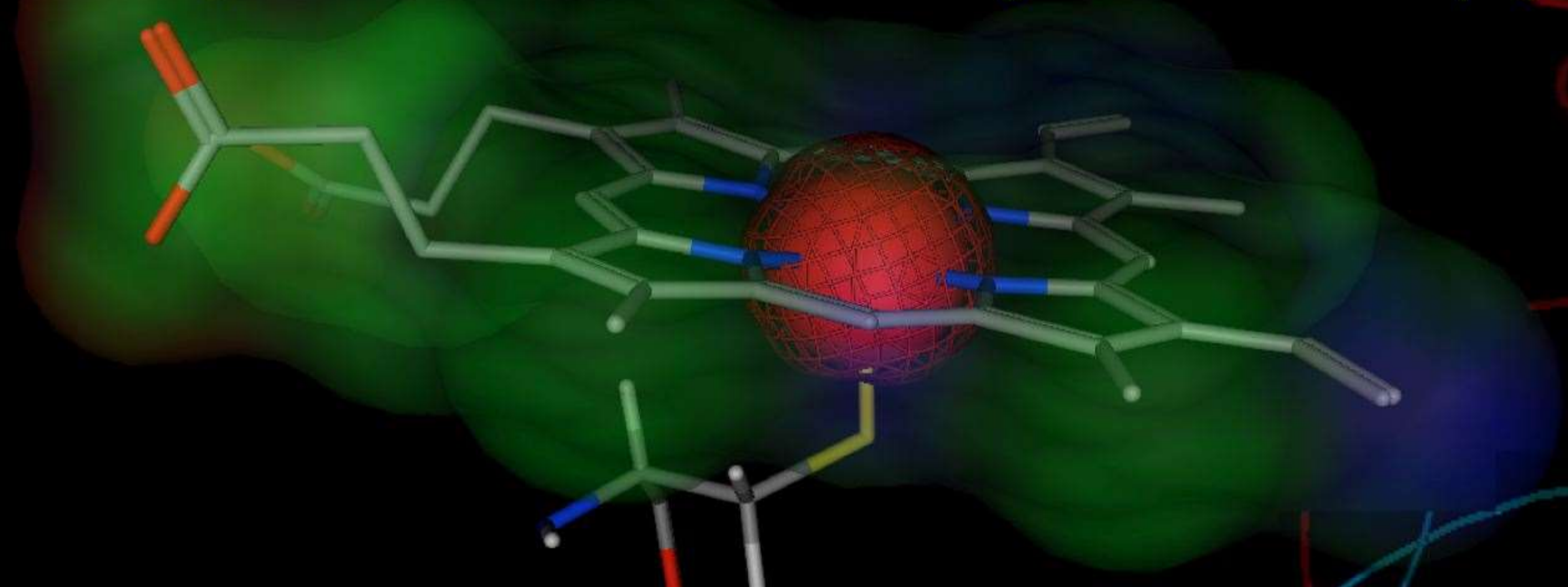


# Engineering the Bioremediation of Explosive Pollutants

Jason Harris, John Anderson, Jerome Baudry

## Introduction:

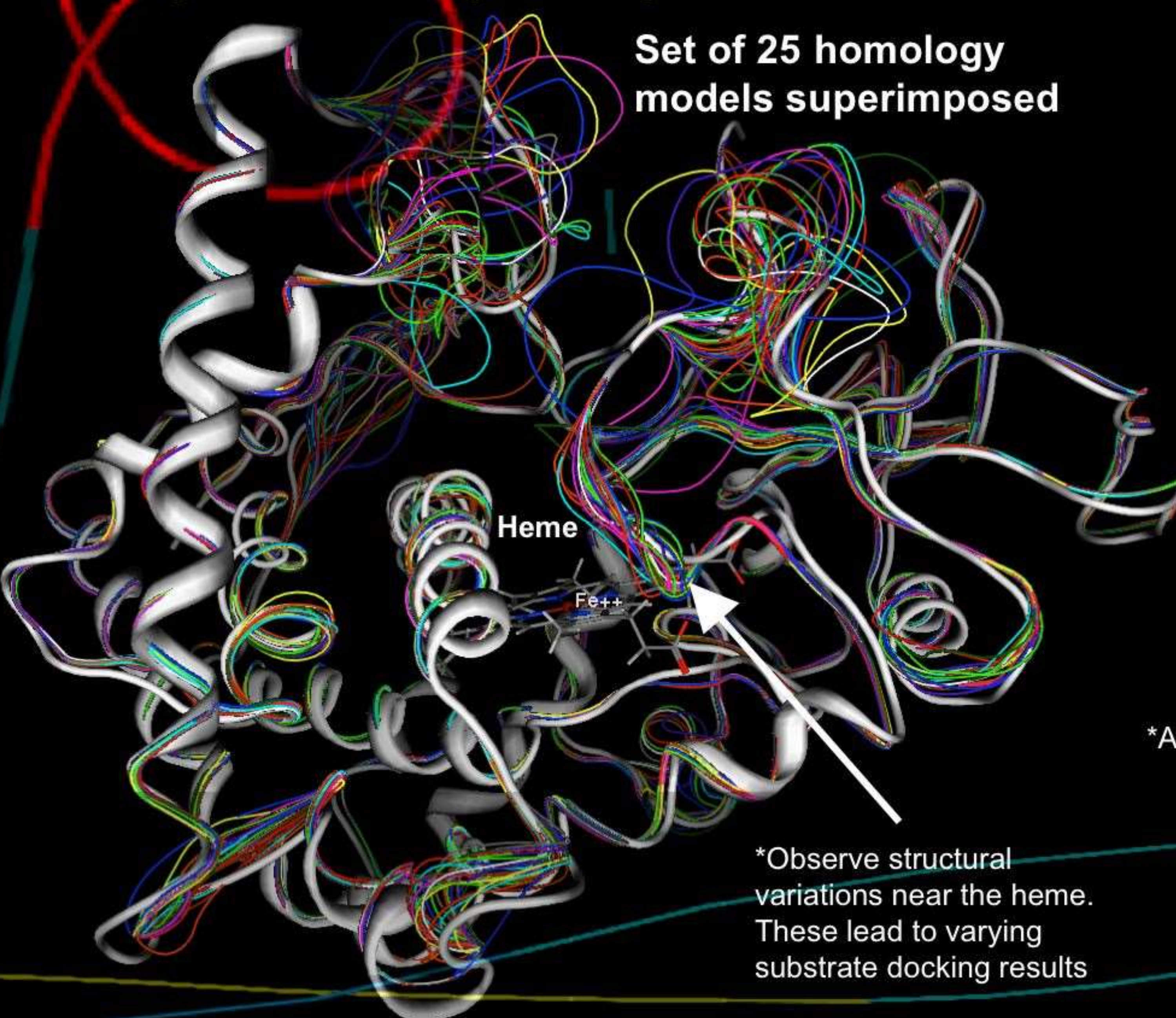
We propose to generate **theoretical models** of a novel **Cytochrome P450** enzyme, **XplA/XplB**, in atomistic detail. XplA **degrades** a recalcitrant weapons **pollutant** called **RDX**. Long term use of this compound along with **similar compounds**, such as **HMX** and **TNT**, has created the **need** for low-cost **bioremediation** steps. This **research** will provide the fundamental knowledge of this **enzyme's structure** and **activity** which will be needed for further **engineering and exploitation** of its unique **properties**. Such knowledge can be used to **elucidate** a detailed **mechanism** of the enzyme's activity and **guide mutagenesis** studies aimed at **harnessing** this P450's detoxifying **abilities** on **similar munitions pollutants**.



