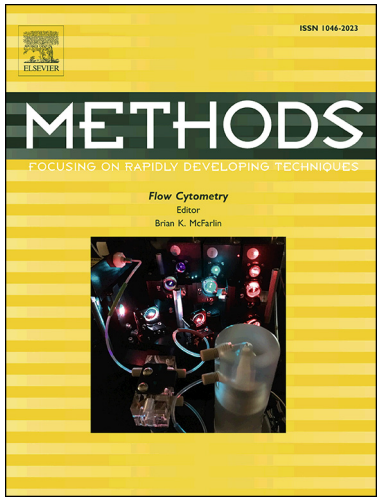

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Efficient computation of co-transcriptional RNA-ligand interaction dynamics

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Abstract

Riboswitches form an abundant class of cis-regulatory RNA elements that mediate gene expression by binding a small metabolite. For synthetic biology applications, they are becoming cheap and accessible systems for selectively triggering transcription or translation of downstream genes. Many riboswitches are kinetically controlled, hence knowledge of their co-transcriptional mechanisms is essential. We present here an efficient implementation for analyzing co-transcriptional RNA-ligand interaction dynamics. This approach allows for the first time to model concentration-dependent metabolite binding/unbinding kinetics. We exemplify this novel approach by means of the recently studied I-A 2'-deoxyguanosine (2'dG)-sensing riboswitch from *Mesoplasma florum*.

Keywords: RNA-ligand interaction, RNA dynamics, co-transcriptional folding, energy landscape, riboswitch

1. Background

Riboswitches are cis-acting regulatory RNAs that undergo an allosteric conformational switch upon binding of a cognate metabolite. They have originally been characterized in bacteria, where they are typically located in 5' untranslated regions (5'-UTR) of mRNAs. The regulatory repertoire of procaryotic riboswitches comprises modulation of the expression of adjacent genes by means of transcription termination or translation initiation. Riboswitches typically consist of two domains, an evolutionary conserved aptamer domain that specifically senses a metabolite and a variable expression platform that can form specific RNA structural elements required for modulation of gene expression [26, 13]. The binary characteristics of a transcriptional ribsowitch, being either premature transcription termination (OFF-switch) or continuation (ON-switch) is triggered by metabolite binding. In this line, aptamer formation, ligand binding and subsequent formation of RNA structures in the expression platform (terminator / anti-terminator) are kinetically controlled co-transcriptional events [32].

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