

Saliency Map on Cnns for Protein Secondary Structure Prediction

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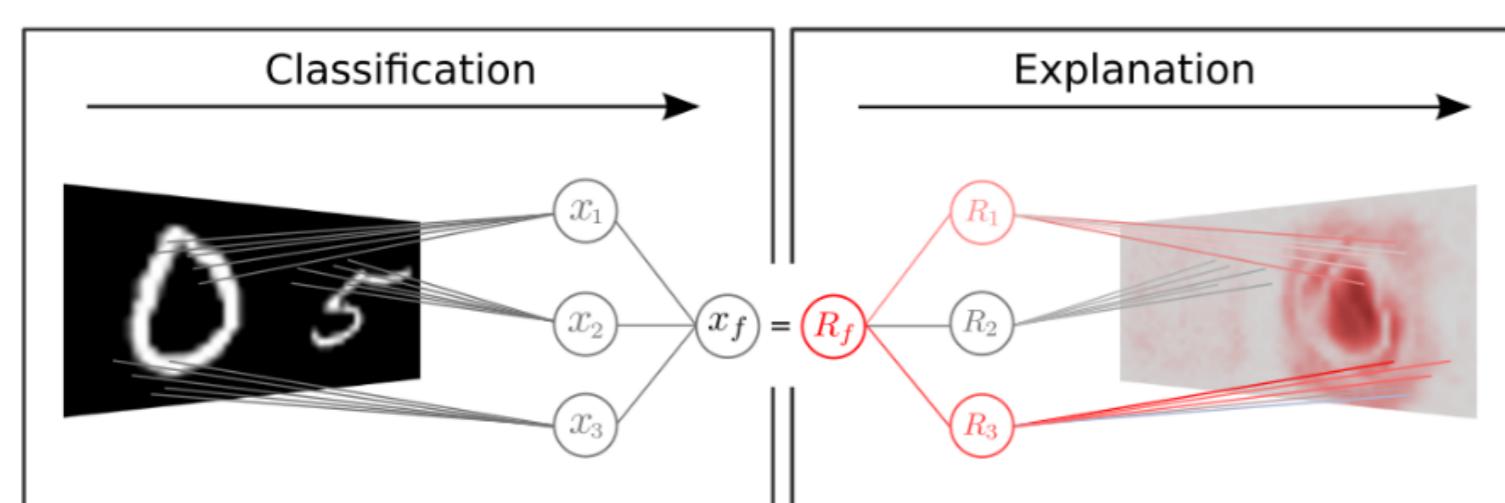
What else can we obtain from our machines?

Machine Learning researchers sometimes fall into a race for accuracy, trying different models and methods without putting excessive attention on the reasons for the successes. Moreover, deep learning architectures are difficult to interpret and typically act as **black boxes**.

Interpretability techniques should be used more often for understanding the underlying processes, spot the key drivers of improvements in accuracy, and detect spurious rules learned by the models. Although a few of such techniques have some level of development, they have barely been applied in bioinformatics.

Main interpretability techniques (from computer vision field):

- **Feature visualisation** (generating synthetic input from the learned model)
- **Saliency maps** (influence map on inputs for specific classification outputs)



