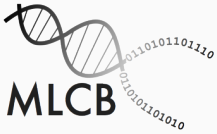
Building a library to evaluate protein generative models

Philip Hartout

May 4, 2022



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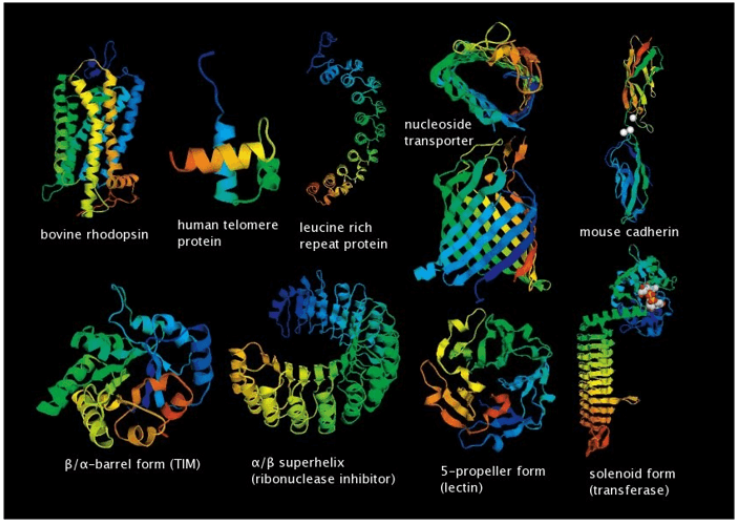
Introduction



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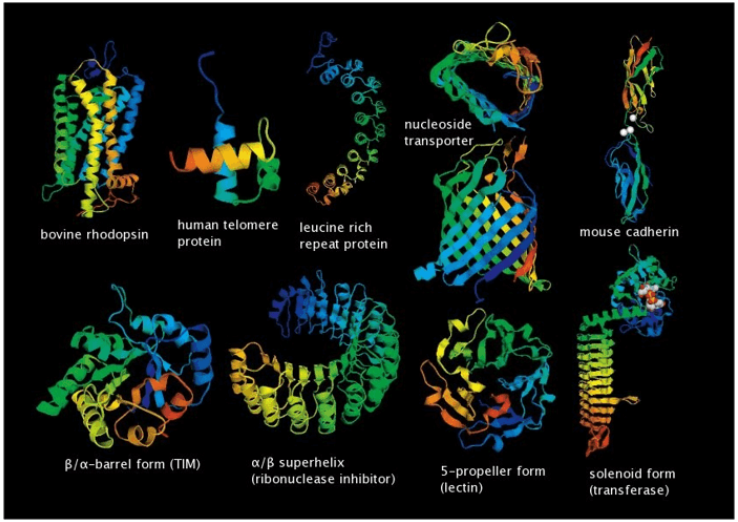

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They support all functions necessary for life.

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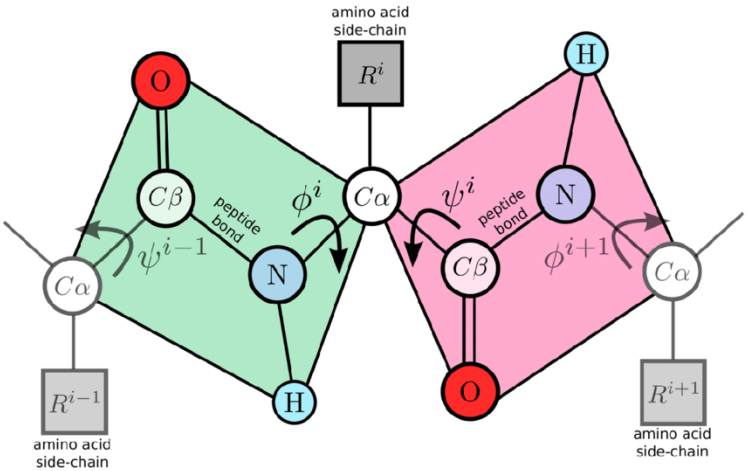

These angles *define* the shape of the protein

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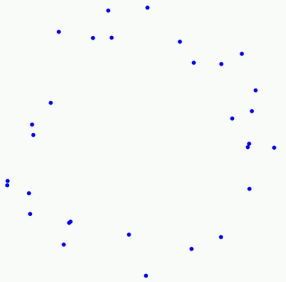

Čech filtrations allows the capture of holes and topological features of proteins

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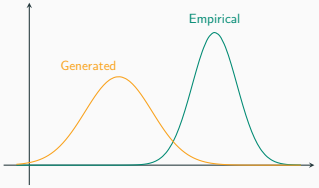
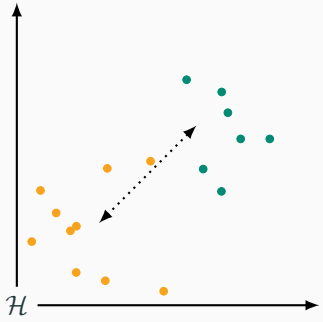
Given a set of proteins, how to we make sure that our model follows the same distribution?



What makes a good protein?

