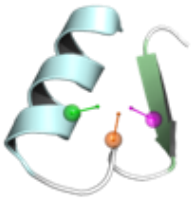
MeCOM Manual



1. Introduction

MeCOM is a versatile tool for the screening, analyzation and comparison of metalloenzymes, which is based on the pharmacophore and α-carbon patterns. It can automatically recognize the active site of the given metalloenzyme, extract the site features and compare with other metalloenzymes to obtain similarity information. MeCOM can generate feature models of the metalloenzyme active site and overlap similar active sites of others to provide information for the study of interaction mechanism between metalloenzyme and ligand. It can also provide new ideas for the design of targeting metalloenzyme inhibitors by combining drug purposing.

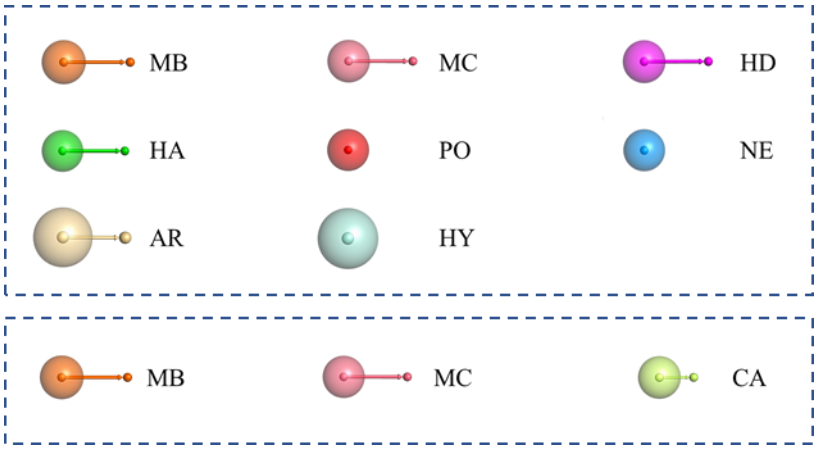


Figure 1. Graphic representation of eight types of pharmacophore features and three types of α-carbon features showed by a PyMOL plugin.

2. Functions

(1) Determine whether a given protein belongs to metalloenzyme

(2) Recognize the active site of a given metalloenzyme

(3) Extract the features information of the active site based on pharmacophore and α-carbon, respectively

(4) Compare the active sites and get the similarity scores

(5) Superimpose two similar metalloenzyme structures for visual analysis

3. Compatibility and Installing

Linux

MeCOM is expected to work on compatible 64-bit Linux systems, and it's tested and feasible on CentOS 7.

Windows

MeCOM current version has been tested on Windows 8/10 without any dependency.

Note: MeCOM old version must depend on C++ compiler suite which should be pre-installed. MinGW (https://osdn.net/projects/mingw/releases/) is recommended.

Mac

MeCOM current version has been tested on macOS 11/12.

Installing

Click the downloaded MeCOM.zip and follow the instructions.

Note: Please send an email to ddtmlab_gbl@sina.com to obtain the unzipping password of the password-protected ZIP file.

4. Usage

Linux

Open the terminal and, if you installed MeCOM in the default location, type:

```
cd /home/MeCOM-centos7/bin
chmod +x MeCOM
./MeCOM --para parameter.txt
```

Windows

Open the Command Prompt after unzipping the package in your install location, type:

```
cd C:\Users\ibm\MeCOM-Window10\bin
./MeCOM.exe --para parameter.txt
```

Mac

Open the terminal and, if you installed MeCOM in the default location, type:

```
cd Desktop/MeCOM-Mac11/bin
chmod +x MeCOM
./MeCOM --para parameter.txt
```

See the parameters for details *via* type: *./MeCOM or .\MeCOM.exe*

Parameters

--para <parameter file (txt format)>

The parameter file contains all of the parameters listed below.

--pro *< protein file (pdb format) >*

--center_x *< X-coordinate of the assigned center by user >*

--center_y *< Y-coordinate of the assigned center by user >*

--center_z *< Z-coordinate of the assigned center by user >*

--radius *< radius of the assigned sphere by user >*

--out *< generated pharmacophore/alpha-carbon file (phore/atoms format) >*

--id *< protein ID for the output folder >*

--ref *< reference pharmacophore/alpha-carbon (phore/atoms format) >*

--query *< query pharmacophore/alpha-carbon (phore/atoms format) >*

--type *< phore or atoms >*

--result *< aligned query file (phore/atoms format) >*

--score *< score (score format) >* *--pro_q* *< protein file of query (pdb format) >* *--pro_o* *< aligned protein file of query (pdb format) >*

5. **PyMol Plugin Usage**

The MeCOM-Plugin.py is included in MeCOM.zip.

