A novel computational approach for identifying protein relationships

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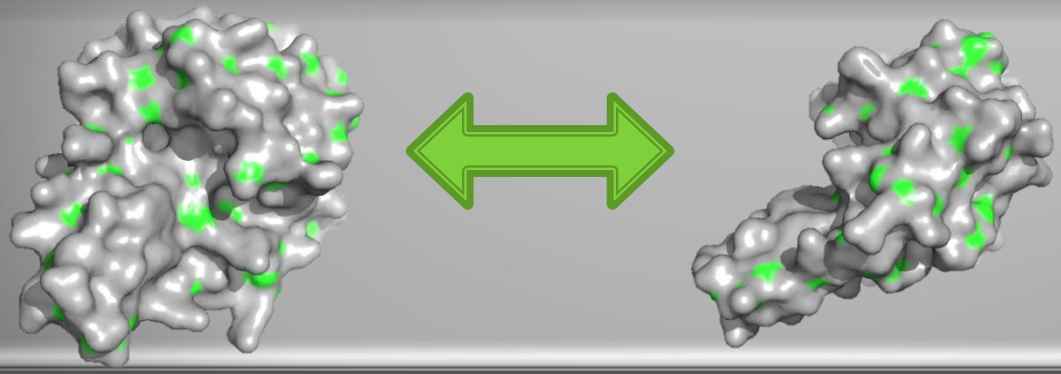
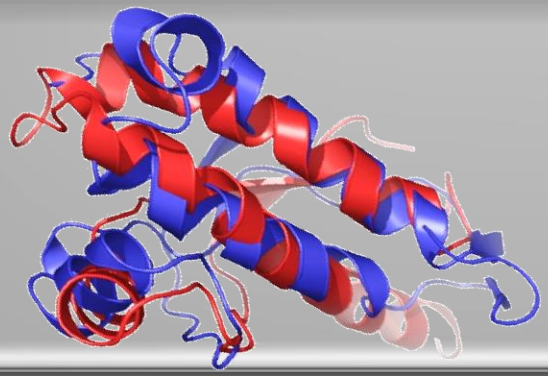
Protein function is commonly inferred by homology

Surface



Structure

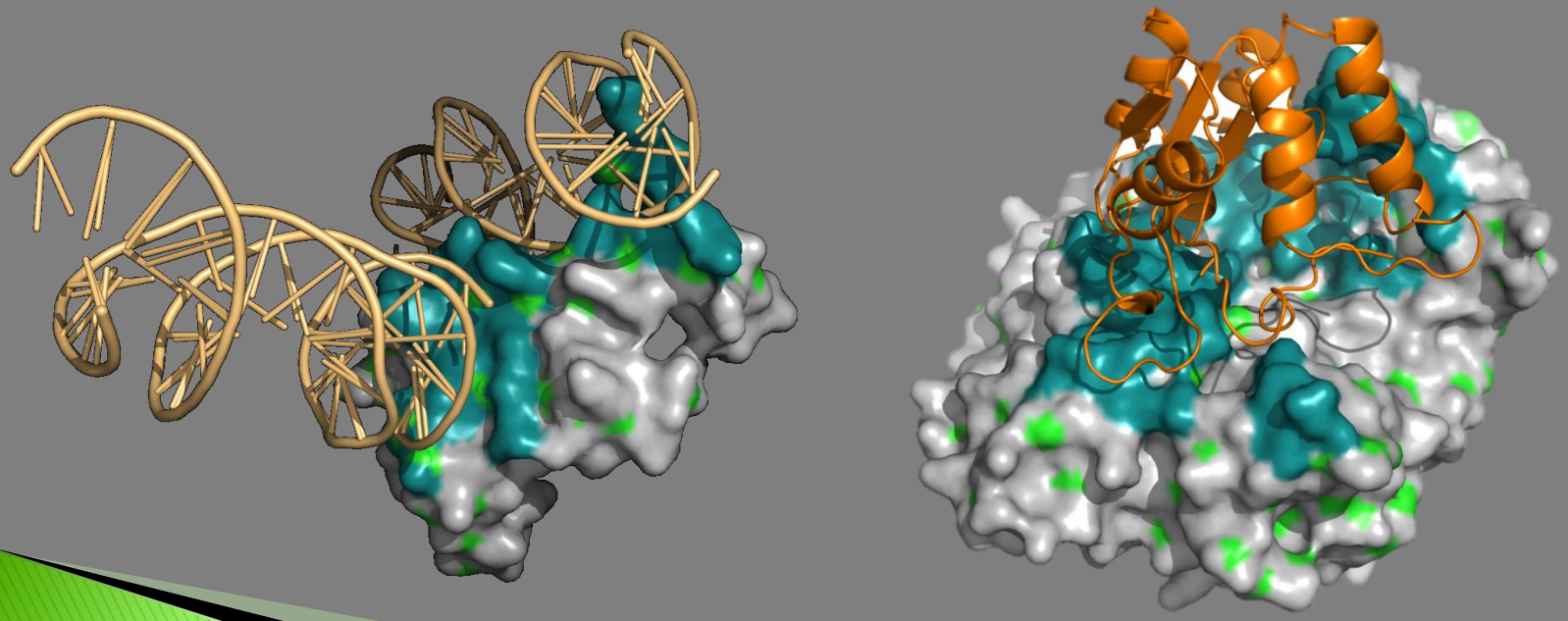


Sequence

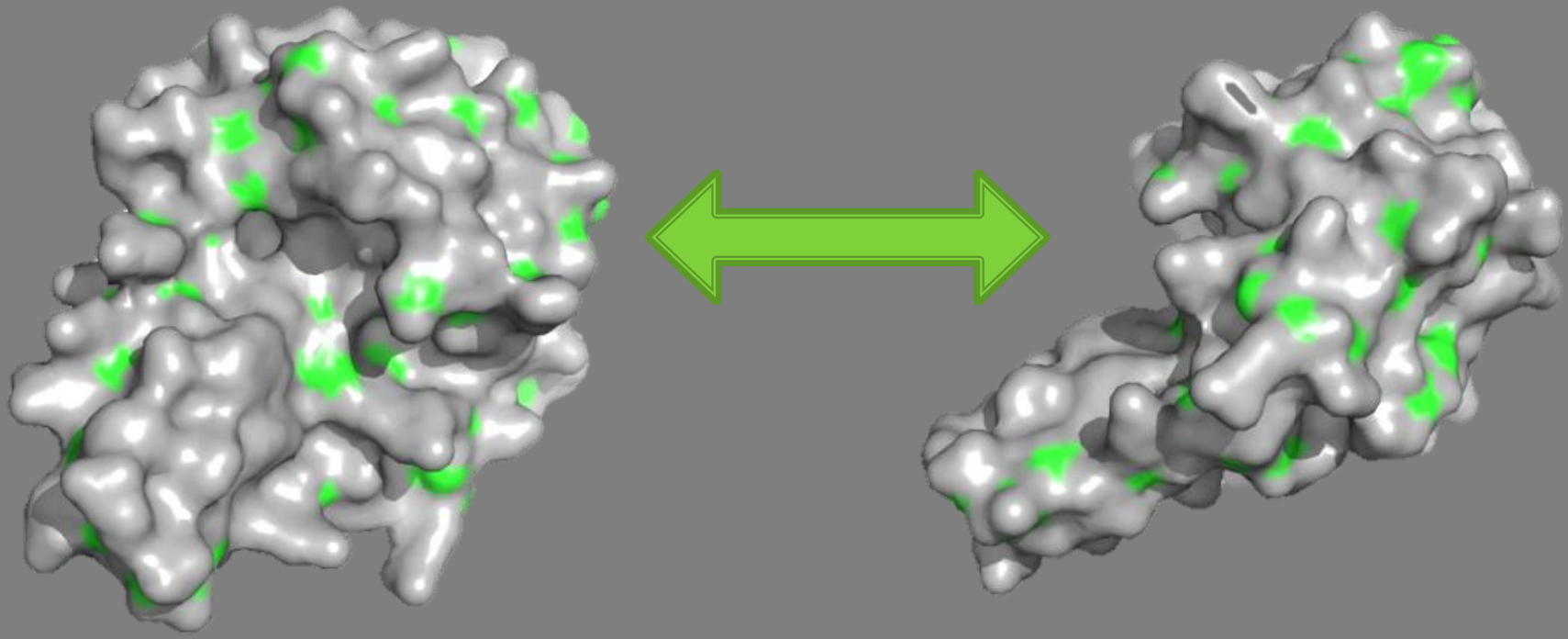
KKILKELEVVSPEEAAHQKAVVE

IKKELKNLSPEEASDQKAVVQKK

The protein surface can provide additional information regarding its interactions with other molecules