Maximum Mean Discrepancy (MMD)

$$\text{MMD}(X, Y) := \frac{1}{n^2} \sum_{i,j=1}^{n} k(x_i, x_j) + \frac{1}{m^2} \sum_{i,j=1}^{n} k(y_i, y_j) - \frac{2}{nm} \sum_{i=1}^{n} \sum_{j=1}^{m} k(x_i, y_j)$$



where:

- $\mathcal{X}$ is some non-empty set.
- $x_i, x_j \subseteq \mathcal{X}$, n is the number of samples in $\mathbf{x}$;
- $y_i, y_j \subseteq \mathcal{X}$, m is the number of samples in $\mathbf{y}$;
- $k : \mathcal{X} \times \mathcal{X} \to \mathbb{R}$ is a valid kernel.

MMD captures distances between 2 sets of structured data on *any* RKHS $\mathcal{H}$.

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Foreshadowing...

– Thesis Goal –

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Overview

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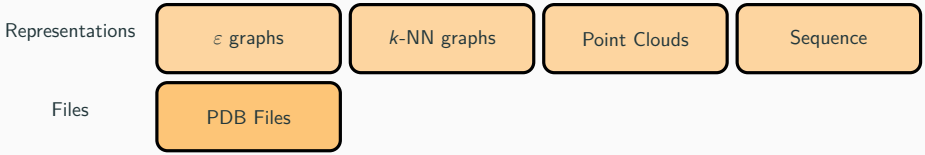
Representations
ε graphs
k-NN graphs
Point Clouds
Sequence
Files
PDB Files

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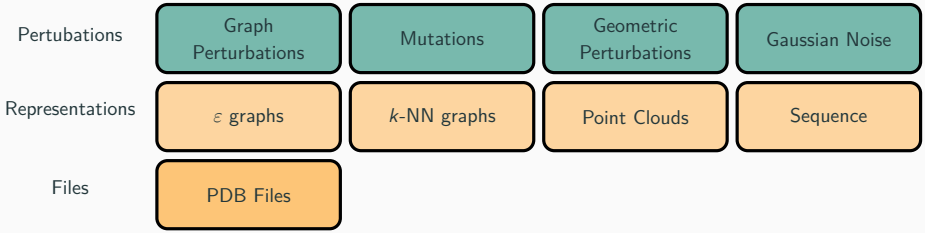
Pertubations
Graph Perturbations
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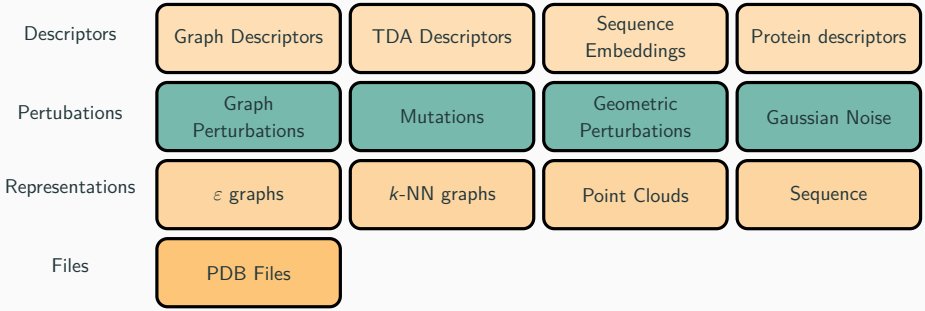
Descriptors
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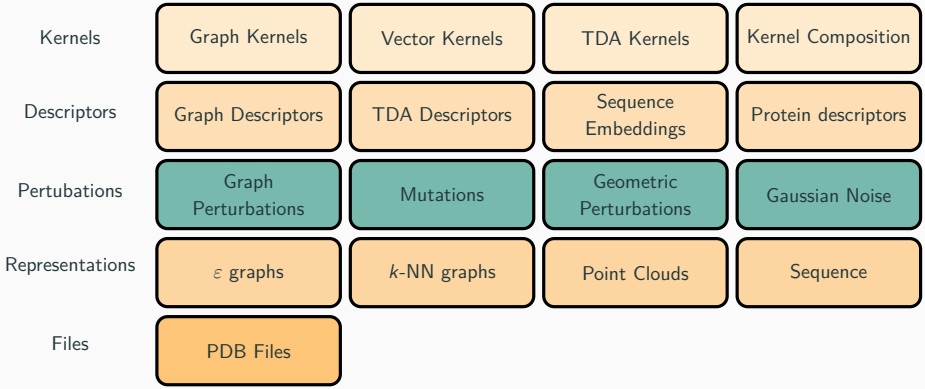
Kernels
Graph Kernels
Vector Kernels
TDA Kernels
Kernel Composition
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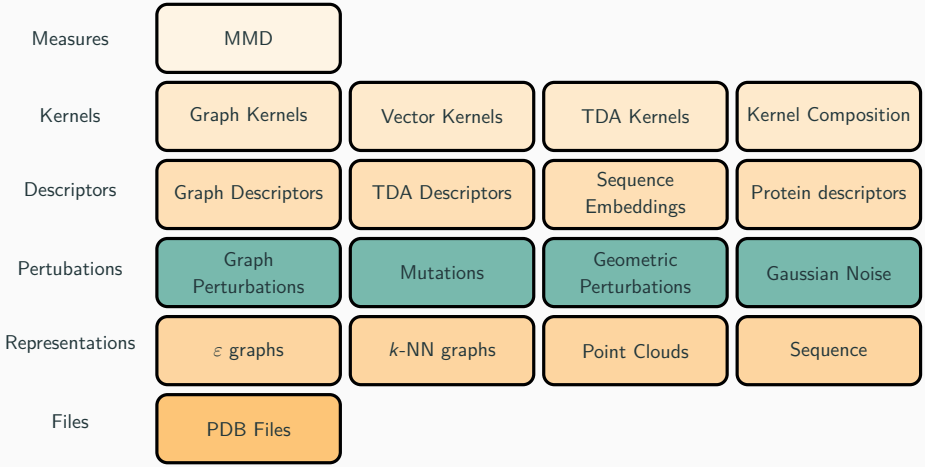
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2. Add twist to proteins to the point cloud and see the results on different kernels
3. Add mutations to proteins to the point cloud and see the results on different kernels

