Dissertation presented at Uppsala University to be publicly examined in Room C10301 (floor 3), Biomedical Center, Uppsala, Saturday, April 29, 2006 at 12:00 for the degree of Doctor of Philosophy. The examination will be conducted in English.

Abstract
Acharya, S. 2006. Some Aspects of Physicochemical Properties of DNA and RNA. Acta Universitatis Upsaliensis. *Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Science and Technology* 164. 74 pp. Uppsala. ISBN 91-554-6518-8.

This thesis is based on nine research publications (**I – IX**) on structure and reactivity of RNA vis-à-vis DNA. The DNA and RNA are made of flexible pentose sugar units, polyelectrolytic phosphodiester backbone, and heterocyclic nucleobases. DNA stores our genetic code, whereas RNA is involved both in protein biosynthesis and catalysis. Various ligand-binding and recognition properties of DNA/RNA are mediated through inter- and intra-molecular H-bonding and stacking interactions, beside hydration, van der Waal and London dispersion forces. In this work the pH dependant chemical shift, pK_a values of 2'-OH group as well as those the nucleobases in different sequence context, alkaline hydrolysis of the internucleotidic phosphodiester bonds and analysis of NOESY footprints along with NMR constrained molecular dynamics simulation were used as tools to explore and understand the physico-chemical behavior of various nucleic acid sequences, and the forces involved in their self-assembly process. **Papers I – II** showed that the ionization of 2'-OH group is nucleobase-dependant. **Paper III** showed that the chemical characters of internucleotidic phosphate are non-identical in RNA compared to that of DNA. **Papers IV – VI** show that variable intramolecular electrostatic interactions between electronically coupled nearest neighbor nucleobases in a ssRNA can modulate their respective pseudoaromatic character, and result in creation of a unique set of aglycons with unique properties depending on propensity and geometry of nearest neighbor interaction. **Paper VII** showed that the cross-modulation of the pseudoaromatic character of nucleobases by the nearest neighbor is sequence-dependant in nature in oligonucleotides. **Paper VIII** showed that the purine-rich hexameric ssDNA and ssRNA retain the right-handed helical structure (B-type in ssDNA and A-type in ssRNA) in the single-stranded form even in absence of intermolecular hydrogen bonding. The directionality of stacking geometry however differs in ssDNA compared to ssRNA. In ssDNA the relatively electron-rich imidazole stacks above the electron-deficient pyrimidine in the 5' to 3' direction, in contradistinction, the pyrimidine stacks above the imidazole in the 5' to 3' direction in ssRNA. **Paper IX** showed that the pK_a values of the nucleobases in monomeric nucleotides can be used to show that a RNA-RNA duplex is more stable than a DNA-DNA duplex. The dissection of the relative strength of base-pairing and stacking showed that the relative contribution of former compared to that of the latter in an RNA-RNA over the corresponding DNA-DNA duplexes decreases with the increasing content of A-T/U base pairs in a sequence.

Keywords: nucleic acids, hydrogen-bonding, stacking, single-stranded, NMR, molecular dynamics

Sandipta Acharya, Department of Bioorganic Chemistry, Box 581, Uppsala University, SE-75123 Uppsala, Sweden

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