Modelling Information Flow in Biological Coding Systems

COST Action CA21169
DYNALIFE WG1 Meeting

PHOTO: Dragoljub Zamurović

BOOK OF ABSTRACTS

Editor: Nataša Mišić

Belgrade, 2023
SERBIA

cost EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

Funded by the European Union

LOLA INSTITUT

unibz Freie Universität Bozen
Libera Università di Bolzano
Università Liedia de Bulsan

The first WG1 Meeting of COST Action CA21169 DYNALIFE, co-located with Belgrade BioInformatics Conference (BelBI2023)

www.dynalife.eu/belgrade-2023

About DYNALIFE

In the mid-twentieth century two new scientific disciplines emerged forcefully: molecular biology and information-communication theory. At the beginning cross-fertilisation was so deep that the term genetic code was universally accepted for describing the meaning of triplets of mRNA (codons) as amino acids. However, today, such synergy has not taken advantage of the vertiginous advances in the two disciplines and presents more challenges than answers. These challenges are not only of great theoretical relevance but also represent unavoidable milestones for next generation biology: from personalized genetic therapy and diagnosis, to artificial life, to the production of biologically active proteins. Moreover, the matter is intimately connected to a paradigm shift needed in theoretical biology, pioneered long time ago in Europe, and that requires combined contributions from disciplines well outside the biological realm. The use of information as a conceptual metaphor needs to be turned into quantitative and predictive models that can be tested empirically and integrated in a unified view. The successful achievement of these tasks requires a wide multidisciplinary approach, and Europe is uniquely placed to construct a world leading network to address such an endeavour. The aim of this Action is to connect involved research groups throughout Europe into a strong network that promotes innovative and high-impact multi and inter-disciplinary research and, at the same time, to develop a strong dissemination activity aimed at breaking the communication barriers between disciplines, at forming young researchers, and at bringing the field closer to a broad general audience.

COST (European Cooperation in Science and Technology) is a funding organisation for research and innovation networks. Our Actions help connect research initiatives across Europe and beyond and enable researchers and innovators to grow their ideas in any science and technology field by sharing them with their peers. COST Actions are bottom-up networks with a duration of four years that boost research, innovation and careers.

Modelling Information Flow in Biological Coding Systems

CA21169 DYNALIFE WG1 Meeting Belgrade 2023

Belgrade, Serbia, Jun 20–21, 2023

Book of Abstracts

Editor: Nataša Mišić

cost EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

Funded by the European Union

LOLA INSTITUT

unibz
Freie Universität Bozen
Libera Università di Bolzano
Università Liedia de Bulsan

The meeting is organized under the auspices of COST (European Cooperation in Science and Technology) as a funding agency for research and innovation networks.

Belgrade
Research and Development institute Lola Ltd
2023

Scientific Committee

Branko Dragovich (MI SASA, Belgrade, SERBIA)

Elena Fimmel (University of Mannheim, GERMANY)

Simone Giannerini (University of Bologna, ITALY)

Diego Luis Gonzalez (CNR-IMM, Bologna, ITALY)

Andrei Khrennikov (Linnaeus University, Växjö, SWEDEN)

Nataša Mišić (R&D Institute Lola, Belgrade, SERBIA)

Local Organizing Committee

Nataša Mišić (R&D Institute Lola, Belgrade, SERBIA)

Branko Dragovich (MI SASA Belgrade SERBIA)

Srećko Manasijević (R&D Institute Lola, Belgrade, SERBIA)

Mirko Ostojić (R&D Institute Lola, Belgrade, SERBIA)

Saša Cvetković (R&D Institute Lola, Belgrade, SERBIA)

Meeting program – DAY 1

Tuesday, 20. June 2023.		
08.30 – 09.00	**REGISTRATION**	
09.00 – 09.15	**OPENING**	
09.15 – 09.45	Diego L. GONZALEZ (IT)	Theoretical Models of the Genetic Code, a Case Study: *Non-Power Integer Number Representations*
09.45 – 11.10	Lutz STRÜNGMANN (DE)	Circular Codes in the Genetic Information
10.10 – 11.35	Branko DRAGOVICH (RS)	Biological Information and the Genetic Code
10.35 – 11.00	Paul SORBA (FR)	Why Group Theory in Biology?
11.00 – 11.30	**REFRESHMENT BREAK**	
11.30 – 11.55	Nataša Ž. MIŠIĆ (RS)	Standard Genetic Code Model that Supports De Duve's Idea of an Evolutionary Game Written into the Fabric of the Universe
11.55 – 12.20	Iván MARQUÉS CAMPILLO (ES)	Life's Genesis, Consciousness and the Fabric of Reality: Shifting Perspectives on Spacetime
12.20 – 13.30	**LUNCH BREAK**	
13.30 – 14.20	**WG1 Meeting I**	
14.20 – 14.45	Ozlem DEFTERLİ (TR)	Investigating the Dynamics of Complex Biological Systems within Modern Mathematical Operators
14.45 – 15.10	Tatiana Valentine GUY (CZ)	Dynamic Distributed Decision Making
15.10 – 15.35	Vladimir JAĆIMOVIĆ (ME)	Evolution as Learning, Natural Selection as a Game: Bayes Meets Darwin
15.35 – 16.00	Stefano PIOTTO (IT)	Meaningful Representations of Protein Sequences
16.00 – 16.30	Steen RASMUSSEN (DK)	Origins of Functional Biological Information
16.30 – 17.00	**REFRESHMENT BREAK**	
17.00 – 17.45	Stuart KAUFFMAN (US)	Is the Emergence of Life an Expected Phase Transition in the Evolving Universe?