Experiment 1 – Gaussian Noise

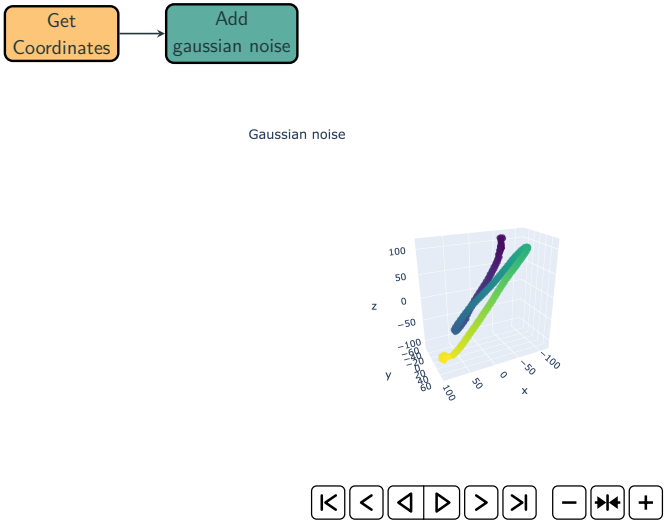

Figure 1: Adding Gaussian Noise. Protein is color-coded according to the index of each amino acid.

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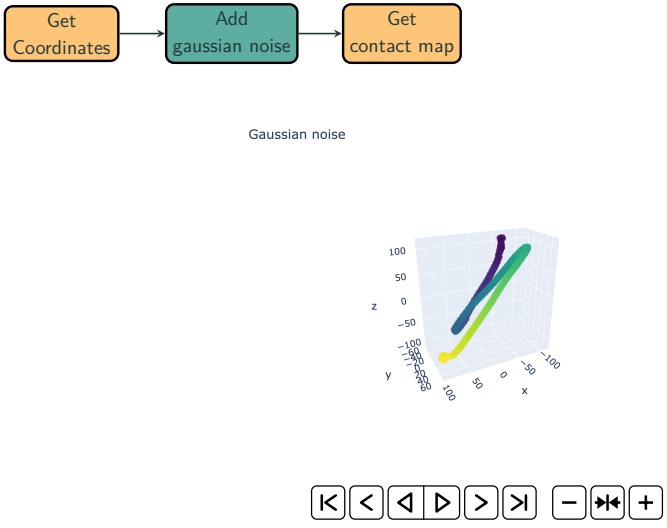

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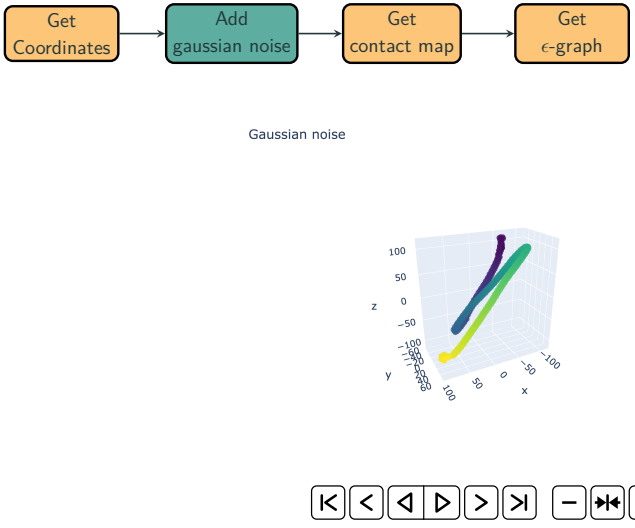

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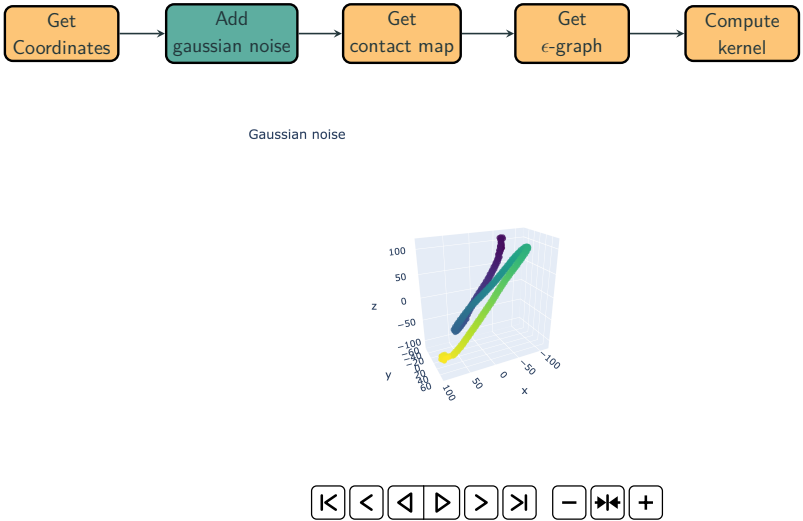

