

Homology modeling and molecular docking recap

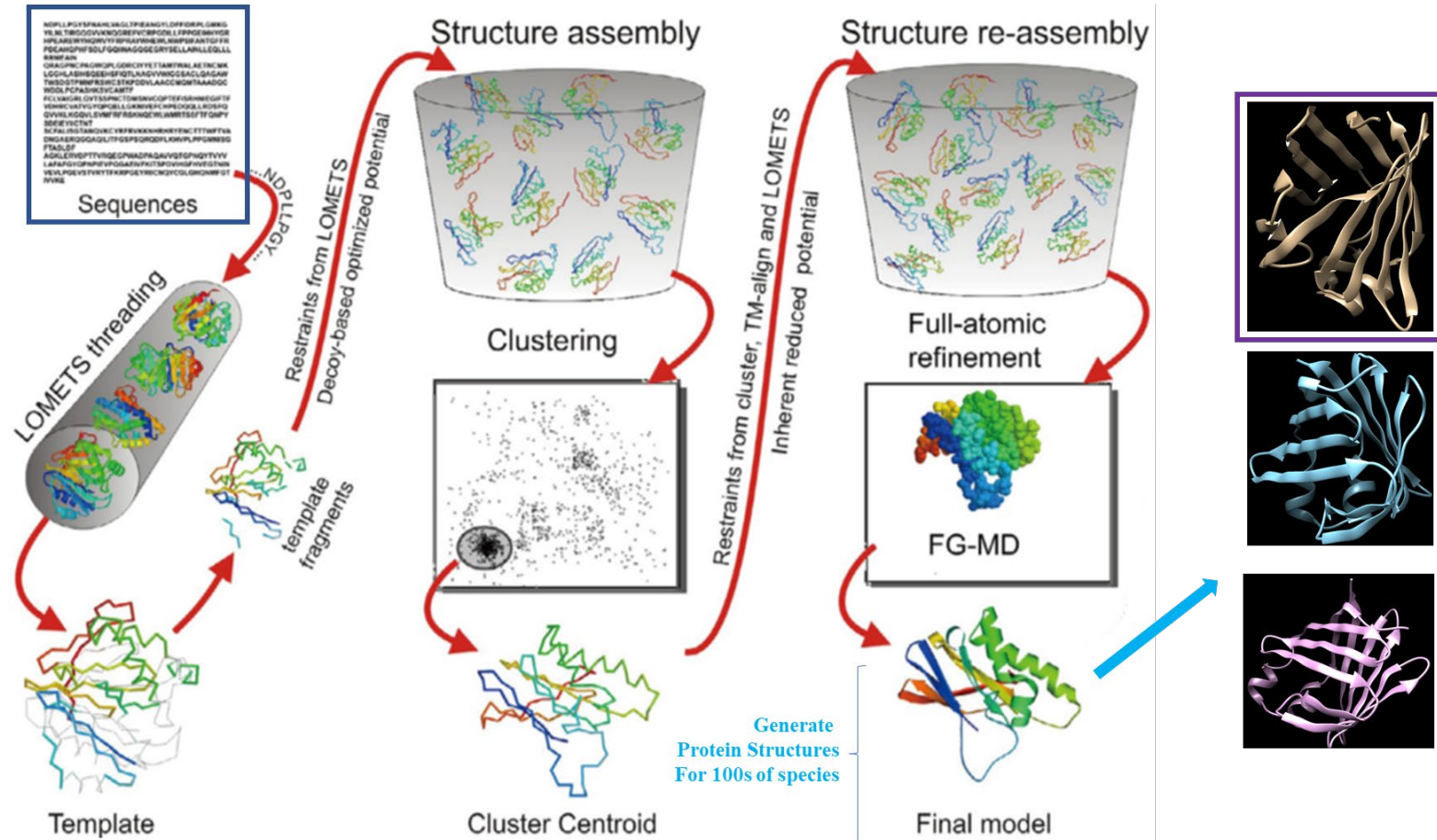
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Overview

- Created homology models for 10 high priority proteins
 - Look at model scores
- Docked thiacloprid and flupyradifurone to models
 - Look at docking scores across species and pesticides
- Compared scores between both docking areas

Creating homology models with the Iterative Threading ASSEmbly Refinement (ITASSER) tool



