

Ribonucleic acid (RNA) is present in all living cells. We all learned in high school about three types of RNAs: messenger RNA (mRNA), transfer RNA (tRNA) and ribosomal RNA (rRNA) and that was all what we were supposed to know! However, this very simplified view of RNAs has been changed by a discovery of RNAs that can perform catalytic reactions. We call these RNAs ribozymes and for the discovery, Sidney Altman and Thomas Cech received the Nobel Prize in 1989.

Today we know that RNAs not only serve as an intermediary between DNA and protein, but also are able to perform catalytic reactions and are involved in a variety of processes in cells, such as translation, transcription, gene expression and more!

The more we learn about RNAs, the more we discover new ways how RNAs could be potentially used in medicine, biotechnology, and basic science. For example, riboswitches are a unique feature of bacteria, and therefore have become a promising target for antibacterial treatment. Fluorescence riboswitches combined with "interchangeable" aptamer domains that can bind various ligands are becoming an important tool in basic science for monitoring metabolites in living cells. It can be a revolution similar to the discovery of the GFP protein (Nobel Prize in 2008). MicroRNAs are used in medicine in new therapies and in science to silence genes of interest. Scientists are investigating CRISP-Cas9 – a prokaryotic immune system - as a tool of genome editing. It seems to be clear that long noncoding RNA are involved in the cancer development. Many questions related to RNA viruses, such as HIV and Influenza, remain to be addressed. We do not the function of newly discovered circular RNAs. Moreover, RNA seems to be ideal for creating nanorobots - biodevices that can be programmed, for example, to detect microRNA related to human diseases in the blood etc.

The world of RNA is very interesting and the knowledge about RNA gives us great opportunities. However, it is not possible to take advantage of these opportunities without the understanding of the structures of these molecules. The proposed project can make this investigation of RNA structures much more efficient.

In order to know the spatial structure of RNA, researchers can use experimental techniques, such as biocrystallography or nuclear magnetic resonance spectroscopy. The experimental techniques, however, are tedious, expensive and require specialized equipment. An alternative to experimental techniques are computer modeling methods. Computer modeling methods are not as accurate as mentioned above experimental methods, but can be successfully used to investigate the function and the mechanism of action of RNA molecules. Unfortunately, despite the fact that these methods are being continuously improved, they often cannot successfully be used to predict the structure of RNA. In the proposed project, we want to take advantage of the observation that RNAs that are homologs fold into the same structure. We want to test if based on modeling of various RNA sequences of the same family, we can improve the process of selecting the final model that can serve as a model of structure for the given sequence. Our preliminary study showed, that the proposed methodology can be successfully used for modeling RNA. We postulate that the new method can significantly improve the RNA structure prediction, and thus become a valuable tool used for studies of the sequence - structure - function of RNA molecules and help us better understand the fascinating world of RNAs!