



HAL
open science

EnzBert: Deep attention network for enzyme class predictions

Nicolas Buton, Yann Le Cunff, François Coste

► **To cite this version:**

Nicolas Buton, Yann Le Cunff, François Coste. EnzBert: Deep attention network for enzyme class predictions. JOBIM 2022 - Journées Ouvertes en Biologie, Informatique et Mathématiques, Jul 2022, Rennes, France. pp.1-1. hal-03780557

HAL Id: hal-03780557

<https://hal.science/hal-03780557v1>

Submitted on 19 Sep 2022

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

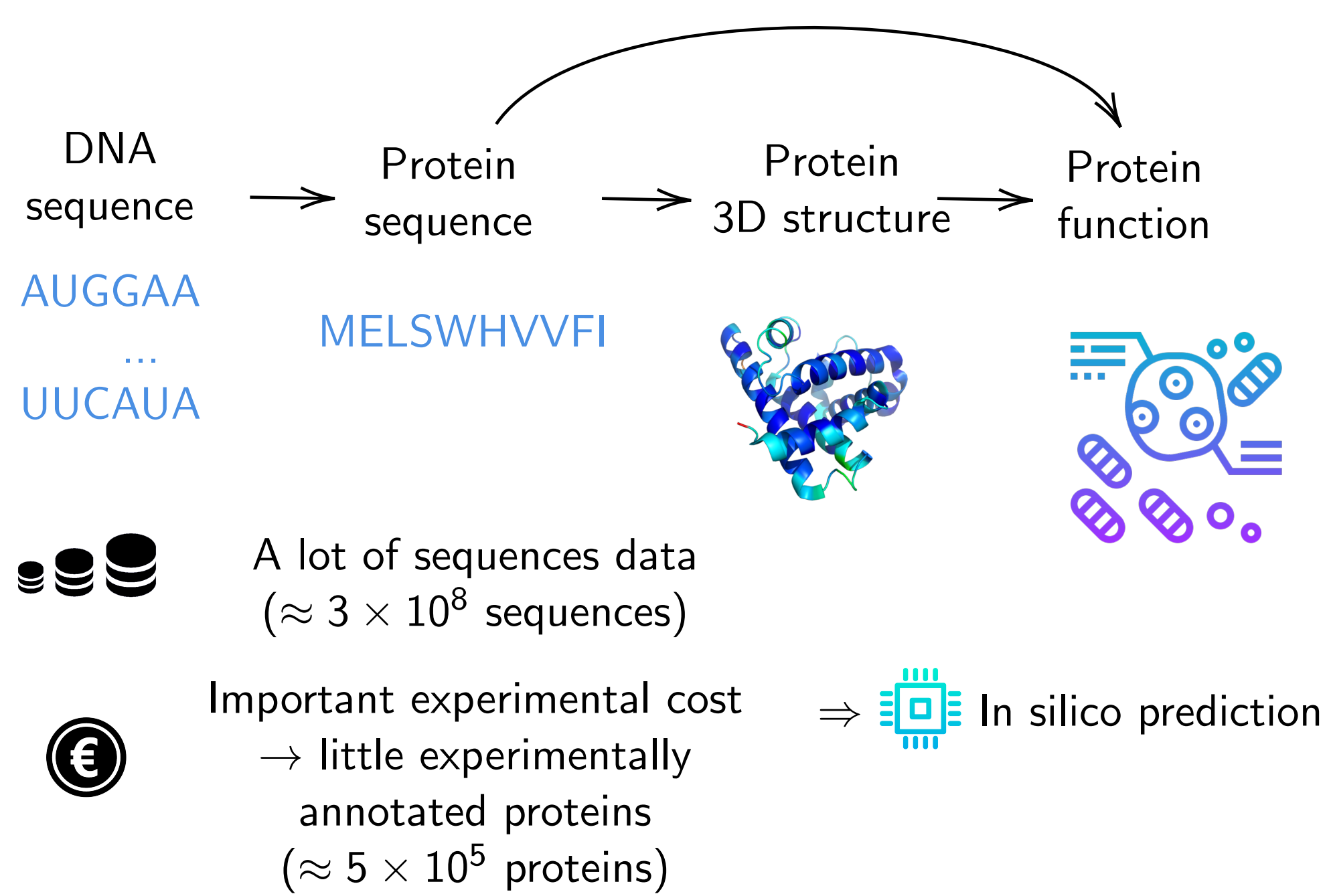


