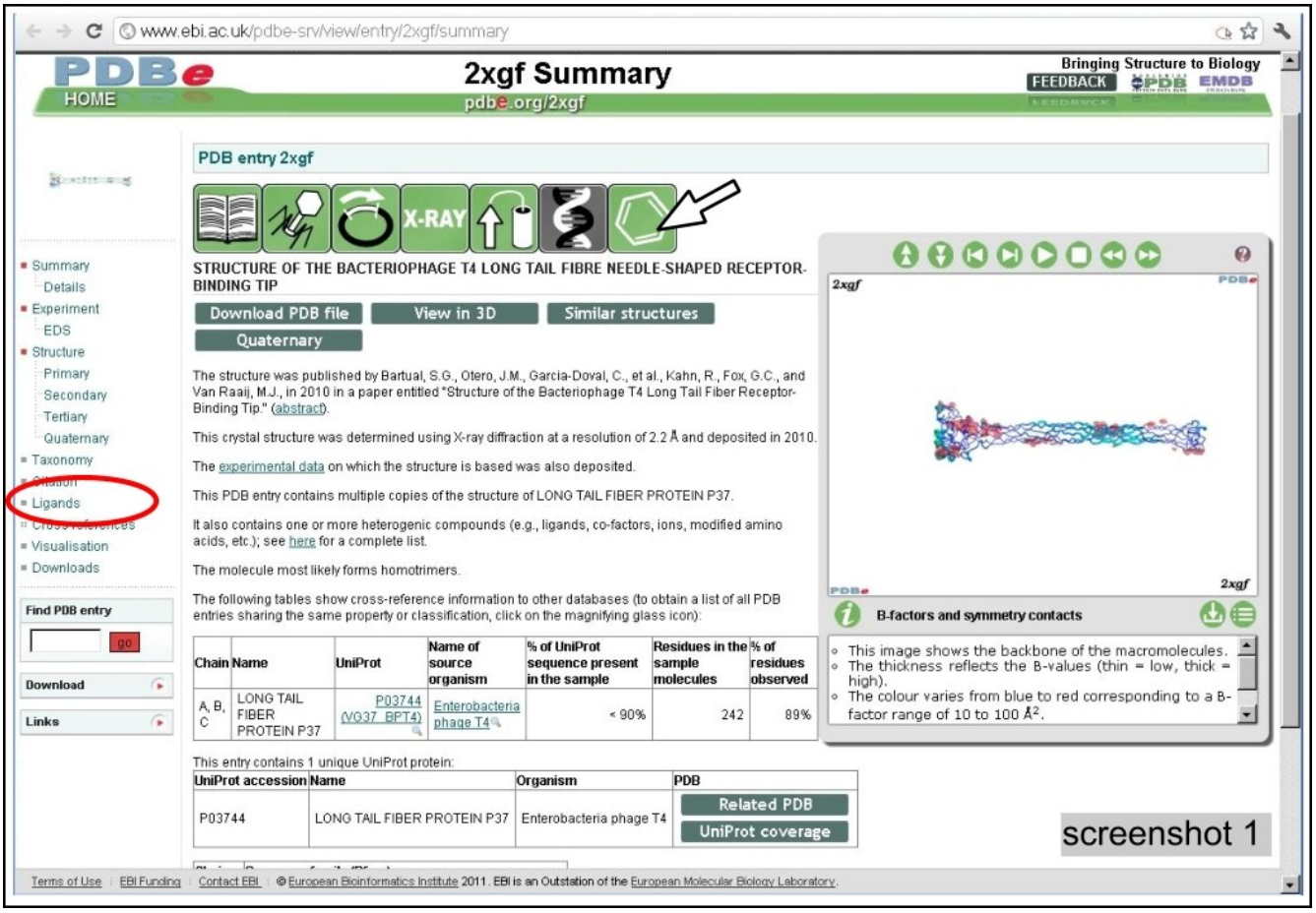
Viewing the 2xgf ligands from its Summary page

Macromolecular structures contain a variety of small molecule compounds. In the PDB archive these are defined as **heterogens** or as **ligands**. Some of them are covalently linked to a macromolecule chain and some are incorporated as modified residues. Even if not directly included in this way, they all get a **three-letter** code and a chain identifier equivalent to a **residue**. To see the small molecule content of a PDB entry you can visit the **Ligand** summary page from the entry's main **Summary** page. As shown in screenshot 1 you click either on the Ligand link (circled in red) or directly on the green **PDBePrints** ligand logo (the benzene ring symbol, arrowed).

