The elaboration of a ***theoretical framework*** for the concurrent ***interpretation of*** various ***neural network*** approaches with the aim of ***identifying relevant features*** in the specific field of bioinformatics

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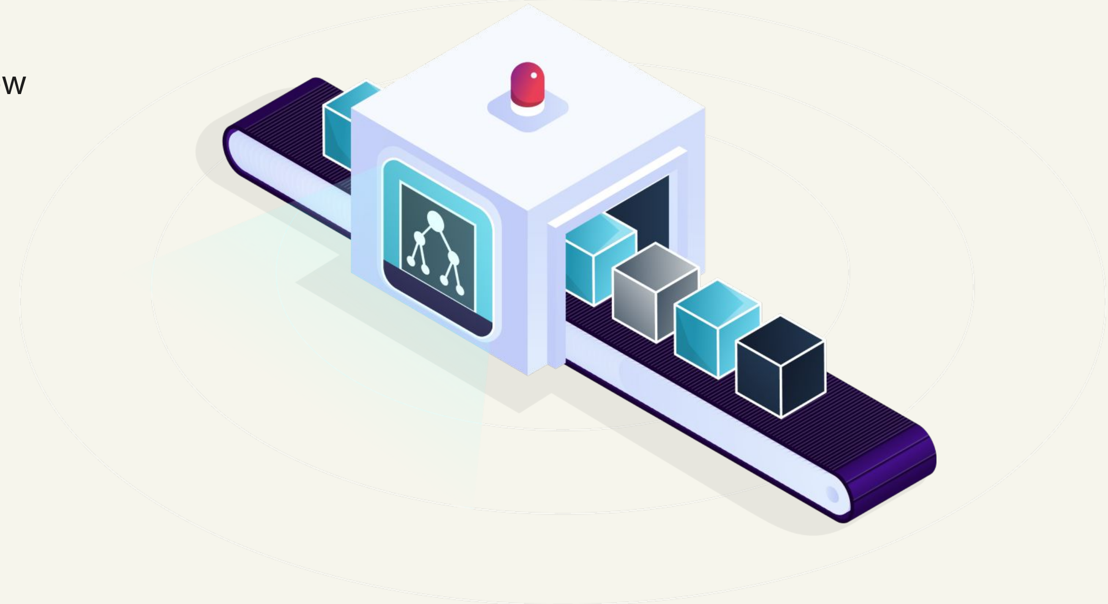
Outline

- Literature & Z-DNA problem overview
- Goals of the research
- The strong Models
- XAI methods
- Interpretation Pipeline
- Feature Extraction Process
- Results
- Conclusion
- References



Explainable AI

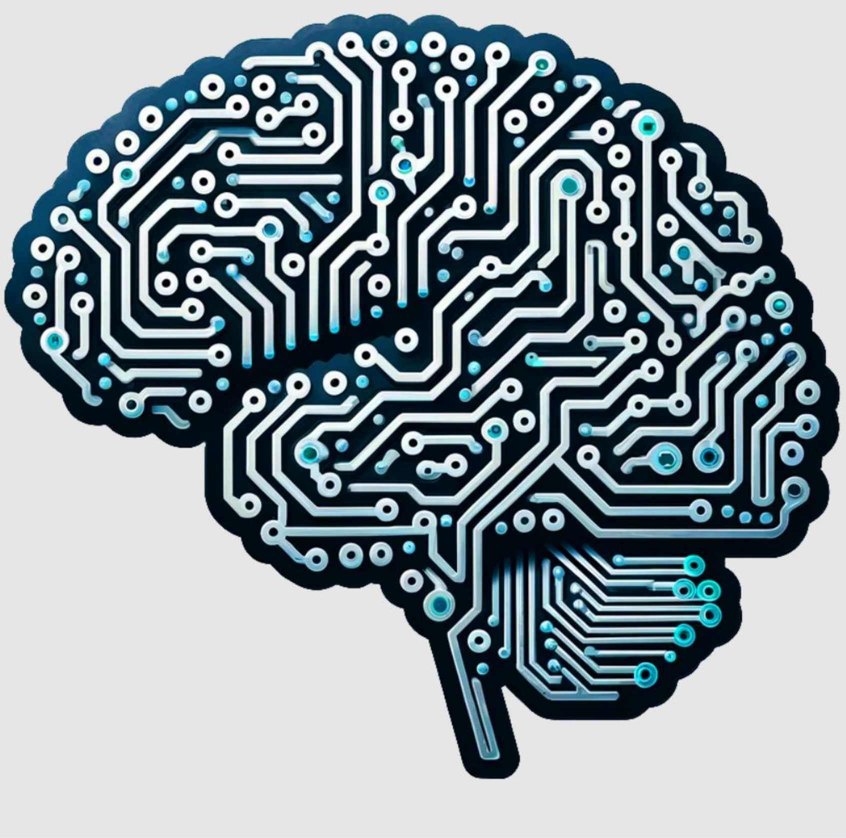
Reasoning behind the predictions:

