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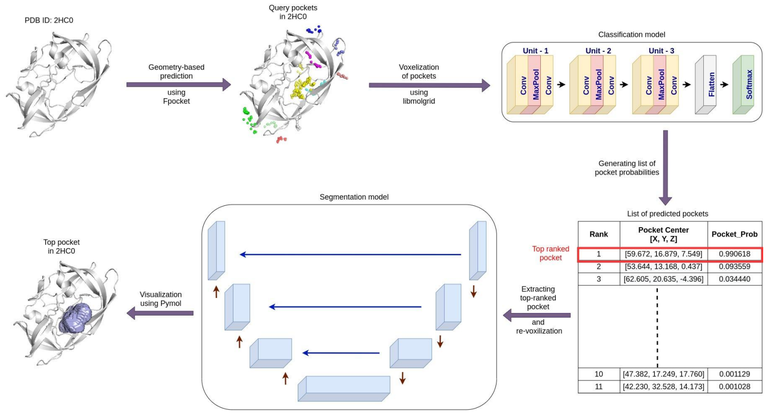
DeepPocket: Ligand Binding Site Detection using 3D Convolutional Neural Networks

ABSTRACT

A Structure Based Drug Design pipeline involves the development of drug molecules or ligands that form strong complexes with a given receptor at its binding site. A prerequisite to this is finding druggable binding sites on the 3D structure of the protein. In this work, we design a novel framework called DeepPocket that utilises 3D Convolutional Neural Networks for the scoring and segmentation of identified cavities on the protein surface.



METHOD

We follow a multi-step approach to get the final pocket location and 3D shape prediction from the input protein structure. We run Fpocket across the structure and calculate the barycenter of each predicted pocket. These become the candidate pocket centers that need to be ranked by the CNN scoring function. Therefore, constant sized grids are placed at each barycenter followed by scoring using the CNN. The top ranked centers are then sent through a CNN segmentation model to get the final pocket structure.

RESULTS

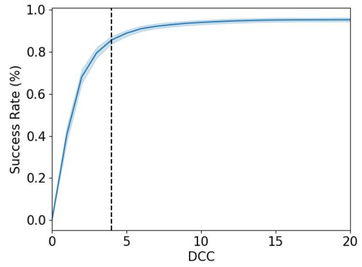
Table 1: DCA results comparison

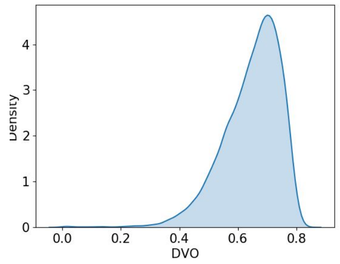
	COACH420		HOLO4K		2018+	
	Top-n	Top-(n+2)	Top-n	Top-(n+2)	Top-n	Top-(n+2)
Fpocket	35.09%	51.25%	36.34%	51.53%	23.99%	37.23%
Deepsite	53.07%	53.07%	51.65%	51.67%	52.94%	65.41%
Kalasanty	63.51%	63.51%	60.89%	60.91%	62.42%	66.23%
P2Rank	**68.24%**	75.48%	70.6%	80.05%	62.9%	75.74%
Deepocket	67.96%	**79.94%**	**73.36%**	**82.97%**	**64.58%**	**83.01%**

RESULTS

There are mainly three metrics used to evaluate binding site detection algorithms:

- **Distance to any atom of the ligand (DCA/PPC)**- It is the shortest distance between the predicted center and any atom of the ligand. Predictions with DCA lesser than 4Å are considered successful.
- **Distance to the center of the binding site (DCC)**- It is the distance between the predicted center and actual center of the pocket.
- **Discretized Volume Overlap (DVO)**- It is the ratio of the volume of intersection of the predicted and actual shapes by the union of their volumes.





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