

# prebiochem : CECAM Workshop "Atomistic simulation in prebiotic chemistry: a dialog between experimentalists and theorists"

([prebiochem.sciencesconf.org](http://prebiochem.sciencesconf.org))

Sorbonne University, Pierre et Marie Curie Campus, 4 Place Jussieu, 75005 Paris (France)  
July 1, 2019 – July 3, 2019

## Abstracts of posters:

### *Natural selection of compartments with autocatalytic reactions*

**Heng Lu\***, **Alex Blokhuis\***, **Cyrille Jeancolas**, **Éstanislau Guilherme**, **Gabrielle Woronoff**, **Rebecca Turk Macleod**, **Eörs Szathmáry**, **Ludovic Jullien**, **Andrew Griffiths** & **Philippe Nghe**

Differential survival and reproduction due to phenotype is a major driving force in biology. It is at present unclear how and when natural selection emerges in chemistry. Using droplet microfluidics we show experimentally and theoretically that compartments containing autocatalytic chemistry (here: formose) can grow, divide and exhibit heritability. Via diffusive coupling, chemically efficient compartments can grow at the expense of inefficient ones, after which sufficiently large droplets are split by shear forces, thus augmenting their frequency in the population. We theoretically prove that the regrowth-division cycles of these fitter droplets can become persistent: they have stable attractors. In a spatial setting, different environments (e.g. neighbor droplets) induce variation in composition, size and growth, which affects the fitness of compartments and the phenotype of their offspring.

Our approach shows that natural selection can be built up from elementary physical-chemical building blocks (here: autocatalysis, diffusion, partition equilibria and shear forces), provided they respect the right separation of timescales. This invites to rethink our conception of protocells, chemical evolution and major evolutionary transitions.

## Computational approaches for prebiotic chemistry

G. Cassone,<sup>1a</sup> F. Saija,<sup>2</sup> M. Ferus,<sup>3</sup> C. Cecchi-Pestellini,<sup>4</sup> F. Pietrucci,<sup>5</sup> A. M. Saitta,<sup>5</sup> J. Sponer,<sup>1</sup> J. E. Sponer,<sup>1</sup>

<sup>1</sup> Institute of Biophysics of the Czech Academy of Sciences, Královopolská 135, 61265 Brno, Czech Republic

<sup>2</sup> CNR-IPCF, Viale Ferdinando Stagno d'Alcontres 37, 98158 Messina, Italy

<sup>3</sup> J. Heyrovsky Institute of Physical Chemistry, Czech Academy of Sciences, Dolejškova 3, 18223 Prague, Czech Republic

<sup>4</sup> INAF, Osservatorio Astronomico di Palermo, Piazza del Parlamento 1, 90134 Palermo, Italy

<sup>5</sup> Sorbonne Universités, Université Pierre et Marie Curie 06, Institut de Minéralogie, de Physique des Matériaux et de Cosmochimie, CNRS, Muséum national d'Histoire naturelle, Institut de Recherche pour le Développement, Unité Mixte de Recherche 7590, F-75005 Paris, France

Owing to the growth of the computing power and to the development of optimized software for molecular simulation, nowadays it has become possible to simulate - *in silico* - a plethora of disparate conditions with unprecedented reliability and precision. Here I present a series of the possible circumstances giving rise to the onset of prebiotically relevant molecules from very simple precursors. In particular, among the many possible reaction pathways underlying the onset of life on Earth, synthesis of simple sugars, along with the formation of nucleobases and amino acids, holds a prominent multidisciplinary interest. For decades, the formose reaction (*i.e.*, the synthesis of sugars from aldehydes) has been the subject of copious research and heated debates [1] mainly because of its first, and rate-limiting, reaction step: the formation of C-C bonds through the synthesis of glycolaldehyde from formaldehyde (*i.e.*,  $2\text{H}_2\text{CO} \rightarrow \text{HOCH}_2\text{CHO}$ ). I present a critical investigation [2] of such a condensed-phase reaction performed through *ab initio* molecular dynamics (AIMD) and an *avant-garde* scheme for the definition of efficient reaction coordinates [3] capable to reveal unexpected mechanisms and, at the same time, providing the free-energy landscape, fully including the effect of the chemical environment and of the thermodynamics. Additionally, I show how intense electric fields are able to trigger the synthesis of (D)-erythrose - the direct ribose precursor - from ubiquitous molecules such as glycolaldehyde and water, without the assistance any catalyst or template [2].