- understandable
- transparent

Main terms: *Explainability and Interpretability*

Further reading:

- ^ Mihály, Héder (2023). "Explainable AI: A Brief History of the Concept" (PDF). *ERCIM News* (134): 9–10.
- Longo, Luca; et al. (2024). "Explainable Artificial Intelligence (XAI) 2.0: A manifesto of open challenges and interdisciplinary research directions". *Information Fusion*. **106**. doi:10.1016/j.inffus.2024.102301.

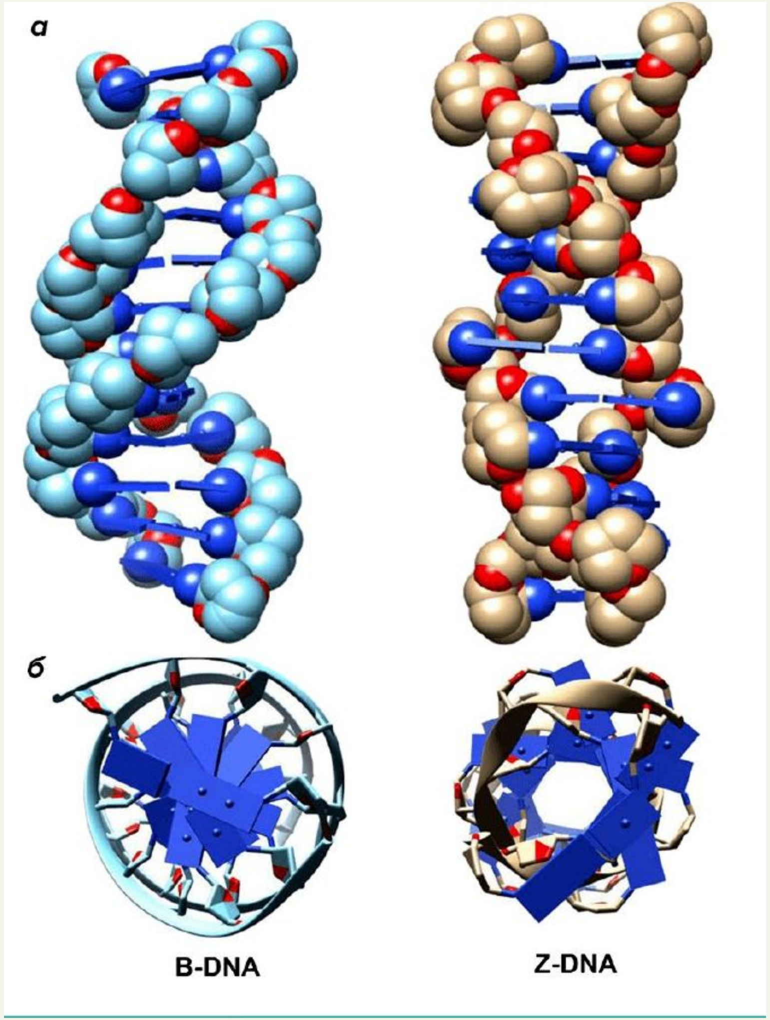


Z-DNA

- Was first found in 1979
- **Left-handed** double helical structure (the helix **winds to the left** in a zigzag pattern)
- Was linked to both cancer and Alzheimer's Disease
- Still **remains a mystery**

Integration of omics data into DL →

→ discover important associations



Goals

Global

- Create a ***flexible framework*** suitable for omics data in genomic problems that ***locates biological dependencies determined by neural network***

Z-DNA Case

- Develop a *strong DL model* for Z-DNA identification
- Extract the *relevant omics features* (biological significance)

Strong Models

- *Indicate the presence of Z-DNA in genome interval*
- *high quality metrics and strong prediction power*

