`GGNNMetrics`, a package for optimizing and understanding MMD parametrization for evaluating generative GNNs on protein datasets.

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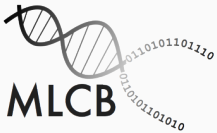

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Introduction

- The following provides an overview of the plan for the thesis
- Aspirational/low priority items are in blue.

General workflow

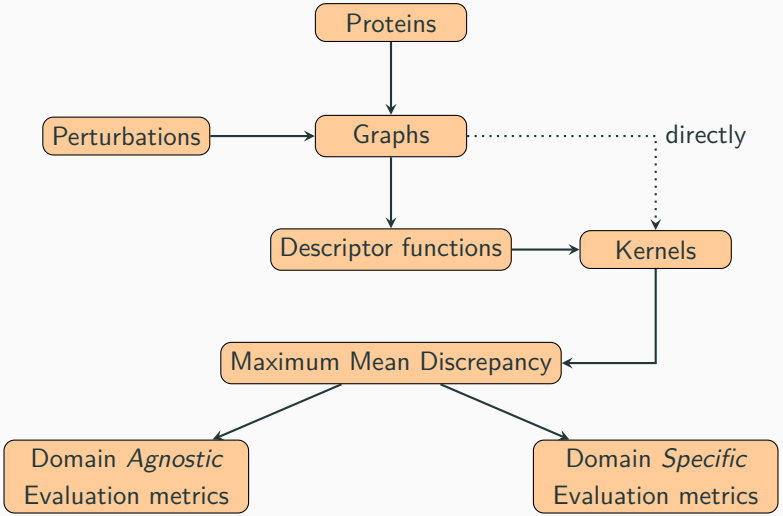

Figure 1: Overview of the library

Protein source datasets

- Start with human proteome from AlphaFold (23390 samples, source)
- Expand to other experimentally datasets & add cleaning handlers

Graph extraction from pdb file

Granularity:

- CA-atom (1 point per amino acid)
- all atoms (loop through each residue to get atom coordinates)
- CB, C, O, ... see `Bio.PDB.Residue`

Graph extraction:

- Contact map (fully connected weighted graph).
- ε-neighborhood graph. [1]
- k-nearest neighbor graph. [10]
- Intramolecular graphs (hydrogen bonds, salt bridges, pi-cation bonds)
- Delaunay graph (through Delaunay triangulation, results in denser graph) [8].

Dependenies: only depend on `Biopython`.

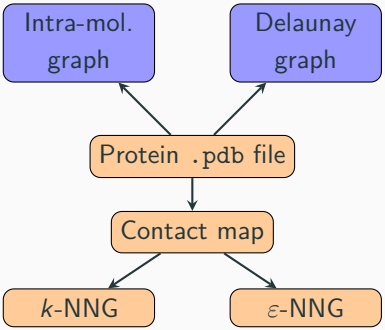

Figure 2: Order of extraction of graphs from `.pdb` files.

Descriptor functions & Kernels

Descriptor functions

Domain agnostic graph descriptors [5]:

- Degree distribution histogram
- Clustering coefficient histogram
- Laplacian spectrum histogram

Topological descriptors (using the weighted, fully connected contact map):

- Persistence diagram, converted to Betti curves, persistence image, persistence landscapes. [7]
- Also possible to obtain vector representation from persistence diagram by applying a heat kernel to it. [6]

Domain specific: t.b.d

Kernels

Conditions for selection: p.s.d & fast

General kernels [5]:

- RBF kernel
- Laplacian kernel
- Linear
- Neighborhood Subgraph Pairwise Distance graph kernel [3]

The last can be used when dicrete edge features are employed.

Domain specific: t.b.d

Maximum Mean Discrepancy

The Maximum Mean Discrepancy (MMD) [4, 2] is defined as follows:

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

where:

- $x_i, x_j \sim \mathcal{X}$, n is the number of samples from non-empty set $\mathcal{X}$;
- $y_i, y_j \sim \mathcal{Y}$, m is the number of samples from non-empty set $\mathcal{Y}$;
- $k : \mathcal{X} \times \mathcal{X} \to \mathbb{R}$ is a valid kernel.

MMD is a kernelized proxy of the distance between two graph distributions G and $G*$ computed as $d_{\text{MMD}}(G, G^*) = MMD(f(G), f(G^*))$, where f is the descriptor function of the graph. A lower $d_{\text{MMD}}(G, G^*)$ indicates a greater similarity between G and $G*$. Potentially look at other metrics for GNNs. [9]

Perturbations to graphs

Domain agnostic [5]:

- edge insertion
- edge removal
- edge rewiring
- node addition

Domain specific:

- t.b.d. (e.g. add edge “disrupting” binding pocket, how to do this?)

Evaluation

Domain agnostic [5]:

- Correlation with perturbation
- Correlation with graph edit distance

Domain specific:

- Alignment
- (estimated) folding energy
- Investigate what makes a “good” protein.

Workflows enabled by the package

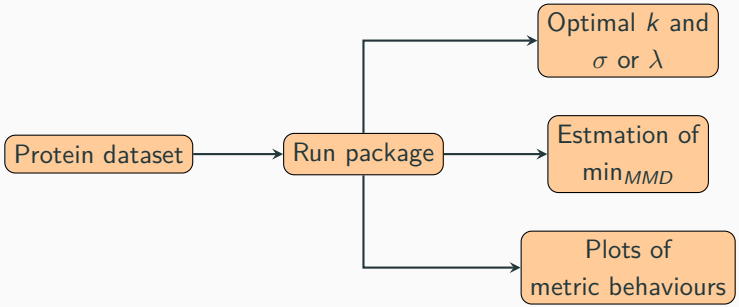

Figure 3: Workflows enabled by the package.

Plots to understand the behaviour of MMD

- Distribution of $\min_{MMD}$ for different random test/train splits.
- Correlation perturbation with MMD values with different parameters
- MMD vs. parameter

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