

Nucleic acids such as DNA and RNA are fundamental carriers of information used by nature to store instructions about the composition of proteins. RNA also serves as a catalyst for many crucial biochemical processes. Explaining how these indispensable for life biomolecules were formed on early Earth is one of the most fascinating challenges for contemporary science.

For the past twenty years, efforts of researchers from various disciplines brought us near to proposing a credible scenario for the emergence of first informational polymers on Earth. These studies allowed to propose high-yielding reaction pathways leading to basic RNA and DNA building blocks, i.e. nucleotides. The key environmental factor providing chemical selectivity of these syntheses is UV irradiation. Several research teams also proposed the reaction sequences and geochemical conditions, which could enable the formation of first self-replicating nucleic acid oligomers. However, unlike nucleotide monomers, exposure of DNA and RNA oligomers to UV irradiation leads to the formation of detrimental lesions. The most frequent lesions, i.e. cyclobutane pyrimidine dimers (CPDs), may effectively suppress their functions. This aspect of prebiotic chemistry is particularly important, because the anoxic Archean atmosphere enabled much higher UV fluxes to reach the surface of our planet. The resulting lack of compatibility between prebiotic synthesis of nucleotides and generation of long oligomers is one of the key unresolved issues in our understanding of the origins of DNA and RNA on Earth.

Living organisms counteract the effects of DNA and RNA photodamage owing to the presence of complicated repairing enzymes, such as photolyases. Photolyases locate and repair CPD lesions through photo-induced electron transfer. However, these complicated enzymes were formed at later stages of evolution of living organisms and first informational polymers could survive harsh conditions of the Archean environment only with more primitive forms of protection from photochemical damages.

In this project, we will focus on studying alternative DNA and RNA nucleosides, which could serve as effective electron donors and mimic the repairing activity of photolyases. According to our preliminary results, even tiny modification of a nucleobase may significantly lower the energy barrier of photochemical electron transfer. These properties may significantly increase the photostability of modified oligomers and enable self-repair of CPDs. Our goal is to identify alternative nucleobases, which apart from these properties would be also compatible with prebiotically credible syntheses of nucleotides, their oligomerization and enzyme-free template copying. Given that some sequences of canonical DNA nucleotides exhibit moderate self-repairing properties, we will also investigate the sequence-dependence of the self-repair process in different canonical and modified oligomers. For this purpose, we will apply highly accurate methods of quantum chemistry to estimate and predict the efficiency of these processes. We will then perform UV-irradiation experiments of selected oligomers in order to confirm our theoretical predictions. This research project will enable addressing the key challenge for prebiotic chemistry, which is the vulnerability of RNA and DNA to the formation of photodamages. Furthermore, these results may also support future development of technologies based on electron transfer in nucleic acid strands and photodynamic therapies, which also involve introduction of alternative nucleotides.