

# CYP4 Arachidonic Acid Selectivity

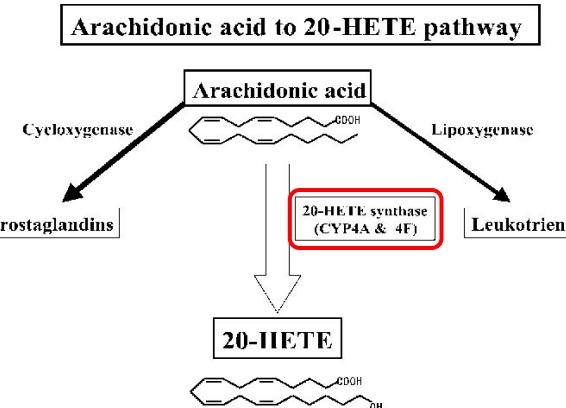
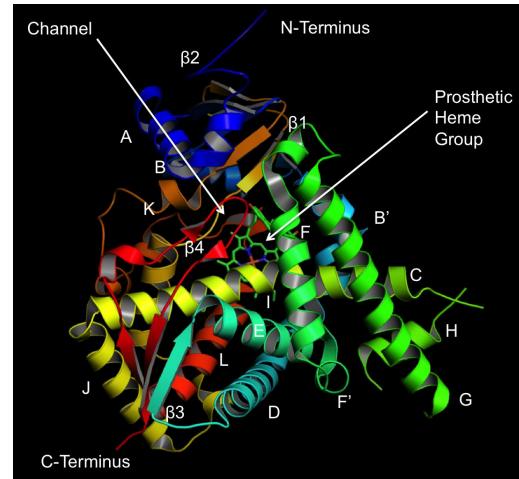
Preetham Bandla, Sanjna Ramesh,  
Sriya Veeramachaneni, David Koes



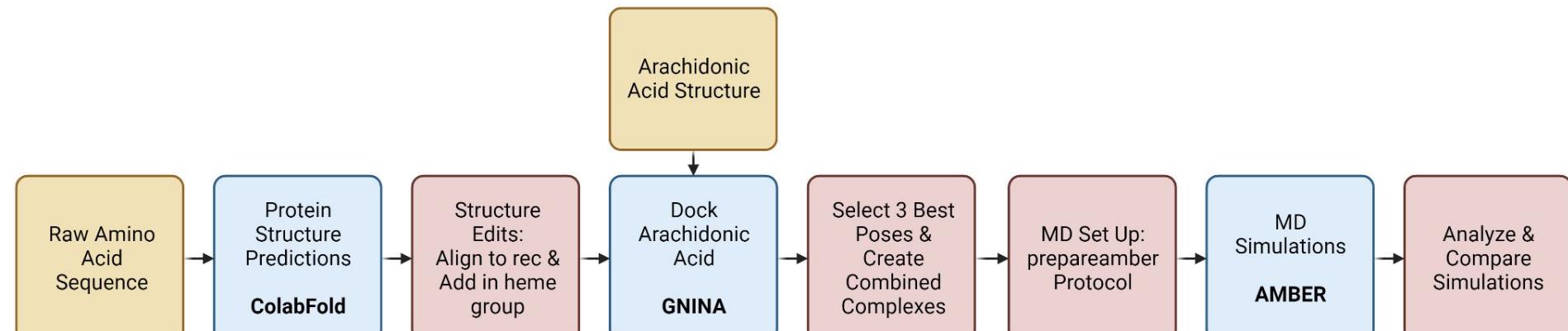
University of  
**Pittsburgh**

# Motivation

- Cytochrome P450s (CYPs/CYP4s) are a superfamily of enzymes containing a heme group & are responsible for a range of functions
- Testing 4 CYPs: CYP4F11, CYP4F2, CYP4F3A, and CYP4F3B
  1. How effectively do different CYPs can convert arachidonic acid (AA) to 20-HETE, a process most active in the liver & kidneys?
    - AA is a polyunsaturated fatty acid present in cell membranes
    - 20-HETE is an eicosanoid metabolite involved in regulation of renal function, vascular tone, development of hypertension & cardiovascular disease, cancer proliferation, etc.
  2. Can computational methods yield comparable results to the existing experimental work?



