

On Secondary Structure Analysis by Using Formal Grammars and Artificial Neural Networks

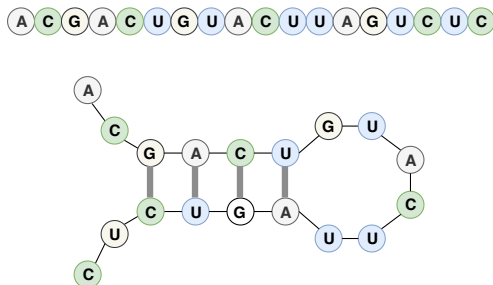
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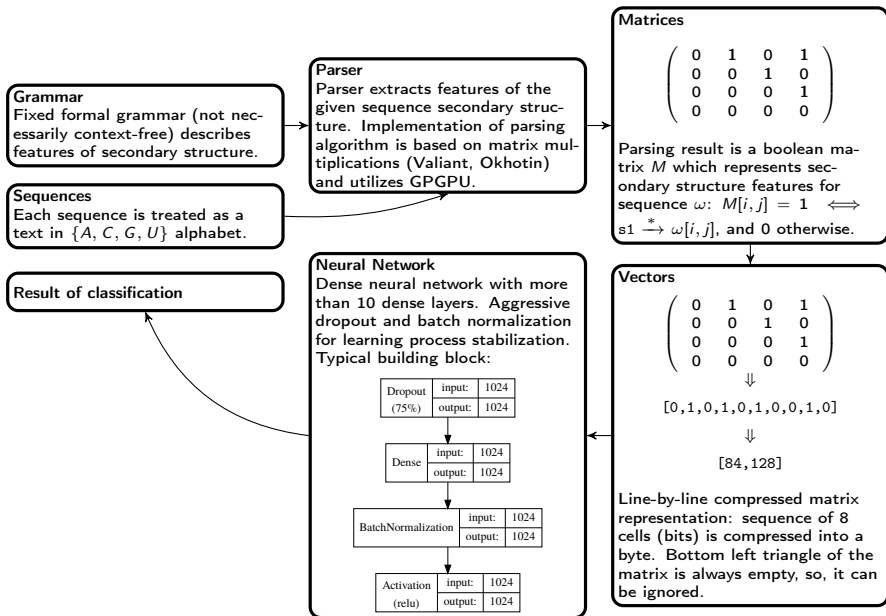
September 6, 2019

Genomic sequences analysis

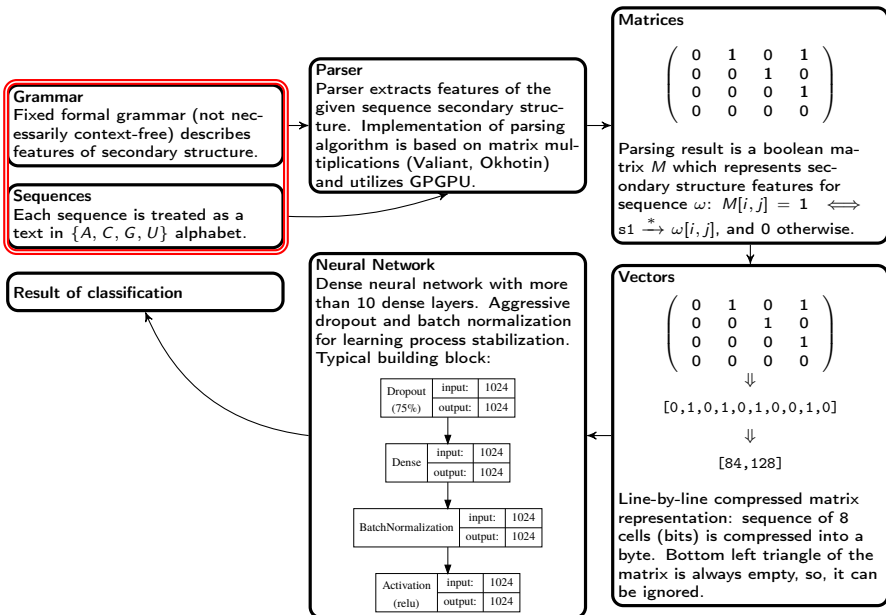
- Problems
 - ▶ Genomic sequences classification
 - ▶ Subsequences detection
 - ▶ Secondary structure prediction
- Secondary structure handling
 - ▶ Covariance models
 - ▶ Hidden Markov Models
 - ▶ Probabilistic grammars
- Probability estimation for noisy data processing