18.00 – 18.40	**NIKOLA TESLA MUSEUM**	Distance: 370 m; Walk: 5 minutes
19.00 – 22.30	**DINNER**	Distance: 1.8 km; Bus line: 24, 26, 27; Walk: 25 minutes

Meeting program – DAY 2

Wednesday, 21. June 2023.		
09.00 – 09.30	Fabio MAVELLI (IT)	Deterministic and Stochastic Modelling of Protocells
09.30 – 09.55	Emiliano ALTAMURA (IT)	Semi-Synthetic Bottom-Up Approach for Photosynthetic Artificial Cell Construction
09.55 – 10.20	Stuart A. HARRISON (UK)	A Biophysical Basis for the Emergence of the Genetic Code in Protocells
10.20 – 10.45	Raquel Nunes PALMEIRA (UK)	A Rudimentary Genetic Code Supports Darwinian Evolution in Protocells
10.45 – 11.00	Lilly BARTSCH (UK)	Biophysical Interactions Underpin the Emergence of Information in the Genetic Code
11.00 – 11.30	**REFRESHMENT BREAK**	
11.30 – 11.55	Andrei KHRENNIKOV (SE)	Medical Diagnostics with Quantum Potential Extracted from Dendrogram Representation for EEG-data
11.55 – 12.20	Oreste PIRO (ES)	Coded Interneural Communication via Chaotically Spiking Neurons
12.20 – 13.30	**LUNCH BREAK**	
13.30 – 13.55	Selcen ÇELİK UZUNER (TR)	The Biological Codes Defined by Epigenetics
13.55 – 14.20	Željko ČUPIĆ (RS)	Modeling the Non-Linear Dynamics of Information Flows in Neuro-Endocrine Systems
14.20 – 14.40	Stefan KUHN (EE)	Simulation of Base Excision Repair in the Calculus of Covalent Bonding
14.40 – 15.05	Paweł BŁAŻEJ (PL)	Some Theoretical Aspects of Reprogramming the Standard Genetic Code
15.05 – 15.35	**POSTERS**	
15.35 – 16.00	**WG1 Meeting II**	
16.00 – 16.30	**CLOSING & REFRESHMENT**	

Contents

Semi-Synthetic Bottom-Up Approach for Photosynthetic Artificial Cell Construction

Emiliano ALTAMURA[1,*], Paola ALBANESE[2,3] and Fabio MAVELLI[1]

*Corresponding author e-mail: emiliano.altamura@uniba.it

[1]*Chemistry Department, Università degli Studi di Bari Aldo Moro, Bari, Italy*
[2]*Department of Biotechnology, Chemistry and Pharmaceutical Sciences, University of Siena, Siena, Italy*
[3]*Department of Earth, Environmental and Physical Sciences, University of Siena, Siena, Italy*

Abstract

A continuous energy supply is a fundamental requirement in the realization of ex novo synthetic cells that can be considered alive or, at least, maintained in homeostatic conditions far from equilibrium. In this contribution, two different approaches for the preparation of artificial photosynthetic cells, i.e., giant phospholipid unilamellar vesicles (GUVs) with the ability to transduce light energy into chemical energy, will be presented and discussed (Altamura et al. 2021a). The first foresees that every single enzyme involved in the bacterial photosynthetic process is extracted and reconstituted in the GUV membrane with the right physiological orientation (Altamura et al. 2017, 2021b); the second is based on the extraction of the entire photosynthetic apparatus in the form of organelles, nanometric bacterial vesicles called chromatophores, capable of carrying out the phosphorylation of ADP into ATP under continuous light irradiation when trapped in the aqueous lumen of GUVs (Altamura et al. 2021c). To demonstrate that a metabolic pathway can be supported by light energy in these artificial cells, a transcription kit was encapsulated that induces the synthesis of RNA molecules fueled by the photoproduced ATP. The transcription process is the first step of protein expression, which is one of the key processes in the life cycle of living organisms.

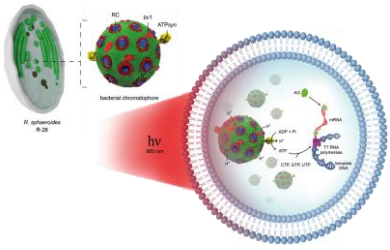


Figure 1. Schematic drawing of a photosynthetic artificial cell entrapping chromatophores, the bacterial light energy transducing compartments

Keywords

Artificial cell, giant lipid vesicles, DNA transcription, photosynthesis.

Reference

Altamura et al. **2017.** Highly oriented photosynthetic reaction centers generate a proton gradient in synthetic protocells. *PNAS* 114(15):3837-3842, https://www.doi.org/10.1073/pnas.1617593114.

Altamura E, Albanese P, Mavelli F, Stano P. **2021a.** The Rise of the Nested Multicompartment Model in Synthetic Cell Research. *Frontiers in Molecular Biosciences* 8:750576; https://doi.org/10.3389/fmolb.2021.750576.

Altamura E et al. **2021b.** Optimizing Enzymatic Photo-Redox Cycles by a Hybrid Protein Complex Chain. *ChemPhotoChem* 5(1):26-31; https://doi.org/10.1002/cptc.202000176.

