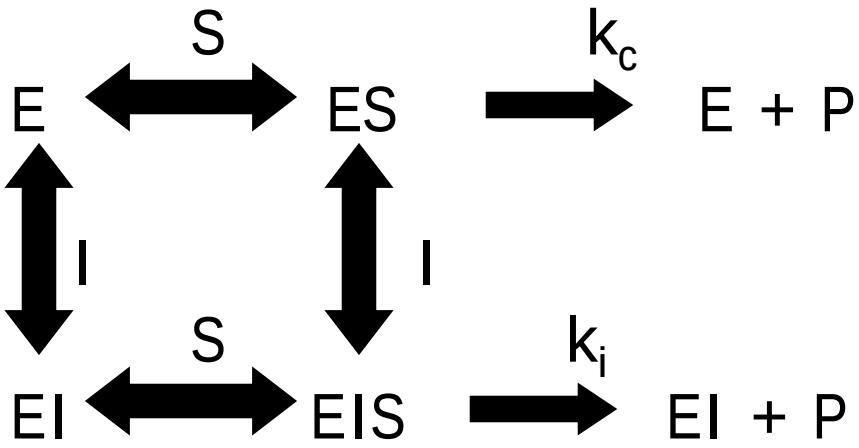
Inhibition

An inhibitor is any compound that causes a decrease in the catalytic rate. We will consider non-covalent ligands that can bind to the enzyme. The general scheme is shown below:



I = inhibitor

Inhibition occurs if

$k_i[EIS] < k_c[ES]$

Competitive Inhibition

Competitive inhibition results from the direct competition between the I and S for the substrate binding site. There is an additional equilibrium constant:

$$EI \rightleftharpoons E + I \qquad K_I = \frac{[E][I]}{[EI]}$$

The velocity under these conditions turns out to be:

$$v = \frac{[S]V_{max}}{\alpha K_M + [S]} \qquad \alpha = 1 + \frac{[I]}{K_I}$$

Uncompetitive Inhibition

Uncompetitive inhibition arises when I can bind at site that is not the same as the substrate binding site. There is an additional equilibrium constant:

$$EI \rightleftharpoons E + I \qquad K_I = \frac{[E][I]}{[EI]}$$

Here the complex IE indicates that the inhibitor does not bind in the same site as the substrate.
The velocity under these conditions is:

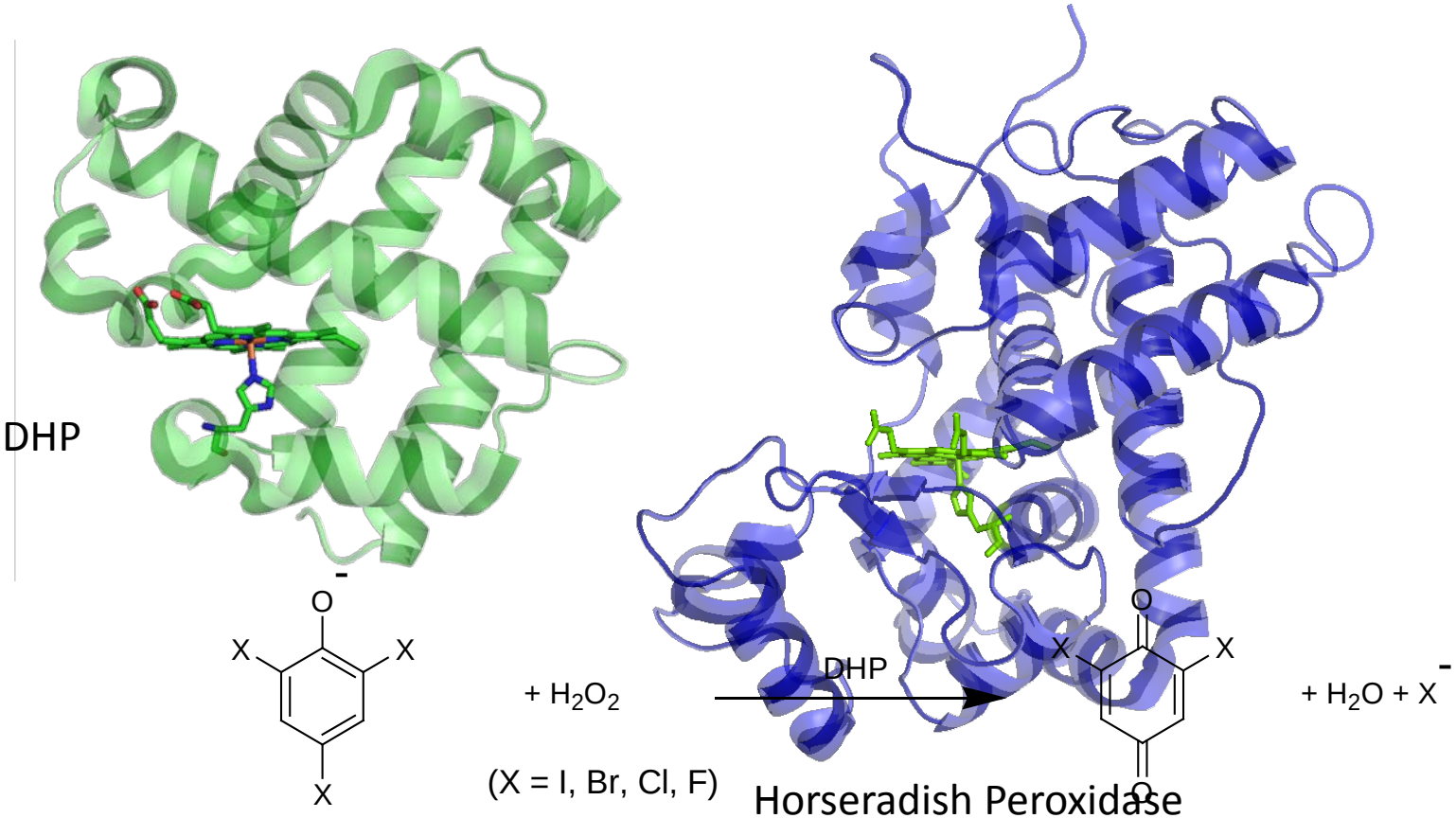
$$v = \frac{v_{max}[S]}{K_M + \alpha[S]} \qquad \alpha = 1 + \frac{[I]}{K_I}$$