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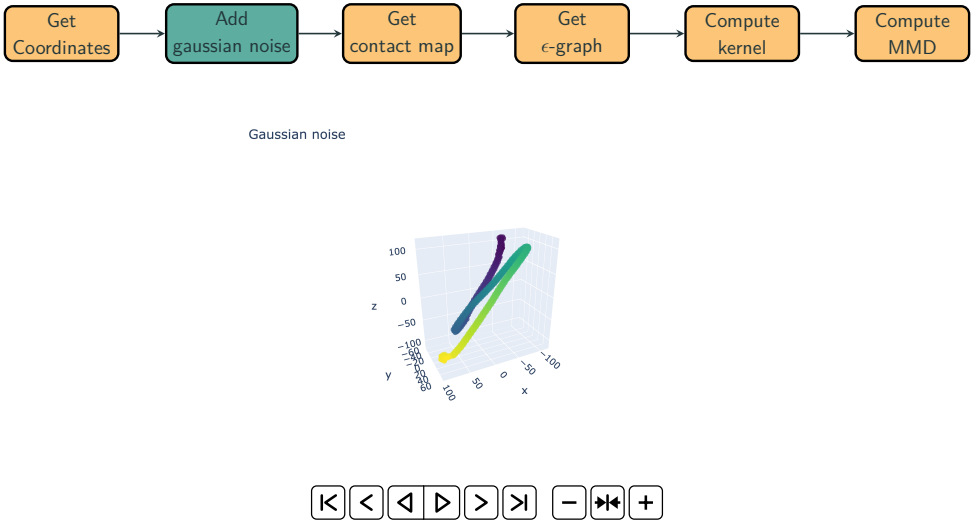

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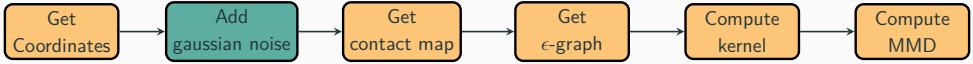

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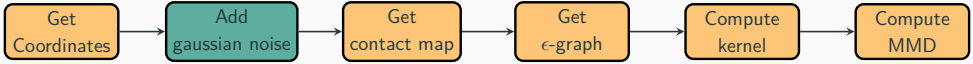

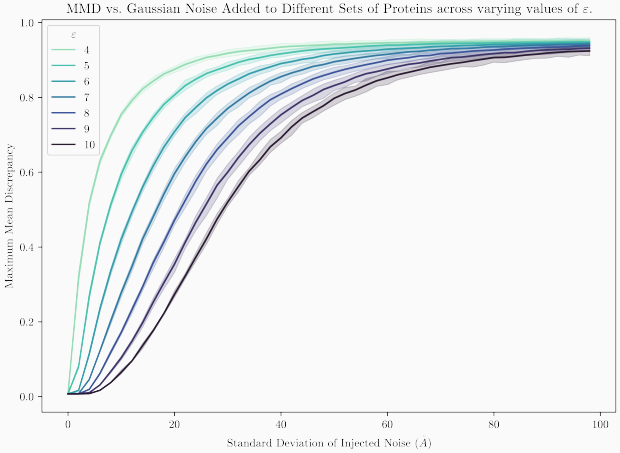

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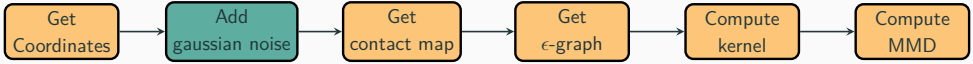

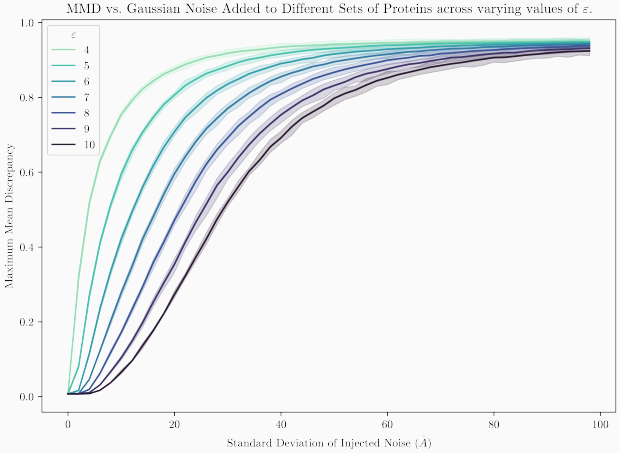

$n = 10$ runs

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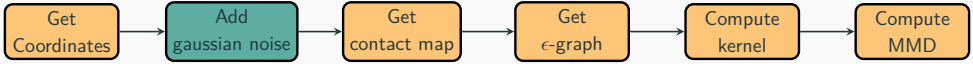

