Design of Hepatitus C inhibitors targeting RNA: Is simulation up to the challenge?

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Biomolecular simulation methods have been developed over the past 40 years and are now routinely applied on nanosecond to microsecond time scales to study protein folding, for structure prediction, to characterize material properties, and also in computer-aided drug design. This has been facilitated by access to large-scale and national computational resources. However, greater power brings new challenges for example by exposing hidden problems in the models and difficulties in handling and analyzing the resulting data. Research in our lab aims to refine RNA structure and characterize drug-RNA interaction through simulation. RNA is a particularly important biomolecule due to its significant roles in protein translation and expression, regulation of genes, and catalysis, among other emerging functional roles. Simulation of RNA is tricky because RNA is a polyelectrolyte that can adopt many different conformations, each of which is very sensitive to the surroundings of water, salt and other potential binders. Unfortunately, we are not yet at the point where we can predict and refine RNA structure through simulation. This will be discussed in the context of large-scale simulation of many RNA structures and structural motifs and recent experience in drug-design based on a novel structure of a drug-bound IRES Hepatitis C virus RNA.