

Comparison of Statistical Algorithms for Predicting Splice Junctions in mRNA Precursors of Mammalian Genes

Yukiyasu Ogawa

ogawa@sunta.csse.muroran-it.ac.jp

Tomomasa Nagashima

nagasima@csse.muroran-it.ac.jp

Sirajuddin Khawaja

Department of Computer Science and Systems Engineering,
Muroran Institute of Technology,
27-1 Mizumoto-cho, Muroran, Hokkaido 050, Japan

Abstract

It is well known that many eukaryotic genes are interrupted by introns, which are removed from mRNA precursors by the RNA splicing mechanism. While it is well accepted that the consensus sequences of exon-intron boundaries in mRNA precursors are important for specifying splice sites, the signals that govern the excision of introns are not well understood yet, because actual splice site sequences are more or less different from the consensus sequences.

So far several statistical methods for predicting actual splice site sequences (splice junctions)in pre-mRNAs of mammalian genes have been proposed. Shapiro-Senapathy gave a method by weight matrix; Iida has proposed a method based on the quantification analysis(categorical discriminant analysis). He applied his method for analyzing the 3'-splice site sequences as well as 5'-splice site and discussed mutational problems in beta-globin genes.

However, while the statistical methods proposed so far have some ability for predicting the splice site sequences in statistical tests, it seems to be far from sufficient when applied to actual problems i.e., predicting the actual splice junctions in complete mammalian genes.

We propose here a new algorithm which can be applicable to predict actual splice junctions in complete mammalian genes and demonstrate its ability by comparing the predicting performances between the algorithms by ours, Shapiro-Senapathy and Iida.

Our algorithm is described as an extension of the categorical discriminant analysis(CDA) by Iida into the hierarchical form i.e., at the first level, we start from the ordinary categorical discriminant analysis and determine the classes of sample sequences which do not fall into the overlapping region of sample scores. For the samples which fall into the overlapping region of the sample scores are treated in the next level. For these data, we apply the categorical discriminant analysis. This process is repeated till the number of the samples which fall into the overlapping region of sample scores becomes to be negligible.

By applying this algorithm to the 3'-splice junctions as well as 5'- splice junctions of Rat Chymotrypsin B gene, we have obtained fairly well predicting performance compared to Shapiro-Senapaty and Iida. In tab.1, we have presented a comparison of the predicting ability obtained by ours and CDA. As shown in tab.1, our algorithm gives fewer potential sequences(candidate) for the splice junctions than CDA. As for Shapiro-Senapaty algorithm, we have also obtained that the algorithm gave more potential sequences than CDA, that implies our algorithm performs well than CDA and Shapiro-Senapaty method.

As a summary, we have developed the algorithm which acts as a filter for selecting the splice signals among a huge number of unknown sequences. We will discuss the details of our algorithm in the symposium.

<i>No. of Introns</i>	<i>(a)</i>	<i>(b)</i>		
	<i>No. of active seq.</i>	I	II	III
6	165	1	4	2
		2	0	6
		3	1	5
		4	1	4

Table 1: Prediction of authentic 5'-splice site sequences of Rat Chymotrypsin B gene by CDA method(a) and proposed algorithm(b)

- I. level number
- II. No. of authentic splice site sequences
- III. No. of non-authentic splice site sequences

References

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