Altamura E, Albanese P, Marotta R, Mavelli F. **2021c.** Chromatophores efficiently promote light-driven ATP synthesis and DNA transcription inside hybrid multi-compartment artificial cells. *PNAS* 118(7):e2012170118; https://www.doi.org/10.1073/pnas.2012170118.

Non-Coding RNAs and Plant Cell Walls

Utku AVCI[1,*]

*Corresponding author e-mail: utku.avci@gmail.com

[1]*Department of Agricultural Biotechnology, Eskisehir Osmangazi University, Eskisehir, Turkiye*

Abstract
Non-coding RNAs (ncRNAs) are RNA molecules that do not encode proteins but have regulatory functions in gene expression. In plants, ncRNAs have been shown to play important roles in various cellular processes, including development, stress responses, and metabolism. Recent studies have also revealed that ncRNAs are involved in the regulation of plant cell wall biosynthesis and remodeling. Specifically, ncRNAs have been shown to regulate the expression of genes involved in cellulose and hemicellulose biosynthesis, pectin metabolism, and lignin biosynthesis. In addition, some ncRNAs have been shown to regulate the expression of transcription factors and other regulatory proteins that control cell wall-related processes.

The findings suggest that ncRNAs are important regulators of plant cell wall structure and function, and provide new insights into the molecular mechanisms underlying plant cell wall biology. Further research in this area is needed to fully elucidate the roles of ncRNAs in plant cell walls and to explore their potential applications in crop improvement and biomass utilization.

Keywords
Biosynthesis, non-coding RNAs, plant cell wall, remodelling.

Biophysical Interactions Underpin the Emergence of Information in the Genetic Code

Lilly BARTSCH[1,*], Aaron HALPERN[1], Kaan IBRAHIM[1], Stuart A. HARRISON[1], Minkoo AHN[2], John CHRISTODOULOU[2] and Nick LANE[1]

*Corresponding author e-mail: lilly.bartsch.20@ucl.ac.uk

[1]*UCL Centre for Life's Origins and Evolution, Genetics, Evolution and Environment, University College London, London, United Kingdom*
[2]*Department of Structural and Molecular Biology, Institute of Structural and Molecular Biology (ISMB), University College London, London, United Kingdom*

Abstract
Several theories on the emergence of the genetic code at the origin of life have been proposed over the past decades. A recurring idea focuses on the possibility of biophysical interactions between amino acids and nucleotides directing codon assignments (Woese 1969). Patterns in the genetic code suggest hydrophobicity as an essential factor (Harrison *et al.* 2022). Despite the fact that the idea continues to reappear in the literature, a comprehensive analysis investigating the proposed interactions has yet to be conducted. We used molecular dynamics simulations to analyse the interactions between all 20 standard proteinogenic amino acids and the four RNA mononucleotides in three different RNA phosphate-backbone charge states (Halpern *et al.* 2023). The simulations appear sensitive to the charge of the backbone, with the -1 charge state exhibiting the strongest interaction preferences of the amino acids for their assigned codons. 50% of the tested amino acids in the -1 state interact best with their middle anticodonic nucleotide, which is suggested as the location of hydrophobicity interactions (Harrison *et al.* 2022). That preference rises to 95% if it includes the middle codonic nucleotide. H1 NMR was used to experimentally demonstrate the presence of the preferential interactions by observing chemical shift changes of proton peaks. Within the tested subset of 4 amino acids, 50% showed a preference for their anticodonic middle base. While not all amino acids preferentially bind according to their codon assignment, the results of the NMR consistently match the simulation results. Both methods show a decreased capacity of biophysical interactions to predict codon assignments of hydrophobic amino acids. Additionally, we investigated a subset of 11 dinucleotides and 6 proteinogenic amino acids using molecular dynamic simulations. Dinucleotides also display a preference for their cognate amino acids, though they appear weaker. This work provides potential evidence for the role of weak biophysical interactions between nucleotides and amino acids in pre-patterning the genetic code and we have shown that molecular dynamics and NMR have the potential to investigate such interactions (Halpern *et al.* 2023).

Keywords
Origin of life, genetic code, biophysical interactions, anticodon, molecular dynamics, NMR.

Reference
Halpern A, Bartsch LR, Ibrahim K, Harrison SA, Ahn M, Christodoulou J, Lane N. **2023.** Biophysical Interactions Underpin the Emergence of Information in the Genetic Code. *Life* 13(5):1129; https://doi.org/10.3390/life13051129.

Harrison SA, Palmeira RN, Halpern A, Lane N. **2022.** A biophysical basis for the emergence of the genetic code in protocells. *Biochimica et Biophysica Acta (BBA) – Bioenergetics* 1863(8):148597; https://doi.org/10.1016/j.bbabio.2022.148597.

Woese C. **1969.** Models for the evolution of codon assignments. *Journal of Molecular Biology* 43(1):235–240; https://doi.org/10.1016/0022-2836(69)90095-3.

Acknowledgment
This research was supported by the Biotechnology and Biological Sciences Research Council to N.L. and from the Natural Environment Research Council to A.H. and N.L., while M.A. and J.C. were supported by a Wellcome Trust Investigator.

