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Designing meaningful measures to evaluate generative graph neural networks on protein datasets.

Master Thesis

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Abstract

This example thesis briefly shows the main features of our thesis style, and how to use it for your purposes.

Contents

Chapter 1

Introduction

Chapter 2

Background & Related Work

This chapter introduces the core concepts built upon in this thesis and surveys recent literature tackling the evaluation of generative graph neural networks and the relevance of this problem in structural biology. Section 2.1 defines core mathematical and biological concepts that will be built upon in the thesis. Section 2.2 will discuss recent advances in the design of measures used to evaluate generative graph neural networks and in structural biology.

2.1 Background

The set of methods investigated in this thesis lies at the interface of structural biology and machine learning. We start by defining some relevant biological properties of proteins, followed by a survey various graph theoretical abstractions derived from the protein structure. We then move on to define generative models and the various classes of measures used to evaluate them.

2.1.1 Proteins

Proteins are large biomolecules that are formed from a sequence of amino acids, performing their functions as determined by their three-dimensional structure, and amino acid sequence. Proteins support a vast array of functions in living organisms, such as catalysing metabolic reactions, DNA replication, providing structural support to cells, transporting molecules and sensing stimuli.

Each protein is made up of one or more chains of amino acids, each of which contain a backbone and different side chains. The atoms in the backbone include a α-carbon, another carbon and a nitrogen atom. An overview of the peptide backbone is shown in Figure 2.1. Interestingly, a plane is forned by two alpha carbons, the carboxyl group, and the hydrogen atom attached

to the nitrogen atom (see Figure 2.1), making the peptide bond between the nitrogen and carbon atom resistant to twisting. That means that the rotations enabling the 3D folding of a protein is governed by the angle of the bonds linking the nitrogen atom to the α-carbon and the other carbon atom to the α-carbon, named φ and ψ. These angles' values are frequently used to validate proteins, characterise the secondary structure of proteins (i.e. structural features observed in certain segments of proteins), etc.

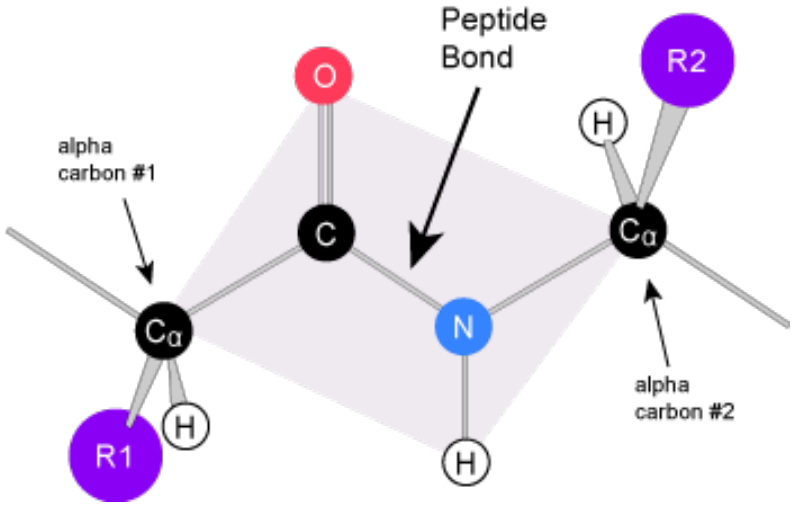

Figure 2.1: Schematic of the backbone of a protein. Two α-carbons are shown as well as a β-carbon in the middle. R1 and R2 represent the side chains of the amino acid.

To visualize such angles, a Ramachandran plot can be constructed for any protein. Such a plot can reveal secondary structural features such as β-sheets, α-helices, etc. An example of such a plot together with a 3D model of a protein can be found in Figure 2.2.

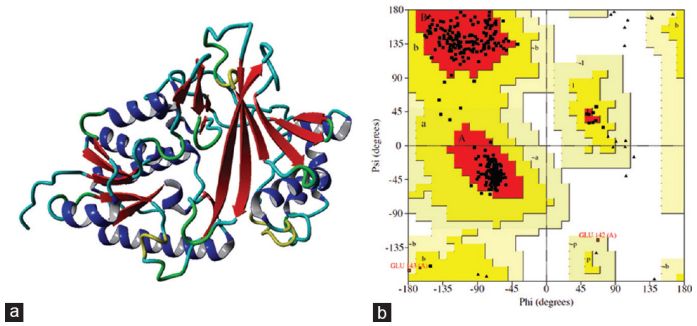

Figure 2.2: 3D structure of uridine diphosphogalactofuranose-galactopyranose mutase with a corresponding Ramachandran plot. The α -helices can be found on the middle left part of the Ramachandran plot, the β sheets on the upper right quadrant, and the left handed α-helices can be found in the middle upper right part of the plot. This figure is adapted from [1].

2.1.2 Graphs

A graph G is a pair of vertices V and edges E such that $G = (V, E)$, $|V| = n$ and $|E| = m$. Two vertices i and j are adjacent if there is an edge between them, i.e. $e_{ij} \in E$. The relationship between between edges can be represented as an $n \times n$ adjacency matrix A, where:

$$A_{ij} = \begin{cases} 1, & \text{if } e_{ij} \in E \\ 0, & \text{otherwise.} \end{cases} \tag{2.1}$$

2.1.3 Topological Data Analysis

2.1.4 Generative models

2.1.5 Kernel methods

2.2 Related Work

2.2.1 Structural Biology

2.2.2 Metrics for Generative Graph Models

2.3 Summary

Chapter 3

Methods

Dummy text.

3.1 Example Section

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3.1.1 Example Subsection

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Example Subsubsection

Dummy text.

Example Paragraph Dummy text.

Example Subparagraph Dummy text.

Chapter 4

Results

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4.1 Example Section

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4.1.1 Example Subsection

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Example Subsubsection

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Chapter 5

Discussion

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5.1 Example Section

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5.1.1 Example Subsection

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Example Subsubsection

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Example Paragraph Dummy text.

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Chapter 6

Conclusion

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6.1 Example Section

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6.1.1 Example Subsection

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Example Subsubsection

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Example Subparagraph Dummy text.

Appendix A

Dummy Appendix

You can defer lengthy calculations that would otherwise only interrupt the flow of your thesis to an appendix.

Bibliography

[1] Tapaswini Nayak, Lingaraja Jena, Pranita Waghmare, Bhaskar C Harinath, et al. Identification of potential inhibitors for mycobacterial uridine diphosphogalactofuranose-galactopyranose mutase enzyme: A novel drug target through in silico approach. *International Journal of Mycobacteriology*, 7(1):61, 2018.

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