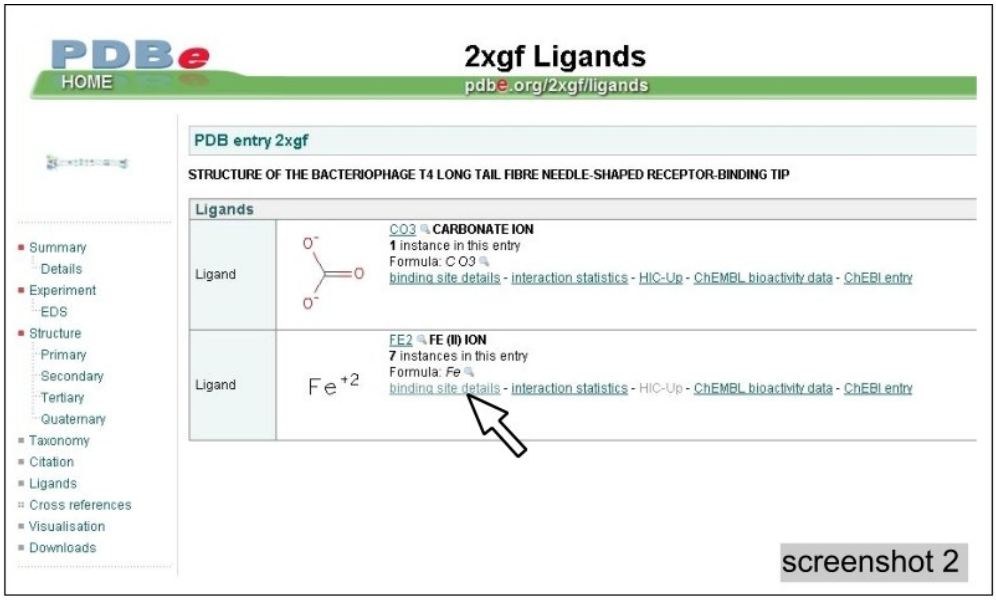
Usefully, ligands only turn the **PDBeMotif** symbol green if they are bound to the macromolecule rather than being modified residues that are incorporated into the backbone of the molecule.



Ligands in the 2xgf structure from its Summary page.
Click on the green Ligand logo in the PDBePrints (arrowed) or on the Ligands link (circled in red).

The list of ligands in 2xgf

This **Ligand** summary page for the phage receptor-binding **gp47** structure shows that it contains one instance of the ligand **CO3** (bicarbonate) and seven instances of **FE2** (iron, Fe2+, ion). You will know from the accompanying **Quips** article that seven iron ions are integral structural components of the **gp47** central needle domain structure. In general metal ions can be bound by protein sidechains and prosthetic groups. To examine the environment that these seven iron ions are bound in by the **gp47** protein you can browse the analysis from the **PDBeMotif** service. This is precalculated for most PDB entries. To view this information click on the '**binding site details**' link under the 'Formula Fe' line for the FE2 ligand (arrowed in screenshot 2).



