NUCLEOBASE PHOTOCHEMISTRY: A SEARCH FOR PREBIOTIC MOLECULAR FOSSILS.

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Introduction: The key components of the reproductive machinery are unlikely to have been selected by a biological evolution that requires that very machinery to begin with. Instead it is conceivable that the choice of the molecular building blocks of life was mediated by a chemical selection that preceded biology. This hypothesis also implies that molecular properties of nucleobases have been preserved unchanged from prebiotic times, possibly providing us with molecular fossils. To probe these intrinsic properties we study isolated nucleobases, employing techniques we developed specifically for this purpose, combining laser spectroscopy and mass spectrometry.

UV hardiness. We have found that the nucleobases that are involved in replication selectively exhibit short excited state lifetimes which provide high intrinsic stability against otherwise harmful UV photo-damage. UV protection comes about when electronic excitation is converted to heat by internal conversion and safely dissipated to the environment at rates too fast for other more harmful reactive pathways to occur. The canonical nucleobases generally decay in less than 1 picosecond, orders of magnitude faster than in most other heterocyclic compounds. This property would have been highly advantageous for the first self-replicating molecules in prebiotic times before modern enzymatic repair and before the formation of the ozone layer that later attenuated the high levels of UV radiation penetrating the early atmosphere. The safe elimination of excess electronic energy in the canonical bases is exquisitely sensitive to molecular structure and much slower relaxation is observed in closely related structures. This suggests that the natural bases were selected in part due to their high intrinsic photostability or UV hardiness and that their photochemistry is a vital property of the set of prebiotic molecules that could give rise to life on Earth or elsewhere in the universe.

Photochemical selection. This intrinsic damage resistance is literally built into the nucleobases. Figure 1, showing selected excited state lifetimes, illustrates the remarkable selectivity of this attribute: the canonical bases are generally protected against UV photodamage while most of their derivatives and even isomers lack this property. This selectivity is so great, that even specific tautomers that are prevalent in RNA and DNA, such as keto-guanine are short lived when excited and thus UV protected. At the same time other tautomers of the very same base, such as the enol form of guanine, are orders of magnitude longer lived and thus prone to photodamage. We have even found the same remarkable selectivity between base pair structures. For example, we found the well-known Watson-Crick structure of the GC pair to be short lived when UV excited, while other equally stable structures of GC that are possible but that do not occur in RNA and DNA, are very long lived. A picture is now emerging in which large differences in response to UV radiation arise from small and very subtle variations in molecular structure between similar derivatives, tautomers, and conformers of nucleobases. Many of those closely related compounds, that are less UV stable, would likely also have been present on an early earth and could have been candidates for alternate genetic lexicons. Thus, this photochemistry may be a relic of the earliest stages of prebiotic chemistry.

Intrinsic properties of nucleobases. We study the intrinsic photochemical properties of nucleobases and base pairs by double resonant spectroscopy in the gas phase of *isolated* bases and clusters. This work has helped motivate a growing number of theoretical studies that model the excited state dynamics with increasing mechanistic insight and begin to map out possible prebiotic photochemical pathways. UV sunlight is an attractive energy source for creating the organic molecules needed to start life on the early earth and not all competing processes are harmful. Generally, the molecular architecture for replication seems to require rigid structures, which tend to be aromatic and therefore inevitably prone to UV absorption. Since UV excitation is unavoidable for such compounds, it is crucial to understand the possible competing pathways available to process the electronic excitation. Nucleobase photochemistry may constrain hypotheses for prebiotic conditions as well as for alternative self-replicating informational polymers that could be important elsewhere in the universe. Understanding this functionality will help provide insight into the emergence of the biochemistry we know today.