On the other hand, the multi-scale shock-compression technique (MSST) [4], when combined to AIMD, is able to simulate intense shock waves propagating in relatively small numerical samples. Based on this technique, we simulated the collision between interstellar grains composed of  $\text{H}_2$  and HNC [5], and demonstrated that a plethora of prebiotically significant species spontaneously arises. Finally, also peculiar planetary atmospheres [6] and other extreme conditions [7] can be nowadays simulated synergistically with laboratory experiments.

[1] R. Shapiro, *Origins Life Evol. Biospheres* **1988**, 18, 71.

[2] G. Cassone *et al.*, *Chem. Commun.* **2018**, 54, 3211.

[3] F. Pietrucci & A. M. Saitta, *Proc. Natl. Acad. Sci. USA* **2015**, 112, 15030.

[4] E. J. Reed *et al.*, *Phys. Rev. Lett.* **2003**, 90, 235503.

[5] G. Cassone *et al.*, *Astrophys. J. Lett.* **2018**, 866, L23.

[6] M. Ferus *et al.*, *A&A* **2018**, 616, A150.

[7] M. Ferus *et al.*, *A&A* **2019**, 626, A52.

<sup>a</sup> Email: [cassone@ibp.cz](mailto:cassone@ibp.cz)

# **NON- ENZYMATIC OLIGOMERIZATION OF 3'-5' CYCLIC RIBONUCLEOTIDES IN PREBIOTIC CONDITIONS**

**Giovanna COSTANZO**

Istituto di Biologia e Patologia Molecolari, CNR, Rome, 00185, Italy

Extant biological DNA and RNA syntheses are based on template copying by highly evolved polymerases and high levels of adaptation and refinement have been achieved in studies on the *in vitro* evolution of polymerizing enzymes (1). Complex chemistries involved in the non-enzymatic polymerization of high-energy monomers to nucleic acids are also well described in the literature (2). However, these are all compounds whose likelihood of prebiotic availability and accumulation is inversely proportional to their intrinsic stability and the elaborate chemistry necessary for their synthesis. In brief, the prebiotic generation of RNA remains undeciphered.

We explored in prebiotic conditions the non-enzymatic polymerization of cyclic nucleotides. Such a template-free polymerization reaction is preceded by the self-assembling of the cyclic precursors utilizing stacking interactions, which mediate the trans-phosphorylations among the pillared monomer units, resulting in covalently bound oligonucleotides. The conditions allowing this chemistry necessarily differ among the different nucleotides and depend on the propensity of the monomers to participate in various intermolecular interactions. Thus, in order to reconstruct the series of chemical events that eventually led to the prebiotic non-enzymatic synthesis of mixed-sequence RNA, the polymerization of each cyclic nucleotide requires a dedicated specific analysis. Starting by our observation of abiotic phosphorylation of nucleosides using phosphate minerals as source of phosphate and the spontaneous formation of cyclic nucleotides, the non-enzymatic polymerization of 3',5'-cGMP, 3',5' cAMP, and 3',5'cCMP has been obtained and characterized (3,4,5).

[1] Costanzo G., Saladino R., Botta G., Giorgi A., Scipioni A. Pino S., Di Mauro E. **2012**, *ChemBioChem* 13(7).

[2] Costanzo G., Pino S., Timperio A.M. , Šponer J.E., Šponer J., Nováková O., Šedo O., Zdráhal Z., Di Mauro E **2016**, *PLoS ONE* 11(11).