A PatchBag approach for comparing protein surfaces

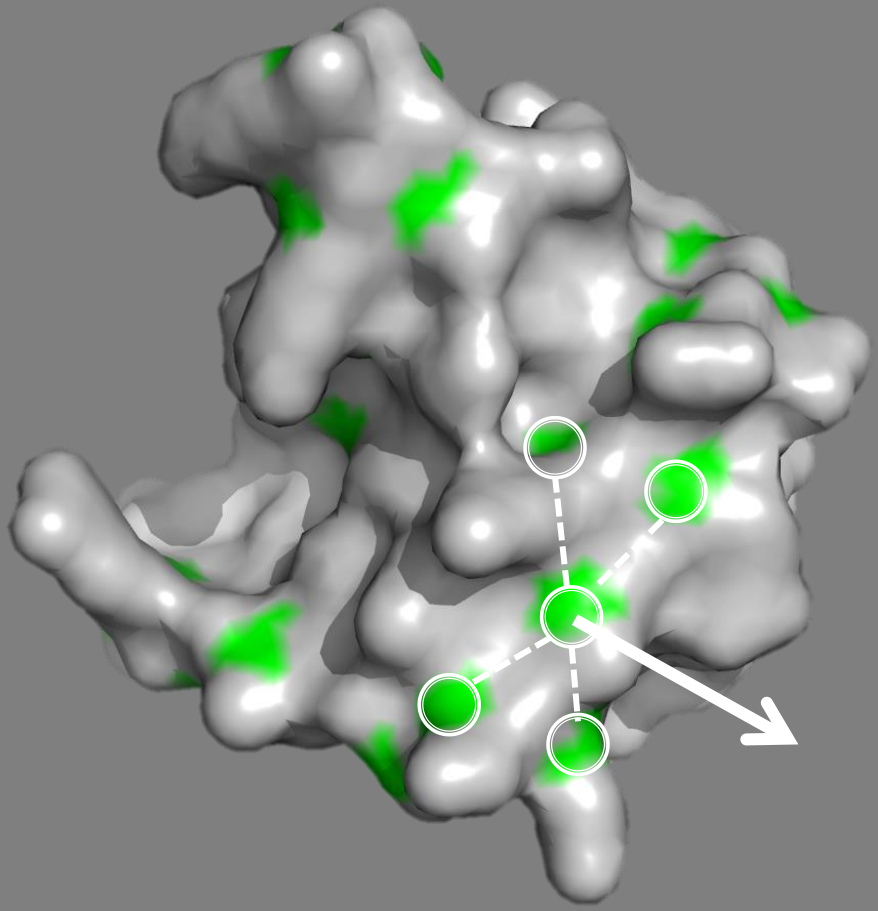


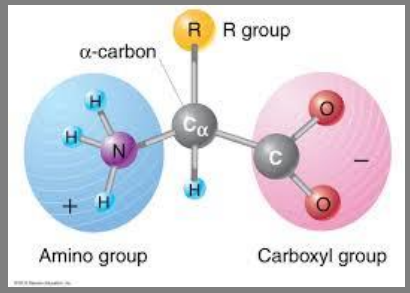
What is a PatchBag approach

PatchBag = Bag of Patches ~ Bag of Words

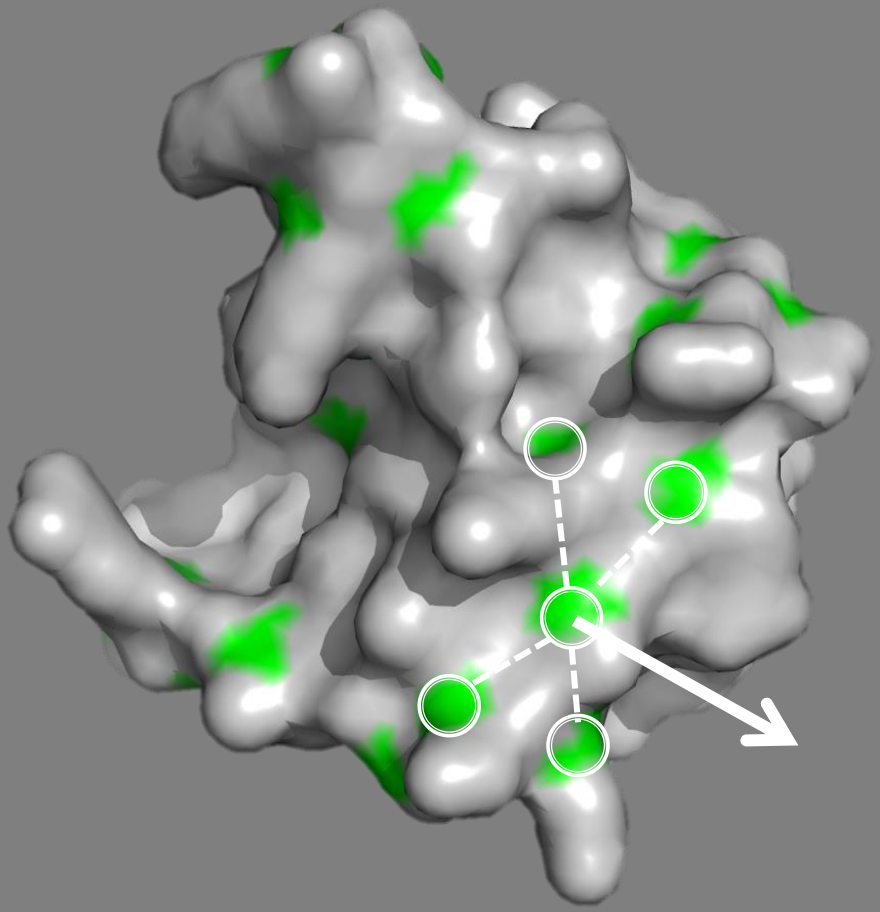
The **bag-of-words model** is a simplifying representation used in natural language processing and information retrieval (IR).
In this model, a text (such as a sentence or a document) is represented as the bag (multiset) of its words, disregarding grammar and even word order but keeping multiplicity.

How do we define words on protein surfaces ?

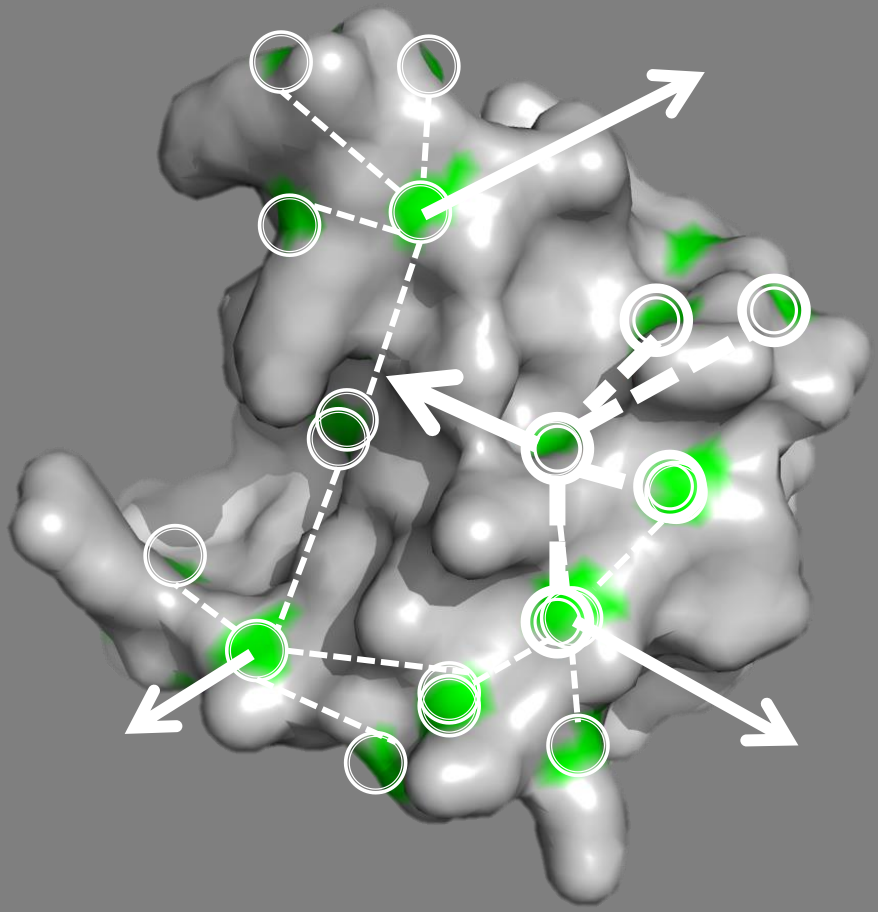




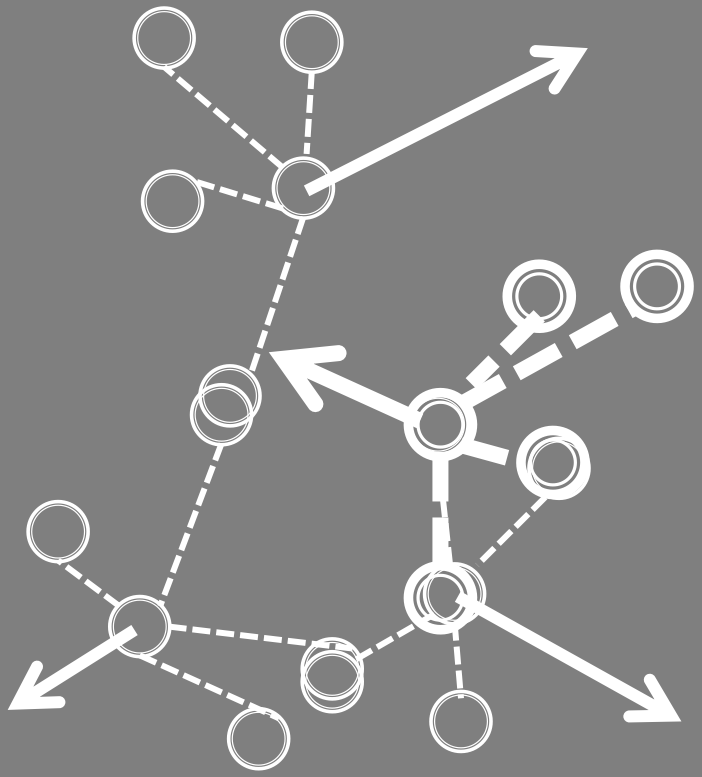
Surface Patch Definition



Surface Patch Definition

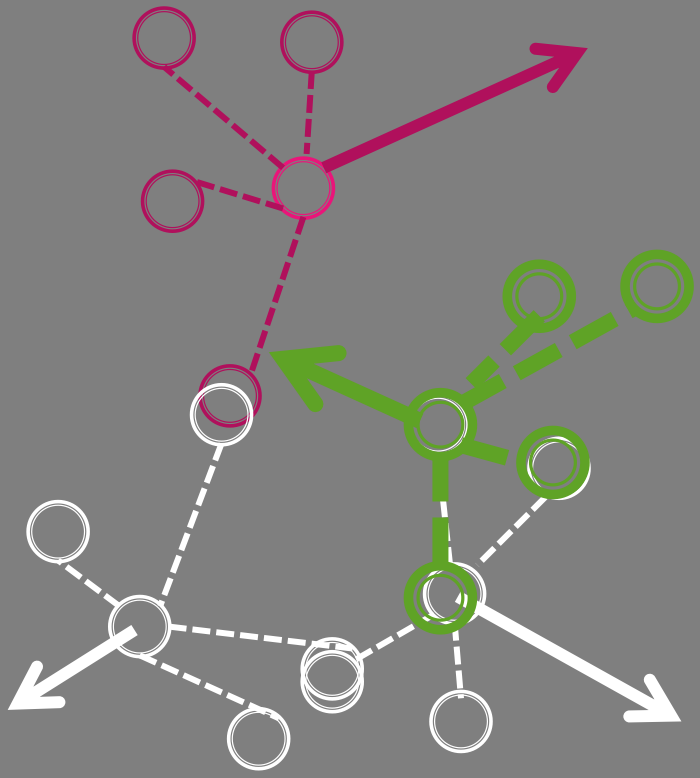


How can we compare Patches

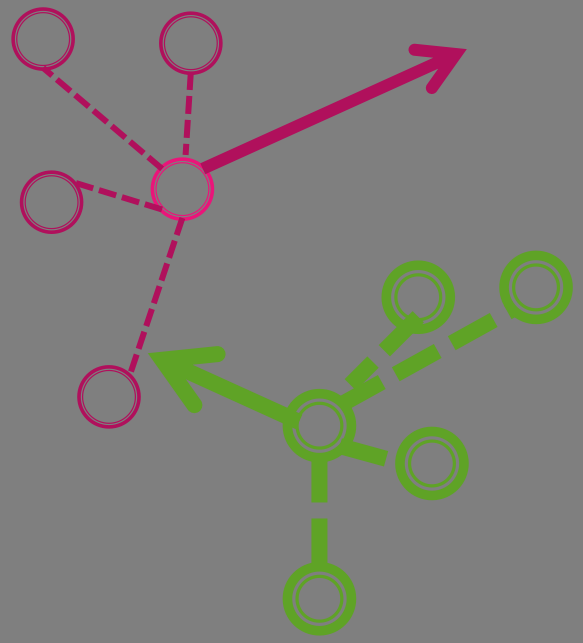


We need a patch dictionary (library) !

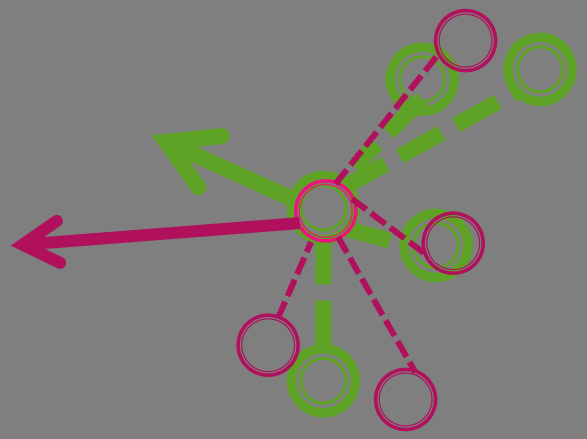
Similarity of 2 Surface Patches



Similarity of 2 Surface Patches

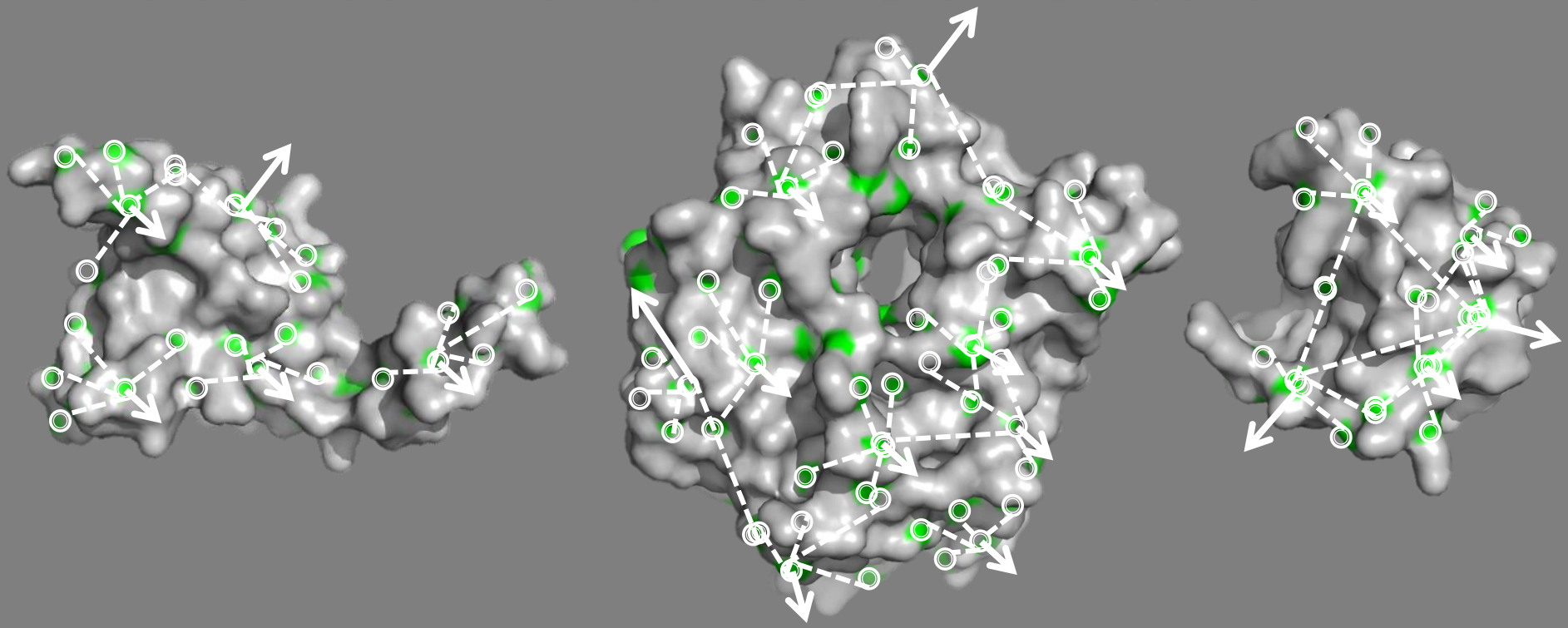


Similarity of 2 Surface Patches



RMSD on the best alignment,
such that normal vectors “agree”

