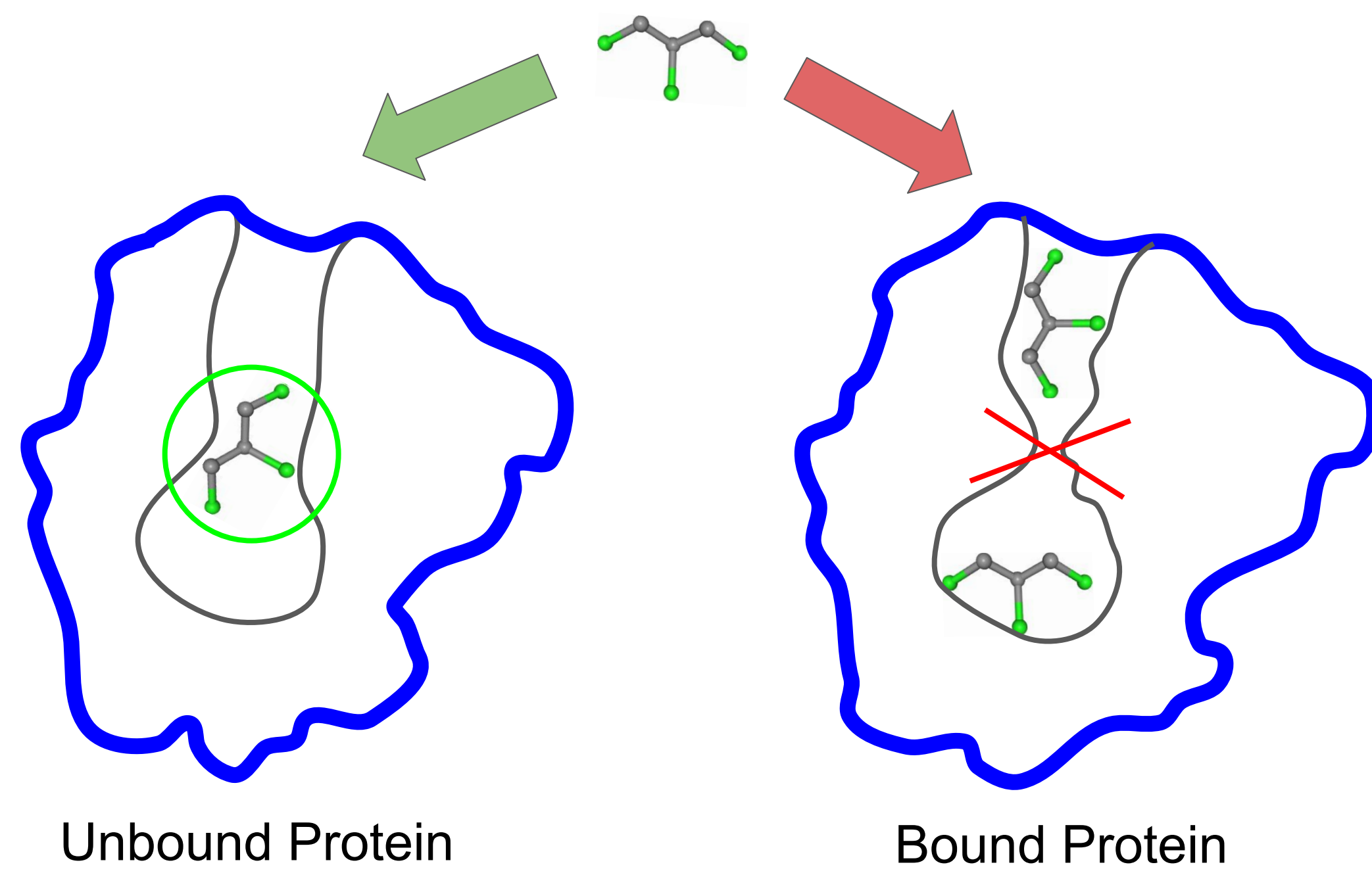


Motivation

- Changes in protein structure after protein-ligand binding affect the accessibility of the binding site
- Accessibility to an active binding site is influenced by the size and energy within protein tunnels



