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# GrAPFI: Graph Based Inference for Automatic Protein Function Annotation

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► **To cite this version:**

Bishnu Sarker, David Ritchie, Sabeur Aridhi. GrAPFI: Graph Based Inference for Automatic Protein Function Annotation. ECCB 2018 - 17th European Conference on Computational Biology, Sep 2018, Athens, Greece. hal-01876907v2

**HAL Id: hal-01876907**

**<https://inria.hal.science/hal-01876907v2>**

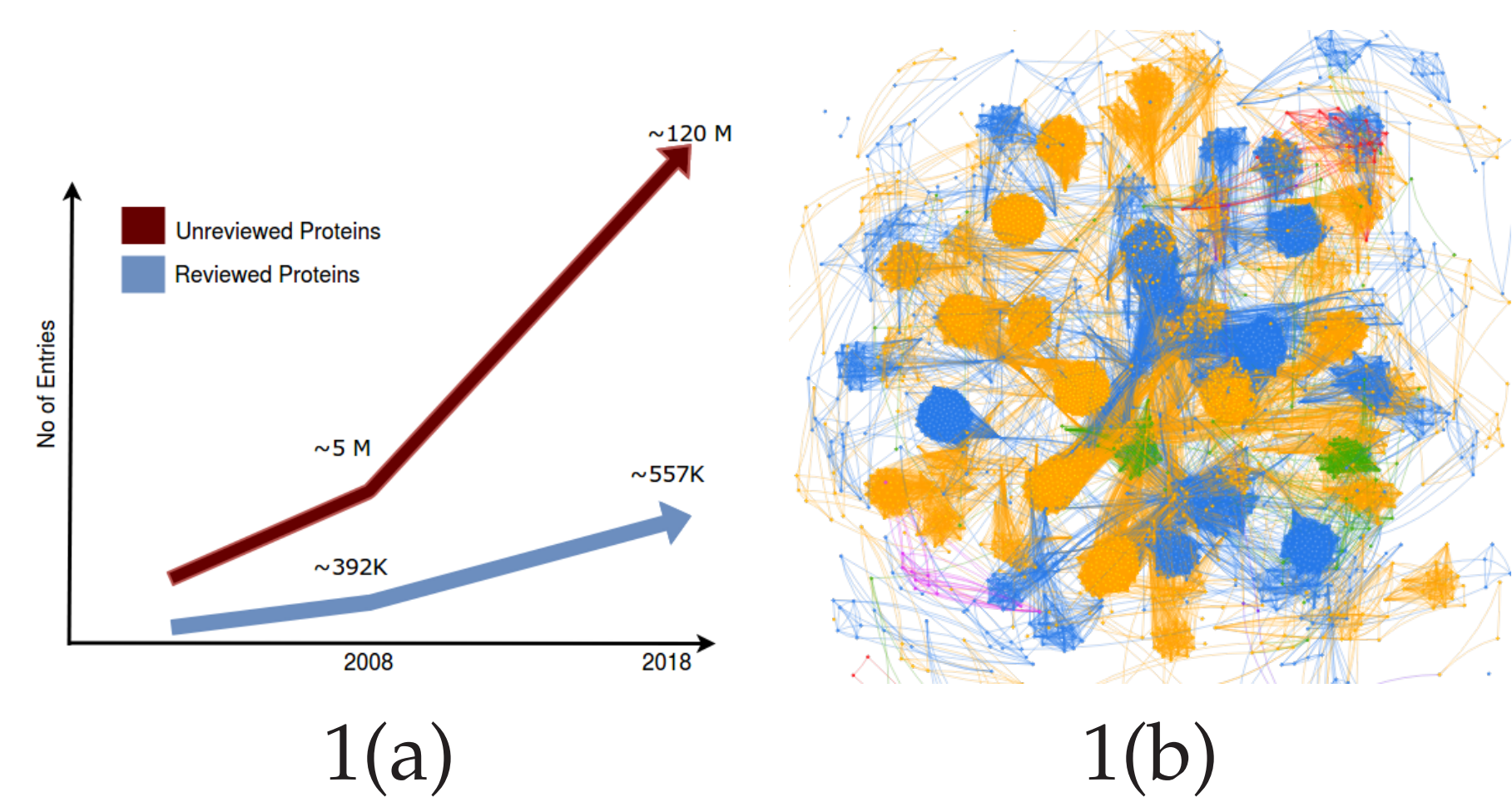
Submitted on 14 Nov 2018

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## Introduction



The growing number of protein sequences in UniProtKB (Fig-1(a)) makes it increasingly expensive to annotate them manually. Here, we present GrAPFI (Graph based Automatic Protein Function Inference), a tool for the automatic functional annotation of proteins with Enzyme Commission (EC) numbers. The EC System uses a four digit numbering with a hierarchical structure. GrAPFI utilizes the domain composition of the proteins. Our general observation is that protein domains shares functional properties. Fig-1(b). illustrates this for proteins from viruses dataset. The 6 different colors in this figure correspond to the 6 different top level EC classes.

## Graph Construction

GrAPFI constructs the protein graph based on domain composition of each protein. Each node of the graph represents a protein, while a link between two nodes means that the proteins exhibit a given minimum level of domain similarity. Each node  $u$  is identified by a set of labels  $L(u)$  (one or more annotations to propagate), has a set of neighbours  $N(u)$ , and for every neighbour  $v$  it has an associated weight  $W_{u,v}$ . If  $u$  and  $v$  have domain composition  $D1=(d1,d2,d3,d4)$  and  $D2=(d1,d3,d5)$ , then,

$$W_{u,v} = \frac{|(d1, d2, d3, d4) \cap (d1, d3, d5)|}{|(d1, d2, d3, d4) \cup (d1, d3, d5)|}$$