## Homology Modeling

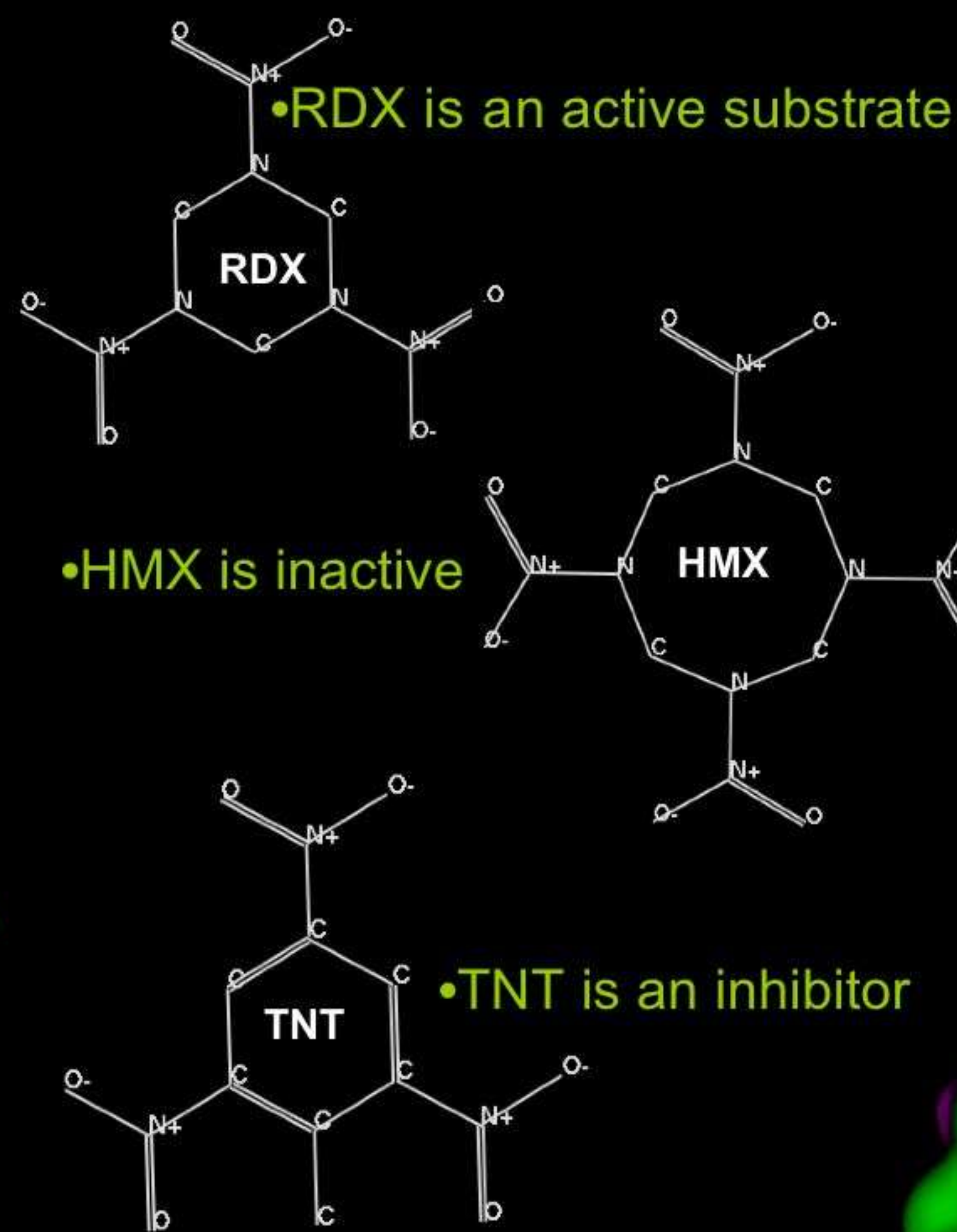
- Already solved P450's of similar architecture are used as templates for generating theoretical models of XplA
- 125 models have been generated thus far and are currently being evaluated through docking simulations.