# Methods



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# Individual CYP Analysis

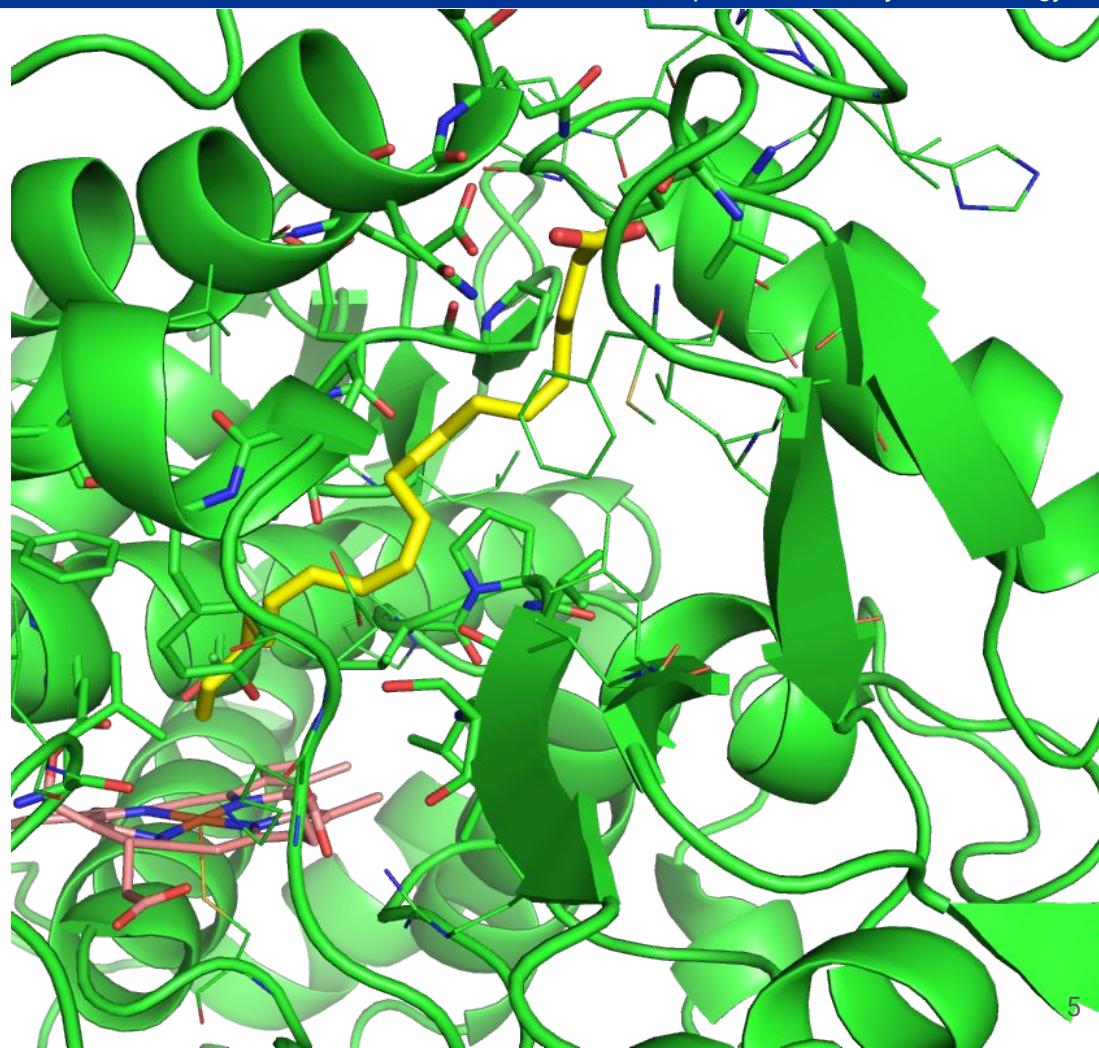
CYP4F11, CYP4F2, CYP4F3A, CYP4F3B

# CYP4F11 - D. Koes

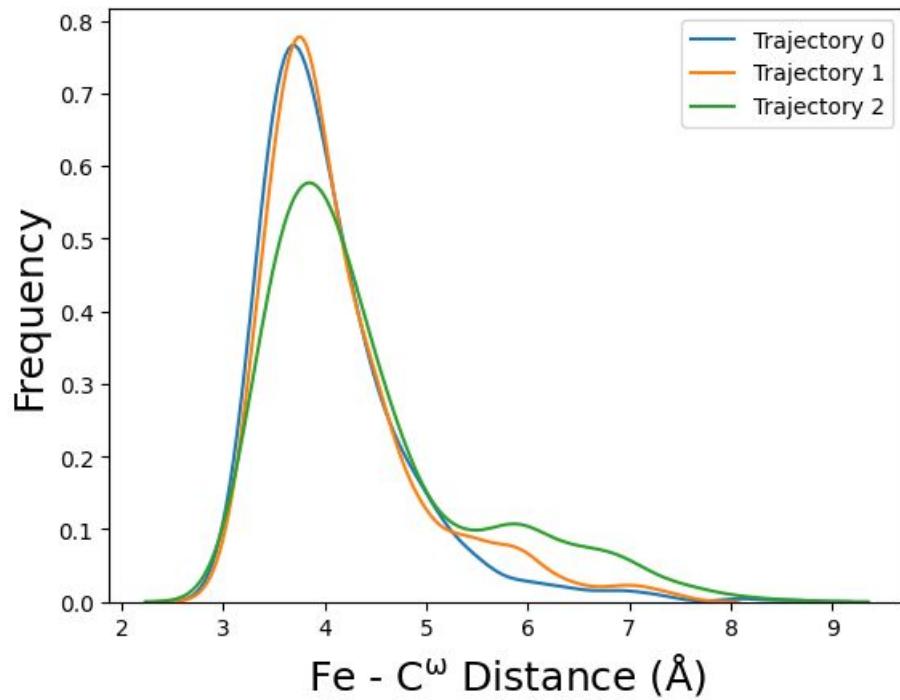
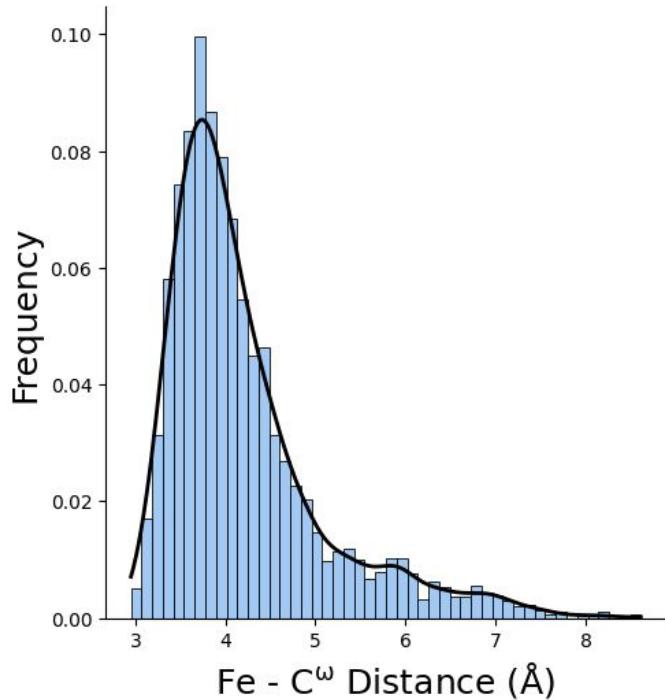
## Key Binding Site Residues

V15	T280
L40	V343
F72	P344
Y73	V345
L76	I346
L85	S347
E181	P450
N184	E451
Q185	L452
F275	I453

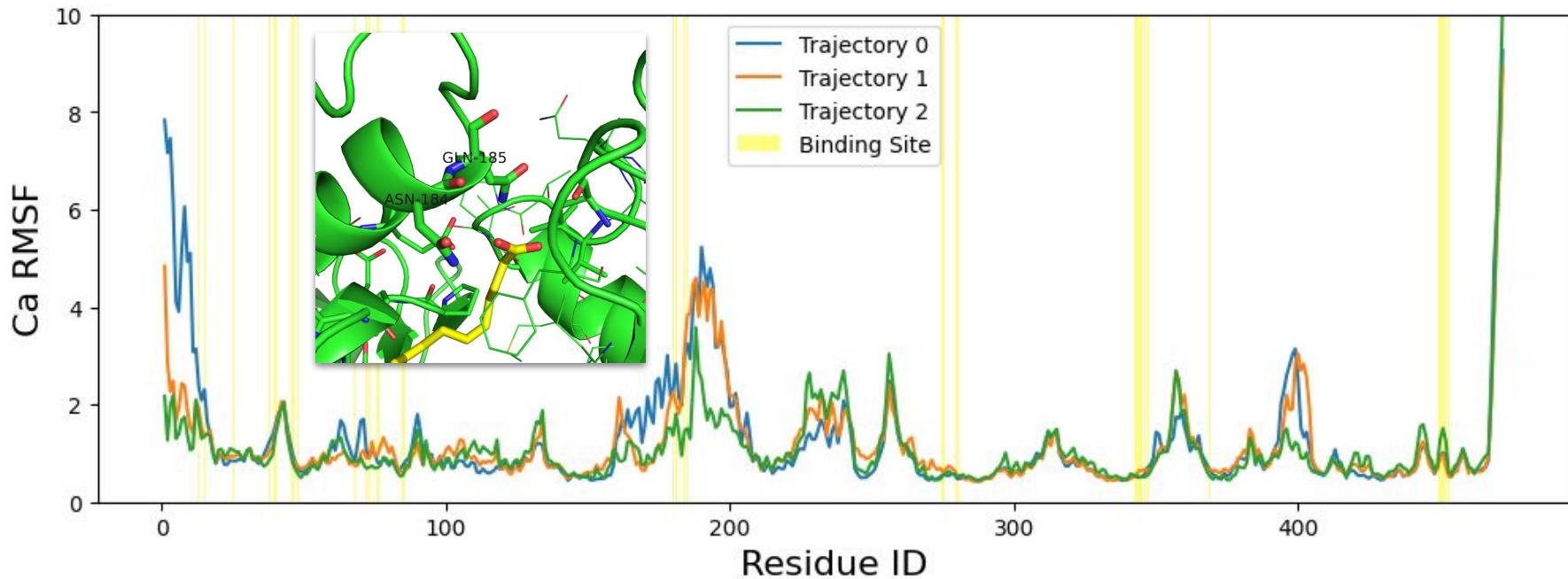
**Note:** First 52 residues truncated



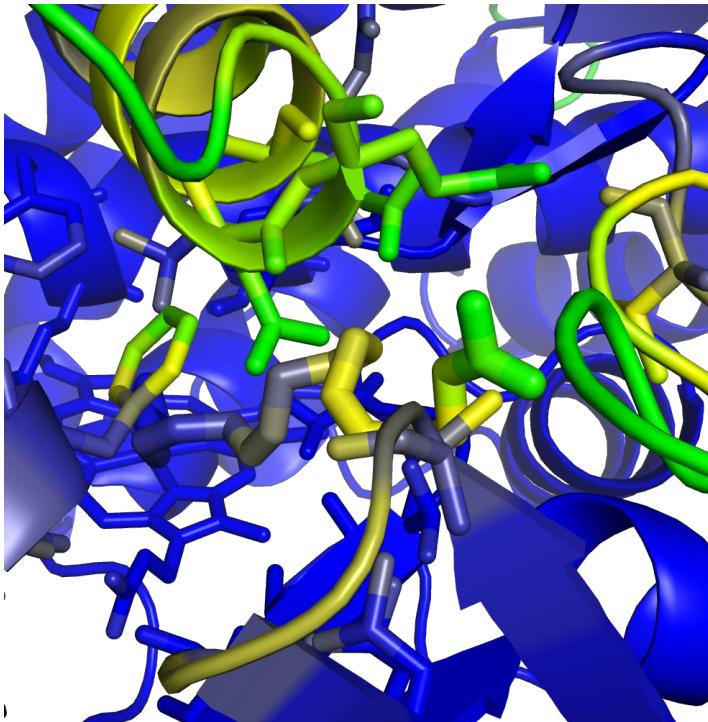
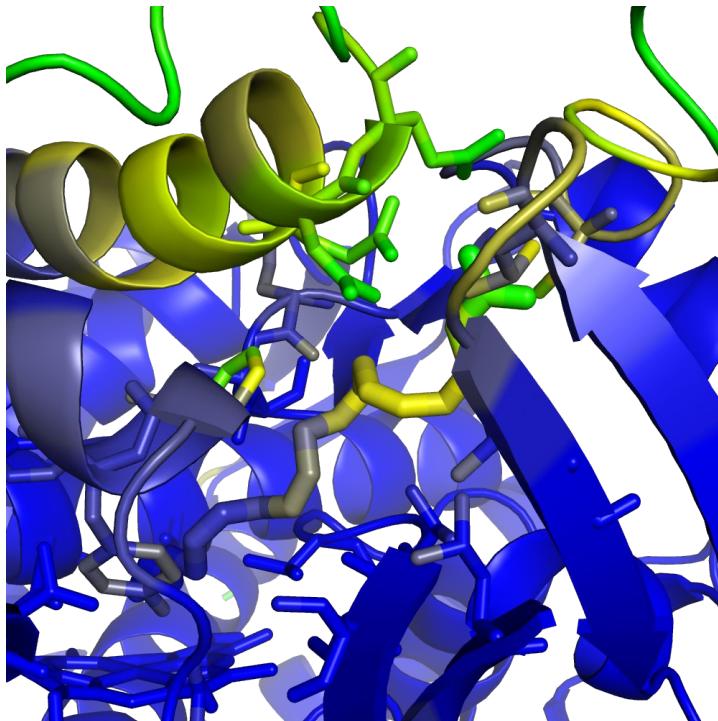
# CYP4F11 $\omega$ -carbon:iron distance