# Oxygen Evolution Reaction at the (110)-Co<sub>3</sub>O<sub>4</sub>/water Interface: electrocatalysis by MetD & DFT-MD simulations

**Creazzo Fabrizio<sup>(a)</sup>, Cassone G.<sup>(b)</sup>, Galimberti D.<sup>(a)</sup>, Pezzotti S.<sup>(a)</sup>, Sponer J.<sup>(b)</sup>, and Gaigeot Marie-Pierre<sup>(a)</sup>**

<sup>(a)</sup> LAMBE UMR8587 CNRS, Université Paris-Saclay & Université d'Evry Val d'Essonne, Evry, France

<sup>(b)</sup> Institute of Biophysics, Czech Academy of Sciences, Brno, Czech Republic

[fabrizio.creazzo@univ-evry.fr](mailto:fabrizio.creazzo@univ-evry.fr)

The processes involved in electrochemistry at the solid-liquid-electrolytic interface in order to produce molecular hydrogen and oxygen is a current key field of research in science and technology, especially of importance for the hydrogen economy, for green technology in a period of time with an ever more growing demand in green-energy. In this context, water splitting at cobalt oxide interfaces has to be investigated in details, and first-principles molecular dynamics simulations are highly relevant in order to understand the mechanisms at play, how the oxides can act as a good catalyst for the water splitting, and how liquid water at the interface can be involved in the overall processes.

Most of the existing first-principles calculations published in the literature on Co<sub>3</sub>O<sub>4</sub> oxides are related to "surface science" calculations<sup>1-4</sup>, where there is no explicit interfacial water molecules.

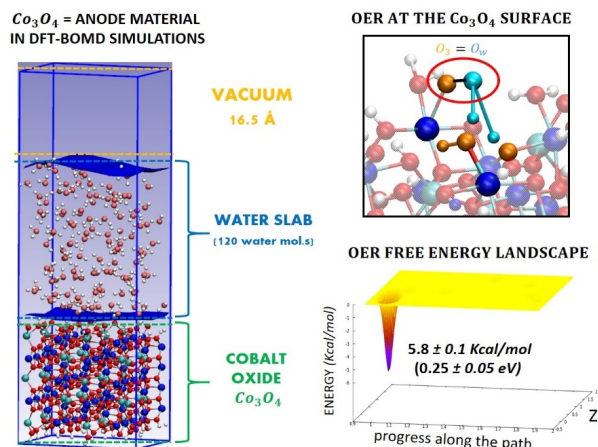
In this poster, we present DFT-based molecular dynamics simulations of (110) Co<sub>3</sub>O<sub>4</sub>-liquid water interfaces<sup>5</sup>, out- and in- electrocatalysis conditions, including a full water slab in direct contact with the (110) Co<sub>3</sub>O<sub>4</sub> solid surface. A detailed characterization of this complex inhomogeneous semi-conductor/water interface will be presented in terms of interfacial structure (solid surface and interfacial water), dynamics, chemical reactivity and how/why water can be found in undisciplined behaviors e.g. H-bond environments, surface speciation, effect of the presence of ions and electrostatic gradients in the simulation box.

In order to reveal the mechanisms of the OER (Oxygen Evolution Reaction) and quantify the associated energetics at aqueous Co-oxides interfaces, biased DFT-MD simulations have been performed and their results will be presented. To that end, biased DFT-MD are within the framework of novel "contact matrix" metadynamics<sup>6</sup>. The free-energy landscapes show how the OER pathway and energetics strongly depend on the catalytic solid surface sites involved in the reaction. Our investigation reveals a prevalent structural motif of  $\mu$ -oxo-Co<sup>3+</sup> surface sites as the active site for the OER at (110) Co<sub>3</sub>O<sub>4</sub>-liquid water interfaces and how the presence of water slab reduces the overpotential required for the OER compared to the gas-phase investigations.

This work is part of a partnership in between simulations (*Université d'Evry Val d'Essonne*) and electrochemical experiments performed in the Allongue's group at the Ecole Polytechnique.

[1] Wu X., Selloni A., *Phys. Rev. B*, **2011**, 83.

[2] Chen J. and Selloni A., *J. Phys. Chem. Lett.*, **2012**, 3.



[3] Chen J. and Selloni A., *J. Phys. Chem. C*, **2013**, 117.

[4] Selcuk S. and Selloni A., *J. Phys. Chem. C*, **2015**, 119.

[5] F. Creazzo, D. R. Galimberti, S. Pezzotti, and M. P. Gaigeot, *J. Chem. Phys.*, **2019**, 150, 4. Chosen as Feature Article by JCP, Chosen as 2018 JCP Editor's Choice, and highlighted by AIP.

