Improving the performance of the RNA AMBER force field by tuning hydrogen bonding interactions

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Abstract

I will introduce our efforts to improve the pair-additive AMBER force field (ff) for RNA. I will explain the limits of the currently used ff form, which we try to circumvent by adding a new simple ff term for tuning of H-bonding called gHBfix. gHBfix is orthogonal to the basic ff terms and can thus improve the simulation performance without causing undesired side effects. I will show that several recently published RNA ff versions have been over-fitted to A-form RNA (based on NMR data on RNA tetranucleotides) and are not suitable for simulations of folded RNAs. Then I will briefly describe our efforts to use MD simulations to capture structural dynamics and partial disorder at protein-RNA interfaces, extending the picture provided by ensemble-averaging experimental methods. Structural dynamics may allow the proteins to read simultaneously multiple RNA targets, to scan the RNA chain, and to de-couple affinity of binding from catalytic activity via transiently populated but highly reactive conformations. Finally, I will briefly comment on limitations of collective-variable-based enhance-sampling methods to capture the essence of folding of DNA quadruplex molecules.

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