Classification of Thiamine-Repressible Promoters Using a Feed-forward Backpropagation Neural Network

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1. Introduction and Objectives

• *nmt1*, *nmt2*, *bsu1*, *pho4*, *thi4* and *thi9* genes in *Schizosaccharomyces pombe* are essential components of the thiamine biosynthesis pathway (Figure 1)

• Promoters of the genes are thiamine-repressible/thiamine-regulated

•Thi1 is a Cys6 zinc finger transcription factor that positively regulates the expression of all known thiamine-repressible genes

• Thi5, another Cys6 zinc finger protein, also regulates the *nmt1* promoter and may work to regulate the expression of *thi1* as well

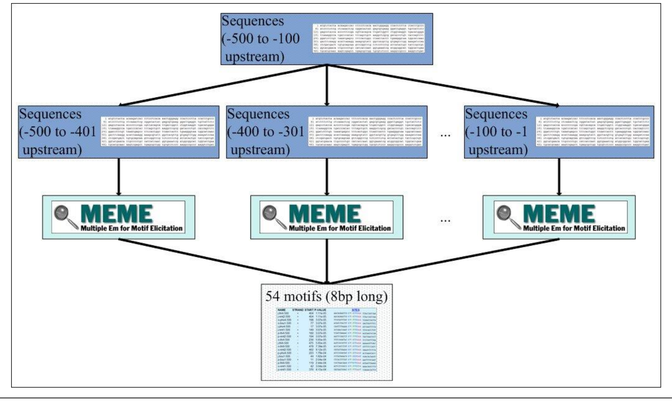
• The sequences for the promoter regions of the thiamine-repressible genes in *S. pombe*, *Schizosaccharomyces japonicus* and *Schizosaccharomyces octosporus* are presumed to be recognized by Thi1 and to thus have some sequence similarities

• The objective of this study is to use a feed-forward backpropagation (FFBP) neural network that may learn to differentiate thiamine-repressible promoter sequences from random, non-thiamine-repressible sequences.

2. Methodology

2.1 Data

• Used sequences from *S. pombe*, *S. japonicus* and *S. octosporus*



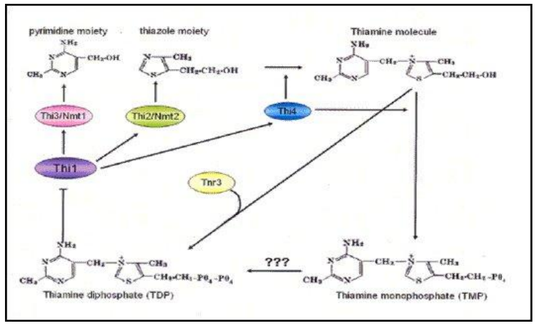


Figure 1. Nmt1, Nmt2 and Thi4 are repressed by the thiamine molecule in the thiamine biosynthesis pathway.

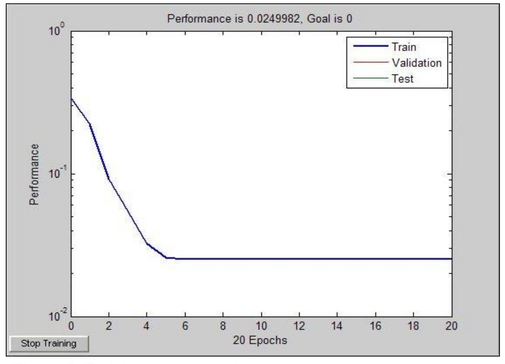


Figure 3. Training of the feed-forward backpropagation neural network using the conjugant gradient method. The neural network was trained 20 times.

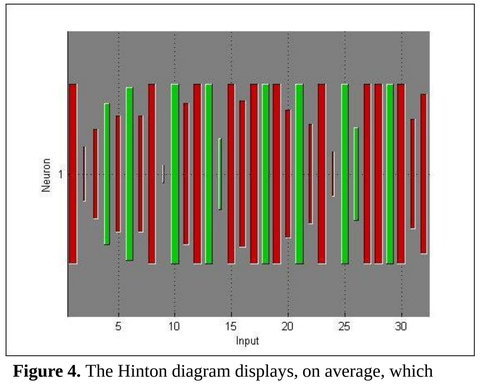


Figure 4. The Hinton diagram displays, on average, which position in the motifs had the most significant weighting in classification (average is based on 100 cycles).

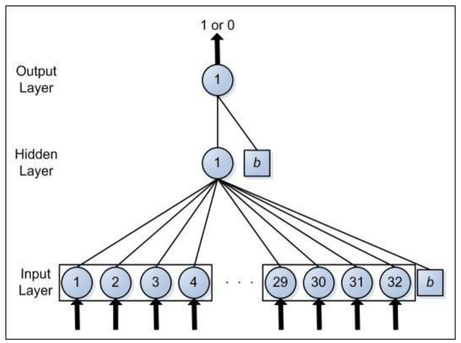


Figure 2. Classification of thiamine-repressible and non-thiamine-repressible promoter sequences by the feed-forward backpropagation neural network. The network has 32 input nodes, one hidden node and one output node. The input layer and hidden layer each have bias weights added to it. The classification output is either 1 (thiamine-repressible) or 0 (non-thiamine-repressible).

2. Methodology

2.2 Feed-forward backpropagation neural network

• Each nucleotide is represented as a set of four binary digits (e.g. A=0100; G=0010; C=0001; and T=1000)

•The feed-forward network consists of two layers - hidden and output layers (Figure 2)

•Weighted inputs are calculated by applying the dot product weight function to inputs

• The net input function calculates the layer's net input by combining its weighted inputs and biases

• Transfer functions transform the output of the layer

• The first and second layers each have a weight as input from the previous layer

• Each layer's weights and biases are initialized by random

3. Results

• Motifs that were consistently classified incorrectly were removed from the dataset

• The best results were achieved when the conjugate gradient method was used for training the neural network

• The neural network was trained 20 times (Figure 3), for 100 cycles

• The input dataset was divided into two-thirds training and one-third validation

• The size of the hidden layer was one neuron

• The best performance of the neural network was 83% accuracy on the validation dataset

• Figure 4 shows which positions in the motifs are significant in classification

4. Conclusion

• The highly conserved DNA binding motifs in thiamine-regulated promoters for the zinc finger transcription factors Thi1 and Thi5 have not yet been identified

• The FFBP neural network can differentiate between thiamine-repressible and non-thiamine-repressible promoter sequences

• The regulatory sequences of the thiamine-repressible promoters may be one of the 30 motifs that were classified correctly by the neural network

• One of the limitations in this study was the small number of known thiamine-regulated genes in the dataset

• A further exploration of this study would be to use longer motifs and to train the neural network with known non-thiamine-repressible promoter sequences