# CYP4F11 $\alpha$ -carbon RMSF

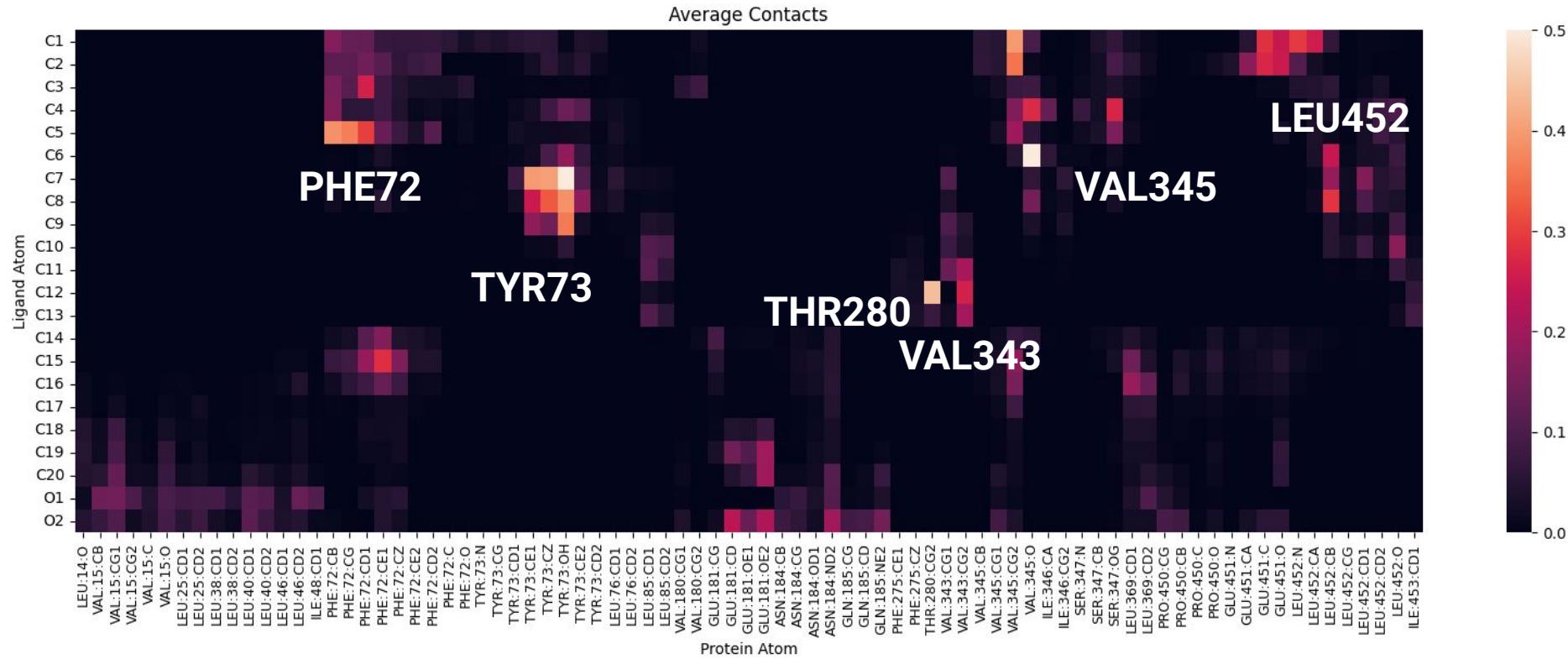


# CYP4F11 All Atom RMSF

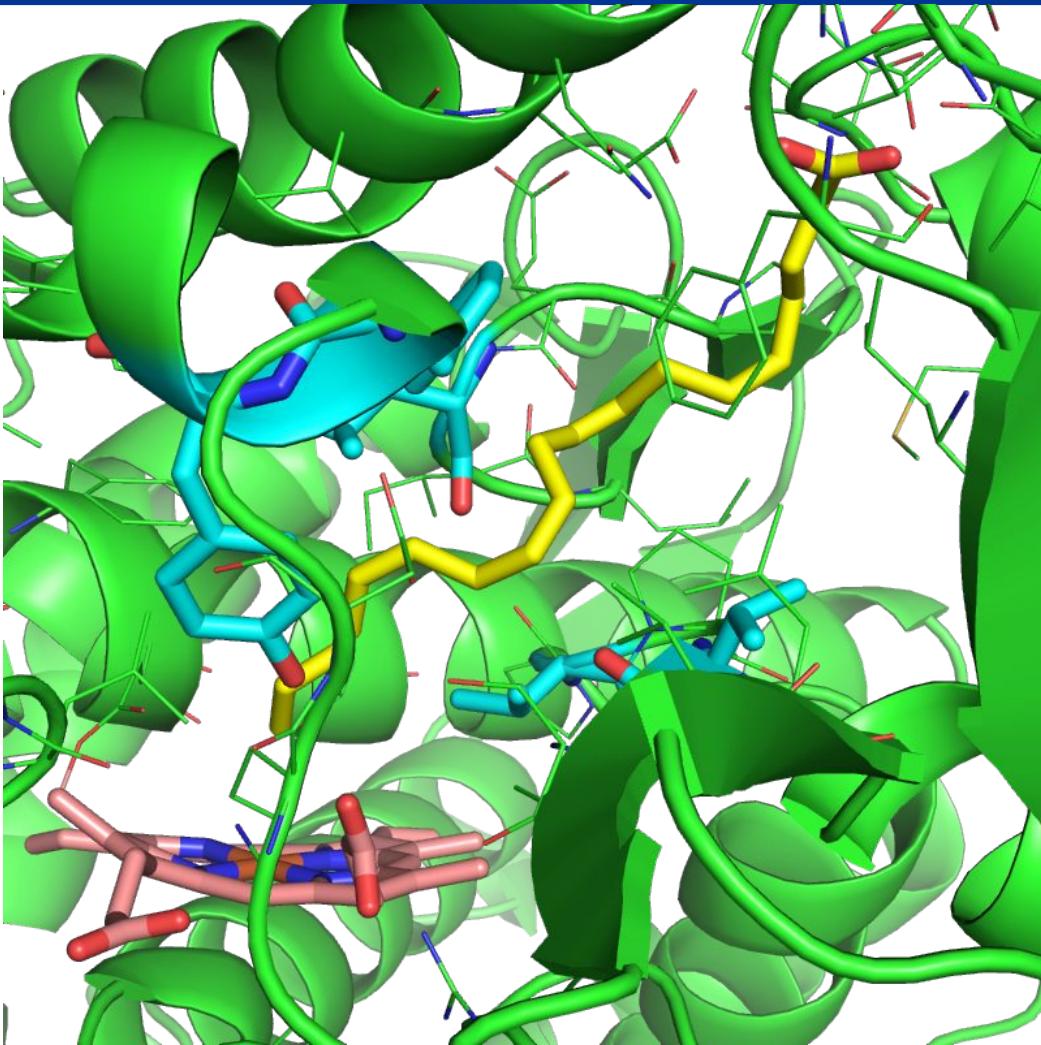


RMSF  
1.0 Å  
2.5 Å  
4.0 Å

# CYP4F11 Ligand Contacts



# Contacts



# CYP4F2 - Sriya

Differences from CYP4F11

V67->I67

P69->S69

I100->R100

E233->T233

N236->H236

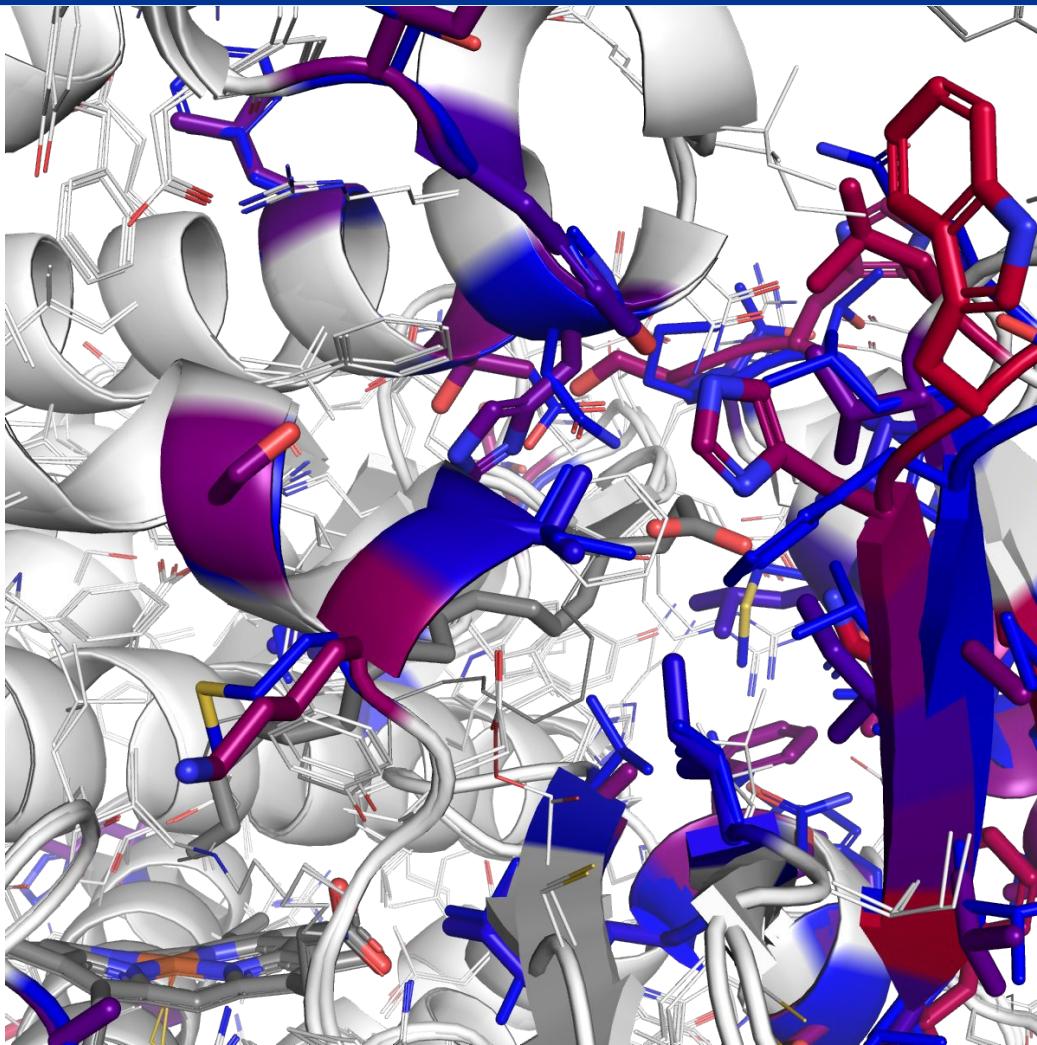
V397->A397

I398 -> V398

N423->S423

I505 -> V505

Work in Progress!