Set of 25 homology models superimposed



\*Observe structural variations near the heme. These lead to varying substrate docking results

## Ligands

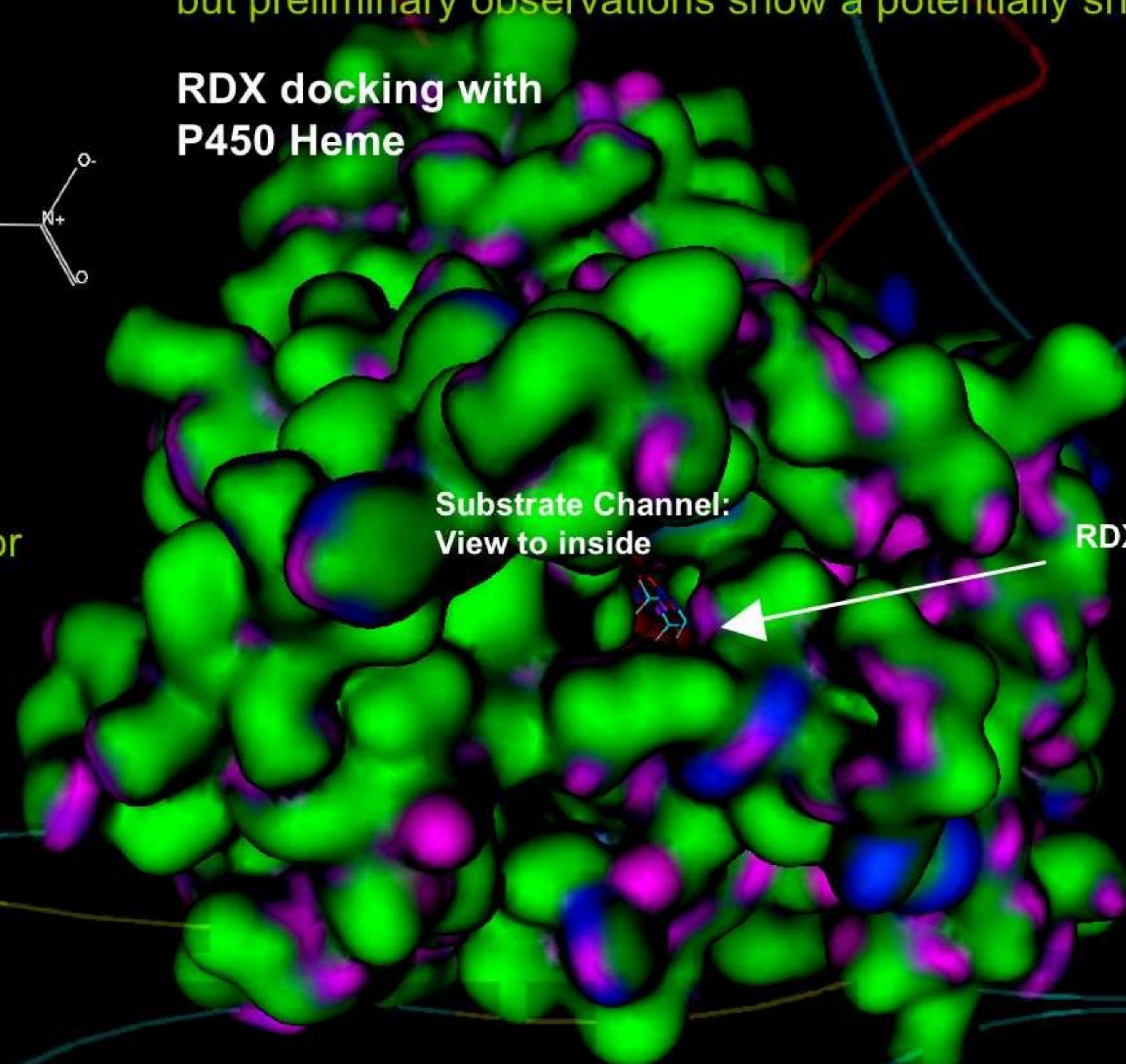


\*All three are nitroaromatic but behave differently

## Molecular Docking

- Computer simulations are used to dock the known ligands of the protein into our theoretical models. Comparisons of the results to experimental data are made.
- Flexible protein docking simulations on all 125 models have been performed using RDX, HMX, and TNT. A more detailed analysis of the results is pending, but preliminary observations show a potentially shared substrate channel.