Patches Libraries Generation



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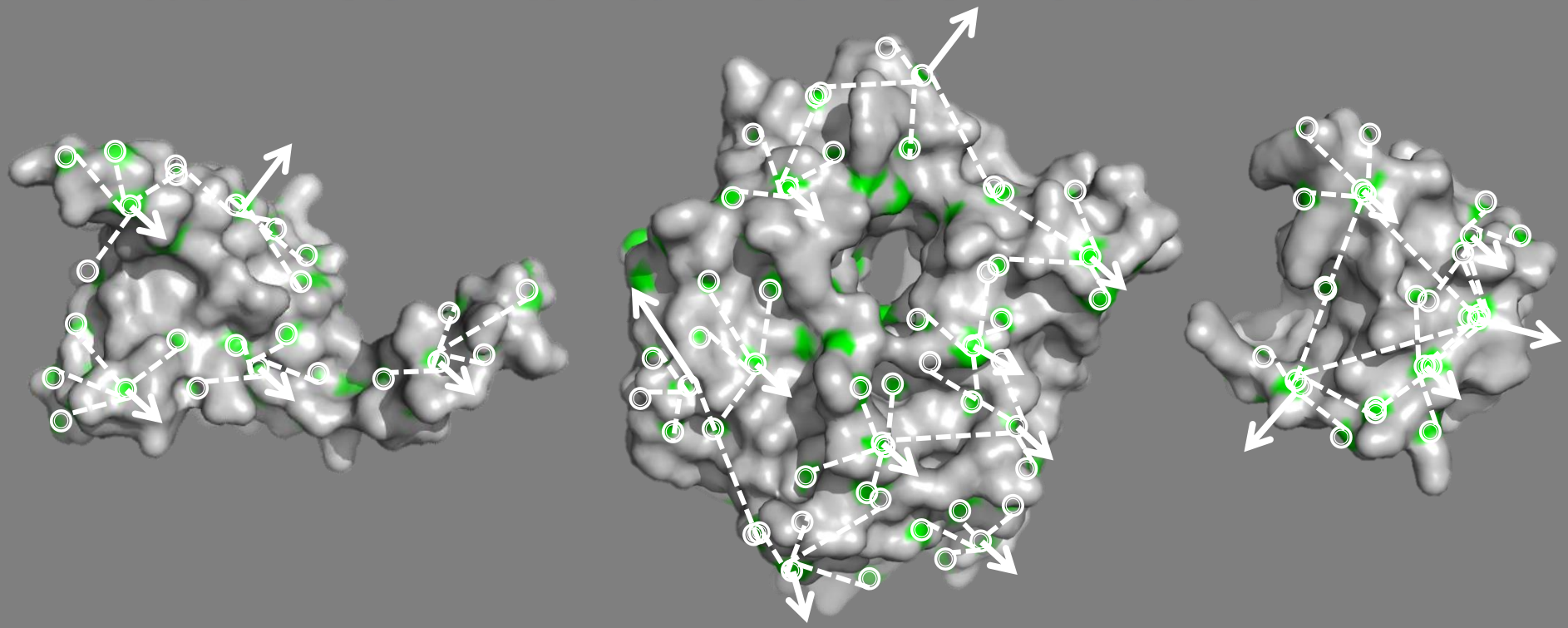

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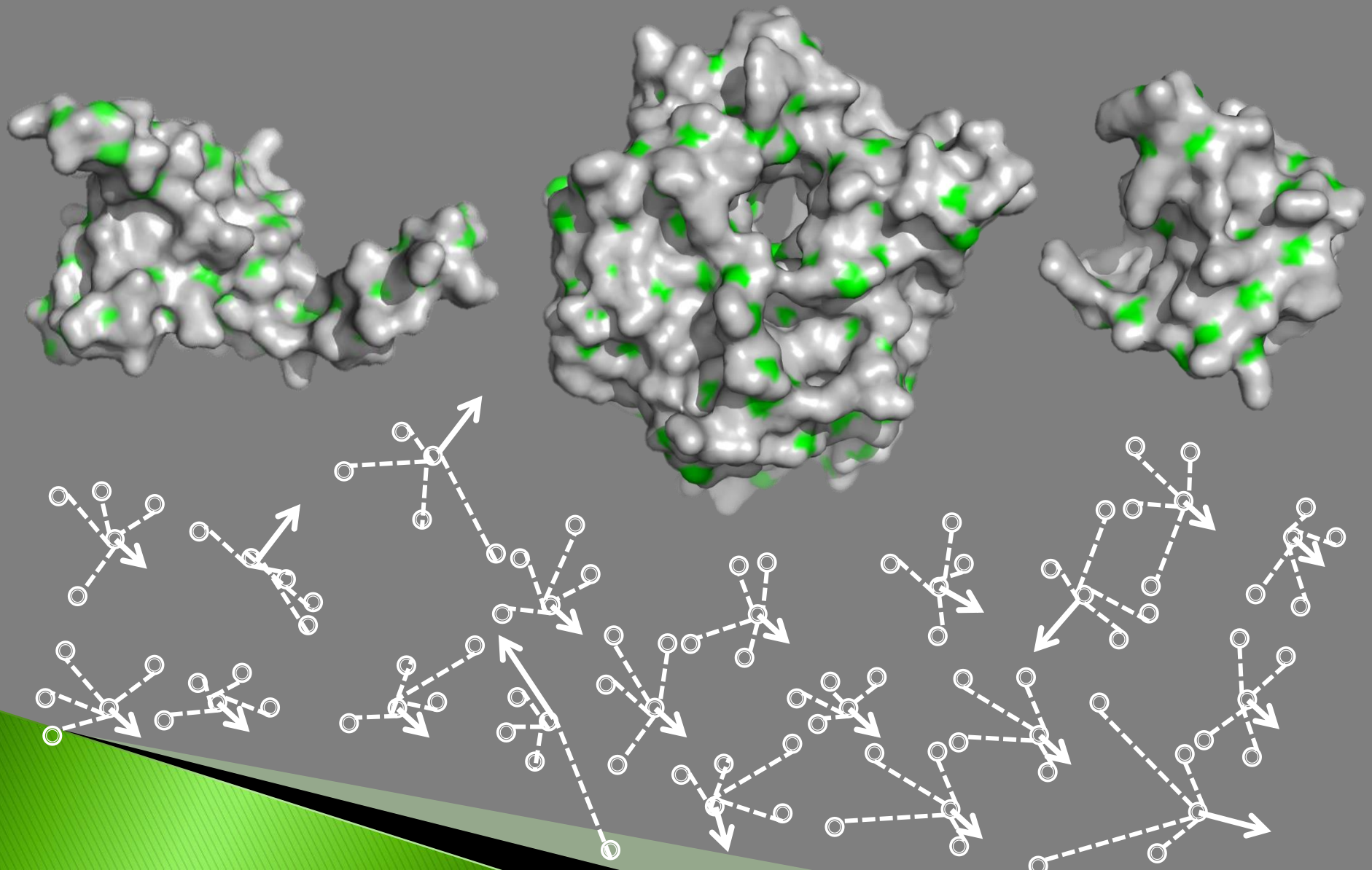

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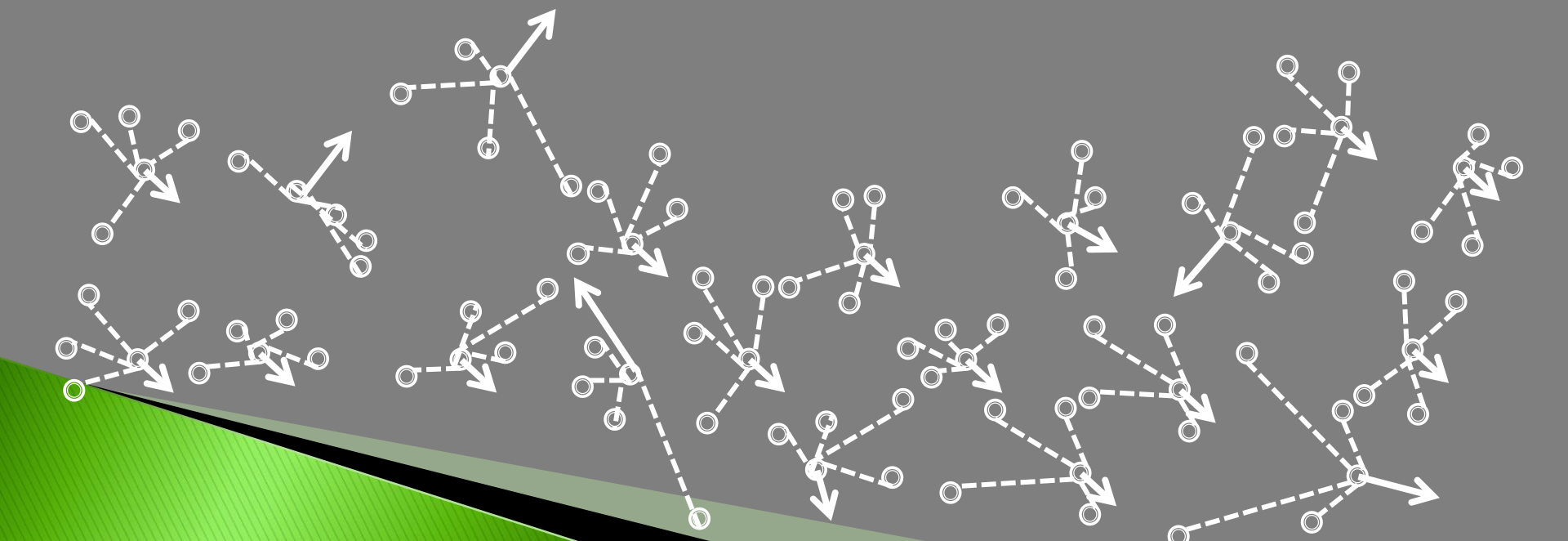