Some Theoretical Aspects of Reprogramming the Standard Genetic Code

Paweł BŁAŻEJ[1,*]

*Corresponding author e-mail: pawel.blazej@uwr.edu.pl

[1]*Department of Bioinformatics and Genomics, Faculty of Biotechnology, University of Wroclaw, Poland*

Abstract
It is believed that the extension of the standard genetic code in order to include non-canonical amino acids opens new prospects for medicine, industry, and biotechnology. Nowadays, there are several methods of code engineering used for storing new genetic information in DNA sequences and producing proteins with new properties. In this talk, we would like to provide a theoretical background for the optimal genetic code expansion. It is assumed that the expanded genetic code includes both canonical and non-canonical information stored in 64 classical codons. Moreover, the new coding system is robust to point mutations and minimizes the possibility of reversion from the new to old information. We presented also the formal procedure in finding the optimal codes with various number of vacant codons that could be assigned to new amino acids. Finally, we discussed the optimal number of the newly incorporated ncAAs and also the optimal size of codon groups that can be assigned to ncAAs.

Keywords
Genetic code, amino acid, code evolution.

Seeking the Genomic Simplicity Towards a Minimum Self-Managing Informational System

Ernesto BORRAYO CARBAJAL[1,*]

*Corresponding author e-mail: ernesto.borrayo@academicos.udg.mx

[1]*Department of Electro-Photonic Engineering, University of Guadalajara, Guadalajara, México*

Abstract

Current understanding of biological-information management mainly stems from the so-called Central Dogma of Molecular Biology, which has shaped the Genocentric Paradigm on the gene-to-functional-transcript perspective. This perspective has impregnated the search for the minimum information required for an organism to sustain a cellular-system-network. The minimum genome exploration has rendered the identification of a fixed number of known genes, as well as genes whose function remains to be identified. Such search has predominantly concentrated the analysis on coding genomic regions which leave other fundamental processes aside, mainly those that include higher-level information management. To cope with this limitation, a non-genocentric approach should be implemented as this would provide an integrative analysis on the information value of all genomic elements, regardless of their coding status.

Once the genocentric perspective has been surpassed, the search for a minimum genome should intrinsically lead to a Minimal Information Management System concept, where the main focus of attention relies on not only in coding elements, but also in those already described functional non-coding transcripts, as well as those undisclosed sequences which are non-coding and non-expressed (non-transcribed at all) and yet play a significant biological role in when, where and which biological functions are executed.

Altogether, coding and non-coding element fragments (or contigs) can be treated as *unitas informationis* and can be analyzed from a comprehensive point of view –regardless of their coding status– taking into consideration their ontological function as their primary attribute. According to this concept, semiotic functional structures can be identified and a functional congruence can be established by their permutation analysis. Thus, it will lead to a deeper insight of elementary genomic sequences that bear the bottom-line/basal information required for the regulation and execution of biological functions.

Keywords

Minimum genome, non-genocentric, biological information flow.

The Biological Codes Defined by Epigenetics

Selcen ÇELİK UZUNER[1,*]

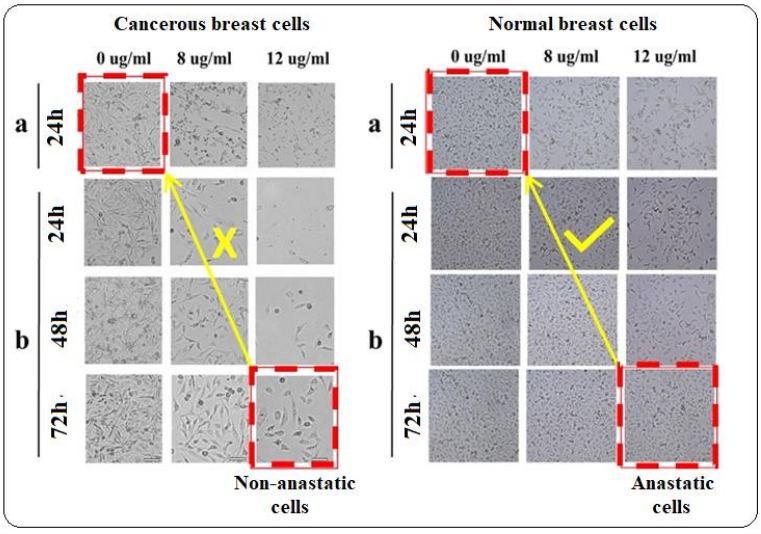
*Corresponding author e-mail: selcencelik83@yahoo.com

[1]*Department of Molecular Biology and Genetics, Karadeniz Technical University, Trabzon, Turkiye*

Abstract

Epigenome is the dynamic representative of the genome that manages all biological processes. It is thought that epigenetics is the main part of the puzzle for understanding gene expression profiles, however there are still numerous mysterious epi-stories that have not been told. I am curious to learn about hidden codes in humans, and strongly believe that what we have known is very less than we have not known yet.

With this motivation, a major part of my studies includes epigenetics. My previous works included the development of the immuno-detection of DNA methylation in mammalian cells. DNA is the epitope surrounded by a different range of proteins preventing the proper accessibility of antibodies to stain DNA methylation. We have revised the classical method to enhance *in situ* detection of DNA methylation by increasing antigenicity of methylated DNA. Although development of new methods is important for appropriate experiments, I personally closed this methodological book. I have now opened a new book to understand the roles of DNA methylation in normal cells and in cancer cells.



My current studies specifically are as follows.

1) *Anastasis by epigenetic regulation:* We found that bee venom induced anastasis in normal cells but not in cancer cells (Figure). Therefore, we aim to reveal the role of epigenetics for this different response of normal and cancerous cells to bee venom in terms of anastasis. We will propose a candidate pathway for this different anastatic response and reveal its epigenetic control.

