Ab-Initio Molecular Dynamics Simulations And Nmr Experiments Of Rna Nucleotides In Hydrothermal Prebiotic Conditions. A. Pérez-Villa[1], T. Georgelin[2], J-F Lambert[2], B. Rigaud[2], F. Guyot[1], M-C. Maurel[3], A. M. Saitta[1] and F. Pietrucci[1].
[1]IMPMC, Université Pierre et Marie Curie - Muséum National d'Histoire Naturelle, 4 place Jussieu, 75005 Paris, France (Email: andrea.perez-villa@impmc.upmc.fr, fguyot@mnhn.fr, marco.saitta@impmc.upmc.fr, fabio.pietrucci@impmc.upmc.fr), [2]LRS, Université Pierre et Marie Curie, 4 Place Jussieu, 75005 Paris, France (Email: thomas.georgelin@upmc.fr, jean-francois.lambert@upmc.fr, baptiste.rigaud@upmc.fr), [3]ISYEB - CNRS - Université Pierre et Marie Curie - Muséum National d'Histoire Naturelle, 57 Rue Cuvier, 75005 Paris, France (Email: mcmaurel@mnhn.fr)

Introduction: "RNA world" is one of the most widely accepted hypothesis about origins of life, due to the experimentally observed versatility of Ribonucleic Acid (RNA) molecules in different chemical processes [1]. RNA is constituted by ribonucleotides, which are composed by three molecular entities: a nitrogenous base, a furanose-ribose and a phosphate group. Several studies have investigated how RNA has been formed in the early Earth, including the catalytic role of mineral surfaces, the presence of salts or lipid compounds, the exposure to drying/wetting cycles, and so forth [2]. Even though, the mechanism of spontaneous formation of ribonucleotides in different primitive scenarios is still a key question in the prebiotic chemistry field.

In this work, we model the chemical reactions for the ribonucleotide formation/degradation under hydrothermal prebiotic conditions, by means of ab initio molecular dynamics in explicit aqueous solution. We exploit free-energy methods [3, 4] combined with a topological approach based on graph theory developed in our group able to accurately track variations of the chemical bonds network along a chemical reaction [5]. From this methodology, we explored different reaction channels related with the nucleotide synthesis/degradation as well as quantitatively reconstruct the free energy profiles associated to the studied chemical reactions in silico. Additionally, we performed a series of NMR experiments for the nucleotide in liquid phase to characterize the different substrates and products and get insights of the reaction rates, providing a complementary information to the simulations and confirming the predicted values obtained from the free-energy calculations.

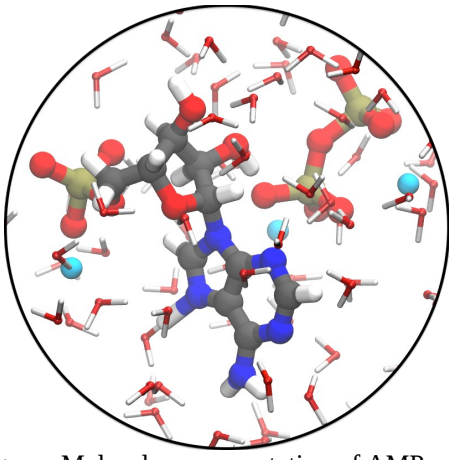

Figure: Molecular representation of AMP solution

References:

[1] W. Gilbert. (1986) Nature, 319, 618.
[2] J. G. Forsythe et al. (2015) Angew. Chem. 127, 10009.
[3] A. Laio, M. Parrinello. (2002) Proc. Natl. Acad. Sci. USA. 99, 12562.
[4] G. M. Torrie, J. P. Valleau (1977) J. Comput. Phys. 23, 187.
[5] F. Pietrucci, A. M. Saitta. (2015) Proc. Natl. Acad. Sci. USA. 112, 15030.