

Introduction

How we wanna do this? We gonna assume a base level of biochemistry amongst our peers, what we had in the last semester.

Proteins that require metallic groups as their ligands are known as metalloproteins, and they compose approximately 40% of all proteins. One such ligand is heme. Heme is employed by many metalloproteins to catalyze a broad range of reactions.

Hemoglobin and myoglobin are likely familiar proteins, and use heme to store and transport oxygen. Other examples of the enzymes that employ heme are peroxidases, catalases (a type of peroxidase), nitric oxide synthases, heme oxygenases, and cytochrome p450s. Peroxidases and catalases catalyze oxidation-reduction reactions using a histidine-bound heme, with catalases in particular specializing in the decomposition of hydrogen peroxide. Nitric oxide synthases catalyze the reaction of L-arginine into nitric oxide, which is vitally important to cellular signaling[Poulos2014]. Free heme molecules may be released upon degradation of hemoproteins, however, heme is prooxidative and therefore toxic to cells; heme oxygenases serve to degrade heme, protecting the cell and forming products preventing vascular inflammation. Heme oxygenases are regarded as potential therapeutics, because of their anti-inflammatory effects.

Last but not least, cytochrome p450 function as powerful monooxygenases. They are capable oxidizing, inserting oxygen into a fantastic amount of substrates, serving to oxidize carbohydrates, steroids, fatty acids; hormone degradation and synthesis; and degrade the vast majority of drugs. Due to their extraordinary utility and range of reactions, cytochrome p450s are of great interest in the protein engineering field. Cytochrome p450s have the potential to be used in industrial biocatalysis, e.g. in pharmaceutical production, bioremediation of environmental pollutants. The

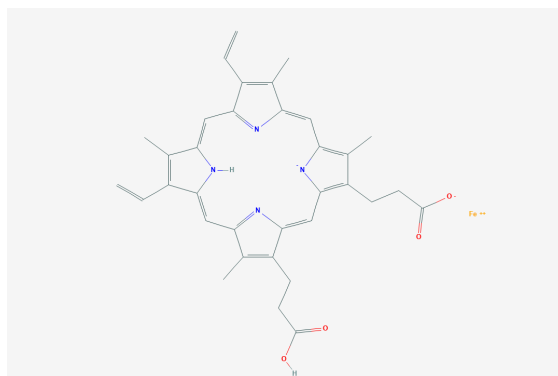


Figure 1: Heme-b (HEM)

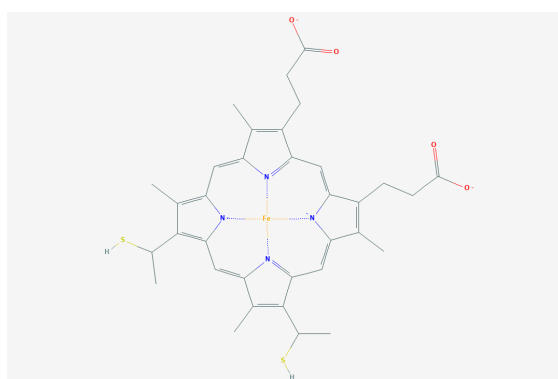


Figure 2: Heme-c (HEC)

limiting factor preventing its deployment has been the struggle to increase enzymatic efficiency and therefore yield of processes employing the enzyme. The struggle to increase enzymatic efficiency, in turn, is due to an incomplete understanding of the binding environment for heme; indeed, the binding environment for *hemes*.

The heme molecule itself has its own variety. There are several “hemes”, structurally and chemically different, that are used to achieve different chemical reactions; in this study, we examined heme-b, heme-c, siroheme, and verdoheme. Their structures are shown in Figures 1-5.

FIXME!! Actually put the reference of this stuff.

The most common “heme”, heme-b, has been discussed above. It binds principally via noncovalent interactions with its binding pocket. Heme-c is derived from heme-b; it binds, with few exceptions, covalently to cysteine residues in the binding pocket, forming thioester bonds between the residues and heme-c vinyl

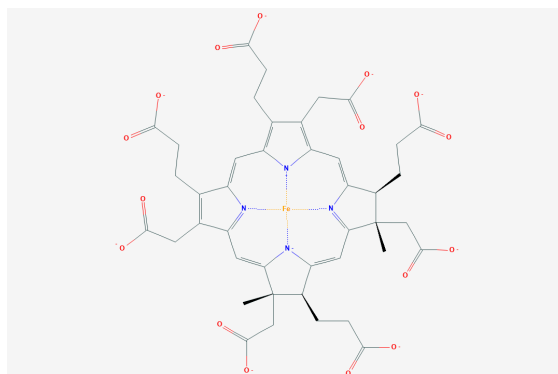


Figure 3: Siroheme (SRM)