$$= \frac{|(d1, d3)|}{|(d1, d2, d3, d4, d5)|}$$

$$= \frac{2}{5} = 0.4.$$

## GrAPFI Annotation Workflow

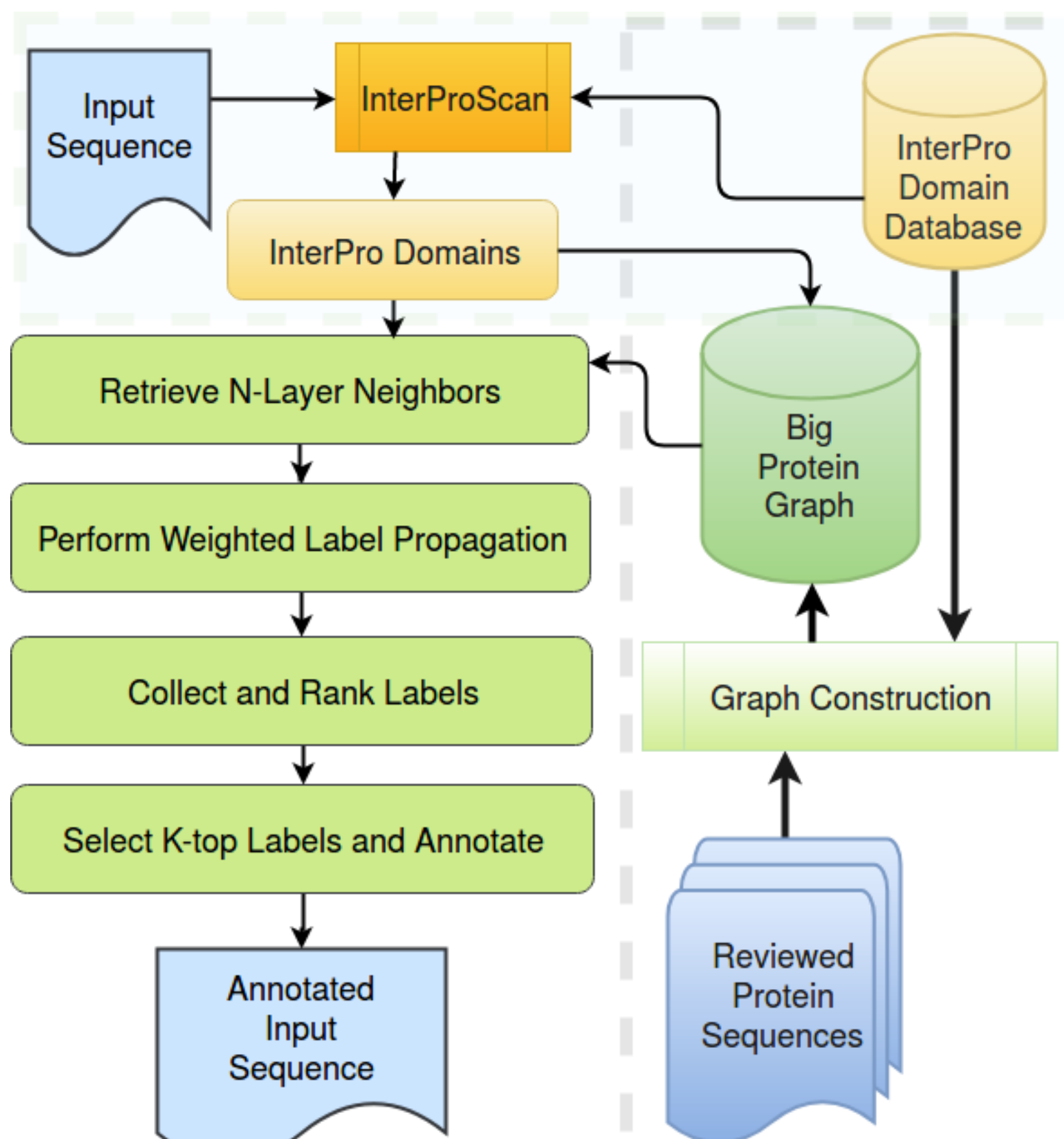


Fig-2: GrAPFI follows the above work-flow to annotate an un-reviewed protein.