Distributed under a Creative Commons Attribution 4.0 International License

EnzBert: Deep attention network for enzyme class predictions

1. Task

1.1 Functional annotation of protein sequences



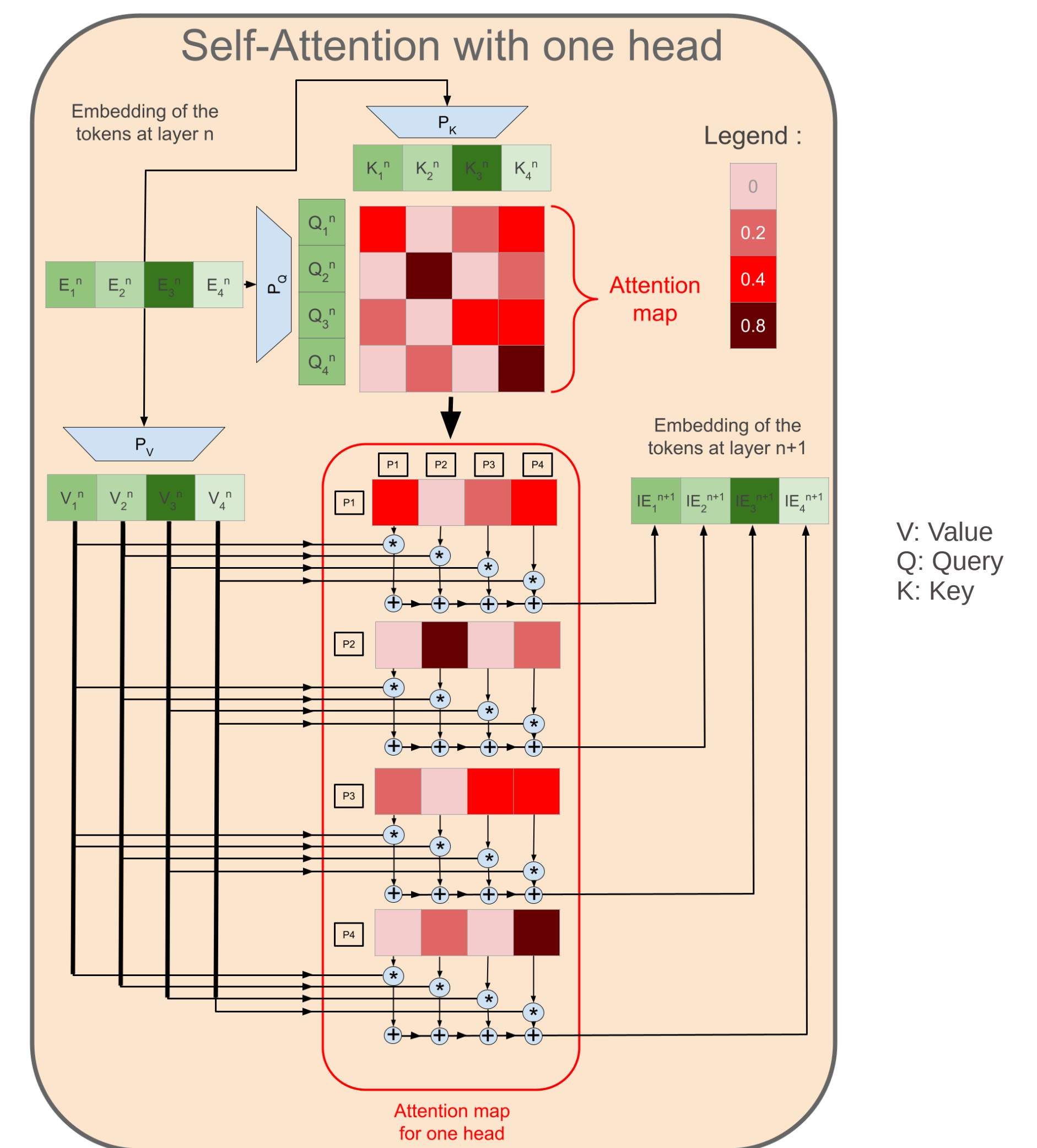
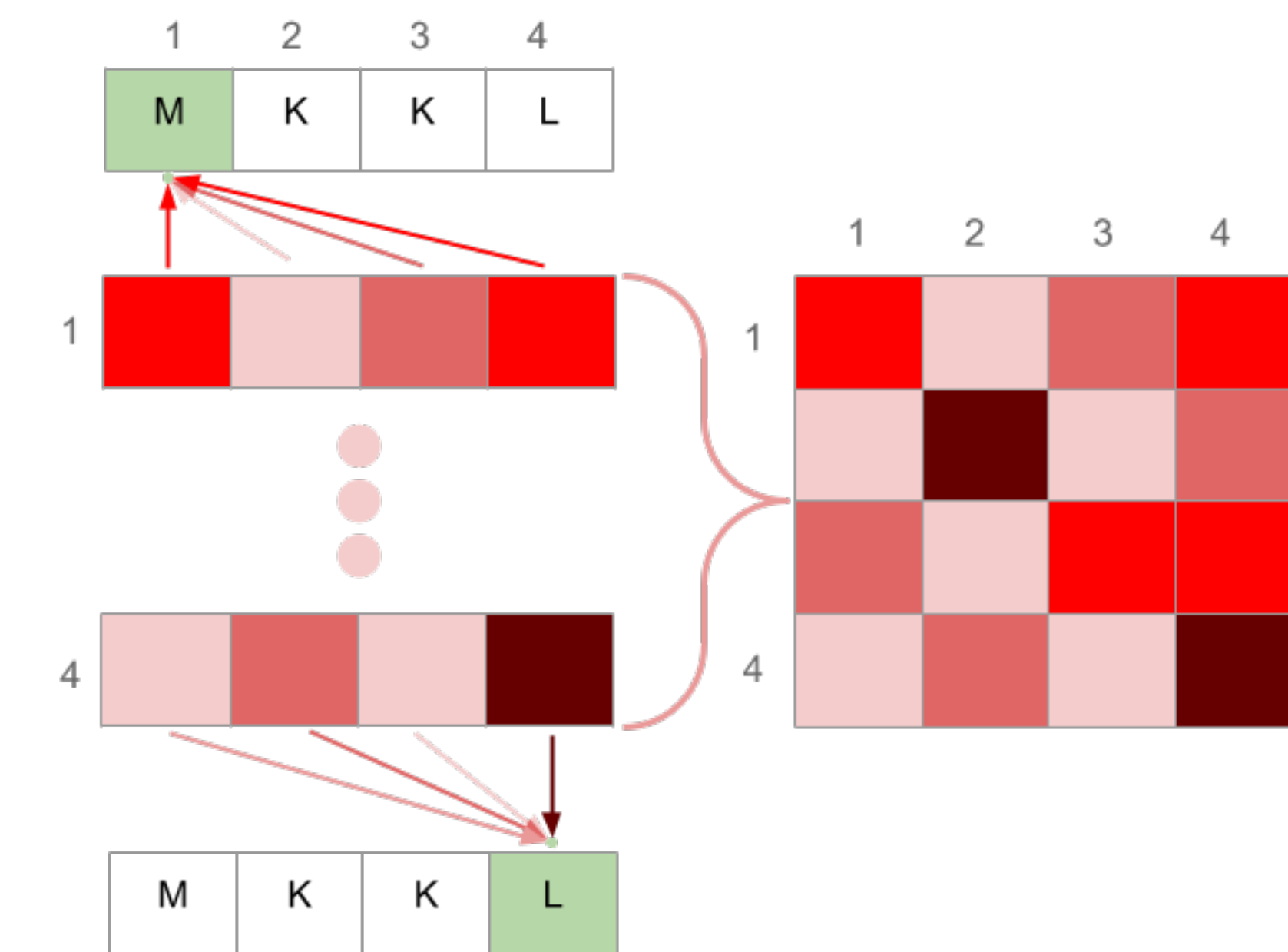
1.2 Challenges