Models created and scores

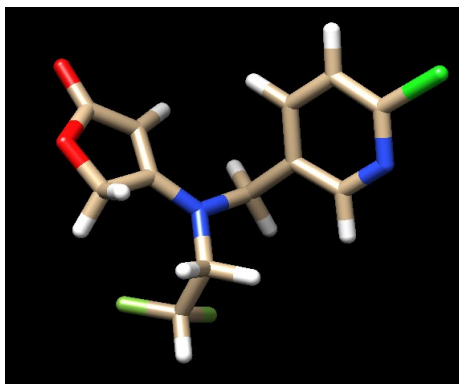
Protein	C-Score	TM-Score	RMSD	decoys	density
CYP6AS11	1.32	0.90+-0.06	4.5+-3.0	7707	0.571
CYP6AS13	1.21	0.88+-0.07	4.7+-3.1	8571	0.533
CYP6BD1	0.68	0.81+-0.09	5.9+-3.7	4028	0.314
CYP9DL5	1.58	0.94+-0.06	4.1+-2.7	6294	0.761
CYP9DM1	1.42	0.91+-0.06	4.3+-2.9	8639	0.65
CYP9DM2	1.23	0.88+-0.07	4.8+-3.1	9784	0.555
CYP9FT2	1.75	0.96+-0.05	3.7+-2.5	5596	0.902
CYP9FU3	1.14	0.87+-0.07	5.0+-3.2	7131	0.486
CYP9FZ2	1.17	0.87+-0.07	4.9+-3.2	7127	0.506
CYP9Q10	1.36	0.9+-0.06	4.5+-3.0	7430	0.605

Project	Protein	Template	Species	Model #	Cscore	TM-Score	RMSD	Decoys	Density
CYP9Q	CYP3A4	1TQN	Human	1 of 5	1.09	0.86+-0.07	5.0+-3.2	3316	0.556
CYP9Q	CYP9Q3	1TQN	Apis mellifera	1 of 5	1.01	0.85+-0.08	5.2+-3.3	4559	0.428
CYP9Q	CYP9Q4	1TQN	Bombus terrestris	1 of 5	0.83	0.83+-0.08	5.6+-3.5	2088	0.365
CYP9Q	CYP9BU1	1TQN	Osmia bicornis	1 of 5	0.57	0.79+-0.09	6.1+-3.8	1579	0.28
CYP9Q	CYP9Q3	None	Apis mellifera	1 of 5	1.07	0.86+-0.07	5.1+-3.3	4515	0.456
CYP9Q	CYP9Q4	None	Bombus terrestris	1 of 5	0.72	0.80+-0.09	5.9+-3.7	3153	0.326
CYP9Q	CYP9BU1	None	Osmia bicornis	1 of 5	0.54	0.79+-0.09	6.2+-3.8	1042	0.272

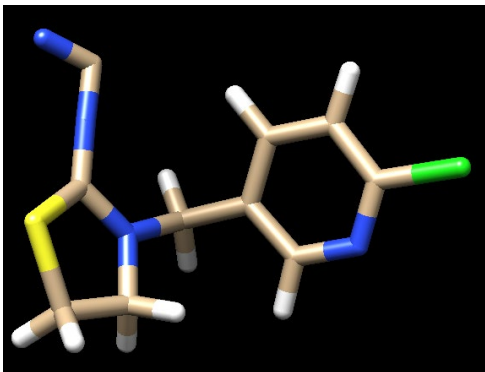
ITASSER scoring text

- Correlation coefficient of C-score of the first model with TM-score to the native structure is 0.91, while the coefficient of C-score with RMSD to the native structure is 0.75
- TM-score >0.5 indicates a model of correct topology and a TM-score <0.17 means a random similarity
- A higher cluster density means the structure occurs more often in the simulation trajectory and therefore signifies a better-quality model

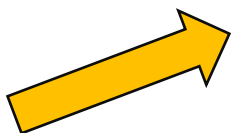
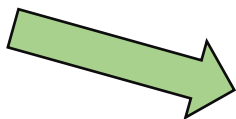
Docking process



Flupyradifurone



Thiachloprid



Docking box areas

EPA:

-17.098,-22.338,-11.492

20,15,15

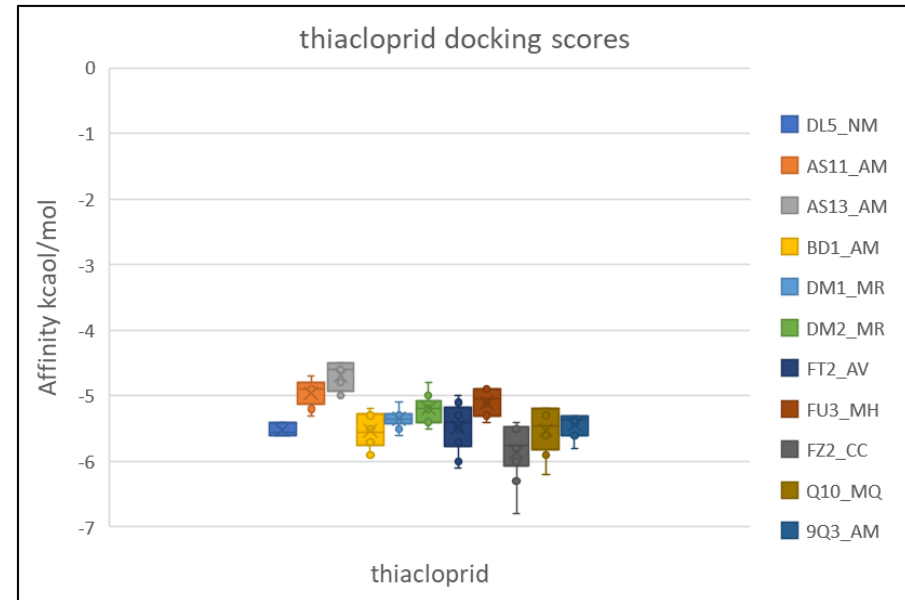
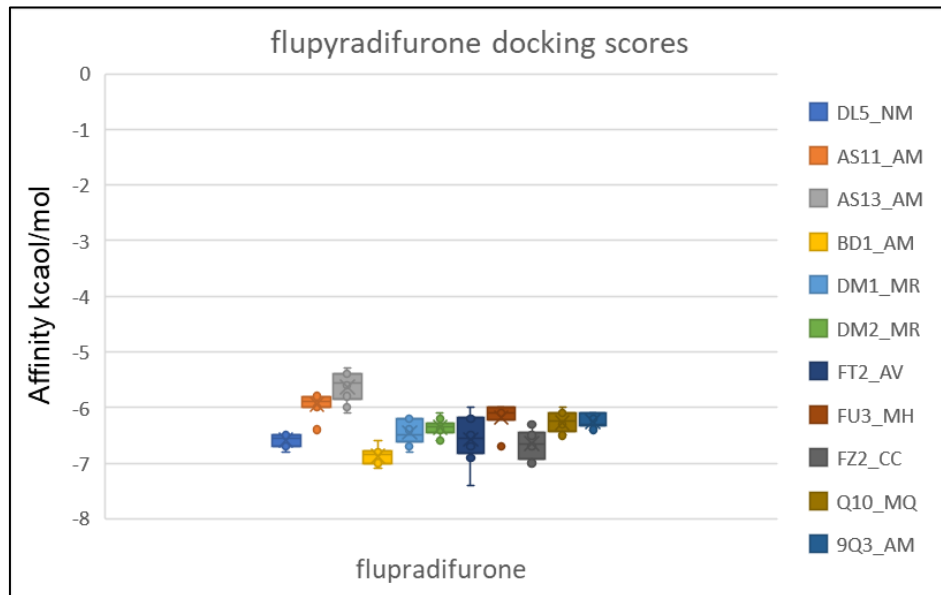
Bayer:

19.7332,25.7236,-4.67613

16.0055,17.7187,23.9048

(Used negative x,y,z coordinates due to location of ITASSER models)

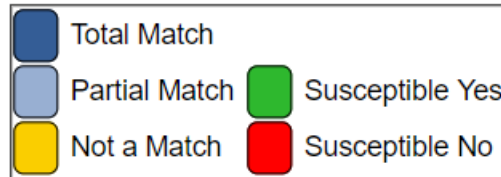
Docking scores between models and boxes



	Average docking scores					
	AS11_AM	AS13_AM	BD1_AM	DM1_MR	DM2_MR	
flupyradifurone	-5.94	-5.63	-6.87	-6.45	-6.36	EPA Box
	-6	-5.68	-6.52	-6.54	-6.24	Bayer Box
thiacloprid	-4.96	-4.69	-5.53	-4.29	-5.19	EPA Box
	-5.3	-4.97	-5.4	-5.32	-4.91	Bayer Box
	flupy	thia				
Reference	-6.25	-5.44	EPA Box			
CYP9Q3_AM	-6.61	-5.64	Bayer Box			

“It includes 5 of the CYP9Q-orthologs we tested and have thiacloprid and flupyradifurone as their confirmed substrate and 5 enzymes (3 from the honey bee and two from Megachile rotundata), where metabolism of those insecticides is not present *in-vitro*.”

Previously made SeqAPASS heat map



NCBI Accession	Scientific Name	Protein Name	Common Name	Similar Susceptibility	Amino Acid 1	Amino Acid 2	Amino Acid 3	Amino Acid 4	Amino Acid 5
XP_006562363.1	<i>Apis mellifera</i>	cytochrome P450 9e2	Honey bee	Y	111G	214N	310S	371V	372L
XP_016922294.2	<i>Apis cerana</i>	LOW QUALITY PROTEIN: cytochrome P450 9e2-like	Asiatic honeybee	Y	111G	214N	310S	371I	372L
XP_017758640.1	<i>Eufriesea mexicana</i>	PREDICTED: cytochrome P450 9e2-like	Orchid bees	N	110K	214M	307T	368I	369A
XP_031775226.1	<i>Apis florea</i>	cytochrome P450 9e2-like	Little honeybee	N	112K	216T	309T	370V	371V
XP_017794730.1	<i>Habropoda laboriosa</i>	PREDICTED: cytochrome P450 9e2-like	Digger bees	N	108K	212L	305T	366I	367V
XP_031837097.1	<i>Nomia melanderi</i>	cytochrome P450 9e2-like	Alkali bee	N	110K	214D	307S	368S	369P

Conclusions

- Models created are “quality models” based off scoring metrics
- Sequence based predictions differ from structural based predictions
- SeqAPASS predictions can be difficult when comparing sequences that don't align with template protein