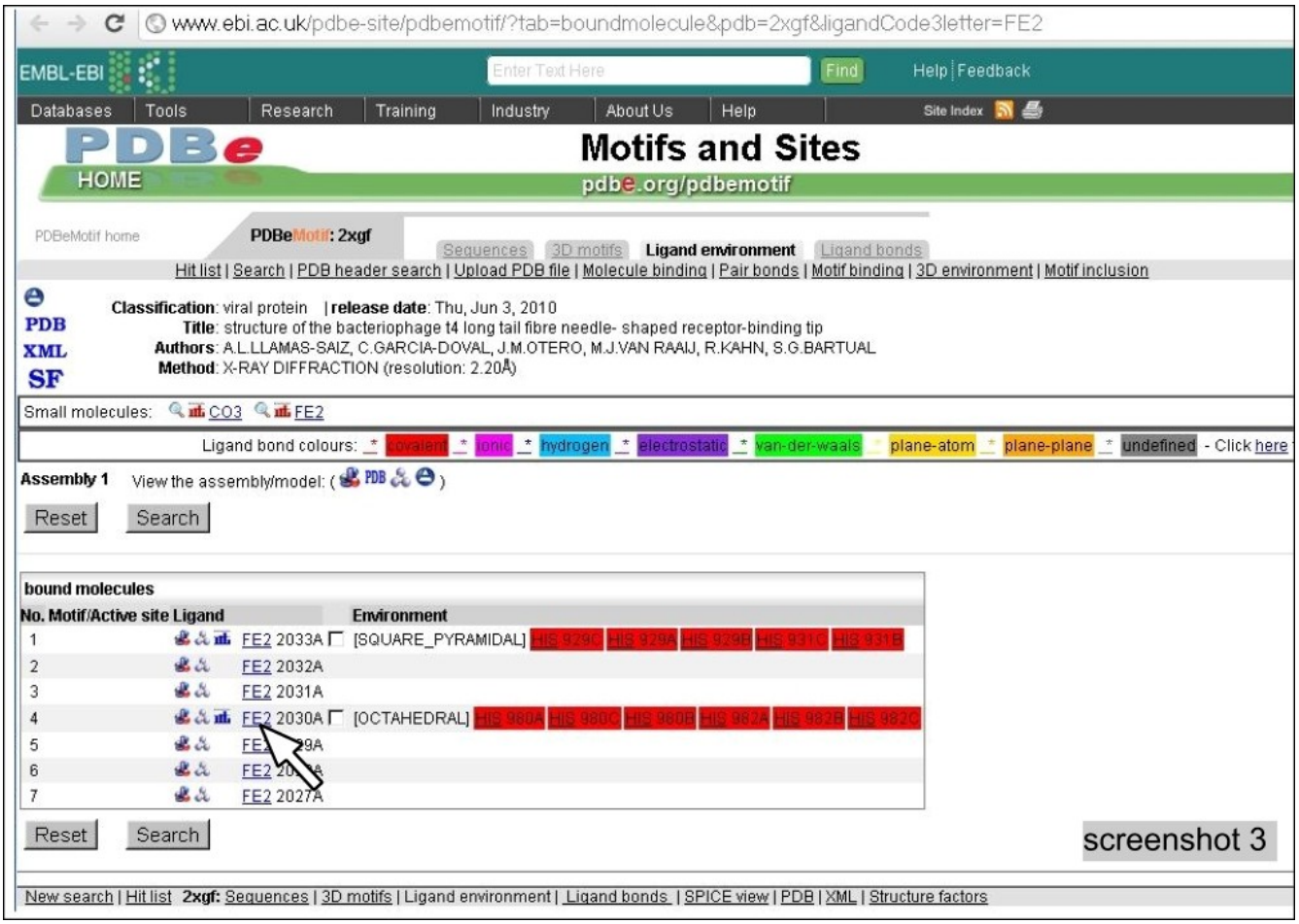
The list of ligands in PDB entry 2xgf.
To examine the environment around the Fe2+, click on 'binding site details' link (arrowed).

'Almost' covalent links to the Fe2+ ions

Metal ions are coordinated by sidechains through donation of electrons to the ions. This **coordination** chemistry gives an association that is not as strong as that from the usual covalent bonds. PDBeMotif analyses the environment aroung the metal ions and also help you explore other similar examples in the PDB archive.

The standard **PDBeMotif** analysis in fact recognizes only one of the seven sites as having a complete set of 'almost covalent' bonds. You can see these shown in red in screenshot 3. For other environments you will also see examples of interactions shown by the colours listed at the top.