Usage and Note:

(1) Open Pymol

(2) Open the tab "Plugin"，click the button "Plugin Manager"

(3) Click the button "Choose file" in the panel "Install New Plugin", import the file MeCOM-Plugin.py, installation completed

(4) Start the plug-in MeCOM: in the tab "Plugin", under the Legacy Plugins option, find the MeCOM plug-in. Click the button "Read alpha carbon file" to read in the file (.atoms) or the button "Read pharmacophore file" to read in the file (.phore), then the corresponding model will show out.

6. Examples

(1) Generate the α-carbon and pharmacophore models automatically for a given metalloenzyme

Command: *./MeCOM --para Examples/Example_1/p1.txt*
Parameters: *--pro Examples/Example_1/4c1e.pdb* *--out Examples/Example_1/* *--id 4c1e*
Results: *Output pharmacophore file and α-carbon file:*

4c1e_1_carbon.atoms
4c1e_1_refphore.phore

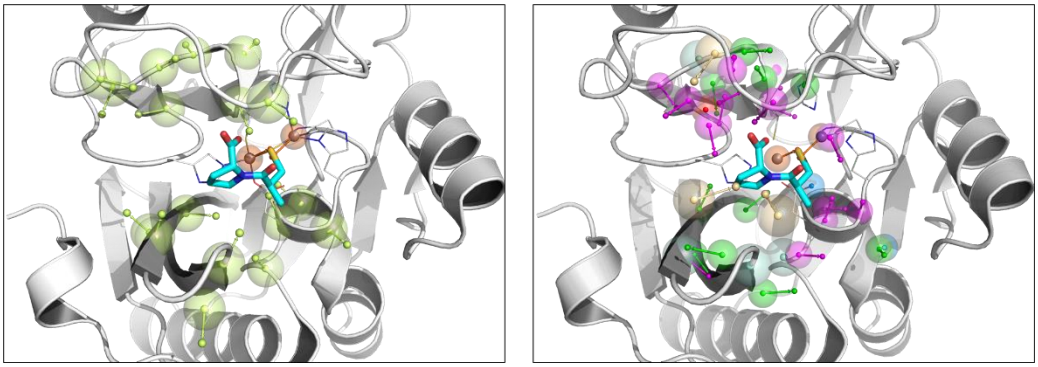


Figure 2. The α-carbon model (left) and pharmacophore model (right)

(2) Generate the α-carbon and pharmacophore models based on the parameters assigned by user for a given metalloenzyme

Command:

./MeCOM --para Examples/Example_2/p2.txt

Parameters:

--pro	*Examples/Example_2/2yz3.pdb*
--out	*Examples/Example_2/*
--id	*2yz3*
--center_x	*34.0*
--center_y	*13.0*
--center_z	*108.0*
--radius	*20*

Results:

Output pharmacophore file and α-carbon file:

2yz3_1_carbon.atoms
2yz3_1_refphore.phore

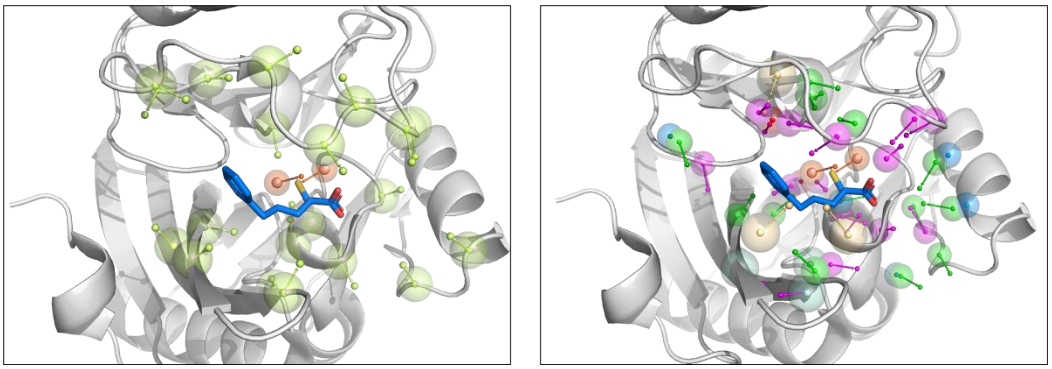


Figure 3. The α-carbon model (left) and pharmacophore model (right)