DHP has a natural peroxidase function

Engineered globin peroxidases

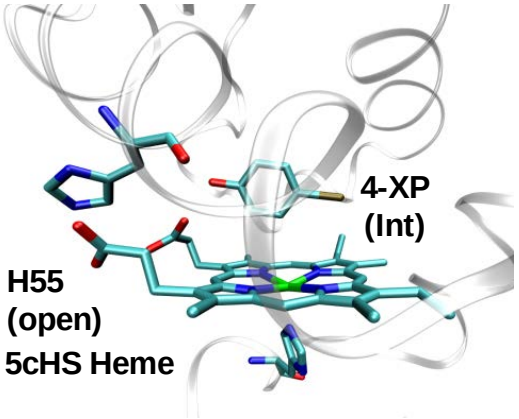
Mauk group

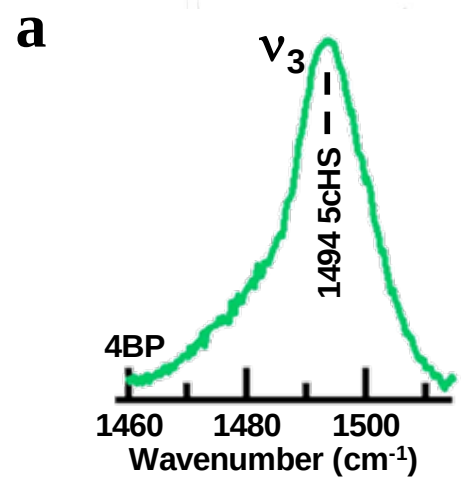
Watanabe group



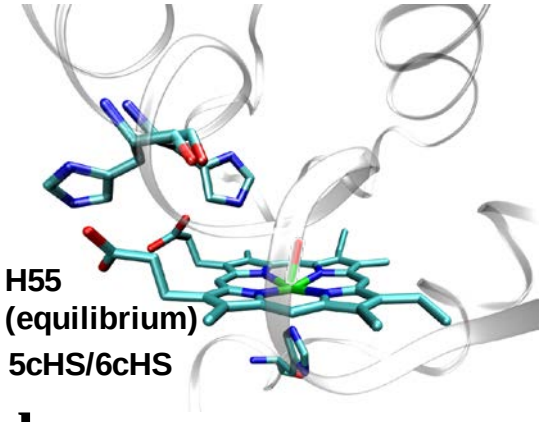
Structural model of inhibitor and substrate binding based on X-ray and resonance Raman.