The protein secondary-structure prediction (SPPS) problem

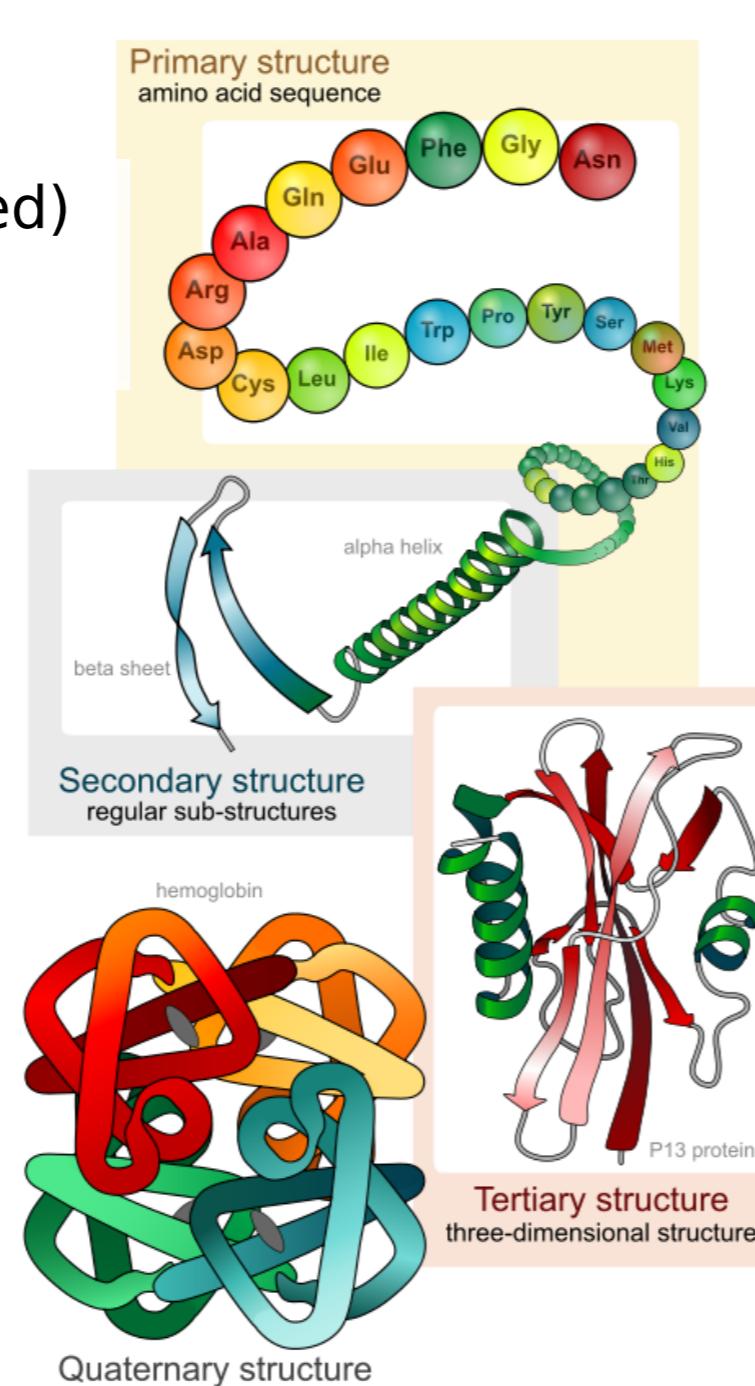
SPPS is a long-time studied problem. Recent machine learning revolution introduced significant advances in performance

Inputs: protein sequences with varying length and width 42:

- 21 amino acid types (one-hot encoded)
- 21 PSSM values (evolutionary)

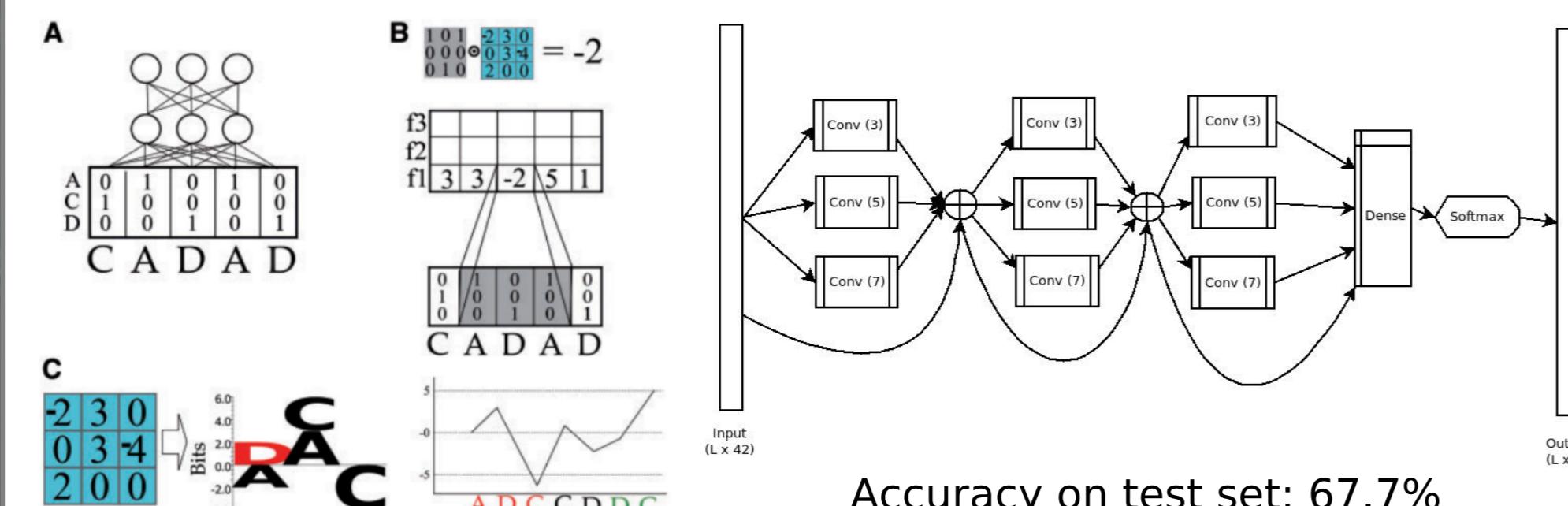
Output: one per amino acid:
8 classes of secondary structures (one-hot)

