Riboswitches, RNA conformational switches and prokaryotic gene regulation

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Metabolite-sensing 5' -UTR (untranslated regions) of certain mRNAs, called riboswitches, have been discovered to undergo a conformational change upon ligand-binding, which thereby can up- or down-regulate the corresponding protein product. For instance, upon the binding of nucleotide guanine, the G-box riboswitch in the 5' UTR of the XPT gene of Bacillus subtilis undergoes a conformational change to create a terminator loop, thereby prematurely terminating transcription of the XPT gene. Since XPT is involved in guanine metabolism, this is an example of negative autoregulation by a riboswitch. Although riboswitches have been postulated to be an ancient genetic regulatory system, first developed in bacteria, the remarkable discovery of Cheah et al. in Nature 2007 suggests that eukaryotes may have co-opted riboswitches to control alternative splicing of genes.

Here we describe a new algorithm RNAbor (Freyhult, Moulton, Clote Bioinformatics 2007) which gives information on possible conformational switches by computing the Boltzmann probability of structural neighbors of a given RNA secondary structure. A secondary structure $T$ of a given RNA sequence $s$ is called a $\delta$-neighbor of $S$ if $T$ and $S$ differ by exactly $\delta$ base pairs. RNAbor computes the number ($N^\delta$), the Boltzmann partition function ($Z^\delta$) and the minimum free energy (MFE$^\delta$) and corresponding structure over the collection of all $\delta$-neighbors of $S$. This computation is done simultaneously for all $\delta \leq m$, in run time $O(m^2n^3)$ and memory $O(mn^2)$, where $n$ is the sequence length. We apply RNAbor for the detection of possible RNA conformational switches, and compare RNAbor with an existent switch detection method. We also provide examples of how RNAbor can at times improve the accuracy of secondary structure prediction.