- Sequence information (2.1)
- Underlying 3D structure (2.1)
- Few examples per category (2.2)
- Interpretability (2.3)

2. Methods

2.1 Attention mechanism and Transformer

Attention is the basis of Transformers, for each position it gives weights to other residues.



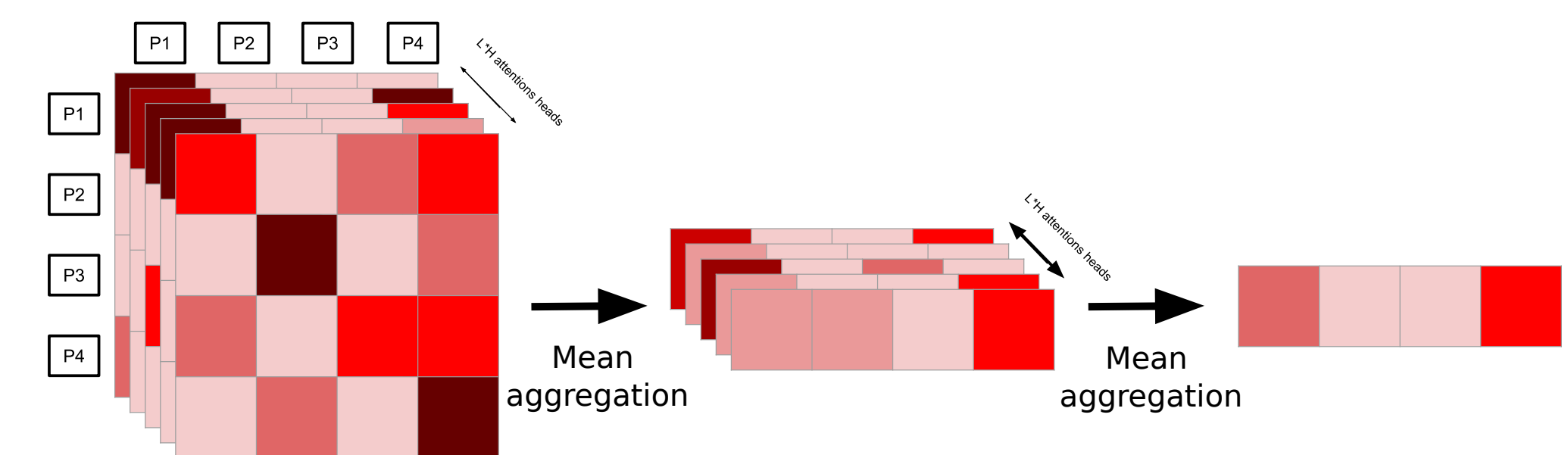
2.2 Two phases training

Unsupervised pre-training on all proteins and supervised fine-tuning step on enzyme classification

Produces a meaningful embedding space for proteins and exploits this during the fine-tuning for better generalization

2.3 Interpretability method

Attention maps from multiple layers and multiple heads. A new interpretability method to get residues' importance scores: attention aggregation.



3. Results

3.1 Enzyme classification

Comparison with state-of-the-art method at level 1 and 2 of the enzyme commission (EC) number on EC40 dataset

Model	Accuracy at level 1	Accuracy at level 2
UDSMProt ¹	0.87	0.84
EnzBert	0.97	0.95

Macro metrics, comparison with state-of-the-art method at different levels of the enzyme commission (EC) number on ECPred40 dataset.

Model	Level	Macro-precision	Macro-recall	Macro-f1
ECPred ²	0	0.78	0.78	0.77
EnzBert	0	0.80	0.80	0.80
ECPred	1	0.69	0.84	0.73
EnzBert	1	0.62	0.55	0.55
ECPred	2	0.48	0.61	0.51
EnzBert	2	0.57	0.60	0.55
ECPred	3	0.50	0.56	0.50
EnzBert	3	0.53	0.57	0.52
ECPred	4	0.43	0.41	0.40
EnzBert	4	0.49	0.49	0.47

3.2 Interpretability

Benchmark: Evaluated on the identification of catalytic residues on enzymes with respect to different interpretability methods.

