize] or [Global Dynamics] to generate the TPL file in advance.

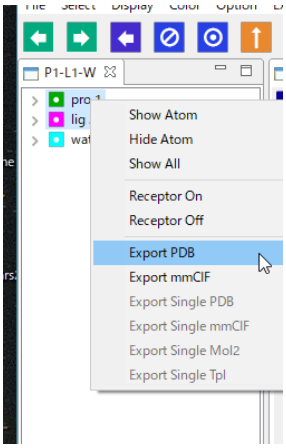
**TPL file:**

Topology file output by tplgeneX and tplgeneL of myPresto. The force field information of the molecule of the system is described. Used in cosgene and sievgene of myPresto.

However, to make it easier to carry over docking calculations on other computing servers, the TPL file for receptors is output when docking calculations are performed.

### 4.10. Multi-molecule file output

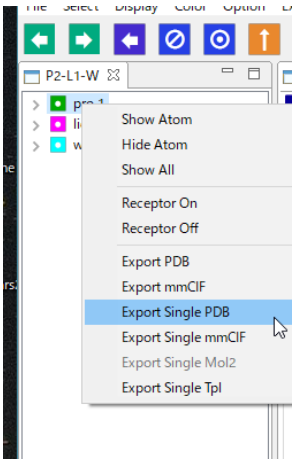
Output multiple molecules together in a single PDB fileor mmCIF file.




If you select multiple molecules on the tree display screen, right-click and select [Export PDB] or [Export mmCIF], you can output the selected molecules together in one PDB file or mmCIF file.
For PDB files, each molecule is separated by a TER.

### 4.11. File output of individual molecules

Output individual molecules to a PDB / mmCIF / Mol2 / TPL file.




Select one molecule on the tree display screen, right-click and select [Export Single PDB], [Export Single mmCIF], [Export Single Mol2], or [Export Single Tpl] to select the selected molecule. You can output in the selected format.

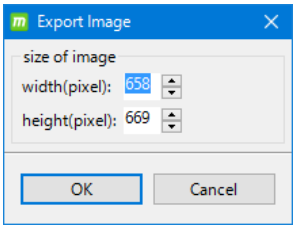
The menu you can choose varies depending on the type and conditions of the molecule.

- Export Single PDB: : Full molecule
- Export Single mmCIF: : Full molecule
- Export Single Mol2 : Compound
- Export Single Tpl: : Compound and TPL file has been generated

## 4.12. 3D display image file output

### 4.12.1. [File] - [Export Image]

Outputs a 3D screen image in png image file format.




When you execute [File]-[Export Image],
A dialog for specifying the image size is displayed.
The image size can be any value up to 4600 x 4600 pixels.

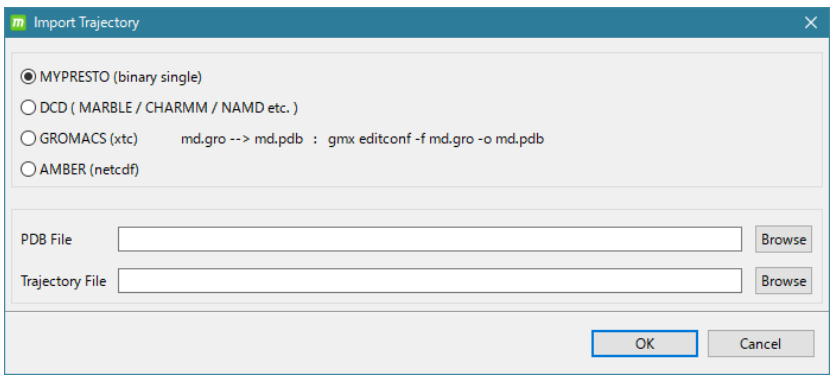
The default value is the size of the 3D screen you are currently displaying.

## 4.13. Trajectori file I/O

### 4.13.1. [File] - [Import Trajectory]

It reads the trajectori files of various MD programs and the PDB files of the reference structure in pairs to create a new project and display the video at the same time.

When [File]-[Import Trajectory] is executed, the following screen is displayed.



There are four types of tradgetry files to choose from:

| project | content |
|---|---|
| MYPRESTO | MyPresto MD program cosgene / cosgene_MPI / psygene / psygene-G tradgetry file output in single binary format<br><br>* cosgene_MPI / psygene / psygene-G are not available in MolDesk Basic. They can be used in MolDesk Screening. |
| DCD | DCDformats such asMARBLE,CHARM, and NAMD |
| GROMACS | xtc format for GROMACS |
| AMBER | AMBER netcdf format |

[Browse] to start the file selection screen.

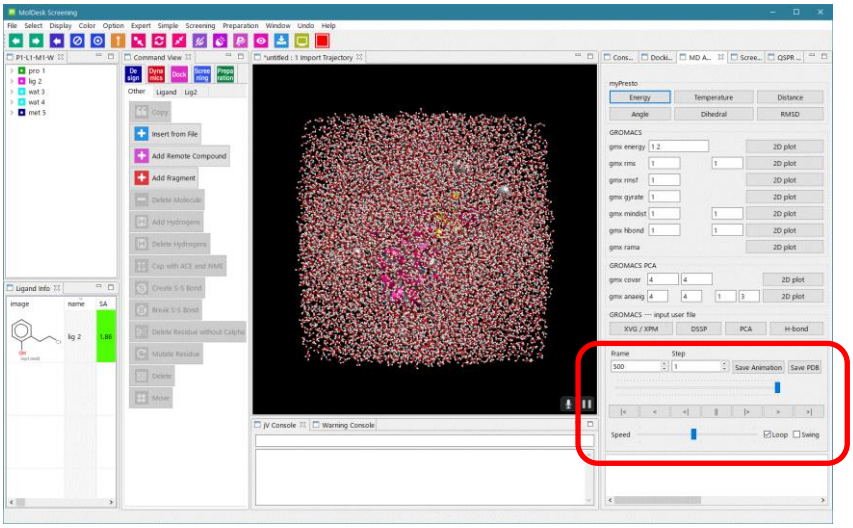
Select the PDB file for the reference structure at the same time.

※ The reference structure file does not correspond to the GROMACS gro format file, so for GROMACS, convertthe gro file to a PDB file and enter it as appropriate.

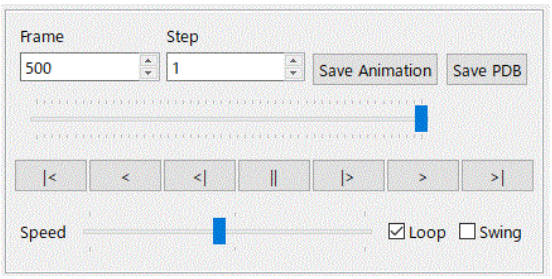
MolDesk Basic -> sample -> trajectory -> AMBER
-> DCD
-> GROMACS

The following PDB files for AMBER, DCD, and GROMACS, all.pdb, and trajectory files are available, so you can try out the video display.

The following is how GROMACS md.pdb and md.xtc are loaded.

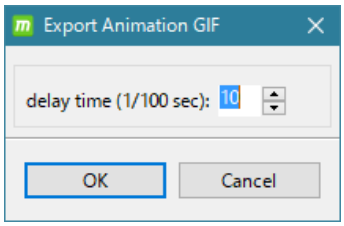


The red frame part is as follows in the animation controller.




Video frame, return, display speed ,Loop /Swing, Weeding (Step)
It can be run in real time while the video is being viewed.

You can also save the displayed video to an Animation GIF file with the [Save Animation] button. At that time, you can set the frame interval time with the following GUI.




The [Save PDB] button allows you to save the trajectory of the video being displayed to a PDB file.
At that time, a directory selector screen will appear so you can specify or create a folder to save the output PDB file.
When cosgene / psygene is used as the MD calculation engine, each snapshot is stored in many PDB files of md.n.pdb (n=1,2,3...), and when GROMACS is used, each snapshot is stored in one PDB file md.pdb with MODEL When using GROMACS, each snapshot is stored in a single PDB file md.pdb, differentiated by MODEL record.

※ When a MYPRESTO or GROMACS trajectory file is entered, a trajectory analysis can also be performed. In the case of GROMACS, edr files, tpr files, and trr files are required. When performing a trajectory analysis for GROMACS, the input screen for missing files will be displayed, so please input them accordingly.

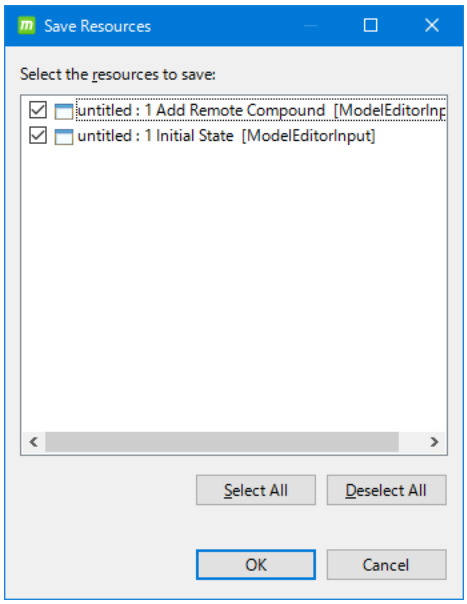
### 4.13.2. [File] - [Export Trajectory]

If a trajectori file exists in the project's viewed history, you can savethe myPresto-formatted trajectori file with any file name on the file selection screen.

## 4.14. How to exit

### 4.14.1. [File] - [Quit]

Exit MolDesk.



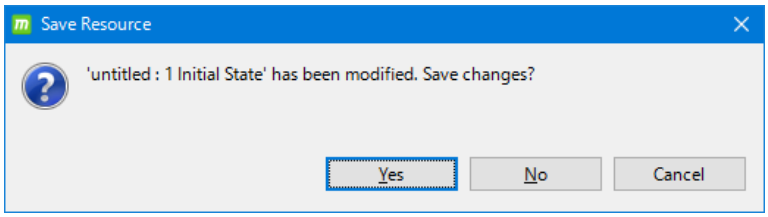

[File] - [Quit] When you run ,
If you have a project that has not been saved,
The dialog to see if you want to save the project
it will be displayed.

Projects marked with ☑ will be saved.
For projects that do not need to be saved,
remove ☑ Click [OK].

### 4.14.2. End project

Closes only the specified project.

When you close a tab on a 3D screen, if the project is not saved, the project
A dialog will appear to confirm whether to save.




Select [YES] if you want to save, or [No] if you don't want to save.
Exits.

## 4.15. 3D display of molecular structure

### 4.15.1. Mouse operation

On the 3D screen, you can use the mouse to rotate and move molecules.

| action | Mouse operation |
|---|---|
| X-axis (left-right axis) rotation<br>Y-axis (vertical axis) rotation | Left drag |
| Z-axis (depth direction axis) rotation | Shift + Right Drag (Left/Right) |
| Move in the X-axis (left and right) direction<br>Move in the Y-axis (up and down) direction | Right drag |
| Move in the Z-axis (depth) direction (scale) | Shift + Left Drag<br>Or wheel rotation |

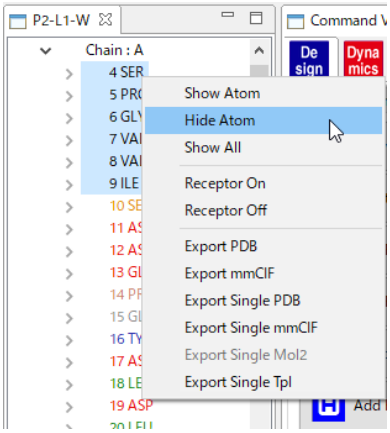
※ For MAC, left-click = click

Right-click = [Command] + Click

### 4.15.2. Selection of molecules, chains, afterts, and atoms

The mouse selects molecules, chains, rests, and atoms, but the operation is different on the 3D screen and the tree display screen.

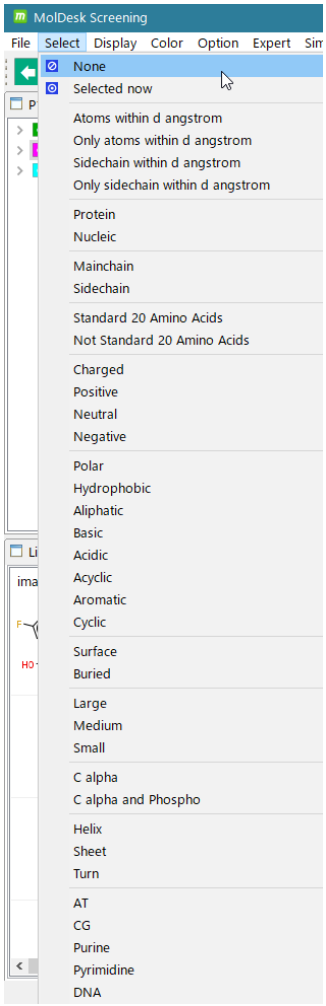
| operation | 3D screen | Tree display screen |
|---|---|---|
| Multiple selection | Ctrl + Click | Ctrl + Click |
| Continuous multiple selection | - | Shift + Click |
| Base selection | Double click | Click the base name |
| Chain selection | Triple Click | Click the chain name |
| Molecular selection | - | Click on the name of the molecule |




It is possible to display and hide multiple molecules, chains, rests, and atoms together.

On the tree view, select multiple, and then right-clickShowAtom  or Hide Atom.
Unhide it with Show All to show everything.

### 4.15.3. Select menu for selecting atoms




You can select selected atoms (clusters) and surrounding atoms together.
You can also selectatomsusing various atomic expressions.

If you make additional selections with atoms (clusters) already selected,the AND(product set)
It will be.

[None] : Deselects all current selections.
Clicking on the background of a 3D screen does the same thing.

[Selected now] : Used to check the selected status.
The currently selected atom is displayed in green.

[Atoms within d angstrom] : Select the atoms that have already been selected and the atomswithin d Å of them .

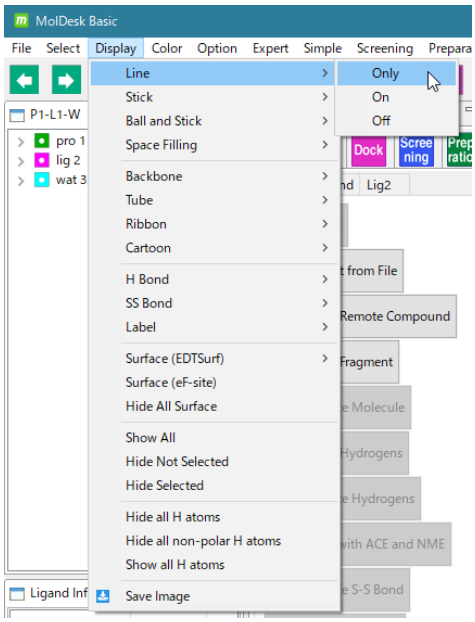
[Only atoms within d angstrom] : Excludes atoms that have already been selected and selects atomswithind Å of them.

[Sidechain within d angstrom]: Select the atoms that have already been selected and the atoms in the side chain of the protein within dÅ from them.

[Only sidechain within d angstrom]: Exclude the atoms that have already been selected, and select the atoms in the side chain of the protein within dÅ from them.

For each other atomicrepresentation (Atomexpression)
See the following sites in MolDesk:
https://www.moldesk.com/moldesk-basic-commands/#Select
The distance d between [Atom within d angstrom] and [Sidechain within d angstrom] can be changed in [Help]-[Preference]-[5.3D View] (default value is 5 Å).
See "5.32.4 3D View" for details.

### 4.15.4. Select display model




Select a molecule, chain, afterseal, or atom, [Display] If you select a model on the menu, You can change the display model to Line, Stick, etc.

The meaning of the option is as follows:
[Only] : Display in 3D with just this display model .
[On]: Apply this display model to other display models Overwrite.
[Off] : Erases this display model .

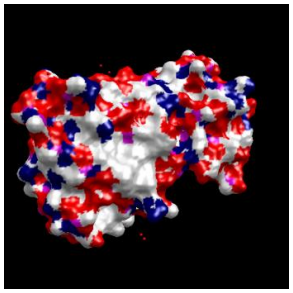
For more display models, see the following sites in MolDesk:
https://www.moldesk.com/moldesk-basic-commands/#Display

### 4.15.5. Surface (EDTSurf) display model

You can view the molecular surface model.

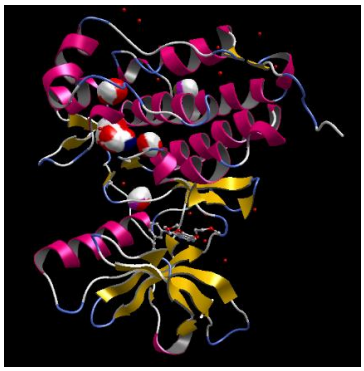
If you select a molecule and select [Display]-[Surface (EDTSurf)] – [Outer and Inner], the selected molecule will overwrite the molecular surface display model created by EDT Surf (*).

※ EDTSurf is a free software for molecular surface creation distributed at the University of Michigan.
https://zhanggroup.org//EDTSurf/

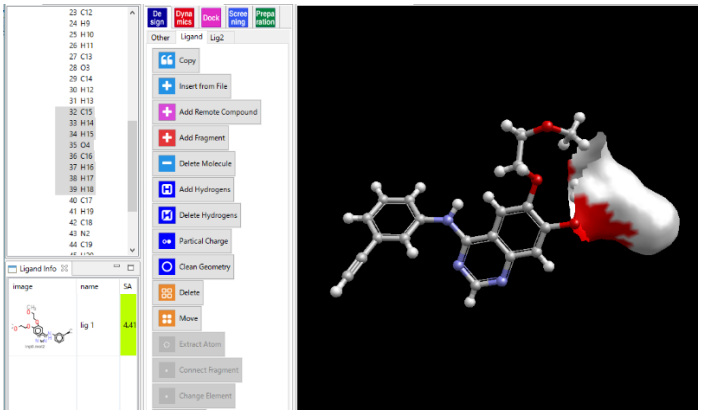


At this time, different types of atoms have different colors.

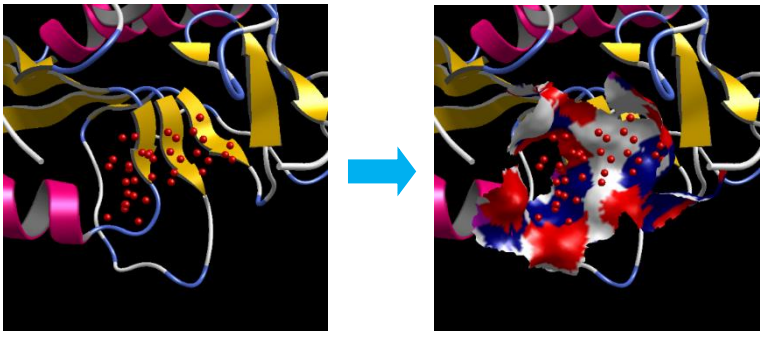
Selecting a molecule and selecting Display-Surface (EDTSurf) - Inner (Cavity) overwrites the selected molecule with Cavity's molecular surface display model created by EDT Surf. If Cavity does not exist in the selected molecule, it will not be displayed.



Selecting  an atom and selecting Display - Surface(EDTSurf)– Selected only overwrites the molecular surface display model created with EDTSurf on the selected atom.



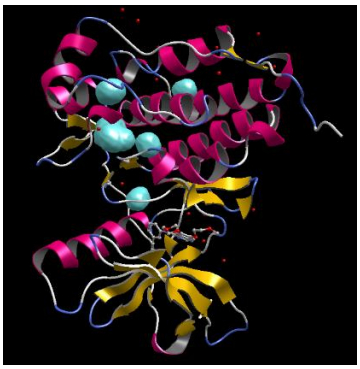

[Make Pocket] Or, [Find Pocket], after you create a pocket (red dots),
[Display] - [Surface (EDTSurf)] - [Pocket] displays the surface of the protein pocket.



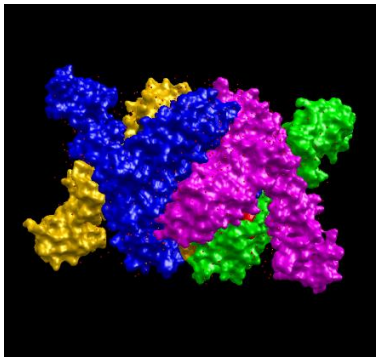
If you want to erase the molecularsurface display model, use [Display] - [Hide All Surface].

You can change the color and transparency of the molecular surface display.

The color selection screen displayed by selecting [Color] - [All Surface] - [Any] allows you to change the color of all molecular surfaces to any single color (the figure below is an example of setting to light blue).

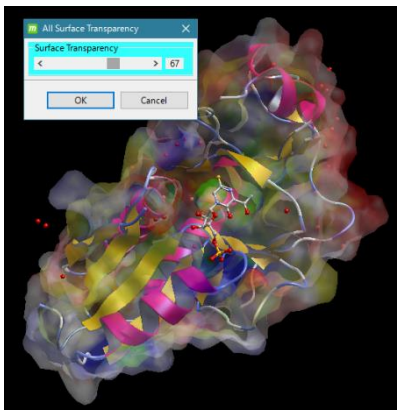


[Color] - [All Surface] - [Each Polygon] can be used to change the color of all molecular surfaces to the single color defined by default in the program for each molecule.



[Color]-[All Surface]-[Reset] restores the color of all molecular surfaces to the original color.

In [Color]-[All Surface]-[Transparency], the transparency of all molecular surfaces can be changed in real time by the slider.




Transparency can be any value between 0 (completely opaque) and 100 (fully transparent).


You can also set the transparency of all molecular surfaces by entering commands on the jV Console screen.

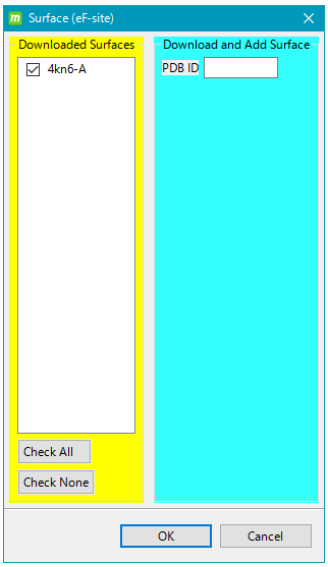
Entering the command "set transparency 0.5" in the red frame in the figure will make the molecular surface display translucent (0.5).

At this time,
the transparency can be set to any value between 0.0 (fully opaque) and 1.0 (fully transparent).

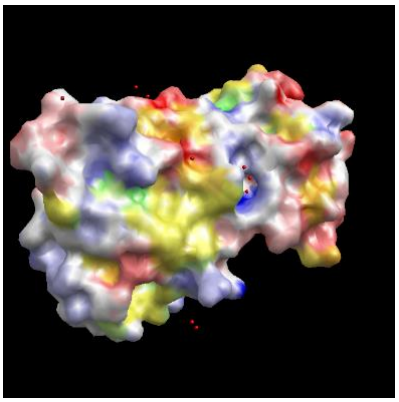
### 4.15.6. Surface (eF-site) display model

You can view the molecular surface model of PDBj's eF-site. The molecular surface of the eF-site is represented by a connolly surface and is colored by the electrostatic potential calculated by the Poisson-Boltzmann equation.

Select a moleculeand select [Display] - [Surface (eF-site)] to display the following screen:

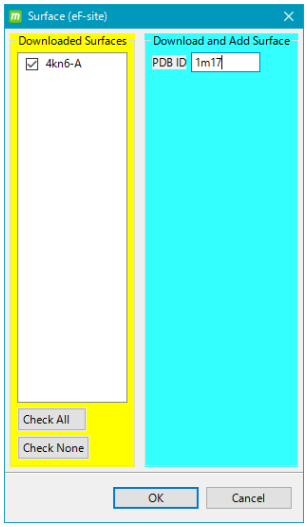



In the example on the left, the molecular surface of the 4kn6 A chain can be displayed.
While checking 4kn6-A, click [OK] to display themolecular surface of the A-chain as shown below.

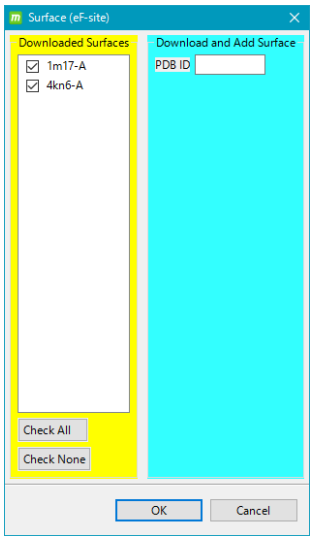


In eF-site, the value of electrostatic potential on the protein surface is blue above +0.1V, red below -0.1V, and above the two lower right color bars between +0.1 and -0.1. If there is an amino acid residue with a hydrophobic side chain near the surface, it is colored with the color of the lower part of the color bar.

Electrostatic potential
hydrophobicity


Enter the PDB ID in [PDB ID] and click [OK]. When the screen shown on the left is displayed again with [Display]-[Surface (EDTSurf)], the entered PDB ID is shown in the figure below. The molecular surface of the eF-site can be selected.
(In the example, 1m17 was entered.) )



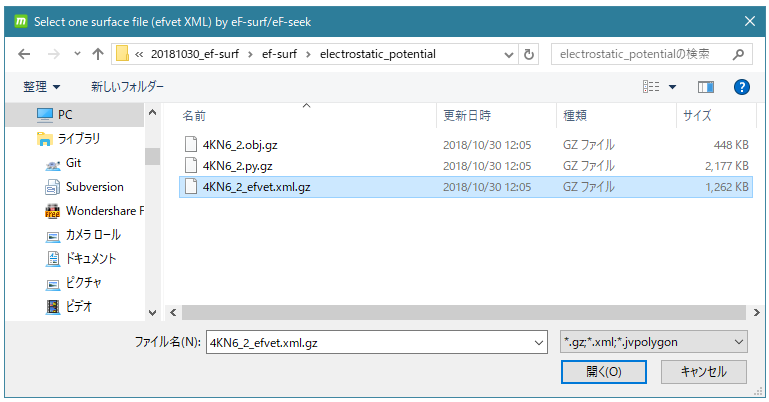

A molecular surface of 1m17-A (1m17 A chain) was added.

If you want to erase all the molecular surface display models displayed above, select [Display]-[Hide All Surface].

### 4.15.7. Surface(eF-surf / eF-seek) display model

You can view the molecular surface model created by PDBj's eF-surf or eF-seek. The molecular surface of eF-site is calculated with the coordinates registered in PDB, but with eF-surf / eF-seek, the molecular surface can be calculated with arbitrary coordinates entered by the user, so MD calculation You can display the rear surface and so on.

Select [Display]-[Surface (eF-surf / eF-seek)] to display the following input file selection screen.




Here, select the efvet xml file (* _efvet.xml.gz file above) calculated by eF-surf or eF-seek.

※ The URLs of eF-surf / eF-seek are as follows.

eF-surf : https://pdbj.org/eF-surf/

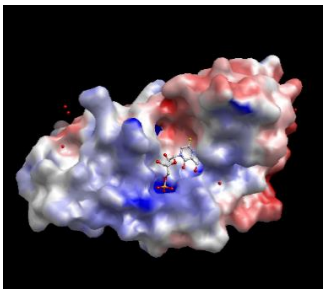
eF-seek : https://pdbj.org/eF-seek/

On this page, enter the user's numerator and follow the email response to get the calculation result data. If you download and unzip the calculation result data (* .tar.gz format),

4KN6_2_efvet.xml.gz

(In this example, the PDB file with PDB ID = 4KN6 is used as the input file) There is a file in his efvet xml format with the filename.

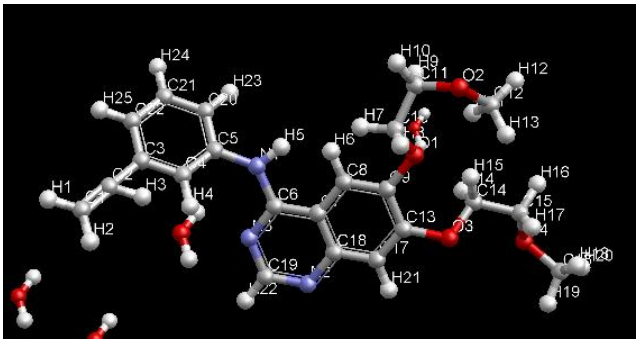
[Open] to see the surface as follows:



To properly overlap the source PDB system with the computed surface, display the PDB in eF-surf / eF-seek in MolDesk, and then enter the surface with this function. (You can do it internally when you create a surface in MolDesk,*. You can also enter and display the jvpolygon file with this function. )

### 4.15.8. Label display model

Select [Display]-[Label]-[*** On] to display the selected atom as a label.



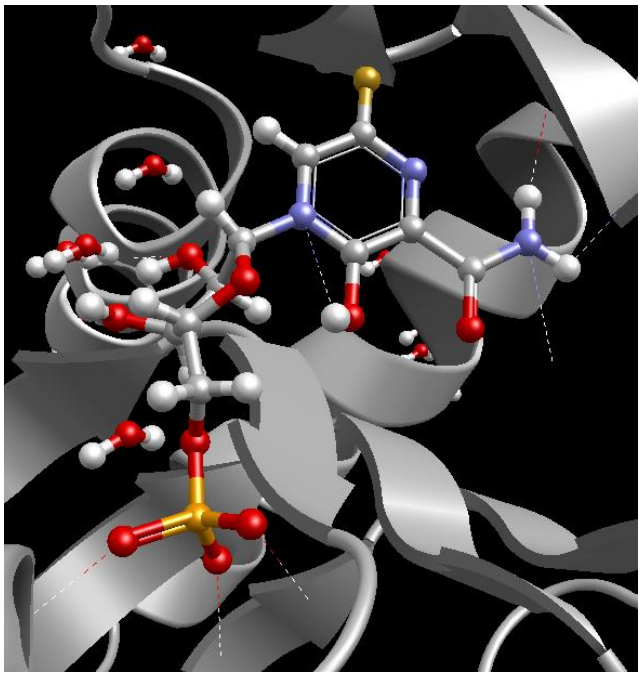

Select from the following nine display strings when displaying labels:

| item | explanation |
|---|---|
| [Atom name] | Atomic name |
| [Atom id] | Atomic ID |
| [Atom name] [Atom id] | Atomic Name + Atomic ID |
| [Residue name] [Atom name] | Remaining name + atomic name |
| [Residue name] [Atom name : Atom id] | Remaining name + atomic name: Atomic ID |
| [Residue name : Residue id] [Atom name : Atom id] | Remaining name : Base number + Atomic name : Atomic ID |
| [Residue name] | Base name (protein only) |
| [Residue id] | Base number (protein only) |
| [Residue name] [Residue id] | Base name + base number (protein only) |

### 4.15.9. Hydrogen bond display model

Select [Display]-[H Bond]-[On] to display all hydrogen bonds related to the selected atom (group), whether intramolecular or intermolecular.

**Hydrogen atoms must be added in advance with the [Add Hydrogens] command.**



This is an example of selecting a compound and displaying all hydrogen bonds related to the compound.

To increase the thickness of the hydrogen bond, select the compound and display
ghbond 0.2
on the jV Console screen.
Enter and execute. (0.2 represents thickness).

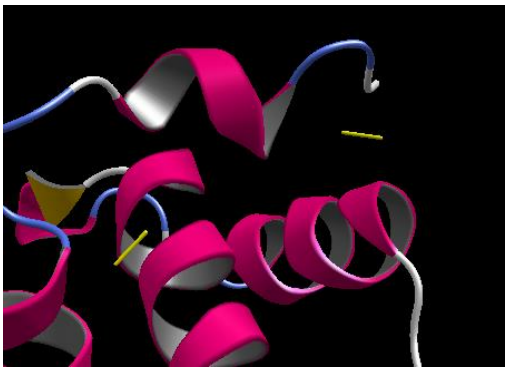
To change the color of the hydrogen bond, leave the compound selected and select [Color]-[H Bond]-[Any] and select any color.

Use [Help]-[Preference]-[4. H Bond] to set the hydrogen bond display.
For details, refer to "5.32.3 H Bond".

### 4.15.10. SS join display model

Select [Display]-[SS Bond]-[On] to display all SS bonds related to the selected atom (group) with a thick yellow bar. When displaying SS bonds, the atom (group) to select is generally the entire protein.

**All SS bonds in the initial structure have been deleted, so if you want to add SS bonds, you need to execute [Create S-S Bond] in advance to generate SS bonds.**



Select Protein
An example of displaying the SS binding of a protein.

To increase the thickness of the SS binding, use the jV Console screen with the protein selected.
ssbond 0.2
And so on. (0.2 represents thickness.)

To change the color of the SS bond, with the protein still selected, select [Color]-[SS Bond]-[Any] and select any color.

### 4.15.11. Hiding non-polar hydrogen

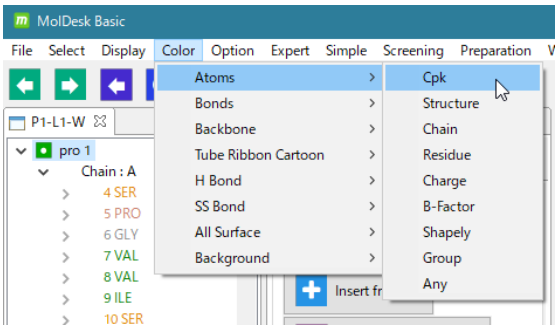
Select [Display] - [Hide all non-polar H atoms] to hide all non-polar hydrogen atoms in the system.

### 4.15.12. Hydrogen display/ hiding

Select [Display] - [Hide all H atoms] to hide all hydrogen atoms in the system.
Select [Display] - [Show all H atoms] to show all (hidden) hydrogen atoms in the system.

### 4.15.13. How to color

You can change the color of molecules, chains, rests, and atoms.
Select a molecule, chain, base, or atom,andselect a color in the [Color] menu to change the color.

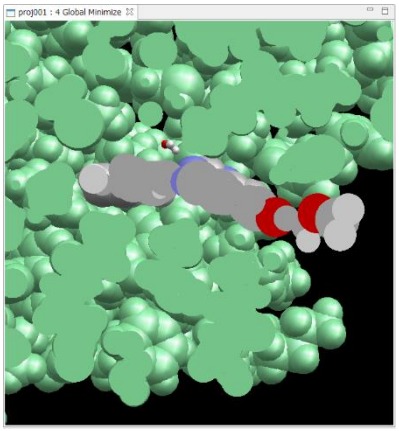



You can also change the color and transparency of all molecular surfaces at the same time with [Color]-[All Surface]. See the Surface Display Model section for more information.

For details on each item in the [Color] menu, refer to the following site of MolDesk.
https://www.moldesk.com/moldesk-basic-commands/#Color

### 4.15.14. How to clip

You can display (clip) the cutting plane of the molecule.



To enter clip mode


Click the button or

[Option] - [Z clip] Run the .

You can use your mouse to control clip mode.

| operate | explanation |
|---|---|
| Ctrl + left drag, or<br>Alt + Left Drag | Move the image cutting plane toward the Z-axis (depth) direction |
| Shift + Left Drag , or<br>Mouse wheel rotation | Move the molecule in the Z-axis (depth) direction while keeping the image cutting plane fixed |
| Ctrl + Shift + Left Drag | Zoom in and out while still visible |

To remove clip mode, click the  button again, or run [Option] - [Z clip].

#### 4.15.15. UNDO for the Run command

The executed command can be re-executed with  [UNDO] and  [REDO].

#### 4.15.16. UNDO mouse selection

You can undo the selection with the mouse with  .

#### 4.15.17. Deselect

Press  to deselect all mouse selections.

#### 4.15.18. Confirm selection

Displays the currently selected atom with  in 3D.

#### 4.15.19. Center Ring

 Or center in the following menu:

[Option] - [Center]
[Option] - [Orient]
[Option] - [Reset]

[Option] For more information about each item inthe menu, see the following sites in MolDesk:
https://www.moldesk.com/moldesk-basic-commands/#Option

#### 4.15.20. View axis

 Or use [Option] - [Axis] to display the coordinate axes. Red, Green, and Blue represent the x, y, and z axes, respectively.

### 4.15.21. Fog View

 Or [Option] - [Fog] allowsyou tofog in the depth direction of a 3D screen and blend into the background. The default is OFF.

### 4.15.22. Projection mode

 Or you can switch the projection mode of the 3D screen to perspective or parallel by selecting [Option] - [Projection]. The default value is perspective.

### 4.15.23. Stereo display

 Or use [Option]-[Stereo] to switch the display to color-coded (anaglyph) stereoscopic display. Stereoscopic viewing is possible with "red-blue glasses" that use red cellophane for the left eye and cyan (light blue) cellophane for the right eye.

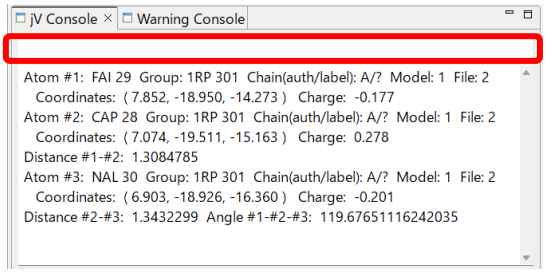
### 4.15.24. Save 3D view

 Or [Display] - [Save Image] to save all current display settings.

Refer to "5.12.1 [File] - [Export Image]" for the procedure to output the 3D screen image to a png image file.

### 4.15.25. Run the jV command

MolDesk uses jV of PDBj as a 3D display program. In MolDesk, you can execute almost all jV commands in the red boxed area of the jV Console screen.
For the jV command list, refer to the following jV site.
https://pdbj.org/jv/manual/index_ja.html



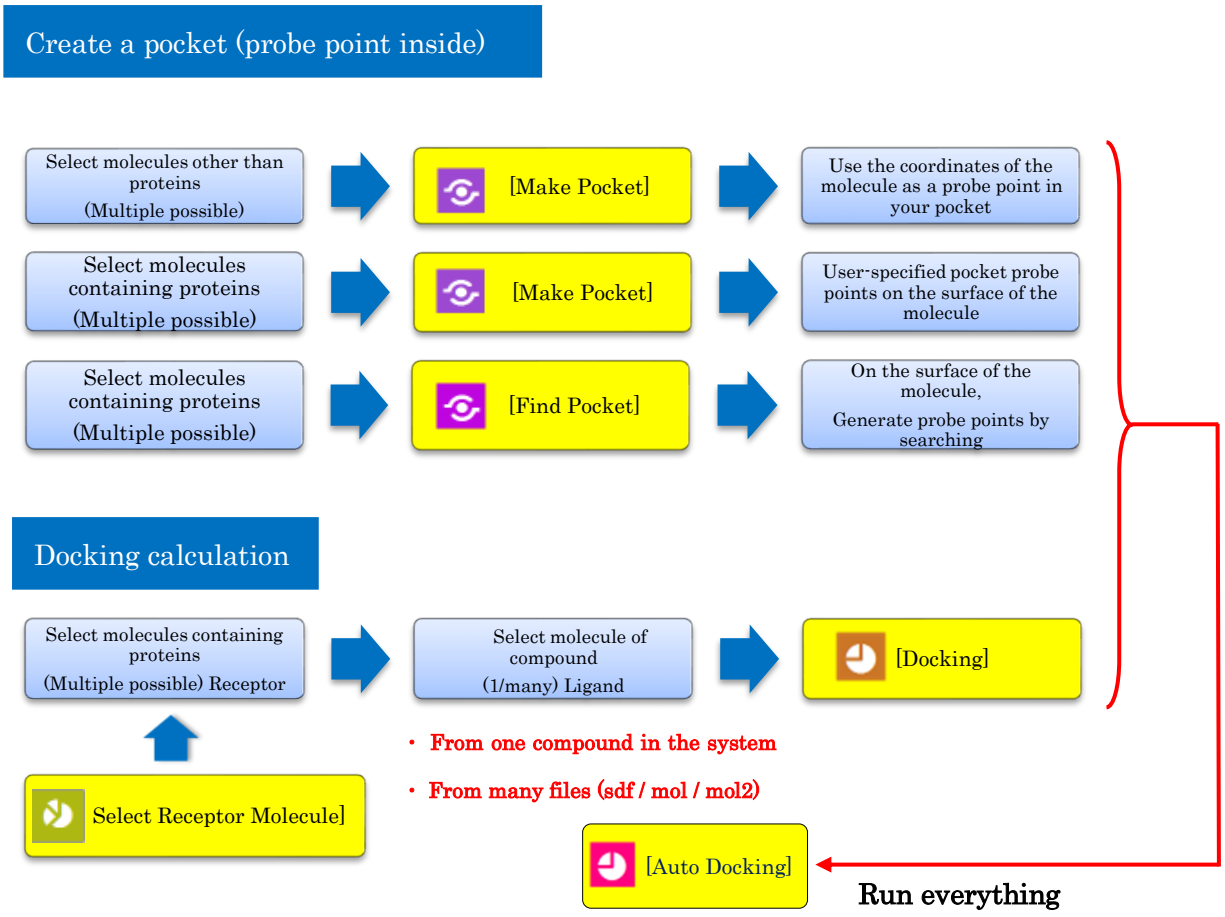

The jV Console screen displays information about the atom you clicked on, including the atom name, the name of the residue to which it belongs, its coordinate value, and its charge.Clicking an atom twice displays the distance between the two atoms, and clicking three times consecutively displays the angle between the three atoms.

## 4.16. Docking calculations in general

Docking calculation is a calculation to search for multiple candidate structures to which a receptor and a ligand are bound by specifying a molecule of a receptor corresponding to a keyhole and a molecule of a ligand corresponding to a key.

When searching for a candidate structure, the structure on the receptor side is fixed, and the dihedral angle of the single bond of the straight part excluding the ring of the molecule is rotated on the ligand side to generate a large number of structures.

The steps for docking calculations in MolDesk are as follows:



※ In addition to proteins, docking to nucleic acid molecules is possible. You can specify either a protein or a nucleic acid molecule as a receptor.

※ [Preference] – [3. Docking], you can select the docking calculation program from sievgene_dual or sievgene2. sievgene2 is a docking program specialized for RNA docking. sievgene2 is generally used for RNA docking. program, generally sievgene_dual (default setting) is used.

A pocket (probe point) must be generated before docking calculations can be performed. There are the following methods for pocket generation:

**How pockets are generated:**

1. How to make the coordinates of the molecule the probe point of the pocket itself.
   It is used when the correct structure of the combined state is known. Let the ligand molecule be the probe point.
   Select molecules other than proteins or nucleic acid molecules. Multiple selections are possible.

2. How to create pocket probe points on the surface of a molecule.
   Select the molecule that contains the protein or nucleic acid molecule. Multiple selections are possible. At this time, the probe points of the pocket are generated in the vacant space, so select the pocket space by excluding the molecules that fill the pocket.
   You can specify where the user will generate the probe point for the pocket, or Find Pocket will automatically search for it.

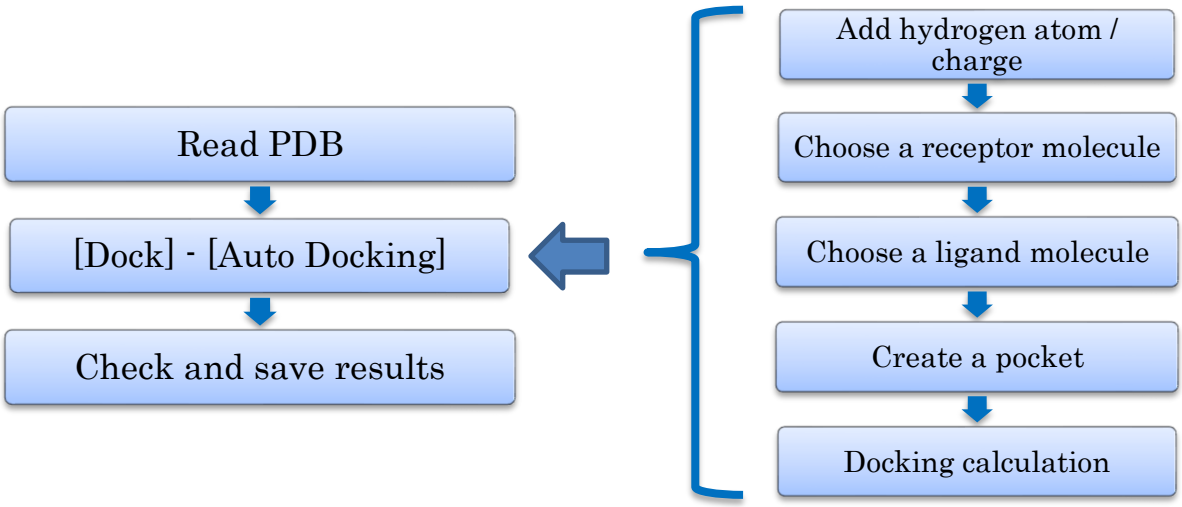
After the pocket formation is complete, specify the receptor and ligand molecules to be used in the docking calculation.
Multiple receptor molecules can be selected, including proteins or nucleic acid molecules. The molecule of the ligand is one compound or glycan.
When selecting a receptor molecule, make sure there is space in the pocket to which the ligand binds.

**MolDesk allows you to specify and calculate exactly the receptor molecule group (must contain at least one protein or nucleic acid molecule) and the ligand molecule (one compound or glycan).**

## 4.17. Docking Calculation1 (Fully Automatic)

Here is an example of performing the simplest docking calculation using fully automatic docking.

The procedure is as follows.




### 4.17.1. Load mmCIF/PDB files over the Internet

Refer to "5.4.4 [File]-[Open Remote mmCIF / PDB]" and read the PDB ID "1m17" from the Internet as test data.
This protein is the EGFR tyrosine kinase domain, which contains the molecule of the anticancer drug Erlotinib.
It is added.

### 4.17.2. Fully automatic docking

Select 

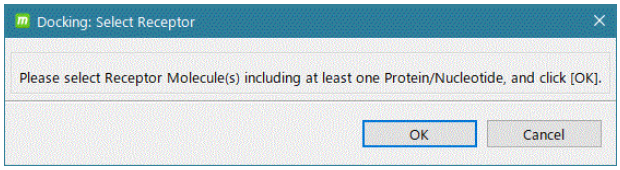
[Dock] -  [Auto Docking] .

Initially, the missing hydrogen atoms will be automatically added to all molecules, and MOPAC7 AM1 will add charge to all compounds or glycans.
For compounds or glycans that cannot be calculated by MOPAC7 AM1, Gasteiger will add the charge.

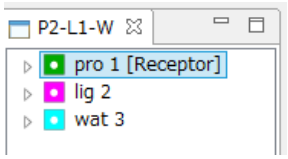
For molecules other than compounds or glycans, charge is added based on the force field selected in [Help]-[Preference]-[Molecule]-[tplgeneX].

### 4.17.3. Choosing receptor and regand molecules

When charging is complete, a message dialog will appear prompting you to select a receptor.



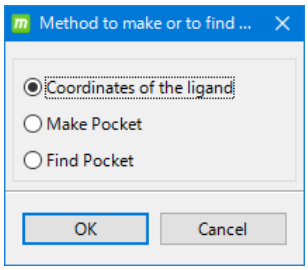

In this example, select pro1 on the tree view screen and click OK.