# CYP4F2 $\omega$ -carbon:iron distance

# CYP4F2 $\alpha$ -carbon RMSF

# CYP4F2 All Atom RMSF

# CYP4F2 Ligand Contacts

# CYP4F3A - Sanjna

Differences from CYP4F11

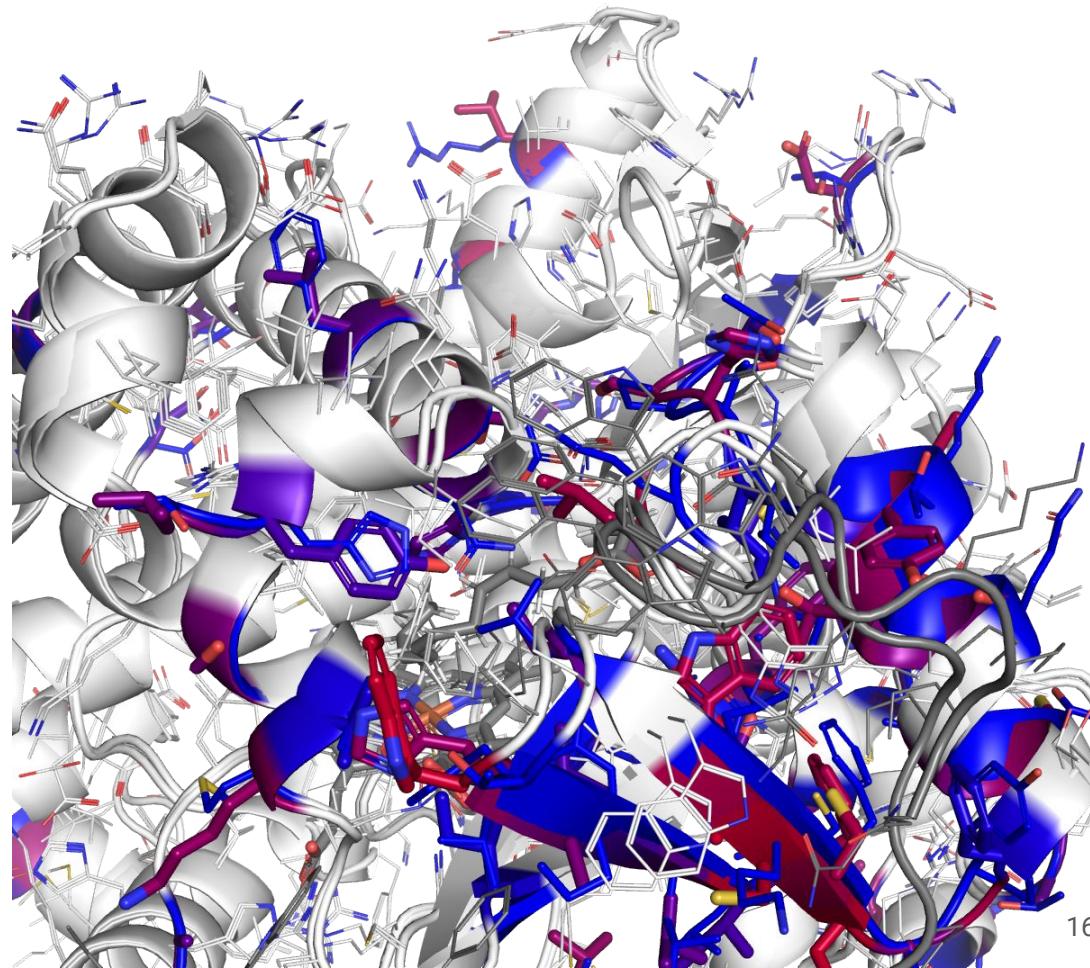
Q62-> L63

V67 -> I67

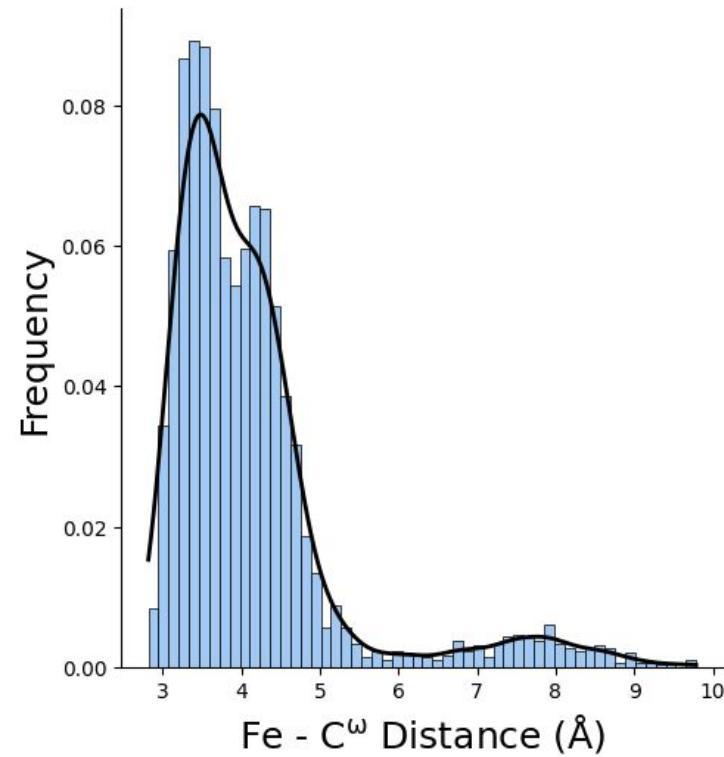
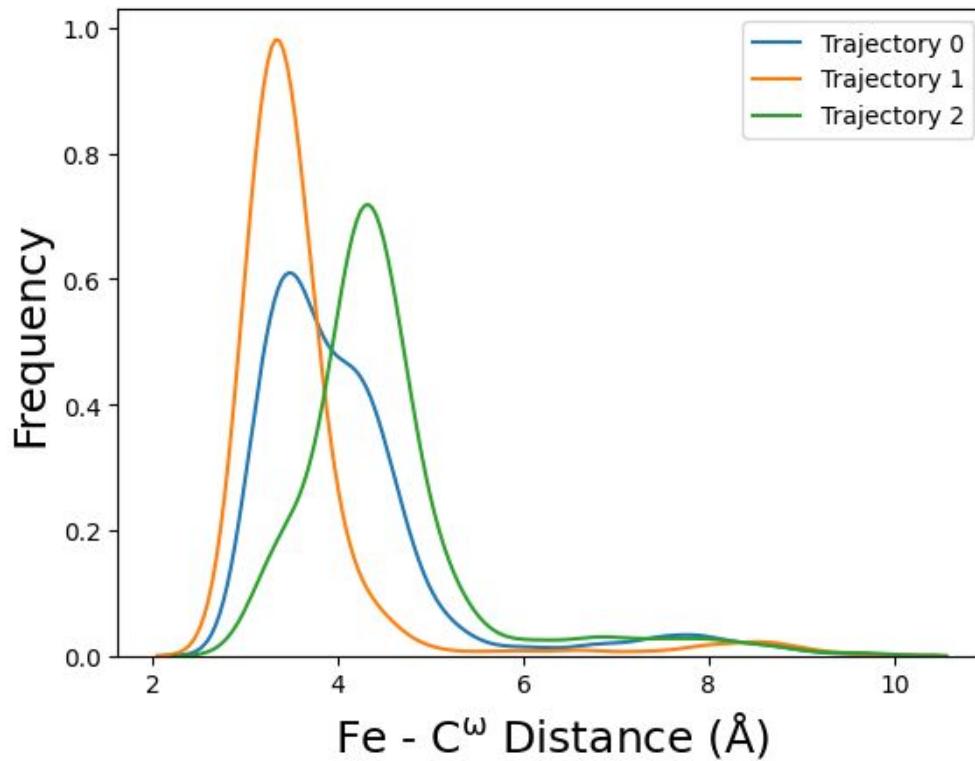
T68->H68

