Conformational dynamics of metabolite-sensing RNAs

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"Riboswitches" are recently discovered metabolite-sensing RNAs that are formed within the untranslated regions of messenger RNAs. When the substrate binds to the metabolite-sensing domain, a structural reorganization of the RNA occurs that unveils (or sometimes masks) a gene-expression signal, often leading to suppression of the production of enzymes that are responsible for the biosynthesis of the detected metabolite. In this way, riboswitches elegantly couple small-molecule recognition with gene regulation in the absence of protein helpers. In this project, it is proposed to study structural dynamics and function of two different biologically relevant riboswitches using single-molecule fluorescence microscopy/ spectroscopy. These RNAs respond to the important enzymatic cofactors TPP and SAM. X-ray structures of both systems have been solved recently, which provide static pictures of the bound ("switched off") states. However, not much is known about the "on" State or the structural transitions that are involved in the switching process. This project focuses on the characterization of the molecular dynamics of tertiary structure formation and the observation of RNA molecular switches in real time at the single-molecule level and shall help to control the factors leading to riboswitch-mediated changes in gene expression.

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