Since pro1 has been recognized as a receptor, the notation of pro1 changes to pro1 [Receptor].

The receptor molecule must contain at least one protein or nucleic acid molecule. It may contain compounds, glycans or metals. However, make sure that there is enough space in the pocket where the ligand binds.

### 4.17.4. Create a pocket




After specifying the receptor, a dialog for selecting the pocket generation method is displayed.

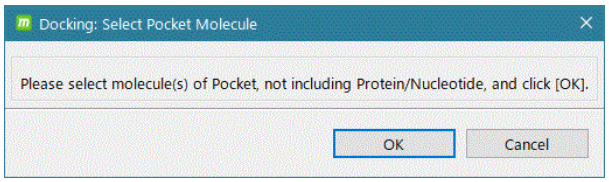
In this example, we know the correct structure, so select [Coordinates of the Ligand] and make the coordinates of the selected ligand itself the probe point of the pocket.

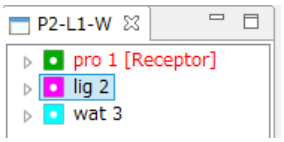
The items in the dialog for selecting a pocket generation method are described below.

| item | explanation |
|---|---|
| [Coordinates of the ligand] | The coordinates of the selected molecule are the probe points of the pocket.<br>Multiple molecules other than proteins or nucleic acid molecules can be selected and made into probe points at once. |

| | |
|---|---|
| [Make Pocket] | Place the pocket sphere on the surface of the selected receptor and generate a pocket probe point inside the sphere. |
| [Find Pocket] | Pocket search is performed on the surface of the selected receptor to automatically generate multiple probe points in order of score. |

A dialog appears to select the molecules (other than proteins or nucleic acid molecules) to be probe points in the pocket.



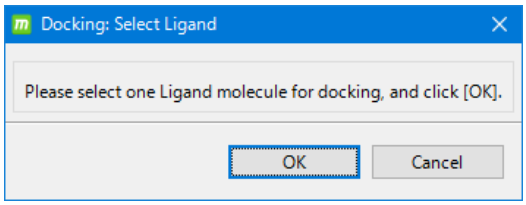




In this example, on the tree view screen, select lig2 and click OK.

At this time, the atoms of the regand molecules become red circles.
This indicates that all atoms of the regand molecule have become probe points in the pocket.

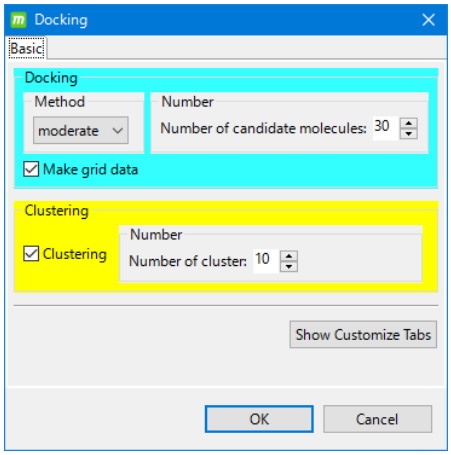
In addition, point4 is displayed on the tree display screen, confirming that the probe point of the pocket has been added to the system.

A message dialog is displayed prompting you to select a ligand.




In this example, select lig2 on the tree display screen,and then click OK.

For the ligand, it is possible to specify a molecule different from the molecule used as the probe point of the pocket.




The docking calculation condition setting dialog is displayed.

In this example, leave the default conditions and click OK.

Click [Show Customize Tabs] to set detailed parameters for docking calculation. For details, refer to "5.18.6 Advanced Docking Calculation Settings".

The items in the docking calculation condition setting dialog are described below.

| item | | explanation |
|---|---|---|
| Docking | Method | fast fast and low accuracy<br>moderate medium accuracy at modeate medium speed (default)<br>precise high accuracy at low speed (Molsite) |
| | Number of candidate molecules | Number of outputs of candidate molecular structures |
| | Make grid data | Calculate grid<br>Required for the first calculation, but with the same receptor name<br>If you use the pocket repeatedly, you can omit it. |
| Clustering | Clustering | Structural clustering |
| | Number of cluster | Make the regand atom the probe point of the pocket. |
| Show Customize Tabs | | Displays a tab for setting detailed parameters.<br>※ Please note that when this tab is displayed, some items on the [Basic] tab cannot be changed (you need to cancel and re-execute to change). |

### 4.17.5. Review results

When the docking calculation is completed, the Docking Info screen will list the compounds used in the docking calculation (lig3) and the 10 molecular structures predicted by the docking calculation (lig5 to lig14) in descending order of score.

The values of the molecular structure attributes are as follows.

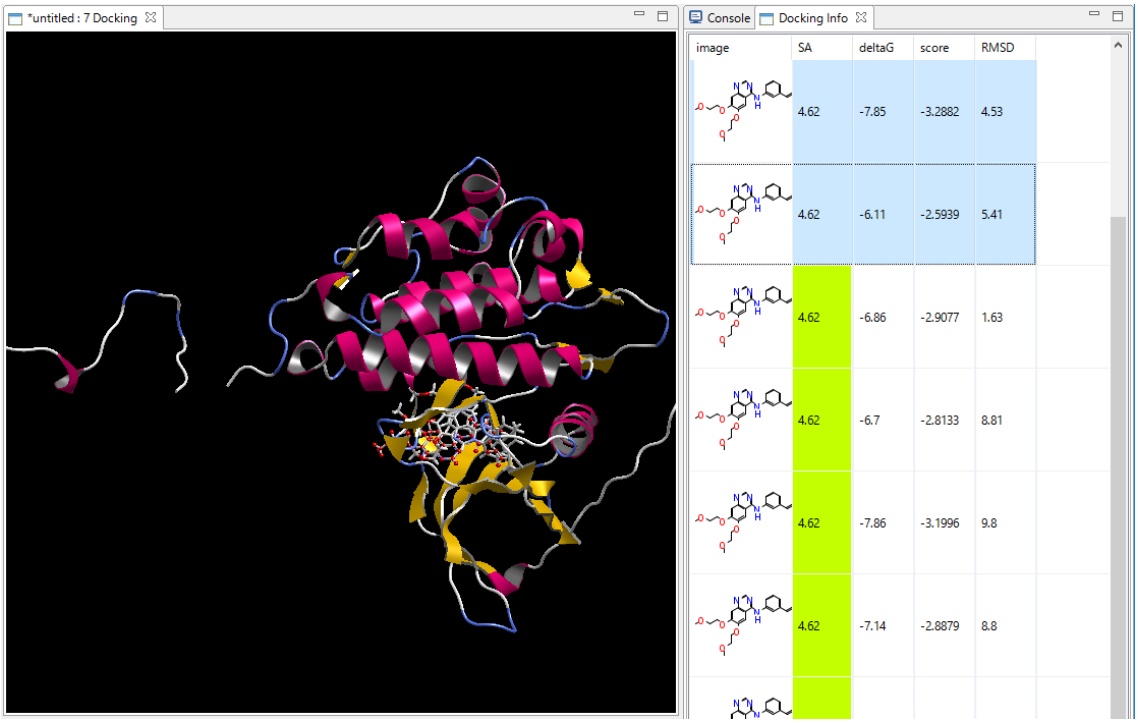
ΔG value (deltaG, free energy)

Score (score, docking score)

RMSD (value for ligand used in docking calculation input)


Click a molecule on the Docking Info screen and click the ↑ ↓ keys to display the selected molecules one by one on the 3D screen.

On the Docking Info screen, you can select multiple molecules with Ctrl + click.



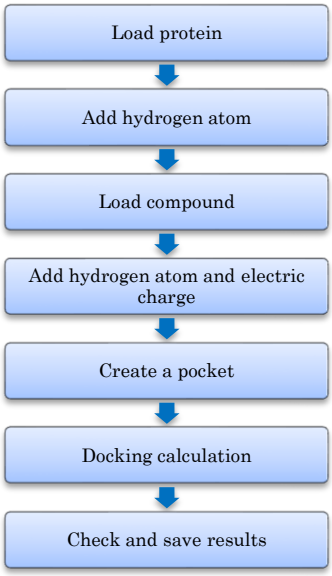

### 4.17.6. Save results

Refer to "5.6 Saving the project" and save the project with a name of your choice.

## 4.18. Docking  calculation2 (one regand)

The following is an example of executing the docking calculation when one ligand is specified.

The procedure is as follows.



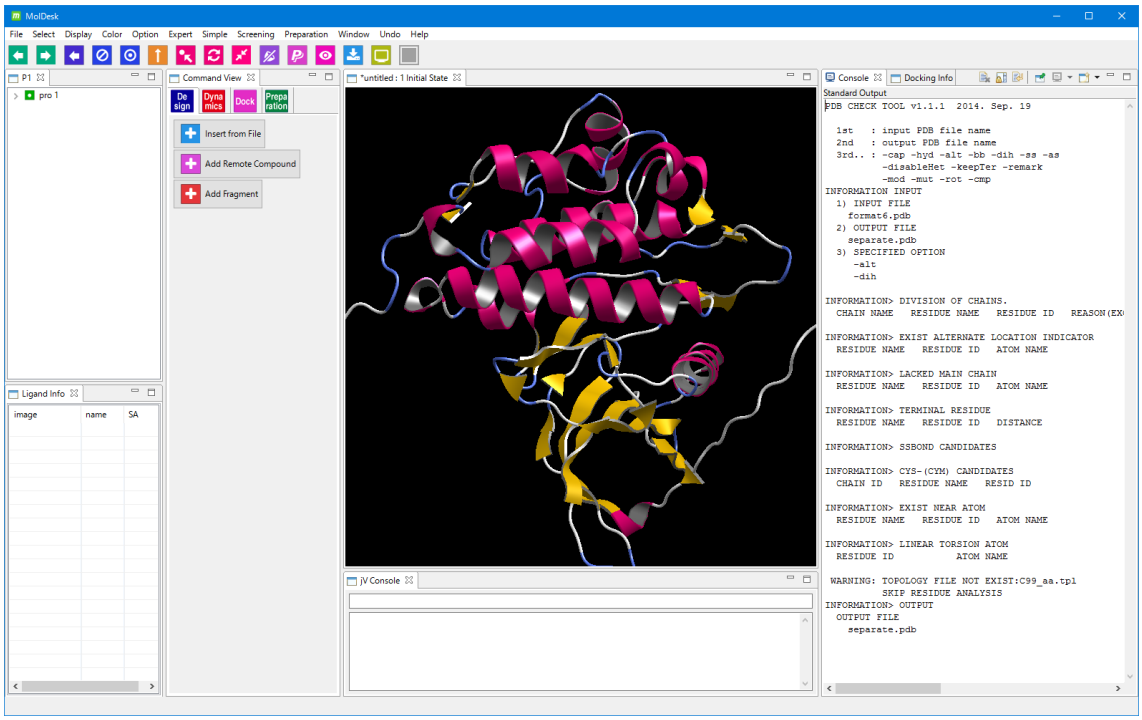

### 4.18.1. Load protein  mmCIF/PDB  file

As test data, download the mmCIF file and PDB file with PDB ID 1m17 and load the mmCIF file. For a description of 1m17, refer to "5.17.1 Reading mmCIF / mmCIF / PDB files via the Internet".

There is a 1m17 PDB file in the MolDesk Basic folder created on the desktop when MolDesk was installed.

Refer to "5.4.2 [File]-[Open Molecular File]" and find it in the MolDesk Basic folder. Read the following file.

MolDesk Basic-> sample-> pdb-> 1m17_protein.pdb




Select pro1 and then click [Add Hydrogens] for the entire protein

Adds missing hydrogen atoms and charges.

**The atom selection status and the buttons on the command button screen are linked.**

The buttons that can be executed for the atoms selected in the tree display screen or 3D screen are displayed on the command button screen.

### 4.18.2. Load the mol2 file for the compound

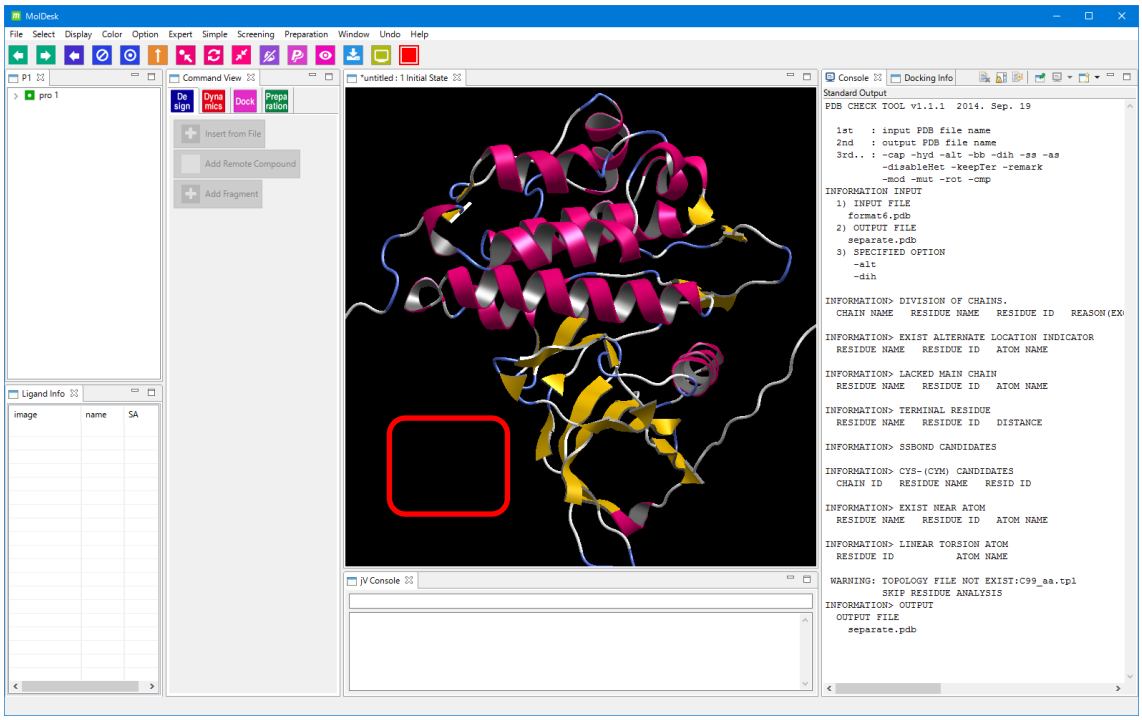
Under [Insert from File], enter the following file.

Load MolDesk Basic-> sample-> mol2-> ERLOTINIB.mol2.

This compound is a molecule of the anticancer drug Erlotinib.

In [Position Select], select [mouse] and click near the red frame in the figure below on the 3D screen.

The molecule is displayed at the click point, and the compound is added with on the tree display screen.




For the explanation of [Position Select], refer to "5.4.1 [File]-[New Project]".

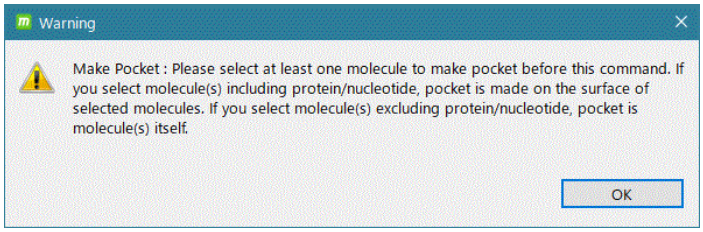
In the tree view or 3D view, click on lig2 to select it, then click on [Add Hydrogens] to add the missing hydrogen atoms to the entire compound in the dissociative state with the -p option. This will add a Gasteiger charge to the compound.

- If the input file is a mol2 file, if the mol2 file contains charge information, that information will be read, but if a hydrogen atom is added, the charge will be regenerated, so please be careful.

### 4.18.3. Pocket creation

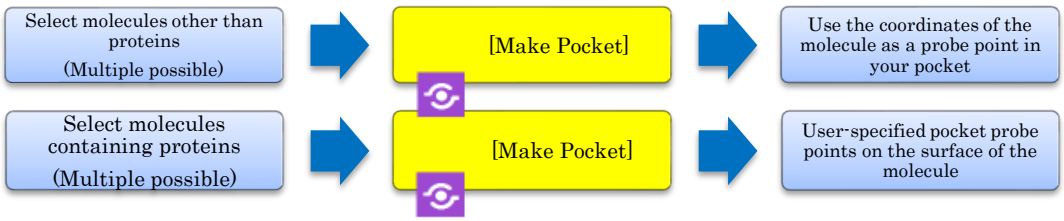
Click Dock [Dock] - [Make Pocket].

Since the molecule has not been selected, the following warning dialog is displayed.




Click OK to dismiss the warning dialog, then select the molecule.

Depending on the type of molecule selected, the process branches in the following two ways.

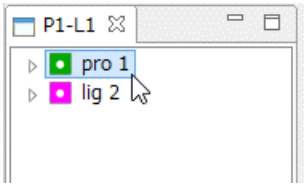



**If the coordinates of the molecule itself are the probe points of the pocket,**

Select molecules that do not contain proteins or nucleic acid molecules. Multiple selections are possible.

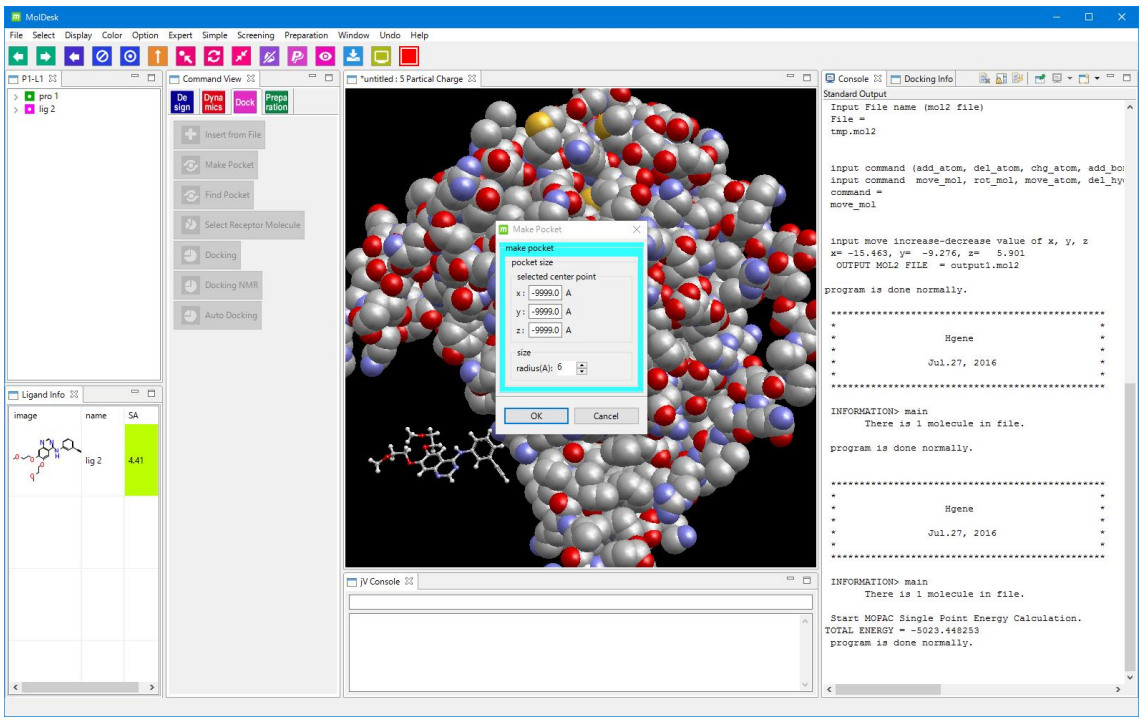
**If you want to create pocket probe points on the surface of a specified molecule,**

Select the molecule containing the protein or nucleic acid molecule (multiple selections are possible). In this case, choose to leave space in your pocket.

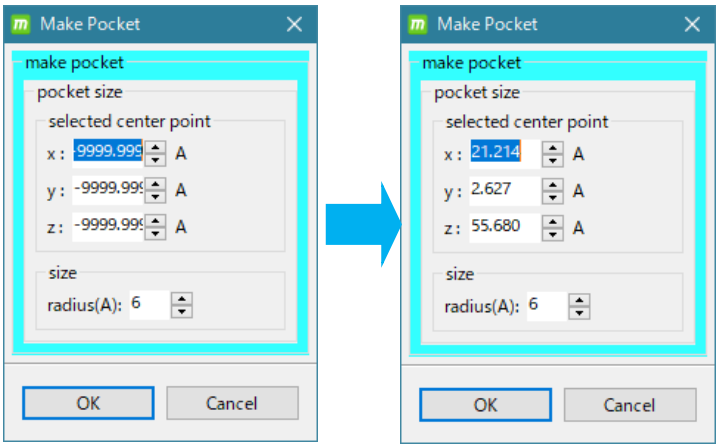



In this example, we will create a pocket on the surface of the molecule, so select the protein pro1 on the tree view screen or 3D screen and click [Make Pocket].

The protein becomes a space fill display model. The pocket selection dialog is displayed.



Enter the center coordinates and radius of the pocket in the pocket selection dialog.




Default
Select 149LEU HD23 atom as center point

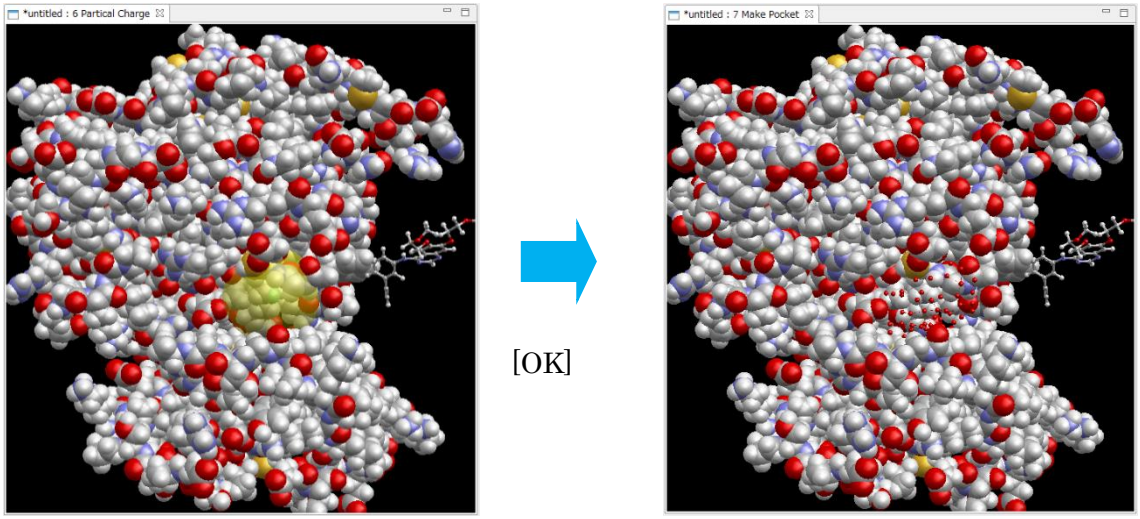
Specify the center coordinates by either of the following methods.

**Enter the numerical value (coordinate value) directly**

**Select atoms on the tree display screen or 3D screen (multiple selections are possible)**

If multiple atoms are selected, their average coordinates will be the center coordinates of the pocket.

The pocket radius can be set in the radius of the dialog.
The following is an example of selecting a 149LEU HD23 atom as the center point and setting the radius to 6 Å.

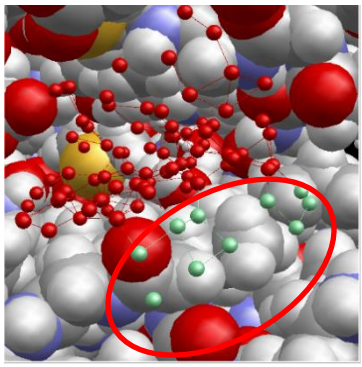


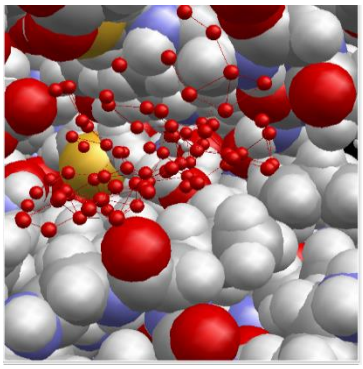

The selected pocket is displayed as a yellow translucent sphere.

Inside the sphere, pocket probe points are generated with red dots.

### 4.18.4. Delete probe points

If there are extra probe points that are out of your pocket, you can remove them by following the steps below.



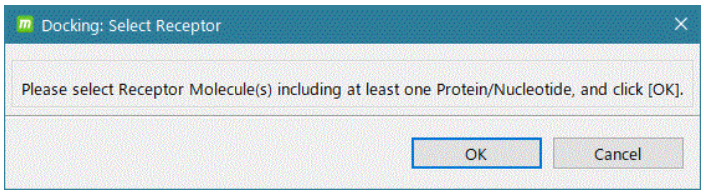
Select extra probe points on the 3D screen (Select multiple by Ctrl + click)

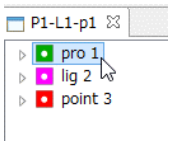
The selected probe point is deleted

### 4.18.5. Docking calculations

Click [Docking].

A message dialog is displayed prompting you to select a receptor.

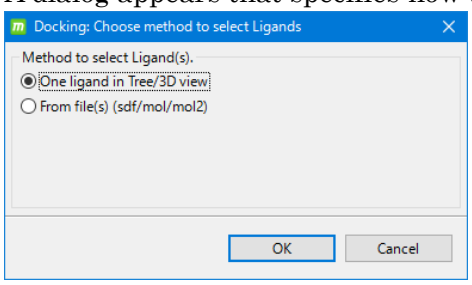


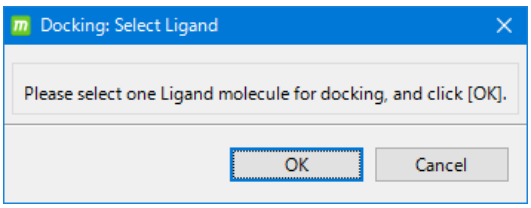

In this example, select pro1 and click OK.

The receptor molecule must contain at least one protein or nucleic acid molecule. May contain compounds, glycans and metals

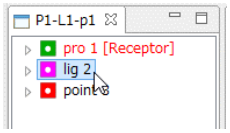
A dialog appears that specifies how to select the regand.




In this example, leave the default One Ligand in Tree / 3D view and click OK.

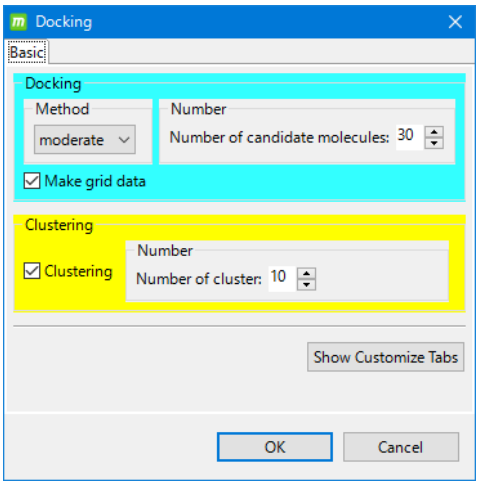



A message dialog is displayed prompting you to select a ligand.
Select one compound or glycan to use as a ligand from the tree display screen or 3D screen.




In this example, select lig 2, and then click OK.

A dialog appears to enter docking calculation conditions.



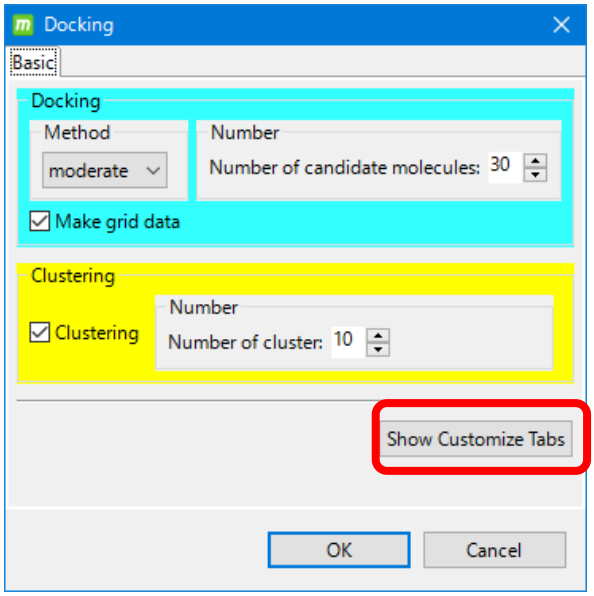

Enter the accuracy of the docking calculation, the presence or absence of structural clustering, and so on.

In this example, it is calculated by default. Click [OK] as it is.

For the meaning of the setting items, refer to "5.17.4 Creating a pocket".

Refer to "5.17.5 Checking Results" and "5.17.6 Saving Results" to check and save the docking results.

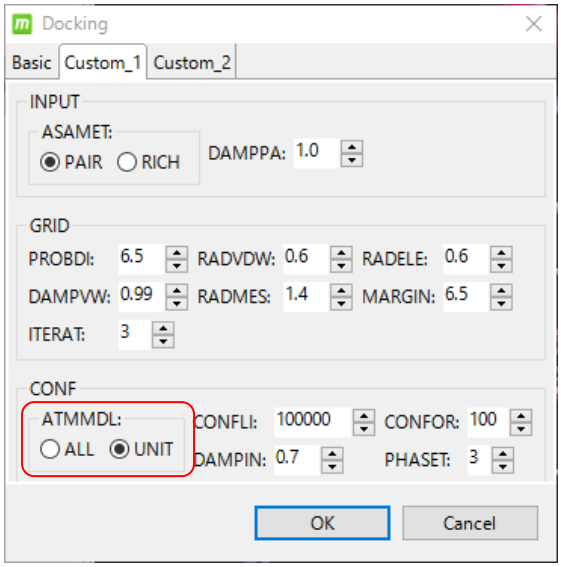
### 4.18.6. Docking Calculation Advanced Settings

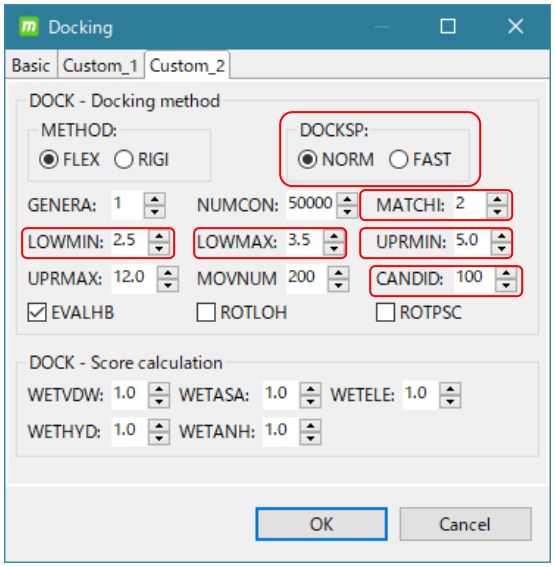



Click the Show Customize Tabs button to display the advanced docking calculation tabs.

The default settings on the Advanced tab depend on the value of Docking-Method.

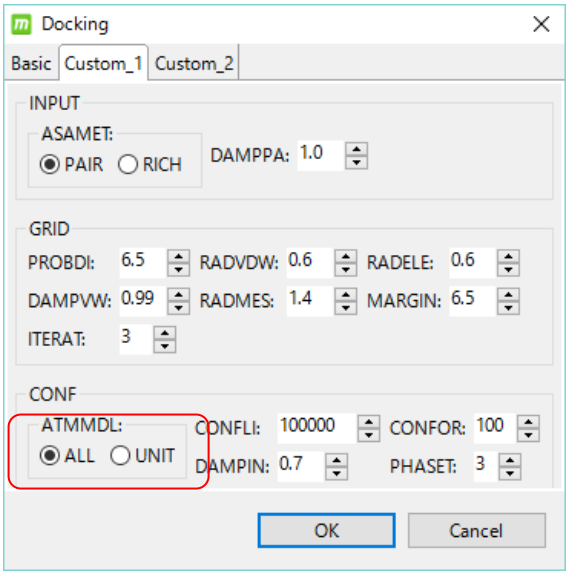
[Docking]-When [Method] is [fast]

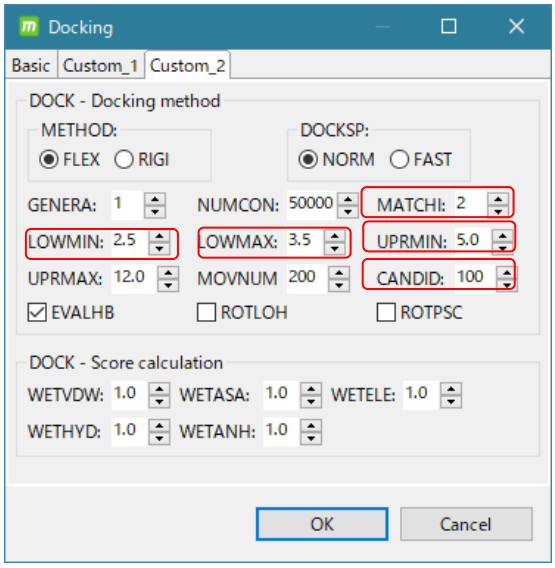



ATMMDL=UNIT、DOCKSP=FAST、MATCH=3、LOWMIN=2. 5、LOWMAX=3. 5、UPRMIN=5.0、CANDID=10

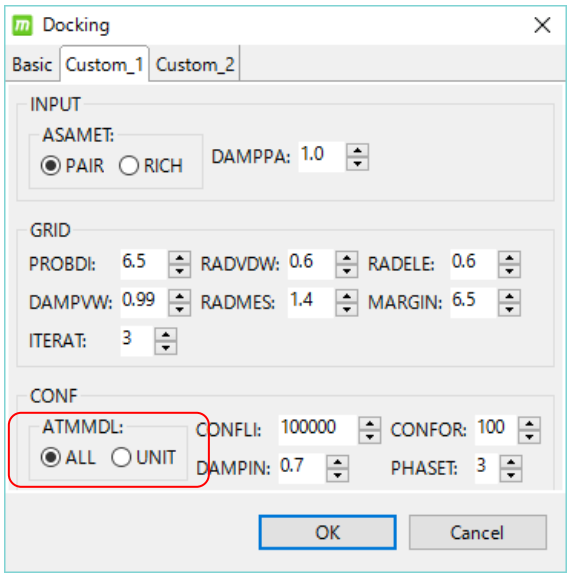
[Docking]-When [Method] is [moderate]

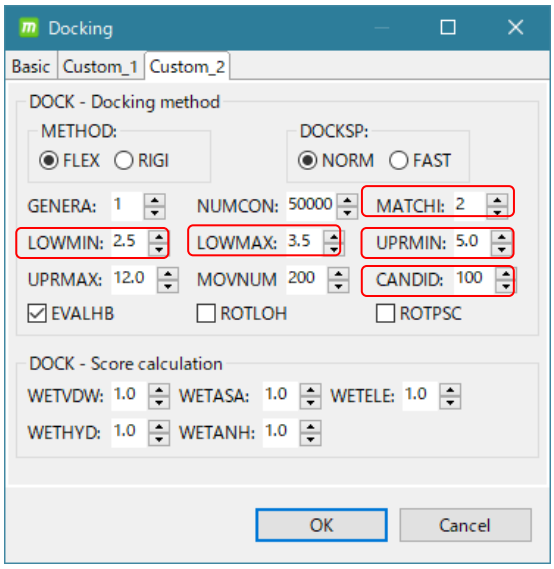



ATMMDL=ALL、DOCKSP=NORM、MATCH=2、LOWMIN=2. 5、LOWMAX=3. 5、UPRMIN=5.0、CANDID=100

[Docking] - [Method] if is[precise]




ATMMDL=ALL、DOCKSP=NORM、MATCH=0、LOWMIN=1.0、LOWMAX=1.2、UPRMIN=3.0、CANDID=100

The description of the items on the Advanced tab is as follows. See the myPresto documentation for more details.

[ INPUT ]

| item | explanation |
|---|---|
| ASAMET | ASA calculation method PAIR / RICH |
| DAMPPA | Coefficient of atomic radius |

[ GRID ] Grid potential generation

| item | explanation |
|---|---|
| PROBDI | Distance upper limit of pocket point and receptor atom |
| MARGIN | GridPotential range margin |
| ITERAT | Smoothing repetitions |
| RADVDW | vdW boundary distance correction |
| RADELE | Electrostatic boundary distance correction |
| RADMES | Probe radius for mesh point generation |
| DAMPVW | Coefficient of vdW radius |

[ CONF ] Regand comformer generation

| item | explanation |
|---|---|
| ATMMDL | Specify atomic model ALL / UNIT |
| CONFLI | Maximum number of attempts for consumer generation |
| CONFOR | Number of seats to generate |
| DAMPIN | Damping factor of the atomic vdW distance of the seat |
| PHASET | Suggestions for torsion rotations |

[ DOCK - Docking method ] Global Search

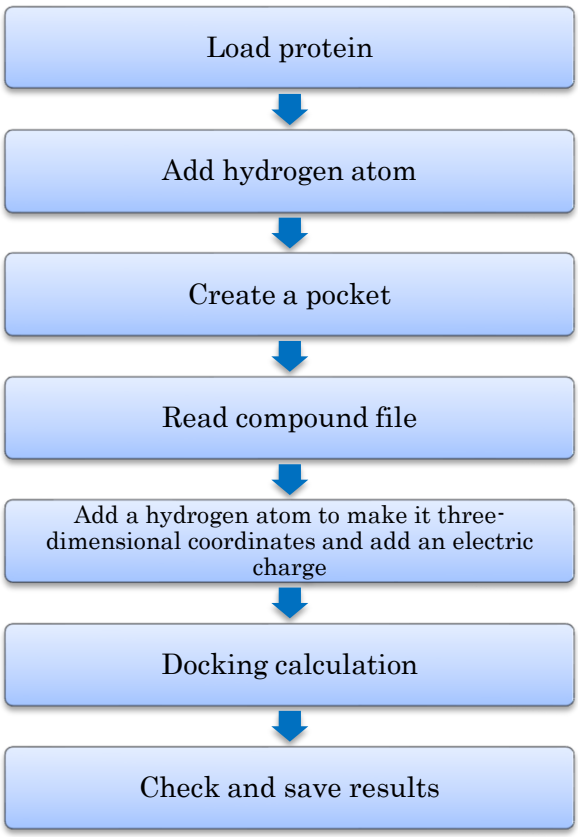
| item | explanation |
|---|---|
| METHOD | Docking Method FLEX / RIGID |
| DOCKSP | Switching docked atoms NORM / FAST |
| CANDID | Number of local searches |
| GENERA | Number of refinees |
| NUMCON | Top score to display |
| MATCHI | Atomic type fit of the bonded surface |
| LOWMIN | Lower minimum value of the edge of the join face |
| LOWMAX | Minimum lower limit of the edge of the join face |
| UPRMIN | Maximum value of the edge of the join face |
| UPRMAX | Maximum edge limit for join faces |
| EVALHB | Evaluation of hydrogen bonds between proteins and rigands considering anthrant sex YES/NO |
| ROTLOH | Rotation of the regand -OH set YES / NO |
| ROTPSC | Hydrogen-binding protein side chain rotation YES / NO |
| MOVNUM | Number of coordinates to be snuthed |

[ DOCK - Score calculation ] Score calculation

| item | explanation |
|---|---|
| WETVDW | Coefficient of vdW during score calculation |
| WETASA | Asa factor during score calculation |
| WETELE | Coefficient of electrostatic power during score calculation |
| WETHYD | Coefficient of hydrogen bond during score calculation |
| WETANH | Coefficient of hydrogen bond between protein and regand considering anthrant sex |

## 4.19. Docking calculation 3 (multiple regands)

Provides an example of performing a docking calculation when multiple regands are specified from a file.




- Many files (sdf / mol / mol2) can be read at once

- Automatically calculated
- It is possible to select not to make it three-dimensional.

### 4.19.1. Read the protein mmCIF / PDB file

Read the protein with PDB ID 1m17 from the file as test data.
Read the PDB file in the same procedure as "5.18.1 Reading the mmCIF / PDB file of protein".

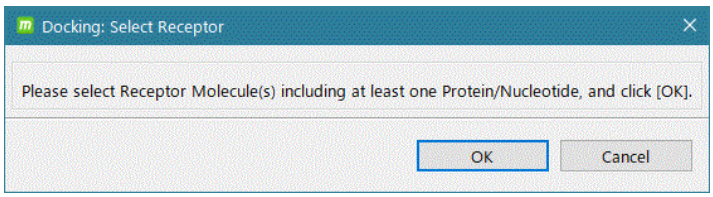
### 4.19.2. Create pockets

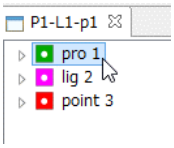
Create a pocket using the same procedure as in "5.18.3 Creating a pocket".

### 4.19.3. Three-dimensionalization of input molecules

Click Dock [Dock] - [Docking].

A message dialog prompts you to select a receptor.

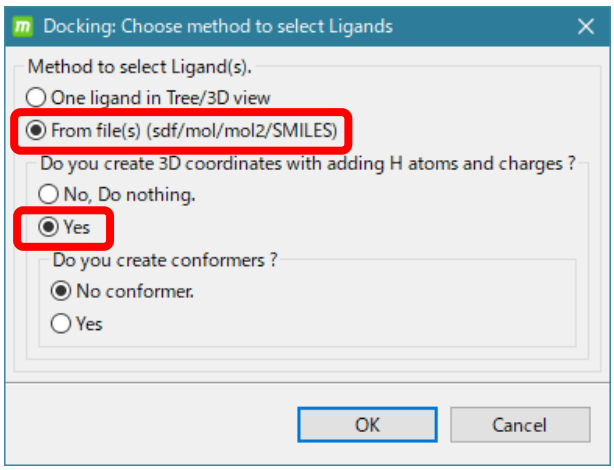



In this example, select pro1 and click OK.

Receptor molecules must contain at least one protein or nucleic acid molecule. It may contain compounds, glycans or metals. However, choose to make the pockets more space.

A dialog appears that specifies how to select a regand.




In this example, select From files (s) (sdf / mol / mol2 / SMILES) and select

Select [Yes] to check whether the ligand molecule is to be three-dimensionally coordinated.

For Conformer generation, select the default No conformer.

Click [OK].

Do you create 3D cordinates * The choice item description is as follows:

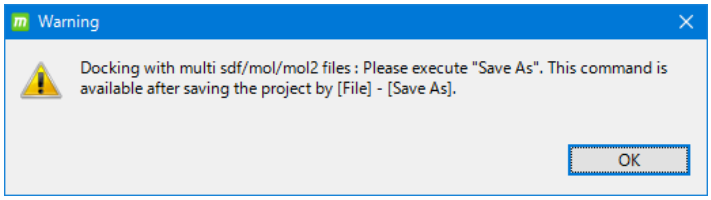
| item | explanation |
|---|---|
| No, Do nothing. | Perform docking calculations using the molecular information (coordinate values, charges, etc.) in the file without manipulating anything on the input file. |
| Yes | Add the missing hydrogen atoms of each regandmolecule, coordinate them in three dimensions, and then charge them withMOPAC7 AM1, and then use them for docking calculations.<br>For 3D coordinates,theamber GAFF2 force field performs energy-to-const sommerization(structural optimization)calculations foreach molecule, and during the calculation, a log (standard output) of the calculation process is displayed on the Console screen. |

Do you create conformers ?The description of the choice item is as follows:

| item | explanation |
|---|---|
| No conformer. | Do not run C onformer generation. |
| Yes | Perform Conformer generation. Use myPresto's confgeneC program. |

If you have not saved the project in advance, the following warning screen will appear.

Save it and click  [Docking] again to perform the same operation.




In the file selection dialog, select the following two files in the MolDesk Basic folder created on the desktop when MolDesk was installed.
(Shift + click to select multiple).

MolDesk Basic -> sample -> mol2 -> ERLOTINIB.mol2 :Contains 1 molecule compound
MolDesk Basic -> sample -> mol2 -> multi3.mol2 : Contains 3 molecule compounds

Click [Open] to perform a three-dimensional calculation for these four-regand molecules.

### 4.19.4. Three-dimensional molecular files

**Normally, it is not necessary to check the result of 3D calculation**. To proceed with the analysis, proceed to "5.19.5 Docking Calculation".

This section describes the storage location of the three-dimensional molecular file. When the 3D calculation is completed, if the folder where the project is saved is [PROJECT], a folder named "mol2_files" will be created under [PROJECT]-> work-> database.

Folders for each molecule are created with serial numbers under the "mol2_files" folder, and mol2 files for each conformer are output with serial numbers in the folders for each molecule.
(Generated for ring structures of 4 or more members. If a chiral center is present in the molecule, an optical isomer is also generated at the same time.) [PROJECT] -> work -> database -> mol2_files -> 3d001 -> 00000001-01.mol2

[PROJECT] -> work -> database -> mol2_files -> 3d002 -> 00000002-01.mol2
[PROJECT] -> work -> database -> mol2_files -> 3d002 -> 00000002-02.mol2
[PROJECT] -> work -> database -> mol2_files -> 3d002 -> 00000003-01.mol2
[PROJECT] -> work -> database -> mol2_files -> 3d002 -> 00000003-02.mol2
[PROJECT] -> work -> database -> mol2_files -> 3d002 -> 00000003-03.mol2
[PROJECT] -> work -> database -> mol2_files -> 3d002 -> 00000003-04.mol2
[PROJECT] -> work -> database -> mol2_files -> 3d002 -> 00000004-01.mol2
[PROJECT] -> work -> database -> mol2_files -> 3d002 -> 00000004-02.mol2

The naming rules for mol2 files are as follows:
[ Molecular number (serial number) ]- [Comfomer number (serialnumber)].mol2

A file (all.mol2) that combines these into one multi mol2 file is also output directly under the "mol2_files" folder.

[PROJECT] -> work -> database -> mol2_files -> all.mol2

If the ligand for docking calculation is input by file input, the mol2_files folder will be generated in the same way even if 3D is not performed.

