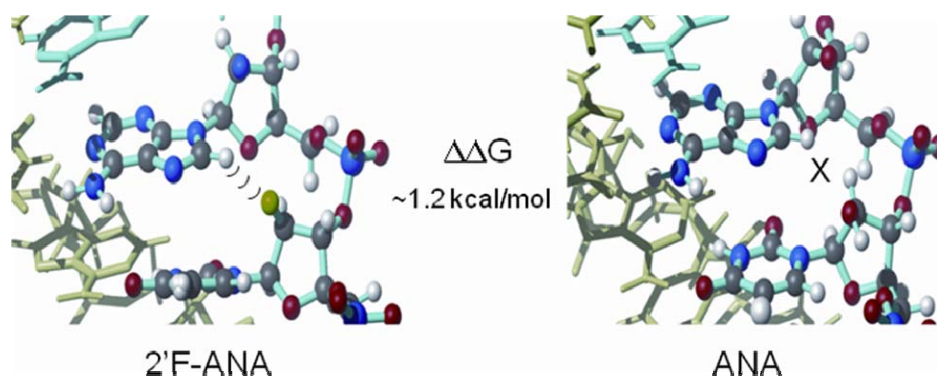




Our research group is interested in the chemical synthesis, biochemical properties and molecular behaviour of nucleic acids and their analogues. Our research goals include gaining a detailed understanding of inter- and intramolecular interactions between various nucleic acid components or between nucleic acids and proteins as key biochemical processes occur. More recently, our group reported the *in situ* synthesis of RNA on microarrays for the study (and discovery of) protein-RNA interactions that are relevant to important biological processes (e.g., RNAi, transcription, etc).

The main methods used in these investigations are solution and solid-phase synthesis; molecular biology techniques (gene silencing via RNAi, antisense, PCR, etc), high resolution NMR, UV and circular dichroism; and molecular modeling. Our research encompasses 2 main areas:

### I. Nucleic acid synthesis, structure and function.



We are interested in developing green chemical technologies for the preparation of nucleoside building blocks, and DNA and RNA chains. Of particular interest are RNA structures including modified siRNA/miRNA, branched RNA and lariat RNA. Our research group has also devoted an enormous effort to study nucleic acid structure. Here, the unique architecture of oligonucleotide analogues serves to induce the formation of nucleic acid structures; e.g. DNA/RNA hybrids, siRNA duplexes, triple and tetra-stranded DNA complexes, etc. Interest in studying these structures, e.g., tetraplexes, has been renewed due to evidence suggesting biological roles *in vivo* (telomeres, DNA recombination), and because the formation and/or stabilization of DNA/RNA and RNA/RNA duplexes provide a basis for artificial control of gene expression (antisense and RNA interference).

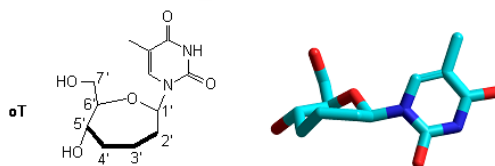
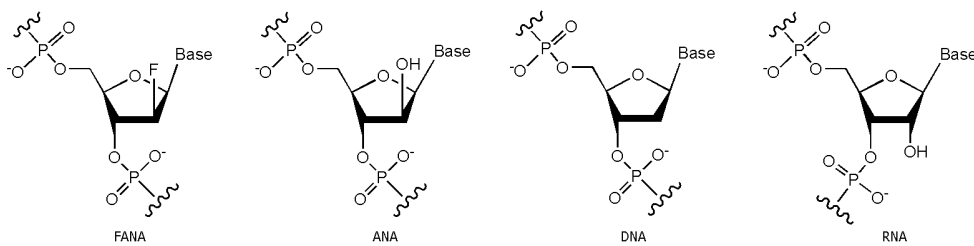


Current efforts are also focused on understanding the recognition of (a) branched RNA (bRNA) by the lariat debranching enzyme and spliceosomal factors, and (b) siRNA duplexes by the RNA-induced silencing complex (RISC). We approach both studies through the use of chemically-modified oligonucleotides.

## II. Nucleosides and oligonucleotides for drug development.

This work has involved biochemical studies with novel chemically modified nucleic acids. Aspects of these studies include modifications that either (i) augment nuclease stability; (ii) improve catalytic cleavage of mRNA by RNase H or within the RNA-Induced Silencing Complex (RISC); or (iii) increase target hybridization accessibility.

Recent examples synthesized in our group are arabinonucleic acids [see (a): 2'-fluoro-ANA; (b): ANA] and oligonucleotides with a 7-membered carbohydrate ring (oxepane nucleic acids, ONA; see "oT"). In collaboration, we are presently examining these compounds as antiviral agents and their ability of to kill primary human leukemia cells in immune compromised mice using antisense and RNAi approaches. We are also adopting the SELEX technique (Systematic Evolution of Ligands by Exponential Enrichment) as a method for generating chemically-modified aptamers with therapeutic utility.



**Masad J. Damha, Ph.D., F.C.I.C.**

James McGill Professor of Chemistry  
McGill University

Otto Maass Chemistry Building – Room 413 A  
801 Sherbrooke St. West, Montreal, QC, Canada  
H3A 2K6

Email: [masad.damha@mcgill.ca](mailto:masad.damha@mcgill.ca)  
<http://www.damha-group.mcgill.ca>