GraphMZC

ROC-AUC = 0.958
F1 = 0.81

ConvMZC

ROC-AUC = 0.979
F1 = 0.88

Strong Models

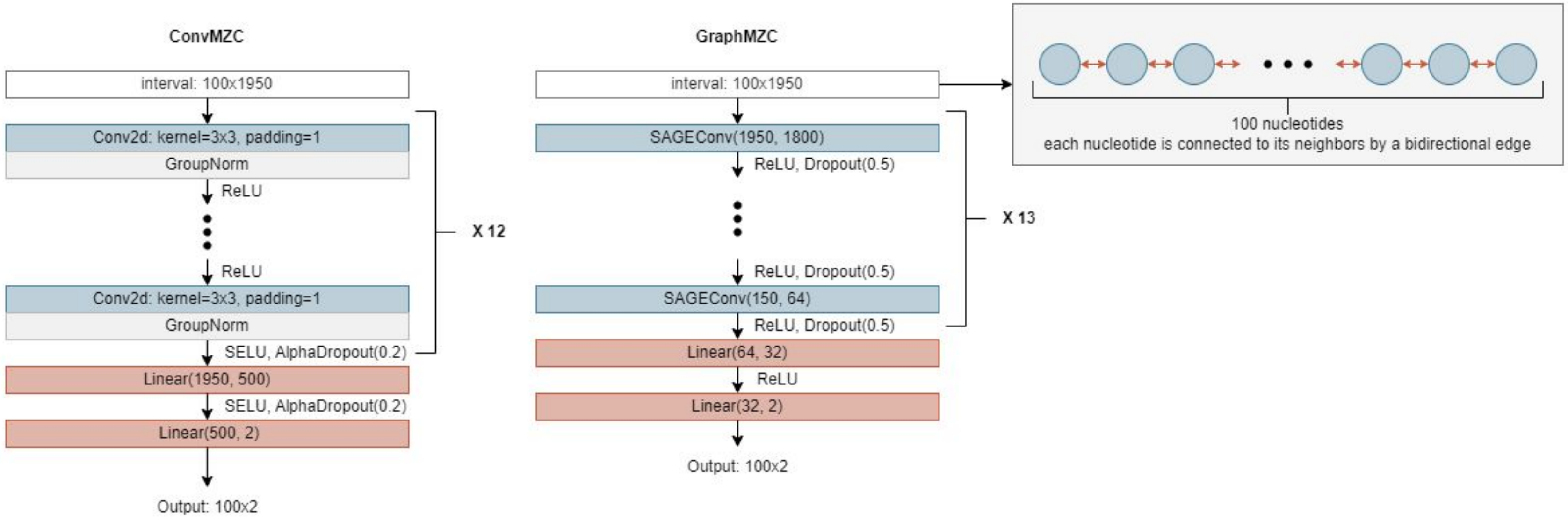


Fig. 3. Architectures of best-performing convolutional and graph models for ZDNA classification task: (A) ConvMZC; (B) GraphMZC

XAI Methods

- *Gradient methods* and other *closely connected techniques* - ***theoretical robustness***
- Accuracy and faithfulness ***required for research in genomics***.