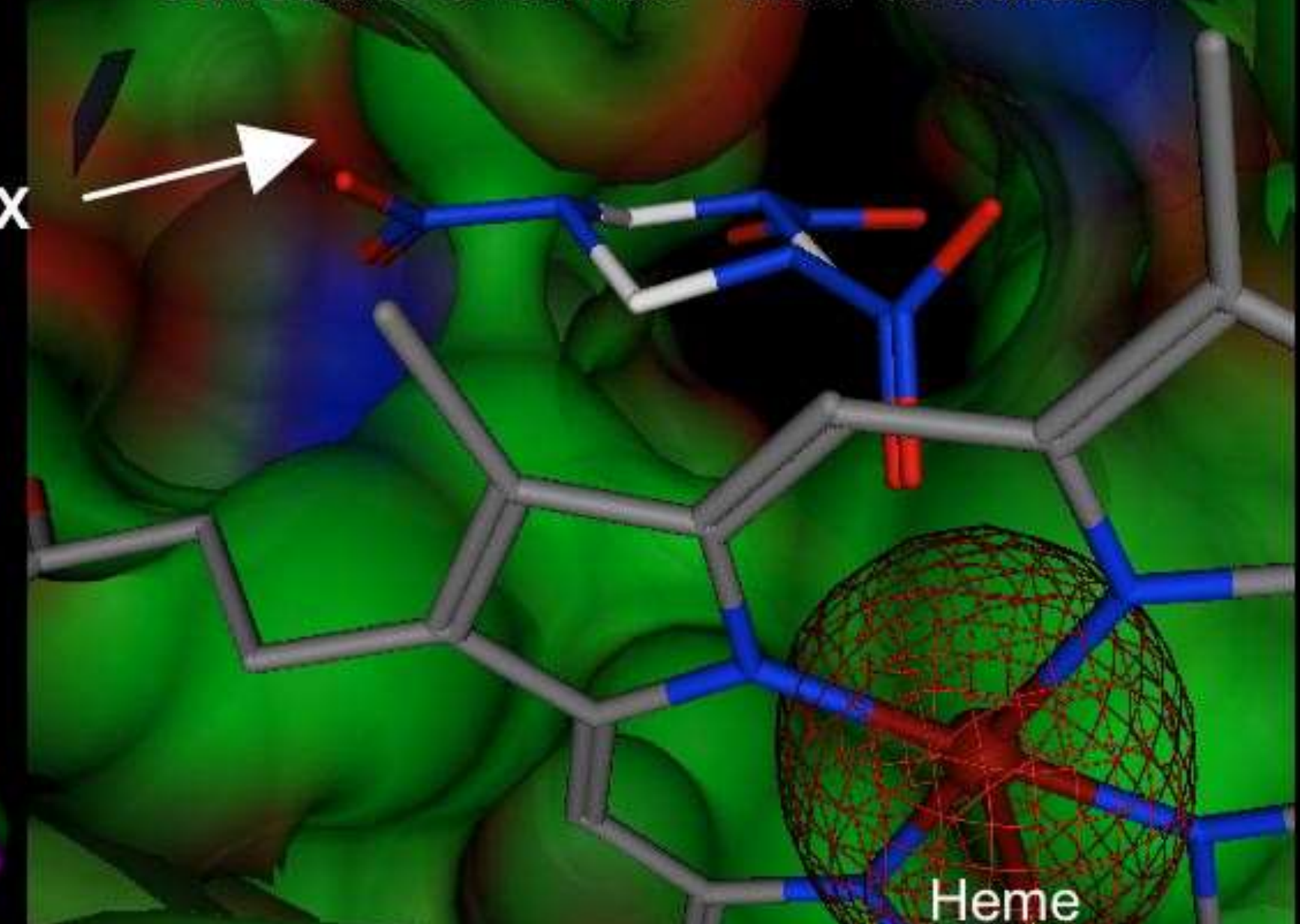
RDX docking with P450 Heme



Substrate Channel: View to inside

\*This particular model only allows RDX to dock near the heme while HMX and TNT can act only to block the channel. This is significant since HMX and TNT are known to be excluded from reactivity and TNT is a known inhibitor of RDX breakdown.

Substrate Channel: View to outside



Heme