UNIVERSITY of VIRGINIA

Deep Motif Dashboard: Visualizing and Understanding Genomic Sequences Using Deep Neural Networks

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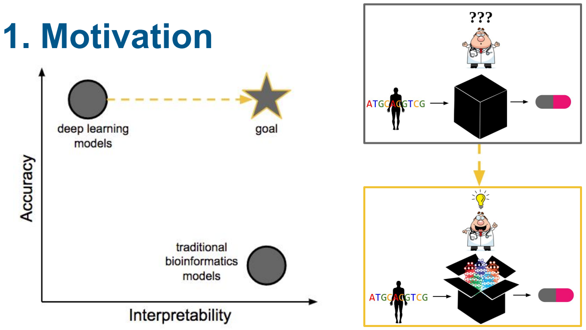
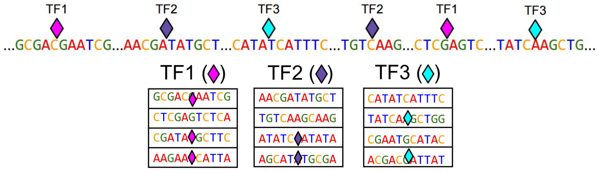
PSB 2017

1. Motivation

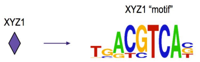


2. Genomic Classification Task

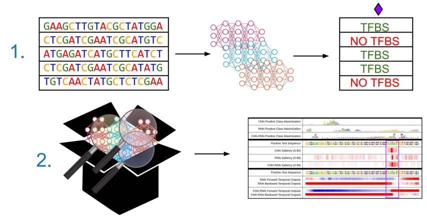
Transcription Factors (TFs) are proteins which bind to DNA and regulate gene expression. Predicting and understanding the **Transcription Factor Binding Sites** (TFBSs), or subsequences where TFs bind is important to biologists.



The binding of a TF is triggered by local sequential patterns within TFBSs, known as "**motifs**". Previous methods predicted TFBSs by constructing motifs using **position weight matrices** which best represented the binding sites.



3. Deep Motif Dashboard



4. NN Models for TFBS Prediction

1. **Convolutional (CNN)**

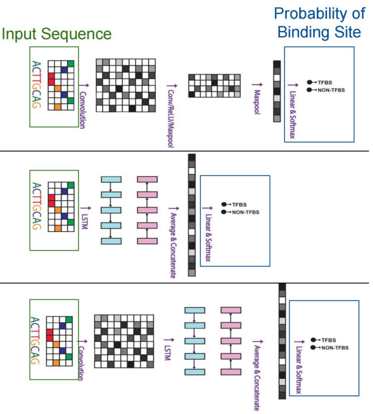
(short local patterns, or motifs)

2. **Recurrent (RNN)**

(long term dependencies)

3. **Convolutional-Recurrent (CNN-RNN)**

(long term dependencies among motifs)

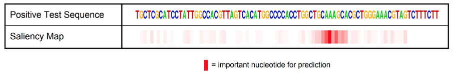


5. Visualization Methods

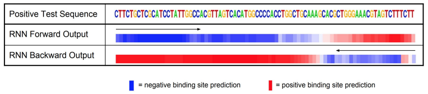
1. Saliency Maps: which nucleotides are most important for classification?

$$S_+(X) \approx w^T X + b = \sum_{i=1}^{|X|} w_i x_i$$

$$w = \left.\frac{\partial S_+}{\partial X}\right|_{X_0} = \text{“saliency map”}$$



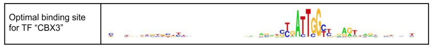
2. Temporal Output Scores: what are the model's predictions at each timestep of the DNA sequence?



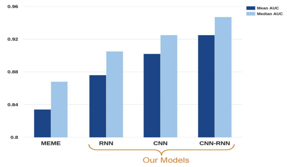
3. Class Optimization: for a particular TF, what does the optimal binding site sequence look like?

$$\arg\max_X S_+(X) + \lambda \|X\|_2^2$$

Where X is the input sequence and the score S_+ is probability of sequence X being a positive binding site

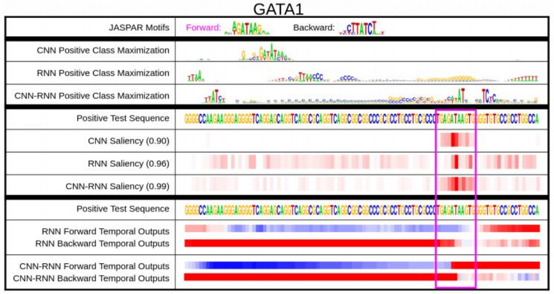


6. Results

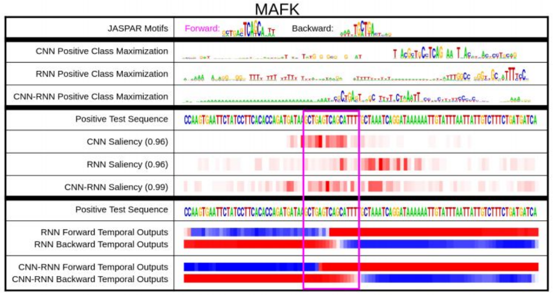


AUC on TFBS dataset from Alipanahi et al., 2015

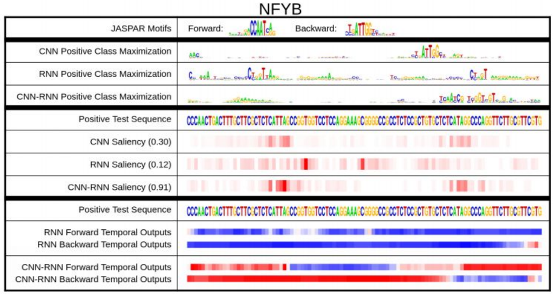
GATA1



MAFK



NFYB


JASPAR Motifs
Forward:
Backward:
CNN Positive Class Maximization
RNN Positive Class Maximization
CNN-RNN Positive Class Maximization
Positive Test Sequence
CNN Saliency (0.30)
RNN Saliency (0.12)
CNN-RNN Saliency (0.91)
Positive Test Sequence
RNN Forward Temporal Outputs
RNN Backward Temporal Outputs
CNN-RNN Forward Temporal Outputs
CNN-RNN Backward Temporal Outputs