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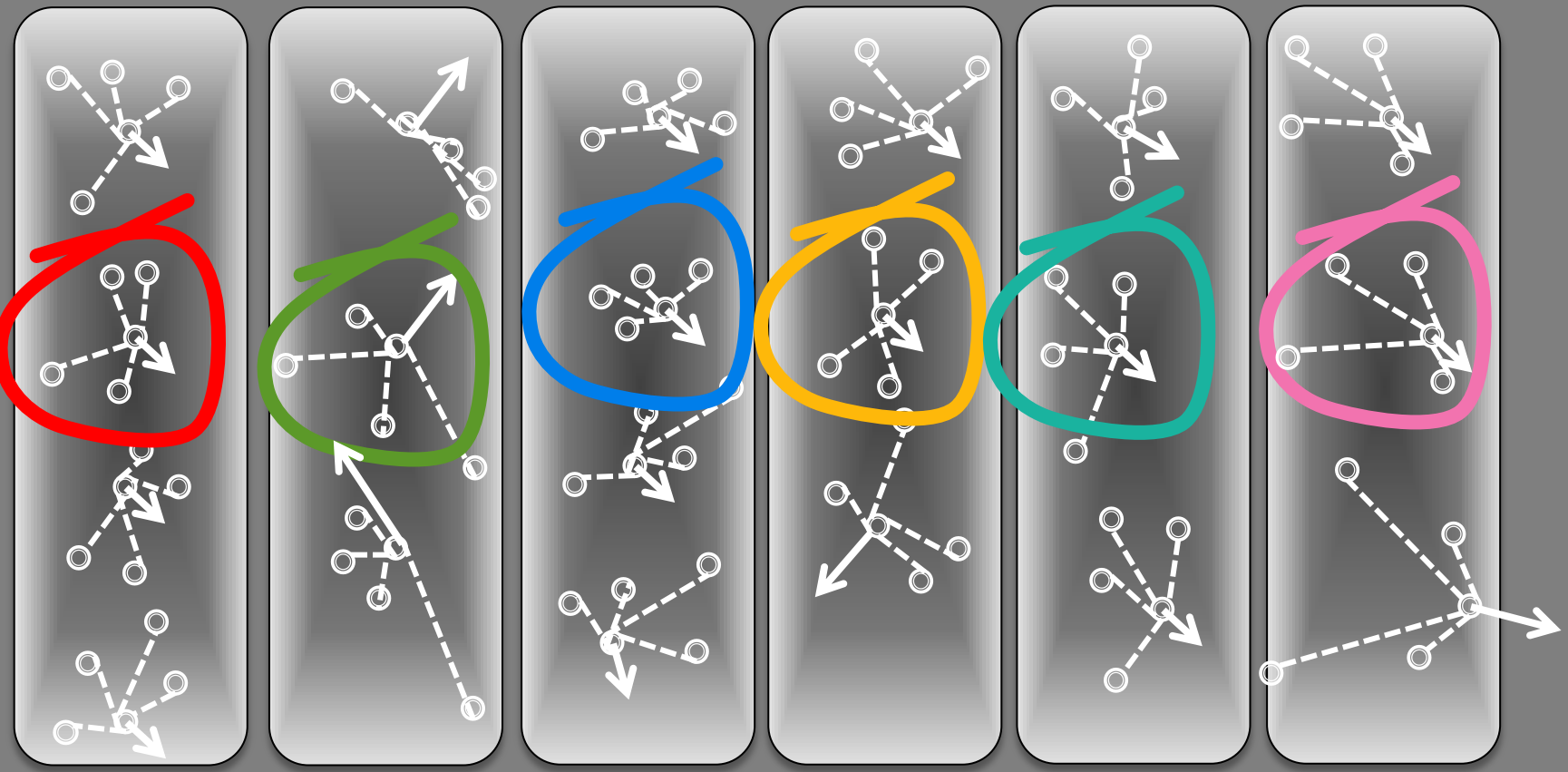

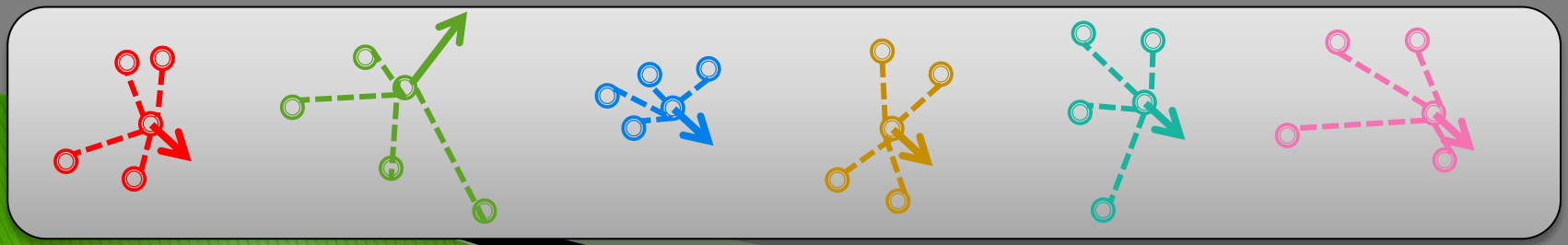

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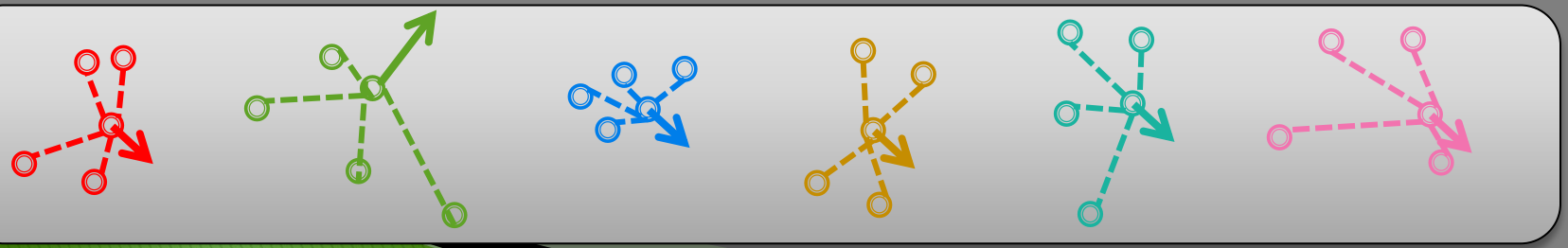
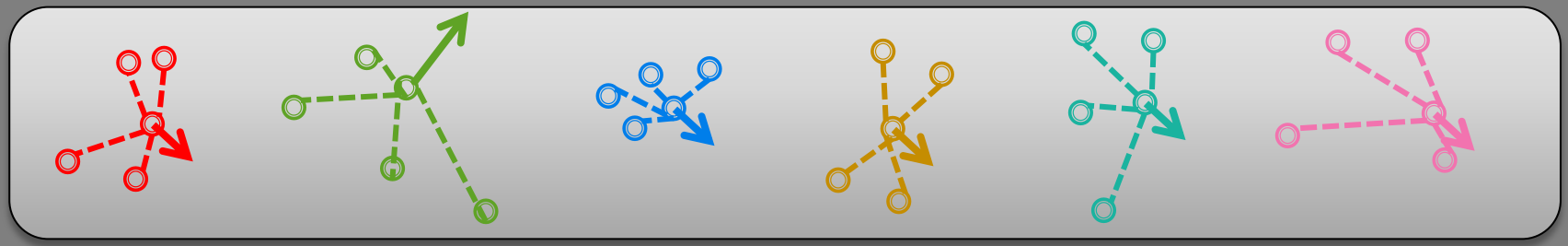
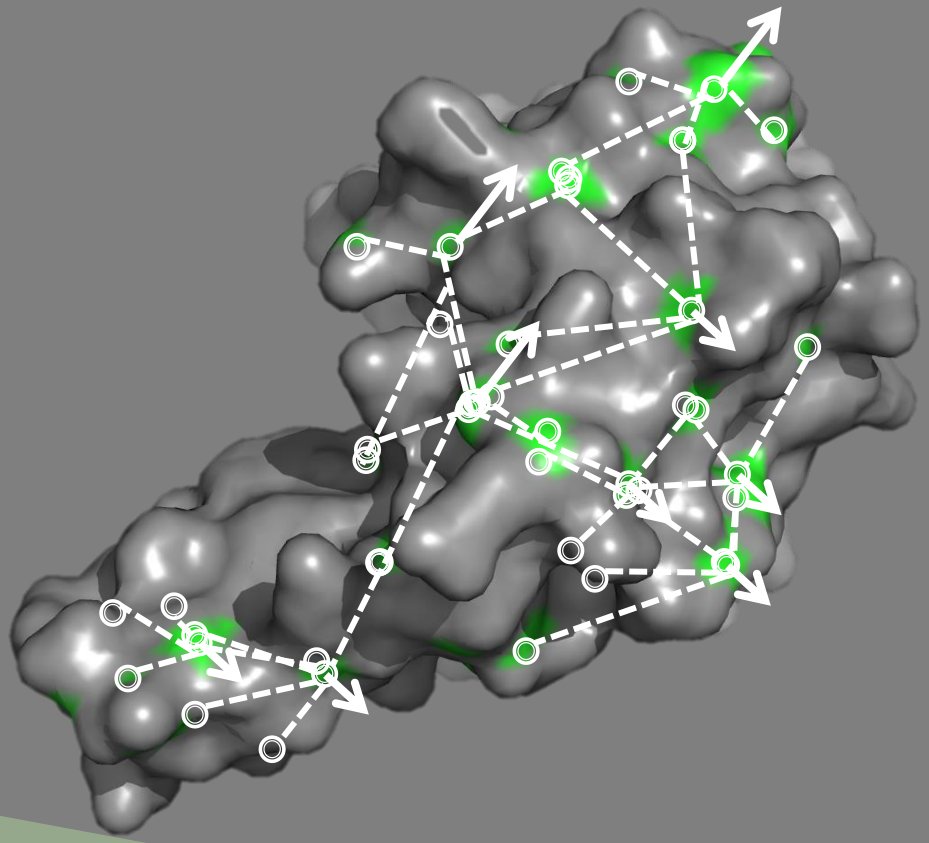
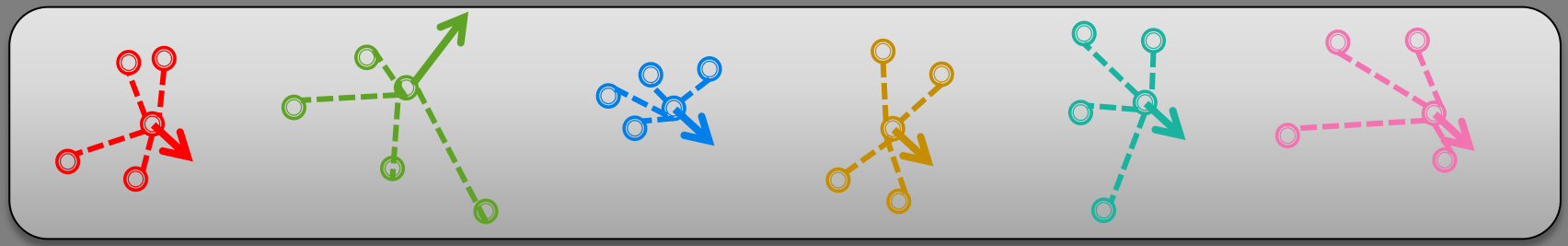