## Example Function Annotation of 2rk2A Enzyme

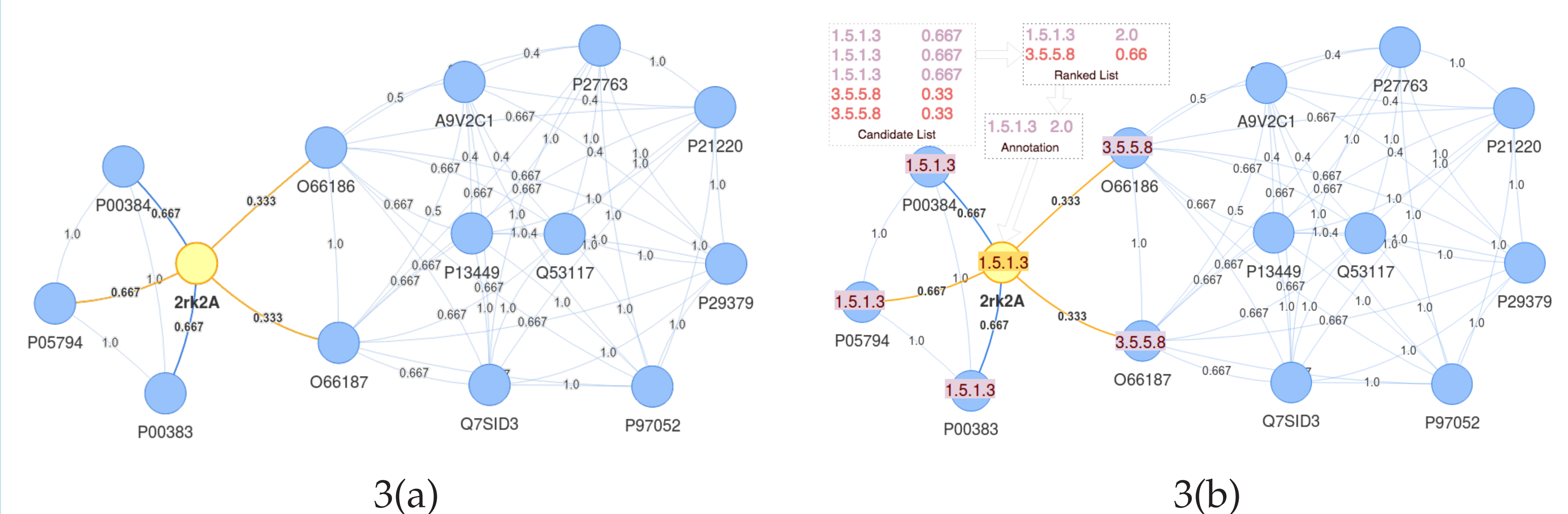
