The Role of Protonated Base Pairs in the Evolution of RNA Function. M. A. Ditzler[1], M. Popović[1,2], P. Fliss[2], and J. D. Stephenson[1], [1]Space Science and Astrobiology Division, NASA Ames Research Center, [2]Blue Marble Space Institute of Science.

Abstract: Ribonucleic acid (RNA) is an essential biopolymer in modern biology and it figures prominently in many scenarios for the origin and early evolution of life. RNA molecules may have played a larger role in ancient biology than they do now, acting both as the primary biocatalysts and as the sole repository of genetic information. Several features of modern biochemistry provide strong support for RNA's dominant role in early life, such as the central role of ribosomal RNA in protein synthesis, the pervasive involvement of nucleotides in enzymatic cofactors, the existence of natural RNAs that bind these cofactors, the existence of multiple catalytic RNAs, and a conserved biosynthetic pathway in which deoxynucleotides are produced from ribonucleotides. Additionally, RNA's potential to serve as the primary biocatalyst is supported by *in vitro* evolution experiments that demonstrate RNA's ability to catalyze diverse chemical reactions.

The ability of biopolymers to support specific functions is defined by their structures and conformational dynamics. Base pairs are a fundamental unit of nucleic acid structure. The protonation state of nucleobases dictates their potential to form hydrogen bonds and therefore impacts RNA base pairing and overall RNA structure. Formation of protonated base pairs is an important aspect of RNA structure at mildly acidic conditions [1] and the stability of $A^{+}C$ pairs at pH 5 has been shown to be comparable to that of AU and GU base pairs at pH 7 [2]. Our data support the evolution of multiple $A^{+}C$ and $A^{+}G$ base pairs at pH 5 [3]. Protonated base pairs likely make a significant contribution to the formation of distinct structures in neutral and acidic environments. The ability to form protonated base pairs under mildly acidic conditions may significantly alter the ability of RNA to evolve specific functions in ancient biology.

References:

[1] Bernhardt, H.S., and Tate, W.P. (2012). *Biology Direct, 7,* 4. [2] Meroueh, M., and Chow, C.S. (1999). *Nucleic Acids research 27*, 1118-1125. [3] Popović, M., Fliss, P., Ditzler, M.A. *(submitted)*.