Integrated Gradients

InputXGradients

Guided Backpropagation

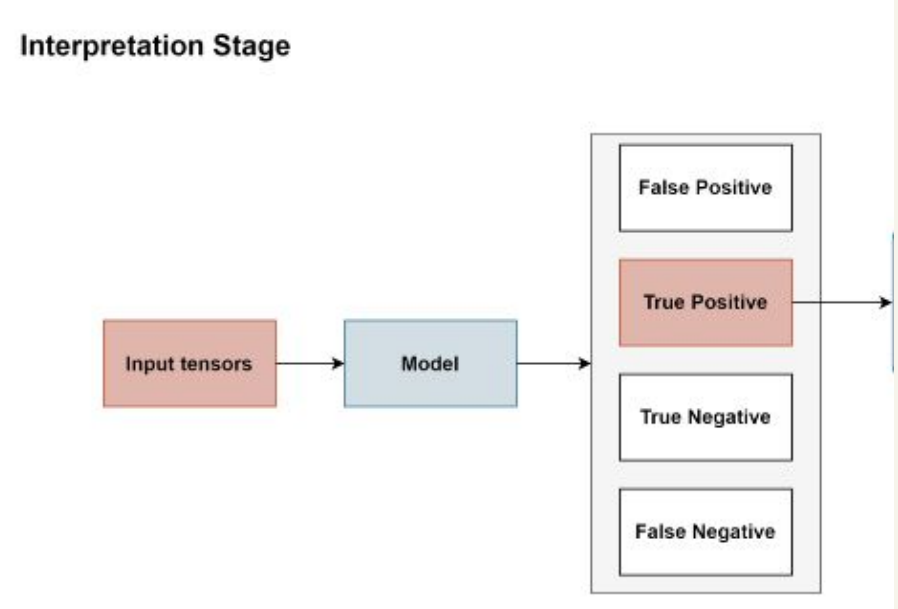
Deconvolution

GNNExplainer

Saliency

Interpretation Pipeline

1. *Choose an input tensor from the interval which contains target*
2. *Get a prediction from well-pretrained model*
3. *Focus on True Positive regions only*

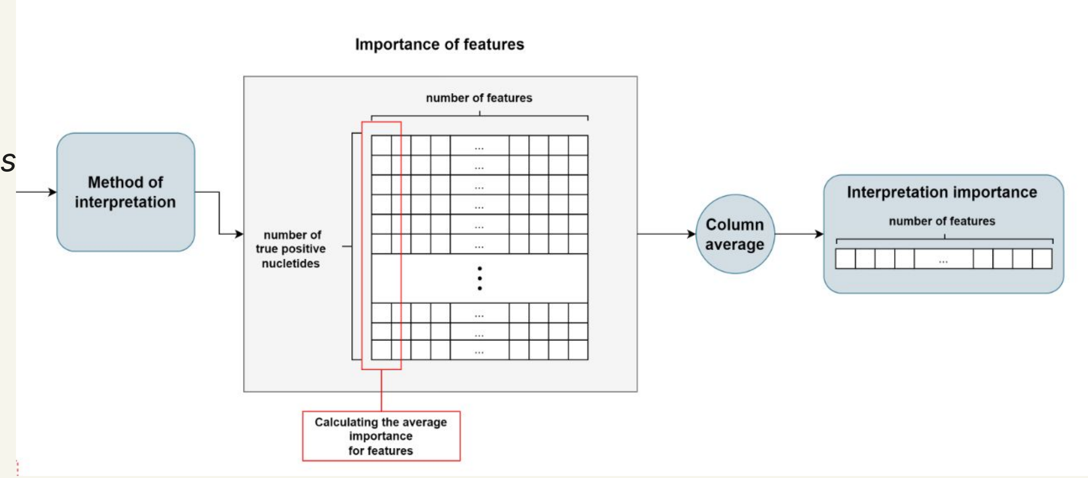


Interpretation Pipeline

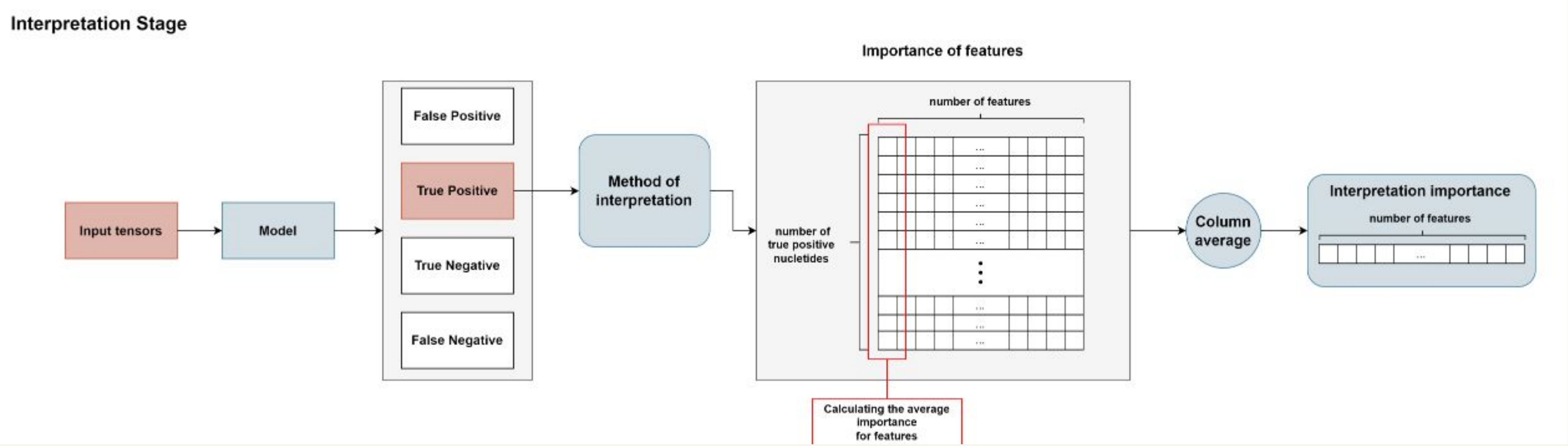
4. Performing interpretation using XAI methods
[number_of_features, 1]