[6] Pietrucci F., Saitta A. M., *Proceedings of the National Academy of Sciences*, **2015**, 112(49), 15030-15035.



## ***Molecular basis for thermophoresis in aqueous solutions***

**Alejandro DIAZ MARQUEZ and Guillaume STIRNEMANN**

Laboratoire de Biochimie Théorique, UPR 9080 CNRS, Institut de Biologie Physico-Chimique, 13 rue Pierre et Marie Curie, 75005 Paris, France

Thermophoresis is a thermally-driven process whereby the composition of a mixture becomes inhomogeneous in a temperature-gradient. Pioneer experiments from the Braun group[1-3] have shown that thermophoresis could contribute to precursor accumulation in prebiotic conditions, a crucial process for the emergence of life in the absence of any compartmentalization. Here, all-atom molecular dynamics simulations have been performed to shed light on the molecular bases of this phenomenon, which remain poorly understood. In particular, we try to understand the relationship between the imposed temperature gradient and the resulting concentration gradient depending on the nature of solutes in aqueous solutions.

[1] Braun, D. & Libchaber, A. *Phys. Biol.* **1**, P1-P8 (2004).

[2] Duhr, S. & Braun, D. *Proc. Natl. Acad. Sci. U.S.A.* **103**, 19678-19682 (2006).

[3] Mast, C. B. & Braun, D. *Phys. Rev. Lett.* **104**, 188102 (2010).

## ***Ab initio study of glycine synthesis in solution: insights into prebiotic scenarios***

**Théo Magrino, Fabio Pietrucci, A. Marco Saitta**

IMPMC, Sorbonne Université, Paris, France

Prebiotic occurrence of amino acids is well-documented in a variety of environments, and experimental results about the possible formation pathways go from the popular Miller experiment to recent studies [1, 2]. In Miller's experiment, featuring water under a reducing atmosphere of ammonia, methane and hydrogen, a spark discharge induced the formation of aldehyde, cyanide and various amino-acids. These and other results are often interpreted in terms of the Strecker multi-component reaction [3] as a candidate synthesis pathway, since it involves e.g. formaldehyde, cyanide and a catalytic ammonia molecule and it leads to glycine, the simplest amino acid.

However, the variety of potential environments in which prebiotic amino acids may have appeared, together with the manifold small molecules existing in such environments as potential precursors, makes the identification of precise synthetic pathways for their apparition a challenge.

We undertook a thorough study of glycine formation in aqueous realistic environments, exploiting DFT-based molecular dynamics in explicit solvent together with enhanced sampling methods, a fruitful methodology which already provided important results in prebiotic chemistry [4, 5, 6]. We computed both free energy differences and free energy barriers for the complex Strecker mechanism in solution, involving about ten steps. Our results are a crucial step for the determination of thermodynamic and kinetic properties of these reactions, and may improve our understanding of prebiotic chemistry by determining the most probable chemical pathway involved in the apparition of protein building blocks.

[1] S. L. Miller, *Science*, 117(3046), 528-259, 1953

[2] K. Planckensteiner, H. Reiner, B. M. Rode, *Mol. Div.*, 10(1), 3-7, 2006

[3] A. Strecker, *Eur. J. Org. Chem.*, 91(3), 349-351, 1854

[4] F. Pietrucci, A. M. Saitta, *PNAS*, 112(49), 15030-15035, 2015

[5] A. Pérez-Villa, A. M. Saitta, T. Georgelin, J.-F. Lambert, F. Guyot, M.-C. Maurel, F. Pietrucci, *J. Phys. Chem. Lett.*, 9(17), 4981-4987, 2018

[6] F. Pietrucci, J. C. Aponte, R. Strarr, A. Pérez-Villa, J. E. Elsilá, J. P. Dworkin, A. M. Saitta, *A.C.S. Earth Space Chem.*, 2(6), 588-598, 2018