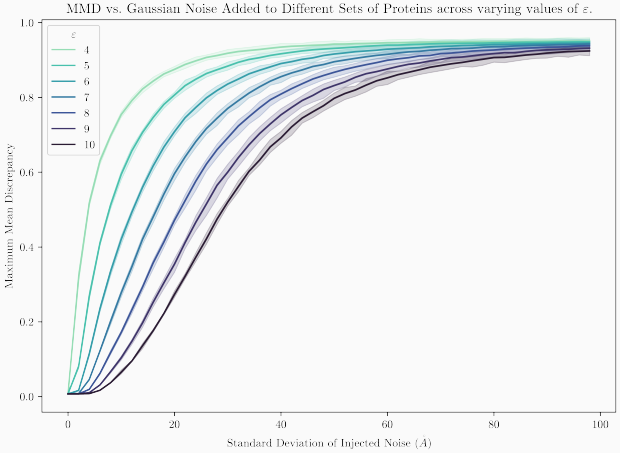

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2 sources of variance:

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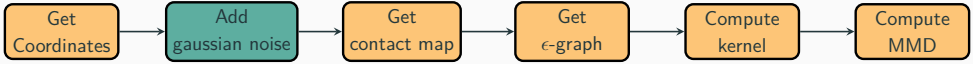

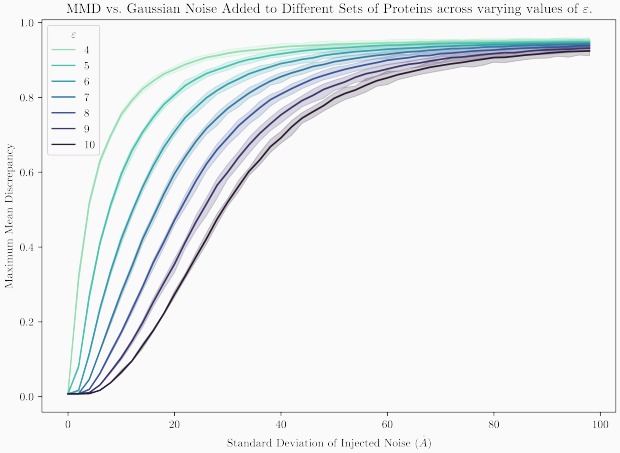

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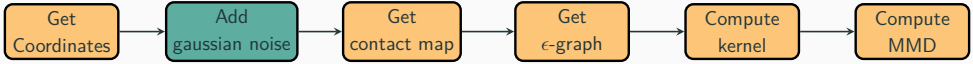

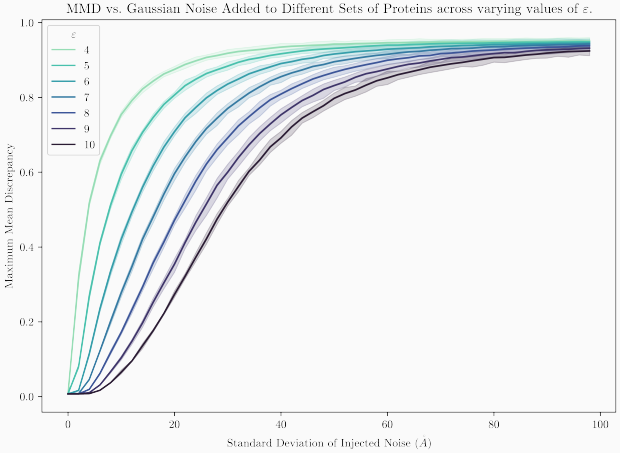

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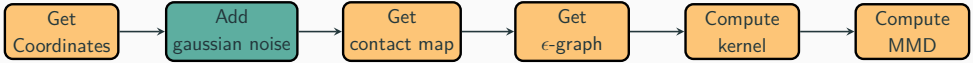

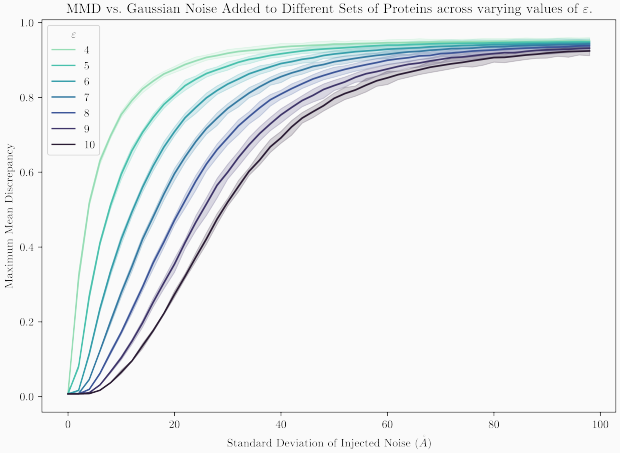

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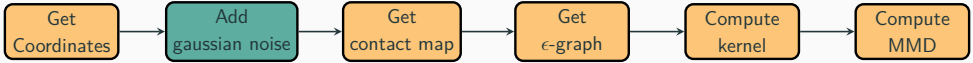

