PREDICTING PHAGE-HOST INTERACTION WITH LANGUAGE MODELS

Project plan

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INTRODUCTION

Recent advancements have highlighted the efficacy of language models over traditional supervised machine learning approaches in the realm of protein structure prediction. Traditional methods rely on evolutionary information sourced from multiple sequence alignment, a process which can be computationally intensive. Conversely, language models have the capacity to derive information directly from single amino acid sequences. Most noticeably, such models can exploit the information encoded in the vast number of unlabeled sequences used for their pre-training. On top of that, language models allow protein-specific predictions, as opposed to other methods which rely on family-averaged alignments.

The information encoded from neural networks are finding a growing number of applications, from protein structure estimation *[1]* to host prediction from a viral protein *[2]*. State of the art results make use of embeddings, which are protein information encoded via transformers architecture like protBERT *[1]*.

This research aims to explore the capabilities of language models in predicting protein-protein interactions. The primary focus will be on assessing the potential interactions between the proteins of a phage and its bacterial host. Successfully predicting such interactions can be indicative of a virus's ability to infect the microorganism.

METHODS

An in-depth investigation of the phages infecting *Escherichia coli* was conducted by *Maffei et al [4].* The data they collected concerns the K-12 MG1655 ΔRM strain and will be the foundation for training and testing this project’s neural model.

The first task requires the labelling of virus-host protein pairs as interacting or not. Such information will be inferred from the occurred infection and knowledge about receptor–receptor binding protein interaction.

Secondly, negative examples of expectedly non-interacting proteins might be added to the dataset in order to reinforce the model understanding of correct protein interaction. On top of that, the protein-class distribution will be assessed to avoid any bias.

The next step contemplates the model realization. The architecture will be based on the work of Gonzales et al, where the host genus is computed from a viral receptor-binding protein embedding [2]. On the other side, the here proposed project’s aim concerns the compatibility prediction of a virus-host protein pair. In detail, the architecture will probably see a protT5 embedding module [1] followed by a random forest classifier.

Lastly, an additional volume of protein sequences will be obtained from ***E. coli*** genomic sequences containing prophages. Infection from these phages is taken heuristically for granted. Further data processing and model training will follow.

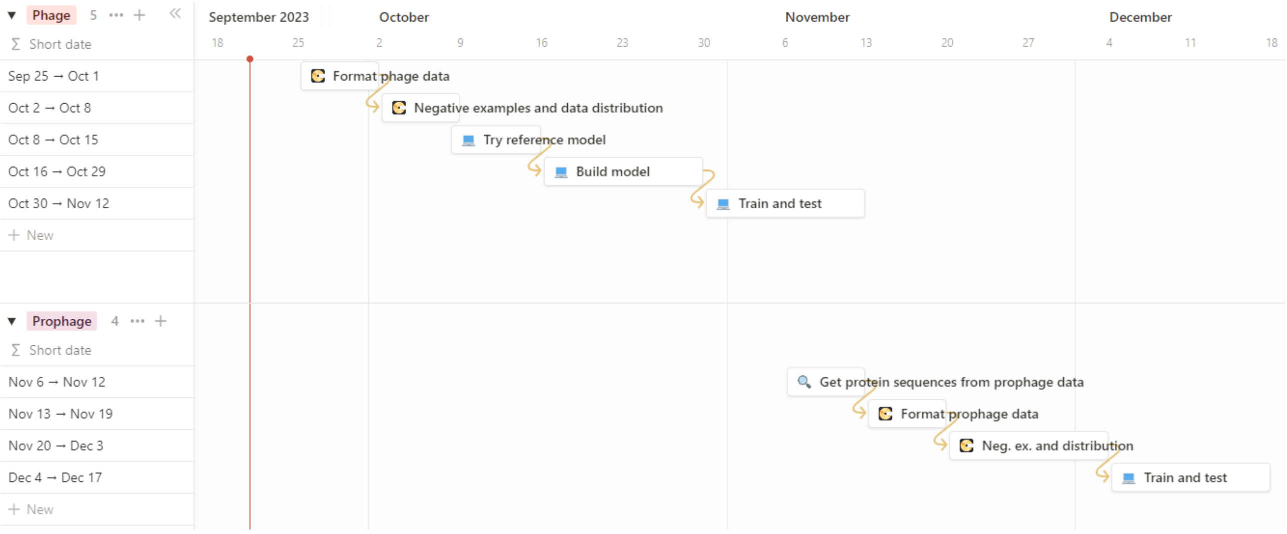
SIDE PROJECTS

The subject is exciting and open to various possibilities. Hereby are listed some possible developments:

- Consider phage interaction with the lipopolysaccharides
- Improve biological knowledge increasing embeddings interpretability - e.g. projection on lower dimensions
- Move the focus on other phylogenetic elements
- Estimate confidence on predictions via evidential learning
- Use protein sets as input to estimate infection instead of protein-protein interactions

PROJECT TIMELINE

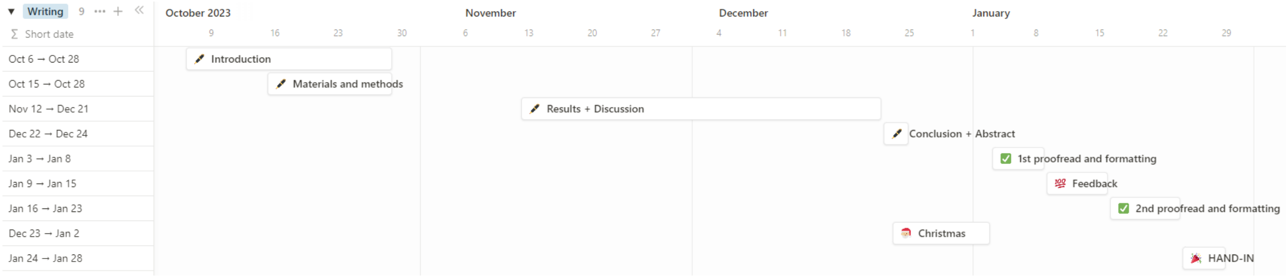
Period: 28/08/2023 – 28/01/2024



Phage 5	
Σ Short date	
Sep 25 → Oct 1	Format phage data
Oct 2 → Oct 8	Negative examples and data distribution
Oct 8 → Oct 15	Try reference model
Oct 16 → Oct 29	Build model
Oct 30 → Nov 12	Train and test
+ New	

Prophage 4	
Σ Short date	
Nov 6 → Nov 12	Get protein sequences from prophage data
Nov 13 → Nov 19	Format prophage data
Nov 20 → Dec 3	Neg. ex. and distribution
Dec 4 → Dec 17	Train and test
+ New	

Figure 1 - Data handling and model development for phages and prophages



Writing 9	
Σ Short date	
Oct 6 → Oct 28	Introduction
Oct 15 → Oct 28	Materials and methods
Nov 12 → Dec 21	Results + Discussion
Dec 22 → Dec 24	Conclusion + Abstract
Jan 3 → Jan 8	✓ 1st proofread and formatting
Jan 9 → Jan 15	Feedback
Jan 16 → Jan 23	✓ 2nd proofread and formatting
Dec 23 → Jan 2	Christmas
Jan 24 → Jan 28	HAND-IN

Figure 2 - Project report writing

REFERENCES

1. Elnaggar et al. – DOI: 10.1109/TPAMI.2021.3095381
2. Gonzales et al. – DOI: 10.1371/journal.pone.0289030
3. Maffei et al. – DOI: 10.1371/journal.pbio.3001424