Multi-scale modelling for RNA structures: a challenge

Julie Bernauer

RNA molecules are involved in most biological processes and are therefore therapeutic targets of interest. The prediction of their 3D structures and interactions at different levels of representation is key in understanding their function.

In silico studies and simulations mainly use physics-based potentials and techniques that could give structural insights in atomic detail but with very limited accuracy, particularly in predicting native like molecular structures of RNA molecules and their complexes.

Recent efforts in RNA structure prediction techniques have shown that parameterized energy functions and knowledge-based techniques largely improve the accuracy of structure prediction.

In this our project, we showed that distance-based RNA KB potentials could be build both in an atomic and coarse-grained setting using mixture models. The obtained potential performed better than the existing tools. We also showed that different knowledge-based strategies (mixture models, machine learning or hybrid potential functions) improve the predictions.

Due to the ruggedness of KB potentials, it is unclear how these will perform in minimizing structure and sampling different conformations, especially in a hierarchical setting. The junction problem should thus be addressed to study large RNA molecules.

We hope our recent models using biogeometry, statistics and machine learning will allow to improve RNA structure modeling, possibly dynamics simulations, junction characterization and protein-RNA interactions.