P69->S69

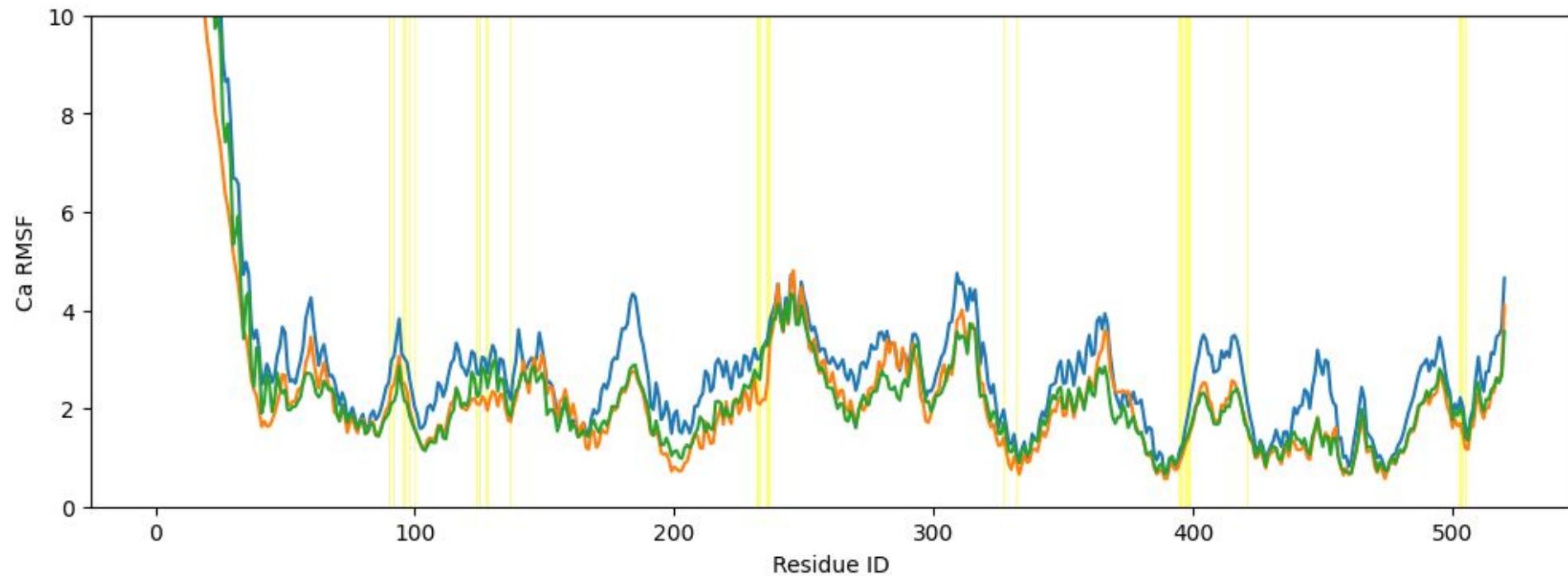
T70->



# CYP4F3A $\omega$ -carbon:iron distance

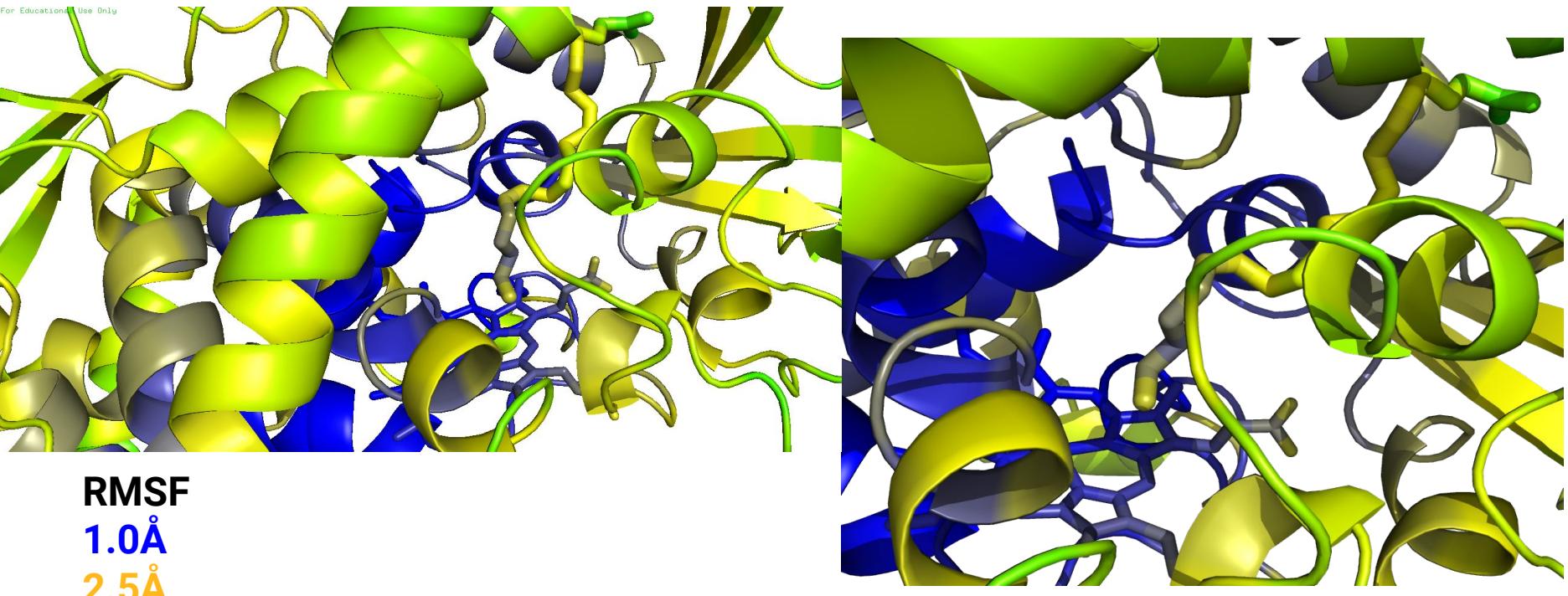


# CYP4F3A $\alpha$ -carbon RMSF



# CYP4F3A All Atom RMSF

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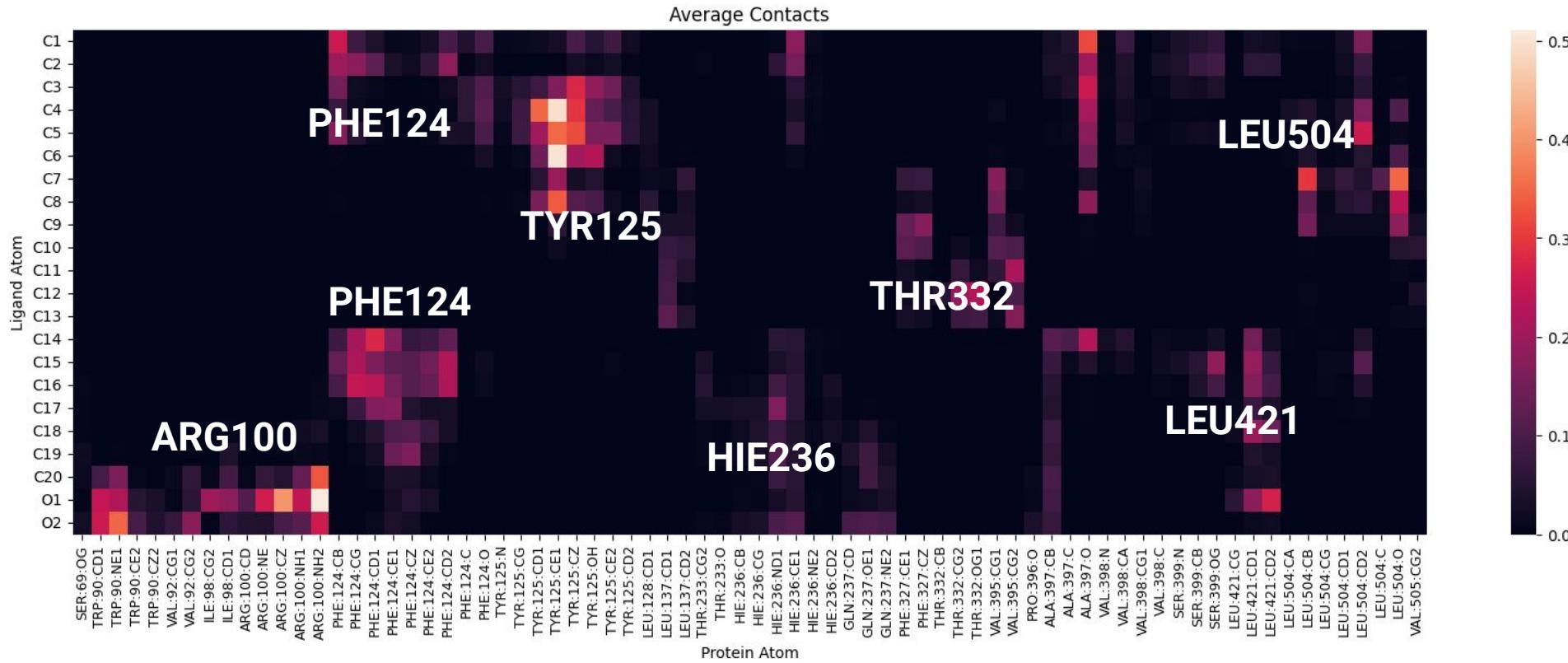
RMSF

