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Abstract. Ribonucleosides, RNA and peptides are prepared to study non-covalent interactions of RNA, aminoacyl- and peptidyl-RNA. Techniques used include chemical synthesis in solution and on solid supports, UV- and NMR-detected thermal denaturation, X-ray crystallography and 1H-NMR spectroscopy for conformational studies, assisted by force-field and \textit{ab initio} calculations.

We synthesize ribonucleosides, RNA, and peptides for the elucidation of non-covalent interactions of RNA, and, most recently, of aminoacyl- and peptidyl-RNA. The goal is to better understand how transfer-RNA-like molecules may be capable of recognizing other RNA strands through 'codon-anticodon' interactions, and how covalently bound amino acids influence the thermodynamics of pairing and conformation of such 'early adaptors'. The biological background of these studies is the messenger-RNA-directed peptidyl-transfer reaction between aminoacylated transfer RNAs, a process involved in ribosomal protein synthesis. The most important techniques used are chemical synthesis in solution and on solid supports, UV- and NMR-detected thermal denaturation for thermodynamic studies, X-ray crystallography, and 1H-NMR spectroscopy for conformational studies, assisted by force-field and \textit{ab initio} calculations.

In the earlier periods of our investigations, we were occupied with synthesizing 15N- and 17O-labelled ribonucleosides and with developing a non-linear fitting procedure that could be used to calculate the thermodynamics of base-pairing from heteronuclear NMR signals [1]. We anticipate using these methods for the measurements of 'codon-anticodon' interactions between synthetic RNA hairpin molecules and synthetic messenger RNA.

More recently, we have investigated the synthesis of enantiomeric L-ribonucleosides [2] and derivatives, such as 1, for their use as potential antiviral drugs and of L-RNA for crystallographic purposes as part of a \textit{CHiral2} project [3]. The crystallization of racemic RNA strands may be of use in obtaining crystal-structure data of aminoacyl- or peptidyl-RNA.

Most recently, we synthesized an aminoacylated ribonucleoside derivative, 3'-alanylamino-3'-deoxyadenosine 2. The conformation of this puromycin analog is being studied by 1H-NMR spectroscopy and calculations [4]. A fully protected derivative thereof is used as the first solid-support-bound nucleoside for the subsequent stepwise synthesis of a peptide and RNA fragment [5]. By means of thermal
We are examining the pairing thermodynamics of RNA hairpin molecules in the absence and presence of amino acids attached [6].

We thank the Swiss National Science Foundation and the Novartis Foundation for continuous financial support.

Replacing Animal Testing by Virtual Experiments: A Challenge in Computational Chemistry

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Abstract. Computer modeling is used to study small-molecule interactions with macromolecular receptors with the aim to reduce in vivo testing of new chemicals and drugs.

The last decade has seen an enormous enhancement in computer power, but the complexity of biochemical events still leaves accurate simulations on a long time scale an unmet challenge. Since the mid 1980s, molecular modeling has been widely used in pharmacological research, partially due to the increasing availability of key protein structures. The impact of molecular modeling on drug development has often been demonstrated, but less obvious is its effectiveness in reducing animal testing. By recognizing inactive or toxic compounds by means of computational screening, undesired substances can be withdrawn from the evaluation pipeline before in vivo experiments become necessary.

Our laboratory develops computational approaches to pharmacological and toxicological screening. In the mid 1990s, a pseudoreceptor-modeling concept for predicting the activity of drug molecules was devised [2][3]. More recently, we have developed a 3D-QSAR concept based on

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