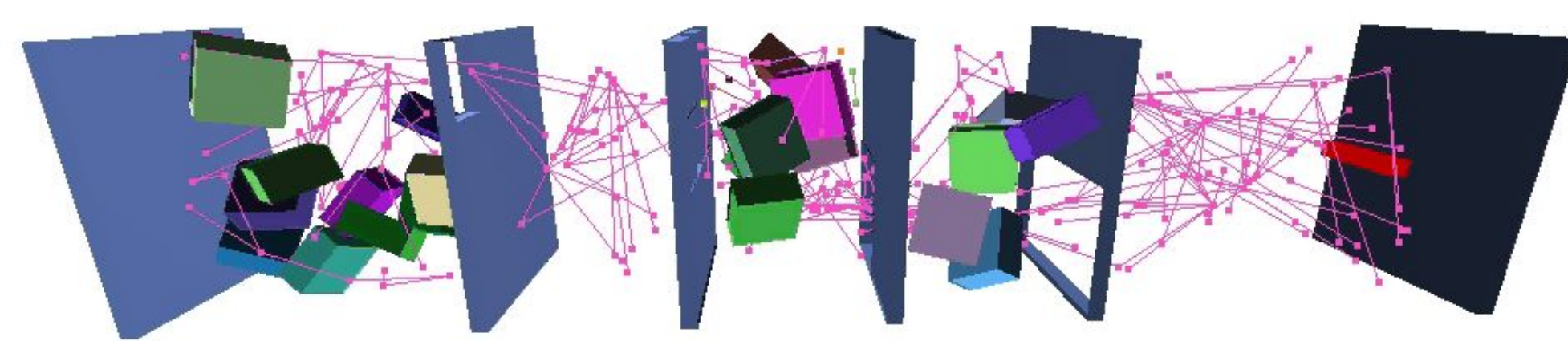
Objective

- Use motion planning to model accessible protein pathways to the active binding site and study the changes that occur between the unbound and bound protein state.