1.0 $\text{\AA}$

2.5 $\text{\AA}$

4.0 $\text{\AA}$

# CYP4F3A Ligand Contacts



# CYP4F3B - Preetham

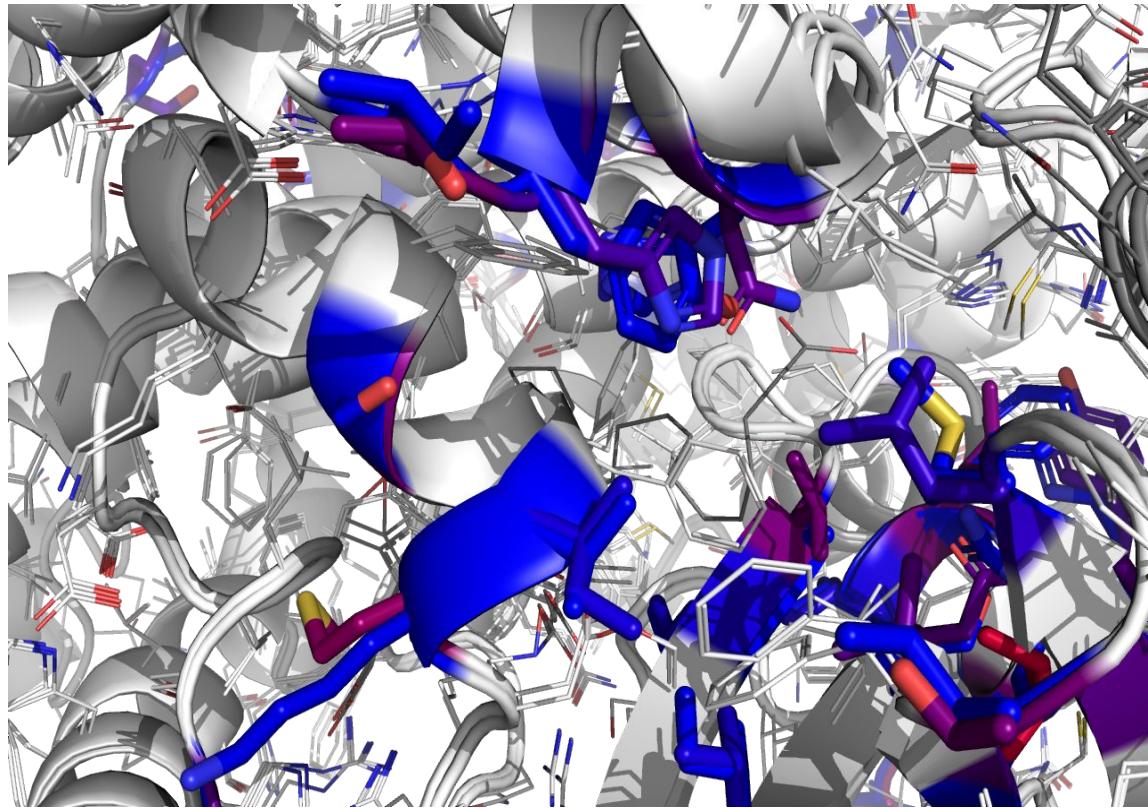
E72 → Q72

T81 → A81

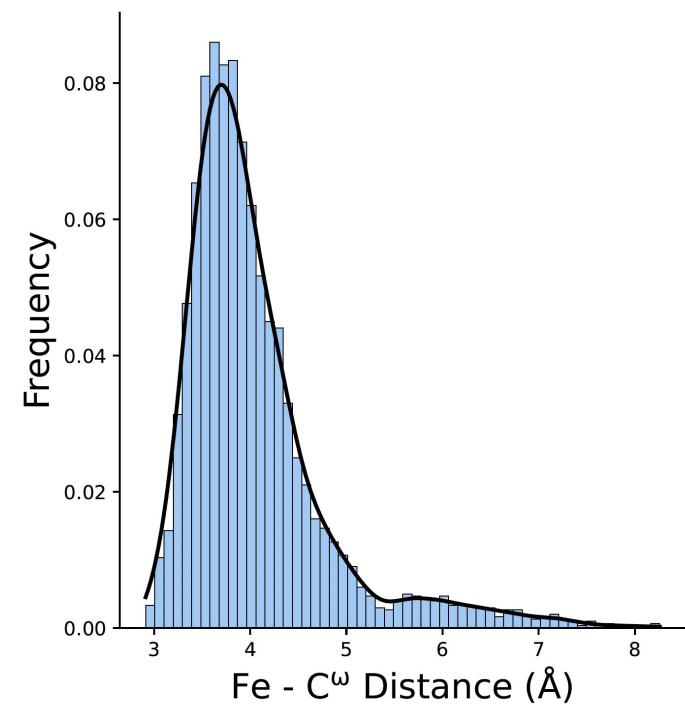
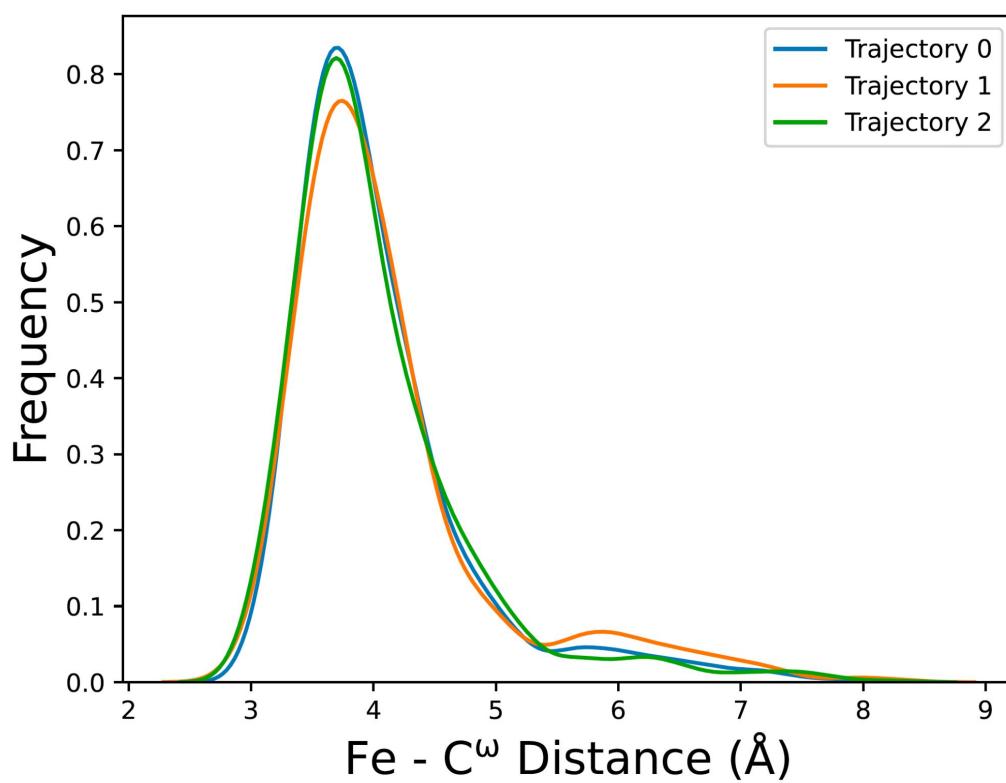
L92 → H92

