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Getting to Know the MetalPDB

Throughout the course of the semester we have been using the Protein Data Bank (PDB) to access structures of biological macromolecules that contain metal binding sites. While this site contains many structures, it does not explicitly identify the metal containing structures, but can be searched using the ligand code for the metal ion or metal cofactor (if it is known). The PDB does not readily provide any information specifically about the metal coordination environment (aside from the *Ligand Interaction* view) and obtaining this information is complicated. MetalPDB is a website that "collects and allows easy access to the knowledge on metal sites in biological macromolecules."[1] As the name suggests, the site uses structures stored in the PDB as a starting point, but curates them according to metal binding sites.

As we move through the remainder of the semester, this site and the associated tools will be useful to gain information about metal-containing biological macromolecules. This exercise will introduce you to the site and allow you to see what type of information can be obtained from the site.

The first step in familiarizing yourself with the site is to watch the video entitled "Basic concepts in MetalPDB" and answer the following questions. [Note: There is no sound with this video and you must expand it to full screen to read all of the text on the slides.]

1. In your own words, please define the following terms.
    a. Metal coordination sphere

    b. Minimal Functional Site (MFS)

    c. Equistructural MFS

2. How is an equivalent MFS distinguished from an equistructural MFS?

[1] http://metalweb.cerm.unifi.it/ (accessed July 6, 2018)

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General Information about Metal-Binding Sites

It is possible to get an overview of the different metals found in biological systems, as well as the ligands that bind to them using the *Statistics* menu. To get an overall picture of the metal-containing structures in the PDB, go to *Statistics* > *Metals in PDB*.

3. What percentage of the structures in the PDB have a metal bound?

4. What are the two most popular coordination geometries for metals and the percentages for each of these geometries?

You can also get an idea of what geometries are adopted by certain metals by choosing *Statistics* > *Per geometry.* From the list of the 37 possible geometries, please choose one geometry (by clicking on the figure in the far-right column) as directed in the instructions for this exercise.

Chosen geometry _____

5. What is the metal that most commonly adopts the geometry that you have chosen?

The *Statistics* > *Per metal* menu will allow you to choose a specific metal and get information about the geometries adopted by that metal and the ligands that bind to the metal. To choose a metal, click the radio button under the element in the periodic table. You can then choose either the **Analyze Geometries** or **Analyze Ligands** buttons found under the periodic table.

Answer the next three questions for the metal you have chosen
Chosen metal _____

6. What is the most common geometry adopted by this metal in MFSs? [**Analyze Geometries**]

7. What is the most common ligand bound to the metal in this geometry? [**Analyze Geometries**]

8. What are the two most common ligands bound to this metal in representative MFSs? [**Analyze Ligands**]

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In this menu, you can also see which metals commonly substitute for other metals in metal binding sites by choosing *Statistics* > *Metal Substitutions*.

9. What metal most commonly substitutes for copper in Cu-binding sites?

Searching for More Specific Information about MFSs

You can search the MetalPDB database in several ways, but for this exercise the most important will be by the PDB ID (*Search* > *Keyword Search* > *PDB ID)* and by the metal (*Search* > *Metal Search*). The PDB ID search can be used when there is a particular structure being investigated. Please search for one structure (using the PDB ID search) that we have looked at to this point in the semester.

10. Identify the structure you chose by both its name and its PDB ID.

11. Using the Summary tab, what is the function of the site?

12. Using the Coordination Sphere tab, what ligands are bound to the metal?

You can also look at the structure graphically by clicking on the image found in the Summary tab. Information about equistructural sites and equivalent sites can be found in the appropriate tabs as well.

The advanced search feature is also quite useful because you can combine search parameters to find commonalities between metal binding sites. In the Advanced Search screen (*Search* > *Advanced Search*), enter the following parameters in the sections noted:

- **{Metal Features}** Metal: Fe
- **{Metal Features}** Geometry: Octahedron
- **{Actions}** Count Results

You can then choose the **Execute** button to begin the search.

13. How many hits were returned from your search?

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Change the action to View Results and choose the **Execute** button.
Choose the second hit on the list (1b2v_1) by clicking on the radio button in the Select column and then choosing the **View** button at the bottom of the page.
In the Summary tab, click on the image to bring up the JSmol viewer.
There are many checkboxes that allow you change the representation and the information displayed.

Under **Coordination Geometry**, you can show the coordination geometry about the metal by choosing **Geometry**.

You can also display the bond lengths between the metals and their ligands by checking the box in the **Measure** section.

You can also find the metal-ligand bond lengths in a table found within the information collected under the Coordination Sphere tab.

14. For the iron in this structure, what are the bond lengths between the iron and the six donor atoms from the attached ligands?

Final Suggestions

Hopefully, this exercise has helped you to become familiar with the MetalPDB site and the information that can be obtained from it. The questions in this exercise were chosen to guide you through the common ways that the database will be used in this course. To learn more about the site, you should take some time and experiment with some searches and other menu choices. You may be pleasantly surprised with what you find!