Click on the FE2 for the octahedral **2030A** site to see the full analysis for it. Notice that the iron ion has a residue number offset from those of the protein residues, but that it has inherited a protein chain id -'**A**'. For ligands this chain will be that closest in space or with a direct contact or bond.

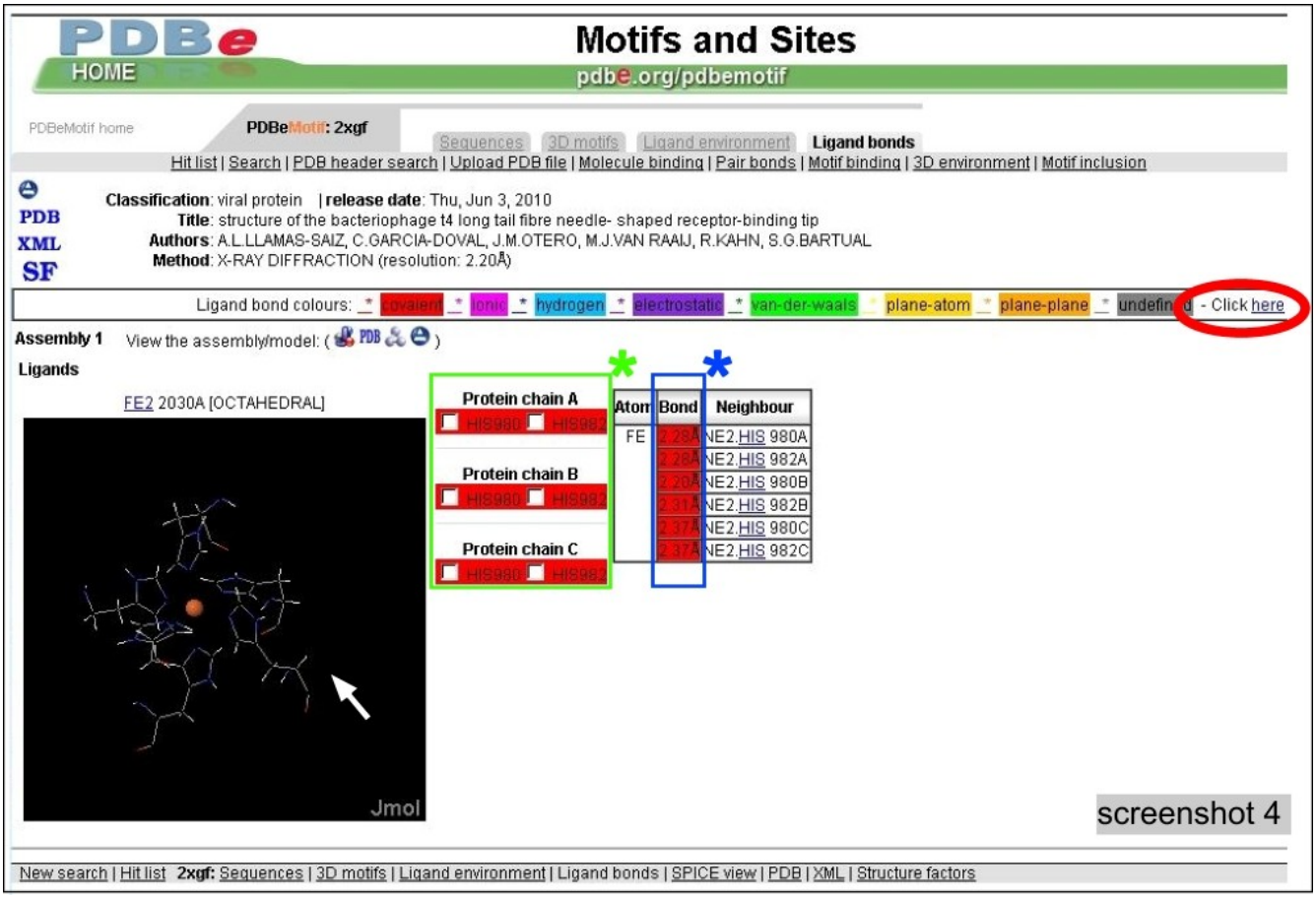


Motifs and Sites analysis of Fe2+ ions environment in 2xgf
*The results from the standard **PDBeMotif** analysis have only two of the Fe2+ sites displayed. In one case only five out of the six His residues are listed. To view the complete octahedral site click on the FE2 2030A link (arrowed).*