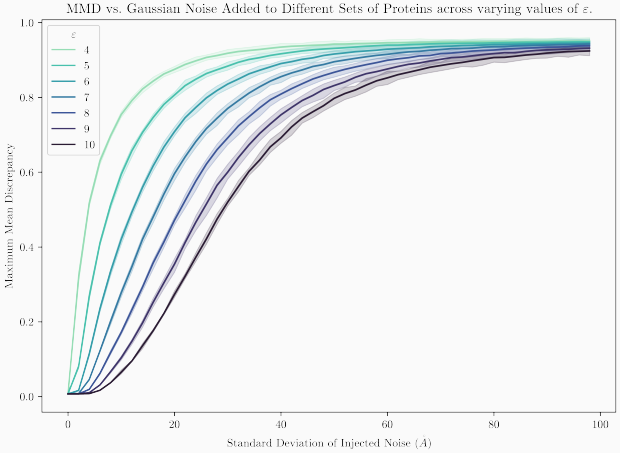

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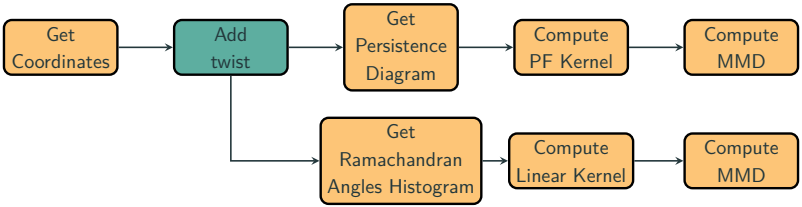
2. Choice of representation influences MMD

Experiment 2 – Twist



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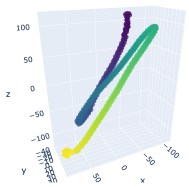

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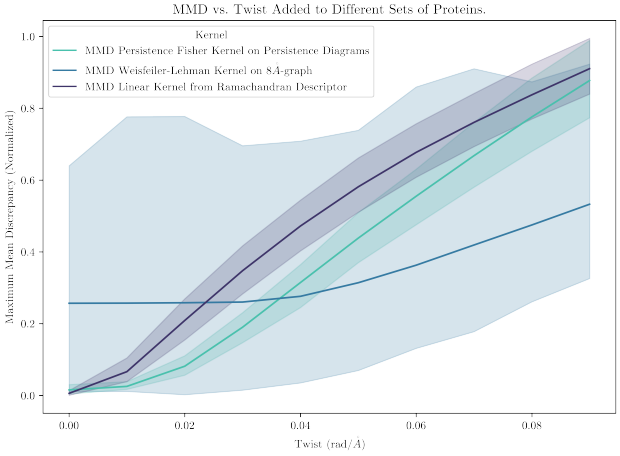

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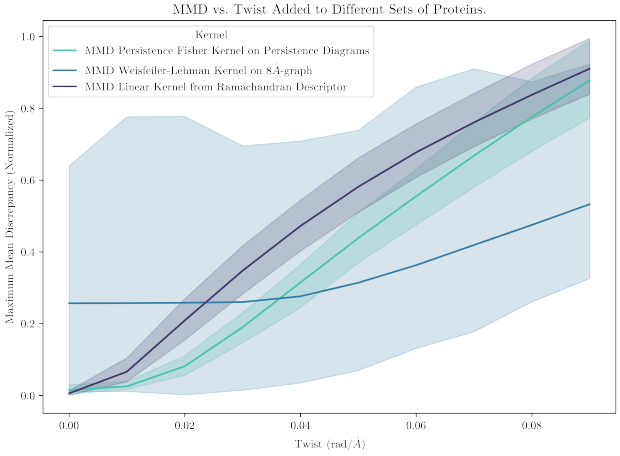

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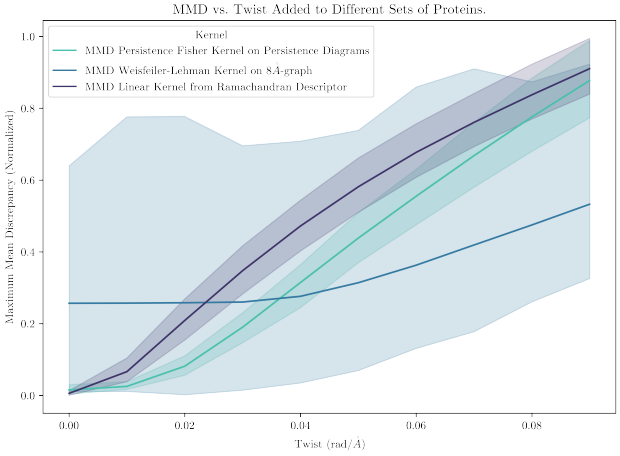

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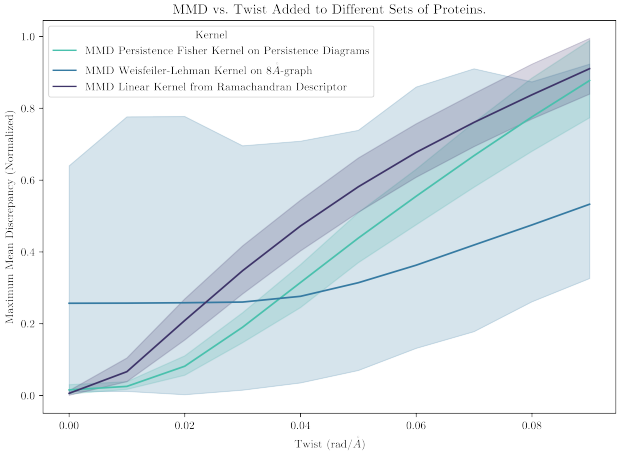