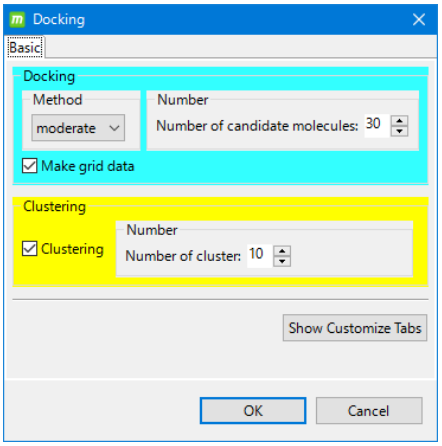
In the generated mol2 file, various characteristic values and titles of the molecule (in red

in the figure below) are described.

```
@<TRIPOS>COMMENT
 LIGANDBOX_ID = 00000001-01
 MOLECULAR_FORMULA = C22H23N3O4
 MOLECULAR_WEIGHT = 393.443
 MOLECULAR_CHARGE = 0
 SUM_OF_ATOMNUMBER = 208
 SUM_OF_ATOMNUMBER_MINUS_CHARGE = 208
 NUM_OF_DONOR = 1
 NUM_OF_ACCEPTOR = 6
 HOMO = -8.7657
 LUMO = -0.8136
 NUM_OF_CHIRAL_ATOMS = 0

@<TRIPOS>MOLECULE
00000001-01
 52 54 0 0 0
SMALL
USER_CHARGES

@<TRIPOS>ATOM
    1 O1        -0.9125    2.2767    1.9916    O.co2 1 UNK -0.5395
    2 C2        -0.3495    1.1177    1.2245    C.2   1 UNK  0.2438
    3 C3         1.1341    0.7531    1.3923    C.3   1 UNK  0.0180
・・・
```

### 4.19.5. Docking calculations

A dialog appears to enter docking calculation conditions.

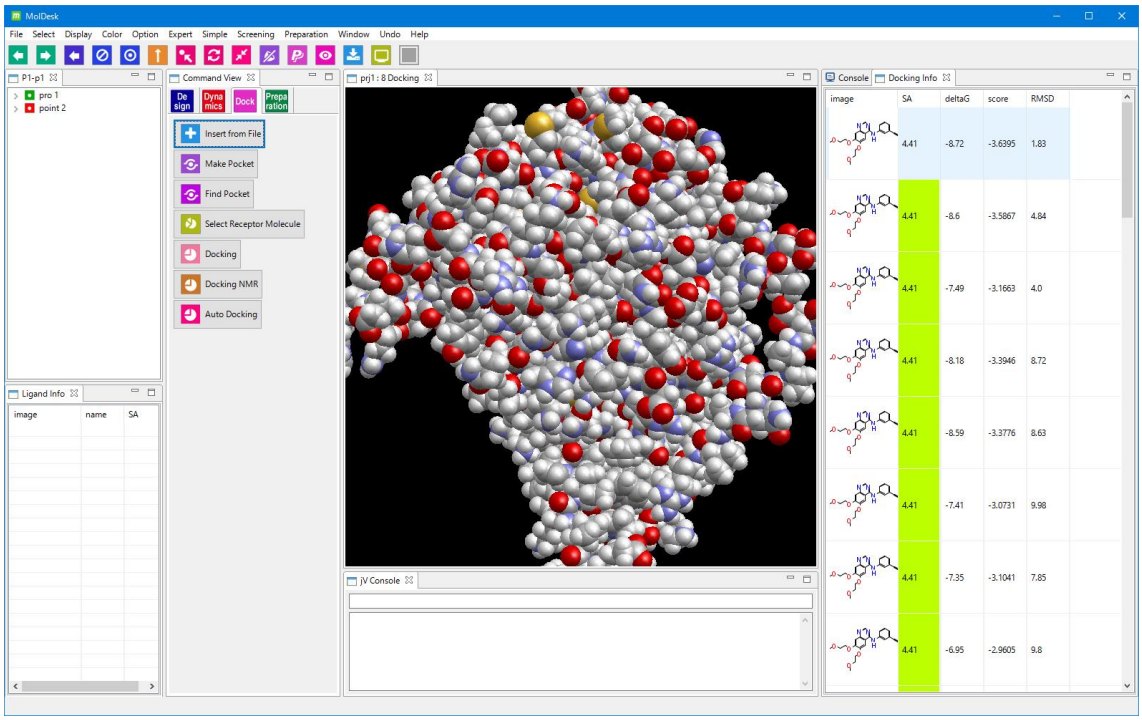



Enter the accuracy of the docking calculation, the presence or absence of structural clustering, and so on.

In this example, it is calculated by default.
Click [OK] as it is.

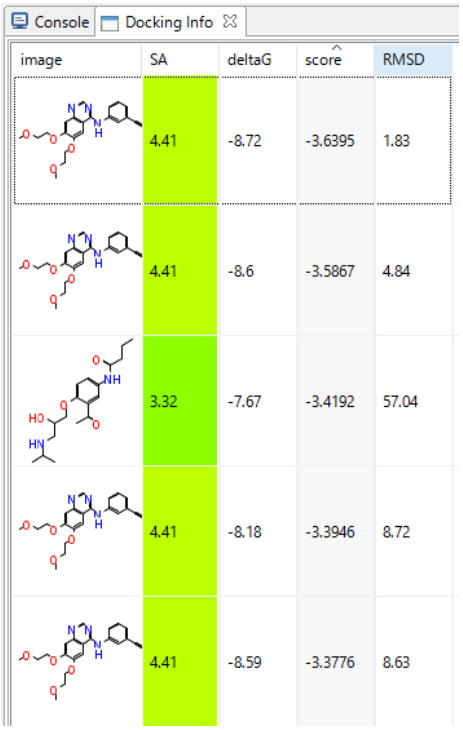
See "5.17.4 Creating Pockets" for more information.

The docking calculation results for the four ligand molecules you entered are listed on the Docking Info screen.



Each item on the Docking Info screen can be sorted in ascending or descending order.

An example of a display sorted by score.




Refer to "5.17.5 Checking Results" and "5.17.6 Saving Results" to check and save the docking results.

## 4.20. Docking Calculation 4 (Pocket Discovery)

Here is an example of running a docking calculation when performing a pocket search.

- Method to determine pockets based on protein shape alone, without docking calculations
- Highly accurate pocket search method using docking calculations (Molsite)

The former is explained here.

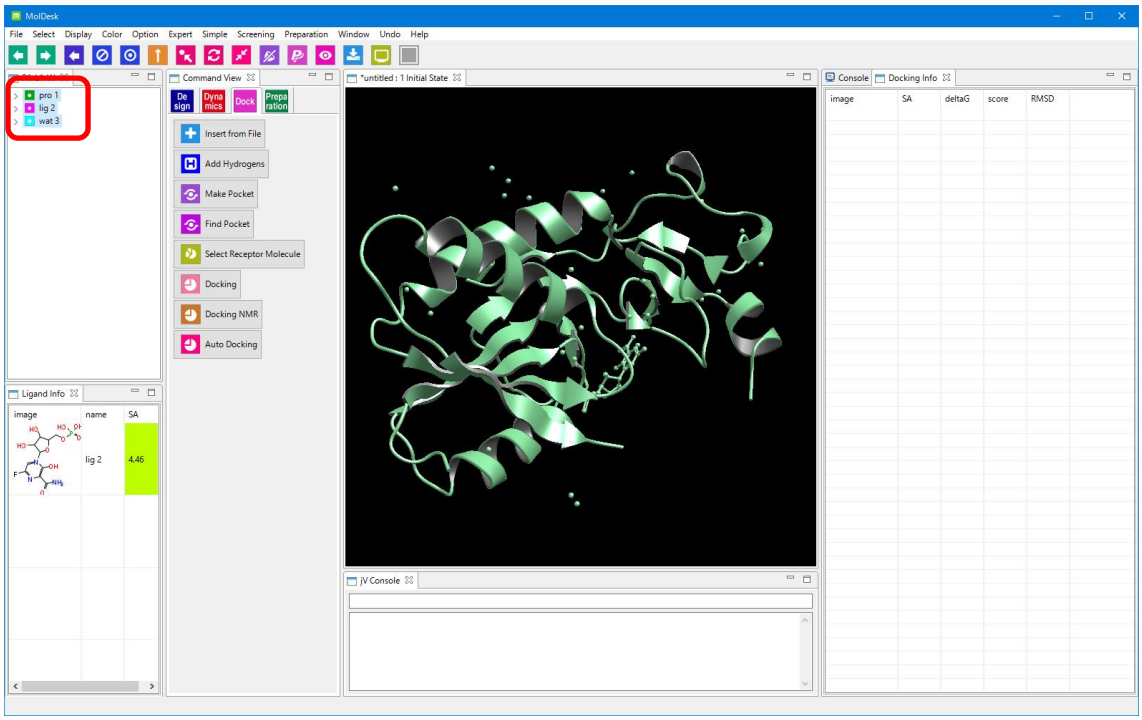
### 4.20.1. Read PDB files and add hydrogen atoms and charges

Refer to "5.4.2 [File]-[Open Molecular File]" and load the following files in the MolDesk Basic folder created on the desktop when MolDesk is installed.

MolDesk Basic-> sample-> pdb-> 4KN6.pdb

See 5.4.4 [File]-[Open Remote mmCIF / PDB] for a description of this data.

On the tree display screen, select protein, compound, and water of crystallization with the mouse (shift + click to select multiple).

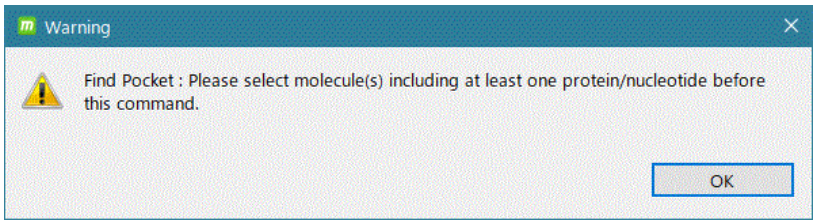


[Add Hydrogens] adds all missing hydrogen atoms (the compound is in the dissociative state with the -p option). In this case, the charge is also added.

### 4.20.2. Pocket Search

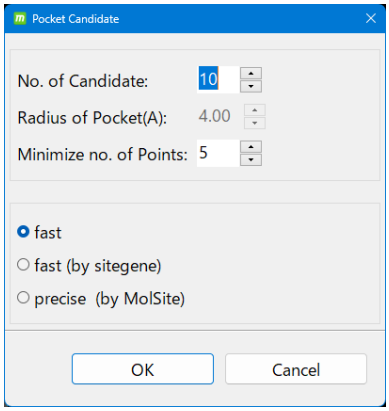
Select pro 1 on the tree view, and thenclick [Find Pocket].

If you run [Find Pocket] without selecting amolecule, the following warning dialog appears: In that case, select the molecule and re-run it.




Here you select at least one protein or nucleic acid molecule. Multiple molecules other than proteins or nucleic acids can be included as long as at least one protein or nucleic acid molecule is selected. A pocket search is performed on the surface of the selected molecule. For this reason, please make sure to select the pocket space to be free.

A dialog box for setting the pocket search conditions appears.

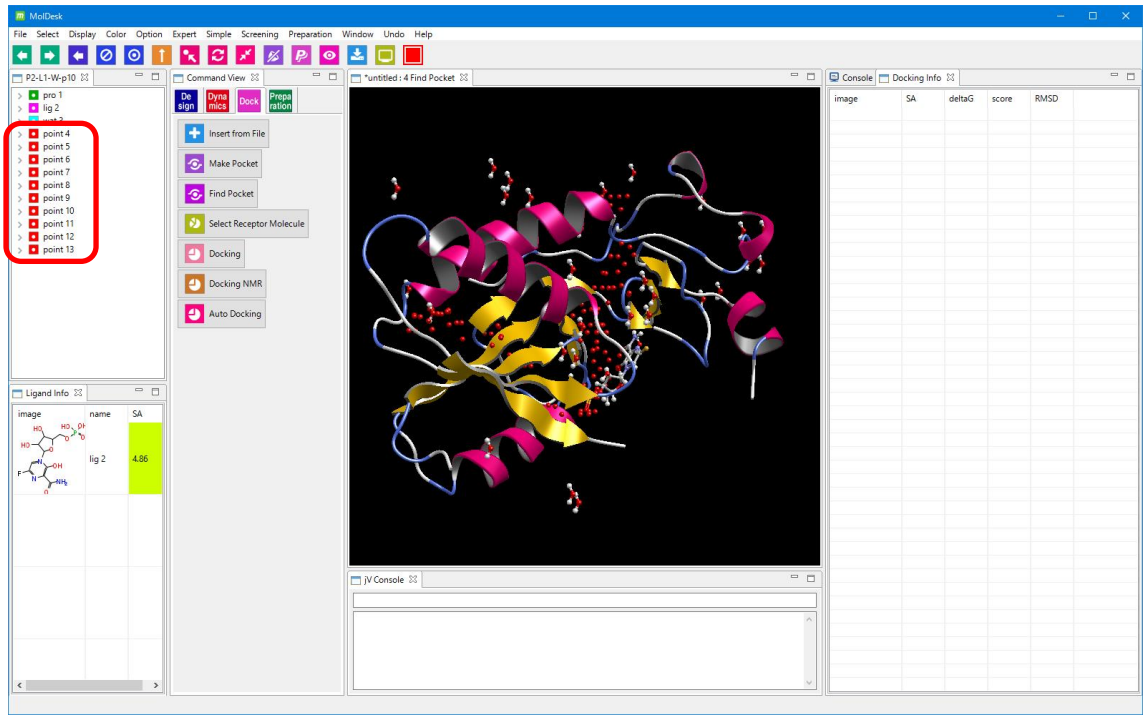



In this example, the default conditions are used for calculation.
Click [OK] as it is.

The explanation of each item is as follows.

| item | explanation |
|---|---|
| No. of Candidate | Number of pocket candidates |
| Minimize no. of Points | Minimum number of probe points in the pocket<br>Pockets with fewer probe points are excluded from the candidate |
| Radius of Pocket(A) | Approximate radius of the pocket (Å).<br>Enter in fast (by sitegene). |
| fast | Fast, low-precision pocket search method. |
| fast (by sitegene) | Fast, low-precision pocket search method (by sitegene). |
| precise | Precise pocket search with Molsite |

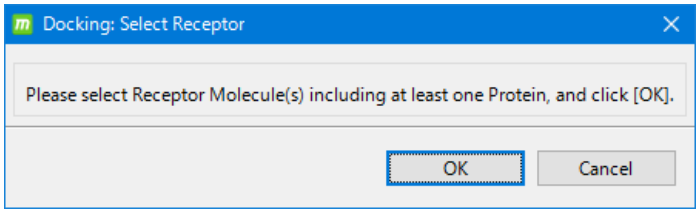
At the end of thecalculation, 10 pocket suggestions are displayed in order of score.

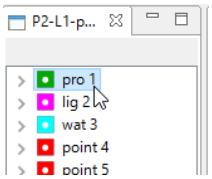


### 4.20.3. Docking calculations

Click  [Docking].

A message dialog is displayed prompting you to select a receptor.

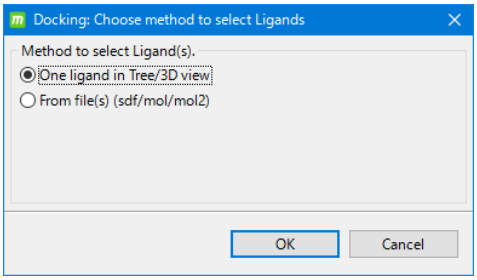


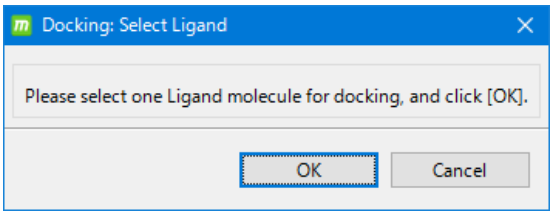

In this example, select  pro1, and then click [OK].

The receptor molecule must contain at least one protein or nucleic acid molecule. It may contain compounds, glycans or metals.

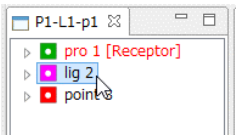
A dialog appears in which you can specify how to select the ligand.




In this example, leave the default [One Ligand in Tree / 3D view] and click OK.

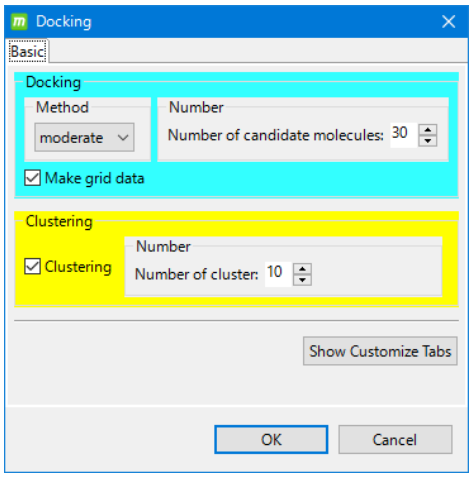



A dialog will appear prompting you to select a ligand.
Select one compound or glycan to use as a ligand from the tree display screen or 3D screen.




In this example, select  lig 2, and then click [OK].

A dialog appears to enter docking calculation conditions.




Docking calculation accuracy, structural cluster Enter the presence or absence of a ring.

In this example, it is calculated by default. Click [OK] as it is.

For the meaning of the setting items, refer to "5.17.4 Creating a pocket".

The docking calculation is performed using the pocket with the best score (the one at the top of the tree view screen in the pocket).

All other pockets will be deleted automatically.

If you want to use a different pocket for the docking calculation, use  [Delete Molecule] to delete all pockets with a better score than the pocket you want to use for the calculation, and then perform the docking calculation.

Refer to "5.17.5 Checking Results" and "5.17.6 Saving Results" to check and save the docking results.

## 4.21. Pocket search and docking calculation by Molsite

The following is an explanation of high-precision pocket search using Molsite.

### 4.21.1. Read PDB file and add hydrogen atoms and charges

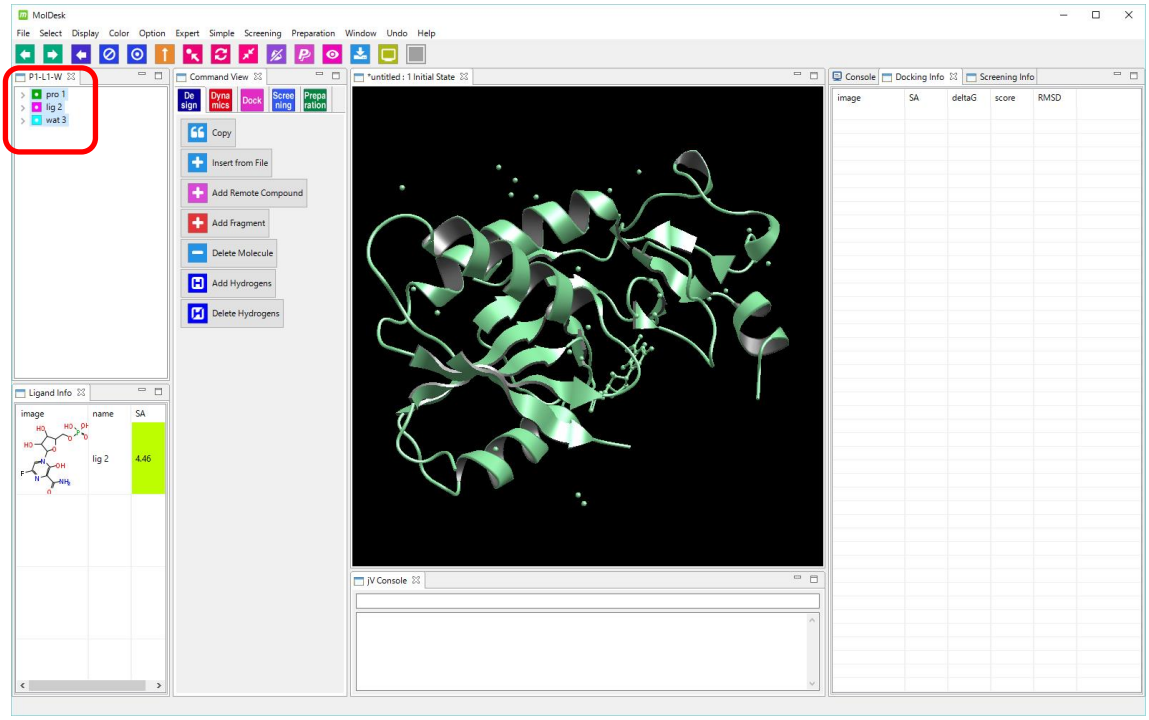
[File] – [Open Molecular File] loads the following files in the MolDesk Basic folder created on the desktop when MolDesk was installed.

MolDesk Basic-> sample-> pdb-> 4KN6.pdb

"4kn6" used in the example is a compound in which ribose-5'-1 phosphate is bound to HGPRT (hypoxanthine-guanine phosphoribosyl transferase), which is one of the purine-

metabolizing enzymes, and favipiravir, a candidate for the treatment of Ebola fever. It is included.

On the tree display screen, select protein, compound, and water of crystallization with the mouse (shift + click to select multiple).




With [Add Hydrogens], add all the missing hydrogen atoms.
At this time, an electric charge is also added to the protein.

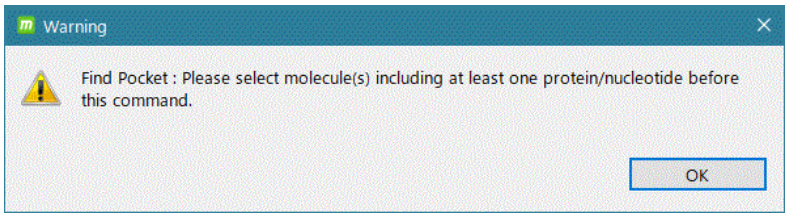
※ For hydrogen atom addition to a compound, there are three options to choose from: -p / -h / -m. Please refer to the "MolDesk Basic Manual" for the details of the contents. Here, the default -p option is selected.

Next, execute [Partial Charge] with lig2 selected, and perform charge calculation with MOPAC7 AM1 to add charge to the compound.

### 4.21.2. Pocket Search with Molsite

Select pro 1 on the tree view screen and click [Find Pocket].

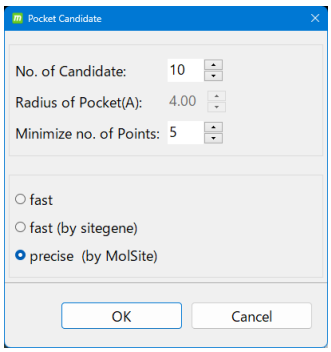
If you execute [Find Pocket] without selecting a molecule, the following warning dialog will be displayed. In that case, select the molecule and try again.




Here, select at least one protein molecule. If you select at least one protein molecule, you can include multiple non-protein molecules. Performs a pocket search on the surface of the selected molecule. For this reason, select the molecule so that there is space in the pocket.

* Molsite supports pocket searches for protein molecules and does not target nucleic acid molecules.

A dialog appears to set pocket search conditions.

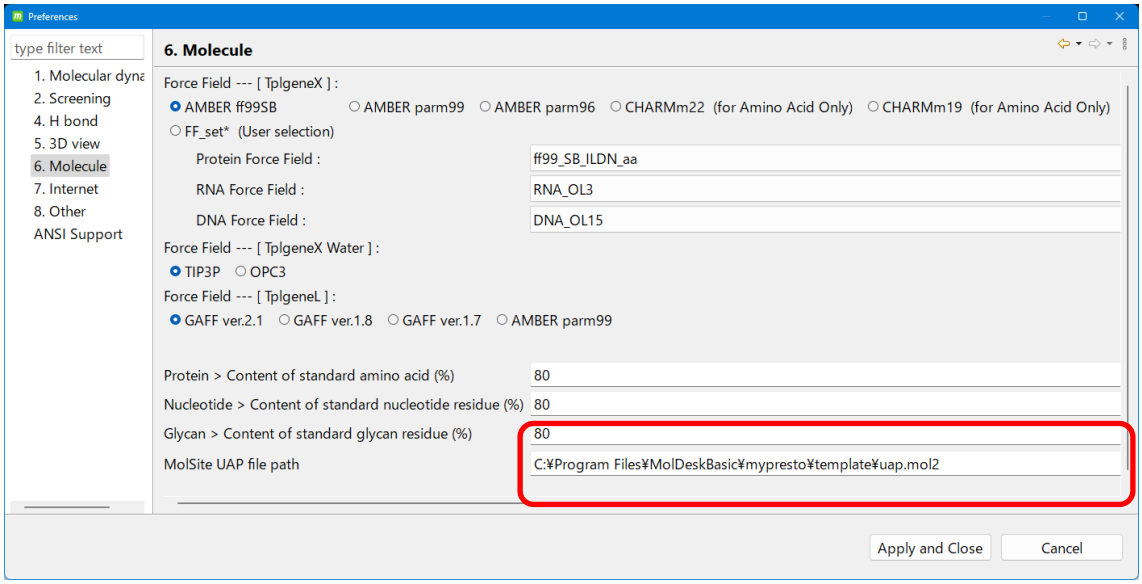



In this example, select precise (by Molsite).

Refer to the MolDesk Basic manual for the explanation of each setting item.

※ * In MolSite, a large number of ligand candidate molecules called UAP molecules are docked to pocket candidates one after another, but UAP molecules are displayed by selecting [Help]-[Preferene]-[Molecule] on the screen below, which is displayed by default. The user can set any molecule other than the set molecule.

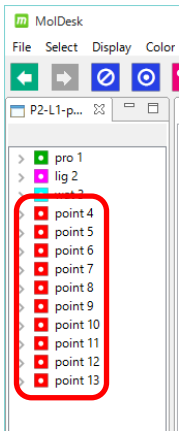
If you want to change the UAP molecule, enter the mol2 file path of the molecule you want to change in the [MolSite UAP file path] below, and click [Apply] or [OK] to confirm and then calculate.




### 4.21.3. Parallel number and time of pocket search by Molsite

The guideline for the calculation time of pocket search by Molsite is as follows.
No special settings are required for parallel computing (thread parallel computing is used).

| | **Intel Core i7-4790K 4.0GHz / 16GB memory / windows8.1** **Run in 8 parallels** |
|---|---|
| PDB 4kn6 (1555 atoms) | 11 minute |
| PDB 1m17 (4744 atoms) | 15 minutes |



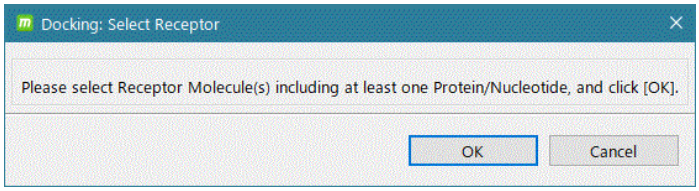

In this example, 10 pocket candidates are displayed in score order after the calculation is completed.

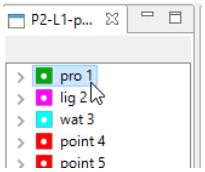
### 4.21.4. Docking calculations

Next, perform the docking calculation.

Click  [Docking].

A message dialog is displayed prompting you to select a receptor.

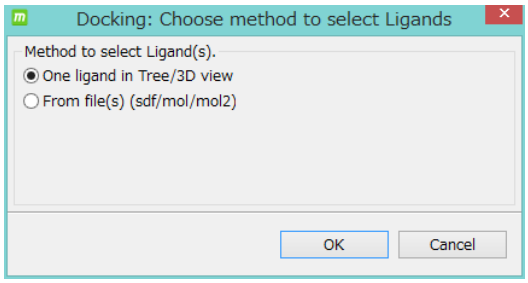


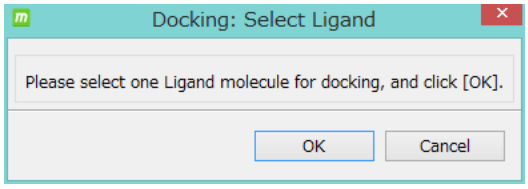

In this example, select  pro1 and click [OK].

Receptor molecules must contain at least one protein molecule. It may contain compounds or metals.

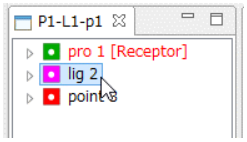
A dialog appears that specifies how to select a regand.




In this example, leave the default One Ligand in Tree / 3D view and click [OK].

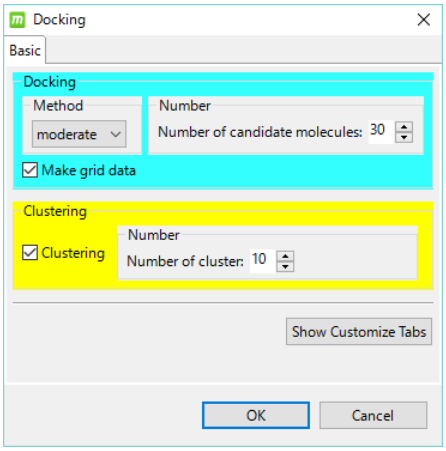



A dialog will appear prompting you to select a ligand.
Select one compound to use as a ligand from the tree display screen or 3D screen.




In this example, select  lig 2, and then click OK.

A dialog appears to enter docking calculation conditions.




Enter the accuracy of the docking calculation, the presence or absence of structural clustering, and so on.

In this example, it is calculated by default.
Click [OK] as it is.

**Docking calculations are performed using the pocket with the highest** score **(the one at the top of the tree display screen in the pocket).**

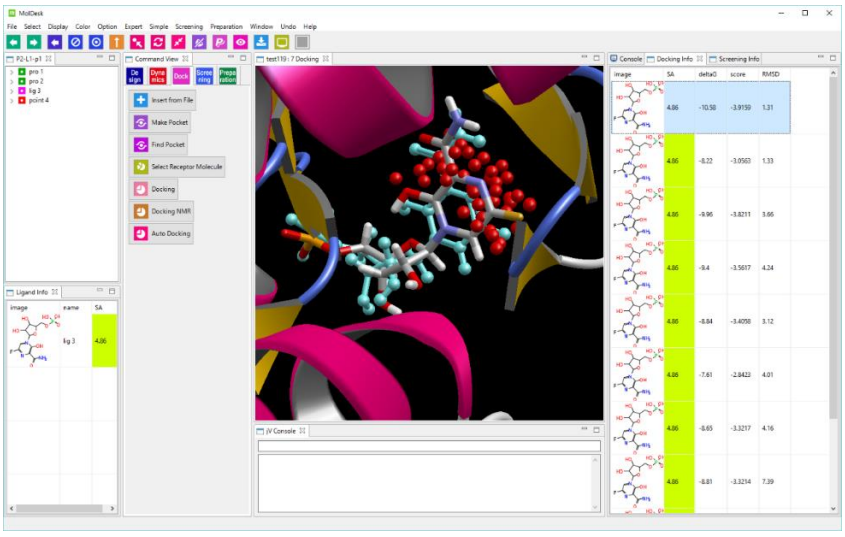
All other pockets will be deleted automatically.

If you want to use a different pocket for docking calculations

Delete all pockets with better scores with  [Delete Molecule]
Perform the docking calculation.

For checking and saving the docking result, refer to preceding paragraph.

In this example, RMSD = 1.31 Å as a result of comparing the predicted structure with the best score and the correct structure (displayed in light blue with lig3, [Color] – [Atom] – [Any]).

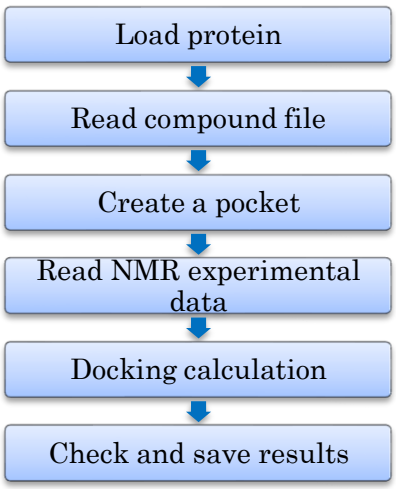


## 4.22. Docking calculation 5 (NMR experimental data )

Provides an example of performing docking calculations when entering solution NMR experimental data for a mixed solution of a protein-compound.

- In solution NMR, collect DIRECTION data of compounds in a mixture of protein-compounds.
- The three-dimensional structure of proteins and compounds is known.
- Protein-When docking a compound, place the compound so that the correlation between the experimental DIRECTION data and the simulated DIRECTION data is maximized to predict the complex structure.

The procedure is as follows.




- For details on docking calculation based on NMR experimental data, refer to "sievgene NMR USER MANUAL" attached to myPresto.

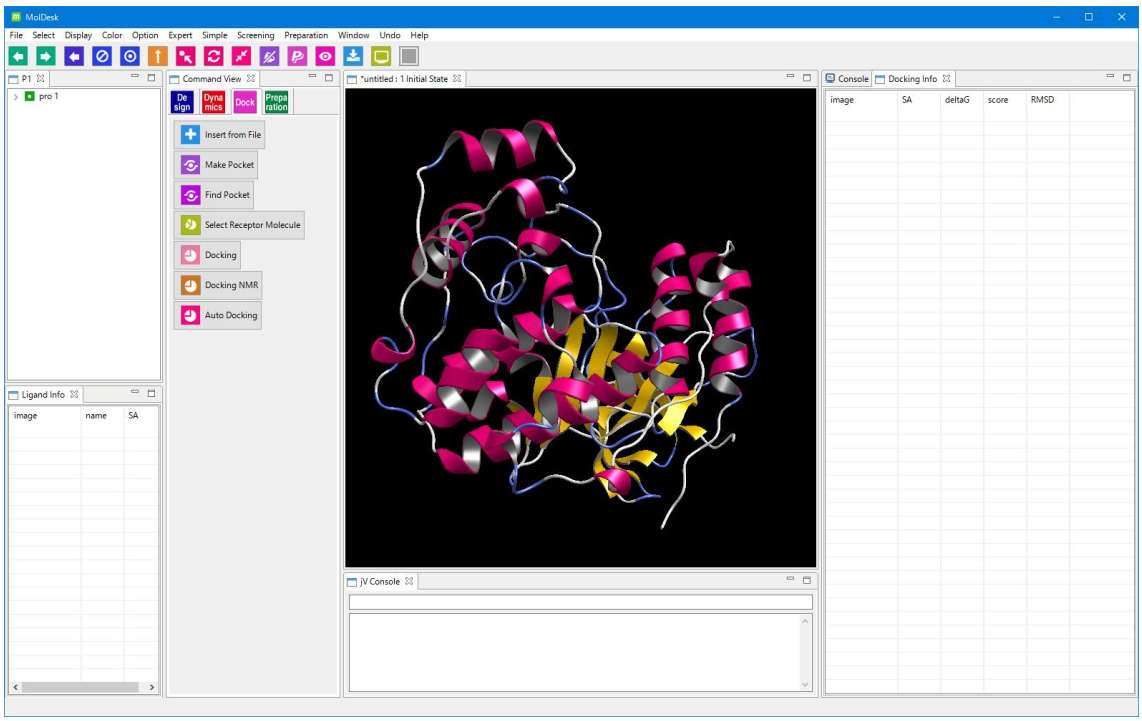
### 4.22.1. Load a protein PDB file

As test data, load the PDB file with PDB ID 1A9U (Mitogen-activated protein (MAP) kinase p38 α ).

There is a 1A9U PDB file in the MolDesk Basic folder that was created on your desktop when you installed MolDesk.

Refer to "5.4.2 [File]-[Open Molecular File]" and load the following files in the MolDesk Basic folder.

MolDesk Basic -> sample -> NMR -> Pro.pdb



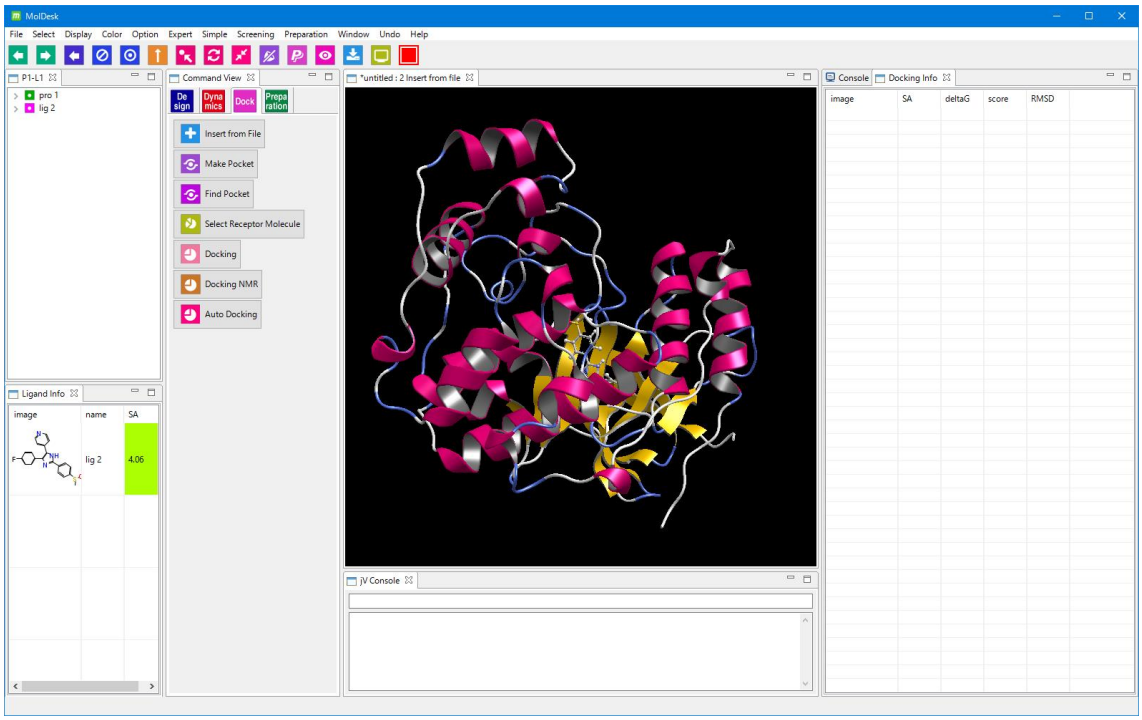

In this test data, since the addition of hydrogen atoms has already been completed, the addition of hydrogen atoms is not performed and the next step is moved.

### 4.22.2. Read the mol2 file of the compound

Under  [Insert from File], enter the following file.

MolDesk Basic-> sample-> NMR-> Lig.mol2
This compound is a molecule of SB203580, a specific inhibitor of MAPK p38 $\alpha$ and p38 $\beta$.

For [Position Select], select [file]. For the explanation of [Position Select], refer to "5.4.1 [File]-[New Project]".




The compound is added to the coordinates of the file, and the compound is also added with on the tree display screen.

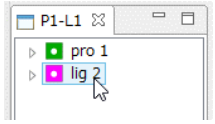
- In this test data, hydrogen atom addition and charge addition have already been completed, so hydrogen atom addition is not executed and the next step is performed.

- If the input file is a mol2 file, the charge in the input file will be saved. No charge calculation is performed at the time of input. For compounds that do not have charge information, perform charge calculation as appropriate.

### 4.22.3. Create pockets

Create a pocket by referring to "5.18.3 Creating a pocket". However, specify the compound lig2 instead of the protein pro1.

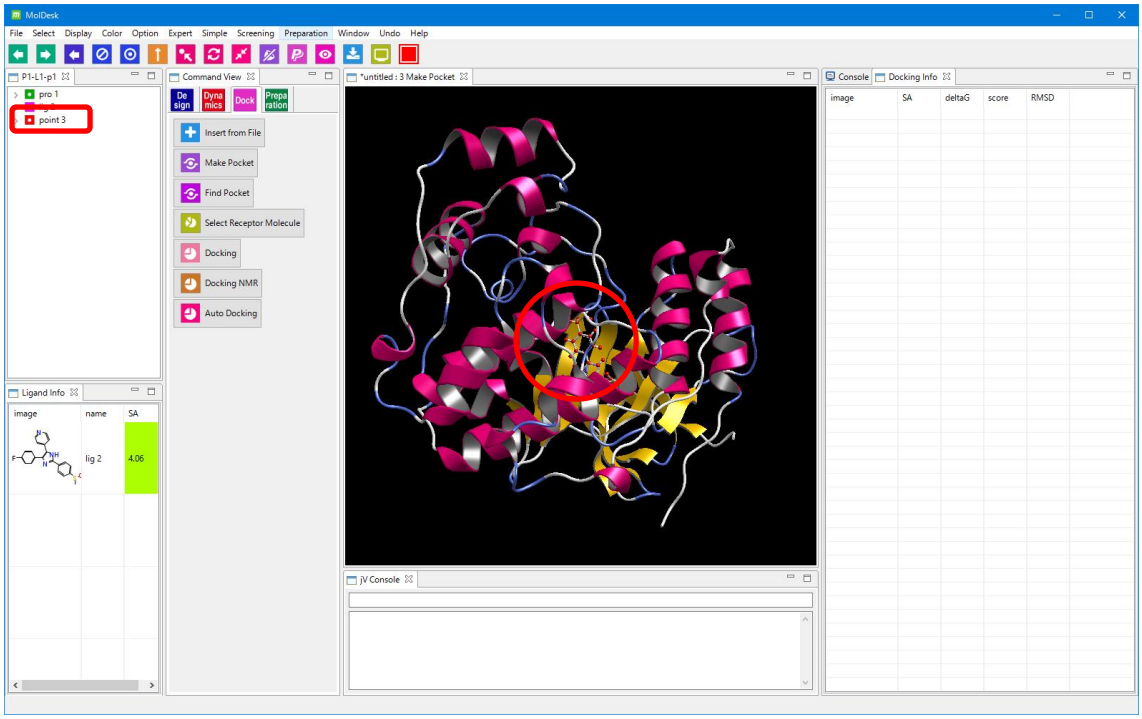
In this example, the compound molecule itself is the probe point in the pocket.




Select the compound lig2 on the tree view screen or 3D screen and click [Make Pocket].

You can see that the atoms of the ligand molecule are circled in red and all the atoms of the ligand molecule are the probe points in the pocket.

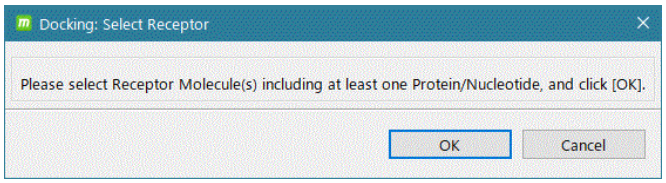
In addition, point3 is displayed on the tree display screen, confirming that the probe point of the pocket has been added to the system.

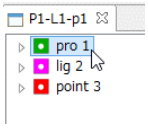



### 4.22.4. Enter NMR experimental data

Click  [Docking NMR].

A message dialog prompts you to select a receptor.

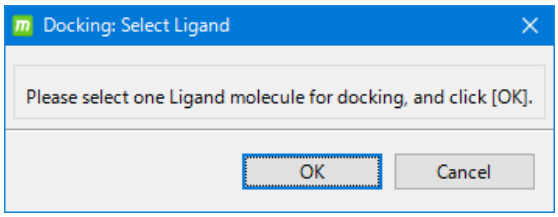


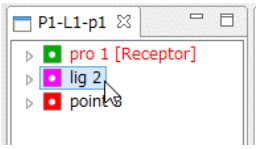




In this example, select pro1, and then click [OK].

Receptor molecules must contain at least one protein molecule. It may contain compounds, glycans or metals.

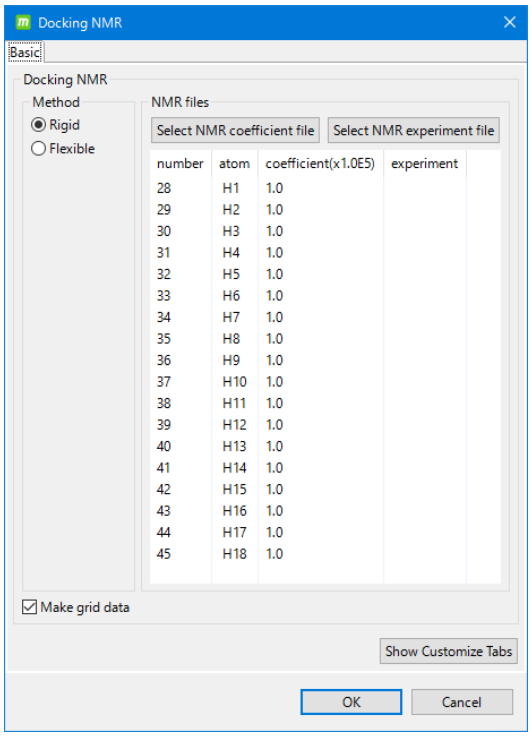
A message dialog prompts you to select a regand.
Select one compound or glycan to use as a regand from the tree display screen or the 3D screen .




In this example, select lig 2, and then click [OK].

A dialog appears in which you can enter information about the total hydrogen atoms of the selected compound.




Select the docking calculation method in [Method].
In this example, select [Rigid].

For details on [Method], refer to "5.21.7 Docking Calculation Using NMR Experimental Data".

Enter the NMR experiment data in [Select NMR coefficient file] and [Select NMR experiment file]

There are two types of NMR experimental data: spin relaxation coefficient data and spin relaxation experimental value data.

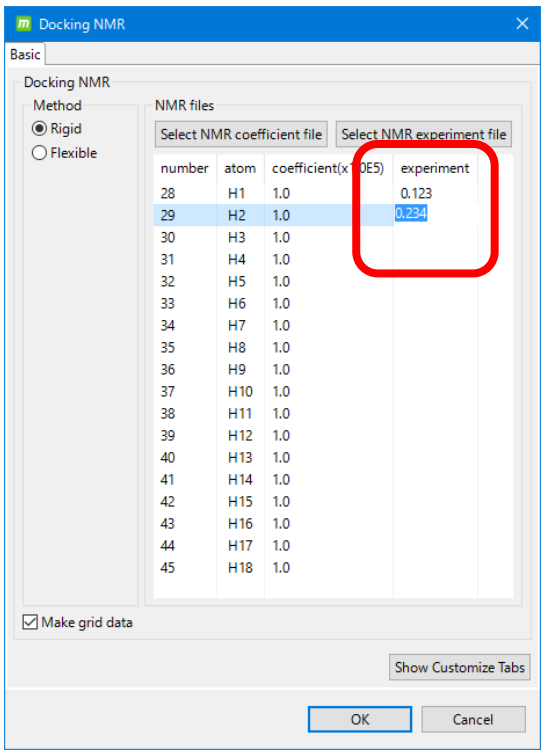
The NMR experiment data is input from the GUI or a file.
In this example, input from a file. Proceed to "5.21.6 File Input of NMR Experiment Data".

For GUI input of NMR experiment data, refer to "5.21.5 GUI input of NMR experiment data".

### 4.22.5. GUI input for NMR experimental data

There are two ways to enter NMR  experimental data: enter it directly in the dialog and  in a file.

If you enter it directly in the dialog, enter the spin relaxation experiment data (experiment) number as follows:
The spin relaxation factor data(coeffficient) defaults to 1.0, but you can change the value.




### 4.22.6. File entry of NMR experimental data

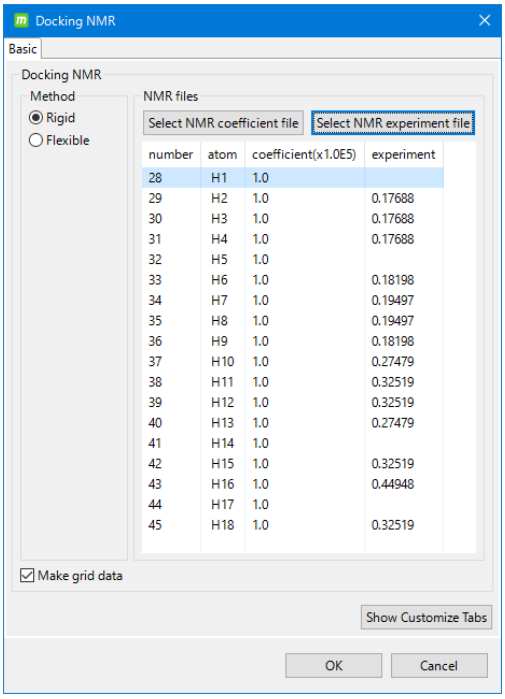
This section describes how to input NMR experiment data from a file.

