

PROTAC mutation section

This section of the tool helps the user to mutate the amino acid sequence of the target protein binding site of the PROTAC molecule.

1) Structure Input:

It takes the input of the PDB ID or structure from the local system, the output file saving location, and the desired output file format (PDB/mmCIF/mol2)

2) Minimization (optional):

Takes the number of steps of Steepest Descent and Conjugate Gradient to run minimization of the mutated structure. This step is optional.

(Note: An Increased number of steps and structure complexity may increase the time of minimization.)

3) Mutation mode:

Allows users to select the type of mutation they want to perform on the structure. It includes,

Single or multiple mutation: Mutate one or more amino acids with any other amino acid. (Discussed in detail in the next section)

Class-wise mutation: Mutate one or more amino acids to all amino acids of any class. (Discussed in detail in the next section)

Enter the number of amino acids that you want to mutate and generate fields for input entry.

The user may also visualize the generated Python script and download it to directly run in Chimera 1.19+ for mutation and minimization, and save the final structures in the desired folder in the desired format.

The screenshot shows the PROTAC Mutation web interface. At the top, it says "PROTAC Mutation" and "Generate ready-to-use UCSF Chimera Python scripts with desired mutation and optional minimization." The interface is divided into three main sections: 1) Structural Inputs, 2) Minimization (optional), and 3) Mutation Mode. In the Structural Inputs section, there are input fields for PDB ID (e.g. 1ABC), Local PDB structure file path (e.g. \\home\user\model.pdb), Output structure location (e.g. \\home\user\out_folder\), and a dropdown for Desired Output Format (PDB). In the Minimization section, there is a checked checkbox for "Select to perform energy minimization", and input fields for "Enter number of Steepest Descent Steps" (e.g. 2000) and "Enter number of Conjugate Gradient Steps" (e.g. 200). In the Mutation Mode section, there are two buttons: "Single / Multiple" and "Class-wise". Below these is an input field for "Enter number of mutations" (1). At the bottom, there are buttons for "Generate Mutation Inputs", "Preview Script", and "Download Script". A "Generated Script Preview" area is visible at the very bottom.

PROTAC Mutation

Generate ready-to-use UCSF Chimera Python scripts with desired mutation and optional minimization.

1) Structural Inputs

PDB ID: Local PDB structure file path:

Output structure location: Desired Output Format:

2) Minimization (optional)

Select to perform energy minimization:

Enter number of Steepest Descent Steps:

Enter number of Conjugate Gradient Steps:

3) Mutation Mode

Single / Multiple: Class-wise:

Enter number of mutations:

(1) (2) (3)

Generated Script Preview

```
from chimera import runCommand
runCommand("open 8ebk")
runCommand(u'swapaa tyr :3.B preserve true')
runCommand(u'minimize nsteps 200 cgsteps 200 nogui true')
runCommand(u'write 0 C:\\Users\\tusha_t46syw9\\Desktop\\trial\\tyr_3_min.pdb')
runCommand("close all")
```

PDB ID or enter pdb structure location from local system

Enter preferred output file saving location

Enter the steps of steepest descent and conjugate gradient for minimization

Select the type of mutation to conduct on desired amino acids

Enter the number of amino acids to mutate

Choose desired output format

Check the box if you want to run minimization on output structures

For the case of single/multiple mutation mode :

1. Enter the Chain ID of the desired amino acid to mutate
2. Enter the residue ID or residue number of the amino acid
3. Choose the amino acid you wish to mutate to

Repeat the same for all the entries

PROTAC Mutation

Generate ready-to-use UCSF Chimera Python scripts with desired mutation and optional minimization.

1) Structural Inputs

PDB ID

8ebk

Local PDB structure file path

e.g. \\home\user\model.pdb

Output structure location

C:\Users\tusha_t46syw9\Desktop\trial\

Desired Output Format

PDB

2) Minimization (optional)

Select to perform energy minimization



Enter number of Steepest Descent Steps

200

Enter number of Conjugate Gradient Steps

200

3) Mutation Mode

Single / Multiple

Class-wise

Enter number of classes

1

Generate Class Fields

Hydrophobic

(1)

A

(2)

3

(3)

Members: A (ALA - Alanine), V (VAL - Valine), I (ILE - Isoleucine), L (LEU - Leucine), G (GLY - Glycine), M (MET - Methionine), P (PRO - Proline)

Preview Script

Download Script

Generated Script Preview

```
runCommand(u'swapaa val :3.A preserve true')
runCommand(u'minimize nsteps 200 cgsteps 200 nogui true')
runCommand(u'write 0 C:\\Users\\tusha_t46syw9\\Desktop\\trial\\val_3_min.pdb')
runCommand(u'swapaa ile :3.A preserve true')
runCommand(u'minimize nsteps 200 cgsteps 200 nogui true')
runCommand(u'write 0 C:\\Users\\tusha_t46syw9\\Desktop\\trial\\ile_3_min.pdb')
runCommand(u'swapaa leu :3.A preserve true')
runCommand(u'minimize nsteps 200 cgsteps 200 nogui true')
runCommand(u'write 0 C:\\Users\\tusha_t46syw9\\Desktop\\trial\\leu_3_min.pdb')
runCommand(u'swapaa gly :3.A preserve true')
runCommand(u'minimize nsteps 200 cgsteps 200 nogui true')
runCommand(u'write 0 C:\\Users\\tusha_t46syw9\\Desktop\\trial\\gly_3_min.pdb')
runCommand(u'swapaa met :3.A preserve true')
runCommand(u'minimize nsteps 200 cgsteps 200 nogui true')
runCommand(u'write 0 C:\\Users\\tusha_t46syw9\\Desktop\\trial\\met_3_min.pdb')
runCommand(u'swapaa pro :3.A preserve true')
runCommand(u'minimize nsteps 200 cgsteps 200 nogui true')
runCommand(u'write 0 C:\\Users\\tusha_t46syw9\\Desktop\\trial\\pro_3_min.pdb')
runCommand("close all")
```

PDB ID or enter pdb structure location from local system

Enter preferred output file saving location

Enter the steps of steepest descent and conjugate gradient for minimization

Select the type of mutation to conduct on desired amino acids

Enter the number of amino acids to mutate

Choose desired output format

Check the box if you want to run minimization on output structures

For the case of class-wise mutation mode :

1. Enter the preferred class of amino acid (all amino acids of each class are listed for reference)
2. Enter the chain ID for the amino acid
3. Enter the residue ID or residue number of the amino acid

Repeat the same for all the entries