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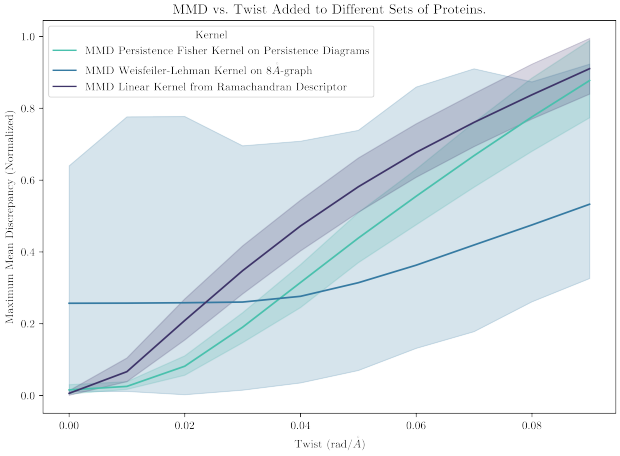
Conclusions

Experiment 2 – Twist



$n = 10$ runs

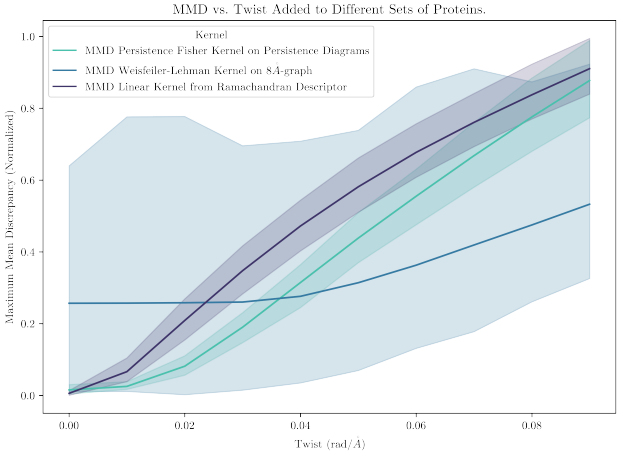
1 source of variance:

- Data

Conclusions

1. Weisfeiler-Lehman kernel is not best to capture geometrical perturbations

Experiment 2 – Twist



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Conclusions

1. Weisfeiler-Lehman kernel is not best to capture geometrical perturbations
2. TDA was difficult to compute but behaves very well

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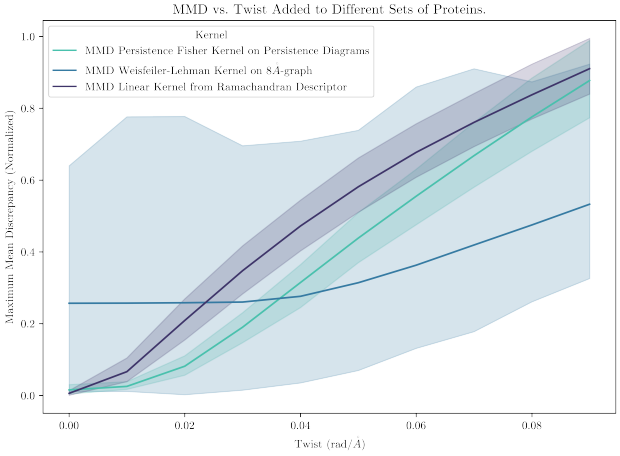

$n = 10$ runs

1 source of variance:

- Data

Conclusions

1. Weisfeiler-Lehman kernel is not best to capture geometrical perturbations
2. TDA was difficult to compute but behaves very well
3. Ramachrandran descriptors capture geometric perturbations very well

Experiment 3 – Mutate

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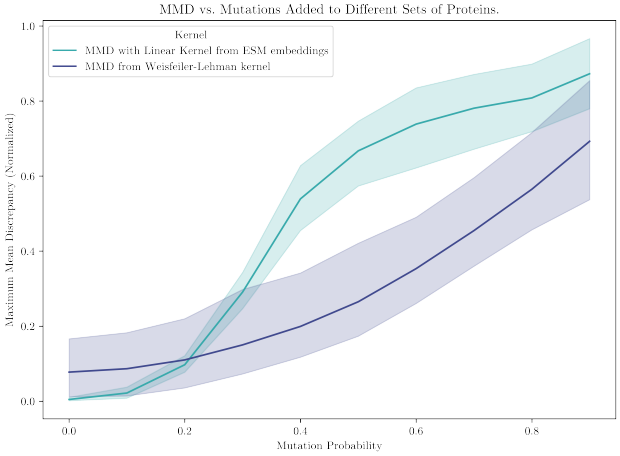
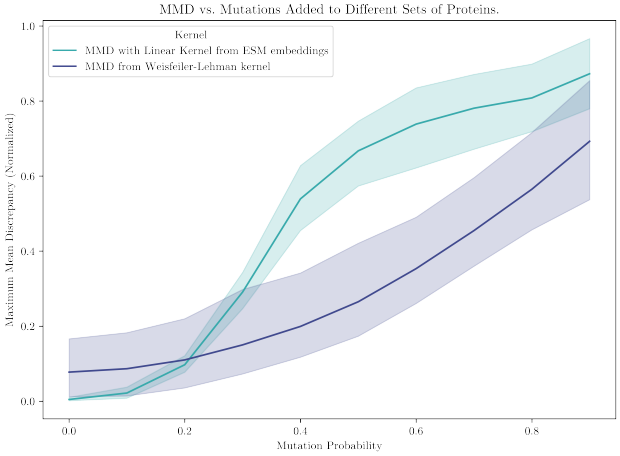