The iron octahedral coordination site in detail

Clicking on the FE2 2030A example of the **gp37** sites gives a fuller analysis (screenshot 4). This shows that it is bound by two histidines from each of the three protein chains (boxed in green). The bond length to each are shown (boxed in blue). You can rotate the view of the site. This page can also be used to search for similar environments in other structures in the PDB archive.

Octahedrally-coordinated iron ions are of course common in the PDB, but much more commonly they are held in the centre of a porphyrin ring which provides four nitrogen atoms in a plane. The out-of-plane contacts to the iron in porphyrins are provided by protein sidechains. This is the basic structure of haem in proteins such as cytochromes and haemoglobin.

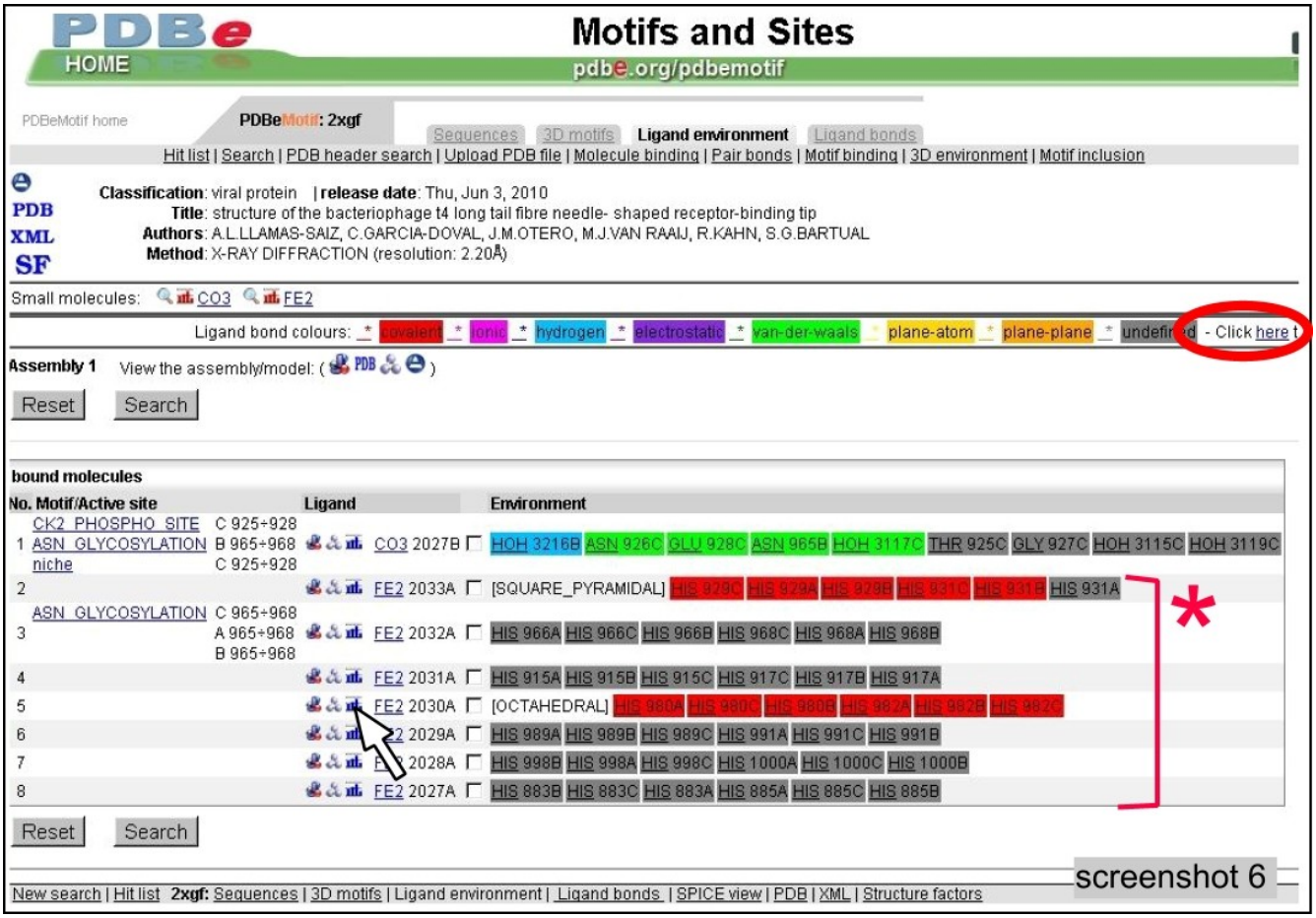


Looking at the best octahedral Fe2+ ion (residue 2030A).
*The PDBeMotif analysis of the environment of Fe2+ 2030A. The notionally covalent bonds to a pair of His residues from each protein chain are listed (boxed in green *) and the bond-lengths are indicated (boxed in blue *). An interactive graphics window shows the arrangement around the iron - you can rotate this with the mouse (arrowed).*

A less restrictive view of the 2xgf sites

You can relax the definition of the length of bonds shown by PDBeMotif. Press the **'click here to show 5 Å bonds '** (circled in red, screenshot 5) to see all of the His residues around each of the seven iron ion.

The results are shown in the screenshot below.



A less restrictive view of the 2gxf sites

*Pressing the '**Click here to show 5 Å bonds**' control (circled in red) picks up all the His sidechain interactions in all of the sites (bracketted in red *). The extra bonds are listed as undefined but can be examined for any site by visiting its summary page as shown previously in screenshot 4. Click on any of the bar-chart icons (arrowed) to search for similar sites throughout the PDB archive.*