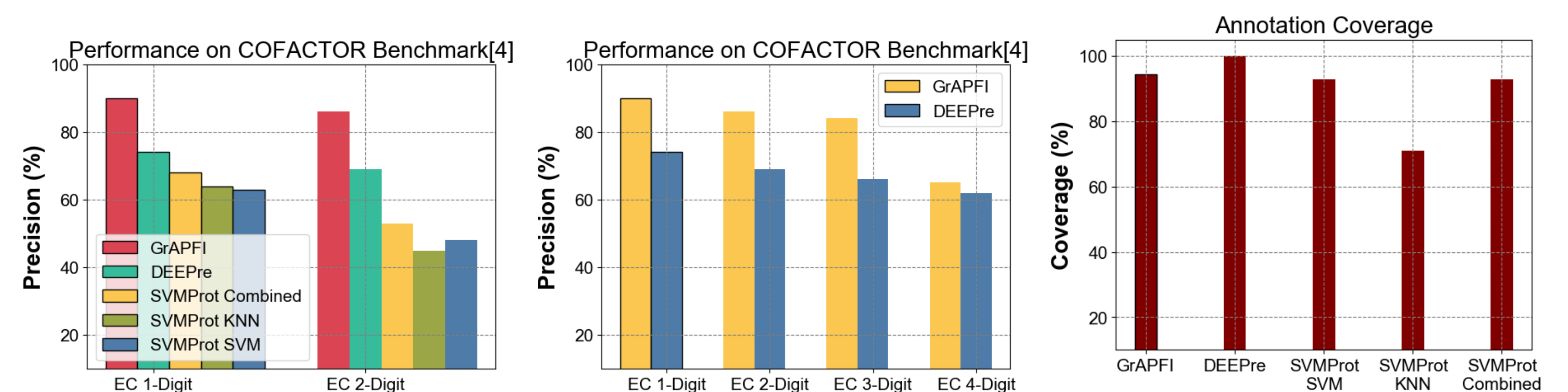
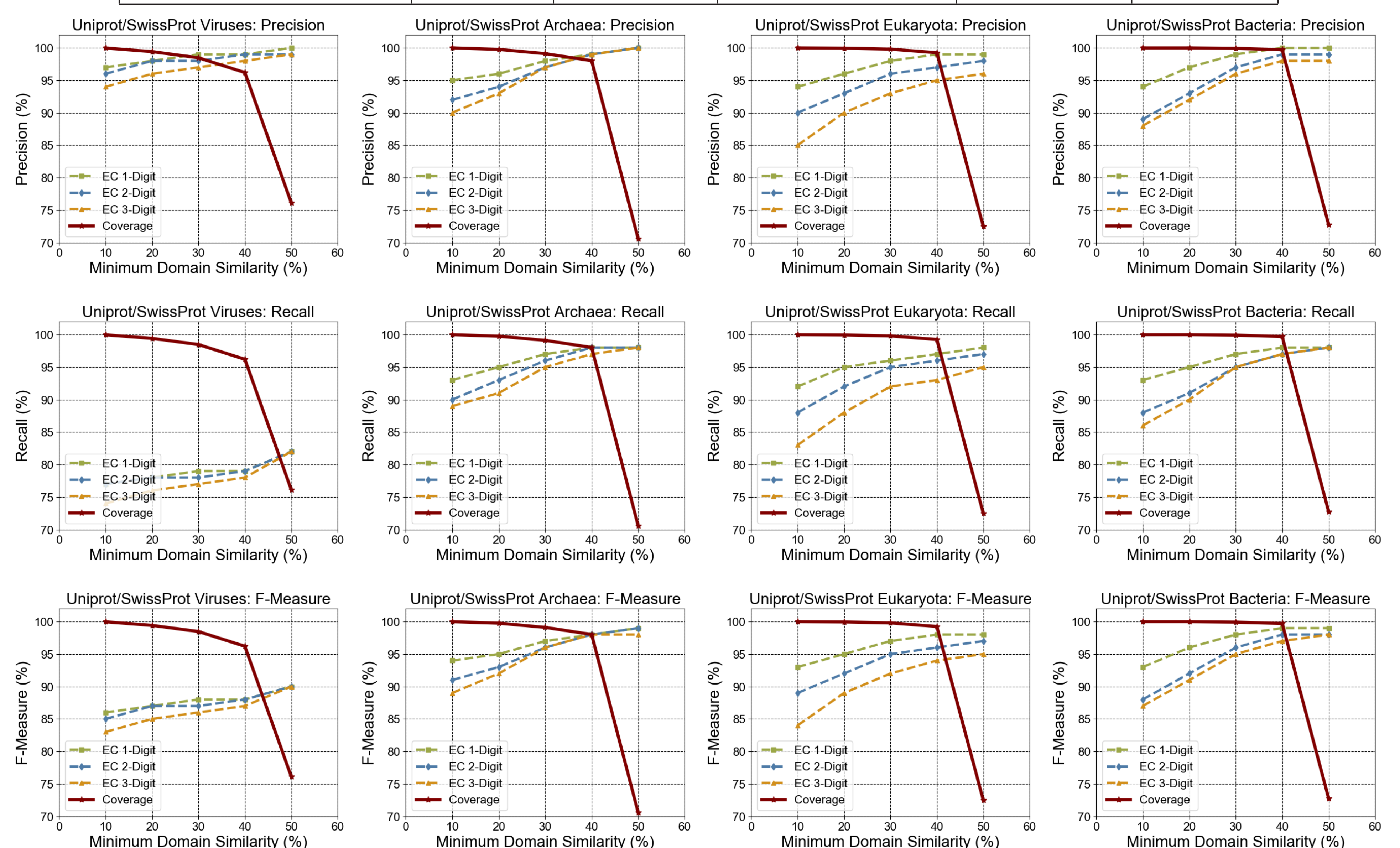