N105 → D105

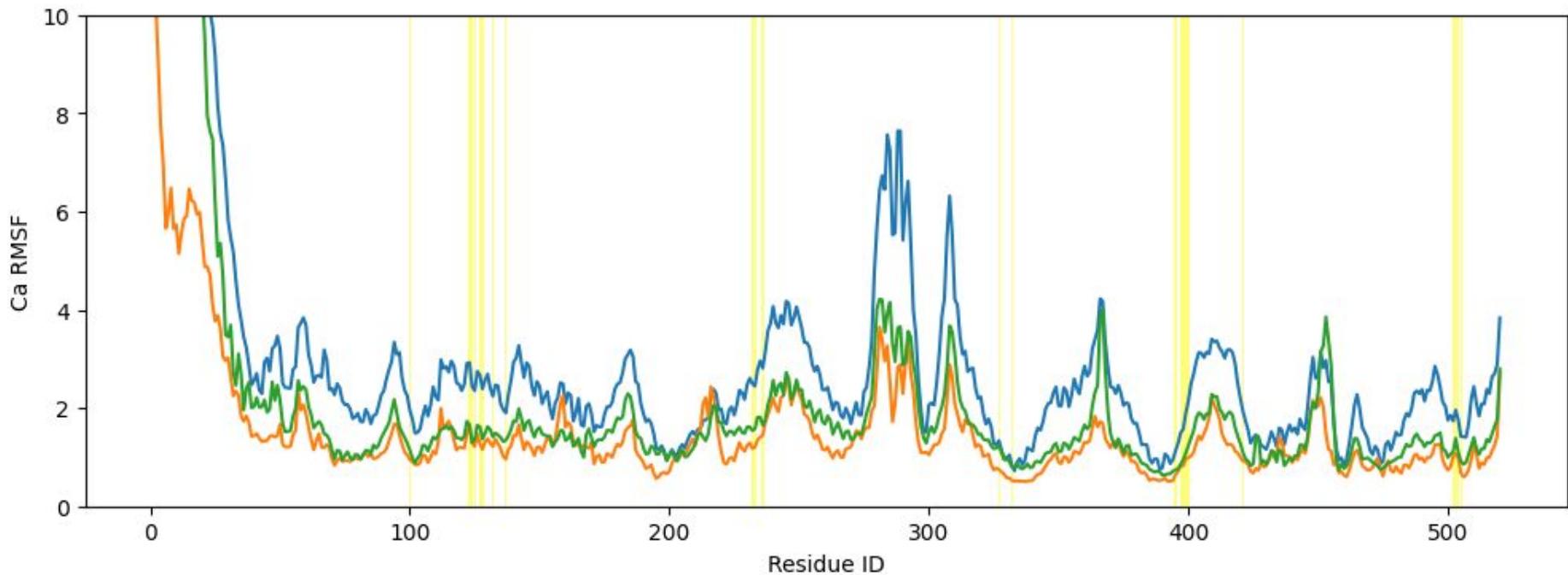
D142 → E142



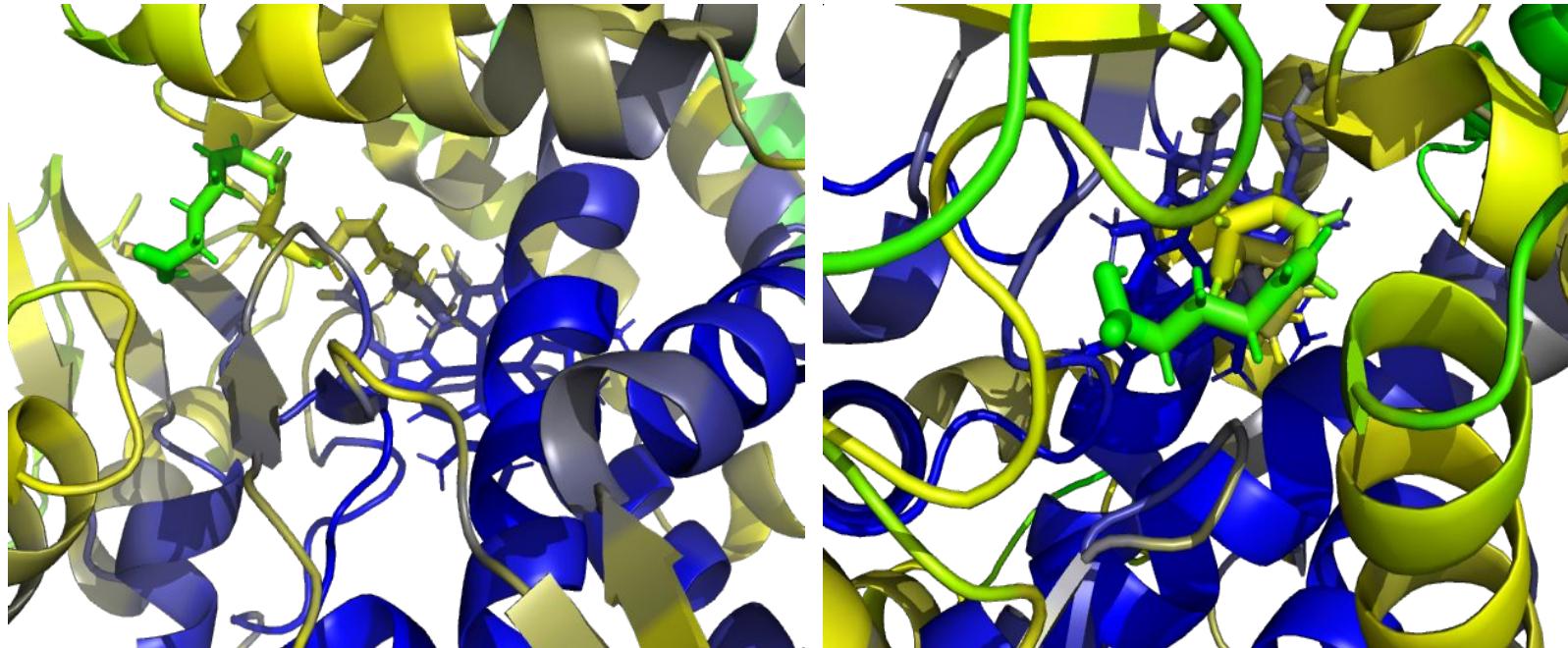
# CYP4F3B $\omega$ -carbon:iron distance