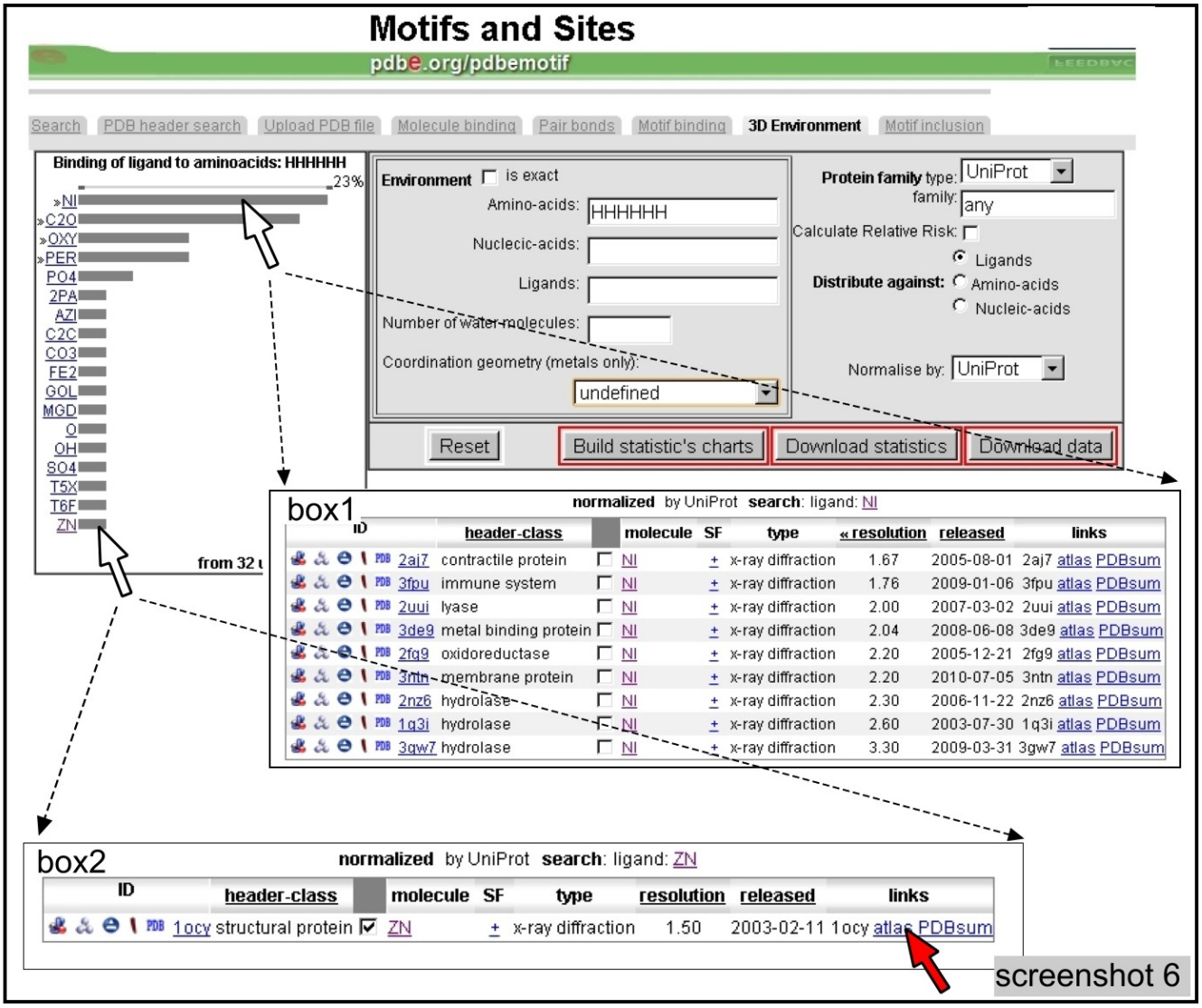
All ligands bound by six Histidine residues

Clicking on any of the statistical analysis links (bar-chart icon - arrowed in screenshot 6) shows the chart below (screenshot 6). This shows all the sites in the PDB archive where six His residues bind a small ligand. Not surprisingly there is a preponderance of Nickel ions bond in this way. You probably know this as a favoured metal coordination that is used in the purification of proteins with an engineered six His tag. In that case only part of the site is provided by the protein and the other by the affinity matrix. If you browse the Ni site entries (box 1 in screenshot 6) you will find that the binding of the nickel ion usually involves additional copies of the coordinating protein chain.

It is interesting that iron ions are not in general bound by six His residues (box 2 in screenshot 6). In fact **2gxf** is the only example in the PDB currently. Perhaps the rarity of six His around iron is owing to the success of the porphyrin co-factor for binding iron octahedrally as **haem** in biological systems.

There are a number of ligands indicated in the chart - each given their **three-letter** code. Click on the

code to see what they are, and click on each bar in the chart (arrowed) to see the list of entries. In fact there are only three metals listed: Ni, Fe, and Zn. The Ni and Fe were explored above, so now explore the Zn binding site by clicking on the 'atlas' link (red arrow) to visit its Summary page.