Q8 grouping	Explanation	%
α -helix	Helix with 4 turns	34.54
3_{10} -helix	Smaller helix with 3 turns	3.91
π -helix	Bigger helix with 5 turns	0.02
β -bridge	Isolated β -bridge	1.03
β -strand	Participates in β -ladders	21.78
Turn	Turns smaller than a helix	11.28
Bend	Curved piece	8.26
Loop	Sometimes also as coil (C)	19.19



State-of-the-art architecture:

1D Convolutional Neural Networks



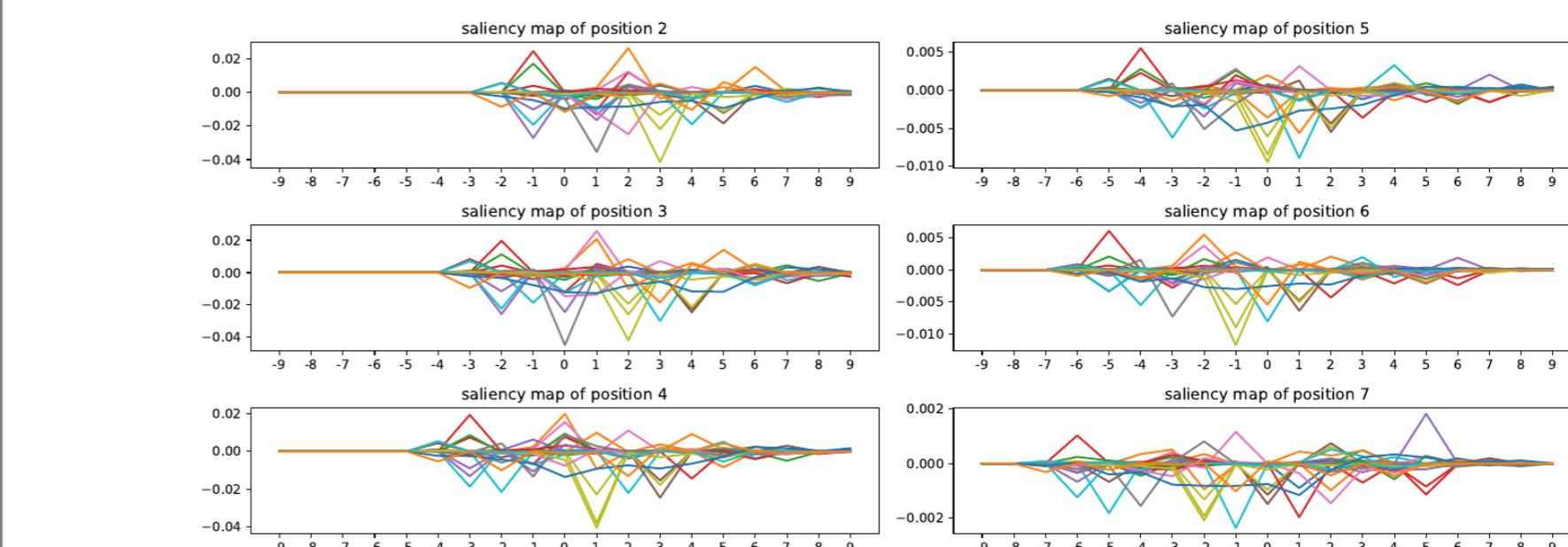
Full paper available at:
<https://ieeexplore.ieee.org/document/8683603>