2) *Fine-tuning argument in molecular biology*: Applications of philosophical approaches to molecular biology is not common, but it needs to be explored. Because science is science only when it is associated with a philosophical base. In this study I propose four parameters including i) position, ii) time, iii) interaction, and iv) amount to conclude the existence of fine-tuning in the human body. I love to look at my inside by a mirror of biology-philosophy.

What I plan to do in the future is to extend the fine-tuning study by modeling fine-tuning parameters (by mathematical and computational approaches). I also would like to prepare a proposal for my hypothesis "a code in the code" in normal cells to understand whether normal cells can rewrite their ontological epigenetic code after they lose the code (experimental and bioinformatics approaches). For both studies, I am highly motivated to collaborate with bioinformaticians, mathematicians and biologists.

I believe that I will benefit from DYNALIFE action while working with WG1 members by theoretical modelling of information flow and management in biological coding systems. These collaborations can improve my current and future work, and I would be very happy to perform experimental parts of projects proposed by all WG members.

Keywords

Epigenetics, anastasis, biological code, fine-tuning argument, cells.

Modeling the Non-Linear Dynamics of Information Flows in Neuro-Endocrine Systems

Željko ČUPIĆ[1,*] and Ana IVANOVIĆ-ŠAŠIĆ[1]

*Corresponding author e-mail: zcupic@ihtm.bg.ac.rs

[1]*Institute of Chemistry, Technology and Metallurgy, University of Belgrade, Belgrade, Serbia*

Abstract

Nonlinear feedback loops inherent to *neuroendocrine systems* are among the most important information flows at the organism level. They support high sensitivity and responsiveness of the living beings to external perturbations. Moreover, nonlinear feedback loops enable efficient control over dynamic physiological states. Often, they can be recognized through emergence of various dynamic phenomena, such as *biological rhythmicity*. Typical examples of such neuroendocrine systems are the hypothalamic-pituitary-adrenal (*HPA*) *axis* and the hypothalamic–pituitary–thyroid (*HPT*) *axis*. They are characterized by rhythmic dynamics with two characteristic periods, circadian (~ 24 h) and ultradian (20 min – 120 min), which allows living organisms to quickly adjust their neuroendocrine activity to fluctuations in their surroundings and/or their internal physiology.

We focus our research on mechanistic modelling of biochemical transformations that underlay complex neuroendocrine networks. Thus far, we have developed several variants of low-dimensional and extended models for the *HPA axis*, as well as, one medium scale model of the *HPT axis*. Both of them are assembled by combinations of the pseudo-reaction steps, describing in essence the information flow through the network of chemical transformations. Their role in physiological system is to maintain basal levels of hormone concentrations, and enable their functionally reasonable change when some need emerges. Our models enable one to emulate in numerical simulations changes in blood level of relevant hormones that constitute the HPA or HPT axis (Jelić et al. 2005, Marković et al. 2011, Čupić et al. 2017, Kolar-Anić et al. 2023).

The high predictive value of our models paves the way for their use in medical diagnostics of neuroendocrine diseases and for more efficient corticosteroid treatment that is applied in various illnesses, by harnessing the power of the underlying nonlinear feedback loops to the dosage of corticosteroid drugs could be significantly decreased, while preserving their efficacy. We pay special attention to the Stoichiometric Network Analysis of reaction network models to identify conditions ensuring the existence of unstable steady states, and in particular, Hopf bifurcation as a most plausible path leading to the oscillatory dynamics. The simplest way to use this template is to replace the text in this file with your own words using the styles provided as far as possible.

Keywords

Neuro-endocrine systems, oscillatory reactions, bifurcations, reaction networks, biological rhythmicity, nonlinear feedback loops.

Reference

Čupić Ž, Stanojević A, Marković VM, Kolar-Anić Lj, Terenius L, Vukojević V. **2017.** The HPA axis and ethanol: a synthesis of mathematical modelling and experimental observations, *Addiction Biology* 22(6):1486-1500.

Jelić S, Čupić Ž, Kolar-Anić Lj. **2005.** Mathematical modeling of the hypothalamic–pituitary–adrenal system activity, *Mathematical Biosciences* 197(2):173-187.

Kolar-Anić Lj, Čupić Ž, Maćešić S, Ivanović-Šašić A, Dietrich JW. **2023.** Modelling of the thyroid hormone synthesis as a part of nonlinear reaction mechanism with feedback, *Computers in Biology and Medicine*, 160:106980.

Marković VM, Čupić Ž, Vukojević V, Kolar-Anić Lj. **2011.** Predictive modeling of the hypothalamic–pituitary–adrenal (HPA) axis response to acute and chronic stress, *Endocrine Journal* 58(10):889-904.

Acknowledgment

This research was supported by Science Fund of Republic of Serbia, Grant No. 7743504, NES.

Investigating the Dynamics of Complex Biological Systems within Modern Mathematical Operators

Ozlem DEFTERLİ[1,*], Sadia ARSHAD[2] and Dumitru BALEANU[1,3]

*Corresponding author e-mail: defterli@cankaya.edu.tr

[1]*Department of Mathematics, Cankaya University, Ankara, Turkiye*
[2]*Department of Mathematics, COMSATS University Islamabad, , Lahore, Pakistan*
[3]*Institute of Space Sciences, Magurele, Bucharest, Romania*

Abstract
Some new and advanced mathematical tools have been proposed over the past few decades to better explain the dynamics of complex systems. To this end, one has to consider fractional modeling, fractional dynamics and hybrid modeling as natural tools. In this direction, fractional calculus has had a significant impact on understanding the dynamics of various processes appearing in the fields of biology, chemistry, medicine, nanotechnology, thermodynamics, mechanics, control theory, etc. Fractional derivatives have the excellent property of capturing the memory effects detected in almost all such important complex systems. The advantage of using models based on fractional calculus is the abundance of fractional kernels (singular or non-singular) that can be adapted to a given dataset. In addition, the order of the fractional derivatives can change, so the applicability of the generated models increases significantly.