5. Get an average interpretation score for a single algorithm
[number_of_features, 1]
average importance score of each feature

6. Gather results for several XAI methods



Interpretation Pipeline



Feature Extraction

Statistical based

- Ranking Stage

Robust, statistical based

Naive Approach

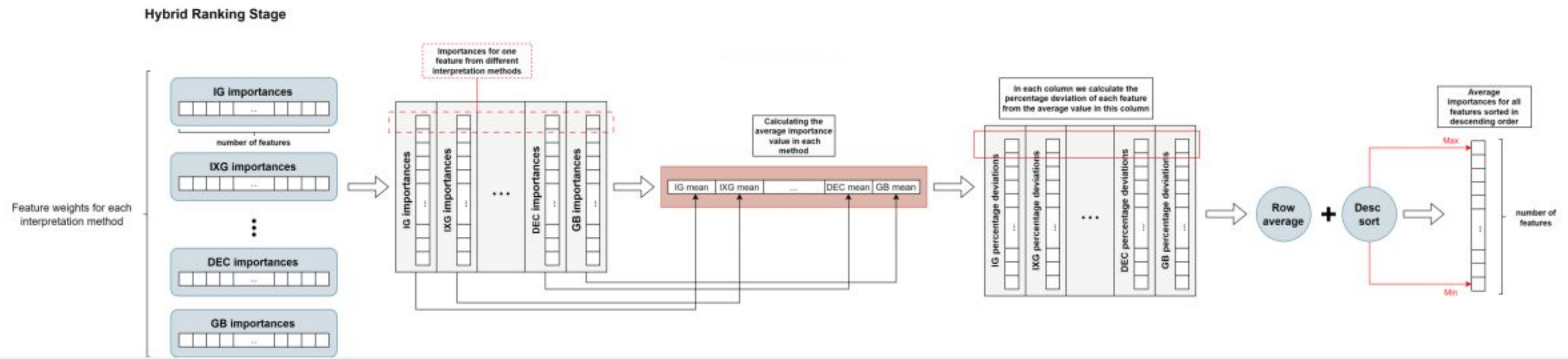
- Sort & intersect
- Extract

Problem: No control

Ranking Stage

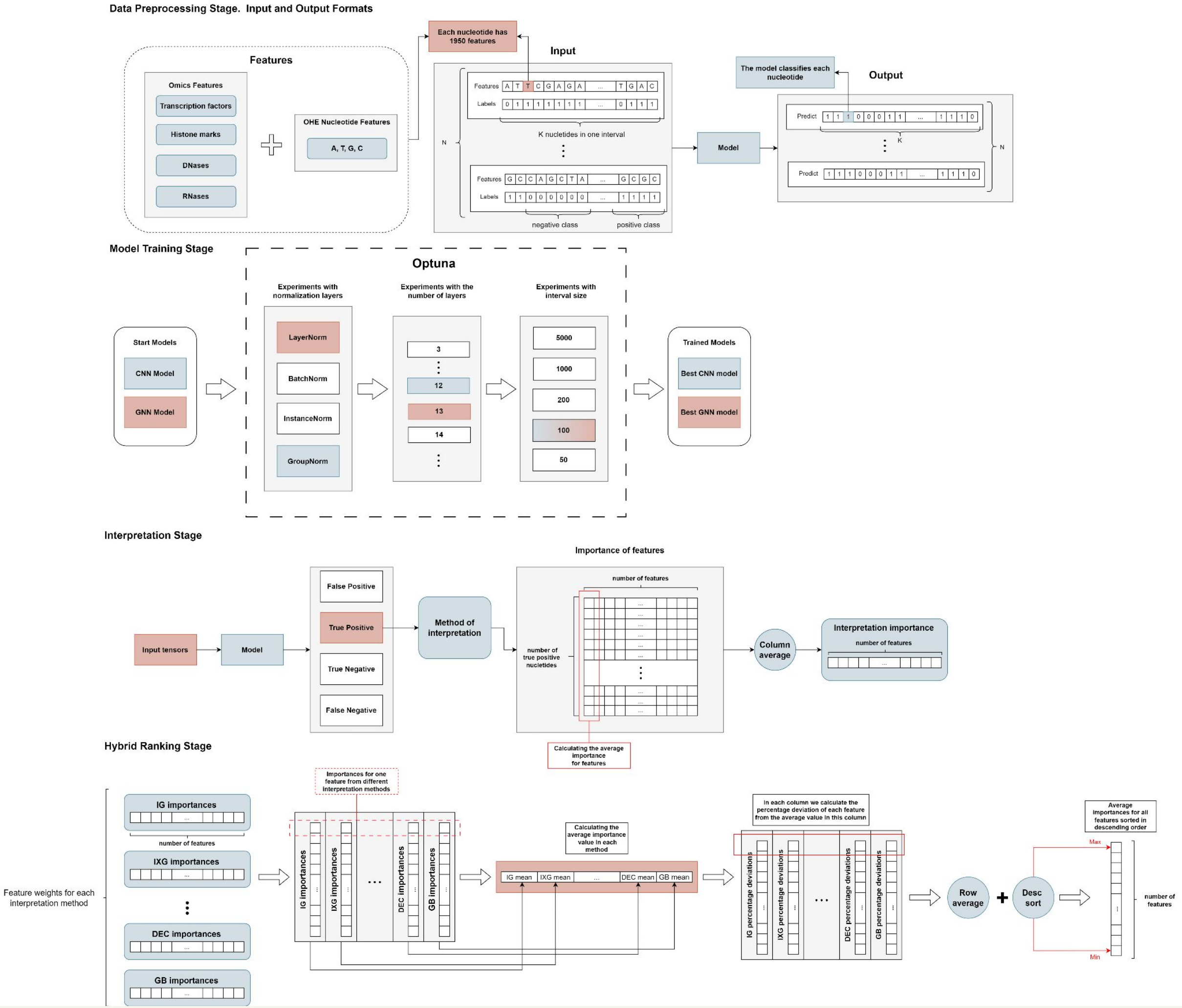
1. *Get the average value of an interpretation tensor for each XAI method.*
2. *For each item in tensor, compute the percentage deviation of its interpretation score from the corresponding mean for each XAI algorithm. So, the interpretation values are transformed into percent deviation scores now.*
3. *Compute the mean percentage deviation of each feature across all XAI methods. As a result, each feature has it's own ranking value.*
4. *Sort the list of ranking values in descending order to get the most important features in the first place.*

Ranking Stage



The Whole Research

Currently we are preparing the paper to publish



Results

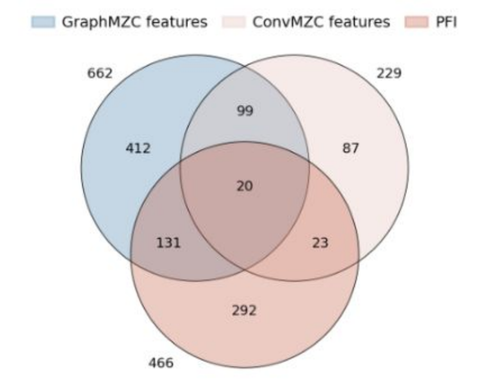
Omics Interpretation Framework

- Interpretation Pipeline + Ranking Stage = ***Omics Interpretation Framework***
- evaluate importance of each feature and extract the most relevant of them
- we provide an implementation of our framework with a user-friendly interface