Extracting saliency maps from many-to-many classification

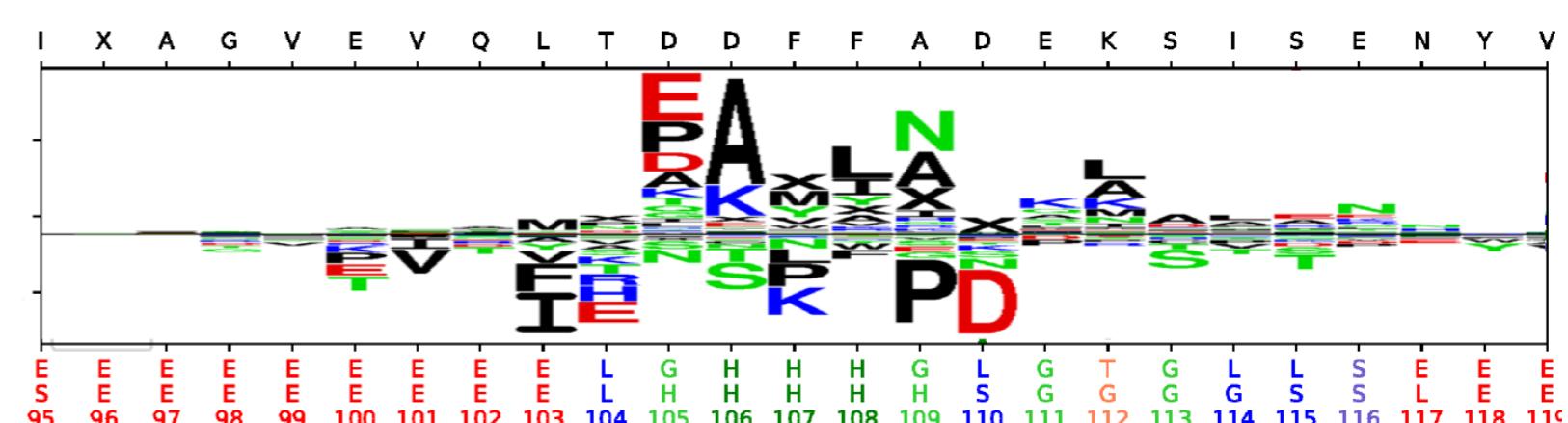
Previous work (on TFBS)[1]: 1 saliency map per sequence

Positive Test Sequence	Saliency Map
TCCTCCATCCTATTGCCACGTTAGTCACATGGCCACCTGGCTCAAACCTGGAACACCTAGTCCTTCCT	

Our work: 1 saliency map per position, 8x42x19 (8 classes, 42 inputs, 19 window size), 1.3M positions.

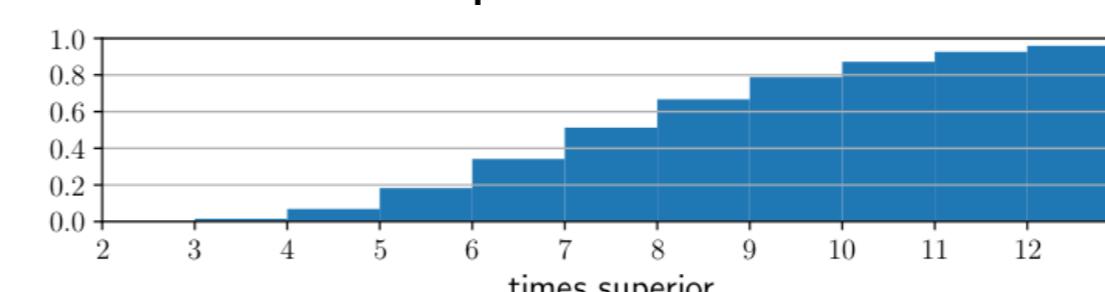


Methods of aggregation: per sequence (below), per class (results), per input type (results), and more