In this presentation, recent progress in mathematical modeling of the dynamics of some important diseases will be discussed via applications. The complex dynamics of such systems will be analyzed by having the advantage of preserving the memory of the system in its evolution. In this direction, the performance of classical derivative and integral operators will be compared with the fractional derivative and integral operators through applications on some real-world problems. A comparative mathematical analysis will be given by simulating both classical and fractional model outcomes with respect some model parameters (Arshad et al. 2019, Arshad et al. 2020, Caputo and Fabrizio 2015, Carrillo et al. 2016). This kind of analysis is important to contribute to the development of the existing medications and new ways of quick, effective and low-cost treatments.

Keywords
Mathematical modelling, system dynamics, mathematical biology, fractional calculus, numerical schemes.

Reference
Arshad S, Baleanu D, Defterli O, Shumaila. **2019.** A numerical framework for the approximate solution of fractional tumor–obesity model. *International Journal of Modeling, Simulation, and Scientific Computing* 10(1):1941008; https://doi.org/10.1142/S1793962319410083.

Arshad S, Defterli O, Baleanu D. **2020.** A second order accurate approximation for fractional derivatives with singular and non-singular kernel applied to a HIV model. *Applied Mathematics and Computation* 374:125061; https://doi.org/10.1016/j.amc.2020.125061.

Caputo M, Fabrizio M. **2015.** A new definition of fractional derivative without singular kernel. *Progress in Fractional Differentiation and Applications* 1:73–85.

Carrillo RAK, Delgadill SE, Chen-Charpentier BM. **2016.** A mathematical model for the effect of obesity on cancer growth and on the immune system response. *Applied Mathematical Modelling* 40:4908–4920; https://doi.org/10.1016/j.apm.2015.12.018.

Acknowledgment
This research is partially supported by the Scientific and Technological Research Council of Turkey (TUBITAK).

Biological Information and the Genetic Code

Branko DRAGOVICH[1,2,*]

*Corresponding author e-mail: dragovich@ipb.ac.rs

[1]*Mathematical Institute, Serbian Academy of Sciences and Arts, Belgrade, Serbia*
[2]*Institute of Physics, University of Belgrade, Belgrade, Serbia*

Abstract
According to the modern scientific developments, the information is getting to be a fundamental notion like space, time and matter. These four fundamental concepts are substantially interconnected and represent the basic form of existence of the universe. Being fundamental, there is no complete definition of the information. According to our intuition, we differ what is the information from what it is not. In the present contribution, I consider information as a very special state of the material system with a meaning. Such very special state of the system determines evolution of another system. Depending on complexity of the system one can speak about physical, chemical, biological and other information.

Biological information (bioinformation) is related to a special state of a biological system – from viruses to multicellular organisms. The main example of the bioinformation system is DNA, which is a special long sequence of pairs of nucleotides. A part of DNA codes proteins, while the other one is mainly related to the regulation functions. The part that codes codons contain genes whose codons code amino acids, which are building blocks of proteins. The special connection between 64 codons and 20 amino acids with the stop signal is known as the genetic code.

In this talk, I plan to speak about basic properties of biological information and about the genetic code as an illustrative example of bioinformation with its functioning. I will also point out the role of p-adic ultrametrics in description of the genetic code.

Keywords
Bioinformation, genetic code.

Reference
Dragovich B, Dragovich A. 2010. p-Adic Modelling of the Genome and the Genetic Code. *Computer Journal* 53(4):432-442; https://doi.org/10.1093/comjnl/bxm083.

Dragovich B, Mišić NŽ. 2019. p-Adic hierarchical properties of the genetic code. *BioSystems* 185:104017; https://doi.org/10.1016/j.biosystems.2019.104017.

Dynamic Distributed Decision Making

Tatiana V. Guy[1,*]

*Corresponding author e-mail: guy@utia.cas.cz

[1]*Adaptive Systems Department, Institute of Information Theory and Automation, 182 00 Prague 8 Czech Republic*

Abstract

The variety of interactions in complex heterogenous systems encourages the study of decentralised models suitable to dynamically interacting independent elements that have their local meaning and costs. The elements can be parts of living matter, human beings, robots, their mixtures and colonies. The elements usually need to collaborate to survive or achieve a common goal. Typically, they have to share space, information and resources. The elements usually interact within a standard time-varying volatile system and have asymmetric and incomplete information (Harsanyi 1967). Besides, the dynamic interaction of individual elements with different (possibly conflicting) goals can cause conflicts and the elements either fight or negotiate.

Generally, interaction can be formulated as a dynamic DM. Its description and influence can be a part of the design and coordination of interconnected decisions distributed among various DM agents. They are acting within a standard system and may solve a problem of mutual interest to survive. Examples of such agents are elements of structures that emerge in ecosystems, technology and governance. Variable network systems of this type return to the process typical of nature. The relative performance of the individual network elements (agents), interactions between them and system variations ultimately determine the global behaviour of the entire system (Wolpert et al 2017). This understanding takes us back to the basic concept of cybernetics (Wiener 1948).

