Exploring RNA flexibility through a coase-grained model and its coupling to experimental data

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Abstract

Thanks to the multitude of possible base pairings, RNA molecules are systems capable of adopting different three dimensional structures in response to the environment. Recent studies have shown how their energy landscape is characterized by the presence of several funnels, making their behavior depart from the simple paradigm of a "folding funnel" that has been successfully applied to globular proteins. The study of the folding and of the large conformational transformations of RNA molecules is therefore essential to understand their interplay in the cell. Atomistic studies are limited in this respect as they can only observe relatively local transformations, the typical size of the systems being too big to address more large-scale questions. The HiRE-RNA coarse-grained model has been developed in recent years to overcome the limitations of atomistic descriptions and to complement them. Its aim is the study the large scale rearrangements of non coding RNAs, to predict folding at least for small systems, to study the interconversions between alternative structures and assembly. In this presentation I will present the basic elements of the model together with the most significant applications showing how it is suited to the study of alternative conformations and rugged landscapes. Given the multitude of possible stable structures for a given sequence, the importance of the environment for the structure that the system adopts in a specific circumstance becomes key. Even with the best modeling tools available, the information coming experiments is essential to understand what particular structure is adopted, and the coupling between models and experiments is more relevant than ever. I will discuss how coarse-grained modeling is particularly apt at incorporating data from experiments and experimental conditions and present our work in progress on how to couple HiRE-RNA to experiments. In particular I will focus on how to incorporate local constraints such as base-paring, the recent developments on how to account for pH, the basis on how to incorporate SAXS data, possible strategies to account for chemical probing and I will present interactive simulations, giving the chance to the user to directly stir the simulation to explore specific structures.

Keywords: RNA, coarse, grain, HiRE, RNA, SAXS, pH

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