Results

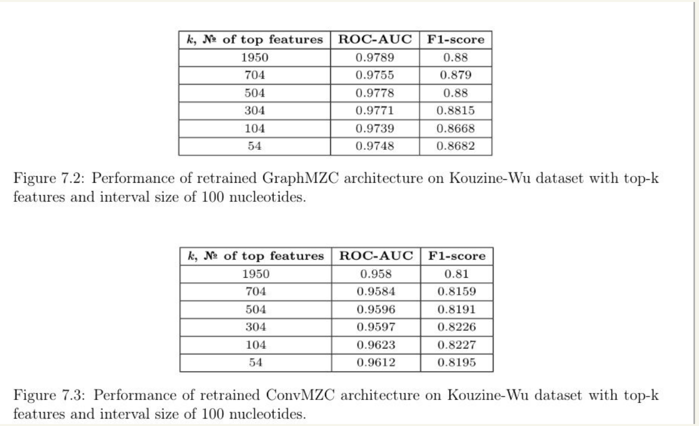
Biological Meaning

- The 20 of 1000 top-extracted omics features



Training Set

- The set suitable for training a high-quality model



k, № of top features	ROC-AUC	F1-score
1950	0.9789	0.88
704	0.9755	0.879
504	0.9778	0.88
304	0.9771	0.8815
104	0.9739	0.8668
54	0.9748	0.8682

Figure 7.2: Performance of retrained GraphMZC architecture on Kouzine-Wu dataset with top-k features and interval size of 100 nucleotides.

k, № of top features	ROC-AUC	F1-score
1950	0.958	0.81
704	0.9584	0.8159
504	0.9596	0.8191
304	0.9597	0.8226
104	0.9623	0.8227
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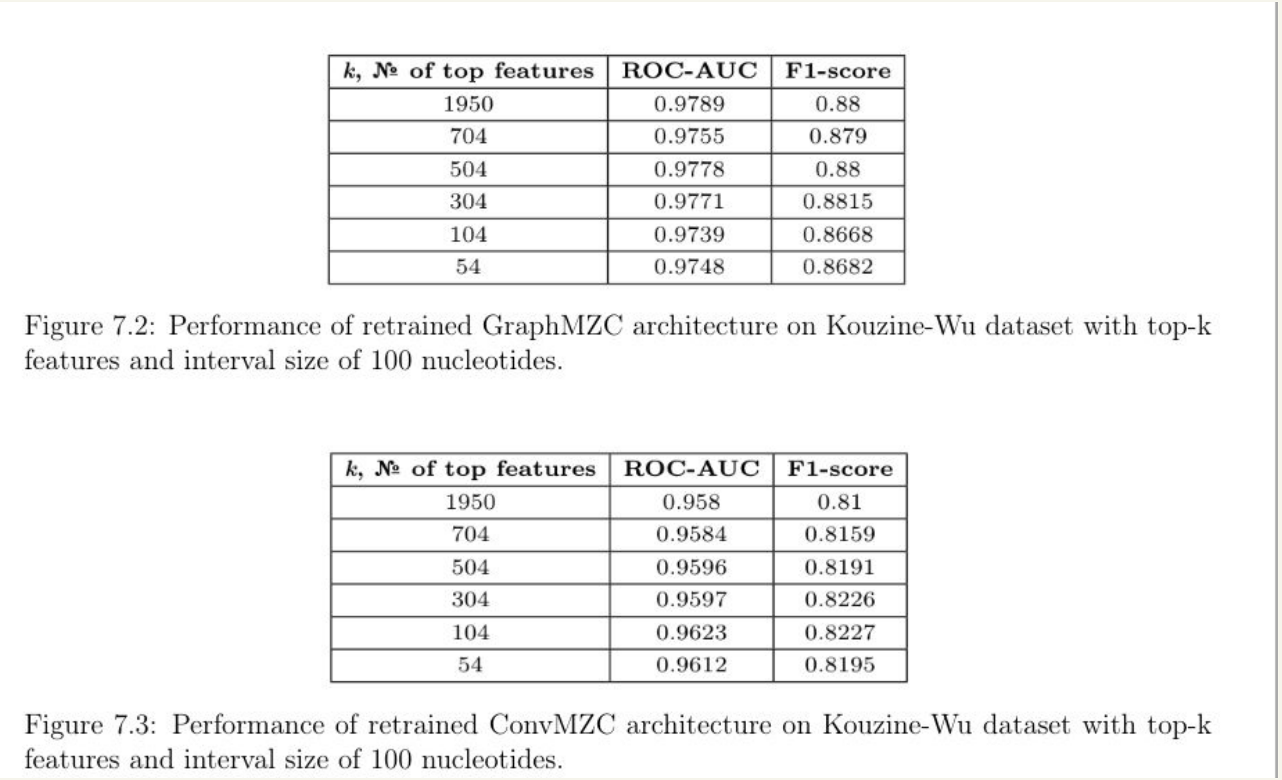
Figure 7.3: Performance of retrained ConvMZC architecture on Kouzine-Wu dataset with top-k features and interval size of 100 nucleotides.