You can enter the spin relaxation experiment value data (experiment) file with the [Select NMR experiment file] button and the spin relaxation coefficient data (coefficient) file with the [Select NMR coefficient file] button.
The NMR experiment data file you select must have a .nmr extension.

In this example, the NMR experiment data file contained in the MolDesk Basic folder created on the desktop when MolDesk is installed is read.

Click the [Select NMR experiment file] button to load the following file.

MolDesk Basic -> sample -> NMR -> expr.nmr




Click [OK].

Lines with blank experiment are not used in the calculation.

Nmr experimental data files are formatted as follows:

**Spin relaxation factor file**

Of the hydrogen contained in the compound, describe the "atom ID", "atom name", and "force coefficient" in this order, separated by spaces, for each line of the hydrogen atom for which the signal is to be calculated.
Blank lines or lines with a';' in the first column are considered comment lines.

The force coefficient is the coefficient of Eq. (5) in "sievgene NMR USER MANUAL". Calculate only the correlation coefficient and specify 0.0 if no force is applied.

```
; NMR signal coefficient (3rd value is force coefficient)
;

29   H2   100000.0
30   H3   100000.0
31   H4   100000.0
・・・
```

**The GUI displays a factor** of **1.0, but for file input,** it describes **a number multiplied by 1.0E5.**

**Spin relaxation experiment value file**

For the spin relaxation experimental values obtained in the NMR experiment, describe the "atom ID", "atom name", and "signal calculation coefficient" in this order, separated by blanks.

Blank lines or lines with a';' in the first column are considered comment lines.

```
; NMR test suits (1aco, use excel sheet calculation)
;

29   H2   0.17688
30   H3   0.17688
31   H4   0.17688
・・・
```

### 4.22.7. Docking calculations using NMR experimental data

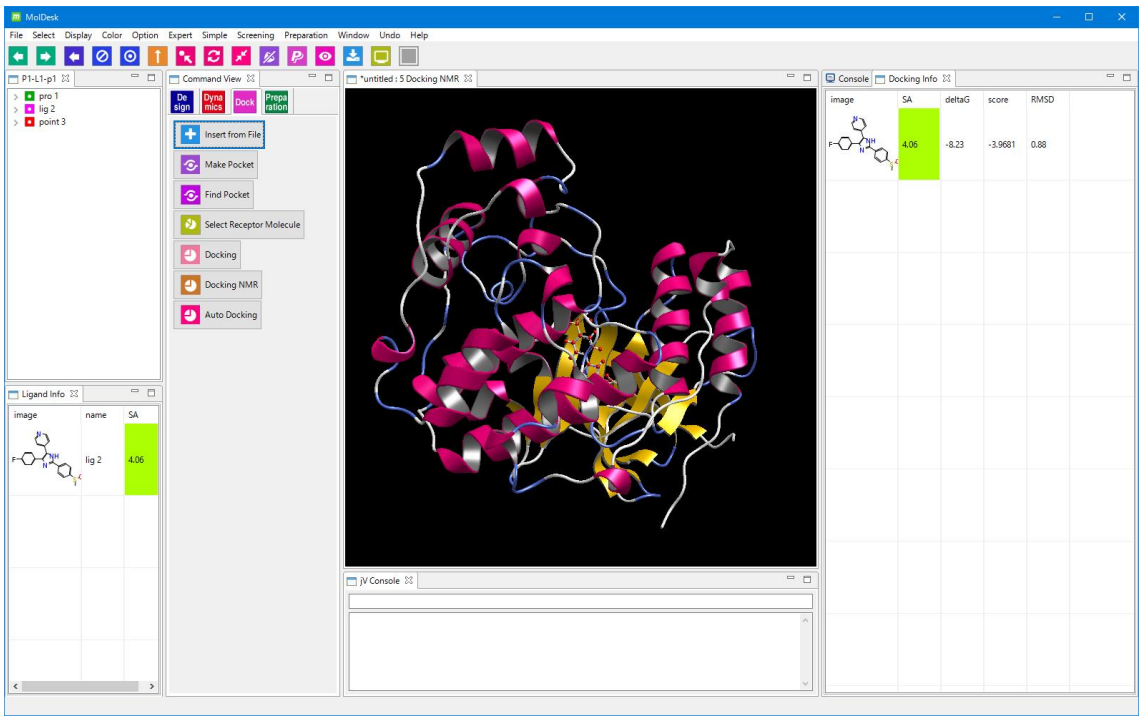
The description of the docking calculation method is as follows.

| item | explanation |
|---|---|
| Rigid | Dock the ligand compound as a rigid body (does not change the conformation) and output one candidate structure. |
| Flexible | Dock the ligand compound while changing its conformation and output 5 candidate structures. |

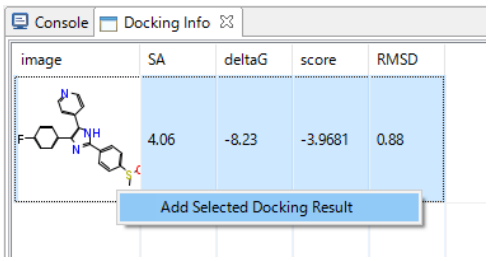
The calculation conditions of the two scripts (nmr_sample_input1.in and nmr_sample_input2.in) in the sievgene NMR sample attached to myPresto are reproduced respectively.

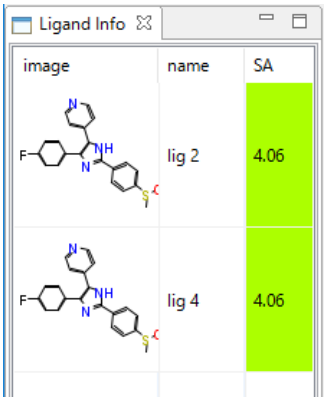
In this example, select Rigid as the calculation method and click OK.

When the docking calculation is finished, one candidate structure is calculated in this example.




You can add the candidate structure to the Ligand Info screen by selecting the candidate structure on the Docking Info screen, right-clicking, and selecting "Add Selected Docking Result".



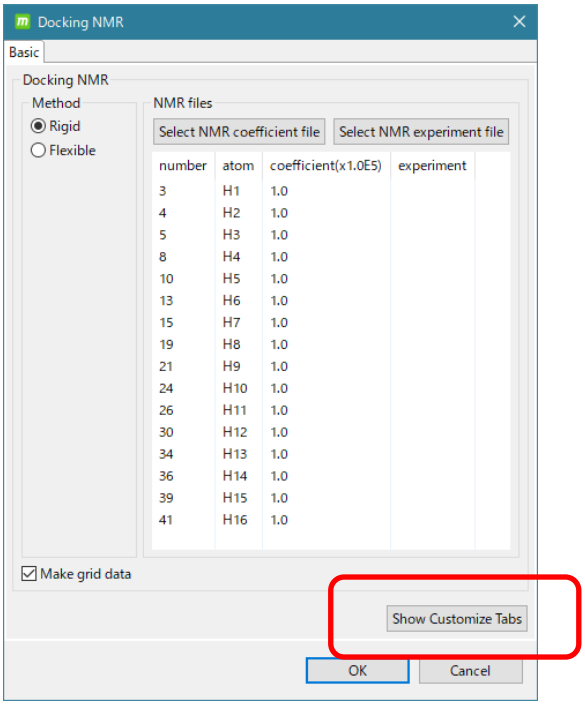



It can be confirmed from the NMR experimental data that the original position (lig2) was slightly modified (lig4).

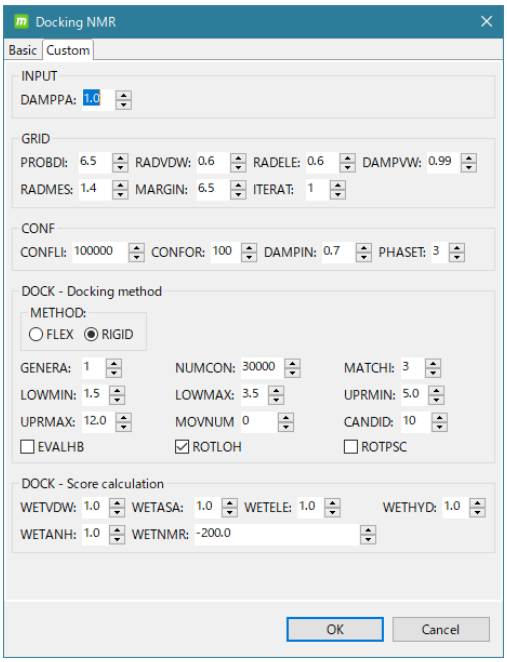
Refer to "5.17.5 Checking Results" and "5.17.6 Saving Results" to check and save the docking results.

### 4.22.8. Docking calculations based on NMR experimental data Advanced settings

[Show Customize Tabs] Click the button to display theAdvancedTab (Custom).



The default settings for advanced settings are as follows:




Please note that when the Custom tab is displayed, the [Method] of the Basic tab cannot be changed. If you want to change the [Method], click "Cancel" to cancel, and then click  [Docking NMR] again.

The description of the item is as follows. For a more detailed explanation,see the myPresto documentation.

[ INPUT ]

| item | explanation |
|---|---|
| DAMPPA | Coefficient of atomic radius of protein |

[ GRID ] Grid potential generation

| item | explanation |
|---|---|
| PROBDI | Distance upper limit of pocket point and receptor atom |
| MARGIN | GridPotential range margin |
| ITERAT | Smoothing repetitions |
| RADVDW | vdW boundary distance correction |
| RADELE | Electrostatic boundary distance correction |
| RADMES | Probe radius for mesh point generation |
| DAMPVW | Coefficient of vdW radius |

[ CONF ] Regand comformer generation

| item | explanation |
|---|---|
| CONFLI | Maximum number of attempts for consumer generation |
| CONFOR | Number of seats to generate |
| DAMPIN | Damping factor of the atomic vdW distance of the seat |
| PHASET | Suggestions for torsion rotations |

[ DOCK - Docking method ] Global Search

| item | explanation |
|---|---|
| METHOD | Docking Method FLEX / RIGID |
| CANDID | Number of local searches |
| GENERA | Number of refinees |
| NUMCON | Top score to display |
| MATCHI | Atomic type fit of the bonded surface |
| LOWMIN | Lower minimum value of the edge of the join face |
| LOWMAX | Minimum lower limit of the edge of the join face |
| UPRMIN | Maximum value of the edge of the join face |
| UPRMAX | Maximum edge limit for join faces |
| EVALHB | Evaluation of hydrogen bonds between proteins and rigands considering anthrant sex YES/NO |
| ROTLOH | Rotation of the regand -OH set YES / NO |
| ROTPSC | Hydrogen-binding protein side chain rotation YES / NO |
| MOVNUM | Number of coordinates to be snuthed |

[ DOCK - Score calculation ] Score calculation

| item | explanation |
|---|---|
| WETVDW | Coefficient of vdW during score calculation |
| WETASA | Asa factor during score calculation |
| WETELE | Coefficient of electrostatic power during score calculation |
| WETHYD | Coefficient of hydrogen bond during score calculation |
| WETANH | Coefficient of hydrogen bond between protein and ligand considering anisotropy |
| WETNMR | Nmr evaluation value score addition factor |

### 4.23. Manual docking calculations

By placing the ligand near the protein pocket (presumably), the structure of the docking pose can be optimized. The position of the protein does not move. No pocket generation is required.

To rearrange the ligand molecule, use the  [Move] command or the like.

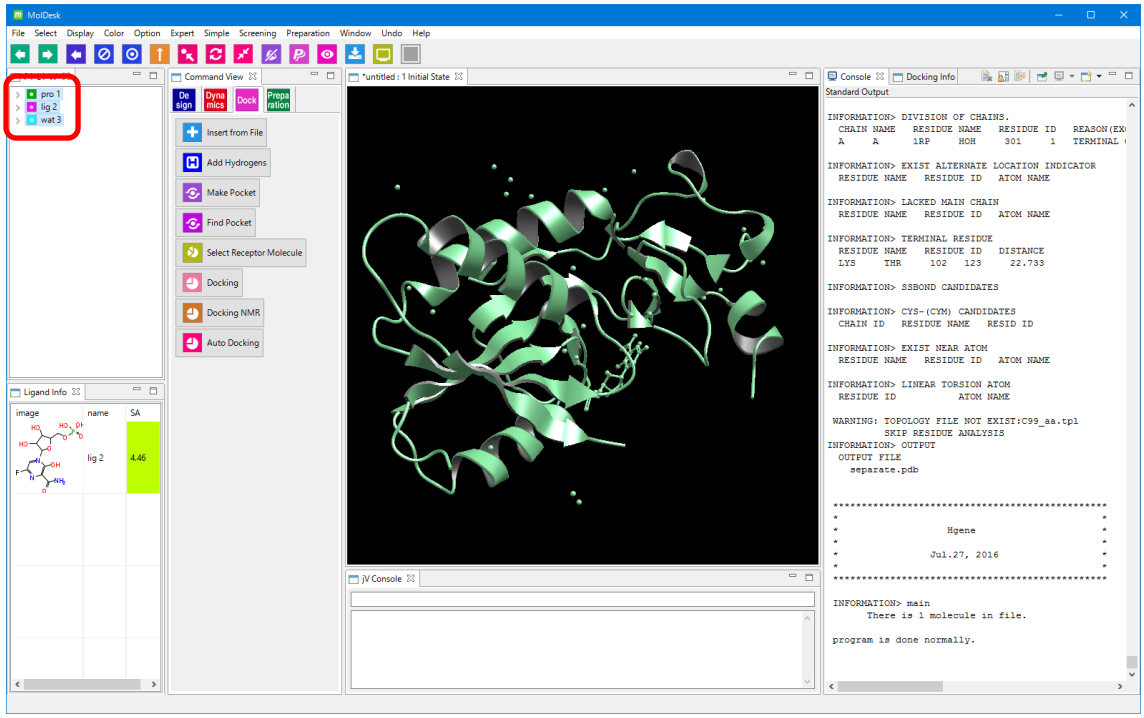
The coupling free energy ΔG value is used as an index for the optimization calculation.

### 4.23.1. Load mmCIF/PDB files over the Internet

Refer to "5.4.4 [File]-[Open Remote mmCIF / PDB]" and load the molecule with PDB ID "4kn6".

### 4.23.2. Addition of hydrogen atoms and charges

On the tree display screen, select three with the mouse: protein, compound, and crystalline water (shift + click multiple selection).




 [Add Hydrogens] adds all missing hydrogen atoms (the compound is in the dissociative state with the -p option). In this case, the charge is also added.

- Be sure to add hydrogen atoms to the protein during manual docking.
  - The addition of hydrogen atoms to the protein is performed by tplgeneX of myPresto, which charges the temperature factor of the protein's PDB file based on the force field selected in [Help]-[Preference] – [Molecule] – [tplgeneX]. The information will be filled in. Manual docking uses this charge information for calculations.

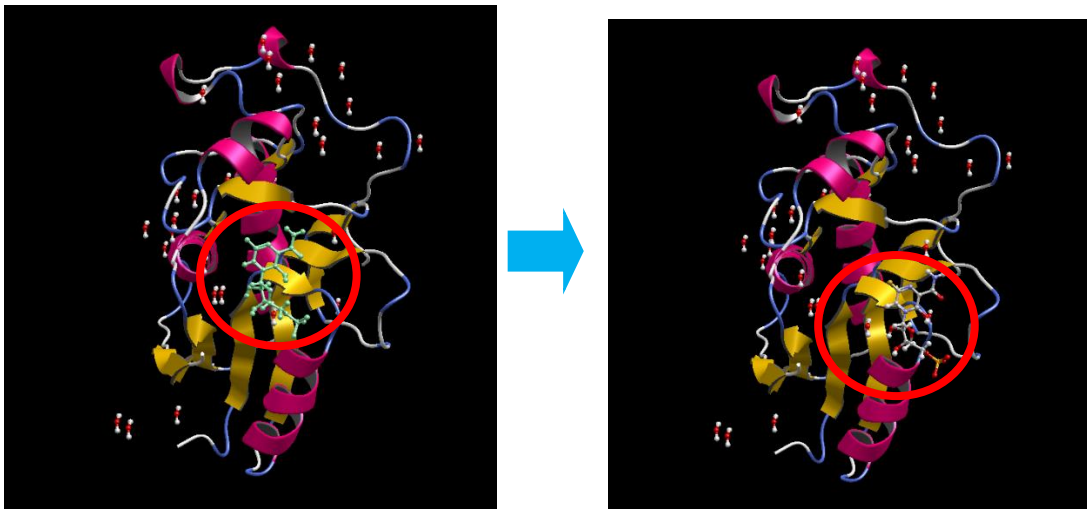
- Compound charging is also required for accurate calculations. When I run Add Hydrogens, myPresto's Hgene program adds charge with Gasteiger.

### 4.23.3. Manual docking

Here is an example of performing manual docking.

Select lig 2, click [Move], and then right-drag lig 2 on the 3D screen (the trick is to drag the end of the molecule) to reposition it slightly.

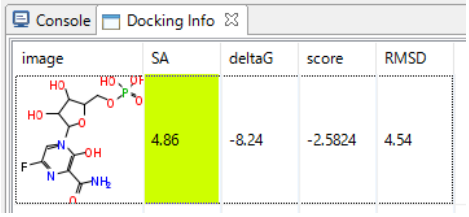
For [Move], refer to "5.23.16 Movement and rotation of atoms (groups)".



Select lig 2 and run [Delta G].

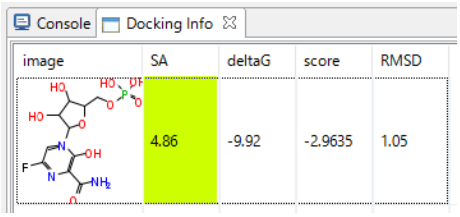
A structural optimization calculation of the docking pose, or manual docking, is performed to get closer to the original correct structure.

At the same time, the free energy deltaG value on the Docking Info screen is updated



Execution of [Delta G] shortens the calculation time because the grid calculation is not required for the second and subsequent calculations using the same pocket.

Select lig 2 again and execute [Delta G]. The calculation is completed earlier than the first time. Also, the deltaG value on the Docking Info screen will be lower than the first time (indicating that the structure is more stable).

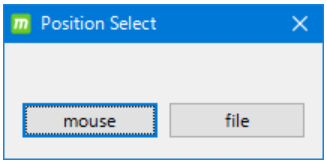



### 4.24. Compound editing

Describes how to edit a compound or glycan. The compound or glycan editing command is in De sign.

#### 4.24.1. Read compounds by file

[Insert From File]: Specify a file to read the molecule.
The file formats that can be read are sdf / mol / mol2 / pdb / mmCIF / SMILES.



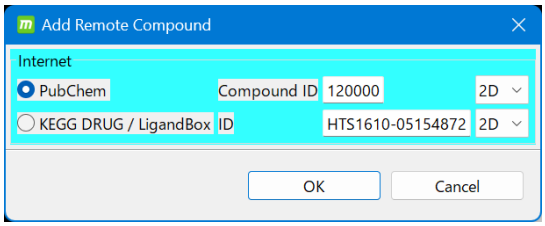

After selecting the file, the [Position Select] dialog is displayed.
[mouse] : Enter the compound at the mouse click point on the 3D screen
[file] : Enter the compound with the coordinates of the compound file

※ If you enter a protein, it will generate an S-S bond by default.

### 4.24.2. Loading compounds over the Internet


[Add Remote Compound]: Read the molecule via the Internet.

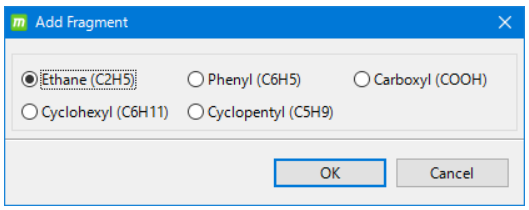
Enter either the PubChem Compound ID or the KEGG DRUG / LigandBox ID. You can choose 2D or 3D.




An example of an ID number to enter is For example, 120000 for PubChem and HTS1610-05154872 for LigandBox.
(As an example, delete the characters that have already been entered and re-enter them.)

### 4.24.3. Loading compounds with templates


[Add Fragment] : Enter the specified molecular species as the initial structure.




There are 5 types of molecules that can be selected.
After selecting the molecule species, the Position Select dialog (see Insert From File description above) is displayed.

### 4.24.4. Addition and removal of hydrogen atoms

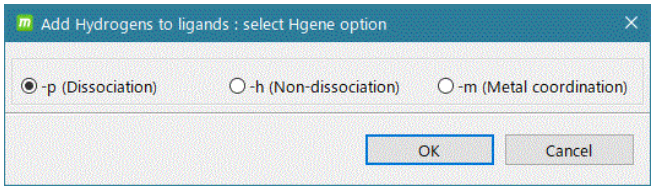
Here, refer to "5.18.2 Reading mol2 files of compounds" as test data, read the following files, and explain in the following chapters.

MolDesk Basic-> sample-> mol2-> ERLOTINIB.mol2

Describes how to add and remove hydrogen atoms.


[Add Hydrogens] to add hydrogen atoms, 
[Delete Hydrogens] to add hydrogen atoms
You can delete it. When adding a hydrogen atom to a compound, the charge is also added at the same time by the Gasteiger method.

If only compounds are selected, the following screen will appear and the hydrogen addition method can be selected from the following three options.




1. -p (Dissociation)

This updates the hydrogenation and formal charge information so that the acidic/basic functional group is in a dissociated state. Dissociation of basic functional groups is available only for amines with sp3 hybrid orbitals, but it is also available for amidine and guanidine structures.

The corresponding functional groups are as follows

Acidic functional group: carboxyl group, phosphoric acid group, sulfonic acid group

Basic functional groups: Molecules with amine, amidine, and guanidine structures mixed with sp3.

In general, this option is selected by default in aqueous solution.

2. -h (Non-dissociation)

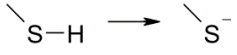
Updates hydrogen addition and formal charge information so that acidic/basic functional groups are non-dissociated.

3.-m (Metal coordination).

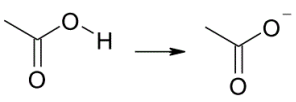
If the metal coordination option (-m) is specified, the hydrogenation and formal charge information is updated so that the specific structure is either dissociated or non-dissociated.

Corresponding structures are as follows

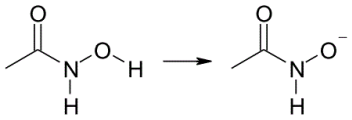
・thiol



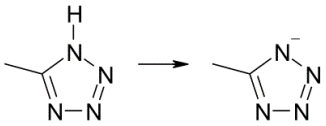

・carboxylic acid



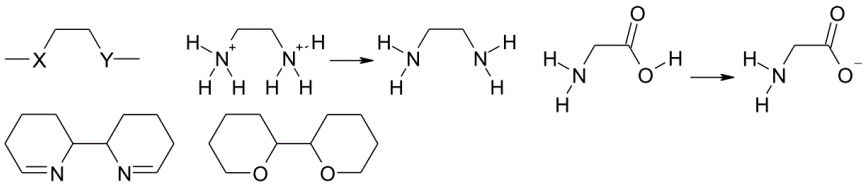
・Hydroxamic acid



・Tetrazole



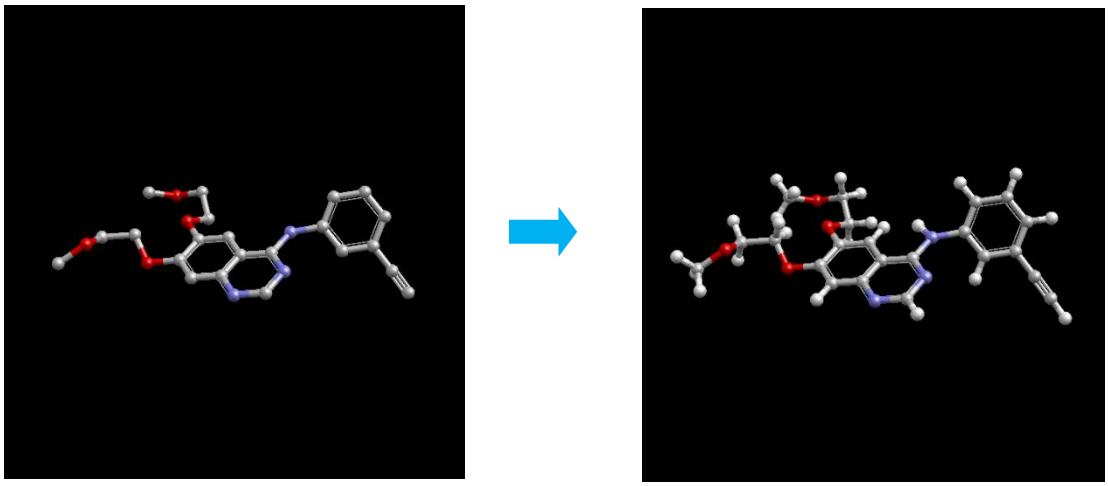
・Chelate type (X,Y are O or N, N is neutral, and those with 3 N bonds and planar structure are not included)



In this example, leave the default -p option and click OK.

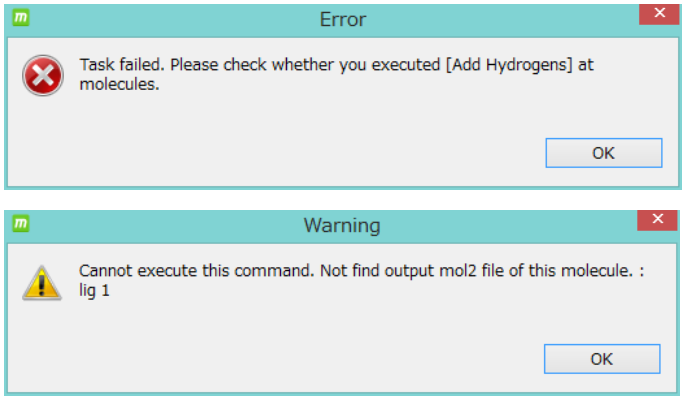
In this example, only one compound is read, but in a system with multiple compounds, multiple compounds can be read at the same time.

You can add or remove hydrogen atoms at once by selecting and performing the above operation.



### 4.24.5. Error when editing compounds

If you see a warning dialog similar to the following when editing a compound, it indicates that it is chemically unedictable.  Therefore, myPresto, which is used as the calculation engine, cannot run.



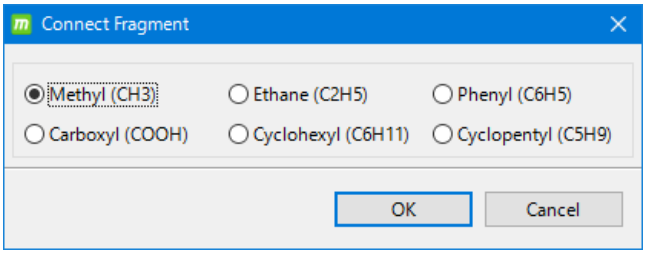

In this case, it is necessary to change the content and procedure of editing to avoid the error.
If it still cannot be executed, it is a molecule that cannot be calculated by myPresto, so delete it from the system.

As a workaround, you may be able to avoid the error by adding a hydrogen atom with  [Add Hydrogens] and then executing it, or by deleting a hydrogen atom with  [Delete Hydrogens] and then executing it.

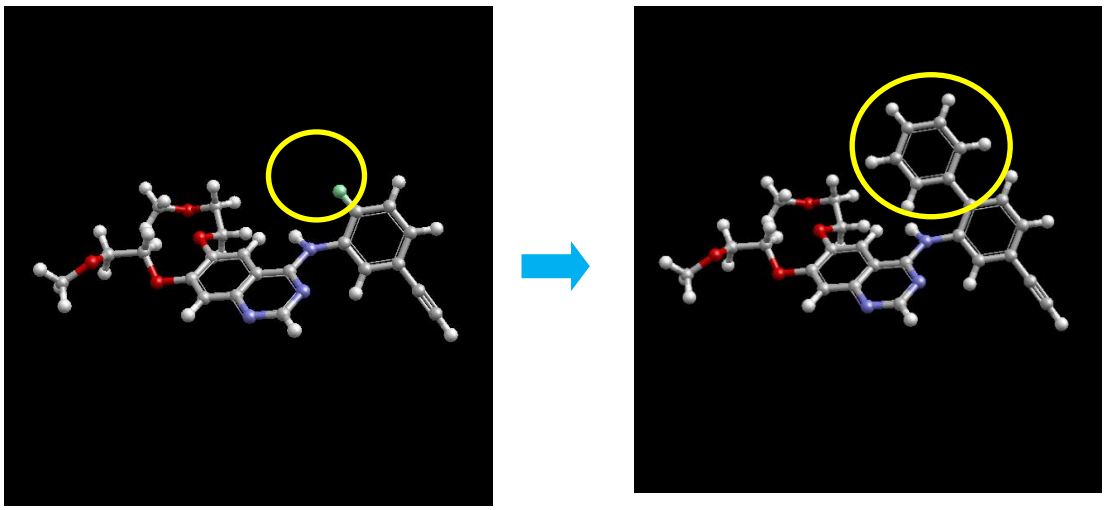
### 4.24.6. Adding chemical structures

Describes how to add a chemical structure.

When  [Connect Fragment] is executed with one atom selected, one of the following chemical structures is added to the selected atom (or the hydrogen atom bonded to the selected atom if it is not a hydrogen atom).

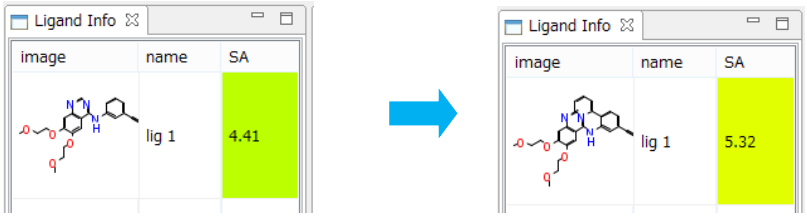



Methyl (CH3)
Ethane (C2H5)
Phenyl (C6H5)
Carboxyl (COOH)
Cyclohexyl (C6H11)
Cyclopentyl (C5H9)



Select hydrogen atoms

Add Phenyl(C6H5 )



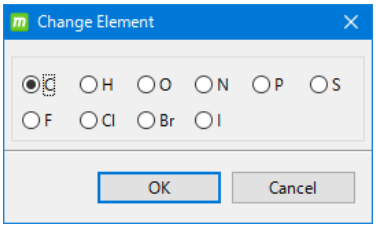

Updates the ligand info screen's 2D structural expression and SA(compositing ease) values.

- Be sure to add hydrogen atoms with [Add Hydrogens] before executing the command.to add
- An error will occur if [Connect Fragment] is executed when a hydrogen atom is not added to the compound.

### 4.24.7. Replacing atoms

Learn how to replace atoms.

You can replace the selected atom with one of C, H, O, N, P, S, F, Cl, Br, or I by executing  [Change Element] with one atom selected.



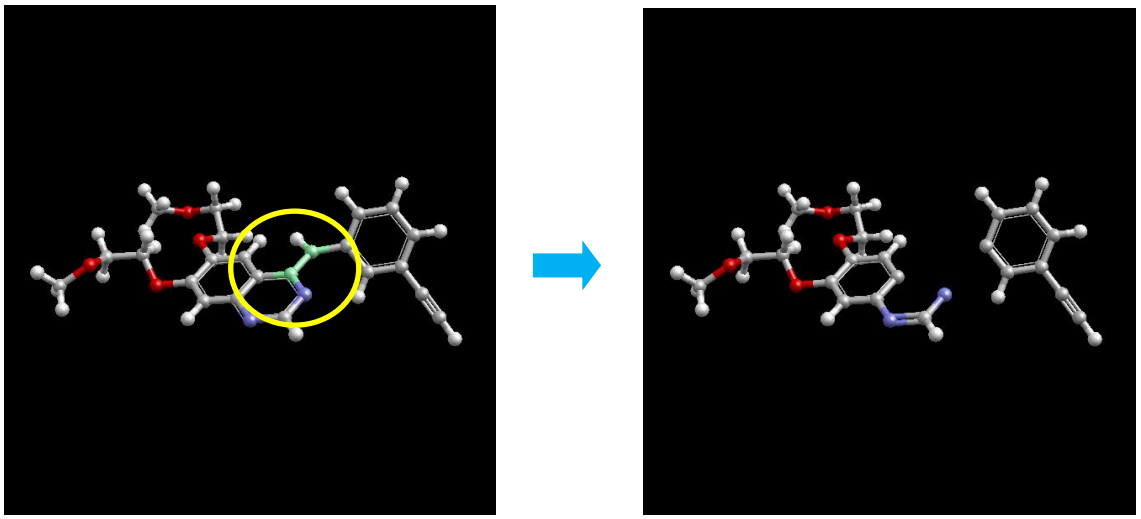

Since an inconsistent number of bonders after atom substitution will result in an error, it is recommended that the hydrogen atoms of the molecule be deleted beforehand by  [Delete Hydrogens] when substituting heavy atoms (other than hydrogen atoms).

### 4.24.8. Removing atoms

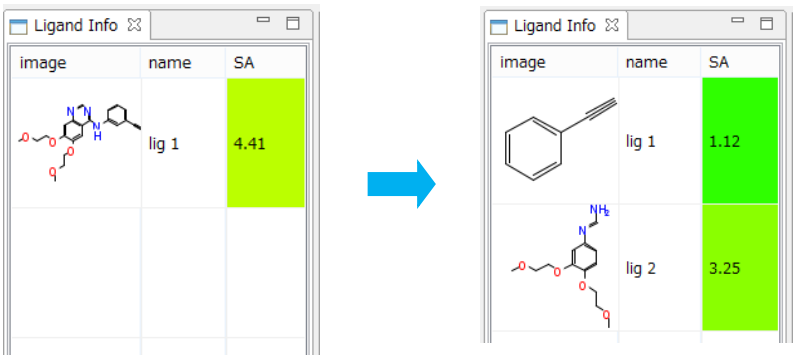
Describes how to delete atoms.

You can delete all at once by executing  [Delete] with one or more atoms selected.

As a result of deletion, if it is divided into multiple molecules, it will be divided.

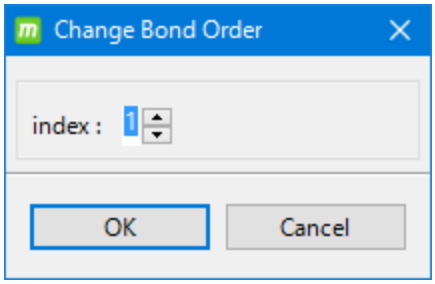


Select two atoms, delete divide them into two molecules.




### 4.24.9. Insert joins, change join number

Learn how to insert joins and change join levels.



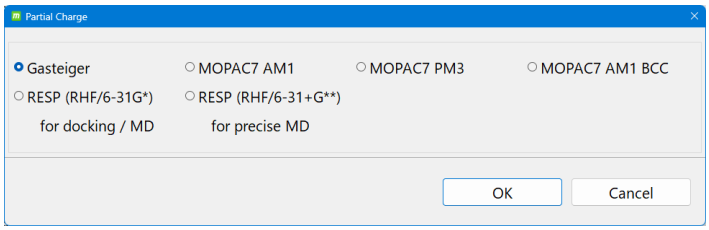

If you execute [Change Bond Order] with two atoms selected, you can insert bonds from 1st to 3rd order between atoms.
If a bond exists, the bond order is changed.

- It is recommended to delete hydrogen atoms with [Delete Hydrogens] before execution. An error will occur if there is a structural inconsistency after changing the join.

### 4.24.10. Charge calculation

Explains how to calculate the electrification of compounds or glycans.

If you execute  [Partial Charge] with any number of compounds or glycans selected, you can calculate the charge of all atoms of the selected compound or glycan at once.



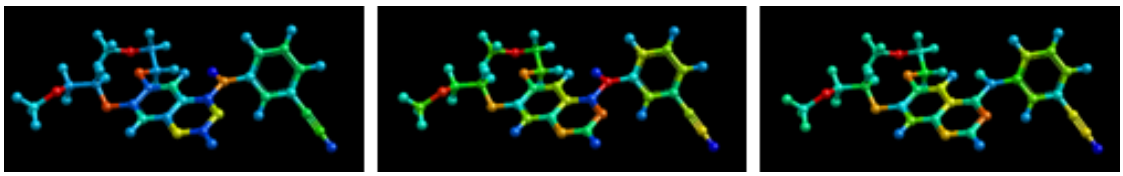

There are 6 approaches to choose from:

Gasteiger, MOPAC7 AM1, MOPAC7 PM3, MOPAC7 AM1-BCC, RESP (RHF/6-31G*), RESP (RHF/6-31+G**)

Gasteiger, MOPAC7 AM1, MOPAC7 PM3, and MOPAC7 AM1-BCC are calculated by Hgene program.
RESP (RHF/6-31G*), RESP (RHF/6-31+G**) is calculated with the AB-initio quantum science program Platypus-QM.

The calculated charge is filled in in the mol2 file.

Gasteiger MOPAC7 AM1 MOPAC7 PM3

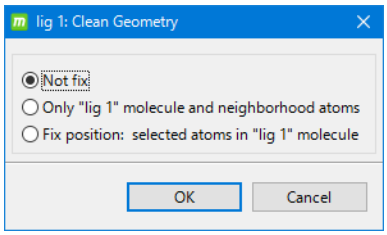


[Color]-[Atoms]-[Charge] to display Color

### 4.24.11. Structural optimization

Describes how to optimize the structure.

If you execute  [Clean Geometry] with a compound or glycan selected, you can perform a structure optimization calculation by cosgene for the selected compound or glycan.




Here's a description of the calculation method choices:

| choice | Explanation |
|---|---|
| Not fix | Structural optimization of only selected compounds or glycans in vacuum, without constraints |
| Only " Molecular Name " molecular and neighborhood atoms | Structure optimization by moving all atoms in the selected compound or glycan and its surroundings (within a cutoff radius of 8.25 Å) and in the pocket, and fixing the rest. |
| Fix position: selected atoms in [ molecular name ] molecular | Position-constrains any atom in the selected compound or glycan and structurally optimizes only the compound<br>※* Select the atom whose position you want to constrain on the 3D screen and click [OK]. |

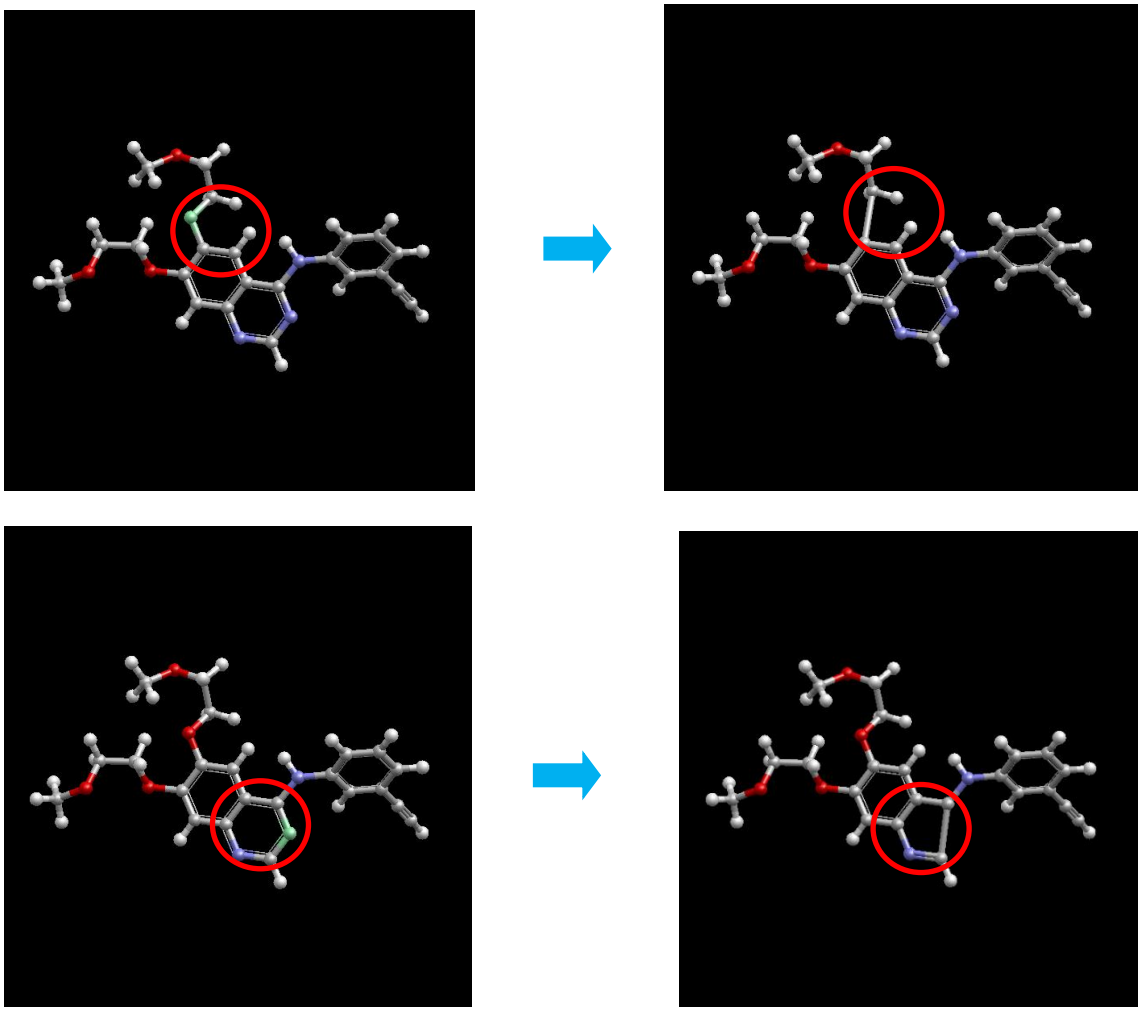
※ The structure optimization calculation of a compound or glycan tends to be easier when a hydrogen atom is not added than when a hydrogen atom is added.
If the structure optimization fails with hydrogen atoms added, try deleting the hydrogen atoms with  [Delete Hydrogens] and then performing the structure optimization  [Clean Geometry].
After that, add hydrogen atoms with  [Add Hydrogens] and perform structural optimization again.

### 4.24.12. Extraction of atoms

Describes how to delete an atom while preserving the bond.

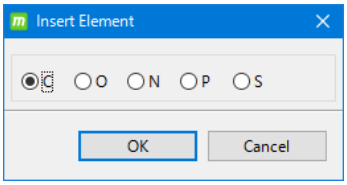
You can delete an atom by executing  [Extract Element] with one atom selected. If the atom belongs to a straight line or a ring, the bond is retained.

Unlike  [Delete], the molecule is not fragmented.

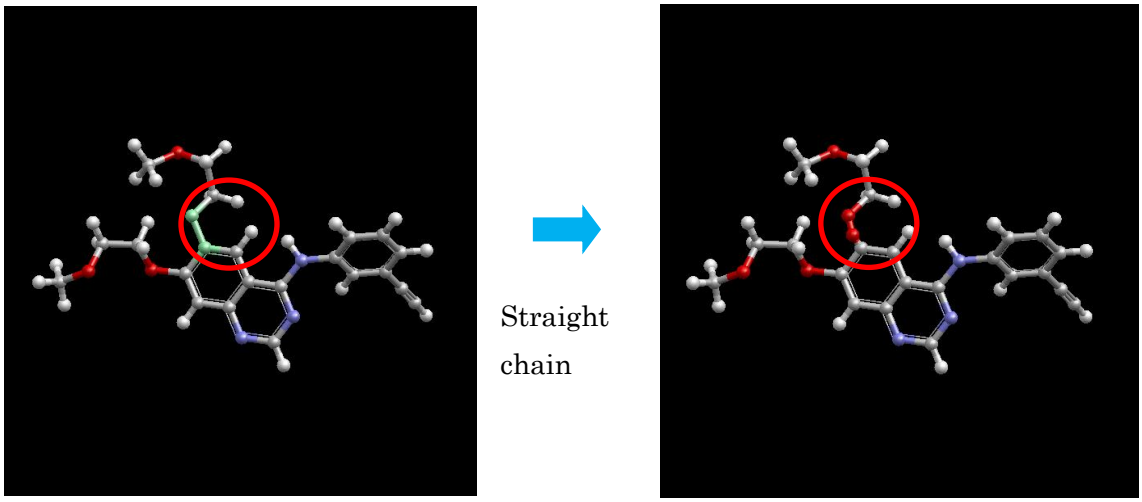


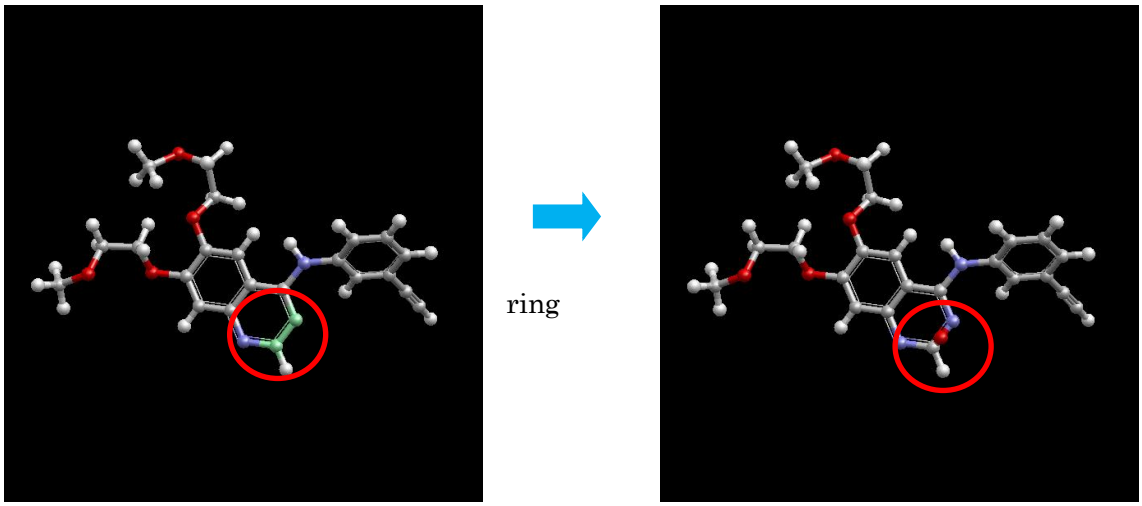
### 4.24.13. Inserting atoms

Describes how to insert atoms while maintaining bonding.




