Ribonucleic acid (RNA) molecules play pivotal roles in living organisms., making them an emerging therapeutic target for new drugs. Well known examples are the RNA pockets of bacterial ribosomes, which are the targets for most known antibiotics. Recently, other RNAs - bacterial riboswitches - have been attracting the attention of scientists. It has been shown that these RNA molecules can also be an attractive target for new antibacterial therapies. Also, viral RNAs, such as HIV-1 and recently also SARS-CoV-2, raise the hopes of scientists for new antiviral drugs.

While the methodology for studying protein interactions with small-molecule ligands is well developed and widely used, analogous solutions dedicated to studying ligand interactions with RNAs do not exist or are in the early stages of development. The lack of such methodology partly translates into a crisis in the development of new antimicrobial and antiviral therapies. Despite a relatively large number of available antibiotics, for several decades, there has been a growing resistance to the drugs used in therapy. Simultaneously, not a single class of new antibiotics has been introduced to the treatment since the 1980s. How helpless humanity is with new viruses has been shown by the recent COVID-19 pandemic caused by SARS-CoV-2 infections. The development of bioinformatic methods focused on RNA is crucial to accelerate research on new small-molecule antimicrobial and antiviral drugs targeting RNA.

This project aims to understand the preference for the interaction of small-molecule ligands with RNA macromolecules. This knowledge will contribute to the identification of new, potential inhibitors of riboswitches and viral RNAs.

We plan to develop a general method to generate a "preference map" for RNA binding pockets. A computer program will determine which molecular fragments best "fit" the RNA binding pockets. The algorithm will propose similar chemical molecules that ideally fit the pocket of interest, thus having a high probability of forming strong interactions with the selected RNA. Preference maps will also allow us to search the databases of existing molecules. We hypothesize that in such database, we may find a compound that aligns perfectly to the binding preferences of a given RNA.

The expected results of this project will be of great importance for understanding the cellular processes that involve the action of RNA molecules, and in the future, they may find practical use in biotechnology and medicine. Results obtained with the use of the new computational methods will contribute to a better understanding of how RNAs interact with small-molecule ligands.