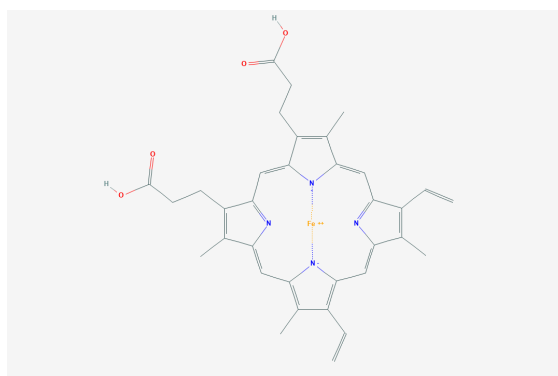


Figure 4: Verdoheme, VEA

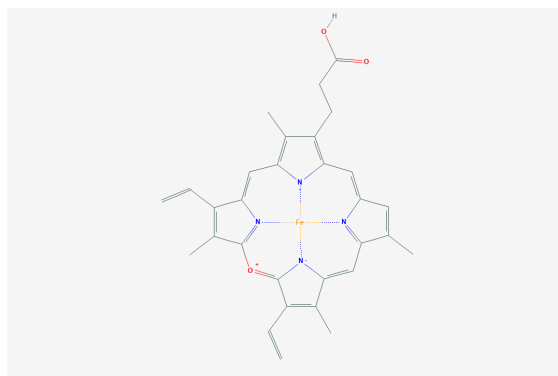


Figure 5: Verdoheme, VER

groups. Its function is much more specific than heme-b, mostly serving as an electron carrier. The reason for this is not abundantly clear, but several studies suggest that because of its covalent bonding, heme-chas an electronic potential that is broader and more specifiable than heme-b.

Siroheme is even more limited in its applications but arguably of greater significance in nature. It is used exclusively in XXX, which in turn is responsible for XX and therefore Y.. Siroheme uniquely is able to transfer 6 electrons or something; one study suggests this is due to its structure of blablabla.

Verdoheme is an intermediate product in the degradation of heme-b by heme oxygenase. When heme oxygenase degrades heme-b, balblabla are produced; verdoheme is the precursor to xx. And while an intermediate, the way verdoheme is at least briefly bound in heme oxygenase (CHECK!!!) is not well documented and may be of interest.

As discussed above, the potential for engineered proteins is huge for these molecules. However, binding environments are not well understood and form a crucial part of the puzzle. Studies have been done engineering hemoproteins, and have concluded the binding environment highly important. Another study blablabla

There have only been a handful of studies dedicated to understanding the structure-chemical relationship between heme and the proteins that use heme for their chemistry (these proteins are known as hemoproteins).

In the most significant previous work, approximately 125 hemoproteins were studied[Li2011]. The study focused on the structural differences between hemoproteins with bound and unbound ligands.

In this study, structures of hemoproteins with bound ligands were examined. Multiple ligands and their binding protein were examined: heme (HEM), heme-c (HEC), siroheme (SER), and verdoheme (VEA/VER).

Yeah so below we get 'em. But no sure how I'd go about stacking em side by side and keeping a caption. So far this gets the job done let's move on homie!

Of particular interest were any qualities that may suggest a requirement for ligand binding. In addition, with several ligands studied, the similarities and differences for binding pockets for the different ligands could be elucidated. Properties of the binding pockets were both predicted and observed from their respective PDB files.

0.1 other stuff to consider adding to the introduction

Although pdbs were thoroughly examined and the datasets were culled, the sample size of this study is very small compared to the amount of hemoproteins available in the pdb a decade later (~10,000 HEM-containing proteins and xx). The dataset is also limited in that there is a somewhat homogenous group of proteins examined (?). The characteristics examined were limited to: xx.

It is hypothesized that the following characteristics all have an impact on the binding of heme and function of the hemoprotein: XXXXXXXXXX.

In this study, some of these characteristics were examined. They include: XX. The remainder are thus far not feasible to calculate. ss All of these characteristics have implications in the field of protein engineering or basic research into hemoproteins. Examples of the uses of these results include [SUPER BLOOD STUDY] and [OTHER PROTEIN ENGINEERING STUFF]. Not sure how much we can reference those other papers besides doing that besides in the conclusion.