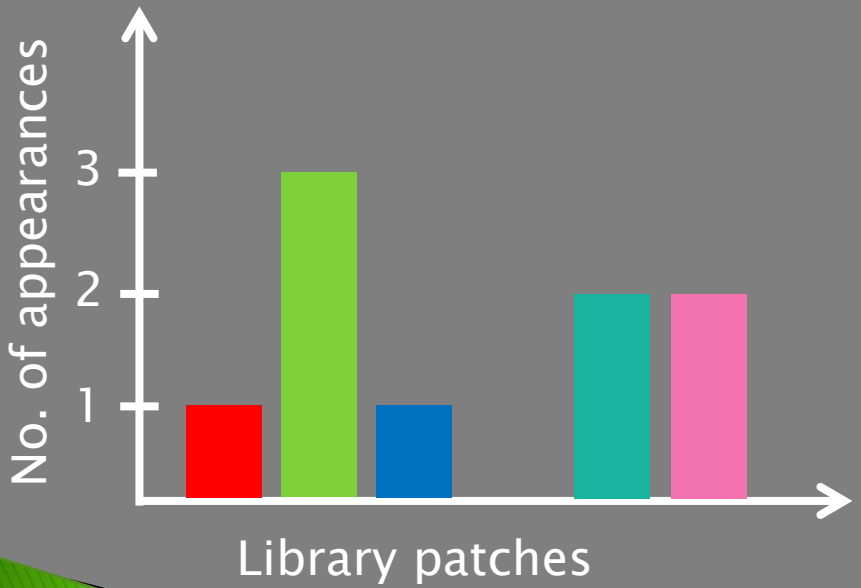
PatchBag

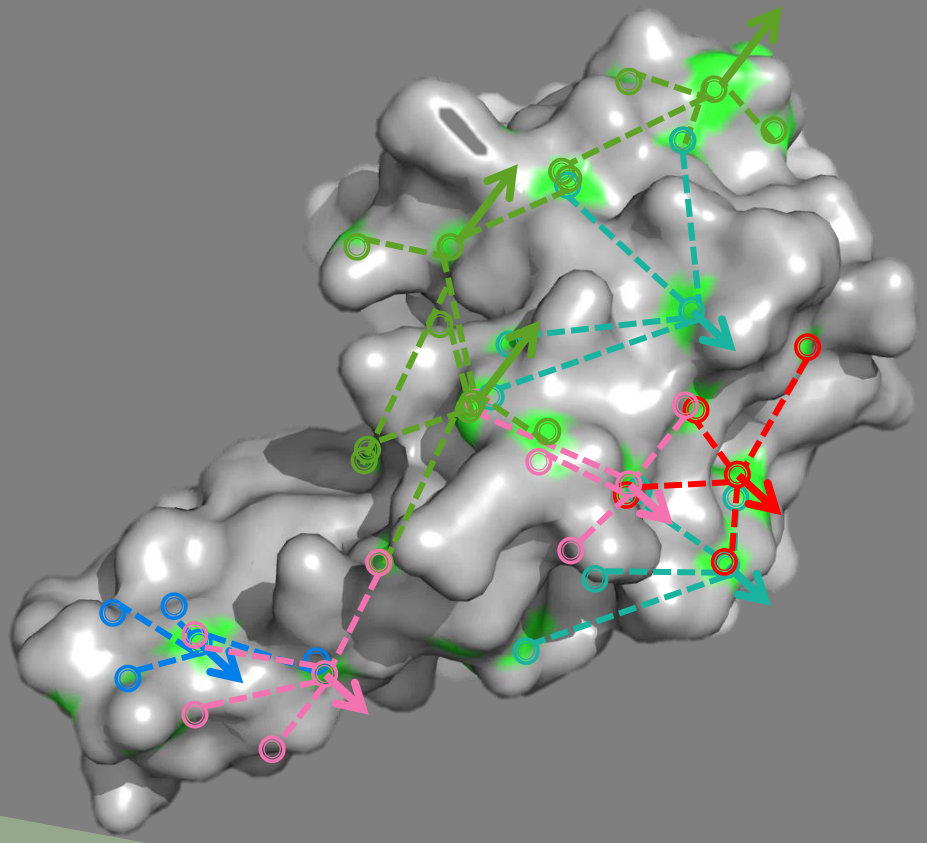




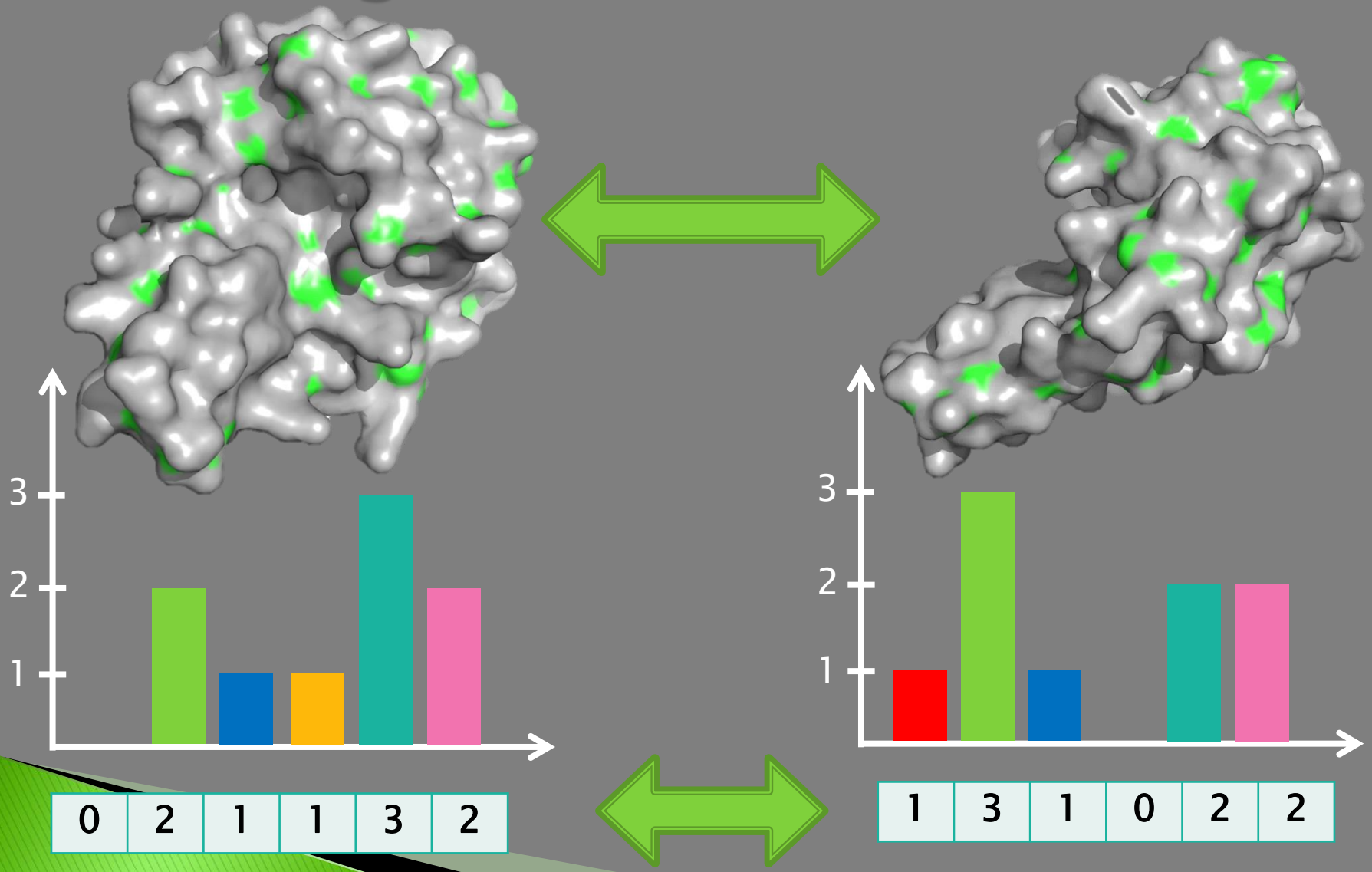
PatchBag



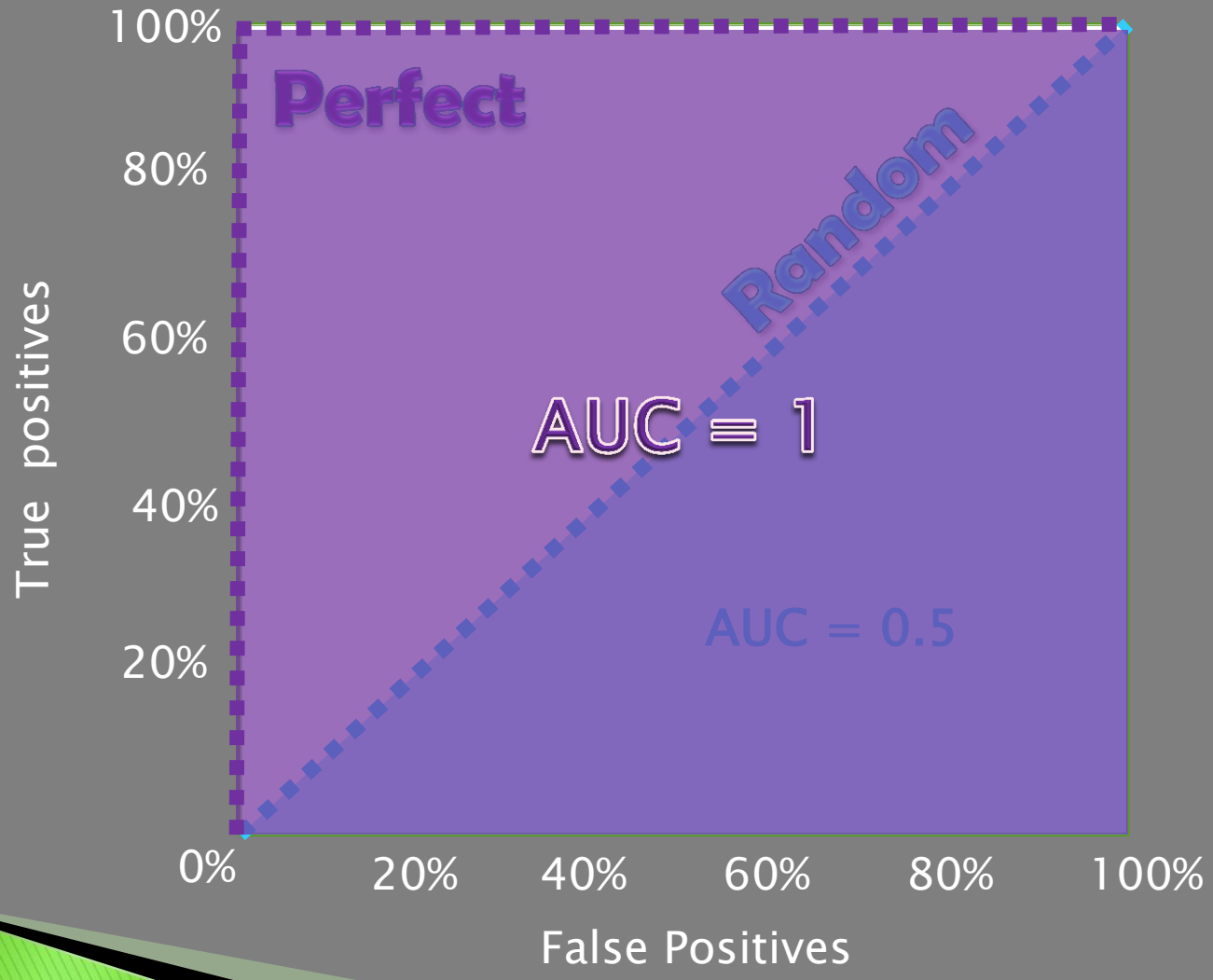




PatchBag



PatchBag detects structural similarities