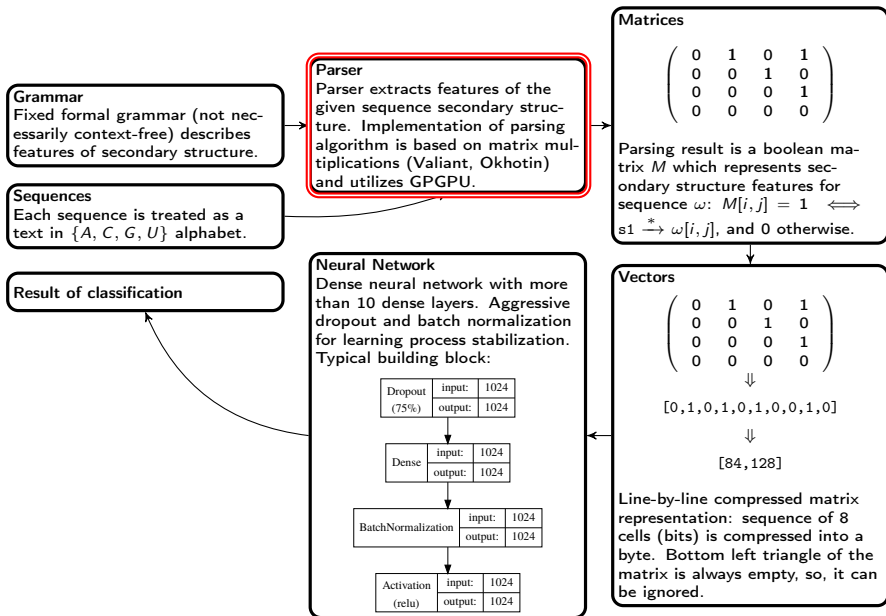
Solution Structure



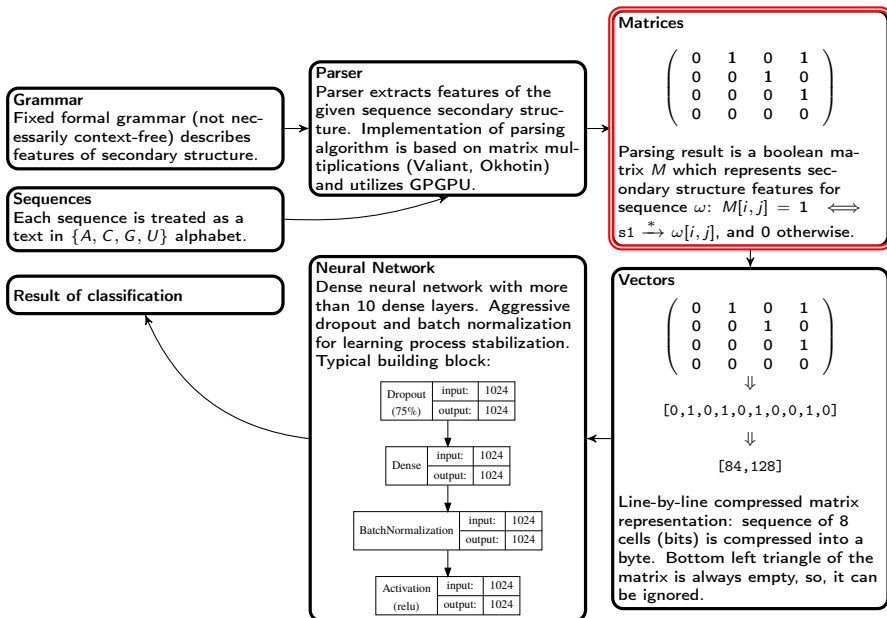
Solution Structure



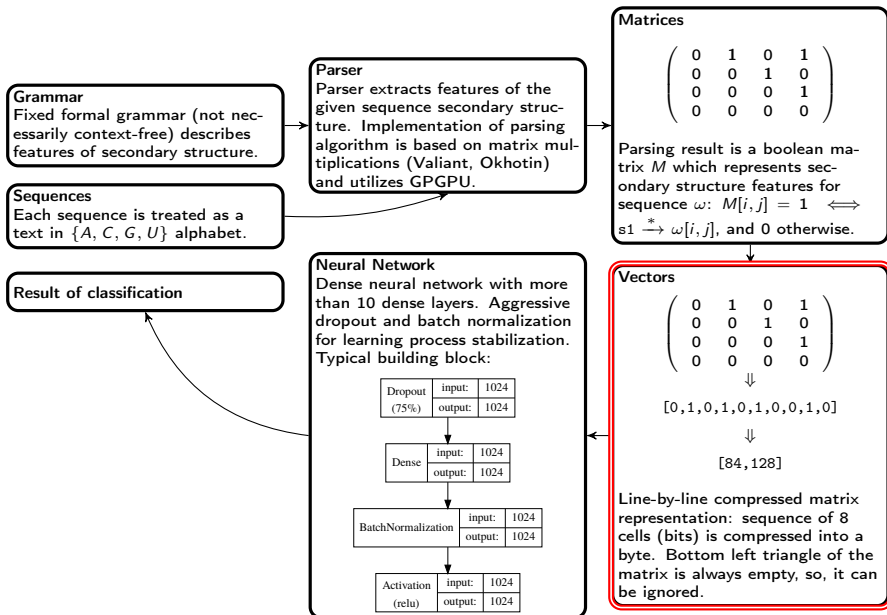
Solution Structure



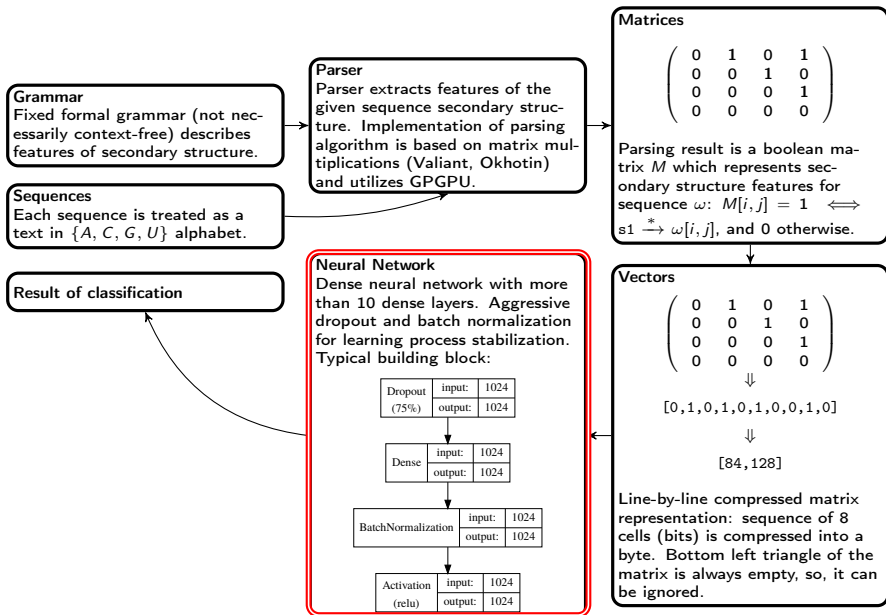
Solution Structure



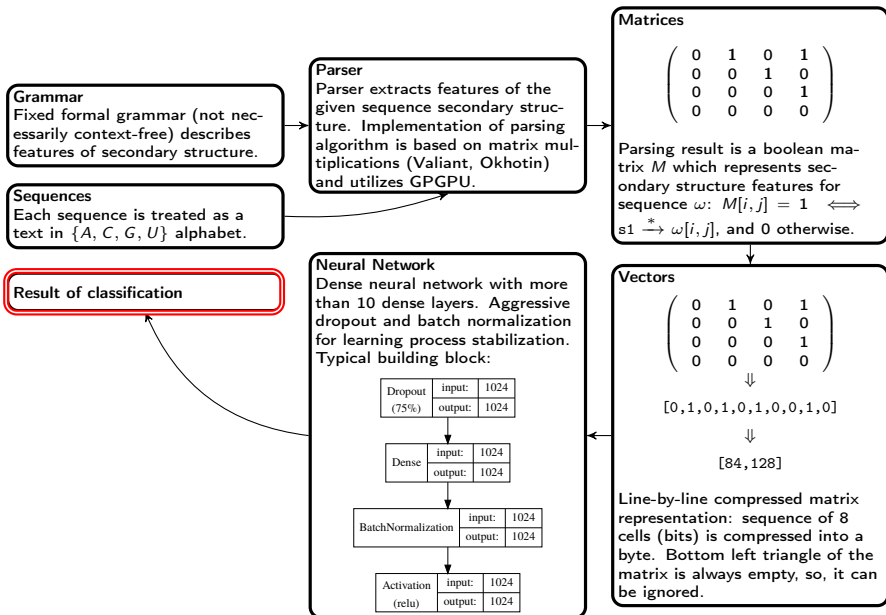
Solution Structure



Solution Structure

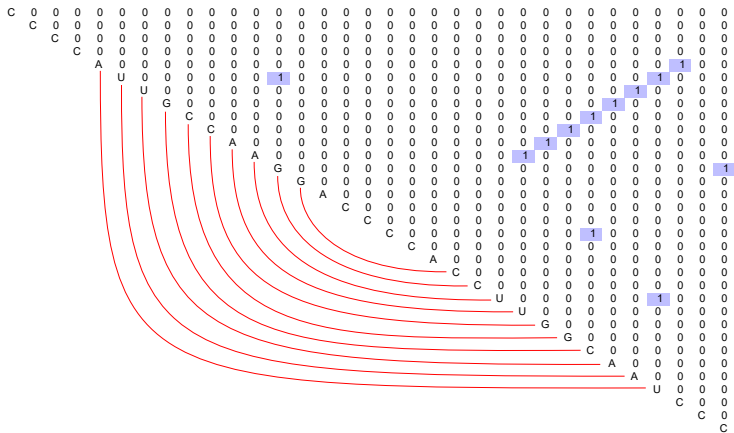


Solution Structure



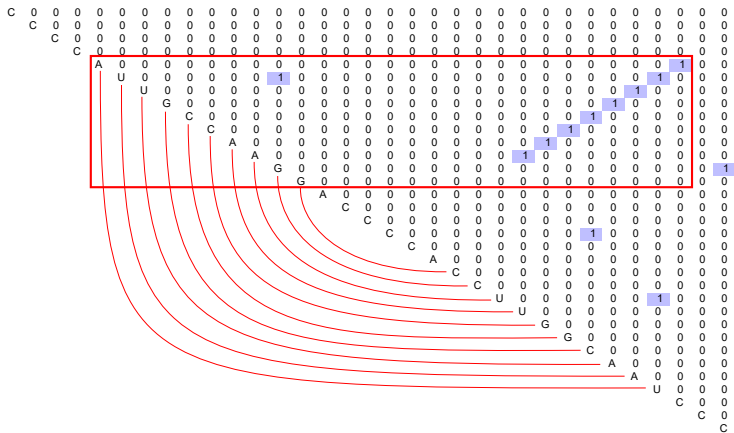
Example

CCCCAUUGCCAAGGACCCCACCUUGGCAAUCCC



Example

CCCCAUUGCCAAGGACCCCACCUUGGCAAUCCC



Data locality preservation

- Represent parsing result as an image
- Use convolutional layers for these images processing
- Compare image- and vector-based networks on the same data

Parsing results representation

Matrices

$$\begin{pmatrix} 0 & 1 & 0 & \dots & 1 \\ 0 & 0 & 1 & \dots & 0 \\ 0 & 0 & 0 & \dots & 1 \\ \dots & \dots & \dots & \dots & \dots \\ 0 & \dots & \dots & \dots & 0 \end{pmatrix}$$

Parsing result is a boolean matrix M which represents secondary structure features for sequence ω :

$M[i, j] = 1 \iff s1 \xrightarrow{*} \omega[i, j]$, and 0 otherwise.

Vectors

$[1, 0, \dots, 1, 1, \dots, 0, \dots, 1, \dots]$

\downarrow

$[84, 128, \dots]$

Line-by-line compressed matrix representation: sequence of 8 cells (bits) is compressed into a byte. Bottom left triangle of the matrix is always empty, so can be ignored. Requires the equal length of the input sequences and breaks the data locality.