# ***Quantum chemical evaluation of inverted membrane stability on the surface of Titan***

**Hilda SANDSTRÖM**

Chalmers university of technology

Saturn's moon Titan is the only other body in our solar system, except Earth, that hosts a dynamic liquid cycle that supports lakes, rivers and rainfall on its surface [1]. The lakes on Titan are predominately made out of liquid methane and ethane [2], and photochemistry in the atmosphere produces a rich a variety of organic compounds [3]. Titan has been proposed as a strict test case for the limits of life, and the possibility for "methanogenic" life has received much attention [4]. In 2015, Stevenson et al. [5] suggested the possible self-assembly of cell membranes made from acrylonitrile under Titan's cryogenic conditions, based on theoretical calculations. The membranes were referred to as azotosomes and were proposed to form due to an enthalpy driven self-assembly through the dipole-dipole interaction of the nitrogen containing groups. Azotosomes were found to be kinetically stable and of comparable flexibility to lipid bilayer membranes on Earth. In 2017, acrylonitrile was detected in Titan's atmosphere by the ALMA radio telescope [6] further fueling speculation of the molecule's importance. To evaluate these claims, we have performed quantum mechanical calculations to estimate the thermodynamic stability of the proposed azotosome membrane relative to the molecular crystal structure of acrylonitrile. Our calculations strongly suggest that azotosome self-assembly is unlikely.

[1] Tokano, T. et al. *Nature* **2006**, 442, 432-435.

[2] Stofan, E. R. et al. *Nature* **2007**, 445, 61-64.

[3] Niemann, H. B. et al. *Nature* **2005**, 438, 779-784.

[4] Lunine, J. I. *Faraday Discuss* **2010**, 147, 405-18; discussion 527.

[5] Stevenson, J.; Clancy, P.; Lunine, J. *Sci Adv* **2015**, e1400067.

[6] Palmer, M. Y. et al. *Sci Adv* **2017**, 3, e1700022

## ***Investigating the origin of life on the Earth : the peptide bond condensation reaction at the air/water interface catalyzed by the “salt of the life”***

**Flavio Siro Brigiano, Daria Ruth Galimberti, Simone Pezzotti  
and Marie Pierre Gaigeot**

Laboratoire Analyse et Modélisation pour la Biologie et l'Environnement, LAMBE UMR-CNRS 8587,  
Université d'Evry val d'Essonne, Université Paris Saclay, Paris, France

[flavio.sirobrigiano@univ-evry.fr](mailto:flavio.sirobrigiano@univ-evry.fr)

The understanding of the formation of biopolymers in the early ages of the Earth is crucial to fully rationalize the origin of life on our planet. In which conditions and how organic compounds polymerized in the primordial soup, before the emergence of catalysts and enzymes, remains a fascinating unresolved question in prebiotic chemistry.

In particular the first peptide bond condensation reaction is a highly debated and controversial topic. The peptide bond condensation reaction is unfavored in bulk water for both thermodynamic and kinetic reasons, and many reaction mechanisms in “exotic conditions” have been proposed by the scientific community in order to account for the peptide bond formation. Recently, Griffith *et al.*<sup>1</sup> have observed the formation of polypeptides between amino acid esters catalyzed by the Cu(II) salt at the air/water interface, suggesting the surface of oceans and water aerosols as suitable environments for the birth of life on the prebiotic Earth.

However, the role of the air/water interface during the reaction and the reasons for which this reaction occurs at the interface and not in bulk water are still unclear.

In our work we simulate the peptide bond synthesis at the air/water interface with biased DFT-based molecular dynamics techniques. We provide comparisons of energetics and reaction mechanisms observed at the air/water interface versus in the bulk water, hence clarifying the role of the interface. We especially identify why the interfacial water network is of utmost importance in catalyzing the peptide bond condensation reaction. This will be presented in this talk.

For the first time such a large and complex reactive chemical environment has been simulated in presence of massive bulk water (560 water molecules in the simulation box) by means of DFT-molecular dynamics simulations. We acknowledge a PRACE (Partnership for Advanced Computing in Europe) funding that made this challenging computational investigation possible.

<sup>1</sup>Griffith EC, Vaida V *In situ observation of peptide bond formation at the water-air interface. Proc Natl Acad Sci USA* **109**(39):15697-1570(2012)