# Riboswitches, RNA conformational switches and prokaryotic gene regulation

Peter Clote

Department of Biology

Courtesy appt. in Computer Science

Boston College

Metabolite-sensing $5'$-UTR (untranlated 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 subtillis* 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 $\mathcal{T}$ of a given RNA sequence $\mathbf{s}$ is called a $\delta$-neighbor of $\mathcal{S}$ if $\mathcal{T}$ and $\mathcal{S}$ differ by exactly $\delta$ base pairs. `RNAbor` computes the number ($\mathbf{N}^\delta$), the Boltzmann partition function ($\mathbf{Z}^\delta$) and the minimum free energy ($\mathrm{MFE}^\delta$) and corresponding structure over the collection of all $\delta$-neighbors of $\mathcal{S}$. This computation is done simultaneously for all $\delta \leq m$, in run time $O(m^2 n^3)$ 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.