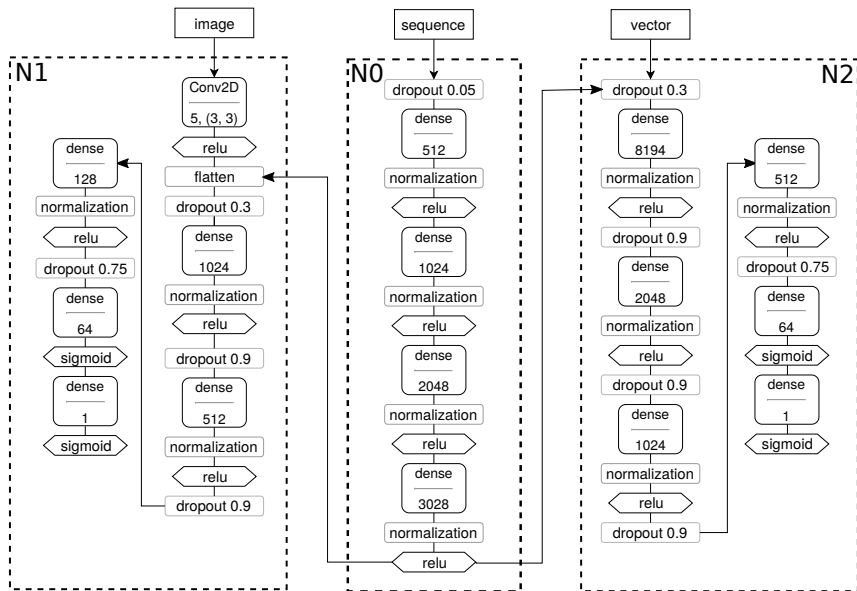
Images



The false bits of the matrix are represented as white pixels and the true bits as black ones. This approach makes it possible to process sequences of different lengths since the images can be transformed to a specified size. Data locality is preserved.

- Create a network which handles initial sequences
- Use two-staged learning
 - ▶ Train network on images or vectors for a given problem
 - ▶ Extend it by several input layers that take the initial nucleotide sequence as an input and convert it to the parsing result

Neural networks



- tRNA sequences analysis tasks
 - ▶ Classification into two classes: eukaryotes and prokaryotes
 - ▶ Classification into four classes: archaea, bacteria, plants and fungi
- Databases
 - ▶ tRNADB-CE
 - ▶ Genomic tRNA database

Results

EP — eukaryotes/prokaryotes task

ABFP — archaea/bacteria/plants/fungi task

Classifier	EP		ABFP	
Approach	Vector-based	Image-based	Vector-based	Image-based
Base model accuracy	94.1%	96.2%	86.7%	93.3%
Extended model accuracy	97.5%	97.8%	96.2%	95.7%
Samples for train:valid:test	20000:5000:10000 (57%:14%:29%)		8000:1000:3000 (67%:8%:25%)	

Results

EP — eukaryotes/prokaryotes task

ABFP — archaea/bacteria/plants/fungi task

Classifier	Class	Vector-based approach		Image-based approach	
		precision	recall	precision	recall
EP	prokaryotic	95.8%	99.4%	96.2%	99.4%
	eukaryotic	99.4%	95.6%	99.4%	99.5%
ABFP	archaeal	91.1%	99.2%	91.6%	98.5%
	bacterial	96.6%	95.1%	95.2%	95.5%
	fungi	98.5%	94.9%	97.5%	94.3%
	plant	99.4%	95.7%	99.2%	94.7%

Conclusion

- The modifications of our approach for biological sequences analysis were implemented
 - ▶ Parsing result in a form of image can be handled by convolutional layers
 - ▶ The parsing step can be removed from the trained model use which allows to run models on the original RNA sequences
- These modification improve the quality of the solution
- The improved version is applicable for real-world problems

- Other RNA sequences analysis tasks
 - ▶ 16s rRNA classification
 - ▶ Chimeric sequences filtration
- Secondary structure prediction by using generative networks
- The use of deep convolutional networks for secondary structure analysis

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Thanks!