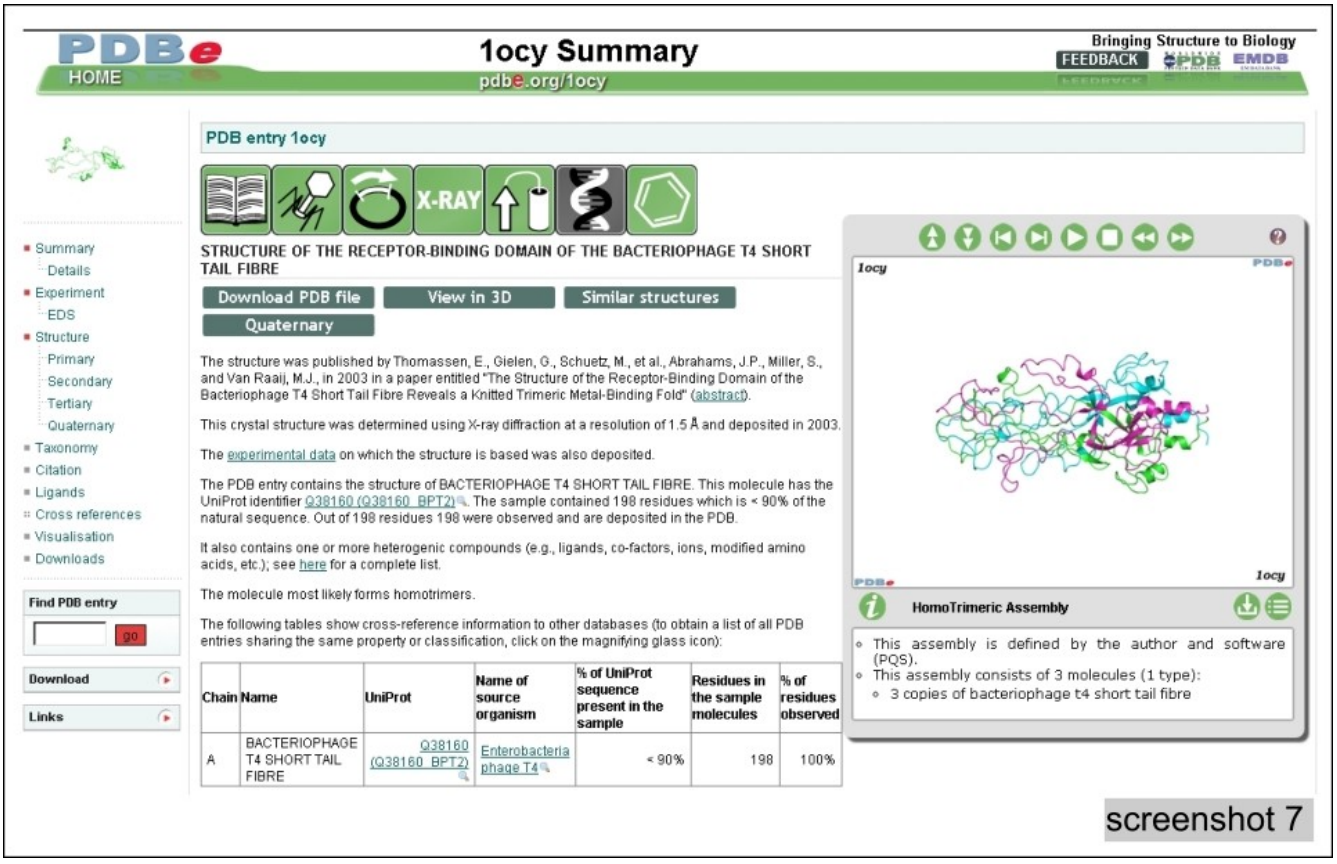
PDBeMotif summary for the HHHHHH environment

These statistics relate to all ligands that are bound by an environment containing six Histidines. Click on the bar in the chart to see the list for each ligand (arrows). Ni is bound in a number of entries (box 1) but Zn is bound only in a single entry (box 2). Click on that atlas link to see details of this (red arrow).

Zn bound by six His residues in the phage T4 short fibre protein

Zn bound by six His residues is observed in PDB entry **1ocy**. This is the short fibre of phage T4. As described in the accompanying **Quips** article this is a trimeric protein with a structural similarity to the extended Fe-binding domain of the long fibre **gp37** protein.

The **PDBeMotif** analysis shows that this similarity extends to the binding site for the metal ion at the centre of the fibre. As you can see, clicking on the **Ligands** link from a protein **Summary** page is a quick way to browse ligand binding sites in the PDB archive.



The summary page for the structure with Zn bound to six Histidines
*The entry **2ocy** is the structure of the short fibre receptor binding region of bacteriophage T4.*