Experiment 3 – Mutate



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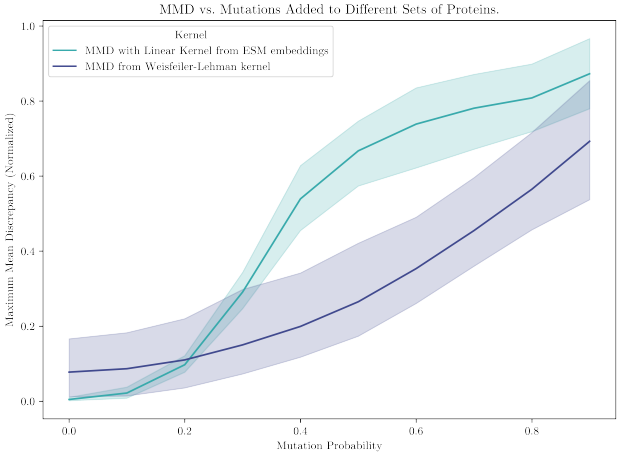
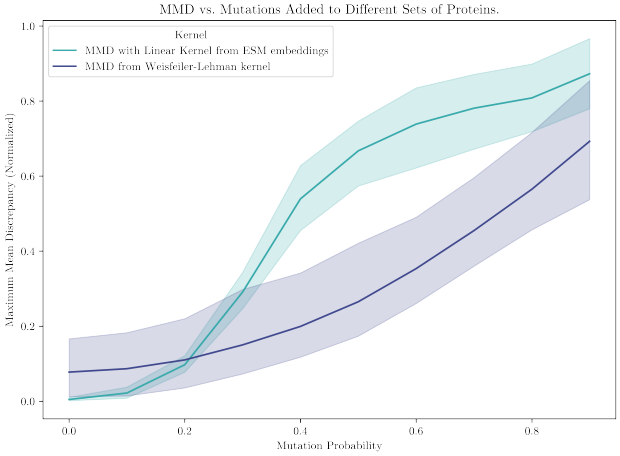
Experiment 3 – Mutate



$n = 10$ runs

2 sources of variance:

Experiment 3 – Mutate



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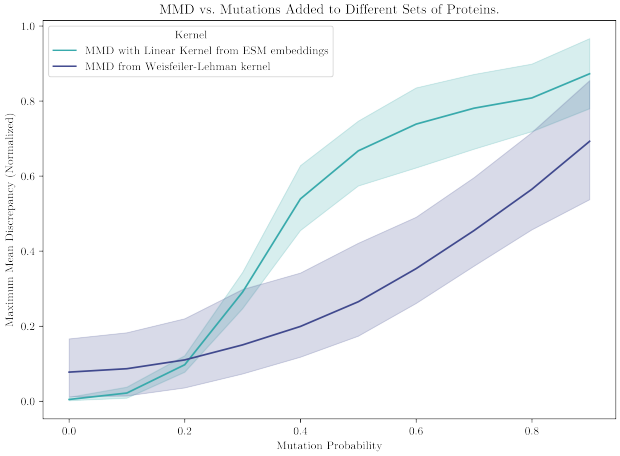
2 sources of variance:

- Data

Experiment 3 – Mutate



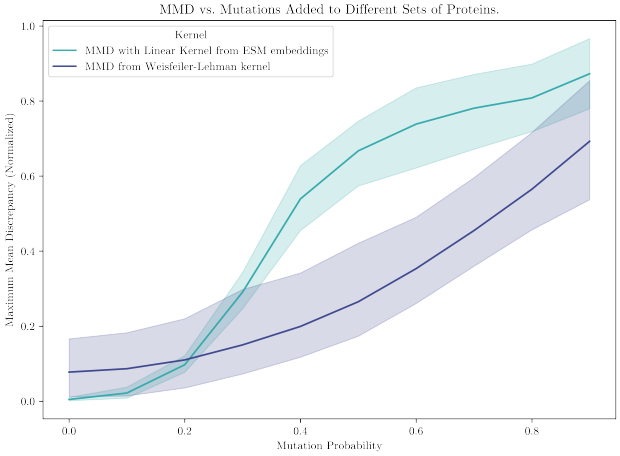
$n = 10$ runs

2 sources of variance:

- Data
- Mutation seed

Conclusions

Experiment 3 – Mutate



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2 sources of variance:

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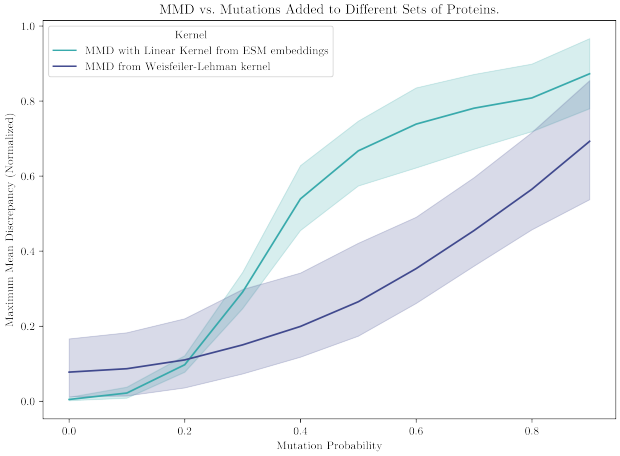
Conclusions

1. Weisfeiler-Lehman kernel does capture node label changes well

Experiment 3 – Mutate



$n = 10$ runs

2 sources of variance:

- Data
- Mutation seed

Conclusions

1. Weisfeiler-Lehman kernel does capture node label changes well
2. ESM also looks ok, but might carry bias from the data.