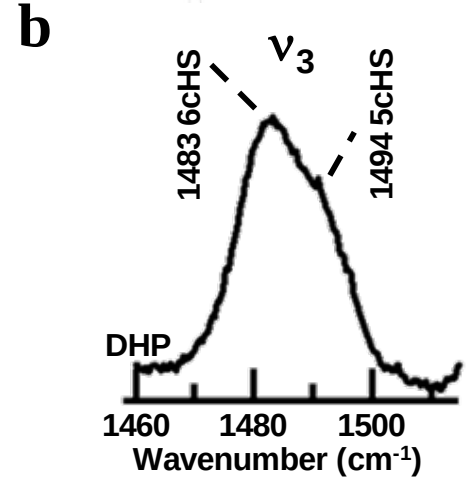
Inhibitor Bound



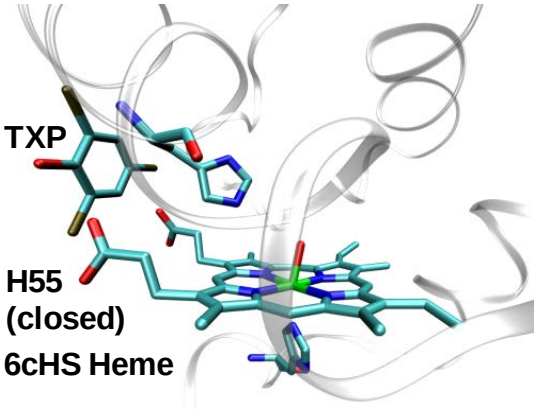


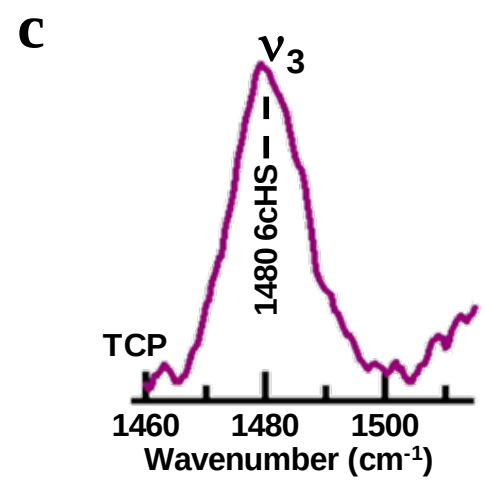
Resting State



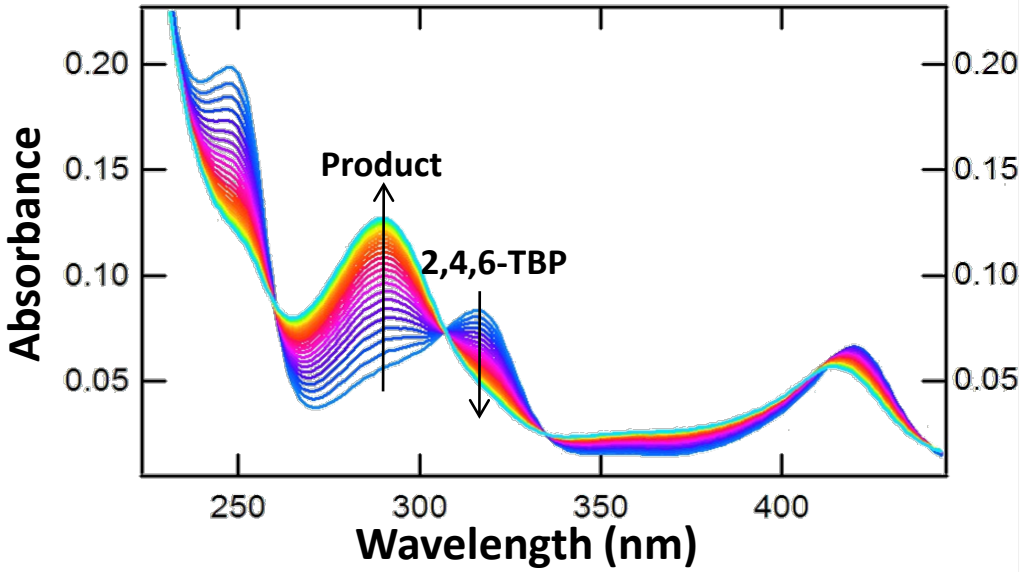


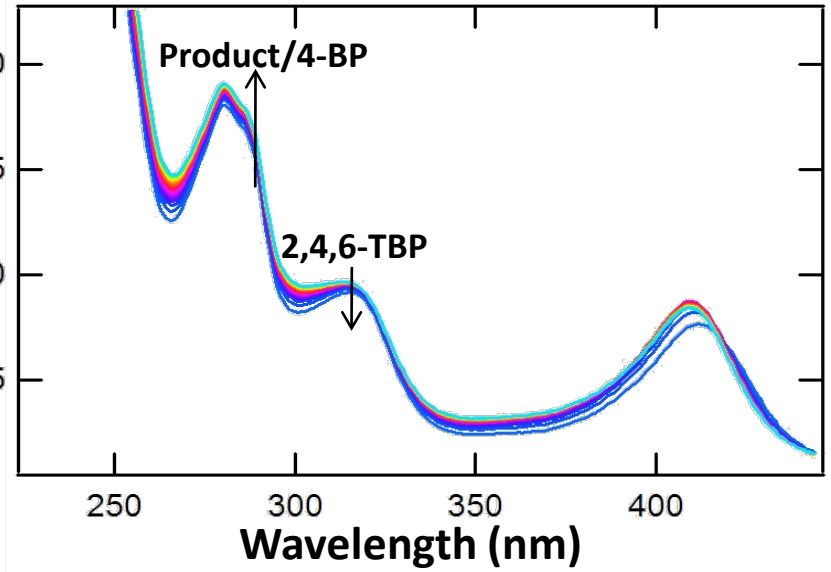
Substrate Bound

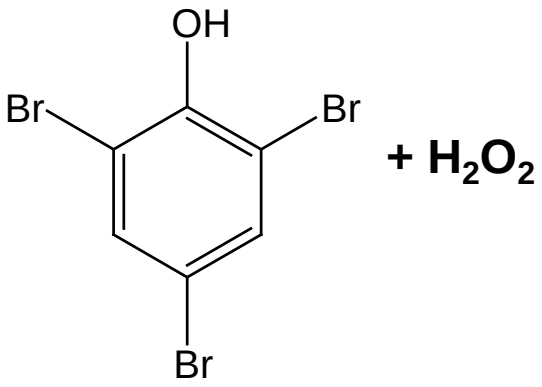




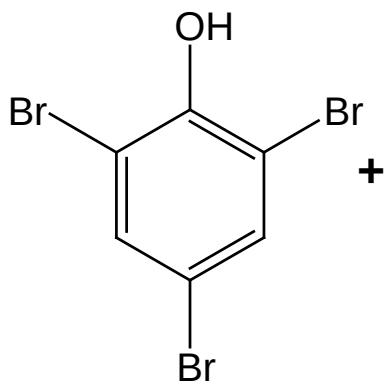
Kinetic analysis showing competitive inhibition under native conditions



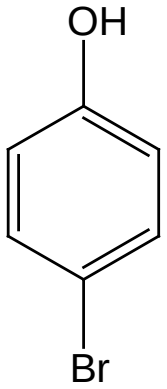




+ H_2O_2



+



+ H_2O_2

Kinetic analysis showing competitive inhibition mechanism