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PhD thesis abstract

“Interactions of synthetic oligomers with ribosomal RNA”

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Synthetic oligomers of nucleic acids, also called oligonucleotides, are short (typically a few to several nucleotides) nucleic acid strands of potential therapeutic and diagnostic applications. First studies describing the interactions of synthetic oligonucleotides with the RNA of living organisms were presented at the end of the eighties of the twentieth century. Currently, the most commonly used oligomers are modifications of natural nucleic acids that exhibit increased stability in a cellular environment and enhanced stability of the complexes formed with RNA and DNA.

This thesis describes the studies of the interactions of 2'-O-methylated RNA and peptide nucleic acid (PNA) oligomers with a functionally important fragment of ribosomal RNA (rRNA). The investigated rRNA region is the so called ribosomal A-site, which serves key functions in the process of translation. This region is mainly responsible for the compliance of the sequences of polypeptide chains synthesised in ribosomes with the information contained in the mRNA template.

The research presented in the thesis includes a comparison of the prokaryotic and eukaryotic ribosomal A-site models as well as characteristics of the interactions of 2'-O-methylated RNA and PNA oligonucleotides with rRNA. The studies were performed with the use of molecular dynamics simulations and experimental methods: absorption and fluorescence spectroscopy, isothermal titration calorimetry and gel electrophoresis. Initial studies employing molecular dynamics revealed the lack of appropriate tools for the analysis of nucleic acids simulations. Therefore, an automatic tool for analysing three-dimensional structures of RNA and DNA molecules, their full-atom molecular dynamics trajectories or other conformation sets, was created. The presented work is a part of a bigger project, which aims to design effective inhibitors of bacterial proteins translation, based on the synthetic oligonucleotides.

The thesis consists of five parts. In the first part, the structure and properties of 2'-O-methylated RNA and PNA oligomers are discussed as well as biological aspects of the study. The second part describes the employed computational and experimental methods. In the third part a novel tool, for the analysis of molecular dynamics trajectories of nucleic acids “MINT” (**M**otif **I**dentifier for **N**ucleic Acids **T**rajectory), is presented. The fourth part describes the results of the computational and experimental studies of the prokaryotic and eukaryotic rRNA models and the interactions of the 2'-O-methylated RNA oligonucleotides with these models. The fifth part is dedicated to the investigation of the potential use of molecular dynamics simulations for prediction of the structural properties and thermal stability of PNA-RNA complexes.