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***Prebiotic origins of DNA&RNA, more questions than answers:
the search for answer through computational modeling***

Abstract:

It is considered that the Earth originated about 4.53 billion years (Gyr) ago, but how did the first RNA/DNA emerge in this prebiotic earth? This and many other fundamental questions remain unanswered about the prebiotic evolutionary selection of the building blocks of nucleic acids. As another example, the β -anomers of the nucleosides(tides) are predominant in modern nucleic acids over their α -counterparts. But why?

Erwin Schrödinger, in 1944, suggested that QM could solve the mysteries of the origins of life. Since then, the world has seen an accelerated development of quantum and computational chemistry, molecular modeling. Thanks to these methods, the *in-silico* modeling of the prebiotic chemistry of ancestral nucleic acids is now at our fingertips. The structural tendencies and propensities in today's nucleic acids can be rationalized based on thermodynamics as a principal driver of evolutionary selection based on the free energies (calculated from quantum chemistry) of the possible reaction paths available to prebiotic Nature.

Hence, by using computational modeling techniques it has been found that the β -anomers of the nucleosides(tides) –predominant in modern nucleic acids - are found to be slightly more stable than their α -counterparts. This small thermodynamic advantage operating over millennia may have contributed to the observed dominance of today's canonical forms. The same theoretical calculations also suggest the possibility that nucleosides(tides) containing the non-canonical amino acid N-(2-aminoethyl)glycine (AEG) and glycerol instead of ribofuranose or 2'-deoxyribofuranose may have assisted in the synthesis of today's nucleosides(tides) if the predominant prebiotic environment was aqueous. Energetic comparisons of ancestral nucleic acids containing arsenate instead of phosphate indicate no thermodynamic advantage for the



phosphate, raising an important open question as to the reason for Nature's selection of the latter. It is also found, computationally, that barbituric acid may have well been a prebiotic precursor of today's nucleobases reinforcing earlier proposals. A more fundamental question may be about the choice of nucleic acids as the carriers of genetic information, in the first place, instead of other contenders such as proteins. A partial answer is formulated by proposing a quantitative account of the "*value*" of information as a new dimension to be added to the traditional "*amount*" (bits) in Shannon's information theory

Biography:

Dr. Lazaro Andres Monteserin Castanedo holds a Bachelor of Science with honors in Chemistry and a Master of Science in Chemistry from the Faculty of Chemistry, University of Havana, Cuba. He earned his PhD in Applied Science at Saint Mary's University in 2024 for his studies on the computational modeling of nucleic acids prebiotic origins.

Dr. Castanedo's research expertise includes the areas of computational and theoretical biochemistry for the modeling of small molecules and biologics, focusing primarily on the modeling of physic-chemical properties of nucleic acids building blocks.

Dr. Castanedo curriculum includes 11 publications, 2 book chapters, 16 scientific presentations and 10 awards & scholarships, including the 2024 Governors' General Gold medal for academic achievements, 2020-2021 Nova Scotia Graduate Scholarship (NSGS), 2020 Scotia Scholar Award and 2020 Abe Leventhal Student Research Award.