Fig-3(a) shows a query protein (yellow node) connected with its five neighbors. Fig-3(b) shows the result of label propagation applied on the graph in Fig-3(a).

## Results

| Dataset             | # Nodes | # Edges   | Average Degree | # Domains | Total EC |
|---------------------|---------|-----------|----------------|-----------|----------|
| SwissProt Viruses   | 3208    | 478447    | 298.28         | 1031      | 150      |
| SwissProt Archaea   | 10619   | 1168710   | 220.12         | 2499      | 727      |
| SwissProt Eukaryota | 55042   | 30753219  | 1117.45        | 6744      | 2832     |
| SwissProt Bacteria  | 193429  | 409837148 | 4237.6         | 6480      | 2902     |



A comparative study is presented based on a benchmark of 318 proteins taken from COFACTOR[4]. After removing proteins that do not have ground truth EC annotation, we had 297 Enzymes to annotate.

## Conclusion

GrAPFI is a novel graph based approach for automatic protein functional annotation. It utilizes a domain based graph representation of the UniProtKB/SwissProt protein database. To evaluate the performance, leave one out cross validation is used on the graph built on four species from UniProt/SwissProt namely Viruses, Archaea, Eukaryota and Bacteria. Average precision,  $Pr_{avg} = \frac{1}{M} \sum_{p \in P} Pr_p$ , recall,  $Re_{avg} = \frac{1}{M} \sum_{p \in P} Re_p$  and F-Measure,  $F_{Measure} = \frac{2 \times Pr_{avg} \times Re_{avg}}{Pr_{avg} + Re_{avg}}$  are used as performance metrics. Our performance comparison shows GrAPFI outperforms other methods e.g. DEEPre[3], SVMProt[2]. The future work aims at using GrAPFI for protein Annotation with GO terms.

## References

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**Acknowledgement** Bishnu Sarker is funded by an INRIA Cordis-S Doctoral Grant.