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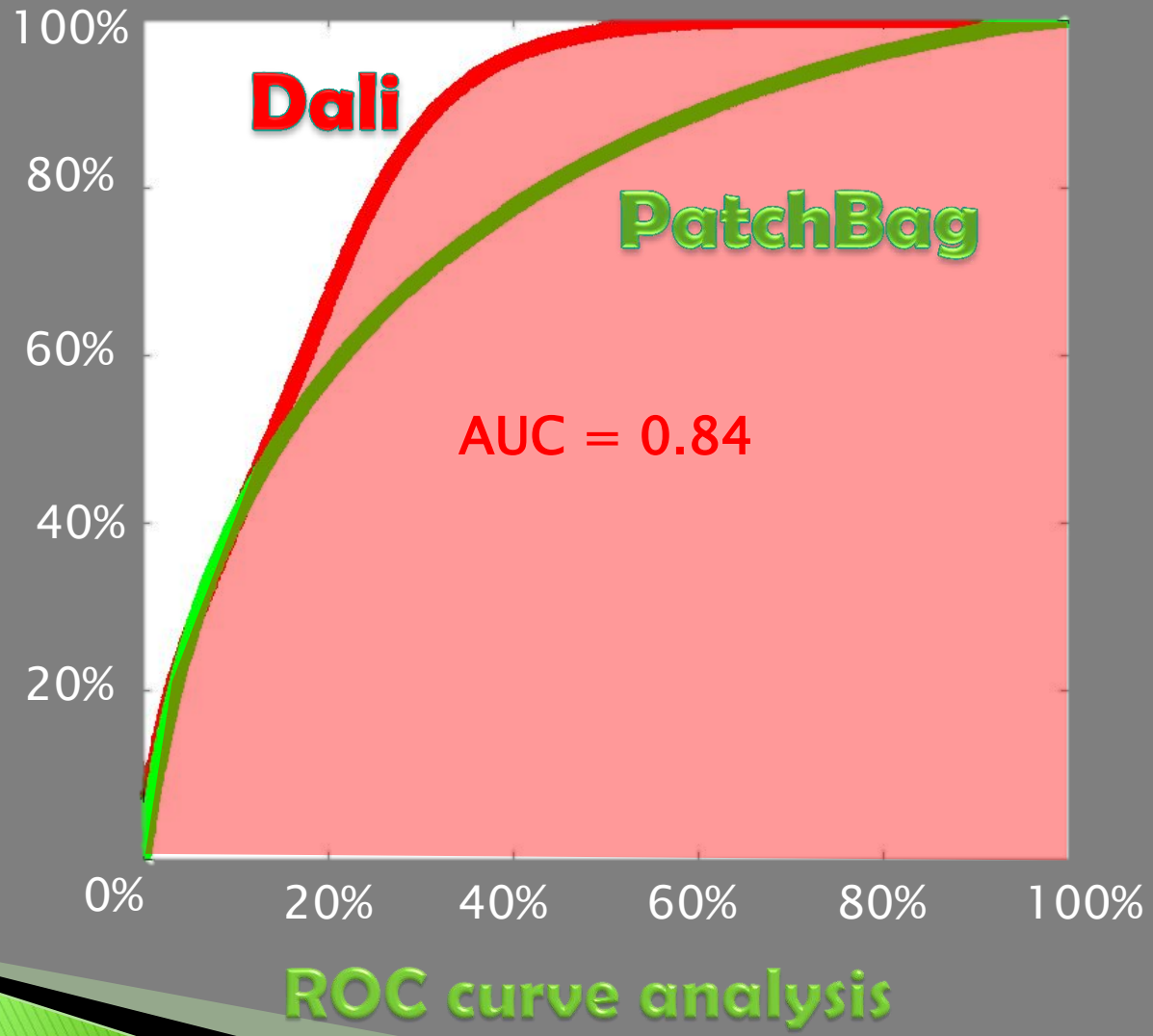
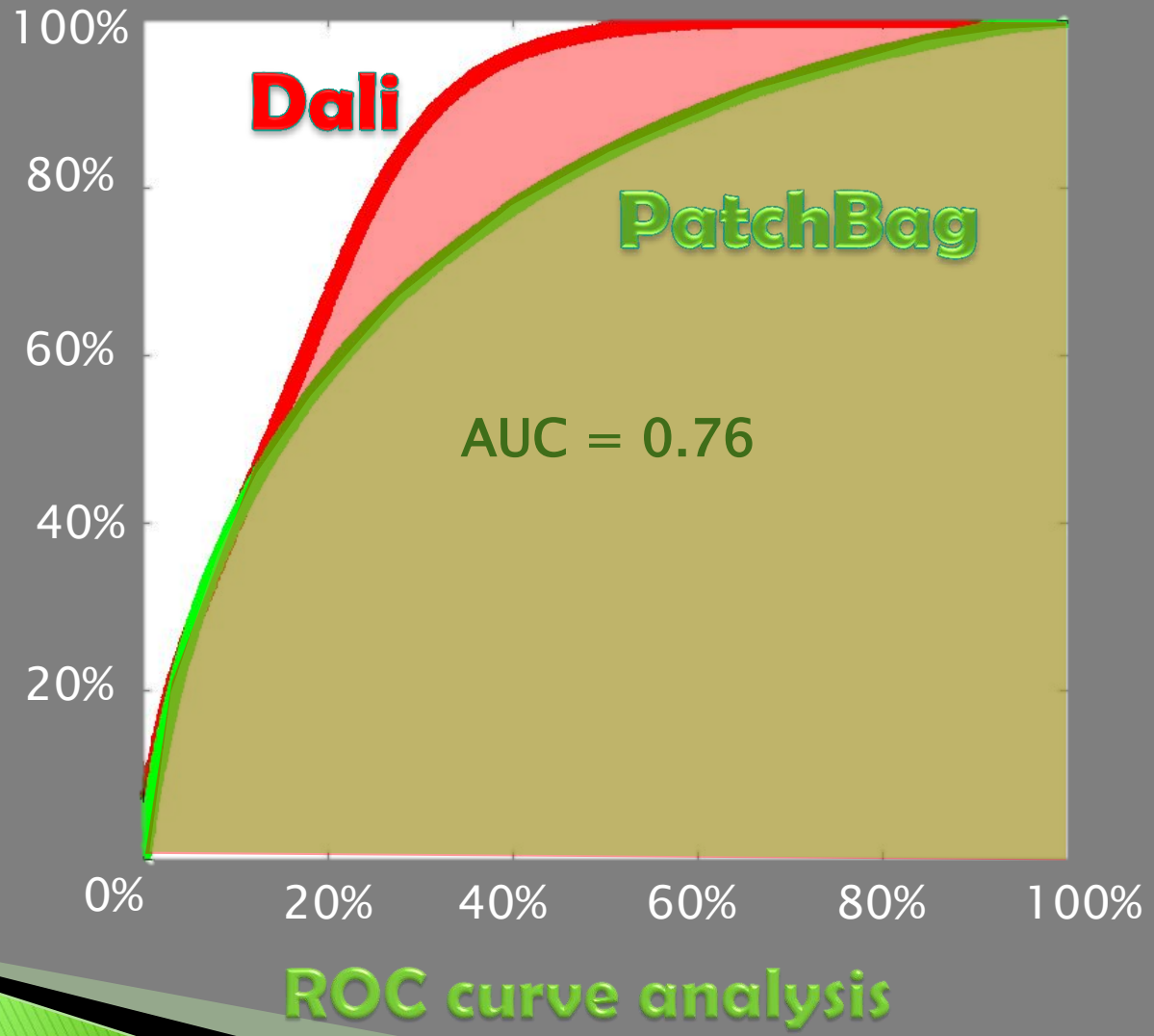
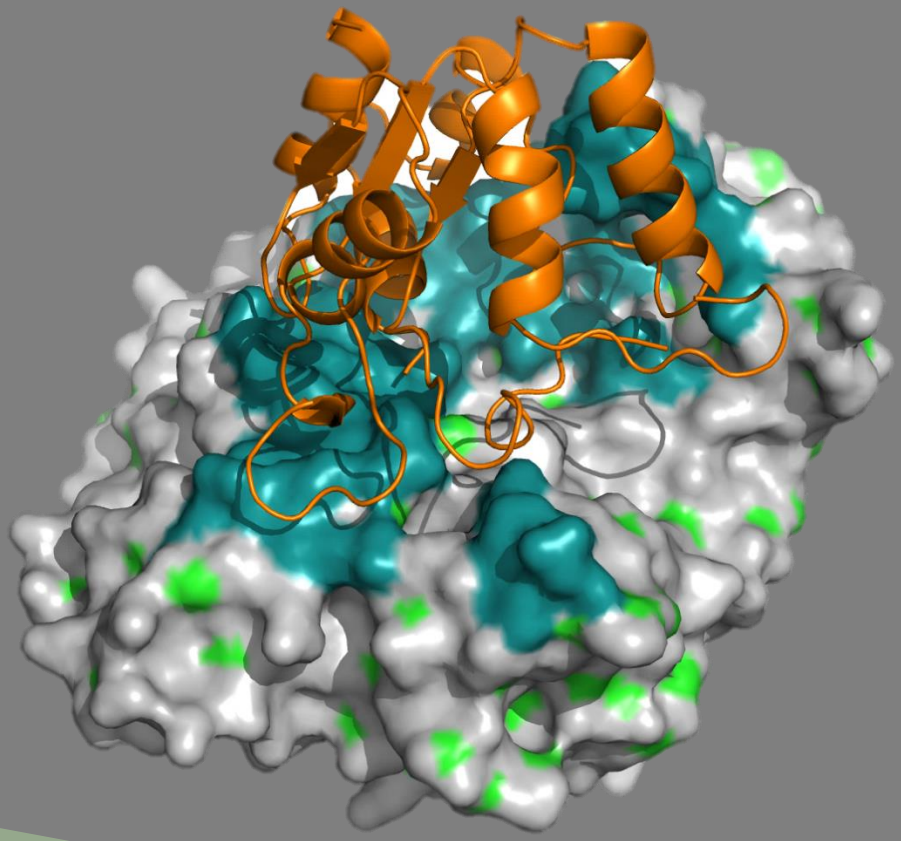


ROC curve analysis

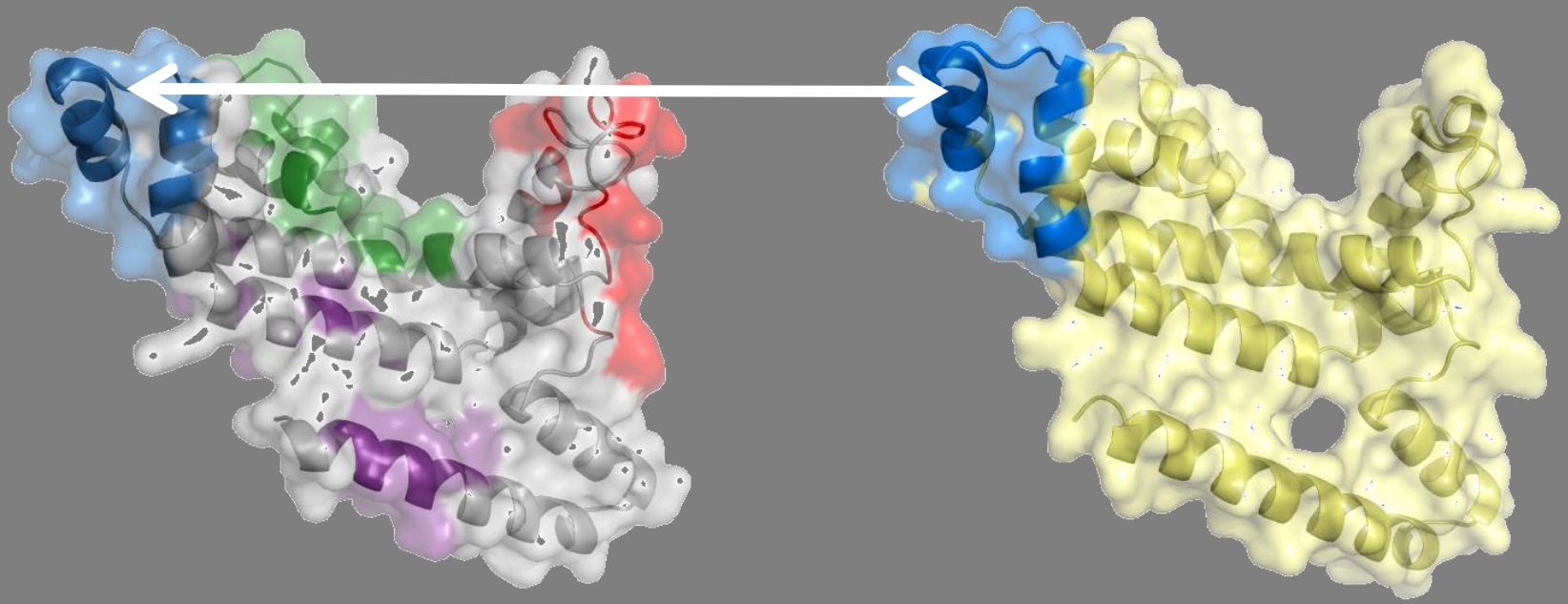
PatchBag detects structural similarities