(3) Compare the active sites of two different metalloenzyme based on pharmacophore

Command:

./MeCOM --para Examples/Example_3/p3.txt

Parameters:

--ref Examples/Example_3/4c1e/4c1e_1_refphore.phore

--query Examples/Example_3/2yz3/2yz3_1_refphore.phore

--type phore

--result Examples/Example_3/result_4c1e_1_2yz3_1.phore

--score Examples/Example_3/result_4c1e_1_2yz3_1_phore.score

--pro_q Examples/Example_3/2yz3.pdb

--pro_o Examples/Example_3/result_2yz3_1_rot_by_phore.pdb

Results:

Output similarity score file, matching pharmacophore file and rotated PDB file:

result_4c1e_1_2yz3_1_phore.score
result_4c1e_1_2yz3_1.phore
result_2yz3_1_rot_by_phore.pdb

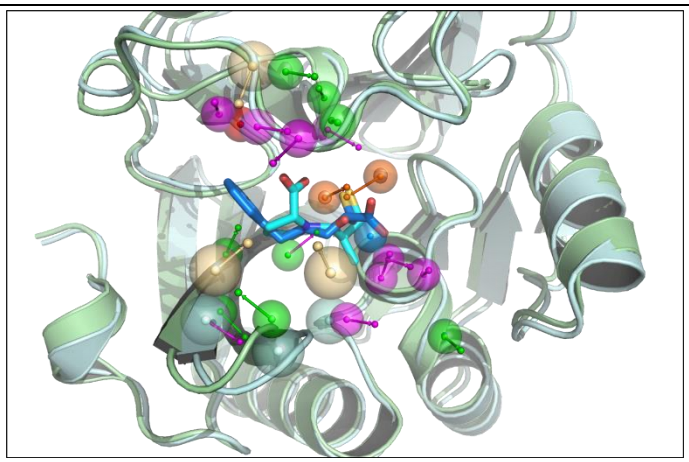


Figure 4. The superposition of 4C1E (green) and 2YZ3 (cyan) based on pharmacophore

(4) Compare the active sites of two different metalloenzyme based on α-carbon

Command:

./MeCOM --para Examples/Example_4/p4.txt

Parameters:

--ref Examples/Example_4/4c1e/4c1e_1_carbon.atoms

--query Examples/Example_4/2yz3/2yz3_1_carbon.atoms

--type atoms

--result Examples/Example_4/result_4c1e_1_2yz3_1.atoms

--score Examples/Example_4/result_4c1e_1_2yz3_1_carbon.score

--pro_q Examples/Example_4/2yz3.pdb

--pro_o Examples/Example_4/result_2yz3_1_rot_by_carbon.pdb

Results:

Output similarity score file, matching α-carbon file and rotated PDB file:

result_4c1e_1_2yz3_1_carbon.score
result_4c1e_1_2yz3_1.atoms
result_2yz3_1_rot_by_carbon.pdb

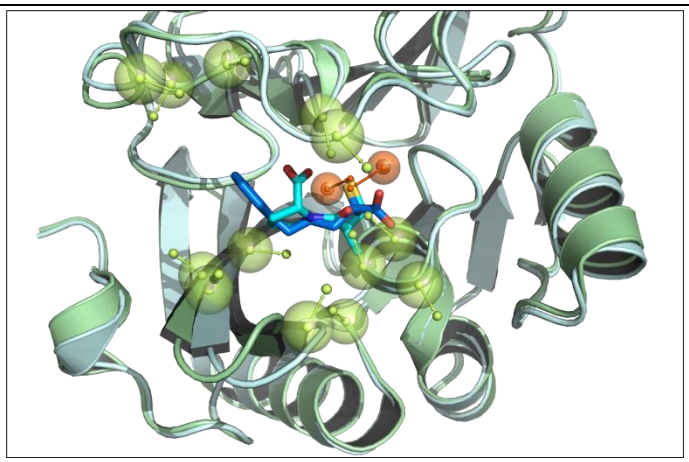


Figure 5. The superposition of 4C1E (green) and 2YZ3 (cyan) based on α-carbon

Thanks for use!

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