You can insert any of the C, O, N, P, or S atoms between them by running [Insert Element] with the two atoms selected. If the atom belongs to a straight line or a ring, the bond is retained.



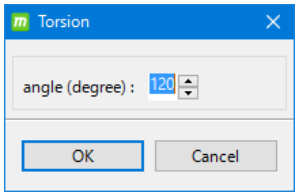



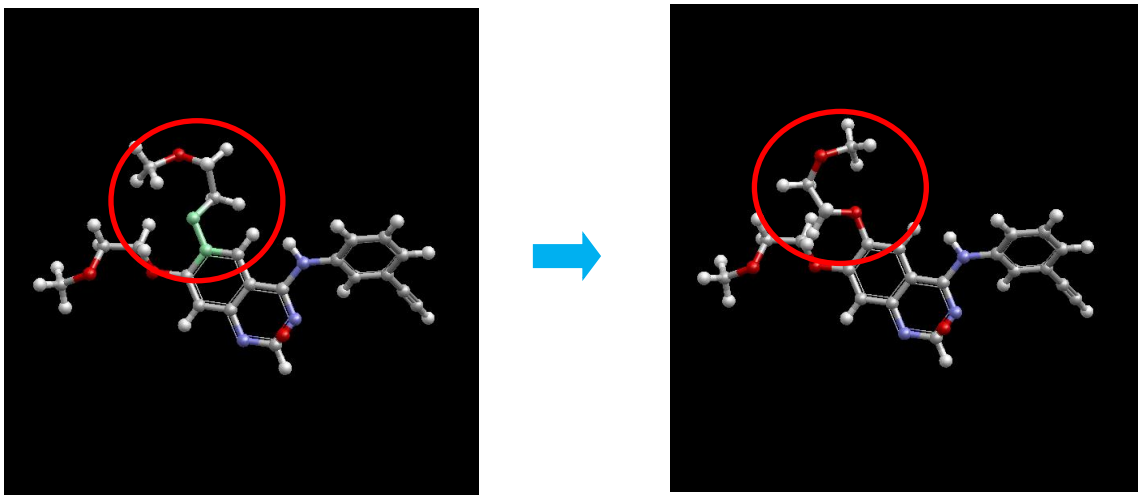

Insert oxygen atoms

### 4.24.14. Rotate join

Describes how to rotate bonds between atoms.

You can rotate the bond between two atoms by any angle by executing  [Torsion] with the two atoms being bonded specified.



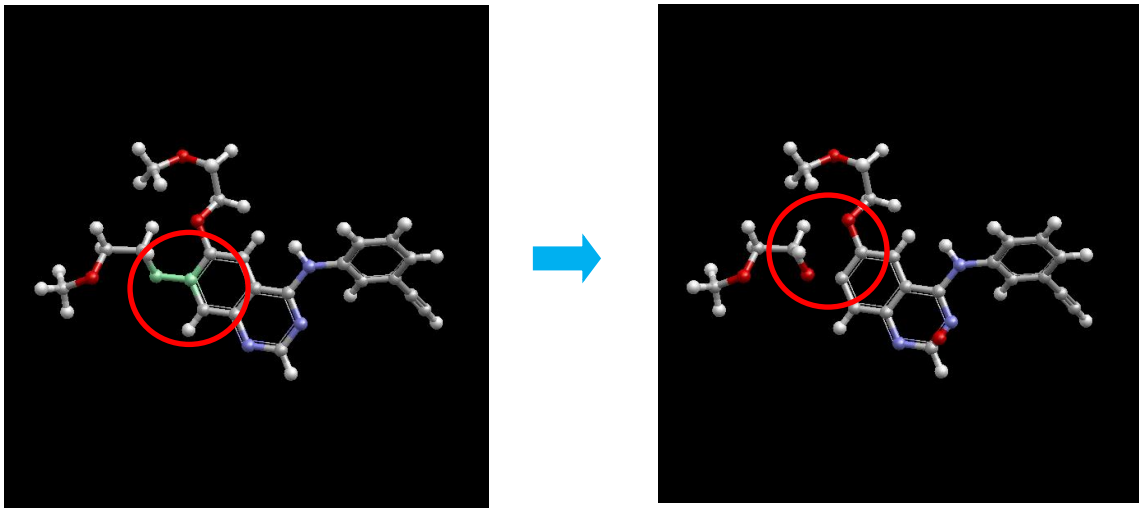



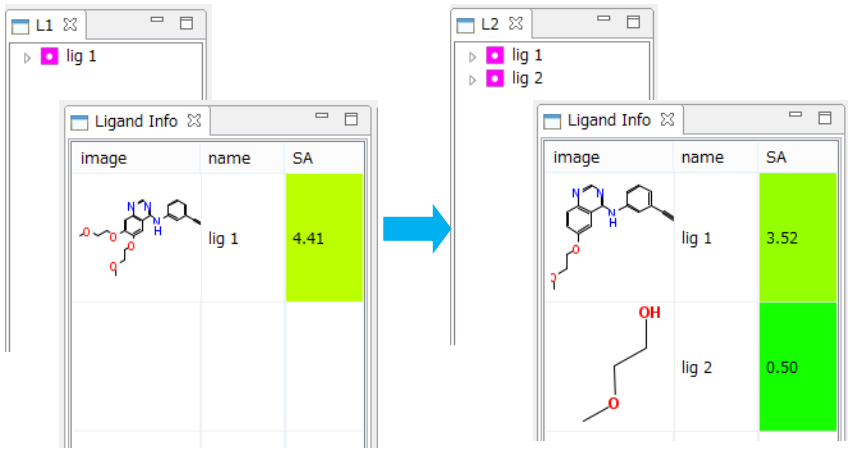
180 degree rotation

### 4.24.15. Delete a join

Describes how to remove the linear bond.

You can delete the linear bond between two atoms by executing  [Delete Bond] with the two atoms bonded in a linear bond selected.



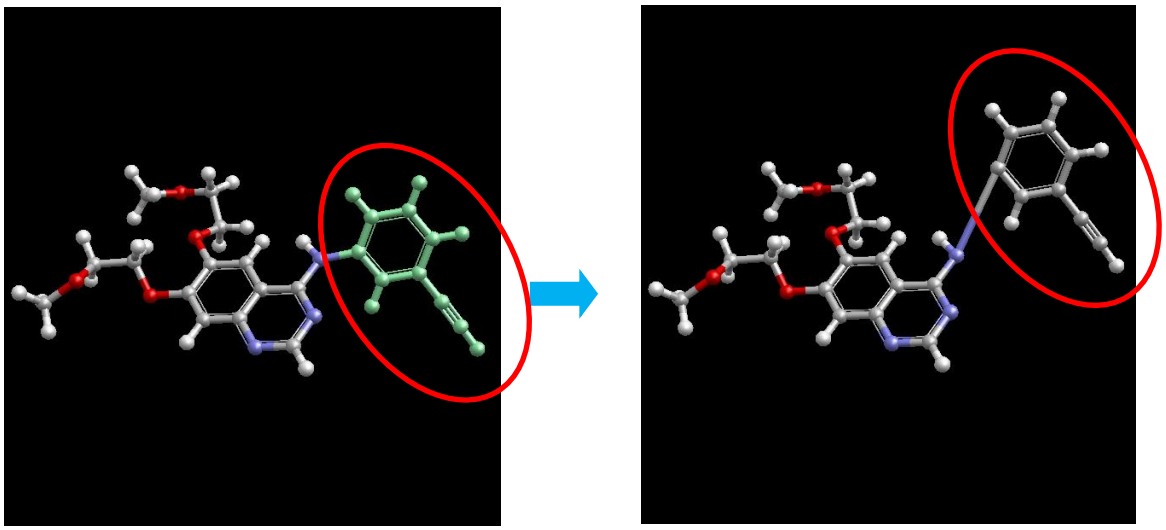



**[Delete Bond] You can only delete straight-chain joins in . An error occurs when attempting to remove a bond in an aromatic ring.**

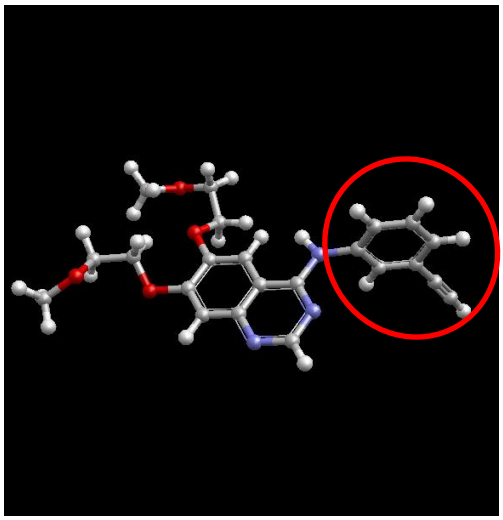
### 4.24.16. Movement and rotation of atoms

Explains how to move and rotate atoms (groups).

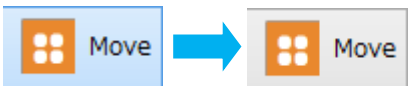
You can translate or rotate the selected atoms (groups) by executing [Move] with one or more atoms selected.



Move side by right drag



Rotate with left drag




After the operation, click to release the Move mode .

## 4.25. Three-dimensionalization of compounds

Prepa ration can be used to make a two-dimensional compound three-dimensional. You can also combine multiple input files up to 999 into one and use it as a ligand input file for docking calculations.

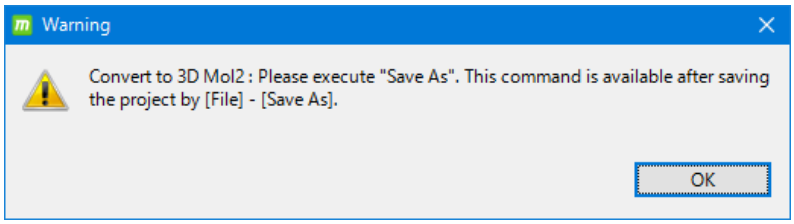
### 4.25.1. Three-dimensionalization of compounds

You can convert specified filea into 3D Mol2 files in three dimensions.

* If the input file is SMILES, the yield will be lower than in the case of input files of other formats.

[Convert to 3D Mol2] makes the coordinates of multiple sdf / mol / mol2 / SMILES files three-dimensional and generates one mol2 file for each molecule. It also merges all the generated mol2 files to create an all.mol2 file.
The procedure is as follows.

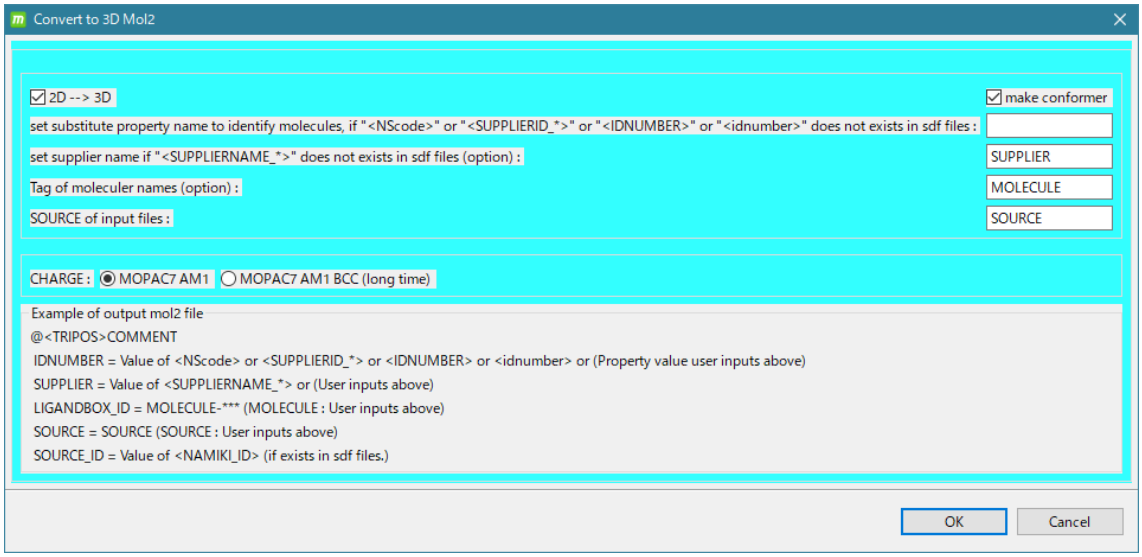
①If you have not created a project, create an arbitrary project by referring to "5.4.1 [File]-[New Project]". Save the project by referring to "5.6.1 [File]-[Save As]". If you execute the following [Convert to 3D Mol2] without saving the project, the following warning dialog will appear.




※ Depending on the size of the input file, a large capacity may be required, so the user specifies the storage location.

※ If the file name of the compound to be entered contains machine-dependent characters, it may not be processed normally. Do not include machine-dependent characters in the file name.

② When you click  [Convert to 3D Mol2], the following dialog will appear. Select the setting conditions for 3D conversion.




Second line,
[set substitute property name to identify molecules, if "<NScode>" or "<SUPPLIERID_*>" or "<IDNUMBER>" or "<idnumber>" does tag does not exists in sdf file :]
Since it is important to enter the character string of, it will be explained in detail below.

This is a useful feature when entering an sdf file. It does not matter for molecular files of other formats.

First, check the contents of the input sdf file with a text editor or the like.

※ If you want to open the sdf file on Windows and check the contents, the free software TeraPad is convenient.

If there is a description of NScode or SUPPLIERID_ * or IDNUMBER or idnumber as the property name as additional information in the sdf file, that is,

```
> <NScode>
***
```

```
> <SUPPLIERID_*>
***
```

```
> <IDNUMBER>
***
```

```
> <idnumber>
***
```

(However, * is an arbitrary string)

When the above is described, MolDesk describes the character string of the above property value of the sdf file in the ID NUMBER = of the comment line of the automatically generated mol2 file as follows.
This makes it possible to identify the output molecule.

(mol2 file description example)

```
@<TRIPOS>COMMENT
 LIGANDBOX_ID = MOLECULE-00000001-01
 SUPPLIER = SUPPLIER
 SOURCE = SOURCE
 IDNUMBER = NS-000000001-0001
 MOLECULAR_FORMULA = C8H9NO4
 MOLECULAR_WEIGHT = 183.163
 MOLECULAR_CHARGE = 0
 SUM_OF_ATOMNUMBER = 96
 SUM_OF_ATOMNUMBER_MINUS_CHARGE = 96
 NUM_OF_DONOR = 5
 NUM_OF_ACCEPTOR = 4
 HOMO = -9.2167
 LUMO = -0.5693
 NUM_OF_CHIRAL_ATOMS = 1

@<TRIPOS>MOLECULE
MOLECULE-00000001-01
 22 22 0 0 0
SMALL
USER_CHARGES

@<TRIPOS>ATOM
```

```
   1 C1        0.2340    0.2060   -0.1420 C.ar    1  LGD      -0.0357
   2 C2        1.5030   -1.9990    0.1260 C.2     1  LGD       0.3443
   3 C3        1.5630   -0.5300   -0.3070 C.3     1  LGD      -0.1662

. . .
```

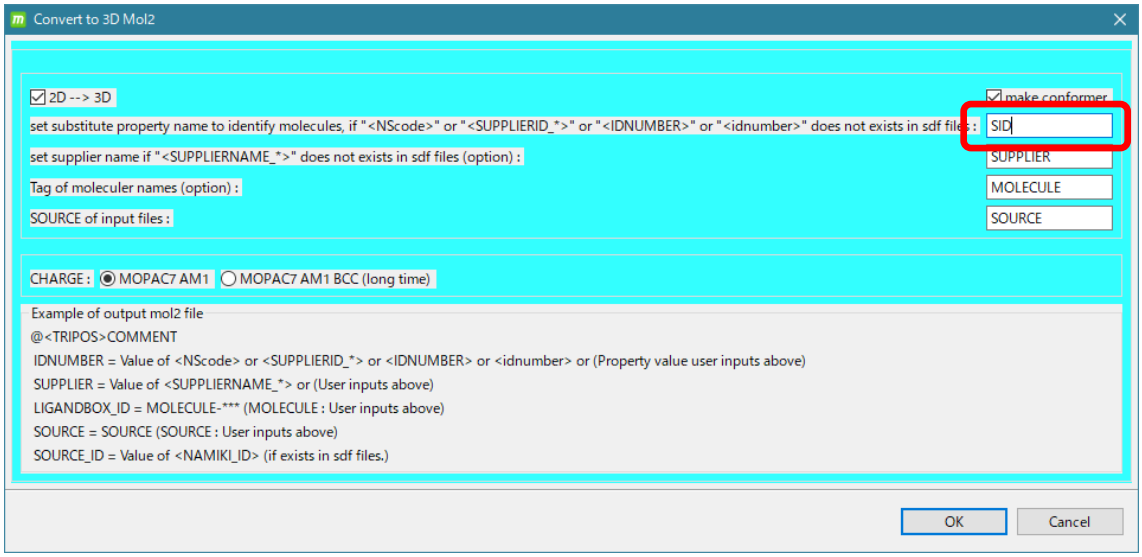
Now, let's say that the molecular description of the input sdf file is as follows, as additional information, as a property name, there is no description of NScode or SUPPLIERID_* or IDNUMBER, or idnumber, andthere is only a deriscing of the property name SID.

```
  Mrv1622910011607582D

 14 13  0  0  0  0            999 V2000
    0.2198    0.0635    0.0000 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.9343   -1.1740    0.0000 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.9343   -0.3490    0.0000 C   0  0  0  0  0  0  0  0  0  0  0  0
    0.2198    0.8885    0.0000 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.4946   -0.3490    0.0000 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.2091    0.0635    0.0000 C   0  0  0  0  0  0  0  0  0  0  0  0
   -0.4946    1.3010    0.0000 C   0  0  0  0  0  0  0  0  0  0  0  0
   -1.2091    0.8885    0.0000 C   0  0  0  0  0  0  0  0  0  0  0  0
    1.6488   -1.5865    0.0000 O   0  0  0  0  0  0  0  0  0  0  0  0
    1.6488    0.0635    0.0000 N   0  0  0  0  0  0  0  0  0  0  0  0
    0.2198   -1.5865    0.0000 O   0  0  0  0  0  0  0  0  0  0  0  0
   -1.9236   -0.3490    0.0000 O   0  0  0  0  0  0  0  0  0  0  0  0
   -0.4946    2.1260    0.0000 O   0  0  0  0  0  0  0  0  0  0  0  0
    3.6524    0.0000    0.0000 Cl  0  0  0  0  0  0  0  0  0  0  0  0
  2  3  1  0  0  0  0
  3  1  1  0  0  0  0
  4  1  2  0  0  0  0
  5  1  1  0  0  0  0
  6  5  2  0  0  0  0
  7  4  1  0  0  0  0
  8  6  1  0  0  0  0
  9  2  2  0  0  0  0
 10  3  1  0  0  0  0
 11  2  1  0  0  0  0
 12  6  1  0  0  0  0
 13  7  1  0  0  0  0
  8  7  2  0  0  0  0
M  END
>  <SID>
NS-000000001-0001

$$$$
. . .
```

In this sdf file, IDNUMBER = cannot be described in the output mol2 file as it is, so the numerator of the input sdf file and the output mol2 file are not linked.

Therefore, instead, the description of the property name SID will be described as ID NUMBER = in the comment line of the mol2 file.

In that case, as shown below, on the second line,
[set substitute property name to identify molecules, if "<NScode>" or "<SUPPLIERID_*>" or "<IDNUMBER>" or "<idnumber>" does tag does not exist in sdf file :]
Describe the SID and the above property name in.




If the property name of the input sdf file is blank, it is not recognizedasa property  name.

> <entry name>
molecule.001

In this case, for example, replace the tag name of the sdf file in bulk with an editor, for example, to eliminate white space before using it.

> <entry_name>
molecule.001

The description of each setting item is as follows.

| item | substance |
|---|---|
| 2D → 3D | If checked, it will be three-dimensional.<br>Follow the procedure below to make it three-dimensional.<br>AMBER GAFF2 Performs three-dimensional calculation by energy minimization calculation by force field. At that time, H atom is added and electric charge is generated. The addition of H atoms is such that acidic / basic functional groups are dissociated in water, and the charge is generated by MOPAC7 AM1.<br>If unchecked, 3D will not be performed. At this time, the Mol2 file is output by reflecting the original structure as it is without adding H atoms or generating electric charges. Also, the COMMENT line is not added. If the molecule does not need to be three-dimensionalized because it has already been three-dimensionalized, uncheck it. |
| make conformer | Check if you want to generate a molecular conformer when making it three-dimensional. Generated for the part of the ring structure with 4 or more member rings. If a chiral center is present in the molecule, an optical isomer is also generated at the same time. |
| set substitute property name to identify molecules, if "<NScode>" or "<SUPPLIERID_*>" or "<IDNUMBER>" or "<idnumber>" does tag does not exists in sdf file : | When the property name of <NScode> or <SUPPLIERID_*> or <IDNUMBER> or <idnumber> does not exist in the input sdf file, describe the property value of another property name in the output mol2 file as IDNUMBER =. Enter another property name that you want to be recognized as IDNUMBER. If there is no entry, the above three property names are automatically determined and set as ID NUMBER.<br>If the above three property names do not exist and the user-input alias property name does not exist, IDNUMBER = is not added to the output mol2 file (again, it can be three-dimensionalized, but the numerator and output of the input sdf file). Molecules in mol2 files cannot be linked). |
| CHARGE: | Select a method for generating the charge to be added to the molecule from MOPAC7 AM1 or MOPAC7 AM1BCC. For MOPAC7 AM1BCC, the calculation time is long. |

The following are options: The specification is not required.

| item | substance |
|---|---|
| Set supplier name if "<SUPPLIERNAME_*>" does not exists in sdf files | When <SUPPLIERNAME_ *> does not exist in the input sdf file, the character string input here can be recorded as SUPPLIER = in the output Mol2 file (it cannot be specified for each molecule).<br>If <SUPPLIERNAME_ *> exists in the input sdf file, that description takes precedence and is described as SUPPLIER = in the output Mol2 file.<br>(The SUPPLIER part below). |
| Tag of moleculer name | Specify the tag to be added to the beginning of the molecule name. The molecule name is the character string described in the next line of @ <TRIPOS> MOLECULE in the output Mol2 file.<br>(MOLECULE part below).<br>This is the molecular recognition ID number that the program independently generates. |
| SOURCE of input files | Specifies the source of the input file.<br>It is described as SOURCE = on the COMMENT line of the output Mol2 file.<br>(The SOURCE part below). |

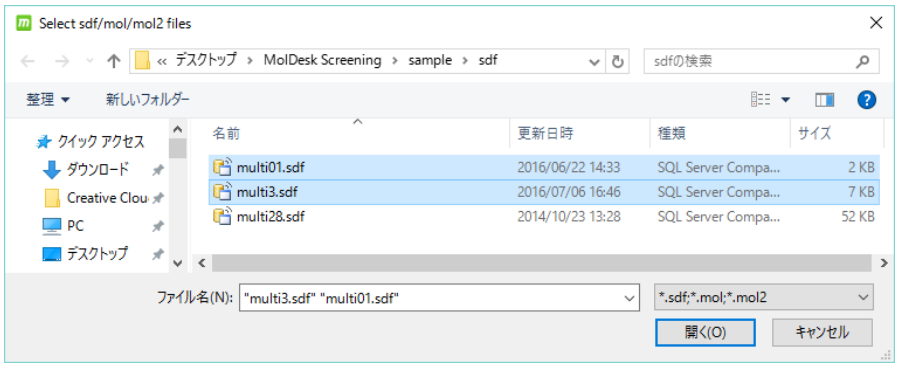
(example mol2 file description)

```
@<TRIPOS>COMMENT
 LIGANDBOX_ID = MOLECULE-00000001-01
 SUPPLIER = SUPPLIER
 SOURCE = SOURCE
 IDNUMBER = NS-000000001-0001
 MOLECULAR_FORMULA = C8H9NO4
 MOLECULAR_WEIGHT = 183.163
 MOLECULAR_CHARGE = 0
 SUM_OF_ATOMNUMBER = 96
 SUM_OF_ATOMNUMBER_MINUS_CHARGE = 96
 NUM_OF_DONOR = 5
 NUM_OF_ACCEPTOR = 4
 HOMO = -9.2167
 LUMO = -0.5693
 NUM_OF_CHIRAL_ATOMS = 1

@<TRIPOS>MOLECULE
MOLECULE-00000001-01
```

③ (3) Click "OK" to display the file selection dialog. Select the file to be converted to a 3D mol2 file.

In this example, MolDesk Basic was created on the desktop when MolDesk was installed.
Select the following 2 files in the folder.

MolDesk Basic-> sample-> sdf-> multi01.sdf ：Contains one molecule of compound
MolDesk Basic-> sample-> sdf-> multi3.sdf ：Contains 3 molecules of compounds




It is also possible to specify multiple files in different formats. The file formats that can be selected are sdf / mol / mol2. They must be in the same folder.

- If the file name contains more than one period, a warning dialog will appear. In that case, change the file name as appropriate.

④ Click [Open] to make the coordinates of the selected file three-dimensional and convert it into multiple mol2 files for the number of molecules.
In the three-dimensionalization of coordinates, the energy minimization (structural optimization) calculation by the AMBER GAFF2 force field is performed for each molecule.

⑤ When the 3D calculation is completed, a mol2 file will be generated under the folder where the project is saved.
If the folder where the project is saved is [PROJECT], a folder named "mol2_files" will be created under [PROJECT]-> work-> database.

Folders for each molecule are created with serial numbers under the "mol2_files" folder, and mol2 files for each conformer are output with serial numbers in the folders for each molecule.

[PROJECT] -> work -> database -> mol2_files -> 3d001 -> 00000001-01.mol2
00000001-02.mol2
[PROJECT] -> work -> database -> mol2_files -> 3d002 -> 00000002-01.mol2
00000002-02.mol2
00000003-01.mol2
00000004-01.mol2

The naming rules for mol2 files are as follows.
[Molecular number (serial number)]-[Comformer number (serial number)] .mol2

The file all.mol2, which combines these into one multi mol2 file, is also output directly under the "mol2_files" folder.

[PROJECT]-> work-> database-> mol2_files-> all.mol2

In the generated mol2 file, various characteristic values and titles of the molecule (in red in the figure below) are described.

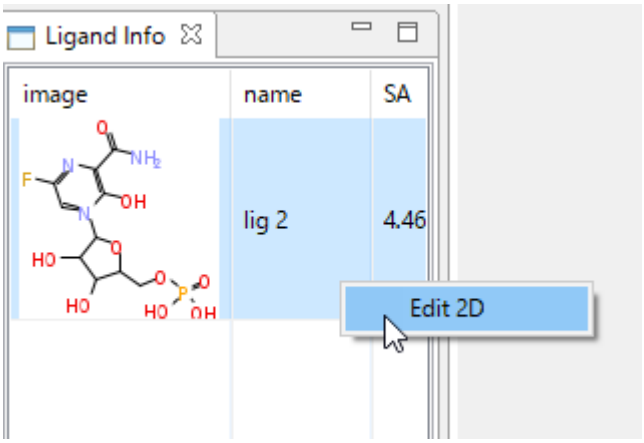
```
@<TRIPOS>COMMENT
 LIGANDBOX_ID = MOLECULE-00000001-01
 SOURCE = SOURCE
 SOURCE_ID = NS-00204087
 SUPPLIER = ENAMINE
 IDNUMBER = Z44490869
 MOLECULAR_FORMULA = C13H18N3O
 MOLECULAR_WEIGHT = 232.307
 MOLECULAR_CHARGE = 1
 SUM_OF_ATOMNUMBER = 125
 SUM_OF_ATOMNUMBER_MINUS_CHARGE = 124
 NUM_OF_DONOR = 3
 NUM_OF_ACCEPTOR = 2
 HOMO = -12.2444
 LUMO = -4.4651
 NUM_OF_CHIRAL_ATOMS = 1
 NOTE = ENAMINE_Z44490869;Enamine(Fragment)_Z44490869;

@<TRIPOS>MOLECULE
MOLECULE-00000001-01
35 36 0 0 0
```

```
SMALL
USER_CHARGES

@<TRIPOS>ATOM
     1 C1              4.1340     -1.4790     -0.0090 C.2          1   LGD
0.3417
     2 N2           3.0250    -0.7110     0.0090 N.am       1  LGD         -
0.3345
     3 N3           4.2490     1.2640    -0.0030 N.2        1  LGD         -
0.1475
. . .
```

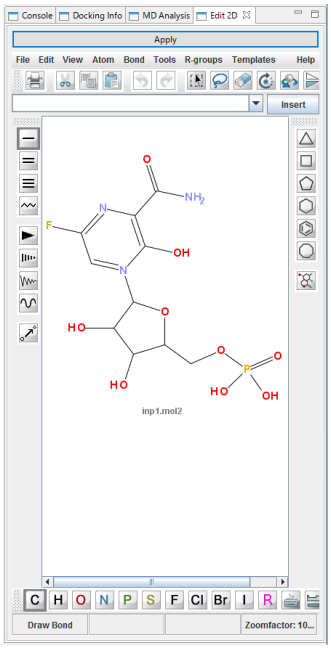
## 4.26. Compound 2D Editor

Right-clicking on a compound or glycan on the Ligand Info screen will bring up the Edit 2D menu. Click this to enter the selected compound or glycan and launch the 2D editor JChemPaint. The version is 3.3-1210 (currently the latest version).

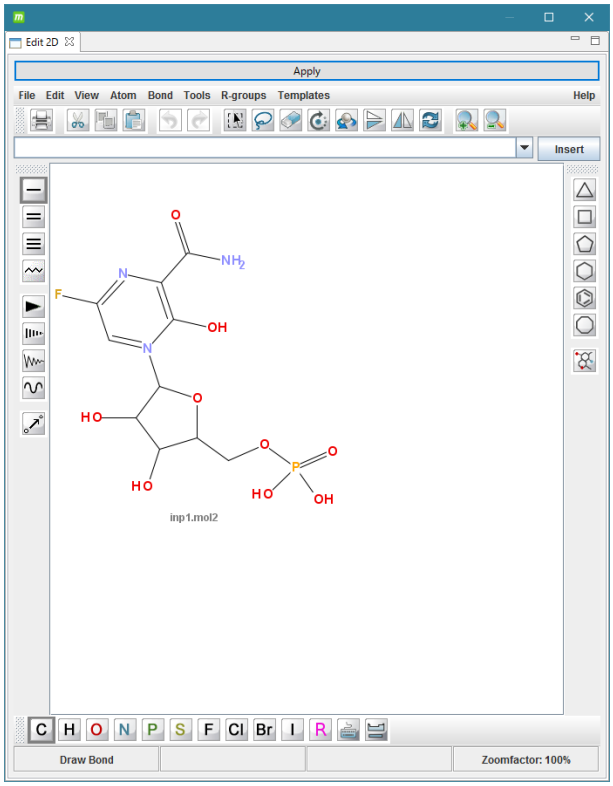
### 4.26.1. Start JChemPaint




The 2D editor J Chem Paint startswiththe selected compound or glycan as the input.




When the screen is small, you can drag the tab out of the MolDesk screen with the mouse to pull the screen out and use it larger.




After editing, click the [Apply] button at the top of the menu to make the edited molecule three-dimensional and import it into MolDesk.

For information on how to use JChemPaint, refer to the JChemPaint Help menu.

## 4.27. Protein editing

You can edit the protein with 

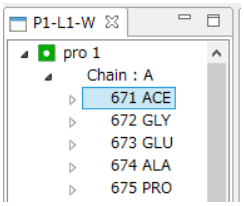
. The residue number of the original PDB file is saved after editing.

### 4.27.1. Terminal treatment

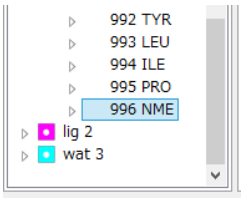
This section describes the procedure for terminal treatment of proteins.

If you execute  [Cap with ACE and NME] with a protein selected, the ACE residue will be placed at the N-terminus of the selected protein and the NME residue will be placed at the C-terminus as appropriate.

It is recommended that the end treatment be performed before "5.26.2 Addition and removal of hydrogen atoms" described later. If a hydrogen atom is added first, an OXT atom will be added to the N-terminal and the NME terminal cannot be added.




The ACE base you add is one less than the base number at the beginning.




The nme base number you add is one greater than the end base number.

### 4.27.2. Addition and removal of hydrogen atoms

Learn how to add and remove hydrogen atoms to proteins.

When you run  [Add Hydrogens] with a protein selected, all missing hydrogen atoms are added to the selected protein.
This process is performed using myPresto's tplgeneX. At the same time, the charge is applied based on the force field specified by [Help]-[Preference]-[Molecule]-[tplgeneX],

and the charge is entered in the temperature factor line of the PDB with the second decimal place accuracy.

If you execute  [Delete Hydrogens] with a protein selected, all hydrogen atoms in the entire selected protein will be deleted.

### 4.27.3. Generate and delete S-S joins

When  [Create SS Bond] is executed with a protein selected, an SS bond is generated when the distance between the S atoms of the two CYS residues of the selected protein is 4.5 Å or less, and the SSBOND line is described in the PDB file. Will be done. The CYS residue that generated the S-S bond is converted to a CYSS residue.

Running  [Break S-S Bond] with a protein selected removes all S-S bonds in the selected protein and also removes the SSBOND line in the PDB file. The CYSS residue that was forming the S-S bond is converted to a CYS residue.

※ MolDesk generates an S-Sbond by default whenyou enter a protein.

### 4.27.4. Delete missing remaining

If you execute  [Delete Residue without Calpha] with a protein selected, the residue will be deleted if the main chain atom of the selected protein is missing.

### 4.27.5. Converting remaining files

Describes how to replace residues.

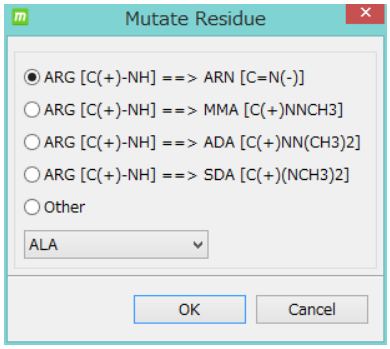
By executing  [Mutate Residue] with one residue in the protein selected, any amino acid in the protein can be converted into 40 types of chemically modified amino acids.

Please refer to the following site of MolDesk for the conversion table.
https://www.moldesk.com/moldesk-basic/#40

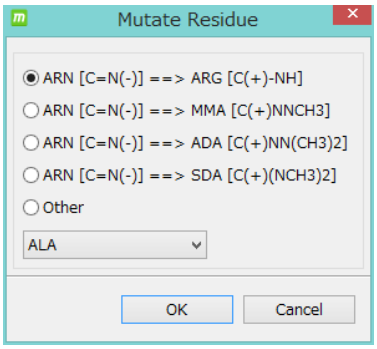
The residues that can be converted are displayed as follows. Select and click the residue you want to convert.

### ARG system

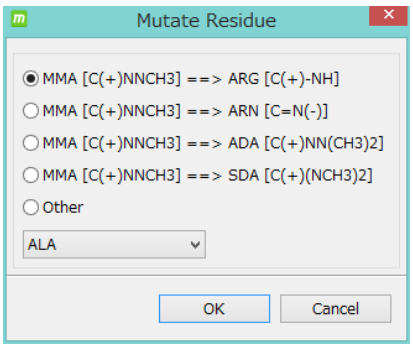
ARG



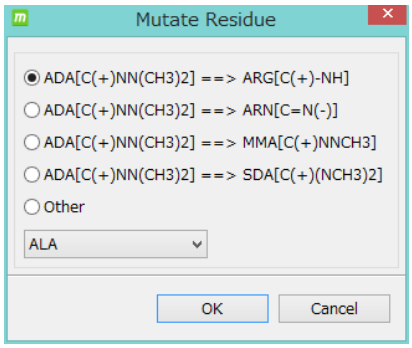

ARN



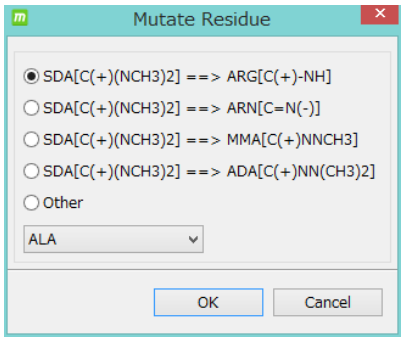

MMA




ADA

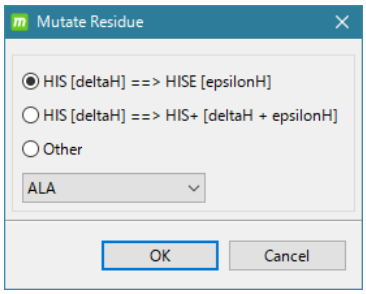



SDA



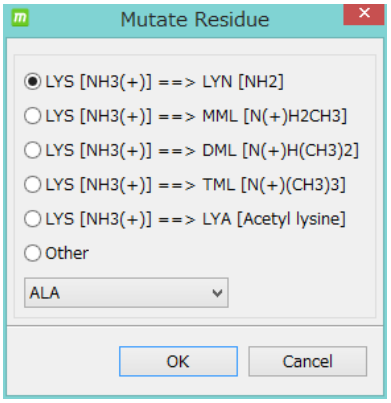

### HIS system

HIS

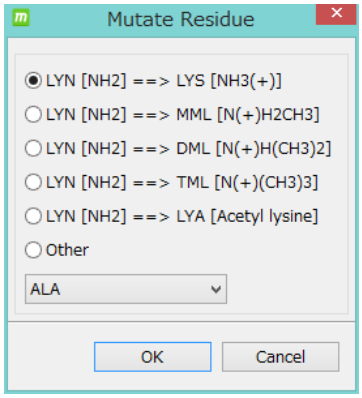


## LYS series

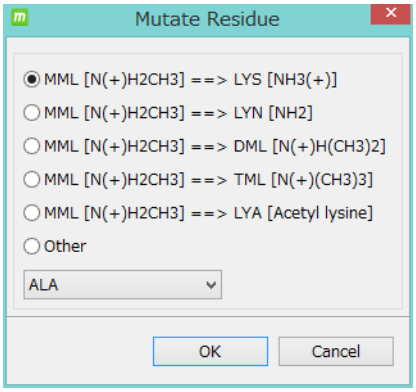
LYS



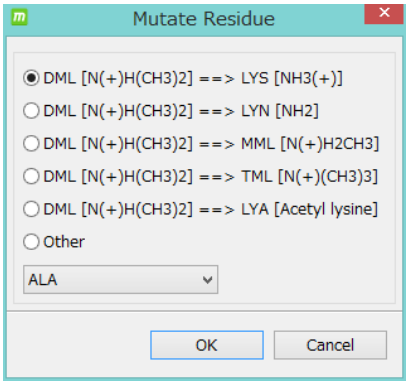

LYN



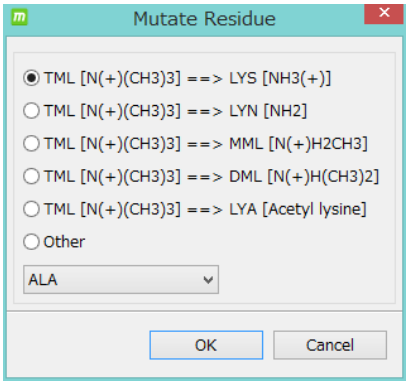

MML



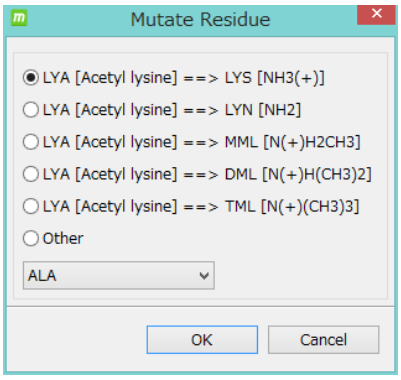

DML




TML

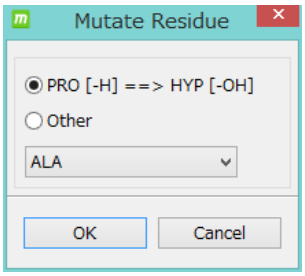



LYA

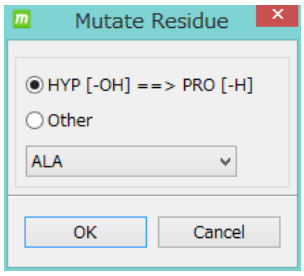



## PRO system

PRO

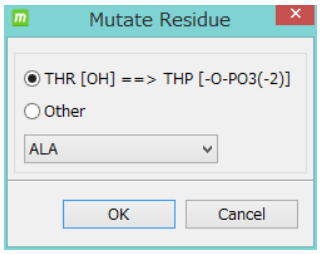



HYP

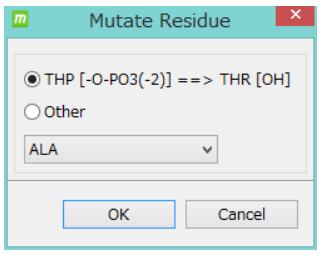



## THR system

THR

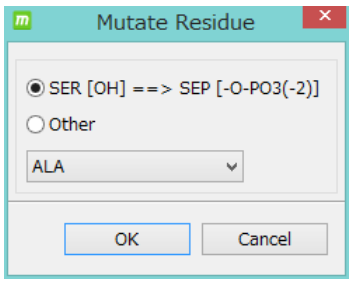



THP

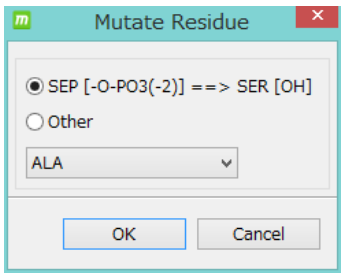


### SER system

SER

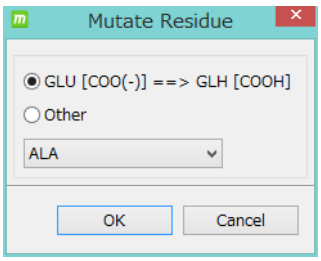



SEP

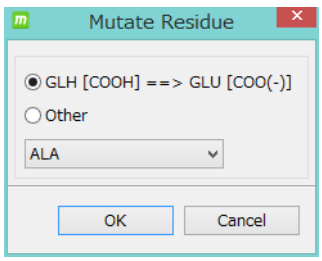



### GLU system

GLU

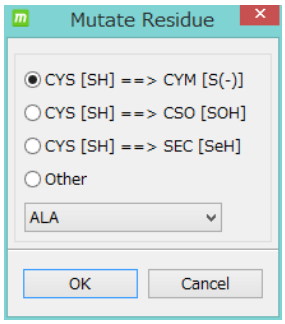



GLH

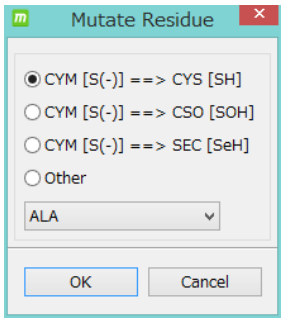



### CYS series

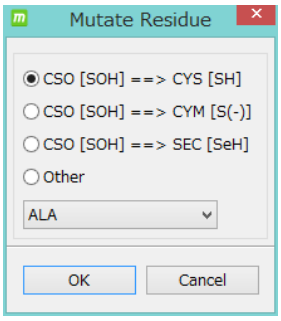
CYS



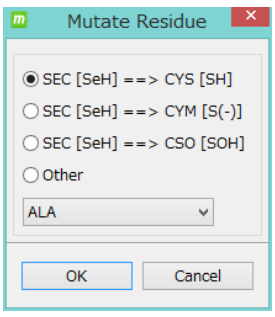

CYM



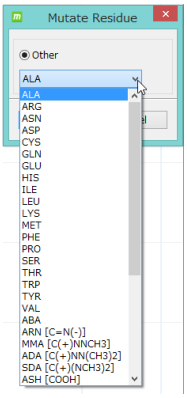

CSO




SEC



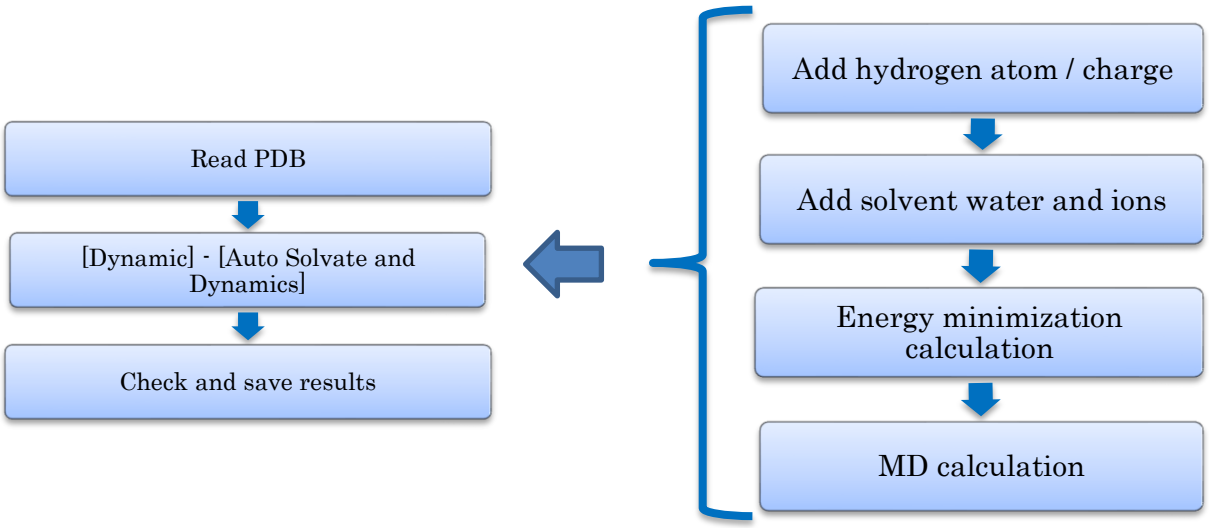

Others (lists all convertable rests)



## 4.28. MD calculation in water 1

The following is an example of executing the simplest MD calculation by automated calculation.

The procedure is as follows.




### 4.28.1. Load PDB files over the Internet

4.4.1Refer to "5.4.4 [File]-[Open Remote mmCIF / PDB]" and load the molecule with PDB ID "4kn6".

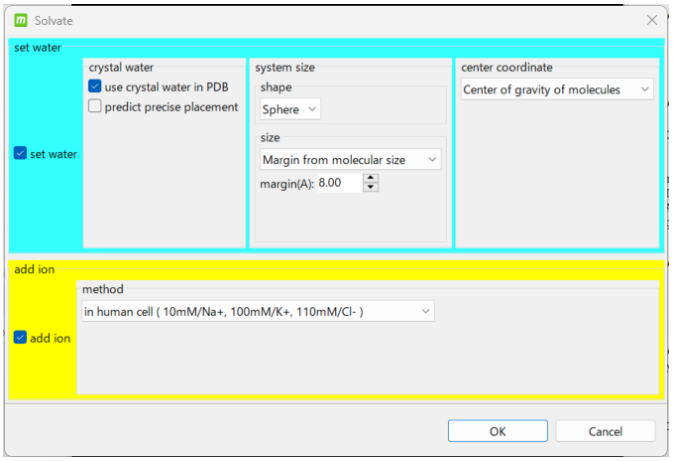
### 4.28.2. Fully automatic MD calculation

Select Dyna mics [Dynamics] - [Auto Solvate and Dynamics].