# CYP4F3B $\alpha$ -carbon RMSF

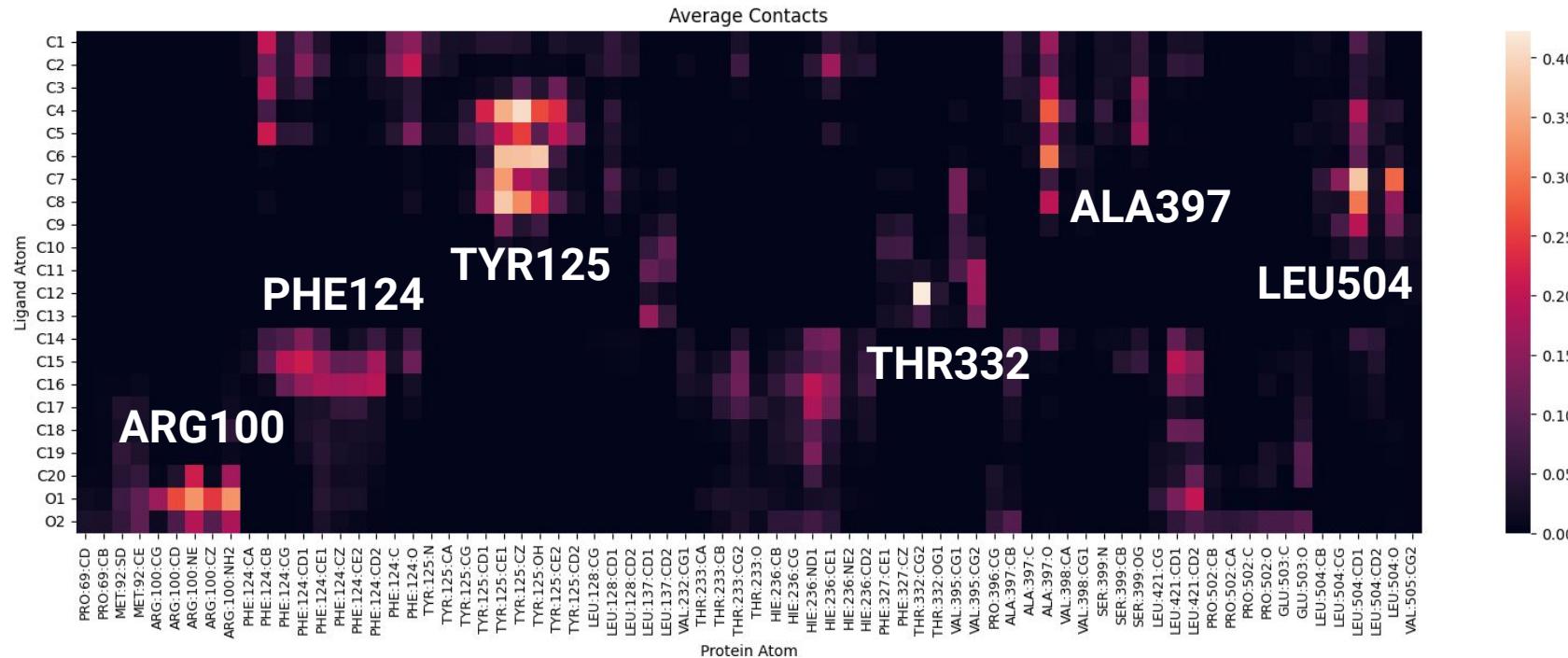


# CYP4F3B All Atom RMSF



RMSF  
1.0 Å  
2.5 Å  
4.0 Å

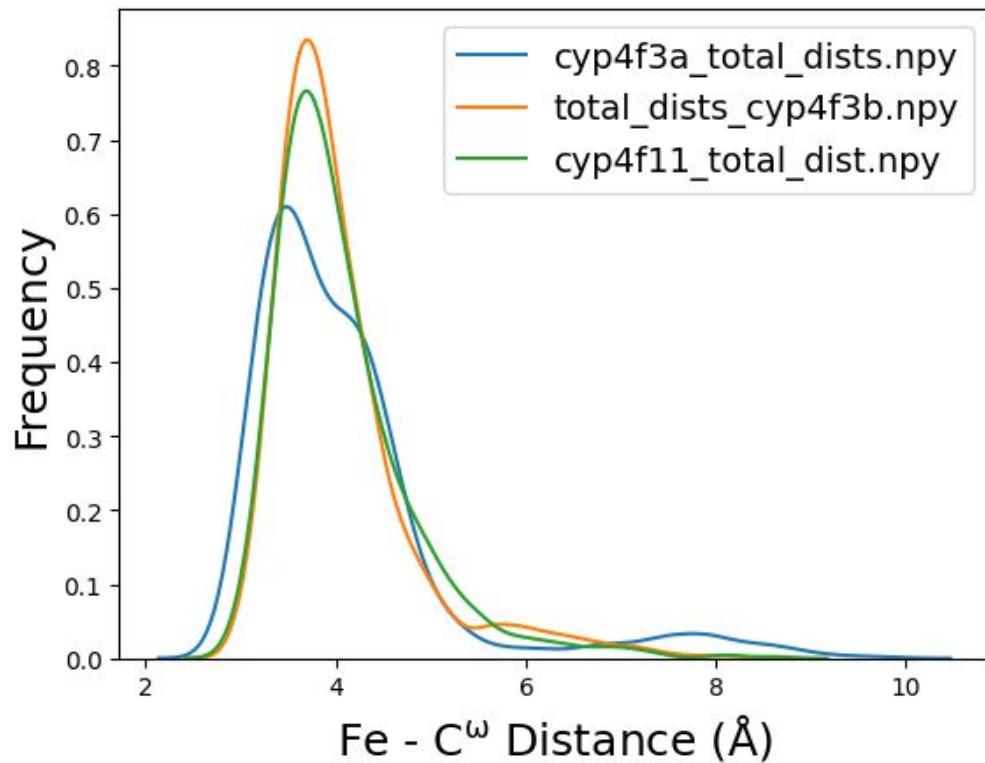
# CYP4F3B Ligand Contacts



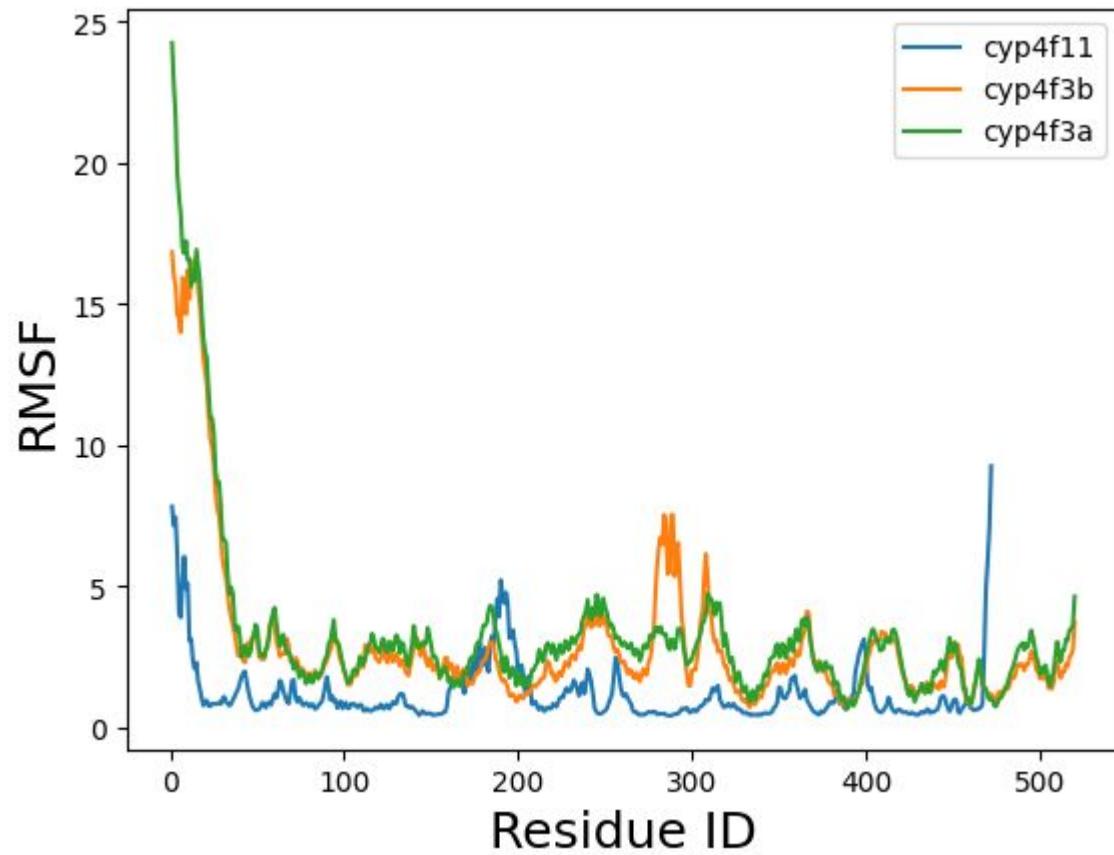
# CYP Comparative Analysis

CYP4F11, CYP4F2, CYP4F3A, CYP4F3B

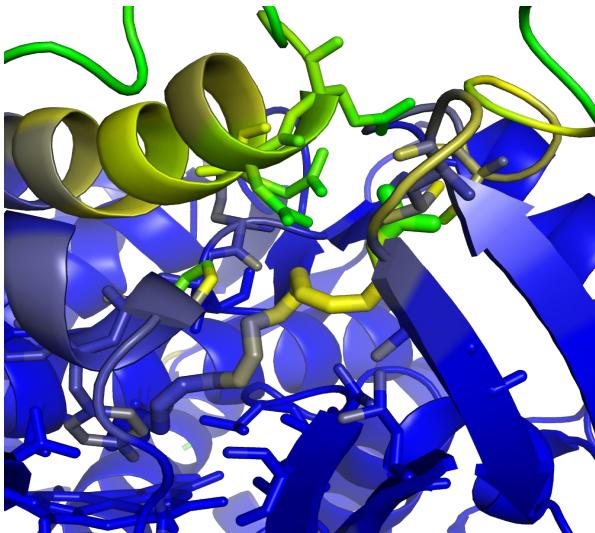
# $\omega$ -carbon:iron distance



# $\alpha$ -carbon RMSF



# All Atom RMSF

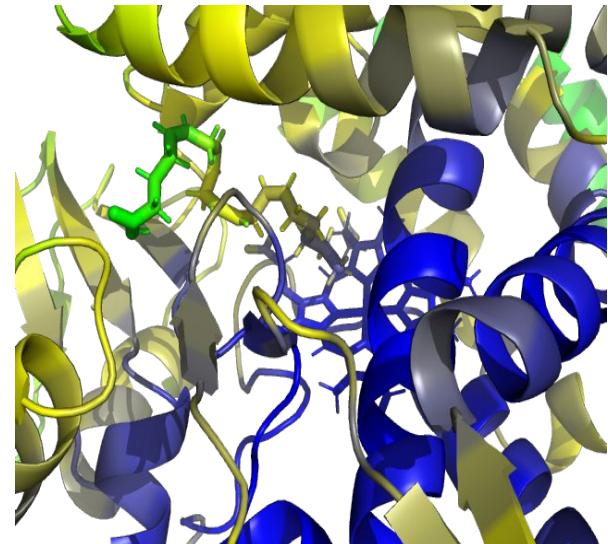
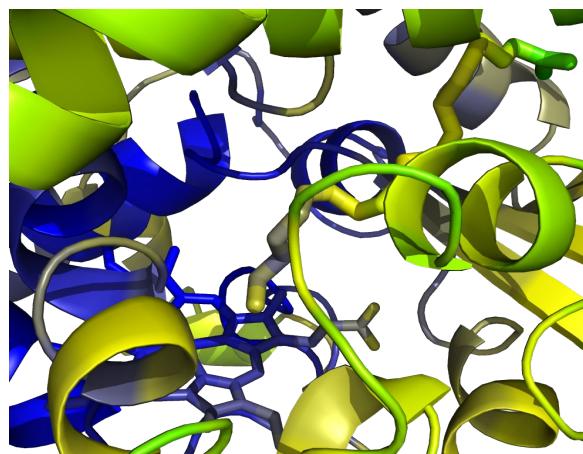


CYP4F11

RMSF

1.0 Å  
2.5 Å  
4.0 Å

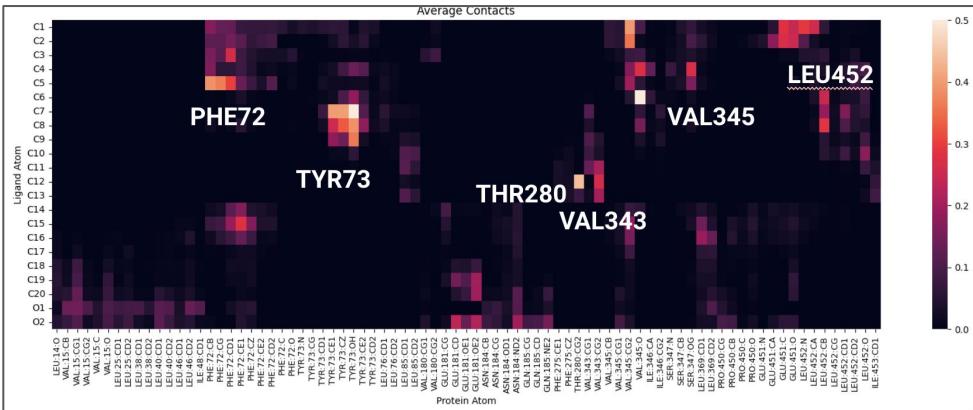
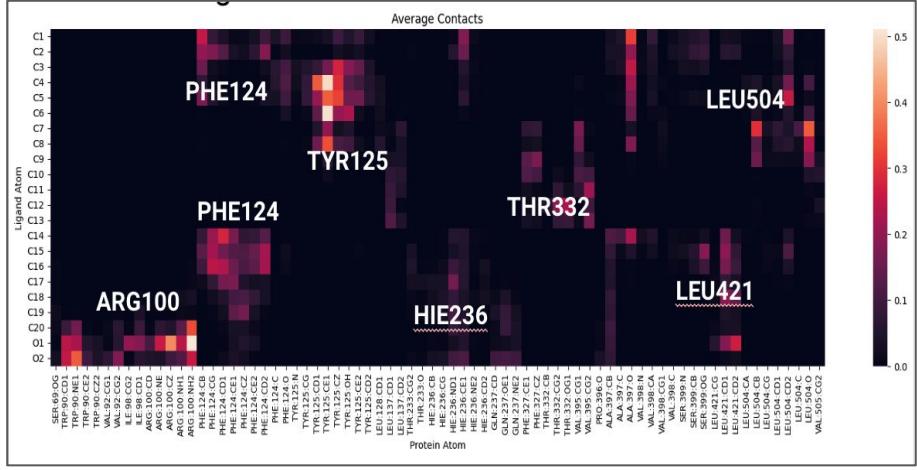
CYP4F3A



CYP4F3B

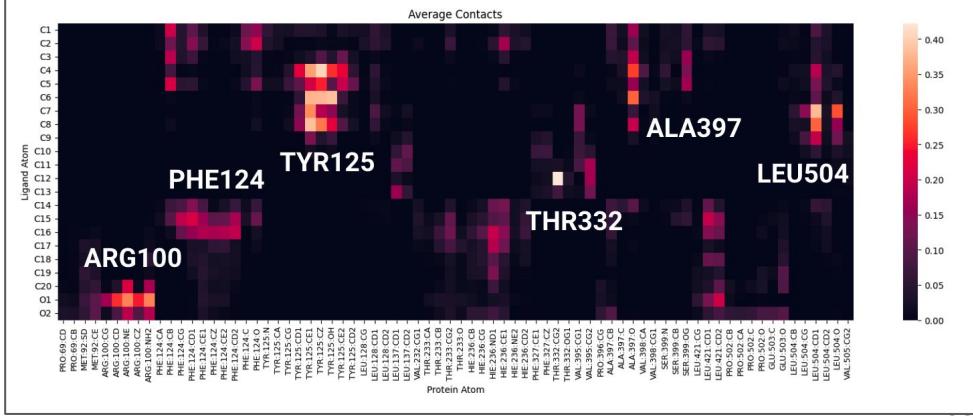
# Ligand Contacts

## CYP4F11



## CYP4F3A

## CYP4F3B



# Conclusions

- CYP4F11 was the most stable protein, followed by 4F3B
- CYP4F11 & 4F3B appear to behave relatively similarly
- CYP4F3A was the least stable protein and shows greater flexibility near Fe