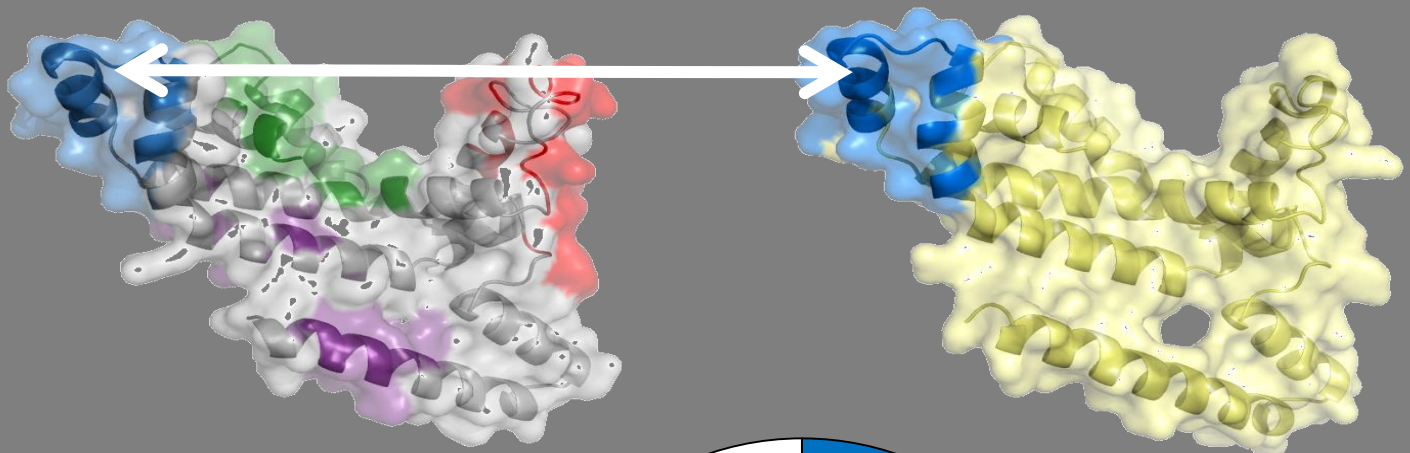
Predicting protein–protein interactions

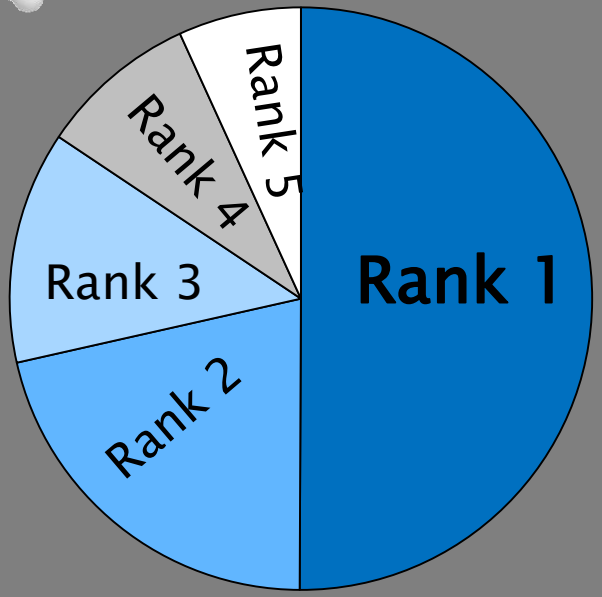


Can PatchBag be employed to detect similarities between sub-surfaces?



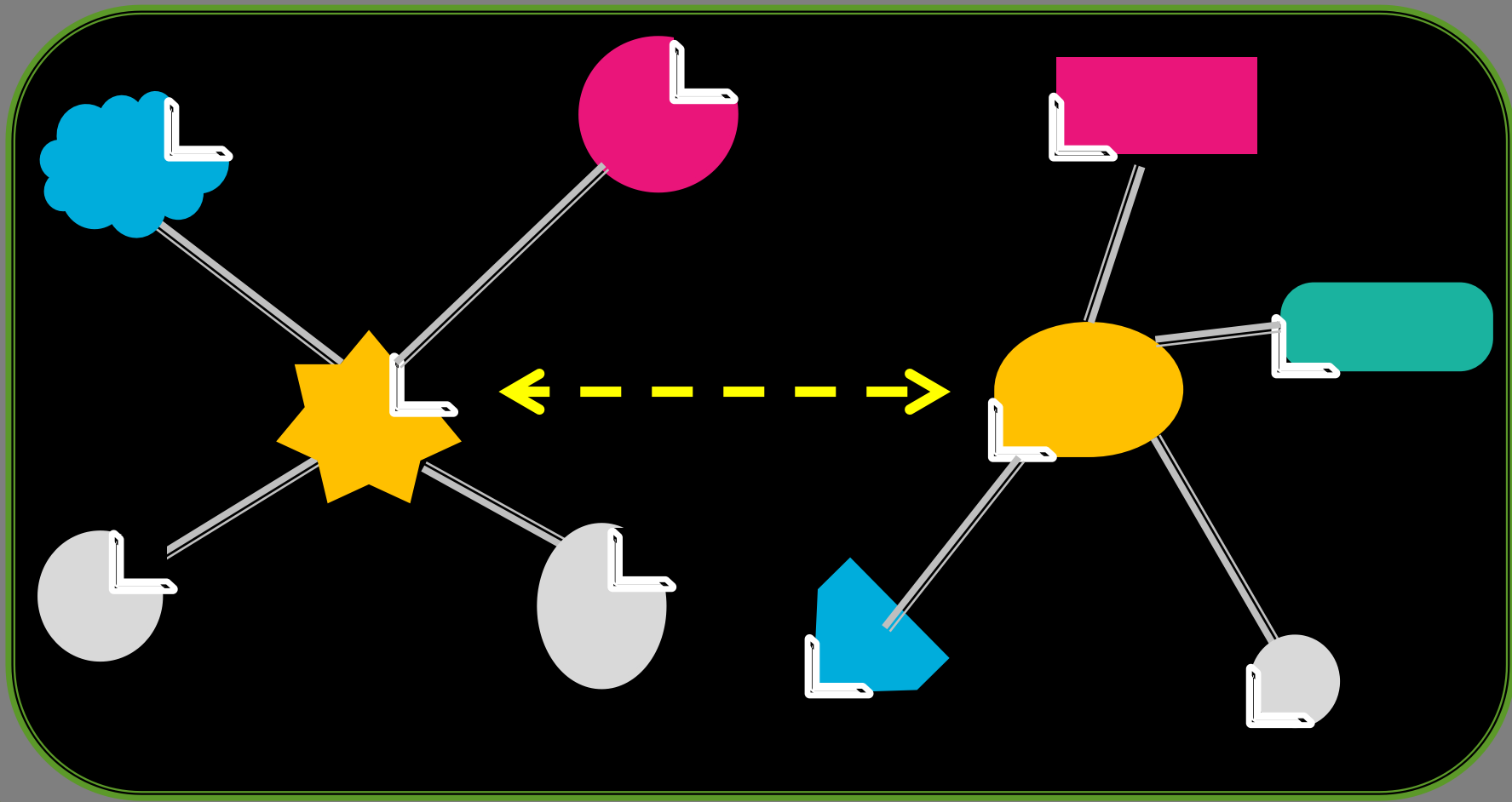
PatchBag can be employed to detect similarities between sub-surfaces





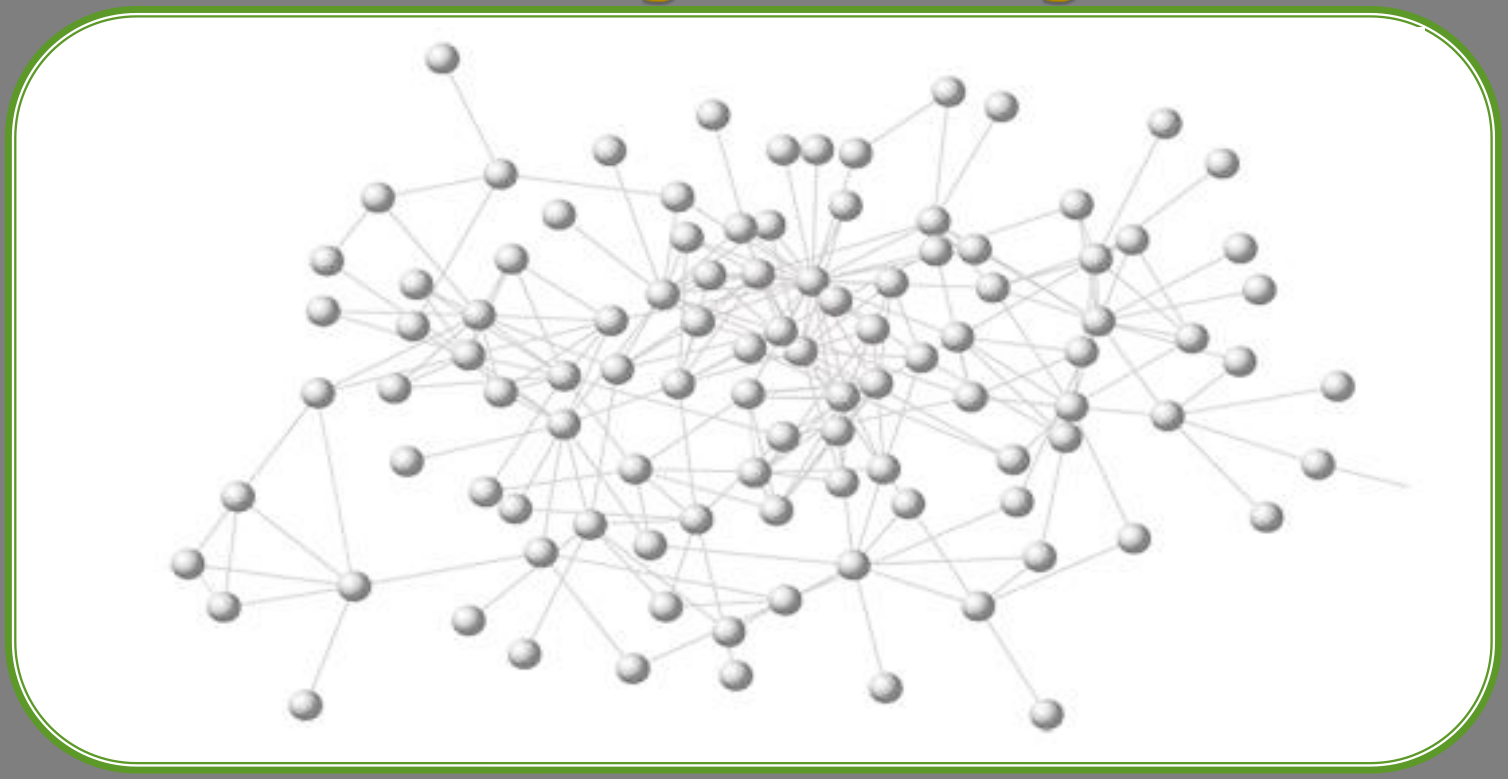
Predicting protein–protein interactions is not an easy task

Guilty by association



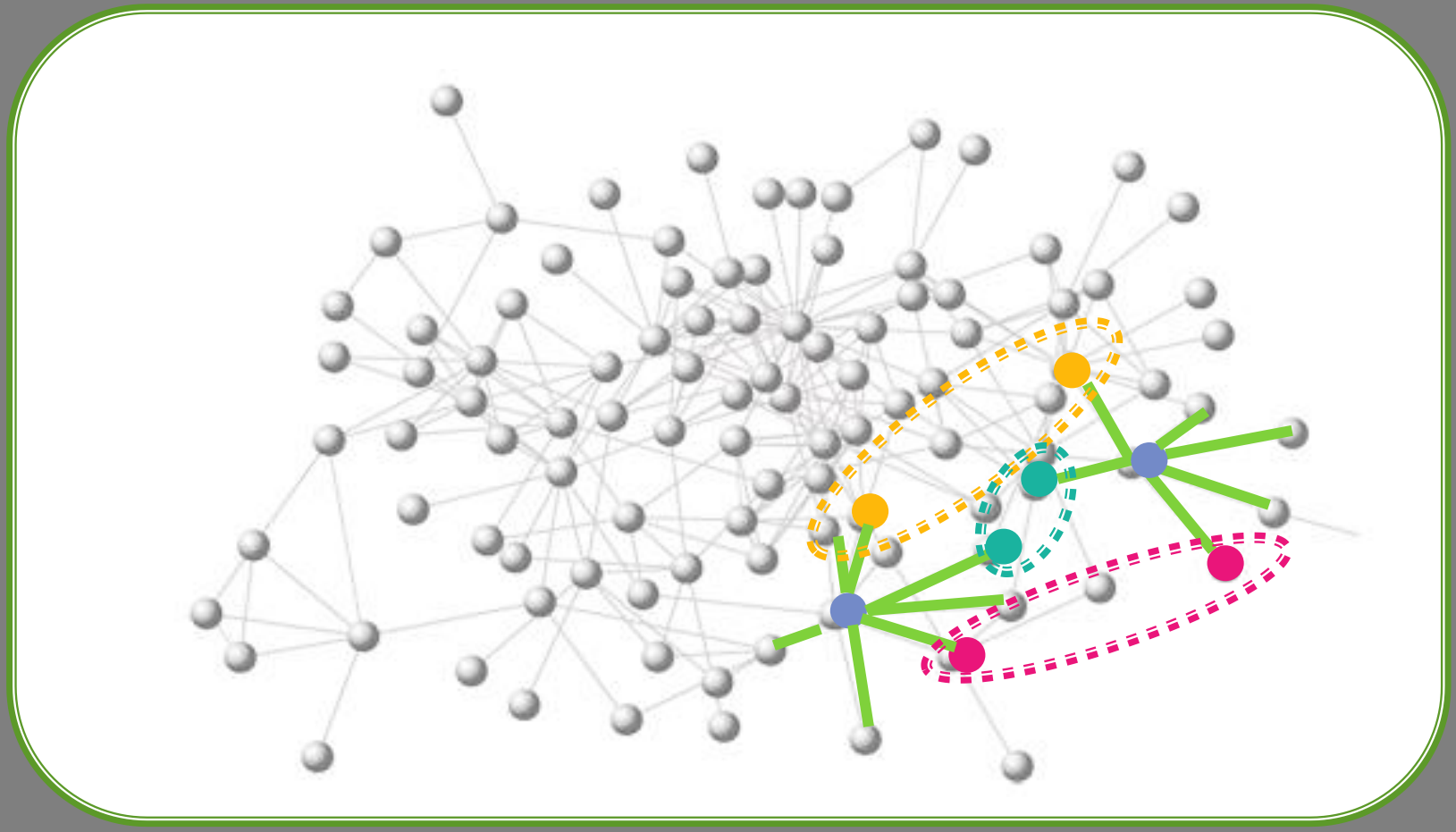
Step 1: Extract a database of known protein-protein interactions