Results

Training Set



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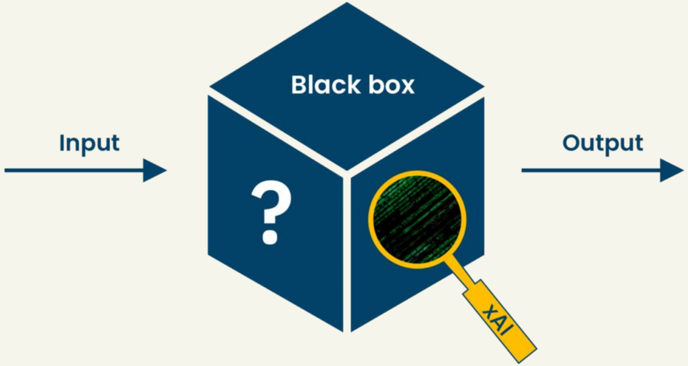
Software Implementation

As a software outcome of our project, we provide ***an implementation of our framework with a user-friendly interface***
(the repository on Github where several folders are available)

1. *CNN model framework folder*
   (runned notebook via link)
2. *GNN model framework folder*
   (runned notebook via link)
3. *Interpretation folder*



Conclusion

In this project we :

1. *Developed the **flexible Omics Interpretation Framework** suitable for omics data in genomic problems that **extracts the most relevant features** and **locates biological dependencies** determined by neural network*
2. *Created the powerful CNN- and GNN-based models **ConvMZC** and **GraphMZC** for Z-DNA identification*
3. ***Applied framework** to Z-DNA problem and **extracted the relevant omics features***

However, there are still more questions to be solved in the explainability of neural networks related to bioinformatics, in particular. We will continue our research on the topic.

References

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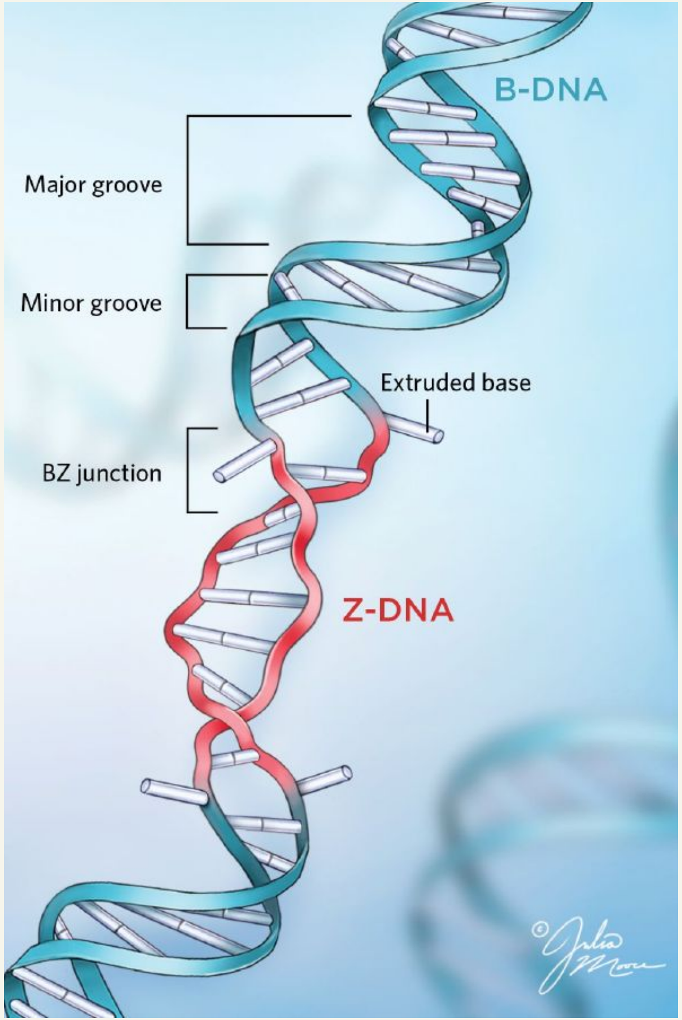

Thank you!

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