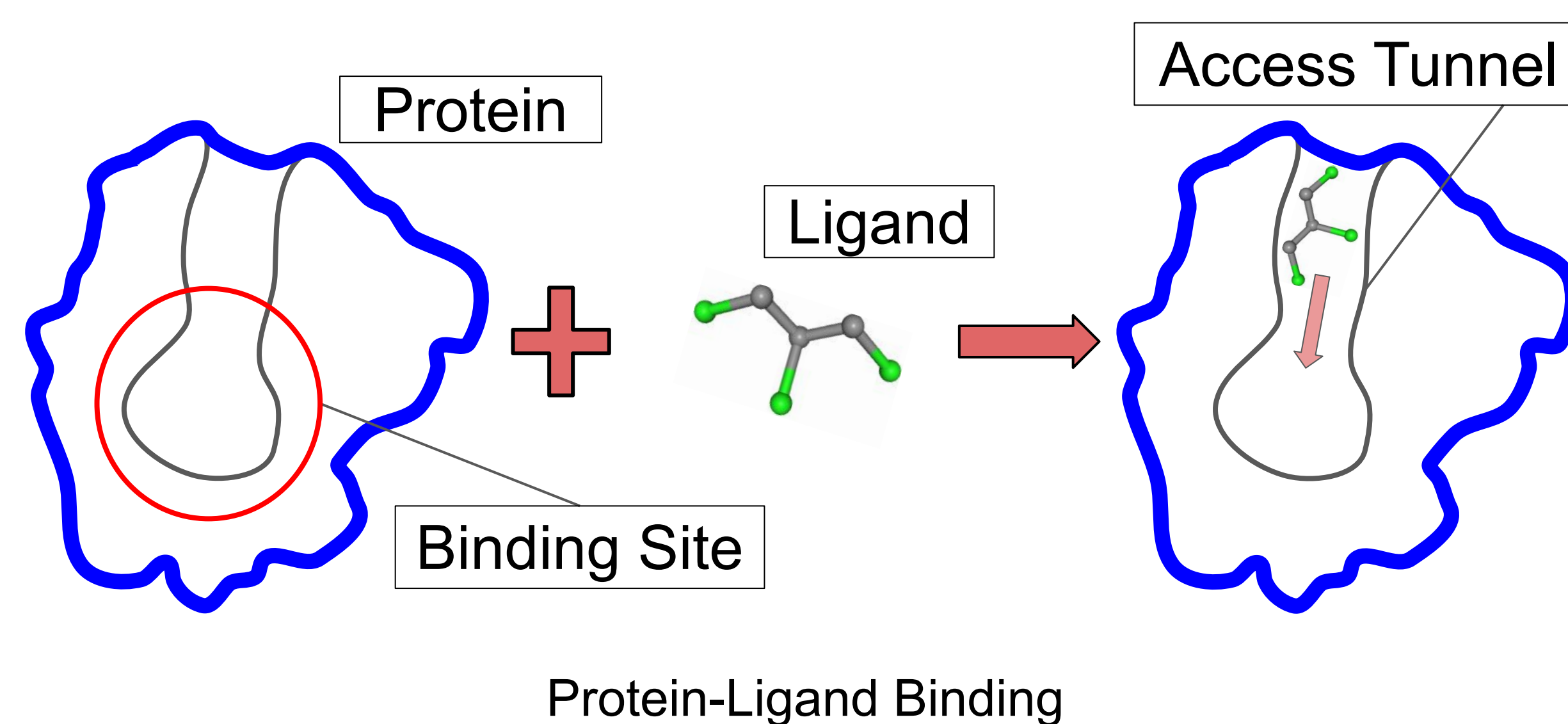
Motion Planning

Purpose

- Finding a valid path from a start to a goal for a movable robot in an environment.

