miRNAss: a semi-supervised approach for microRNA prediction

Cristian Yones, Georgina Stegmayer, Diego Milone
Research Institute for Signals, Systems and Computational Intelligence, sinc(i), FICH-UNL, CONICET, Ciudad Universitaria UNL, (3000) Santa Fe, Argentina.

Background

MicroRNA (miRNAs) play essential roles in post-transcriptional gene regulation in animals and plants. Precursors of miRNA (pre-miRNA) are characterized by their hairpins structure. However, a large amount of similar sequences can be folded into this kind of structure. Several existing computational approaches have been developed to predict which hairpins can be pre-miRNAs, but they require a sufficient number of known pre-miRNAs and non pre-miRNAs as learning samples. However, most sequenced genomes have a very small number of miRNAs reported and most of the sequences are unlabeled. The semi-supervised approach proposed in this work takes advantage of these sequences to achieve better prediction rates than state-of-the-art methods [1].

Proposed method

The first step is to build a similarity matrix among the sequences using the euclidean distance between their feature vectors. Then, a vector of labels **y** is defined, having a positive value for known miRNAs, negative for non-miRNAs and zero for unlabeled sequences. Thus, the scores **z** to assign a class to the unlabeled sequences is obtained solving the optimization problem

$$argmin_{\mathbf{z}} \quad \mathbf{z}^T L\, \mathbf{z} + c\,(\mathbf{z}-\mathbf{y})^T C\,(\mathbf{z}-\mathbf{y})$$
$$subject\ to \quad \mathbf{z}\,\mathbf{1} = 0 \quad \text{and} \quad \mathbf{z}^T\mathbf{z} = n$$

where *C* is a diagonal matrix that allows different misclassification cost per sequence, *c* is a regularization parameter and *L* is the normalized Laplacian of the similarity matrix [2]. The first term of the objective function forces similar sequences to have the same labels. The second term penalizes errors in the labeled sequences. The matrix *C* allows to compensate the imbalance in the learning samples, increasing the weights of the minority class (the pre-miRNAs). The first restriction avoids the trivial solution where all sequences have the same label. The second restriction eliminates scaled versions of **z** in the solution space.

Results

To test the prediction power of miRNAss, we have compared it with a similar approach [3] that uses few training examples. Table 1 shows that miRNAss has outperformed it in most cases in the same experiments with human data.

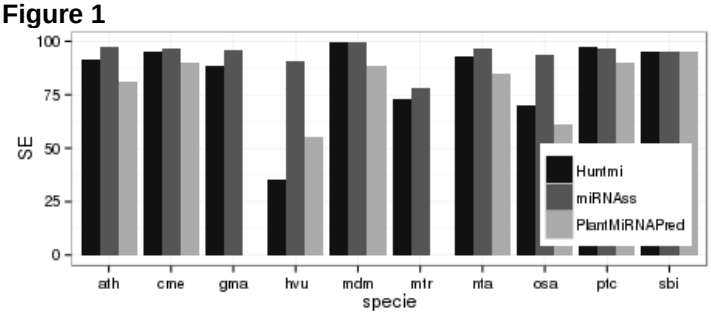
Furthermore, to test miRNAss predictivity in other species, the plant datasets provided by Gudyś *et al*. [4] have been used. In Figure 1 can be seen that, trained with miRNAs from mirBase 17, miRNAss predicted more miRNAs of mirBase 19 than two of the best plant prediction algorithms nowadays: microPlantPred and HuntMi [4].

Table 1

# learning samples	MiRank [3]	miRNAss
1	56.55 %	77.48 %
5	77.85 %	76.41 %
10	79.28 %	82.39 %
15	81.30 %	86.65 %
20	81.48 %	87.42 %
50	82.09 %	89.09 %

Geometric mean of sensibility and specificity with different number of learning samples.

Figure 1



Sensibility for predicting pre-miRNAs included in mirBase 19.

Conclusion

We have presented a new miRNA prediction method called miRNAss. It uses a semi-supervised approach to face the problem of very few training samples within complete genomes. The experiments showed that miRNAss can effectively achieve better results than state-of-the-art methods with very few training samples and that it is versatile enough to be used in genomes of several species.

Reference

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