The processing is performed in the following order.

- Missing hydrogen atoms are added to all molecules.
- Charges are added to all compounds or glycans.
  - The charge is added by MOPAC7 AM1 (if the charge cannot be calculated by MOPAC7 AM1, the charge is added by Gasteiger).
- Charges are added to molecules other than compounds or glycans based on the force field selected by [Help]-[Preference]-[Molecule]-[tplgeneX].

- A dialog appears to select the method of adding a water solvent and ions.




In this example, the default settings are used.

About water solvent

-The center of gravity of the system is the center of the solvent, and the size is a sphere of 8 Å from the boundary of the solute.

About Ion

・ Ion concentrations in human cells, adding Na+, K+ and Cl-.

* In this example, the explanation is based on the case where a calculation engine other than GROMACS is selected as the MD calculation engine.
When GROMACS is selected, the water solubilizer is a Cube instead of a Sphere in order to calculate with periodic boundary conditions.

The explanation of the setting items are as follows.

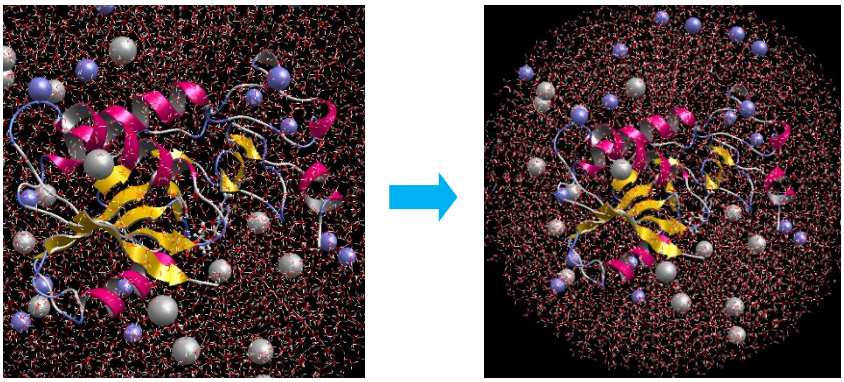
Select whether or not to Set water (add water solvents) by checking the check box.

| | | |
|---|---|---|
| crystal water | use crystal water in PDB | Include PDB crystalline water in the system |
| | predict precise placement | Generate crystalline water with good accuracy (requires several minutes of calculation time) |
| shape size | Sphere | margin (Distance from solute Å) |
| | | radius (Å) |
| | Cube | margin (Distance from solute Å) |
| | | x,y,z (x,y,z direction length Å) |
| center coordinate | Center of gravity | |
| | Setting of the central coordinate (User-specified coordinates) Specify the central atom with a mouse click) | |

Select whether to add ion (Na+, K+ and Cl- ion addition) or not with the check box.

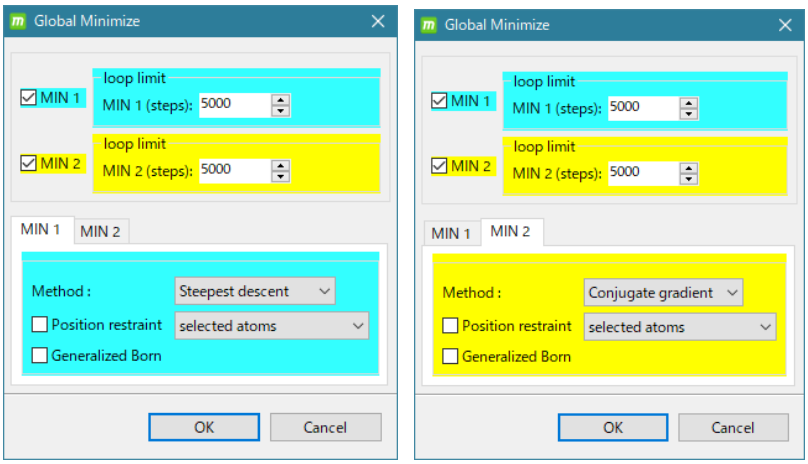
| | |
|---|---|
| method | direct input of number of ions |
| | minimum number of ions to neutralization |
| | saline solution<br>(0.00277/Na+, 0.00006/K+, 0.00283/Cl-) |
| | in human blood plasma<br>(154mM/Na+, 4mM/K+, 158mM/Cl-) |
| | in human cell<br>(10mM/Na+, 100mM/K+, 110mM/Cl-) |
| | in bacteria<br>(10mM/Na+, 200mM/K+, 210mM/Cl-) |
| | in densities of Na+, K+ and Cl- in mM |
| | in % densities of Na+, K+ and Cl-<br>(100mM=0.18015%) |

After specifying the water solvent and ion addition method and clicking "OK," the solvent water and ions are added.



Click  to display the entire system in the center of the screen.

The energy minimization calculation condition setting dialog is displayed.




In this example, the default is used. The meaning is as follows.

・Energy minimization calculation by cosgene is performed twice in succession.

・The first time is the steepest descent method, 5000 steps, no position constraint, no Generalized Born method

・ The second time is the conjugate gradient method, 5000 steps, no position constraint, no generalized Born method.

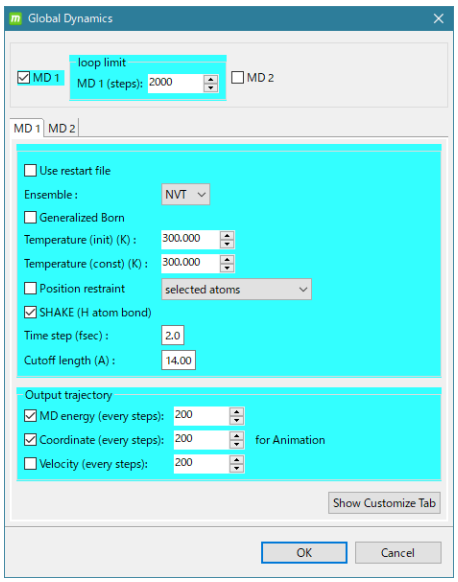
The energy minimization calculation can be performed twice in a row (uncheck MIN 1 or MIN 2 if you do not want to run it continuously).
Set MIN 1 for the first run and MIN 2 for the second run.

| | |
|---|---|
| loop limit（Number of time steps）Default 5000 | |
| Method | Steepest descent |
| | Conjugate gradient |
| Position restraint | Selected atoms<br>(Position constrains the atom (group) specified by the user with the mouse) |
| | Main chain (proteins & DNA/RNA) |
| | Heavy atoms (proteins & DNA/RNA) |
| Calculated by the Generalized Born method | |

- If GROMACS is selected as the calculation engine, the Generalized Born method cannot be calculated, so the checkbox for the Generalized Born method is not displayed.

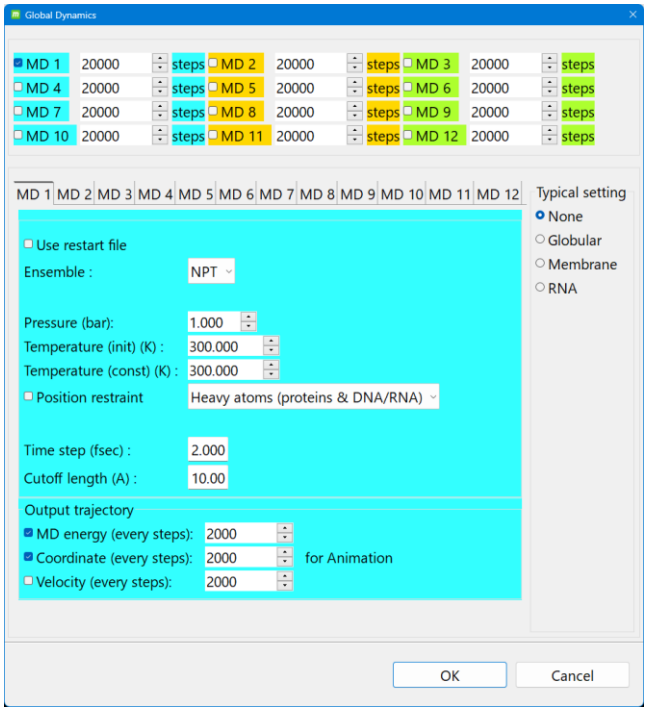
When the energy minimization calculation is completed, the MD calculation condition setting dialog is displayed.

This example runs with the default settings.




- Execute only once
- The number of steps is 2000
- NVT ensemble
- No Generalized Born method
- Initial temperature 300K
- 300K temperature constant
- No position constraint
- SHAKE calculation
- Time step is 2.0 fsec
- Cutoff radius is 14.0Å
- There is energy file output (Every 200 steps)
- Trajectory file output available(Every 200 steps)
- Long-distance Coulomb force calculation by FMM method

- The force field is set to AMBER GAFF2 for compounds or sugars and AMBER ff99SB for others (e.g. proteins) by default.
  (Force field can be changed by [Help] - [Preference] - [Molecule] - [tplgeneX])



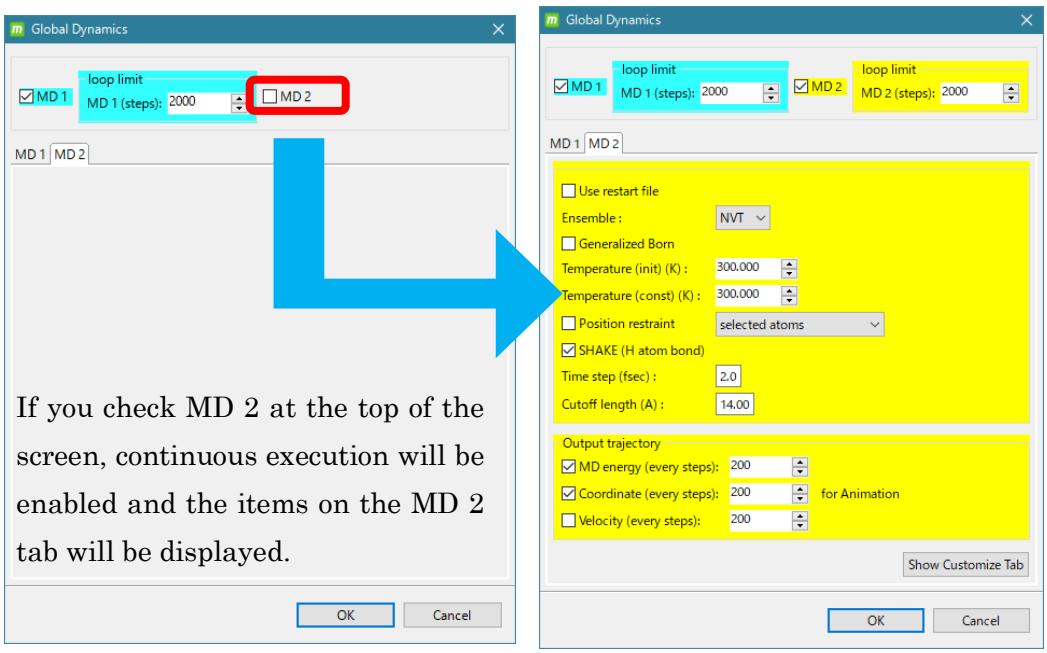

- When GROMACS is selected as the calculation engine, the dialog for setting conditions for MD calculation can be executed 12 times instead of 2 consecutive executions.
- When GROMACS is selected as the calculation engine, the Generalized Born and SHAKE checkboxes are not displayed because the Generalized Born and SHAKE methods cannot be used for calculation. Also, long-range Coulomb forces are calculated

using the PME method, not the FMM method. The default setting for the ensemble is the NPT ensemble.

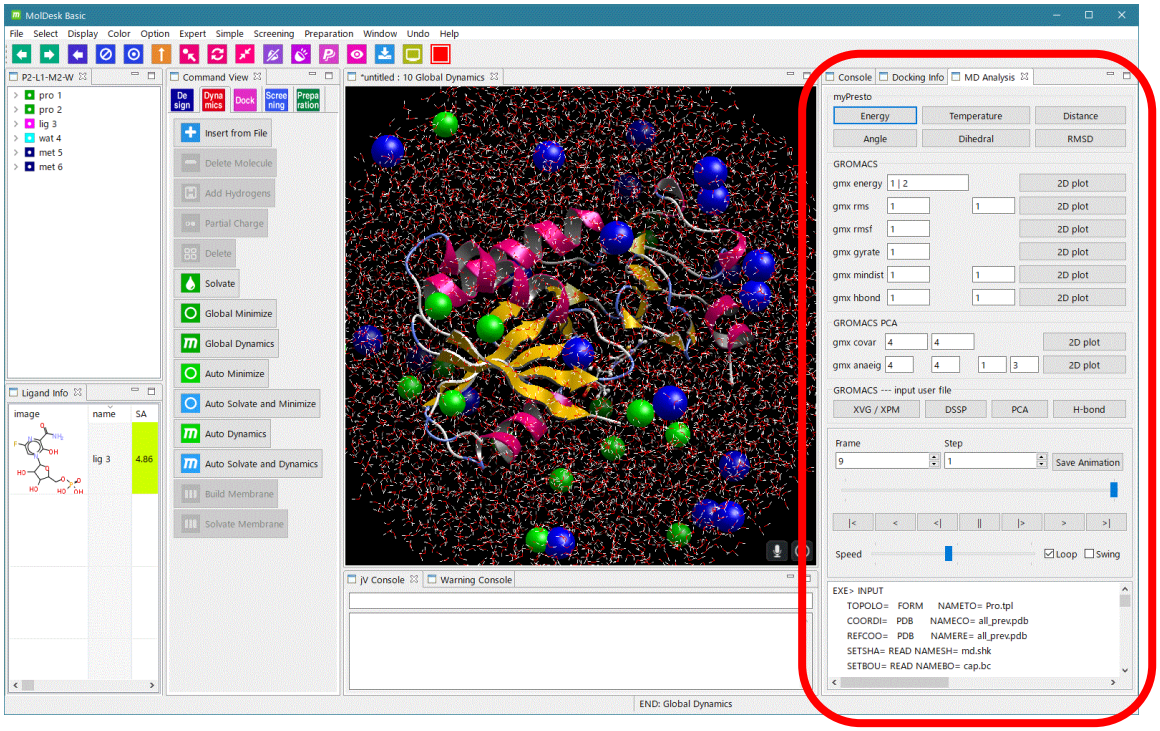
The explanation of the setting items is as follows.

| | |
|---|---|
| Loop limit (number of time steps) Default 2000 | |
| Use restart file Default：OFF | |
| Ensemble | NVT（Canonical ensemble） |
| | NPT（NPT ensemble） |
| | NVE（Microcanonical ensemble） |
| Calculated by the Generalized Born method | |
| Pressure (bar)　Air pressure　Display when NPT ensemble | |
| Temperature (init)　Initial temperature K | |
| Temperature (const)　Constant temperature K (NVE ensemble is not set) | |
| Position restraint | Selected atoms<br>(Position constrains the atom (group) specified by the user with the mouse) |
| | Main chain (proteins & DNA/RNA) |
| | Heavy atoms (proteins & DNA/RNA |
| SHAKE Fixing hydrogen atom bonds | |
| Time step (fsec) | |
| Cutoff length（Å） | |
| Output trajectory | MD energy (interval between output steps for each energy value) |
| | Coordinate (interval between output steps of coordinates) |
| | Velocity（Interval between x, y, z speed output steps） |

MD calculation can be executed twice in a row (12 times when GROMACS). Set the settings for the first execution in MD 1 and the settings for the second execution in MD 2.




When the MD calculation is finished, the button on the command button screen becomes executable.



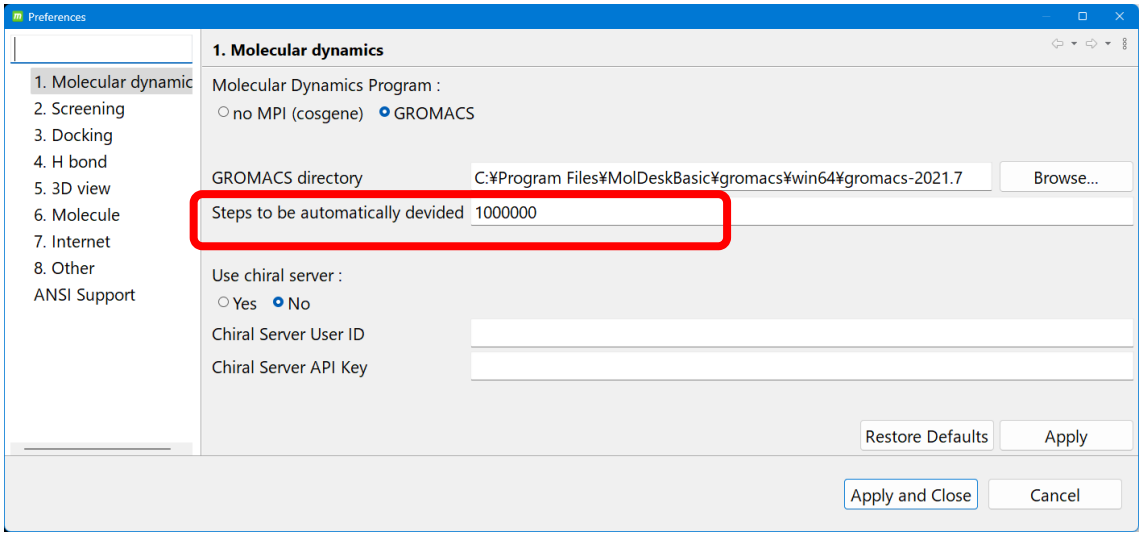

Refer to "5.6 Saving the project" and save the project with a name of your choice.

In GROMACS, the following settings can be selected under **[Typical setting]**.

| | |
|---|---|
| **None** | No setting |
| **Globular** | Relaxation conditions for globular proteins<br><br>[MD1] 10atm, NPT/300K, time step = 0.1 fs, 20,000 step<br>[MD2] 5atm, NPT/300K, time step = 0.2 fs, 20,000 step<br>[MD3] 3atm, NPT/300K, time step = 0.5 fs, 20,000 step<br>[MD4] 1atm, NPT/300K, time step = 0.5 fs, 20,000 step<br>[MD5] 1atm, NPT/300K, time step = 1.0 fs, 20,000 step<br>[MD6] 1atm, NPT/300K, time step = 1.0 fs, 20,000 step<br>[MD7] 1atm, NVT/300K, time step = 2.0 fs, 20,000 step<br>[MD8] 1atm, NVT/300K, time step = 2.0 fs, , 50,000,000 step (sampling) |
| **Membrane** | Relaxation condition for membrane system<br><br>[MD1] 10atm, NPT/300K, time step = 0.01 fs, 20,000 step<br>[MD2] 5atm, NPT/300K, time step = 0.02 fs, 20,000 step<br>[MD3] 3atm, NPT/300K, time step = 0.05 fs, 20,000 step<br>[MD4] 1atm, NPT/300K, time step = 0.1 fs, 20,000 step<br>[MD5] 1atm, NPT/300K, time step = 0.2 fs, 20,000 step<br>[MD6] 1atm, NPT/300K, time step = 0.5 fs, 20,000 step<br>[MD7] 1atm, NPT/300K, time step = 0.5 fs, 20,000 step<br>[MD8] 1atm, NPT/300K, time step = 0.5 fs, 20,000 step<br>[MD9] 1atm, NPT/300K, time step = 1.0 fs, 20,000 step<br>[MD10] 1atm, NPT/300K, time step = 1.0 fs, 20,000 step<br>[MD11] 1atm, NVT/300K, time step = 1.5 fs, 20,000 step<br>[MD12] 1atm, NVT/300K, time step = 1.5 fs, 70,000,000 step (sampling) |
| **RNA** | Relaxation conditions for RNA<br><br>[MD1] 10atm, NPT/300K, time step = 0.01 fs, 200,000 step<br>[MD2] 5atm, NPT/300K, time step = 0.02 fs, 200,000 step<br>[MD3] 3atm, NPT/300K, time step = 0.05 fs, 200,000 step<br>[MD4] 1atm, NPT/300K, time step = 0.1 fs, 200,000 step<br>[MD5] 1atm, NPT/300K, time step = 0.1 fs, 200,000 step<br>[MD6] 1atm, NPT/300K, time step = 0.2 fs, 200,000 step<br>[MD7] 1atm, NPT/300K, time step = 0.2 fs, 200,000 step<br>[MD8] 1atm, NPT/300K, time step = 0.5 fs, 200,000 step<br>[MD9] 1atm, NPT/300K, time step = 1.0 fs, 200,000 step<br>[MD10] 1atm, NPT/300K, time step = 1.0 fs, 200,000 step<br>[MD11] 1atm, NVT/300K, time step = 1.5 fs, 200,000 step<br>[MD12] 1atm, NVT/300K, time step = 1.5 fs, 70,000,000 step (sampling)<br><br>* Using the temperature rise process, the solvent freezes and a volume change occurs.<br>Since we only need to take the strain out of the system, we use a short time step, without changing the temperature, and with a high pressure to keep the system from exploding.<br>Even though the time step is short, the temperature is room temperature, so the water does not freeze and the RNA is less likely to be stretched because the volume change is small.<br>The next step is stretched by LINCS, but 1.5 fs is the upper limit. |

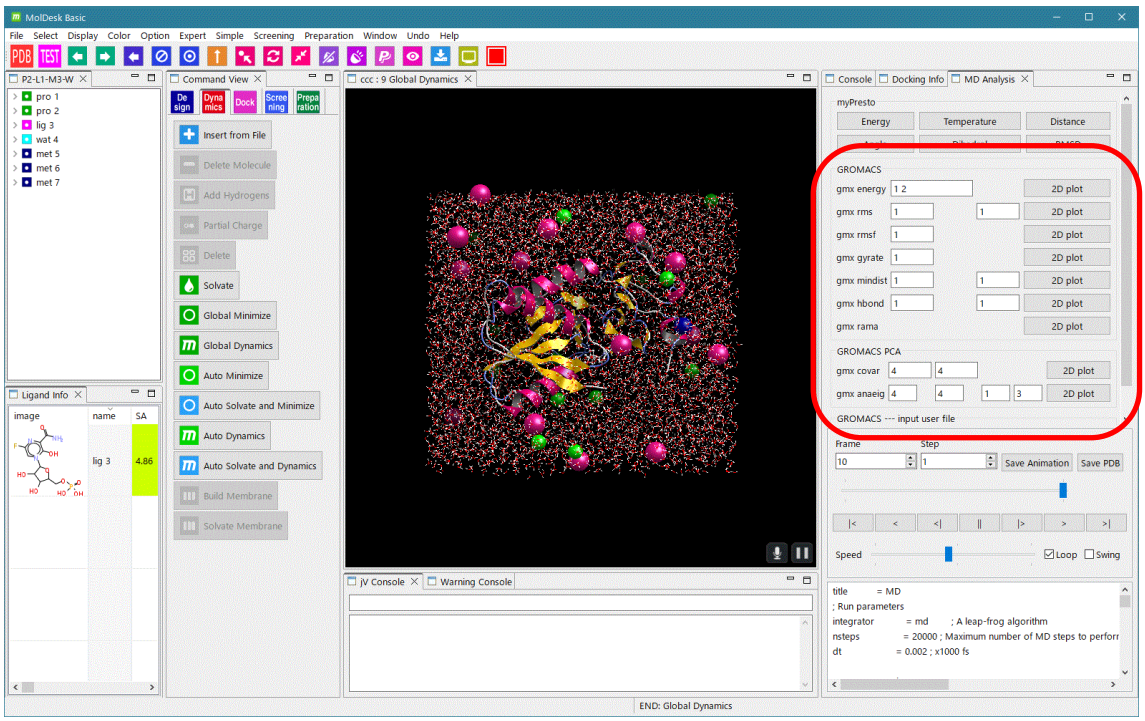
Each relaxation step takes longer than the others because the molecular motion of water at the interface, such as rotational relaxation of water at the surface of hydrophilic molecules, is slower, 1/10 that of the bulk.

In GROMACS, when the number of time steps is 1000000 steps (default value) or more, the MD calculation is automatically divided into 1000000 steps each. This allows the user to check the progress of the MD calculation on the 3D screen over a long period of time. The number of time steps to be divided can be changed in the [Preference] - [1.Molecular dynamics] setting screen (red frame in the figure below).



### 4.28.3. Trajectory Analysis (MD calculation with GROMACS)

Perform the following trajectory analysis to display graphs with time axis linked to the video.




General

(1) gmx energy

Enter the energy term you wish to display and click [2D plot].

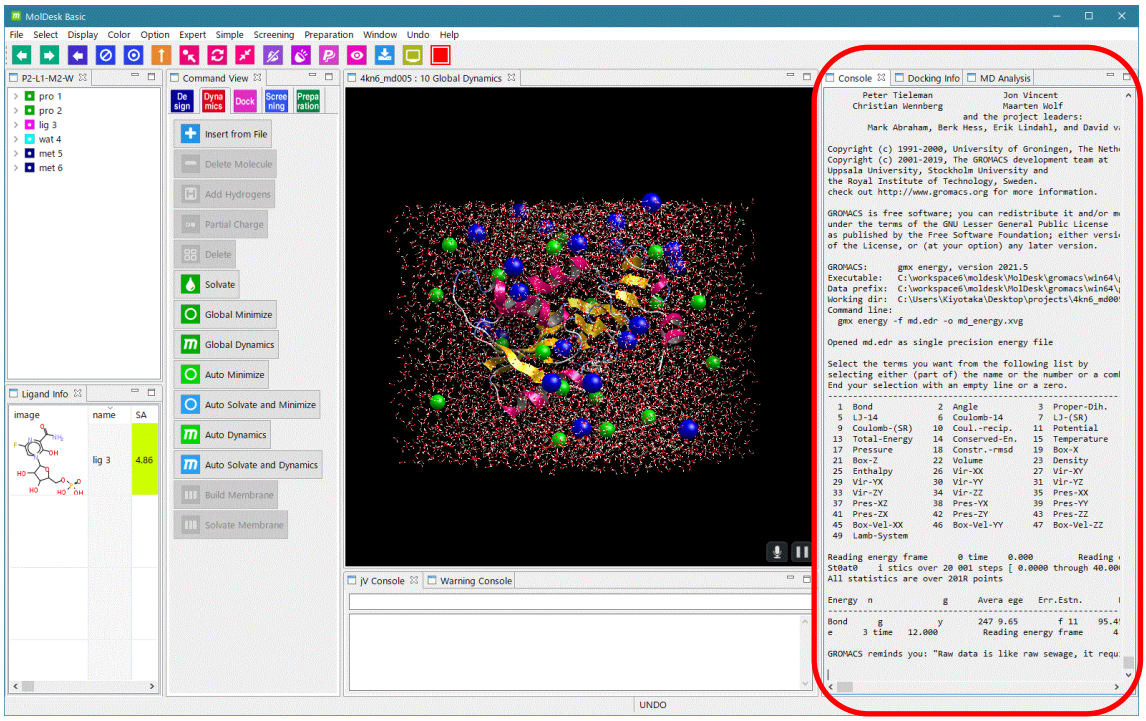
Output file: energy.xvg

The energy term can be confirmed in the output of the Console screen displayed when you click [2D plot] once for a trial run.

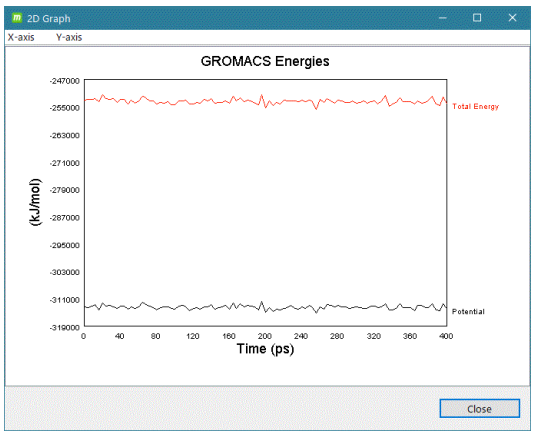
If you want to display two or more items at the same time, connect them with space, e.g., "1 2".

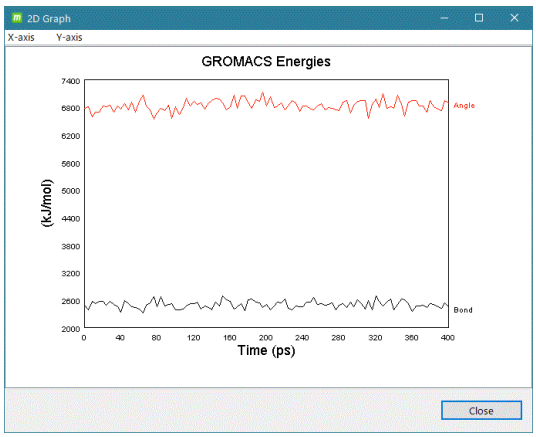
Example of Console screen display

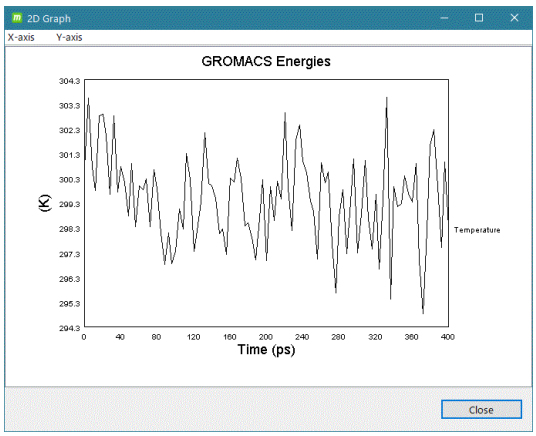
```
-------------------------------------------------------------
  1  Bond            2  Angle           3  Proper-Dih.     4  Improper-Dih.
  5  LJ-14           6  Coulomb-14       7  LJ-(SR)         8  Disper.-corr.
  9  Coulomb-(SR)   10  Coul.-recip.    11  Potential      12  Kinetic-En.
 13  Total-Energy   14  Conserved-En.   15  Temperature    16  Pres.-DC
 17  Pressure       18  Constr.-rmsd    19  Box-X          20  Box-Y
 21  Box-Z          22  Volume          23  Density        24  pV
 25  Enthalpy       26  Vir-XX          27  Vir-XY         28  Vir-XZ
 29  Vir-YX         30  Vir-YY          31  Vir-YZ         32  Vir-ZX
  . . .
```




energy.xvg：Example of graph display)



(2) gmx rms

Enter the group to be fitted by the least squares method (fit group) and the Enter the group for which the RMSD calculation will be performed (rmsd group) and click [2D plot].

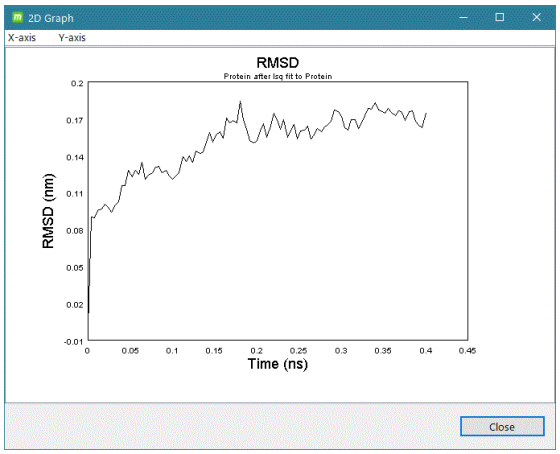
Output file: rmsd.xvg

The group can be confirmed in the output of the Console screen that is displayed when you click [2D plot] once to run the simulation.

(Example of Group display on Console screen)

```
Group     0 (          System) has 23327 elements
Group     1 (         Protein) has  3102 elements
Group     2 (       Protein-H) has  1537 elements
Group     3 (         C-alpha) has   192 elements
Group     4 (        Backbone) has   576 elements
Group     5 (      MainChain) has   770 elements
Group     6 (   MainChain+Cb) has   950 elements
Group     7 (    MainChain+H) has   957 elements
Group     8 (      SideChain) has  2145 elements
Group     9 (    SideChain-H) has   767 elements
Group    10 (    Prot-Masses) has  3102 elements
Group    11 (    non-Protein) has 20225 elements
Group    12 (          Other) has    36 elements
Group    13 (            L00) has    36 elements
Group    14 (             NA) has    20 elements
Group    15 (             CL) has    18 elements
Group    16 (          Water) has 20151 elements
Group    17 (            SOL) has 20151 elements
Group    18 (      non-Water) has  3176 elements
Group    19 (            Ion) has    38 elements
Group    20 (            L00) has    36 elements
Group    21 (             NA) has    20 elements
Group    22 (             CL) has    18 elements
Group    23 ( Water_and_ions) has 20189 elements
```

rmsd.xvg : Example of graph display)

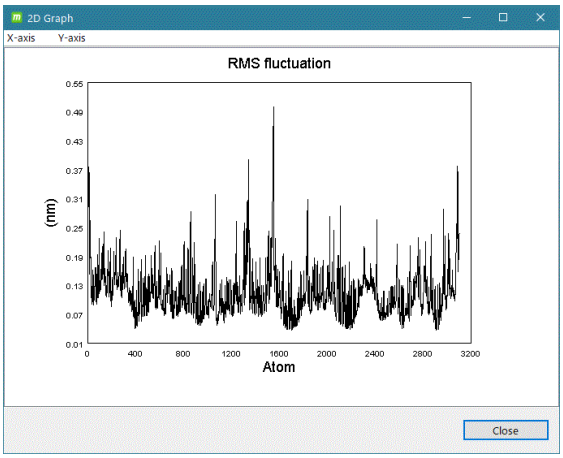


(3) gmx rmsf

Enter the group for which the RMSF calculation is to be performed and click [2D plot].

Output file: rmsf.xvg

rmsf.xvg : Example of graph display)

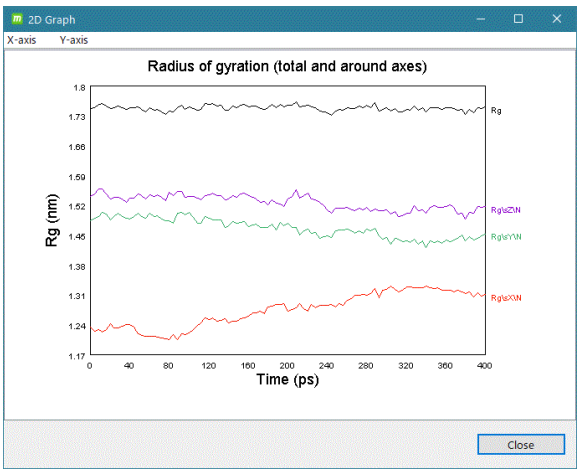



(4) gmx gyrate

Calculates the radius of gyration of a molecule and the radii of gyration about the x-, y-, and z-axes as a function of time. Enter a group and click [2D plot].

Output file: gyrate.xvg

gyrate.xvg : Example of graph display)



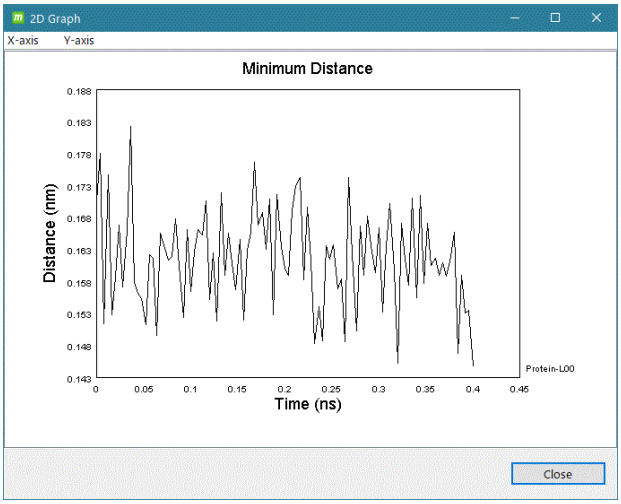
(5) gmx mindist

Calculate the distance between one group and another. Both the minimum distance (between any pair of atoms from each group) and the number of contacts within a given distance are written to two separate output files.

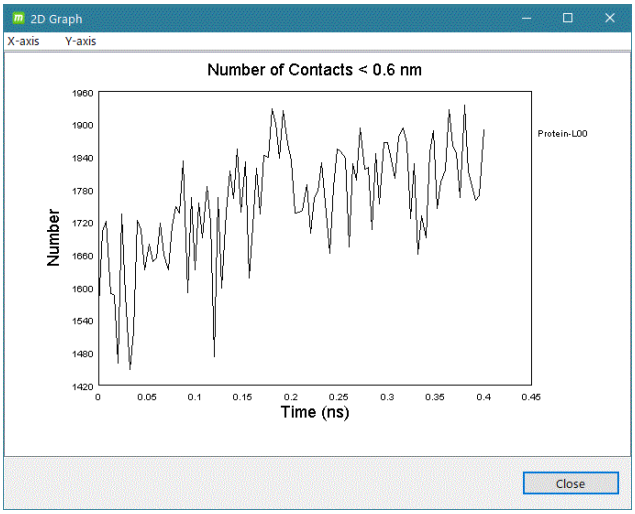
Output files: mindist.xvg

numcount.xvg

mindist.xvg : Example of graph display)




numcount.xvg : Example of graph display)




(6) gmx hbond

Various hydrogen bonding analyses between one group and another.

Perform the following options

-num –ac –dist –ang –hx –hbm –life –dan –nhbdist –don

Output files: hbnum.xvg

hbac.xvg

hbdist.xvg

hbang.xvg

hbhelix.xvg

danum.xvg

hblife.xvg

hbmap.xpm

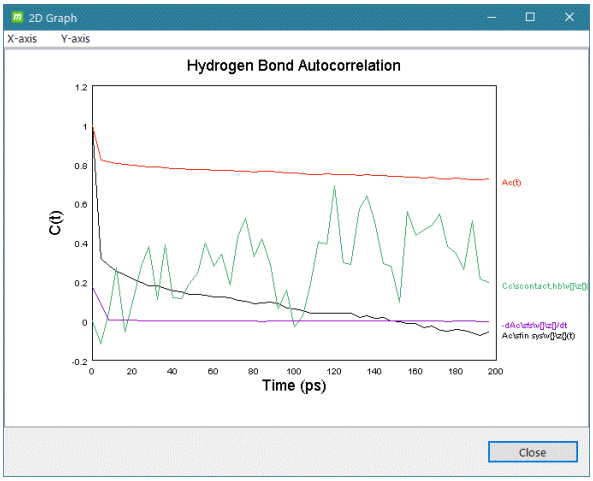
hbond.ndx

nhbdist.xvg

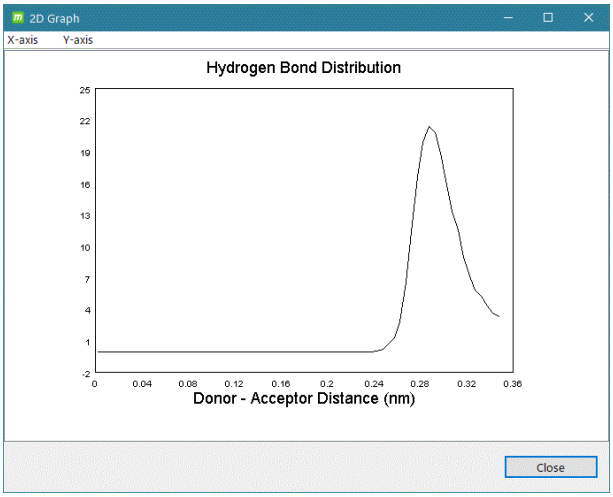
donor.xvg

hbond.log

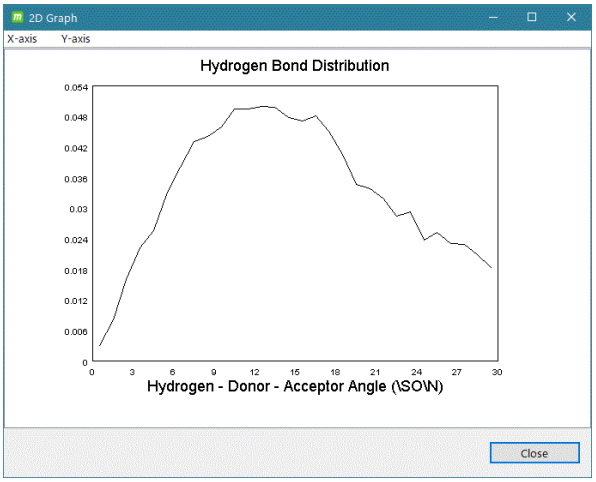
hbac.xvg : Example of graph display)



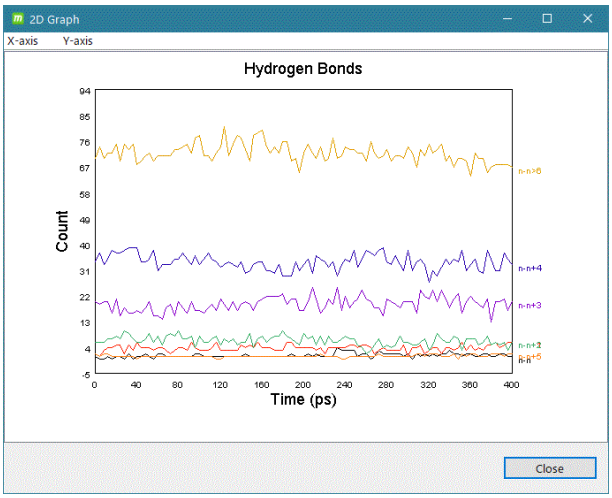

hbdist.xvg : Example of graph display)



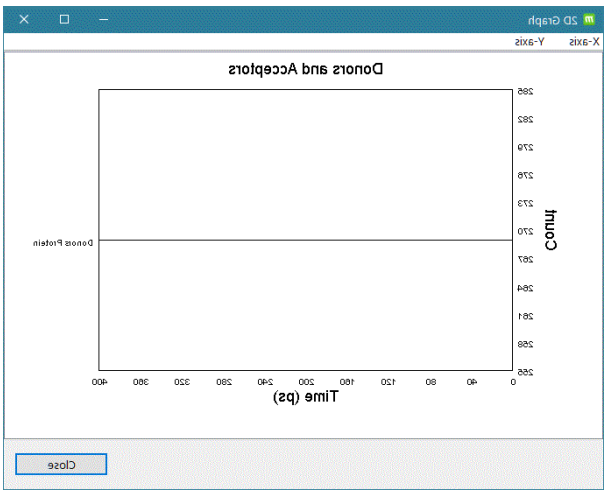
hbang.xvg : Example of graph display)



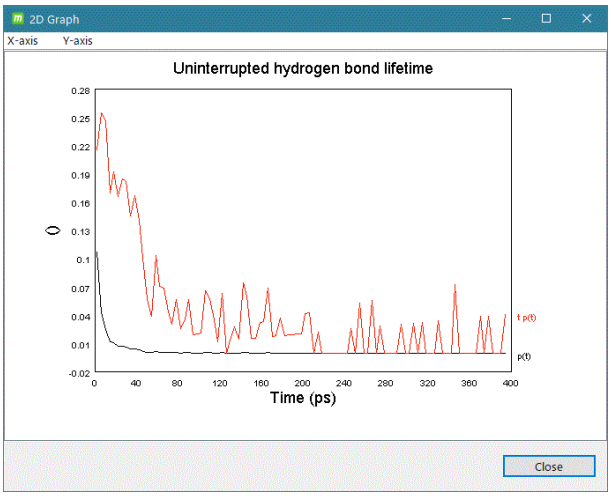

hbhelix.xvg : Example of graph display)



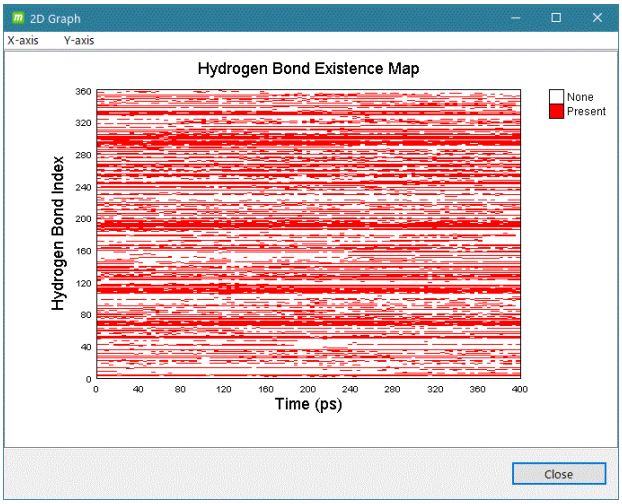

danum.xvg : Example of graph display)



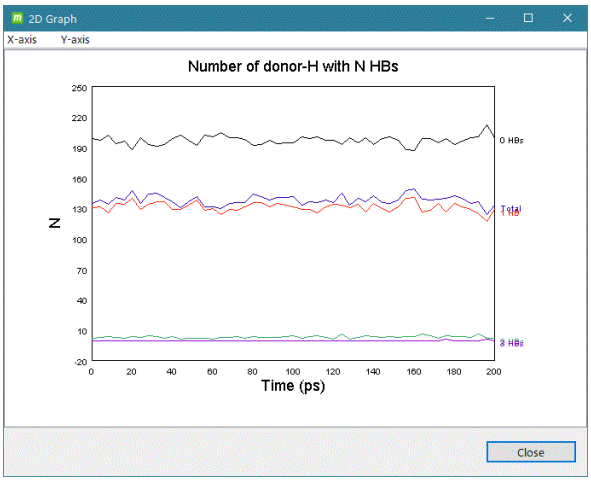
hblife.xvg : Example of graph display)




hbmap.xpm : Example of graph display)




nhbdist.xvg : Example of graph display)

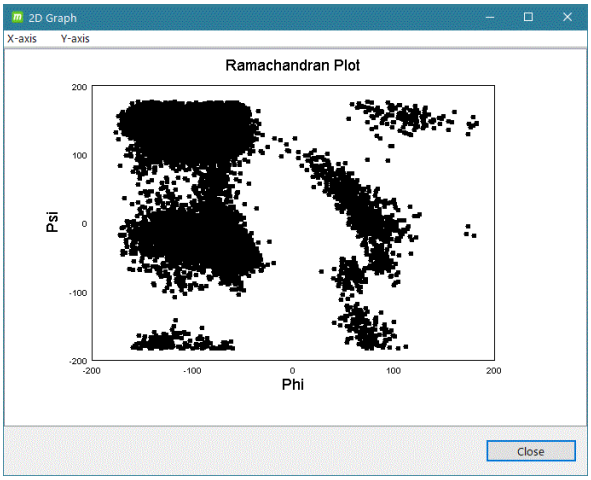


(7) gmx rama

Ramachandran plot. Click [2D plot].