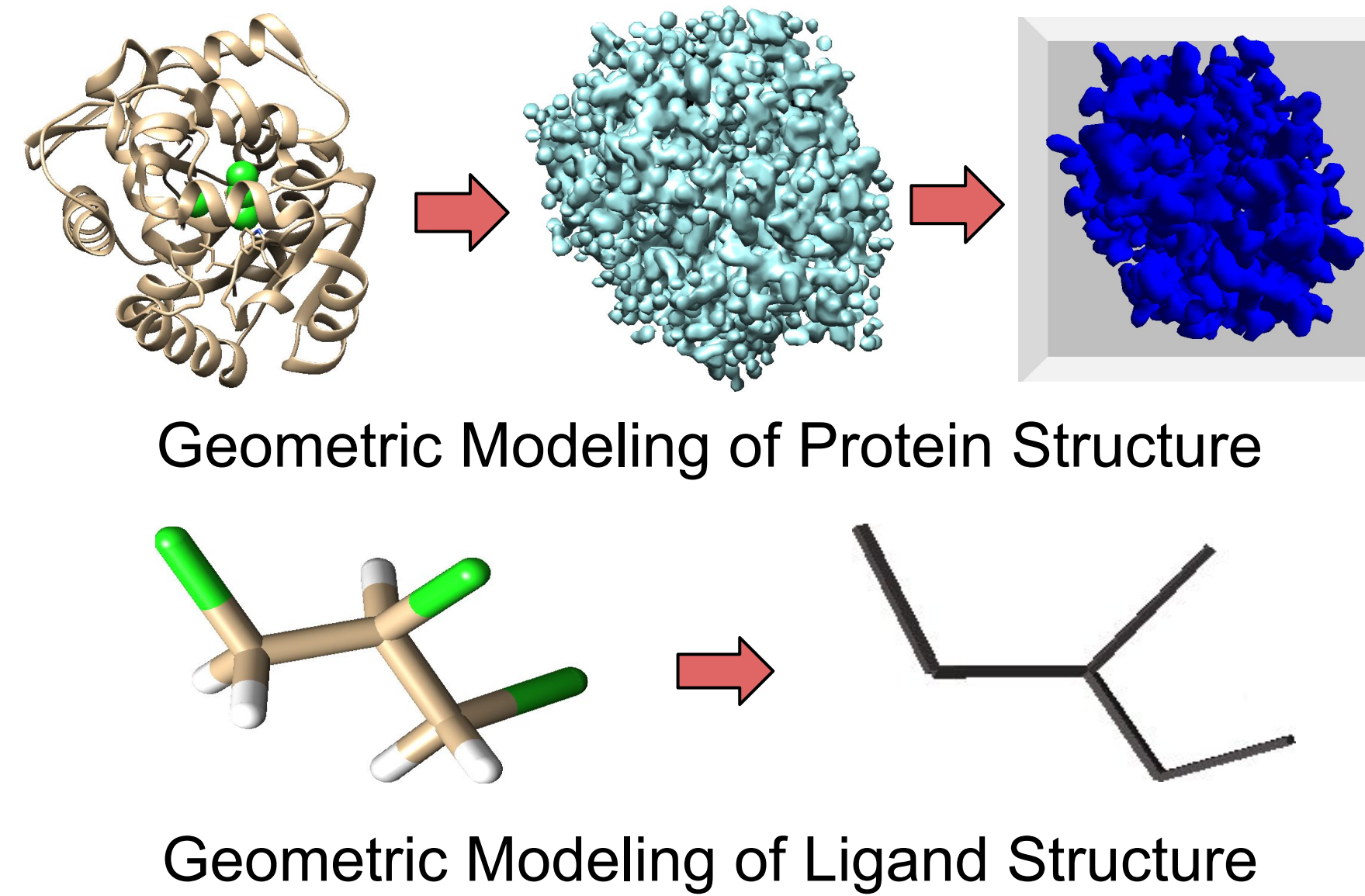


Application in Computational Biology

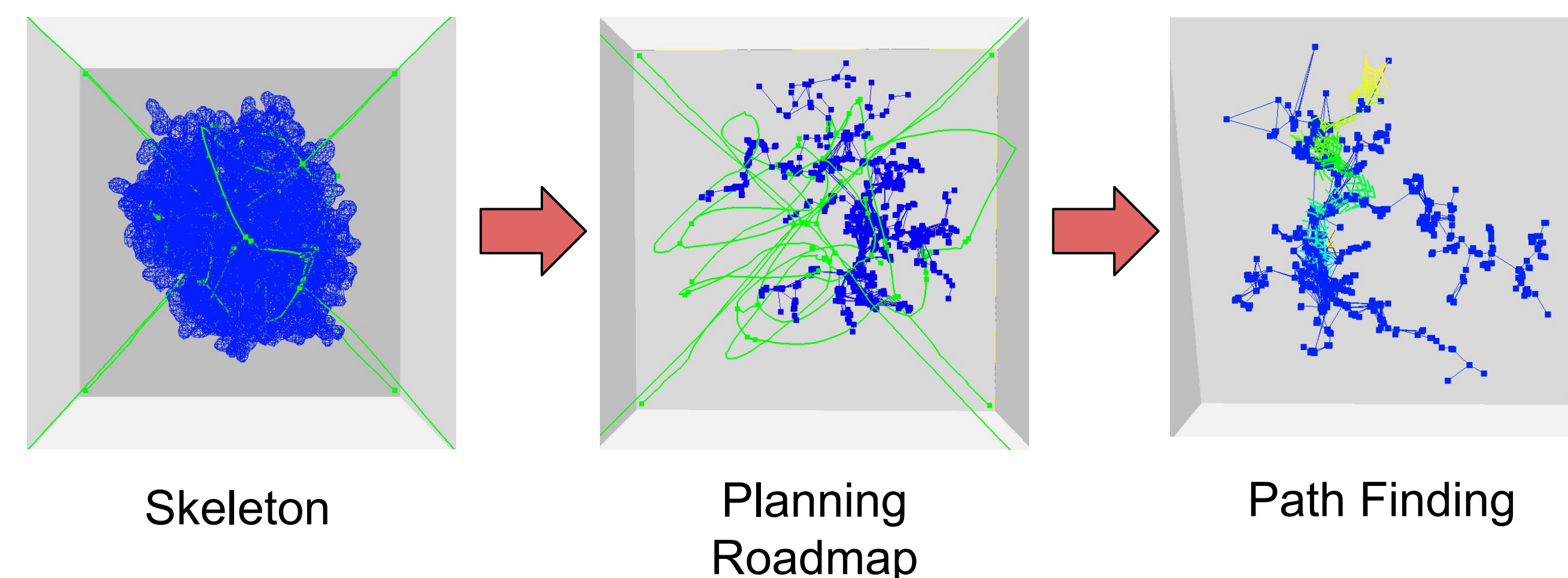


Methods

Modeling



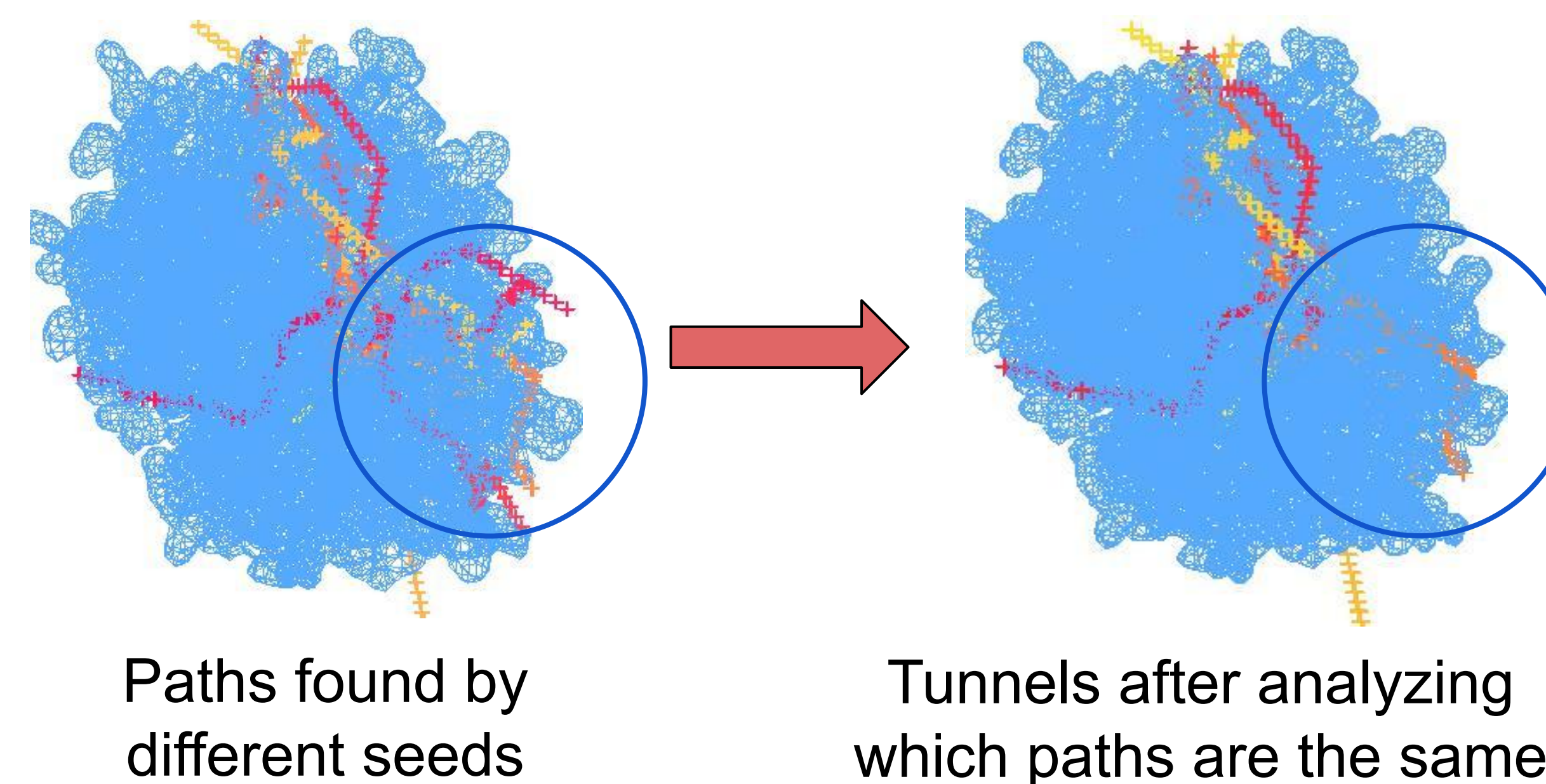
Planning



Analysis

- Score accessibility on a scale from 0.0 to 1.0 based on tunnels found and energy levels
- Tunnel Score**
$$\text{Num Seeds} \cdot w_0 + \text{Min Energy} \cdot w_1 - \text{Max Energy} \cdot w_2$$
- Protein Score**

$$\text{Num Tunnels} \cdot w_0 + \text{Avg. Tunnel Score} \cdot w_1 + \text{Min Energy} \cdot w_2 - \text{Max Energy} \cdot w_3$$



Experiments

- Ran experiments on two sets of protein pairs:
 - DhaA31
 - HCV NS5B
- Compiled data on cost and quality of roadmap construction
- The table shows analyzed data for the unbound and bound proteins of HCV NS5B to demonstrate specific changes in the finding of valid pathways

Protein	Score	
	Unbound	Bound
DhaA31	0.69	0.57
HCV NS5B	0.78	0.57

Protein Name (PDB ID)	HCV NS5B RNA polymerase	
	Unbound (1c2p)	Bound (2ijn)
Image of All Valid Tunnels in Protein		
Avg. Run Time	207	3211
Num. Tunnels Found	9	6
Avg. Min/Max Energy	-1.79 / 217	-3.68 / 806
Avg. Tunnel Score	0.39	0.24

Conclusion

- Pathway accessibility decreases from the unbound to bound protein state due to fewer pathways to the binding site and higher energy levels that inhibit a ligand's ability to move through a tunnel.
- For future work, we would like to add to the data set of proteins and improve the scoring function.

Acknowledgments

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