A decision system is considered from the viewpoint of a single selfish agent. In the supposed setup, the agent is an autonomous decision-maker aiming to influence the behaviour of some part of the World (*environment*), in the desired way. To do that, the agent has at its disposal a set of possible actions related to the environment. Thus, an agent is characterised by DM goals, constraints and information. It uses the information to create its DM strategy, generating actions in order to reach its DM goal. The desired methodology operates with the agent's environment model (describing the environment's reactions to applied actions and already realised part of behaviour) and a model of the agent's DM goals and constraints. Both models evolve dynamically and stochastically and should be adaptively learned, (Peterka 1981), (Karny 2014).

The proposed concept provides for the absence of a central coordinator but encourages the need to respect at least partially other agents (neighbours). The agent's goal determines the degree of respecting others. This DM formulation is the only scalable and suits complex ecosystems. An analytical examination of emerging computational aspects is almost impossible. However, the existence of life confirms the hypothesis that inherently selfish agents can find group benefit by banding together into coalitions.

The proposed framework captures situations where agents may benefit from cooperation. It requires a consistent theory that allows the agent to build and update a dynamic model of its changing stochastic environment (Berger, 1985) as well as build and update a randomised value function model. The so-called fully probabilistic design of optimal policies (Kárný Guy, 2006) provides an appropriate theory and allows Bayes' methodology to be used, too.

Keywords

Fully probabilistic modelling, cooperation, selfish agent, complex interactions.

Reference

Berger JO. **1985.** Statistical decision theory and Bayesian analysis / James O. Berger. New York: Springer Verlag.

Harsanyi JC.**1967.** Games with Incomplete Information Played by "Bayesian" Players, I-III. Part I. The Basic Model Management Science Vol. 14, No. 3, Theory Series.

Kárný M, **2014.** Approximate Bayesian recursive estimation, Information Sciences Vol.285, 1, p. 100-111.

Kárný M, Guy TV. **2006.** Fully probabilistic control design. Systems & Control Letters, 55, 4, 259-265.

Peterka V. **1981.** Bayesian system identification, In: P. Eykhoff ed., Trends and Progress in System Identification, pp 239-304, Pergamon Press, Oxford.

Wiener N. **1948.** Cybernetics: or Control and Communication in the Animal and the Machine. 2 Cambridge, MA: MIT Press.

Wolpert DH, Grana J,Tracey B, Kohler T, Kolchinsky A. **2017.** Modeling Social Organizations as Communication Networks arXiv preprint arXiv:1702.04449.

Theoretical Models of the Genetic Code, a Case Study: *Non-Power Integer Number Representations*

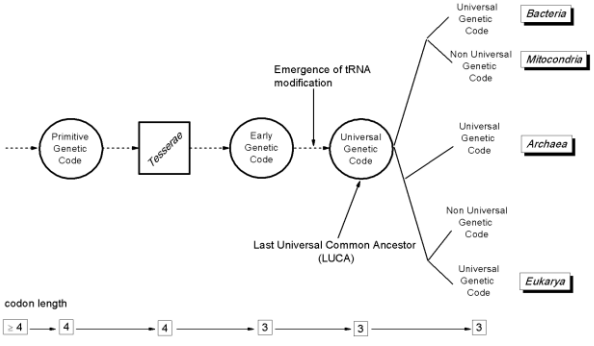
Diego L. GONZALEZ[1,2,*], Simone GIANNERINI[2]

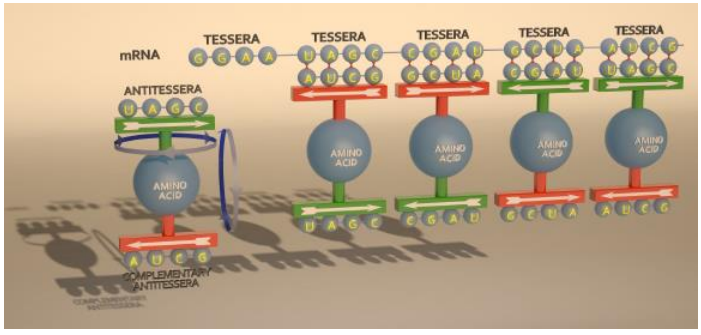
*Corresponding author e-mail: Gonzalez@bo.imm.cnr.it

[1]*Istituto per la Microelettronica e I Microsistemi, IMM-CNR, Bologna, Italy*
[2]*Dipartimento di Scienze Statistiche "Paolo Fortunati", UNIBO, Bologna, Italy*

Abstract
In this contribution we illustrate a case study for the theoretical modelling of the genetic code based on first principles from number theory. The model allows to develop a paradigm that goes from theory, to the study of real coding sequences, to the hard problem of the origin of life.

From the mathematical point of view, the model is based on a particular representation of integer numbers: *the redundant non-power positional system*. On this basis, the degeneracy of different variants of the genetic code can be described. In addition to the properties of the non-power representations, the symmetries of the different variants of the code represent a key aspect for the development of the respective models and applications. In particular, different dichotomic partitions of the genetic code are identified leading to *dichotomic classes* i.e., binary partitions of the genetic code that have a definite biochemical meaning. In turns, this approach allows to study real coding sequences uncovering unexpected universal properties having also definite biochemical meaning. Moreover, the modelling of the (more symmetric) vertebrate mitochondrial genetic code, allows for a biochemical interpretation of the origin of degeneracy based on the symmetry of putative ancient adaptors; in turns, it can be shown that this approach has interesting consequences from the point of view of the origin and evolution of the genetic code. Ancestral symmetries lead to conserved quantities, implying that some present symmetries of the code can be interpreted as evolutionary relics going back close to the origin of the code; in turns, such conserved quantities need to be related to important biological functions and, thus, they contribute to shed light on important molecular mechanisms of present forms of life.