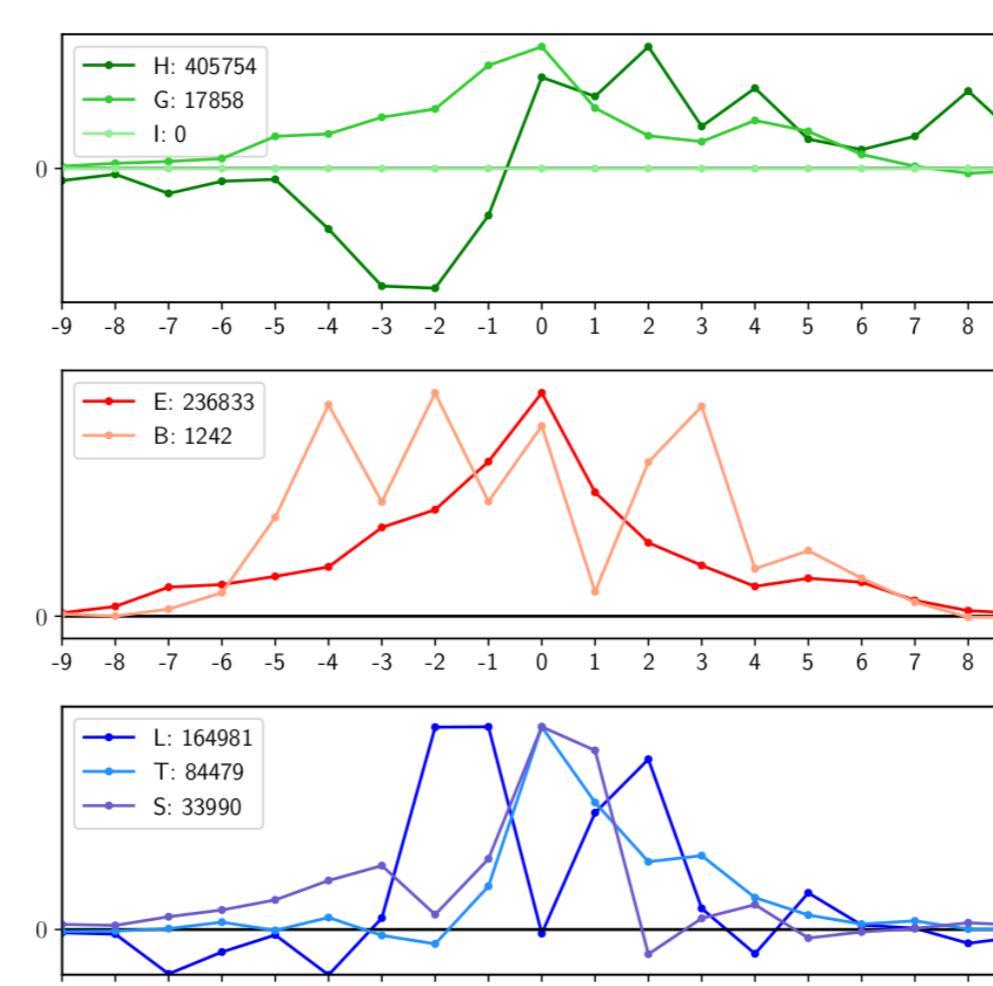
Results

Relevance of inputs: **PSSM values over one-hot amino acids**



Cumulative histogram with relative strength of **PSSM saliency scores** as compared to **amino acid saliency scores**

Spatial relevance of surrounding positions per class



- H class predicted more from one side
- Periodicity

Empirical validation

Re-training modified networks

- With PSSM input only
- With right-side positions only (predicting H)

Labels	Architecture	Accuracy
Q8	Original PSSM-only	69.23% 69.36%
H / non-H	Right positions only Left positions only	86.60% 80.81%

Conclusions

Saliency maps are helpful at extracting insights from learned models. We showed some ways to apply them to CNNs on the SPPS problem and arrived at two main findings: 1) PSSM input is much more valuable than one-hot amino acids, 2) the prediction of α -helices relies more on future amino acids (right side). We have tested the findings on modified CNN architectures.

References

- [1] J. Lanchantin, R. Singh, B. Wang, and Y. Qi, *Deep Motif Dashboard: Visualizing and Understanding Genomic Sequences Using Deep Neural Networks*, arXiv:1608.03644, 2016.
- Saliency map image:** G. Montavon, S. Lapuschkin, A. Binder, W. Samek, & K. R. Müller. *Explaining nonlinear classification decisions with deep Taylor decomposition*. Pattern Recognition, 2017. <https://doi.org/10.1016/j.patcog.2016.11.008>
- 1D CNN image:** J. Zhou, O. Troyanskaya, *Supervised Convolutional GSN for Protein Secondary Structure Prediction*. ICML 2014
- Protein structures image:** Jeremy Conn (Creative Commons Attribution-NonCommercial-ShareAlike 3.0 Unported License) <http://www.clearbiology.com/about/>

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