Output files: rama.xvg

rama.xvg: Example of graph display)




Covarience analysys, PCA

(8) gmx covar

Enter the group for the least squares fit (fit group) and the group for the covariance analysis (covar group) and click on [2D plot].

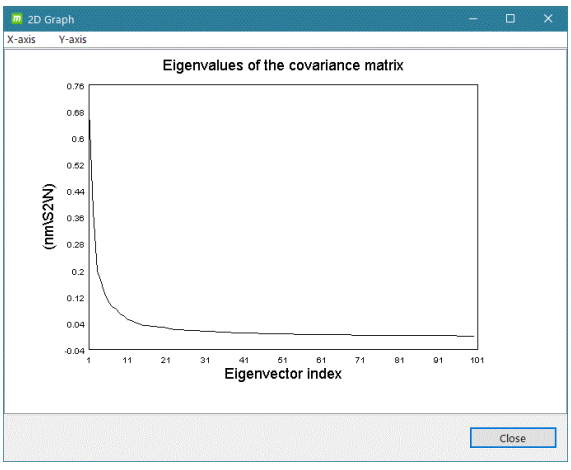
Output files: eigenval.xvg

eigenvec.trr

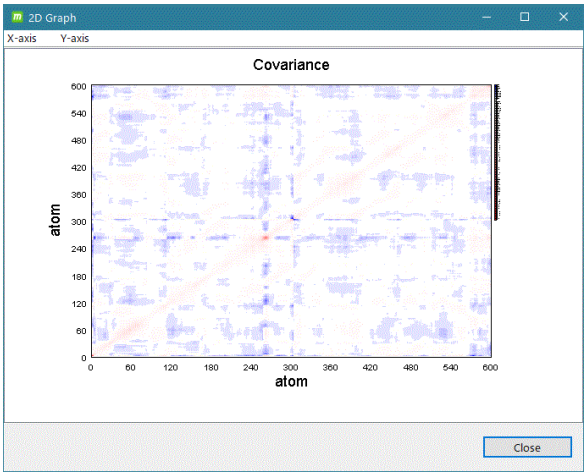
covara.xpm

average.pdb

eigenval.xvg: Example of graph display)



covara.xpm: Example of graph display)




(9) gmx anaeig

Analyze eigenvectors/normal modes. PCA.

Perform the following options

-proj -2d –comp –rmsf -3d –extr

Input files: eigenvec.trr

eigenval.xvg

(md.tpr md_noPBC.xtc)

＊gmx covar output file is input, so gmx covar execution is required.

Output files: proj.xvg

proj2d.xvg

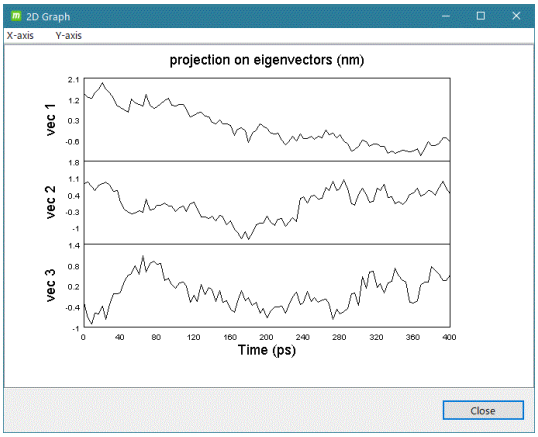
eigcomp.xvg

eigrmsf.xvg

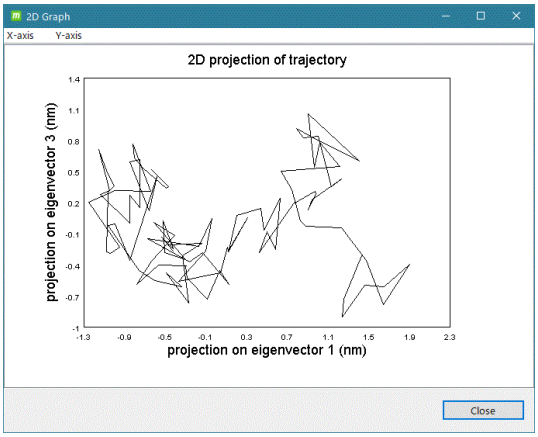
proj3d.gro

extreme.pdb

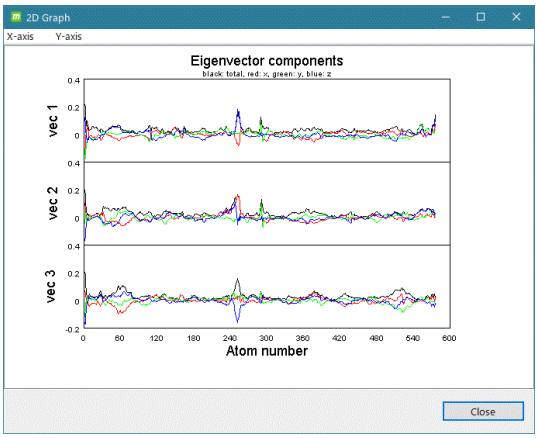
proj.xvg: Example of graph display)



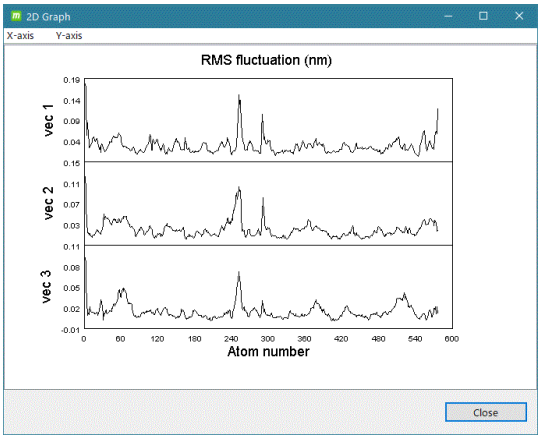

proj2d.xpm: Example of graph display)



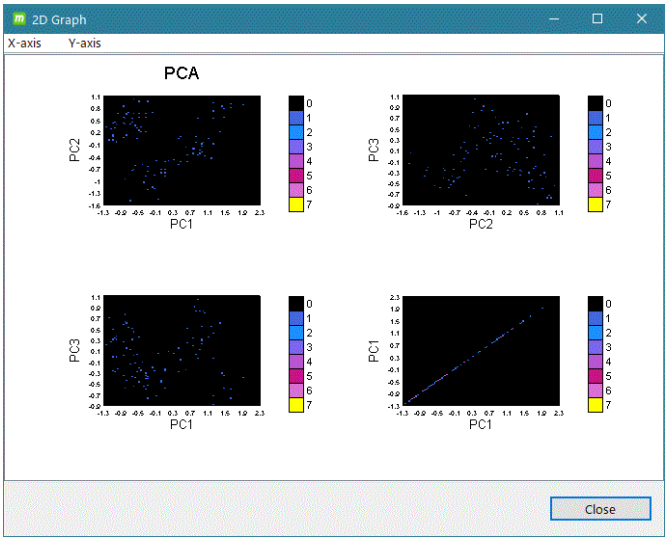

eigcomp.xvg: Example of graph display)



eigrmsf.xpm: Example of graph display)



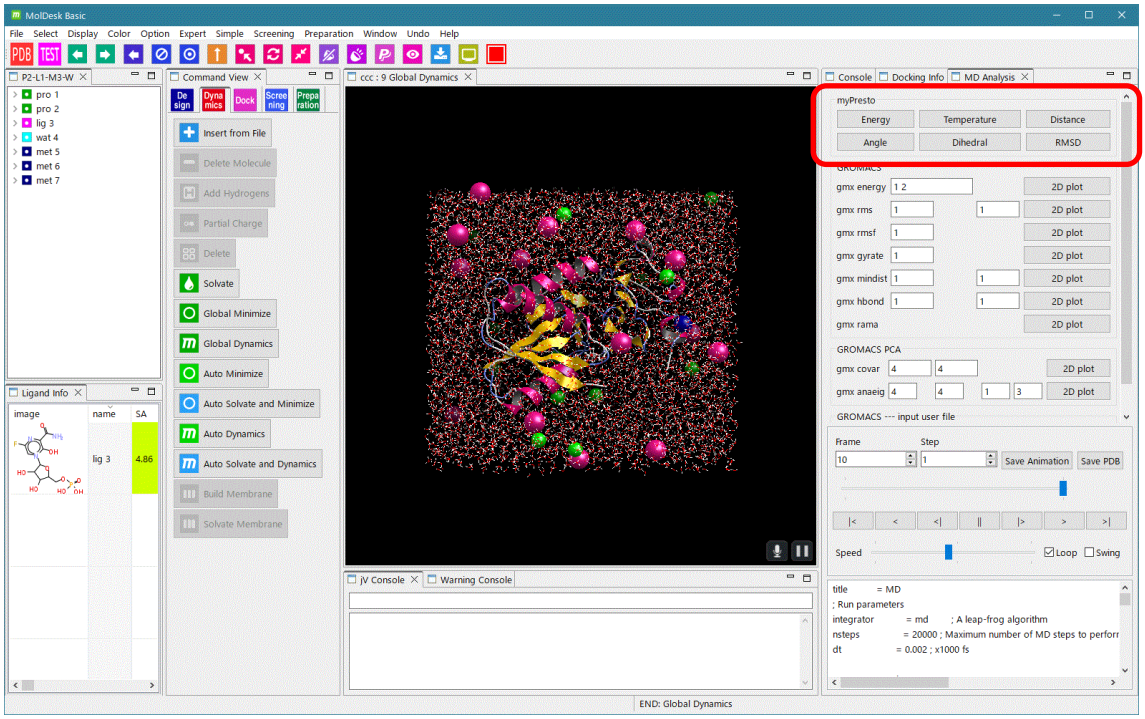

proj3d.gro: Example of graph display)




* For details on trajectory analysis by GROAMCS, refer to the GROMACS manual.

### 4.28.4. Trajectory Analysis (MD calculation by other than GROMACS)

Perform the following trajectory analysis, and graphs with time axis will be displayed in conjunction with the video.




Click the **Energy** button to display a time-varying graph of each energy.

Click the **Temperature** button to display the temperature change graph over time. You can display a two-dimensional graph in which the video and the time axis are linked. Also, by clicking the 2D graph, you can see the video (structure) of the time of the click point.

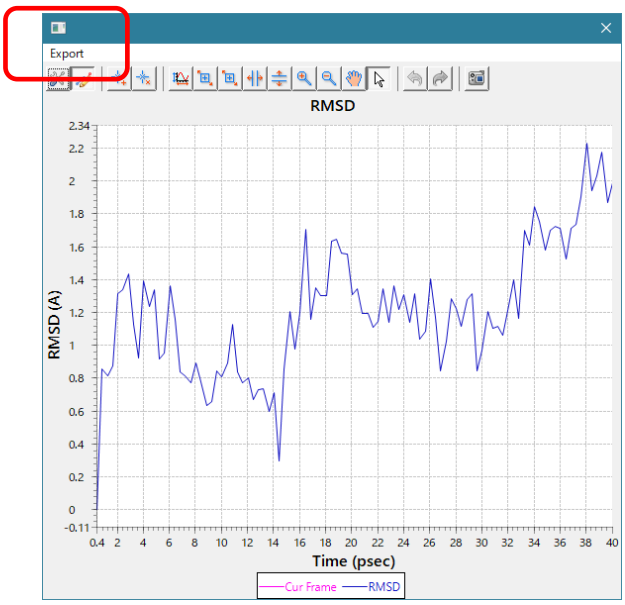
Click the **Distance** button and then select two atoms with the mouse to display a time-varying graph of the selected two-atom distance. You can display a two-dimensional graph in which the video and the time axis are linked. Also, by clicking the 2D graph, you can see the video (structure) of the time of the click point.

Click the **Angle** button and then select 3 atoms with the mouse to display a time-varying graph of the angles formed by the selected 3 atoms. You can display a two-dimensional graph in which the video and the time axis are linked. Also, by clicking the 2D graph, you can see the video (structure) of the time of the click point.

Click the **Dihedral** button, then select 4 atoms with the mouse, and in the order you selected, 2 planes between the planes of the 1st and 2nd atoms and the planes of the 3rd and 4th atoms. Display the time change graph of the corner. You can display a two-dimensional graph in which the video and the time axis are linked. Also, by clicking the 2D graph, you can see the video (structure) of the time of the click point.

After clicking the **RMSD** button, select one molecule on the tree display screen with the mouse to display the RMSD time change graph with respect to the initial coordinates of the selected molecule. You can display a two-dimensional graph in which the video and the time axis are linked. Also, by clicking the 2D graph, you can see the video (structure) of the time of the click point.

You can export the data to a CSV file by clicking the **[Export]** menu (shown below) above the graph.




### 4.28.5. 3D Video Display and File Output

By working with the Animation controller on the MD Analysis screen,the 3D screen animates the time change (trajectory) of the atomic movement.

By clicking the [Save Animation] button, you can output the file to an animated GIF as it is displayed. At that time, you can also set the frame time interval.

Click the [Save PDB] button to save each snapshot of the trajectory of the entire system to a PDB file.

The MD Analysis screen displays the contents of the input file for MD programs (such as cosgene).

The Console screen outputs the standard output of cosgene's MD calculations.
In this example, you can see that the position-constrained atoms are applied to the 36 atoms of the compound.

```
INFORMATION>  READING POSITION RESTRAINT LIST.
 INFORMATION> INPUT POSITION RESTRAINT FILE
     3     1  LGA  O1       1  3103    16.0000
     3     1  LGA  P2       2  3104    30.9700
     3     1  LGA  O3       3  3105    16.0000
     3     1  LGA  O4       4  3106    16.0000
     3     1  LGA  O5       5  3107    16.0000
     3     1  LGA  C6       6  3108    12.0100
     3     1  LGA  C7       7  3109    12.0100
     3     1  LGA  O8       8  3110    16.0000
     3     1  LGA  C9       9  3111    12.0100
     3     1  LGA  O10     10  3112    16.0000
     3     1  LGA  C11     11  3113    12.0100
     3     1  LGA  O12     12  3114    16.0000
     3     1  LGA  C13     13  3115    12.0100
     3     1  LGA  N14     14  3116    14.0100
     3     1  LGA  C15     15  3117    12.0100
     3     1  LGA  O16     16  3118    16.0000
     3     1  LGA  C17     17  3119    12.0100
     3     1  LGA  C18     18  3120    12.0100
     3     1  LGA  F19     19  3121    19.0000
     3     1  LGA  N20     20  3122    14.0100
     3     1  LGA  C21     21  3123    12.0100
     3     1  LGA  C22     22  3124    12.0100
     3     1  LGA  O23     23  3125    16.0000
     3     1  LGA  N24     24  3126    14.0100
     3     1  LGA  H25     25  3127     1.0080
     3     1  LGA  H26     26  3128     1.0080
     3     1  LGA  H27     27  3129     1.0080
     3     1  LGA  H28     28  3130     1.0080
     3     1  LGA  H29     29  3131     1.0080
     3     1  LGA  H30     30  3132     1.0080
     3     1  LGA  H31     31  3133     1.0080
     3     1  LGA  H32     32  3134     1.0080
     3     1  LGA  H33     33  3135     1.0080
     3     1  LGA  H34     34  3136     1.0080
     3     1  LGA  H35     35  3137     1.0080
     3     1  LGA  H36     36  3138     1.0080
        TOTAL NUMBER OF ATOMS :          36
```

Refer to "5.6 Saving the project" and save the project with a name of your choice.

## 4.29. MD calculation in water 2

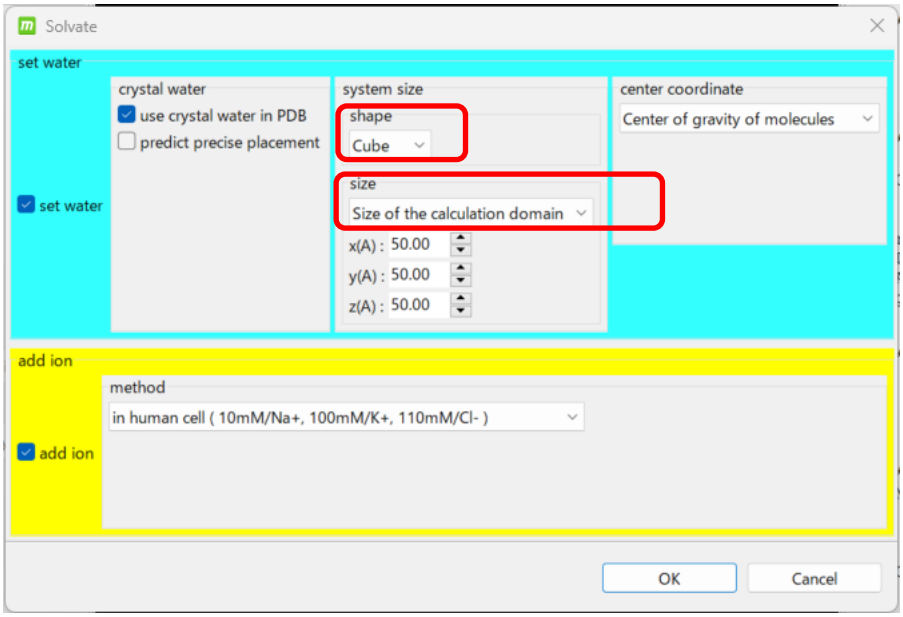
An example of performing MD calculation of proteins and compounds in an aqueous solvent is shown below.
No automatic calculation is performed. Position constraint is performed. Outputs the trajectory file.

### 4.29.1. Preparation of proteins and compounds, addition of hydrogen atoms and charges

Refer to "5.20.1 Read PDB file and add hydrogen atom / charge", open the PDB file with PDB ID "4kn6" and add hydrogen atom and charge.

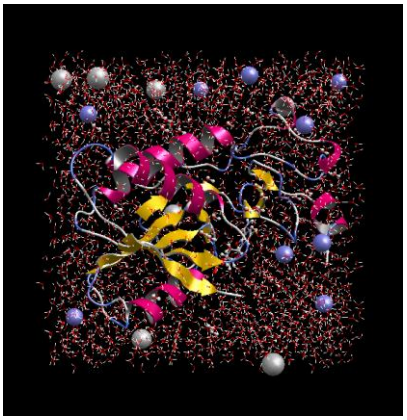
### 4.29.2. Addition of solvent water and ions (periodic boundary conditions)

Click Dyna mics [Dynamics] - [Solvate].




In this example, change [shape] to [Cube] and change [size] to [Size of the calculation domain].
The center of gravity of the system is the center of the solvent, and the size of one side is a rectangle of 50 Å. Leave the default conditions for ion addition. (Refer to "5.25.2 Fully automatic MD calculation" for the setting details.)

Specify the method of adding a water solvent and ions, and click "OK" to add solvent water and ions.



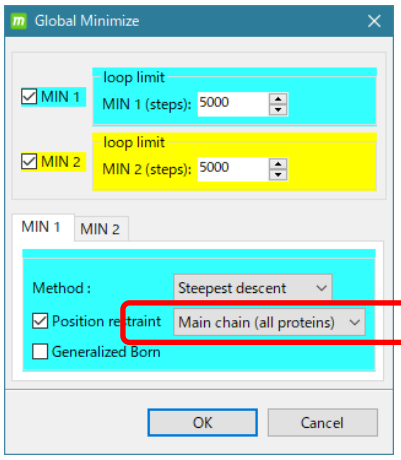
Click  to display the entire system in the center of the screen.

- If the solvent water has a rectangular shape, the PME method is used to calculate the long-range Coulomb force, and periodic boundary conditions are applied.
  - In the PME method, it is necessary to set the number of meshes according to the size of the system, so the optimum value of the number of meshes is automatically calculated from the size of the system.

### 4.29.3. Energy to the smallest calculation

Provides an example of performing an energy-to-the-dize calculation.

 [Global Minimize] Click.The settings dialog for energy-to-the-ion calculations is displayed.




In this example, we're setting it up like this:

Min1,MIN 2 in both
[Position restraint] ON
[Main chain (all proteins)] ] is selected.

Calculates the energy minimization of the entire system. Execute cosgene twice under the following calculation conditions.

5000 steps with the Steepest descent method

5000 steps with Conjugate gradient method

At that time, in the first energy minimization calculation by the Steepest descent method and the energy minimization calculation by the second Conjugate gradient method, the main chains of all proteins are constrained.

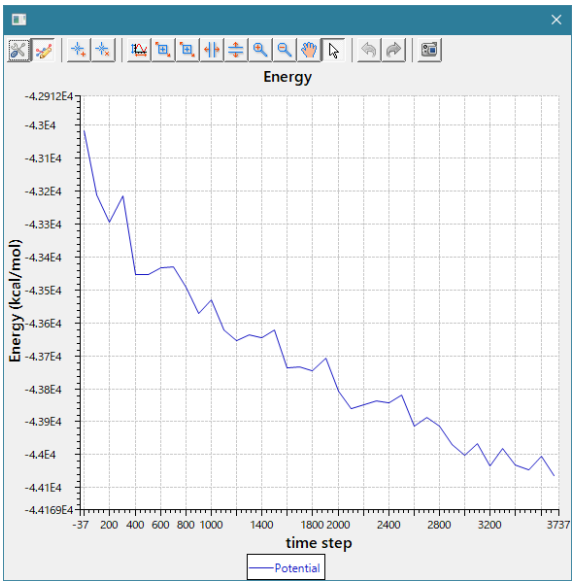
For details on the settings, refer to "5.27.2 Fully Automatic MD Calculation".

Refer to "5.6 Saving the project" and save the project with a name of your choice. (You can calculate without saving)

※ In MolDesk Basic, MD is calculated by sequential calculation by cosgene, so it takes several hours. In MolDesk Screening, MD can be calculated faster by parallel calculation by cosgene_MPI.

### 4.29.4. Confirmation of energy ultra-small calculation results

After the energy destulification calculation is finished,click the Energy button on the MD Analysis screen to view a time change graph of potential energy.

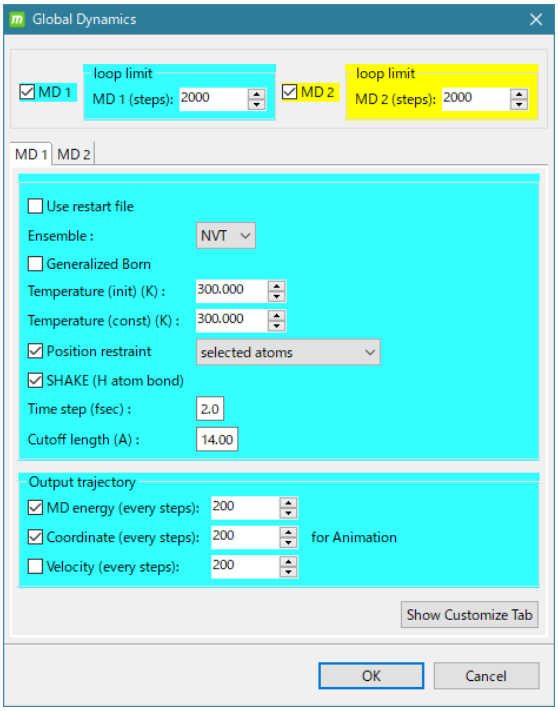


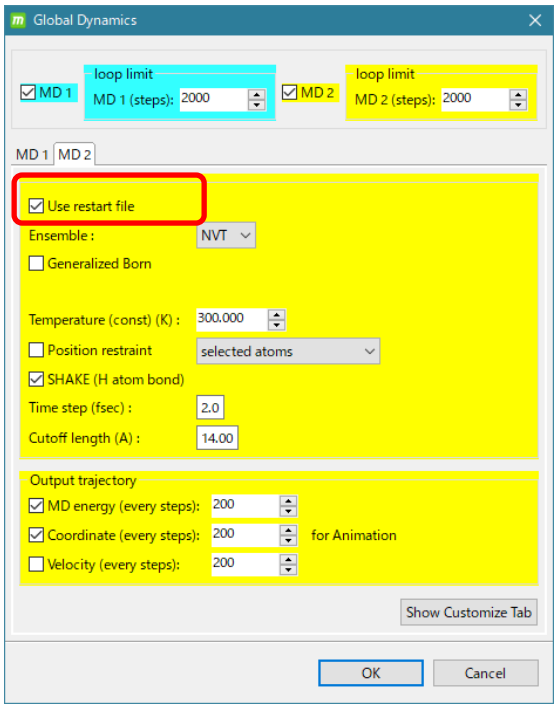

Graph when energy is calculated by the second Conjugate gradient method in the above example

### 4.29.5. MD calculation

Provides an example of performing an MD calculation.

Click [Global Dynamics]. The MD calculation settings dialog is displayed. In this example, MD calculation is performed twice.




The first calculation condition is set in MD 1.

2000 steps, NVT ensemble, no generalized Born method,

Initial temperature 300°C,300°C constant,position-constrained(user-selected atoms),shake calculation, time step width Δt 2.0 5 dsec, cutoff length 14.0 Å,

Energy and coordinate values traversal file output every 200step

For the user-specified atom you wantto position, select lig3 in the tree diagram.

The second calculation condition is set in MD 2.

2000 steps, NVT ensemble, no generalized Born method,

Use the first restart file (initial temperature is the last temperature of the firsttime),

300°C temperature constant, no position constraint, SHAKE calculation,

Time step width Δt 2.0 5 dsec,cutoff length 14.0 Å,

Energy, coordinate values trajectori file output every 200step

The explanation of the setting items is as follows.

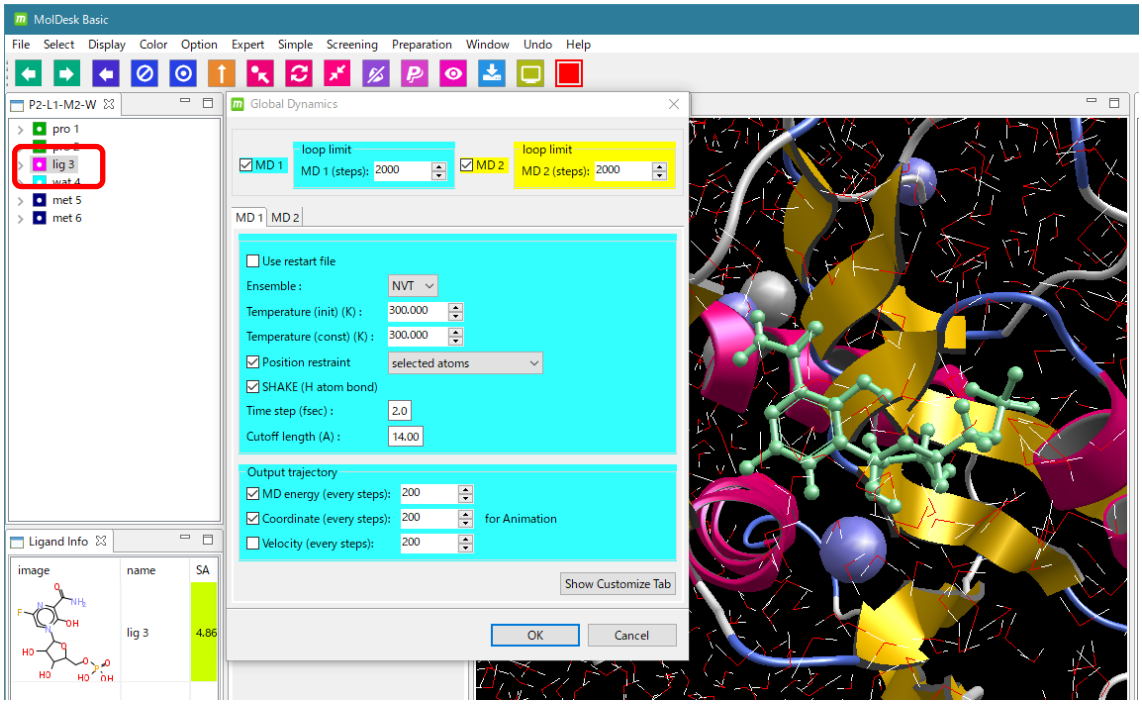
| | |
|---|---|
| Loop limit (number of time steps) Default 2000 | |
| Use restart file Default：OFF | |
| Ensemble | NVT（Canonical ensemble） |
| | NPT（NPT ensemble） |
| | NVE（Microcanonical ensemble） |
| Calculated by the Generalized Born method | |
| Pressure (bar)　Air pressure　Display when NPT ensemble | |
| Temperature (init)　Initial temperature K | |
| Temperature (const)　Constant temperature K (NVE ensemble is not set) | |
| Position restraint | Selected atoms<br>(Position constrains the atom (group) specified by the user with the mouse) |
| | Main chain (proteins & DNA/RNA) |
| | Heavy atoms (proteins & DNA/RNA |
| SHAKE Fixing hydrogen atom bonds | |
| Time step (fsec) | |
| Cutoff length（Å） | |
| Output trajectory | MD energy (interval between output steps for each energy value) |
| | Coordinate (interval between output steps of coordinates) |
| | Velocity（Interval between x, y, z speed output steps） |

- By default, the force field used in MD calculations is set to AMBER GAFF2 for compounds and lipid molecules, and AMBER ff99SB for others (proteins, etc.). (You can change the force field with [Help] – [Preference] – [Molecule] – [tplgeneX].)
- I didn't use it this time, but if I'm applying a position constraint if I do the secondMD calculation, the position constraint is applied to the same atom (group) as the first time.
- Set it to 0.5 fsec if you donot want to apply SHAKE, such as an NPT ensemble. If SHAKE is applied, the time step interval can be 2.0 fsec.
- When GROMACS is selected as the calculation engine, the Generalized Born and SHAKE checkboxes are not displayed because the Generalized Born and SHAKE methods cannot be used for calculation. Also, long-range Coulomb forces are calculated using the PME method, not the FMM method. The default setting for the ensemble is the NPT ensemble. Also, the dialog for setting conditions for MD

calculation can be run 12 times instead of 2 consecutive runs.

Describes how to specify position-constrained atoms( clusters).
With the MD calculation settings dialog displayed, select the atoms to be positioned from the tree display screen or the 3D screen.

This example selects 36 atoms of the compound lig 3 molecule.




[OK] to start the MD calculation.

Trajectory analysis and 3D movie display and file output after MD calculation are the same as described in the previous section, so please refer to the previous section.

## 4.30. Creation of membrane protein systems

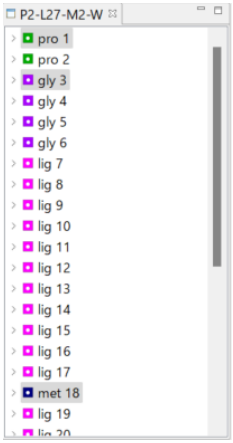
[Build Membrane] [Solvate Membrane] makes it easy to create systems by adding lipid double membrane + water + neutralization ions to membrane proteins.

### 4.30.1. Membrane protein input

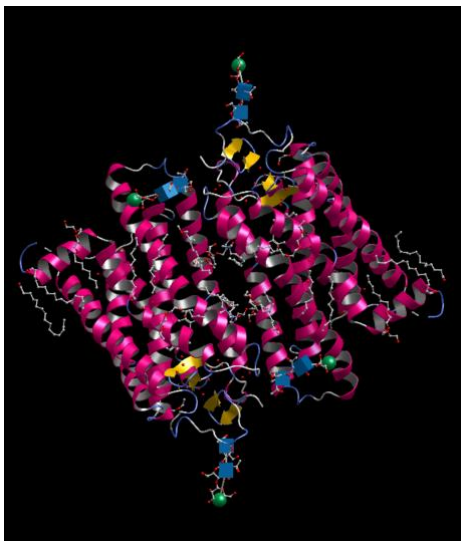
From the File – Open Remote mmCIF / PDB] menu, load the PDB ID: 1gzm.
1gzm is the membrane protein bovine rhodopsin.

### 4.30.2. Formation of membrane protein (+ glycan + metal) + lipid double membranes

First, select the molecule that contains the protein you want to place in the lipid double membrane. In this example, we select three molecules.

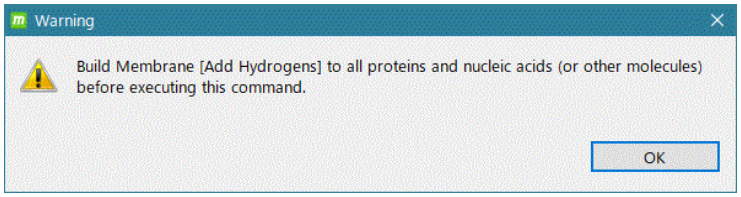



In the tree view, hold down the [Control] key (Command key on Mac) and click to select three molecules: pro1, gly3, met18 protein, sugar chain, and zinc atom.



After selecting the molecule containing the protein as described above, the Dynamics] - [Build Membrane] button will be available.

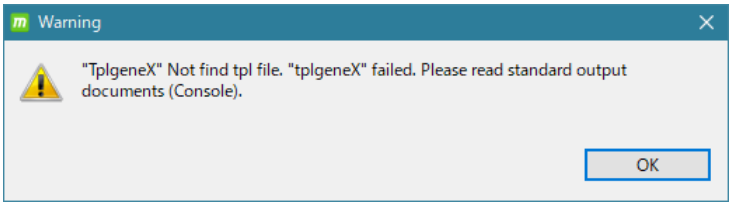
In this state, click Dynamics] - [Build Membrane].




Then, the Warning screen where the hydrogen atom is missing appears as shown above. Before running [Build Membrane], the original PDB is missing a hydrogen atom, so it is

necessary to add a hydrogen atom.

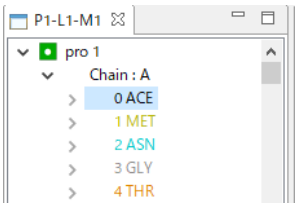
Select pro1 and gly3 and click [Add Hydrogen] to add a hydrogen atom.
(gly3 with the default -p option).
At this point, the following warning screen appears, indicating that TplgeneX's [Add Hydrogens] has failed.




Looking at the [Console] screen, there are the following comments.

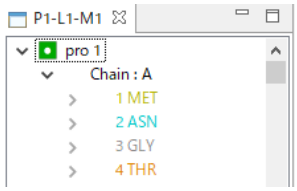
```
 ERROR> setCoordinate
        All the atom positions are not defined.
        The next atoms should be checked again.
N=      1  CA     RES=     0  ACE    MOL=     1
N=      2  HH31   RES=     0  ACE    MOL=     1
N=      3  HH32   RES=     0  ACE    MOL=     1
N=      4  HH33   RES=     0  ACE    MOL=     1
N=      8  H      RES=     1  MET    MOL=     1
```

This indicates that some of the atomic coordinates of the ACE residue, which is the Cap residue pre-added to pro1, are unknown, so the [Design] -[Delete] command is used to delete the ACE residue of the pro1 protein. You can delete it with..



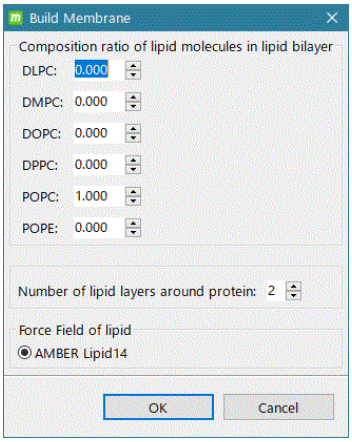

Select the ACE residue of the pro1 molecule in the tree diagram and click the [Delete] button.

After execution, the ACE rest isdeleted, as shown below.




In this state, select pro1 and gly3 in the tree diagram again and click [Add Hydrogens]. This time, a hydrogen atom is added normally.

Now again, in the tree view, select pro1, gly3, met18, then click [Dynamics] - [Build Membrane].

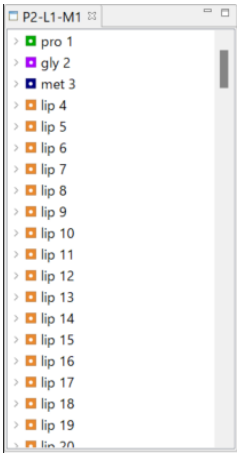


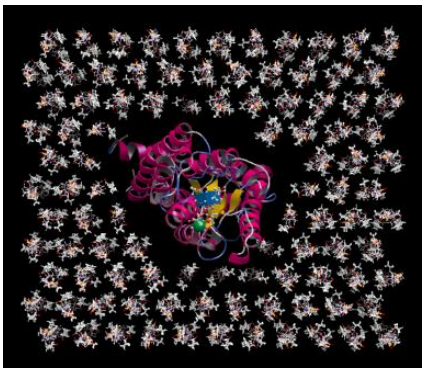

On this screen, set the composition ratio of the six lipid molecules.

Also, select how many layers of lipid molecules should be placed around the protein.

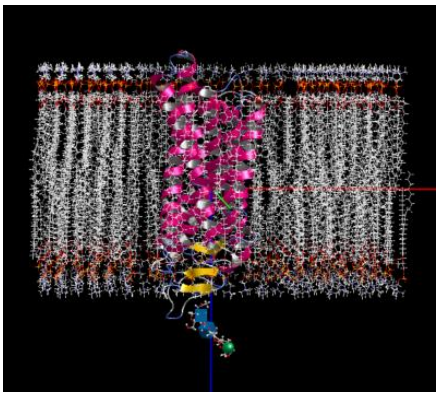
For now, leave the defaults so that the lipid molecules contain only POPC, select the conditions for placing two layers of lipid molecules around the protein, and click OK.

Then, the selected membrane protein, compound and metal are placed in the lipid molecule as shown below.



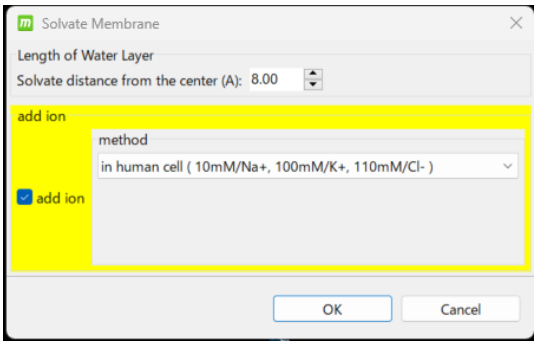
Rotated diagram



* The generated lipid molecules aregenerated by the amber lid14 force field charge, so there is no need to add a charge.

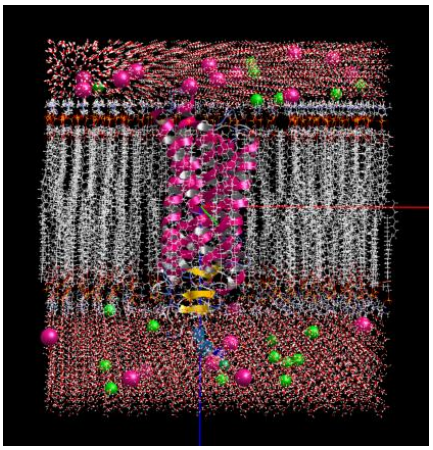
### 4.30.3. Membrane protein (+ glycan + metal) + lipid double membrane system + water + neutralization ion system creation

Click [Dynamics] - [Solvate Membrane].




Here, select the margin in the z direction from the center of the protein in the aqueous solvent and whether or not to place the neutralizing ion.

Here, leave the defaults as they are, selecting a margin of 8 Å and add neutralizing ions at the human cell ion concentration, and click [OK]. The aqueous solution and neutralizing ions (Na+, K+ and Cl-) will be added to the system as shown below.



You can then click [Dynamics] - [Global Minimize] to perform the energy minimization calculation.

In addition, you can perform MD calculations by clicking [Dynamics] - [Global Dynamics].

※ The created membrane protein system is suitable for calculation with GROMACS or with psygene-G, a fast MD calculation program with GPU and MPI supported by MolDesk Screening, because of the large size of the system and the large number of atoms.

※ Lipid molecules generated by [Build Membrane] are limited to the AMBER Lipid14 force field for MD calculations. Other lipid molecules, glycans and compounds default to the AMBER GAFF2 force field, while others (e.g. proteins) are set to AMBER ff99SB. (For these molecules, the force field can be changed by [Help] - [Preference] - [Molecule] - [tplgeneX]).

※ When energy minimization and MD calculations are performed, glycans are recognized as compounds. This is because myPresto does not support the GLYCAM force field, so the glycan residue names are not stored.

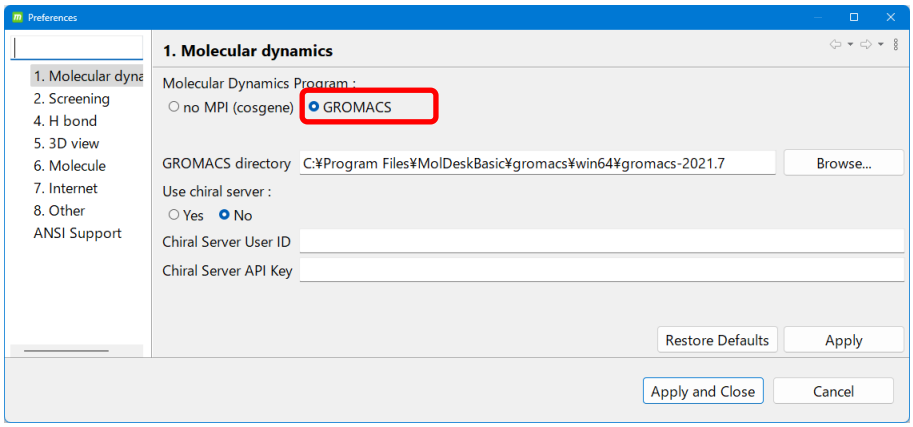
※ For MD calculations of lipid bilayer systems, we recommend using the NPT ensemble because the NVT ensemble tends to separate lipid bilayers.

## 4.31. GROMACS : MD calculation

### 4.31.1. [Preference] - [Molecular dynamics] settings

- **On the [Help]-[Preference]-[Molecular dynamics] screen, select [GROMACS] under [Molecular Dynamic Program : ]**

  Perform energy minimization and MD calculations with GROMACS on a computer with MolDesk Basic installed.




Here, on Linux and MAC, the user must install GROMACS and set the [GROMACS directory] of the installed GROAMCS.
On Windows 10 and Windows 11, this setting is not necessary since the GROMACS executable program is implemented beforehand.

The [GROMACS directory] should be set to the directory where **share** and **bin** exist.

※In the current version, GROMACS is executed in **bin/gmx** without specifying the number of parallels.
If **bin/gmx** does not exist in the installation directory, GROMACS cannot be executed.
The parallel number of OpenMP and thread MPI depends on the automatic parallel number specification function of GROMACS. MPI is not used.

- **On the [Help]-[Preference]-[Molecular dynamics] screen,**
  **If you select Yes in the [Use chiral server : ].**

  The energy minimization and MD calculations are performed by GROMACS on the cloud server provided by Chiral : Chiral Computing Cloud.
  A separate contract between the user and Chiral is required.

### 4.31.2. Energy minimization calculation

Basically, the operation is the same as for energy minimization calculations using cosgene in myPresto.
However, the following restrictions apply.

1. only [Cube] is available as a solute geometry created by [Solvate]. Systems created with [Sphere] cannot be calculated. This is because the calculation is based on periodic boundary conditions.
2. The calculation conditions are as follows, and the PME method is used.
   From the GUI, only nsteps, integrator, and define can be modified.

min.mdp example

```
; min.mdp - used as input into grompp to generate min.tpr
; Parameters describing what to do, when to stop and what to save
define          = -DPOSRES  ; position restrain
integrator      = steep     ; Algorithm (steep = steepest descent minimization)
emtol           = 1000.0    ; Stop minimization when the maximum force < 1000.0 kJ/mol/nm
emstep          = 0.01      ; Minimization step size
nsteps          = 5000      ; Maximum number of minimization steps to perform

; Parameters describing how to find the neighbors of each atom and how to calculate the interactions
nstlist         = 1         ; Frequency to update the neighbor list and long range forces
cutoff-scheme   = Verlet    ; Buffered neighbor searching
ns_type         = grid      ; Method to determine neighbor list (simple, grid)
coulombtype     = PME ; Treatment of long range electrostatic interactions
rcoulomb        = 1.0       ; Short-range electrostatic cut-off
rvdw            = 1.0       ; Short-range Van der Waals cut-off
pbc             = xyz       ; Periodic Boundary Conditions in all 3 dimensions
```

### 4.31.3. MD Calculation

Basically, the operation is similar to the MD calculation for cosgene in myPresto. However, in the current version, the items that can be set from the GUI are limited, with the following restrictions

1. the calculation conditions are as follows for the NVT ensemble, using the PME method. From the GUI, **define, nsteps, dt, nstxout, nstvout, nstenergy, nslog, nstxout-compressed, continuation, gen_vel, gen_temp, tcouple, ref_t, pcouple, rvdw, rcoulomb** can only be modified, the others are currently fixed. md.mdp example

```
title                = MD
define               = -DPOSRES  ; position restrain
; Run parameters
integrator           = md        ; A leap-frog algorithm
nsteps               = 20000     ; Maximum number of MD steps to perform
dt                   = 0.002     ; x1000 fs

; Output control
nstxout              = 2000
nstvout              = 2000
nstenergy            = 2000
nstlog               = 2000
nstxout-compressed   = 2000
compressed-x-grps    = System

; Initial Velocities
continuation         = no
gen_vel              = yes
gen_temp             = 300.0     ; temperature for Maxwell distributions
gen_seed             = -1        ; generate a random seed

; Neighbour Searching
cutoff-scheme        = Verlet    ; Buffered neighbor searching
ns_type              = grid      ; Method to determine neighbor list (simple, grid)
nstlist              = 10
rcoulomb             = 1.0       ; short-range electrostatic cutoff (in nm)
rvdw                 = 1.0       ; short-range van der Waals cutoff (in nm)

; Electrostatics
coulombtype          = PME
pme_order            = 4         ; cubic interpolation
fourierspacing       = 0.16      ; grid spacing for FFT

; Vdw
DispCorr             = EnerPres  ; account for cut-off vdW scheme

; Constraints
constraints          = h-bonds
constraint_algorithm = lincs
lincs_iter           = 1
lincs_order          = 4

; Temperature
tcoupl               = V-rescale ; modified Berendsen thermostat
tc-grps              = System
tau_t                = 0.1       ; time constant, in ps
ref_t                = 300.0     ; reference temperature, one for each group, in K

; Pressure
pcoupl               = no

; Periodic boundary conditions
pbc                  = xyz       ; Periodic Boundary Conditions in all 3 dimensions
```

2. the calculation conditions are as follows for the NPT ensemble, using the PME method. From the GUI, only define, **nsteps, dt, nstxout, nstvout, nstenergy, nslog, nstxout-compressed, continuation, gen_vel, gen_temp, tcouple, ref_t, pcouple, ref_p, rvdw and rcoulomb** The others are currently fixed.

   md.mdp example.

```
title          = MD
define               = -DPOSRES  ; position restrain
; Run parameters
integrator           = md        ; A leap-frog algorithm
nsteps               = 20000     ; Maximum number of MD steps to perform
dt                   = 0.002     ; x1000 fs

; Output control
nstxout              = 2000
nstvout              = 2000
nstenergy            = 2000
nstlog               = 2000
nstxout-compressed   = 2000
compressed-x-grps    = System

; Initial Velocities
continuation         = yes
gen_vel              = no

; Neighbour Searching
cutoff-scheme        = Verlet    ; Buffered neighbor searching
ns_type              = grid      ; Method to determine neighbor list (simple, grid)
nstlist              = 10
rcoulomb             = 1.0       ; short-range electrostatic cutoff (in nm)
rvdw                 = 1.0       ; short-range van der Waals cutoff (in nm)

; Electrostatics
coulombtype          = PME
pme_order            = 4         ; cubic interpolation
fourierspacing       = 0.16      ; grid spacing for FFT

; Vdw
DispCorr             = EnerPres  ; account for cut-off vdW scheme

; Constraints
constraints          = h-bonds
constraint_algorithm = lincs
lincs_iter           = 1
lincs_order          = 4

; Temperature
tcoupl               = V-rescale ; modified Berendsen thermostat
tc-grps              = System
tau_t                = 0.1       ; time constant, in ps
ref_t                = 300.0     ; reference temperature, one for each group, in K

; Pressure
pcoupl               = Parrinello-Rahman ; Pressure coupling on in NPT
pcoupltype           = isotropic ; uniform scaling of box vectors
tau_p                = 2.0       ; time constant, in ps
ref_p                = 1.0       ; reference pressure, in bar
compressibility      = 4.5e-5    ; isothermal compressibility of water, bar^-1
refcoord_scaling     = com

; Periodic boundary conditions
pbc                  = xyz       ; Periodic Boundary Conditions in all 3 dimensions
```

3. the calculation conditions are as follows for the NVE ensemble, using the PME method. From the GUI, define, **nsteps, dt, nstxout, nstvout, nstenergy, nslog, nstxout-compressed, continuation, gen_vel, gen_temp, tcouple, pcouple, rvdw, rcloulomb**; the rest are currently fixed.

   md.mdp example.

```
title          = MD
define               = -DPOSRES  ; position restrain
; Run parameters
integrator           = md        ; A leap-frog algorithm
nsteps               = 20000     ; Maximum number of MD steps to perform
dt                   = 0.002     ; x1000 fs

; Output control
nstxout              = 2000
nstvout              = 2000
nstenergy            = 2000
nstlog               = 2000
nstxout-compressed   = 2000
compressed-x-grps    = System

; Initial Velocities
continuation         = yes
gen_vel              = no

; Neighbour Searching
cutoff-scheme        = Verlet    ; Buffered neighbor searching
ns_type              = grid      ; Method to determine neighbor list (simple, grid)
nstlist              = 10
rcoulomb             = 1.0       ; short-range electrostatic cutoff (in nm)
rvdw                 = 1.0       ; short-range van der Waals cutoff (in nm)

; Electrostatics
coulombtype          = PME
pme_order            = 4         ; cubic interpolation
fourierspacing       = 0.16      ; grid spacing for FFT

; Vdw
DispCorr             = EnerPres  ; account for cut-off vdW scheme

; Constraints
constraints          = h-bonds
constraint_algorithm = lincs
lincs_iter           = 1
lincs_order          = 4

; Temperature
tcoupl               = no

; Pressure
pcoupl               = no

; Periodic boundary conditions
pbc                  = xyz       ; Periodic Boundary Conditions in all 3 dimensions
```

※ NVE ensemble calculations are unstable

### 4.31.4. Graph Display by User's Input File

Trajectory files created by MD calculation with GROMACS and calculation result files of various GROMACS trajectory analysis programs can be input at the same time to display a two-dimensional graph in which video and time axis are linked (a red vertical line is displayed on the two-dimensional graph corresponding to the time of the video). (A red vertical line is displayed on the 2D graph corresponding to the time of the video.) The horizontal and vertical axes of the 2D graph can be enlarged and displayed as desired. The horizontal and vertical axes of the 2D graph can be zoomed in as desired.