Step 2: Construct a network connecting proteins based on their surface similarity using PatchBag



- Every node in the network is a protein in the 3did database
- An edge in the network represents a significant PatchBag score

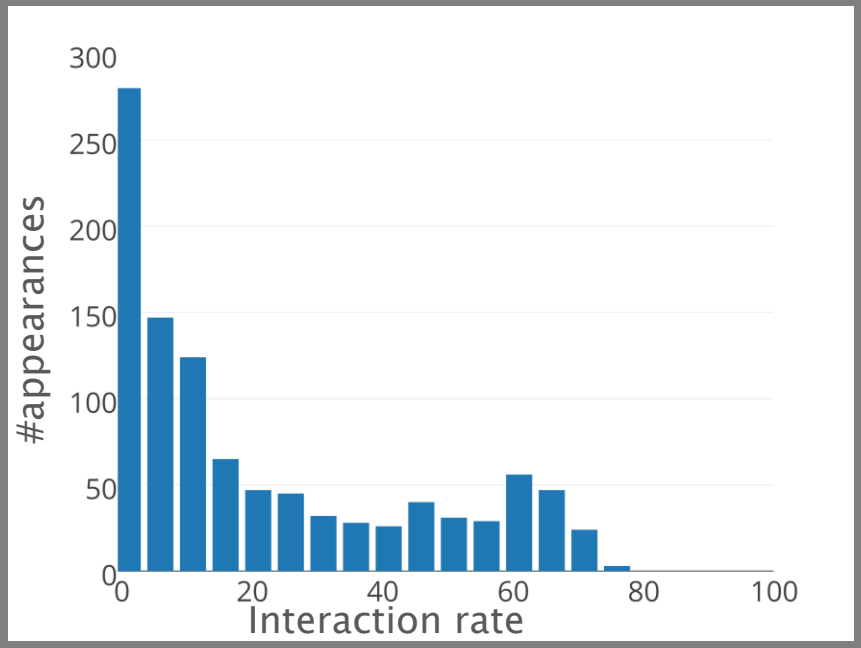
Step 3: Evaluate the percent of known protein pairs among highly connected sub networks



$$\text{Interaction rate} = \frac{\text{\# of known pairs}}{\text{Degree of the sub network}}$$

Interaction rate distribution

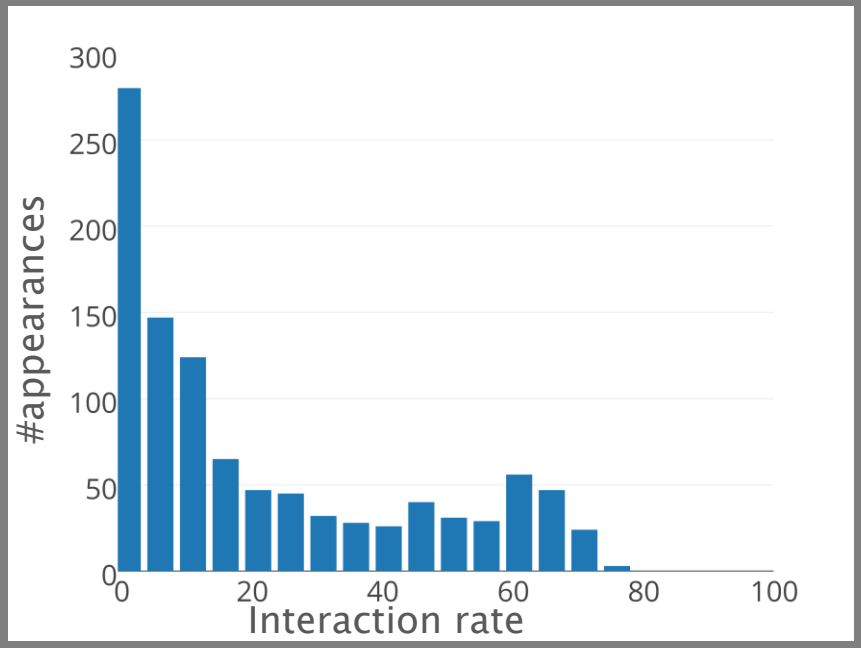
PatchBag on Interface Residues



Mean interaction rate: 35.7

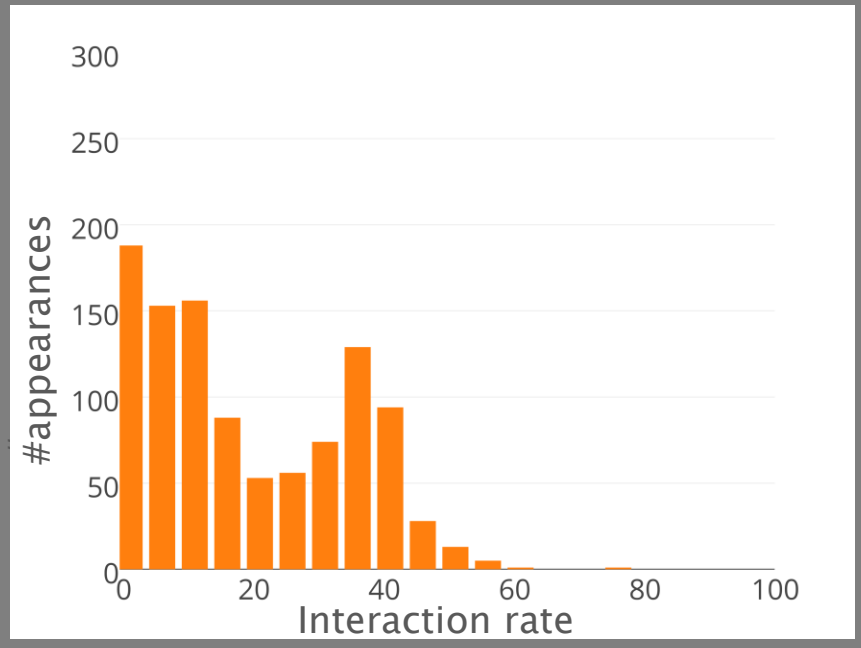
PatchBag network has significantly higher interaction rates relative to random network

PatchBag on Interface Residues



Mean interaction rate: 35.7

Random Network

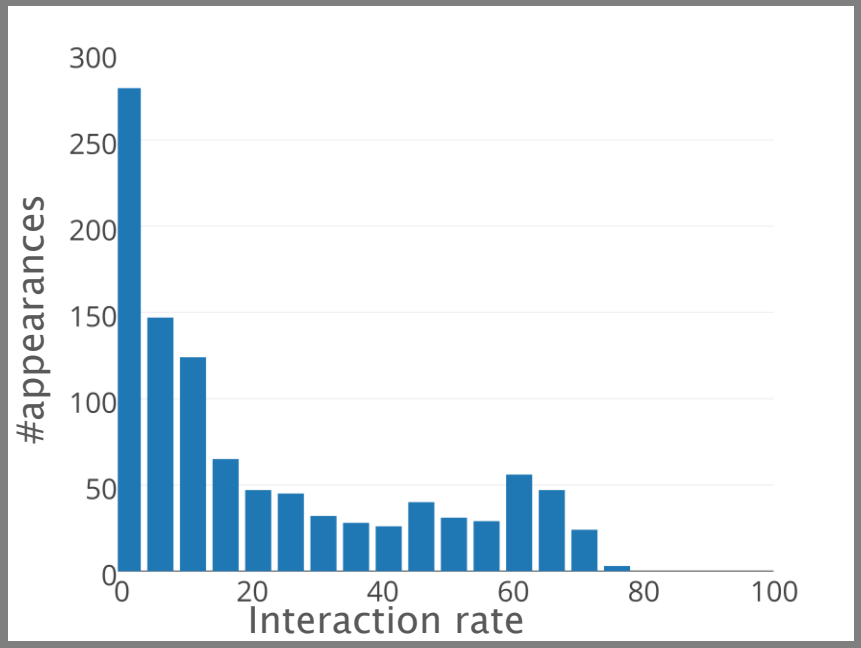


Mean interaction rate: 21.8

Mann-Whitney U test P-value: 2.52×10^{-37}

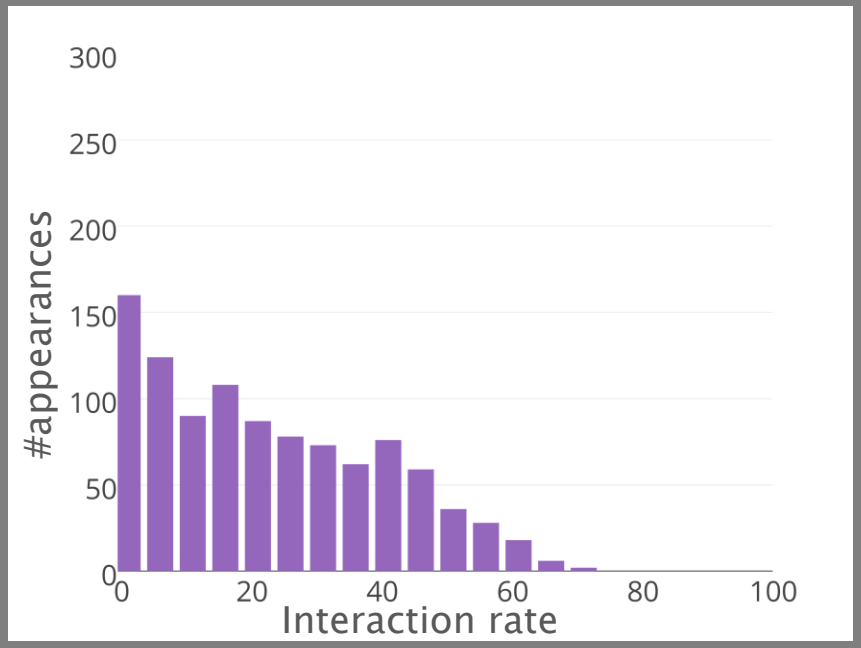
PatchBag network has significantly higher interaction rates relative to scattered network

PatchBag on Interface Residues



Mean interaction rate: 35.7

PatchBag on Scattered Surface Residues



Mean interaction rate: 26.8

Mann-Whitney U test P-value: 1.15×10^{-14}

Take home

- We introduce PatchBag, a fast and accurate method for identifying similar surfaces and interfaces on proteins
- PatchBag can be used for identifying novel molecular interacting surfaces
- PatchBag can be used to predict protein-protein interaction

Thanks to :

Inbal Budowski-Tal

Dr. Rachel Kolodny (Haifa University)

http://yaelab.technion.ac.il