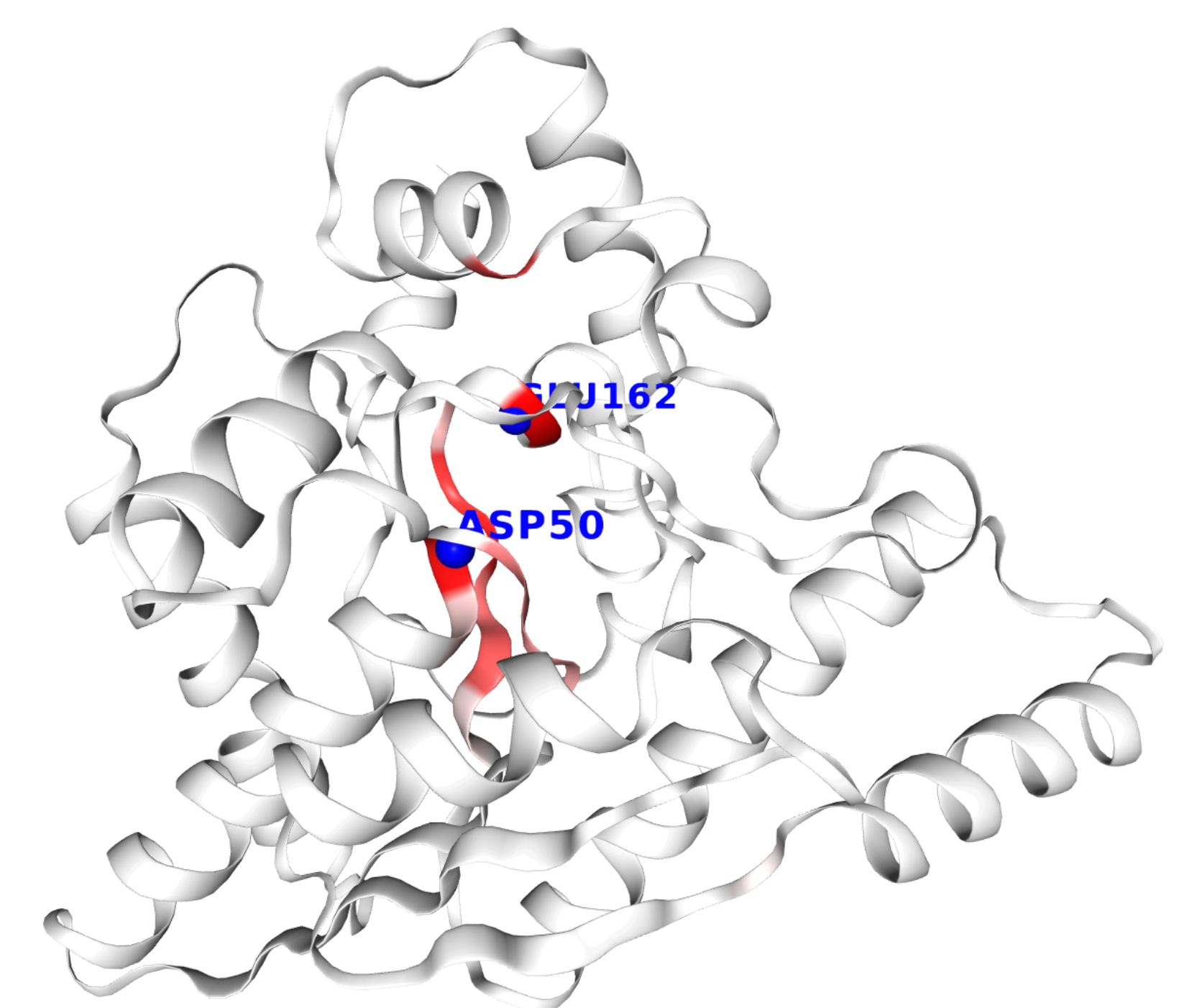
Method type	PRG-AUC (x100)	max F-Gain (%)	Time (s)
Random	42.54 ± 4.37	69.85 ± 1.04	-
Grad	75.01	81.27	4.64
Grad X input	63.62	78.66	7.74
Integrated grad	76.41	81.70	2.48 × 10 ²
Attn last layer	87.80	85.62	2.87
Attn aggregation	98.01	96.05	3.72
Rollout	66.08	76.77	2.95
TGLRP	90.92	88.56	4.05 × 10 ¹
TGradCam	81.00	76.77	4.35 × 10 ¹
LIME	93.46	91.44	1.73 × 10 ⁴

Attention-based interpretability performs best

4. Conclusion

- State-of-the-art prediction on enzymes' classes from sequences only for our model EnzBert
- New interpretability method for Transformers that works very well on enzymes
- Prospects: Considering the hierarchy of Enzyme Commission (EC) number may improve our results

NH(3)-dependent NAD(+) synthetase enzyme



MSMQEKIMRE LHKVPSIDPK QEIEDRVNFI KQYVKTGAK GFVLGI...STLAGRLAQ LAVESIREEG GDAQFIAVRL PHGTQDEDD AQLKFKPK
1 DKSMKFDIKS TVSAFSDQYQ QETGDLTDF NKGAVKARTR MIAQYATGGQ EGGLEL...AVTGFPT KYGGDADLL PLTLTKRQG RTLLKELGAP
2 ERLYLKPTA DLLDEKPKQS DETELGIS...EIDDVLEKGE VSAKVSEALE KRYSMTEHR QVPASMFDDW WK

Fig. : Top 5% of residues' importance score of our interpretability method are highlighted in red and catalytic sites are represented by blue spheres.

The two highest scores on attention aggregation correspond to the two catalytic residues of the enzyme.

Nicolas Buton

Yann Le Cunff

François Coste

Univ. Rennes, Inria, CNRS, IRISA, Rennes, France