RNA (ribonucleic acid) is a unique chemical molecule that can function in living organisms in various different ways. On the most basic level of chemical structure, RNA resembles DNA. Like DNA, it is a linear polymer of nucleotide residues, A, C, G, and U, bound together into a sequence, like beads on a string. To a first approximation, RNA looks like a half of a DNA double helix, and exhibits only a few ostensibly small chemical differences. The basic building blocks of DNA and RNA are very similar, only RNA has an extra oxygen atom on its sugar, ribose (which makes it different from deoxyribose in DNA, and explains why the RNA has an R and DNA has a D). Besides, one of its nucleobases in RNA, uracil (U), lacks a small chemical group called methyl, compared to thymine (T) in DNA.

In cells of living organisms, including humans, RNA fulfills very different roles from the ones reserved for DNA. It can be a messenger of genetic information, and it passes the information from DNA to proteins. In addition, many RNA molecules have been shown to catalyze chemical reactions in the cells. Further, RNA molecules perform a plethora of regulatory roles that are the key to the metabolism of the cells, for instance they can turn on and off or regulate up and down processes carried out by other biological molecules. RNA molecules are master regulators of cells, and are absolutely essential for life at the molecular level.

The cellular and molecular functions of RNA molecules depend on their spatial structures, which in turn are encoded in RNA sequence of the building blocks, and it depends on how the building blocks interact with each other. Interestingly, the four basic building blocks in RNA can be chemically modified by the cellular machinery in many various ways, giving rise to more than 150 variants, each with a different potential to interact with others! These alterations of the basic building blocks can affect the structure of RNA molecules, and influence their ability to interact with other molecules in the cell.

The structure of the RNA can be studied experimentally, but it is a long and laborious research process. A complementary approach is to use computational simulations. Various computational methods have been developed by researchers for the modeling of how the RNA sequence folds in 3D to assume its biologically relevant structure, including SimRNA developed in our laboratory. However, none of these methods is capable of taking into account the effect of the chemical modifications of the four basic building blocks on the folding of the RNA molecules.

In this research project, we propose to develop new computer software for molecular modeling of RNA containing chemical modifications. We will start with the existing prototypes of our computer programs and will extend them based on a series of analyses, involving a combination of computational and experimental research. The project will be carried out by an interdisciplinary team of researchers, including computer programmers, researchers specializing in computer simulations and data analysis, and biochemists who analyze RNA molecules experimentally.

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 better understanding of the relationships between sequence, structure, and function of RNA molecules.