Title:	Understanding the binding specificities of mRNA targets by the mammalian Quaking protein
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Abstract:	Mammalian Quaking (QKI) protein, a member of STAR family of proteins is a mRNA-binding protein, which post-transcriptionally modulates the target RNA. QKI protein possesses a maxi-KH domain composed of single heterogeneous nuclear ribonucleoprotein K homology (KH) domain and C-terminal QUA2 domain, that binds a sequence-specific QKI RNA recognition element (QRE), CUAAC. To understand the binding specificities for different mRNA sequences of the KH-QUA2 domain of QKI protein, we introduced point mutations at different positions in the QRE resulting in twelve different mRNA sequences with single nucleotide change. We carried out long unbiased molecular dynamics simulations using two different sets of recently updated forcefield parameters: AMBERff14SB+RNA$_{\chi}$OL3 and CHARMM36 (with CMAP correction). We analyzed the changes in intermolecular dynamics as a result of mutation. Our results show that AMBER forcefields performed better to model the interactions between mRNA and protein. We also calculated the binding affinities of different mRNA sequences and found that the relative order correlates to the reported experimental studies. Our study shows that the favorable binding with the formation of stable complex will occur when there is an increase of the total intermolecular contacts between mRNA and protein, but without the loss of native contacts within the KH-QUA domain.
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