Also, by clicking on the 2D graph, you can view the movie at the time of the clicked point.

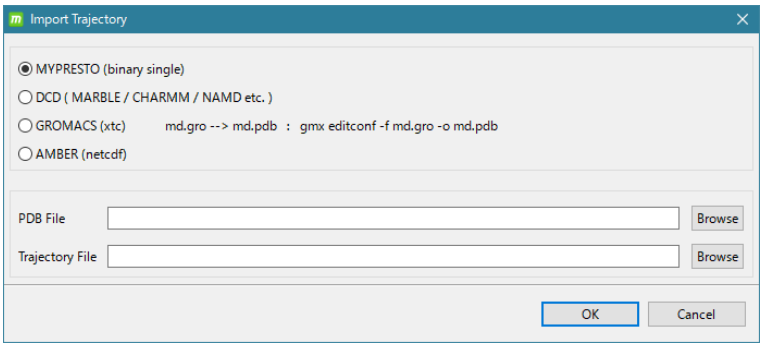
(1) Input file

The input files available are as follows:

| indication | File type |
|---|---|
| video | PDB file (*.pdb or *.ent)<br>And<br>trajectori file (*.xtc) |
| 2D graph | *.xvg or *.xpm |
| 2D Graph (DSSP: Secondary Structural Analysis) | *.xpm |
| 2D Graph (PCA Analysis) | *.gro |
| 2D graph (hydrogen bond analysis) | *.ndx and *.*.xpm |

(2) Video display

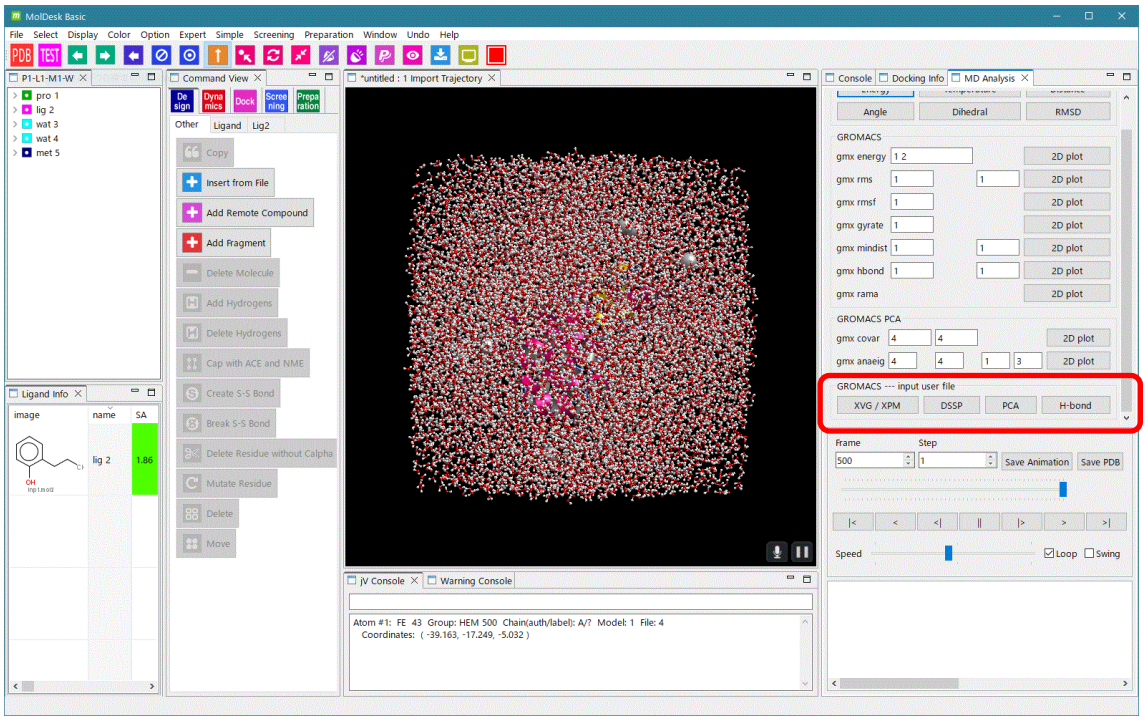
When [File]-[Import Trajectory] is executed, the following screen is displayed.




GROMACS(. xtc ) and select

MolDesk Basic -> sample -> trajectory -> GROMACS

Select all .pdb and md.xtc asPDB File and Trajetory File, respectively,and then clickOK.



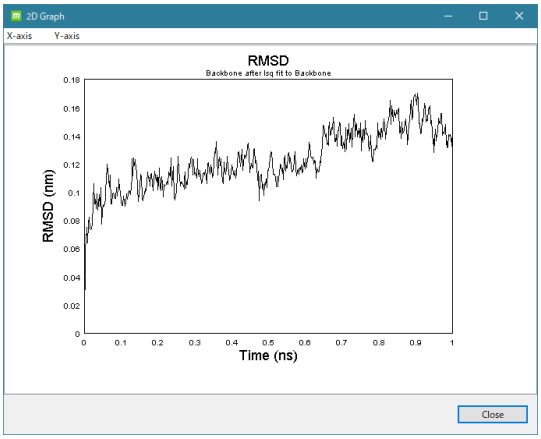

The buttons in the gromacs frame can representa two-dimensional graph of the various GROMACS analysis files. The input files available are as follows:

| button | File type | Chart type |
|---|---|---|
| XVG / XPM | *.xvg or *.xpm | Common 2D charts |
| DSSP | *.xpm | Secondary structural analysis |
| PCA | *.gro | PCA analysis |
| H-bond | *.ndx katsu *.*.xpm | Hydrogen bond analysis |

(3) 2D Graph [ XVG / XPM ]

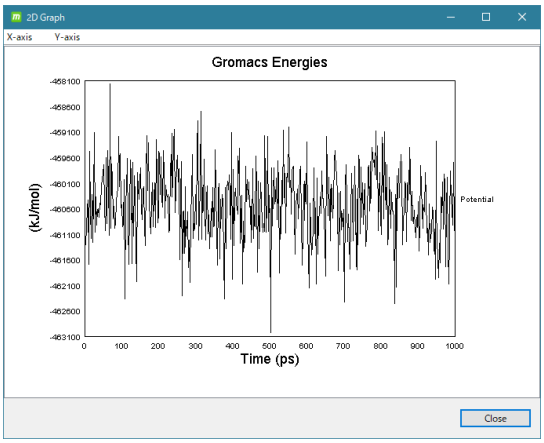
MolDesk Basic -> sample -> trajectory -> GROMACS -> rmsd.xvg

When you load .



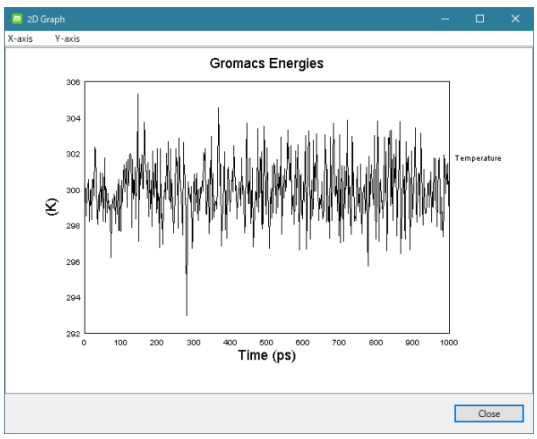

MolDesk Basic -> sample -> trajectory -> GROMACS -> potential.xvg

When you load .




MolDesk Basic -> sample -> trajectory -> GROMACS -> temperature.xvg

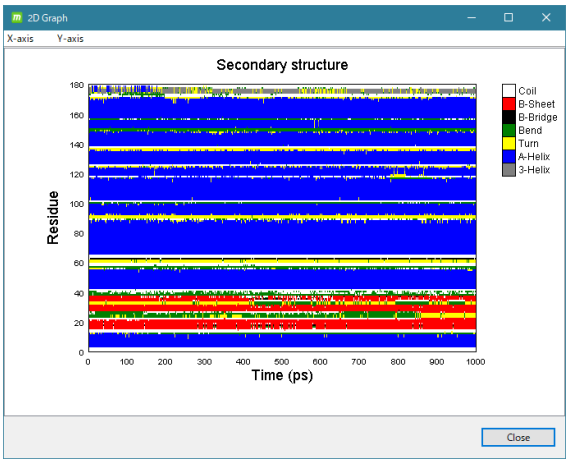
When you load .



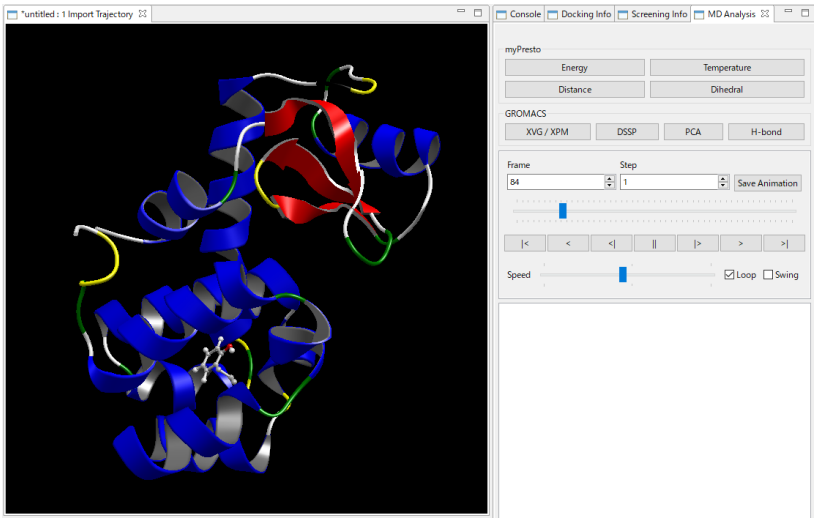
(4) 2D Graph [ DSSP ]

MolDesk Basic -> sample -> trajectory -> GROMACS -> dssp.xvg

When you load .



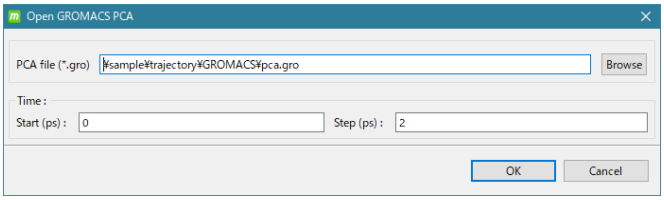

※ The GROMACS secondary structure analysis result file can also be displayed with the [XVG / XPM] button, but to reflect the GROMACS secondary structure analysis result in the video as shown below, load it with the [DSSP] button. Please.




(5) 2D Graph [ PCA ]

GROMACS PCA analysis is output in gro file format.

Click [PCA] and the following screen will appear.

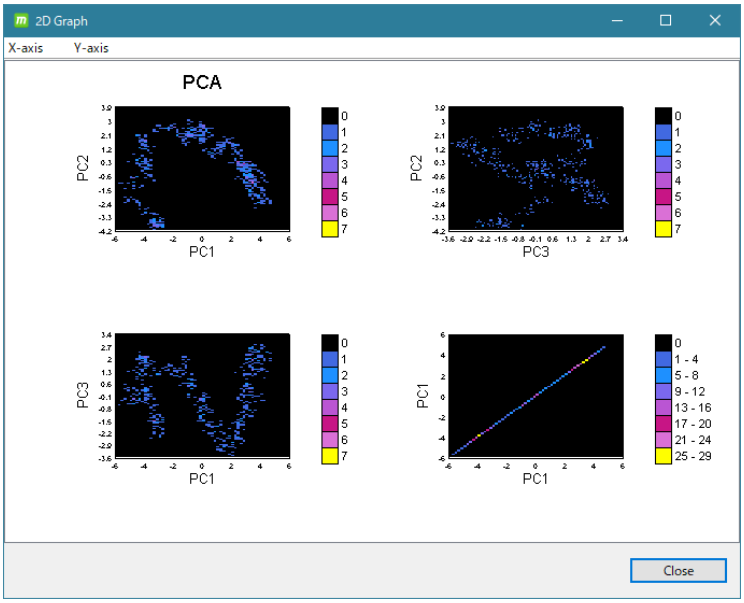


In [Browse]

MolDesk Basic-> sample-> trajectory-> GROMACS-> pca.gro

Read.

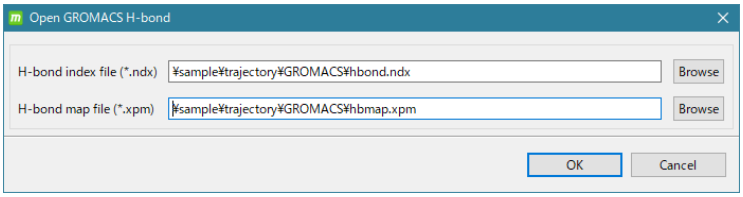
Specify the start time (ps) and step (ps) to synchronize the time between the video and the 2D graph. In this case, the trajectory is from 0 to 1000 psec, and the calculation data is collected every 2 psec, so Start (ps) is 0 and Step (ps) is 2.




In conjunction with the video, the points corresponding to that time will glow white. The PCA graph cannot display a video of the click point time when clicked.

(5) 2D Graph [ H-bond ]

[H-bond] to the following screen.

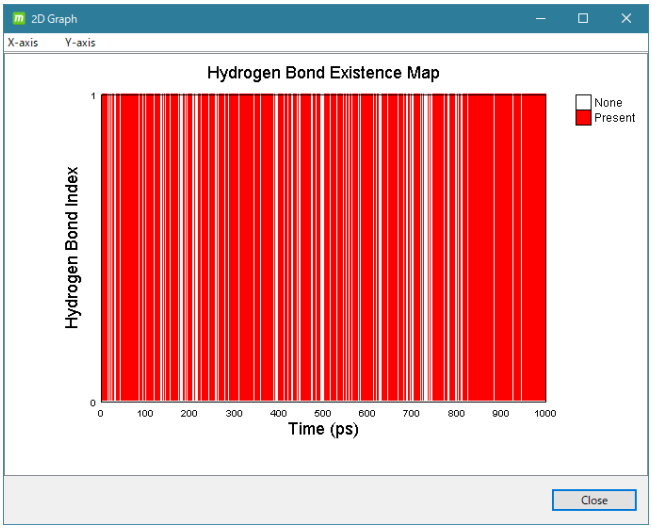



[Browse] reads the ndx and xpm files at the same time.

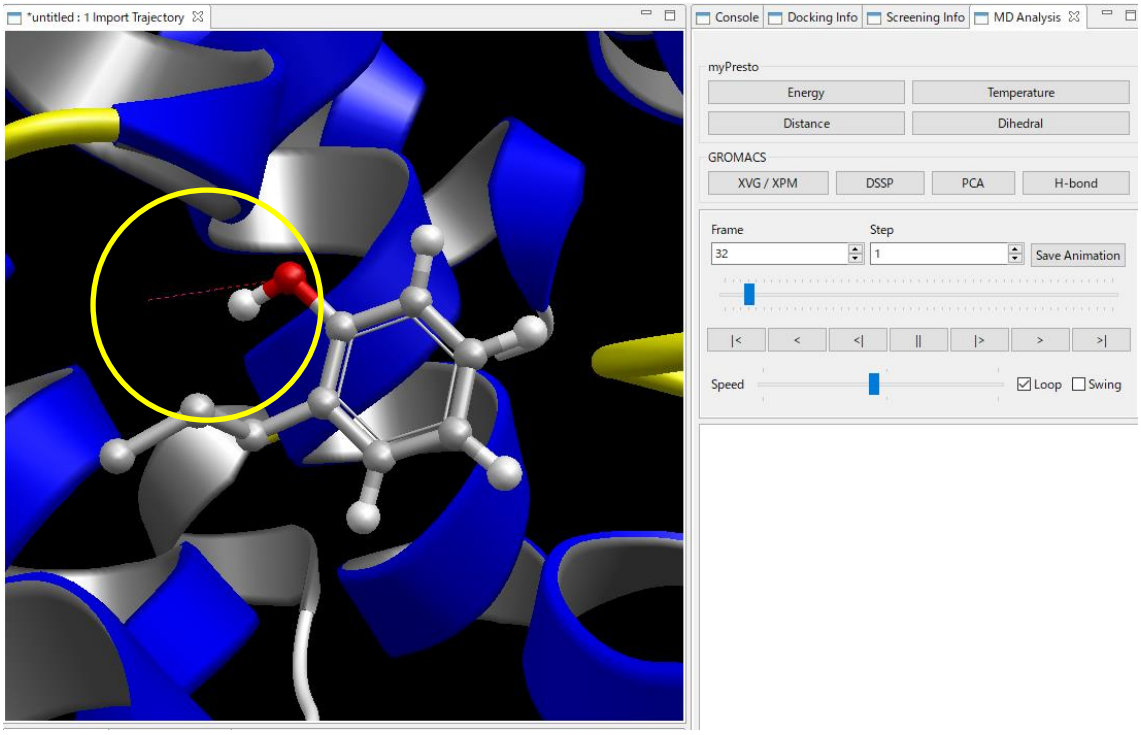
MolDesk Basic -> sample -> trajectory -> GROMACS -> hbond.ndx

hbmap. xpm

※ The ndx file contains a list of hydrogen bonds to be displayed, along with donor and acceptor atom information.



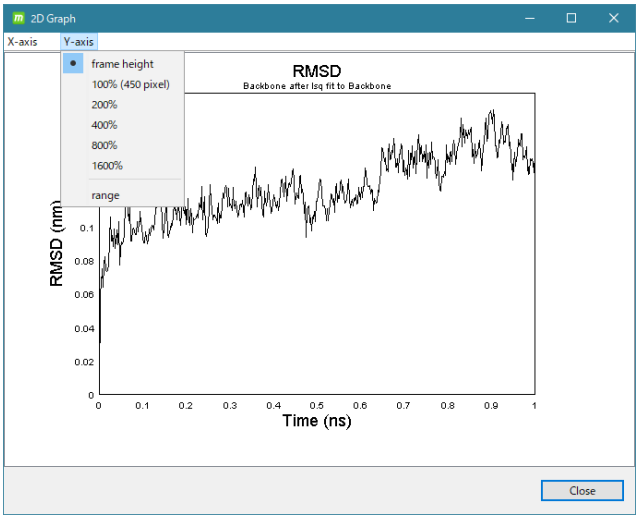

※ The result file of hydrogen bond analysis of GROMACS can also be displayed with the [XVG / XPM] button, but in order to display the hydrogen bond in the video as shown below, click the [H-bond] button to display the ndx file and xpm file. Please read at the same time.




The hydrogen bonds for the time corresponding to the video described in the hbmap.xmp file are displayed as dashed lines (inside the yellow circle).

(5) Enlarge the vertical and horizontal axes of a two-dimensional graph

2D graphs can be scaled from the menu independently in the x-axis and y-axis directions.




## 4.32. Fully automatic calculation

Learn about fully automatic calculations.

There are five menus for fully automatic calculations:

 [Auto Minimize]

 [Auto Solvate and Minimize]

 [Auto Dynamics]

 [Auto Solvate and Dynamics]

 [Auto Docking]

### 4.32.1. [Auto Minimize]

After adding missing hydrogen atoms to all molecules, charge is added to all compounds or glycans by MOPAC7 AM1 (Gasteiger method if not possible), and structural optimization is performed by energy minimization calculation in vacuum (without water solvent). increase. Molecules other than compounds or glycans add charge based on the force field selected in [Help]-[Preference]-[Molecule]-[tplgeneX]. The [Global Minimize] setting dialog is displayed on the way. Set the calculation parameters as necessary.

### 4.32.2. [Auto Solvate and Minimize]

After adding missing hydrogen atoms to all molecules, charge all compounds or glycans with MOPAC7 AM1 (Gasteiger method if not possible), and for molecules other than compounds or glycans, [Help] – [Preference]-[Molecule] – Adds a charge based on the force field selected with [tplgeneX].
After adding an aqueous solvent, the structure is optimized by calculating the energy minimization.
The [Solvate] and [Global Minimize] setting dialogs are displayed on the way. Set the calculation parameters as necessary.

### 4.32.3. [Auto Dynamics]

After adding the missing hydrogen atom to all molecules, charge is added to all compounds or glycans by MOPAC7 AM1 (Gasteiger method if not possible) calculation, and for molecules other than compounds or glycans, [Help] – [Preference]-[Molecule] – Adds charge based on the force field selected with [tplgeneX].
After performing structural optimization by energy minimization calculation in vacuum (without water solvent), MD calculation of the entire system is also performed. Along the way, the Global Minimize and Global Dynamics settings dialogs are displayed. Set the calculation parameters as necessary.

### 4.32.4. [Auto Solvate and Dynamics]

After adding the missing hydrogen atom to all molecules, charge is added to all compounds or glycans by MOPAC7 AM1 (Gasteiger method if not possible) calculation, and for molecules other than compounds or glycans, [Help] – [Preference]-[Molecule] – Adds charge based on the force field selected with [tplgeneX].
After adding the aqueous solvent, the structure is optimized by the energy minimization calculation, and then the MD calculation of the entire system is performed.
Along the way, the Solvate, Global Minimize, and Global Dynamics settings dialogs are displayed. Set the calculation parameters as necessary.

Please refer to "5.27 MD calculation in water 1" for a concrete execution example.

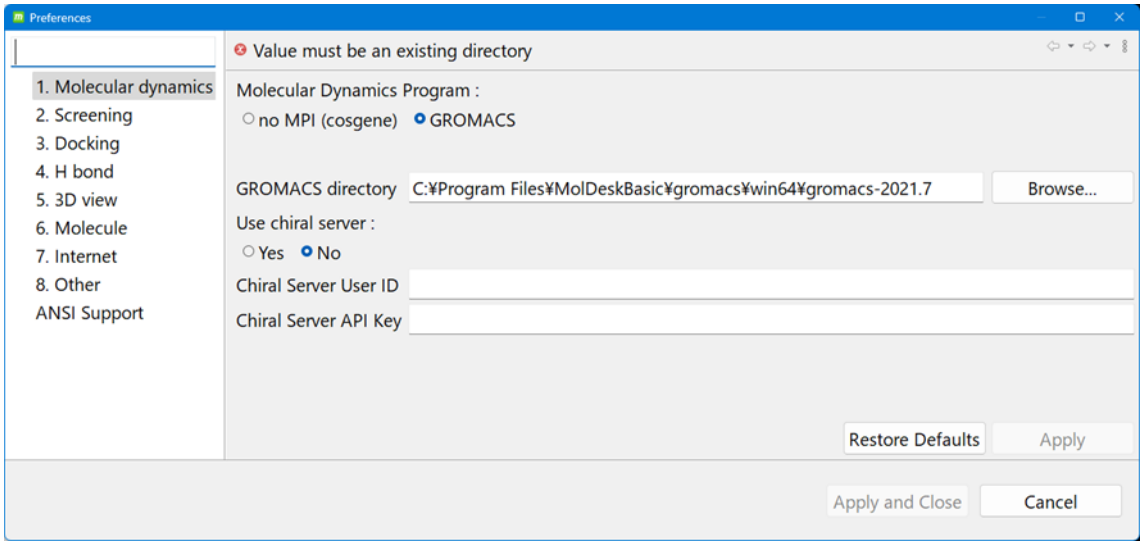
### 4.32.5. [Auto Docking]

After adding the missing hydrogen atom to all molecules, charge is added to all compounds or glycans by MOPAC7 AM1 (Gasteiger method if not possible) calculation, and for molecules other than compounds or glycans, [Help] – [Preference]-[Molecule] – Adds charge based on the force field selected with [tplgeneX].
Create pockets and perform docking calculations.
Along the way, the [Make Pocket] and [Docking] settings dialogs will appear. Set the calculation parameters as necessary.

Refer to "5.17 Docking Calculation 1 (Fully Automatic)" for a concrete execution example.

## 4.33. Preference settings

You can set various Preference values with [Help] – [Preference].

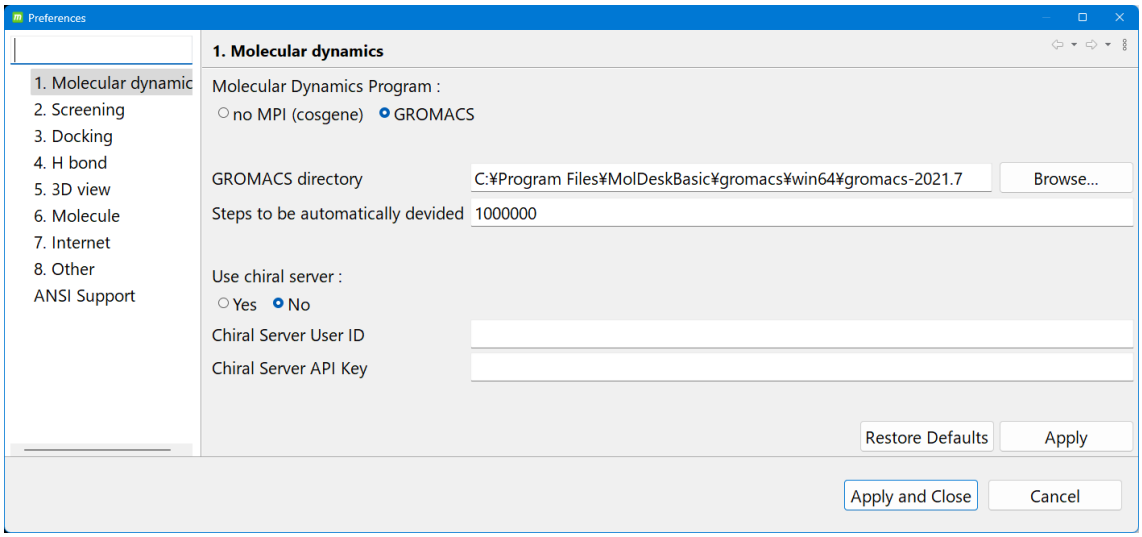



The description of each item is as follows.

| item | explanation |
|---|---|
| Molecular Dynamics | Settings Related to Molecular Dynamics Program |
| Screening | Setting up screening calculations<br>Not set in MolDesk Basic |
| Docking | Settings related to docking calculation programs |
| H Bond | Setting up the display of hydrogen bonds |
| Molecule | Setting up molecular species |
| Internet | Internet settings |
| Other | Other settings |

### 4.33.1. Molecular Dynamics

Configure settings related to the Molecular Dynamics program.



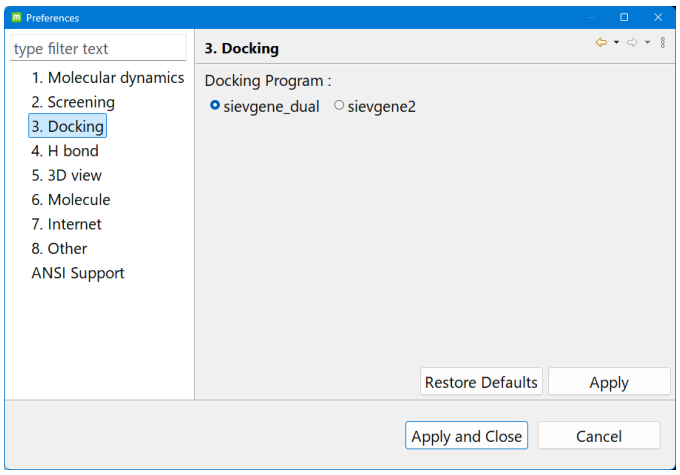

| item | explanation |
|---|---|
| Molecular Dynamic Program | Select no MPI (cosgene) / GROMACS<br><br>If you select GROMACS, please click the next [GROMACS directory] setting is required. |
| GROMACS directory | Set the directory of GROMACS installed by the user.<br>The directories specified here are the installed GROMACS<br>share<br>bin<br>of the installed GROMACS.<br>In the case of Windows, the executable program is implemented, so no setting is required (default setting is OK). |
| Steps to be automatically devided | Number of time steps to automatically split a long MD calculation in GROMACS in order to check the progress during the calculation on the 3D screen. |
| Use chiral server | Yes or No |
| Chiral Server User ID | User ID issued by Chiral |
| Chiral Server API key | API key issued by Chiral |

### 4.33.2. Screening

Because of the MolDesk Screening feature, it is not set in MolDesk Basic.

### 4.33.3. Docking

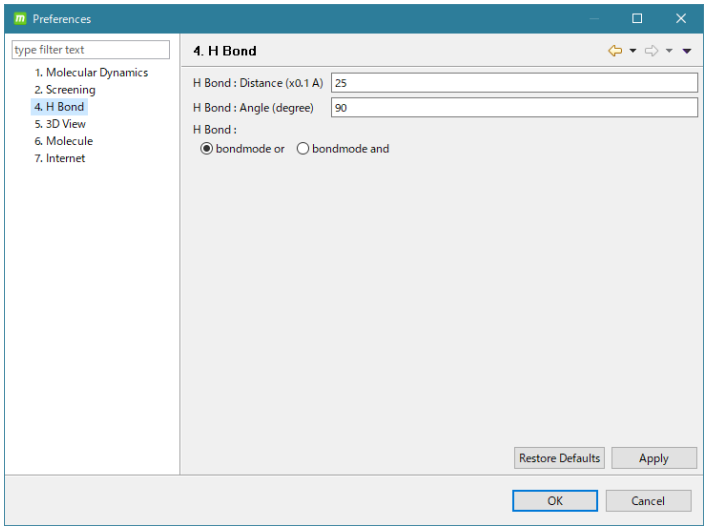
Set the docking calculation program to be used in docking calculations.




| item | explanation |
|---|---|
| sievgene_dual | Normally, this is used. |
| sievgene2 | The calculation program that the RNA docking accuracy, which can generate ring conformations, is almost equal to the protein docking accuracy, but it is time-consuming. |

### 4.33.4. H Bond

Set the values related to "5.15.9 Hydrogen bond display model".



| item | explanation |
|---|---|
| H Bond : Distance (*0.1Å) | Default:2.5Å<br><br>Distance threshold for determining hydrogen bonds in hydrogen bond calculations.<br>Higher values recognize more hydrogen bonds. |
| H Bond : Angle (degree) | Default:90 degrees<br><br>Threshold of the angle of the hydrogen bond determination in the hydrogen bond calculation.<br>Smaller ones recognize more hydrogen bonds. 1<br>Nolonger selected at 80 degrees. |
| H Bond : bondmode or bondmode and | Default:bondmode or<br><br>Settings in hydrogen bond display. Select one or the other.<br>bondmode or : Displays a hydrogen bond when one or more of the atoms involved in the hydrogen bond are selected.<br>bondmode and : Displays hydrogen bonds when both atoms involved in hydrogen bonding are selected. |

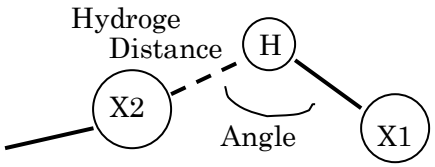
If there is a generation of two hydrogen bonds from one atom, only the dedy bonds are currently displayed.

About specifying the angle.

H Bond Angle <Angle [X2-H-X1] and Angle [X2-H-X1] <= 180

When the H Bond Angle is 180 degrees, hydrogen bonds are no longer caught.

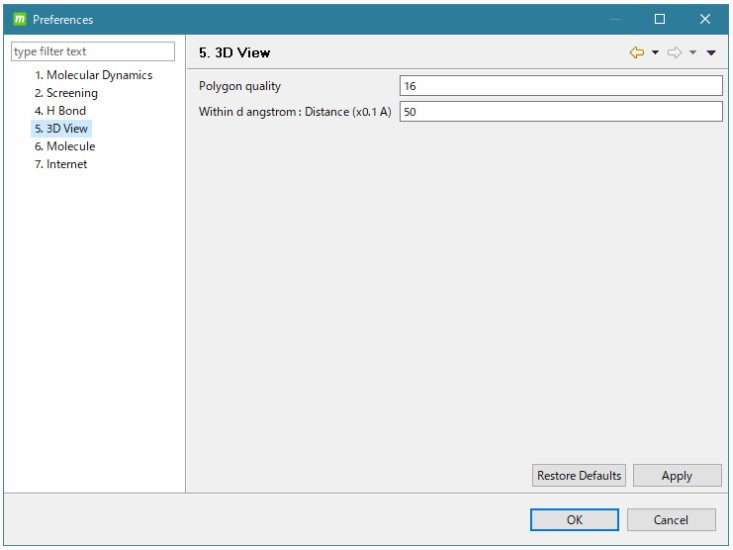
When the H Bond Angle is 0 degrees, water bonds at all angles are caught.




O atoms / N atoms / halogen O atoms / N atoms / halogen

### 4.33.5. 3D View

Values related to 3D polygon display and atomic selection conditions.

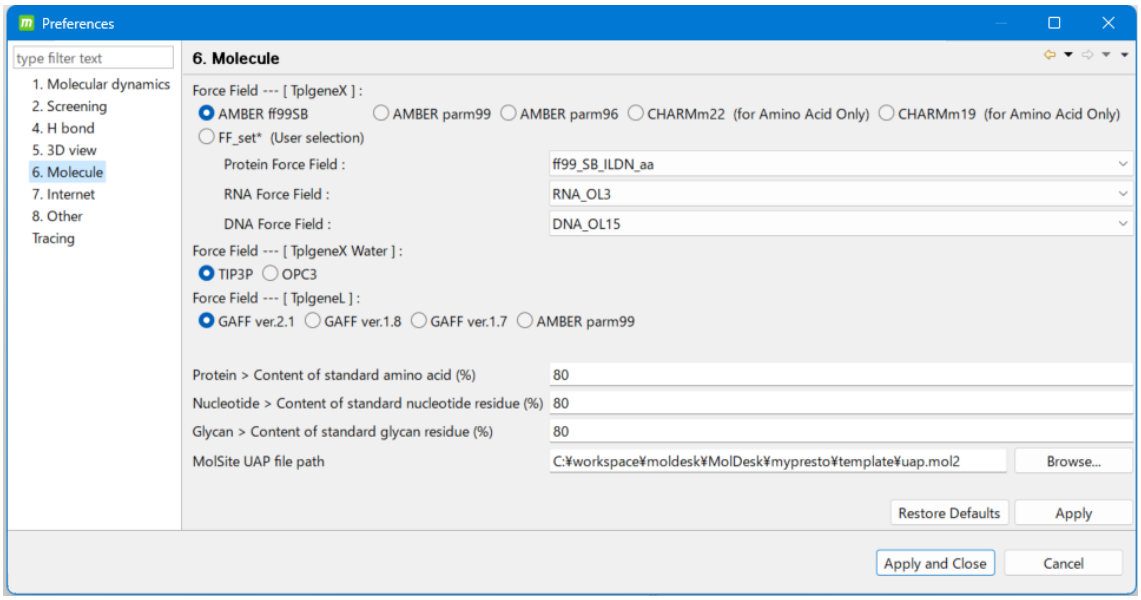



| item | explanation |
|---|---|
| Polygon quality | Default: 16<br><br>The fineness of the polygons in the 3D display. The higher the number, the finer it is.<br>On high-spec machines,it works lightly even if it is as large as20.<br>On low-spec machines, keep the numbers low. |
| Within d angstrom : Distance (*0.1Å) | Default:5Å<br><br>[Select] - Atomwithin d angstrom or<br>[Select] - In Sidechain within d angstrom<br>Selects from the selection to the atoms within this distance. |

### 4.33.6. Molecule

Select the force field of the molecule for each molecular species.

Set the criteria for determining proteins.



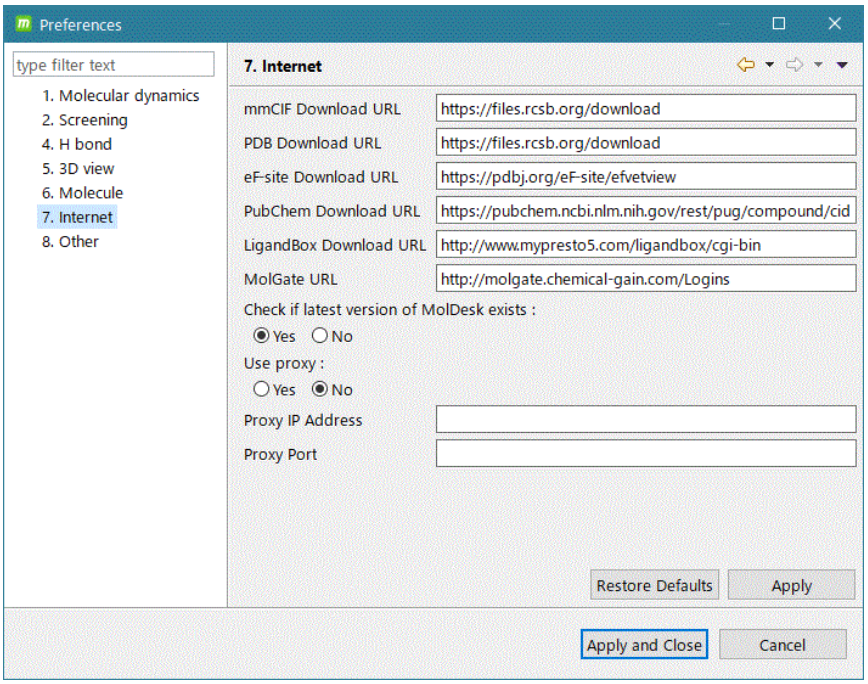

| item | explanation |
|---|---|
| Force Field --- [TplgeneX] | Default:AMBER ff99SB<br><br>a force field used to calculate non-compound and non-glycan molecules such as proteins, nucleic acids, lipids, metals, and ions<br>There are six types to choose from: AMBER ff99SB, AMBER parm99, AMBER parm96, CHARMm22, CHARMm19 and FF_set*.<br><br>When FF_set* is selected, the combination of Protein Force Field, RNA Force Field, and DNA Force Field can be further selected. Each of the following force fields can be selected.<br>Protein Force Field : ff99_SB_ILDN_aa, ff99_SB_aa, ff14_SB_aa<br>RNA Force Field : OL3, LJbb, ROC, YIL, Shaw, modrna08<br>DNA Force Field : OL15 |
| Force Field --- [TplgeneX Water] | Default: TIP3P<br>Force field used in the water molecule calculation.<br>Select from two types, TIP3P and OPC3. |
| Force Field --- [TplgeneL] | Default:GAFF ver.2.1<br><br>a force field used in calculating compounds<br>GAFF ver.2.1, GAFF ver.1.8, GAFF ver.1.7, amber parm99. |
| Protein > Content of standard amino acid (%) | Default:80%<br><br>The amino acid base name per molecule is the basis for determining what % amino acid base is contained as a protein. |

| | |
|---|---|
| | Molecules that are not determined as proteins are treated as compounds or glycans. Proteins, nucleic acids, lipids, metals, ions, etc. are processed by a program in myPresto called tplgeneX and tplgeneL for compounds and glycans. If this value is reduced, more molecules are treated as compounds and more molecular species can be calculated. Around 80%is appropriate. |
| Nucleotide > Content of standard nucleotide residue (%) | Default:80%<br><br>This is the standard for determining the percentage of nucleotide residues contained in the residue name per molecule to determine if it is a nucleotide.<br>Molecules that are not determined to be nucleotides are treated as compounds. Proteins, nucleic acids, lipids, metals, ions, etc., other than compounds or glycans are processed by tplgeneX, and compounds or glycans are processed by tplgeneL, a program in myPresto. |
| Glycan > Content of standard glycan residue (%) | Default:80%<br><br>This is the standard for determining the percentage of glycan residues contained in the residue name per molecule to determine if it is a glycan.<br>Molecules that are not determined to be glycans are treated as compounds. Proteins, nucleic acids, lipids, metals, ions, etc., other than compounds or glycans are processed by tplgeneX, and compounds or glycans are processed by tplgeneL, a program in myPresto. |
| MolSite UAP file path | Default: The path of the mol2 file that collects drug-like small molecule ligands<br><br>Path of the mol2 file of UAP (Univarsal Active Probe) small molecule compounds for use in the protein pocket discovery program MolSite.<br>User-created ones can be specified. |

※ Structures that are not registered in the force field cannot be calculated.

### 4.33.7. Internet

Sets the URL of a site on the Internet. You can also set whether to enable version checkingover the Internet or to connect to the Internet using the Proxy server.
Normally, you don't need to change it from the default.



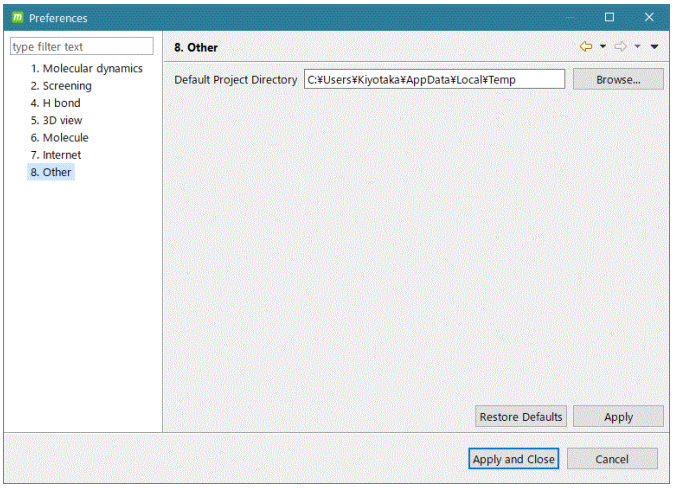

| item | explanation |
|---|---|
| mmCIF Download URL | Default :<br>https://files.rcsb.org/download<br>URL of mmCIF. Used with [File]-[Open Remote mmCIF / PDB]. |
| PDB Download URL | Default :<br>https://files.rcsb.org/download<br>URL of the PDB. Used with [File]-[Open Remote mmCIF / PDB]. |
| eF-site Download URL | Default :<br>https://pdbj.org/eF-site/efvetview<br>URL of eF-site. Used in [Display]-[Surface (eF-site)]. |
| PubChem Download URL | Default :<br>https://pubchem.ncbi.nlm.nih.gov/rest/pug/compound/cid<br>PubChem URL. Used with [Add Remote Compound]. |
| LigandBox Download URL | Default :<br>http://www.mypresto5.com/ligandbox/cgi-bin<br>The URL of the LigandBox. Used with [Add Remote Compound]. |
| MolGate URL | Default :<br>http://molgate.chemical-gain.com/Logins<br>URL of BY-HEX MolGate. (Currently unavailable) |
| Check if latest version of MolDesk exists | Default:Yes<br>Whether to display a warning screen at startup when a newer version of MolDesk than the one installed by the user exists. |
| Use Proxy | Default:No<br>Whether to use a Proxy server for internet connection |
| Proxy IP Address | When Use Proxy is Yes<br>Proxy server IP address |
| Proxy Port | When Use Proxy is Yes |

| | |
|---|---|
| | Proxy server Port number |

### 4.33.8. Other

Set the default directory (folder) for creating a new project.

New projects can be selected in this directory (folder)
MoldeskProject00000
MoldeskProject00001
MoldeskProject00002
・・・
created as .




| item | explanation |
|---|---|
| Default Project Directory | Default: The system default tmp directory.<br>It is different for Windows, Linux, and MAC. |

## 5. List of commands

The latest version of the command list is available on the MolDesk site.
https://www.moldesk.com/moldesk-basic-commands/

## 6. About myPresto

For more information about myPresto, please visit:
https://www.mypresto5.jp/

The source code and complete documentation of myPresto can be downloaded from the above site.