Keywords
Theoretical models, genetic code, non-power representation systems, symmetry, evolution, dichotomic classes

References

Gonzalez DL. **2008.** The Mathematical Structure of the Genetic Code. In: *The Codes of Life,* Chapt. 6 (M. Barbieri, Ed.), Springer Verlag.

Gonzalez DL, Giannerini S, Rosa R. **2019.** On the origin of degeneracy in the genetic code, *Royal Society Interface Focus* 9(6):20190038; https://doi.org/10.1098/rsfs.2019.0038.

Gonzalez DL, Giannerini S, Rosa R. **2016.** The non-power model of the genetic code: a paradigm for interpreting genomic information, *in DNA as Information, Philosophical Transactions of the Royal Society of London Series A* 374(2063):20150062; https://doi.org/10.1098/rsta.2015.0062.

A Biophysical Basis for the Emergence of the Genetic Code in Protocells

Stuart A. HARRISON[1,*], Aaron HALPERN[1], Lilly BARTSCH[1], Raquel Nunes PALMEIRA[1] and Nick LANE[1]

*Corresponding author e-mail: stuart.harrison.17@ucl.ac.uk

[1]*Centre for Life's origins and evolution, Genetics evolution and environment, University College London, London, United Kingdom*

Abstract

The origins of the genetic code is an abiding mystery in biology and poses a unique problem at the origins of life. A 'code within the codon' hints at biophysical interactions between amino acids and nucleotides but these patterns have resisted interpretation. In our recent paper (Harrison et al. 2022) we present a new hypothesis, grounded in an autotrophic protocell model. Considering the genetic code in relation to an emergent protometabolism that starts from CO_2 and H_2, allows the prediction of most modern codon assignments.

We show that the first letter of the codon corresponds to the amino acids distance from CO_2 with the those encoded by purines being closer than those encoded by pyrimidines. These associations suggest that amino acids were incorporated into the genetic code as a protometabolic network expanded. The second position of the anticodon corresponds with hydrophobicity of the amino acid – or some related property – suggesting a mechanism by which amino acids become assigned to codons. Follow up work (Halpern et al, 2023) has shown that these interactions between anticodonic nucleotides and amino acids can be observed both by molecular dynamics simulations and corroborated by NMR. We additionally observe that third position redundancy is not randomly distributed within the genetic code and non-synonymous amino acids can be specified based on size.

These simple rules in combination imply an iterative expansion of the genetic code over time specified by stereochemical interactions between amino acid nucleotide species and can explain a substantial proportion of the extant genetic code with minimal effort. Thus, even the earliest RNA polymers may lead to non-random peptides and provide a means of selection in protocells facilitate the emergence of information.

Keywords

Protometabolism, genetic code, information, origins of life, evolution.

Reference

Halpern A, Bartsch LR, Ibrahim K, Harrison SA, Ahn M, Christodoulou J, et al. **2023.** Biophysical Interactions Underpin the Emergence of Information in the Genetic Code. *Life* 13(5):129; https://doi.org/10.3390/life13051129.

Harrison SA, Palmeira RN, Halpern A, Lane N. **2022.** A biophysical basis for the emergence of the genetic code in protocells. *Biochimica et Biophysica Acta (BBA) – Bioenergetics* 1863(8):148597; https://doi.org/10.1016/j.bbabio.2022.148597.

Acknowledgment

This research was supported by Biotechnology and Biological Sciences Research Council (BBSRC).

Evolution as Learning, Natural Selection as a Game: Bayes Meets Darwin

Vladimir JAĆIMOVIĆ[1,*]

*Corresponding author e-mail: vladimirj@ucg.ac.me

[1]*Faculty of Natural Sciences and Mathematics, University of Montenegro, Podgorica, Montenegro*

Abstract

The basic mathematical framework for modeling evolutionary processes is provided by Evolutionary Game Theory (EGT). EGT has been established in 1970's as a subfield within the broad field of Game Theory focused on explaining population dynamics and evolution in biological systems. John Maynard Smith is widely credited as a founder of EGT, due to his seminal work (Maynard Smith 1972). Later, the Viennese research group made a great contribution to the development of EGT into a prominent and well-established mathematical theory (Hofbauer and Sigmund 1998).

Nevertheless, evolution is not exclusively a biological concept. EGT have found its applications in linguistic evolution (Komarova et al. 2001), learning and cognition (Suchow et al. 2017), and some other fields.

On the other hand, since pioneering efforts in mathematical biology in 1930's and 1940's, there has been an intuition that information theory can be the most important mathematical tool for deeper understanding of biological systems. Evolutionary dynamics in biological systems can be treated as learning, that is - as information transmission within the population and between population and environment. This point of view brought some successes in specific highly focused areas, such as: (a) the maximum entropy principle in ecology (Harte 2011); (b) Shannon and Renyi entropies as measures of biodiversity (Leinster 2021); and (c) thermodynamic study of individual cells (England 2013).

In the present talk, I put a strong emphasize on the notion of "potential information" in evolutionary biology. In has been shown that the "potential information" serves as a Lyapunov function in various dynamical systems modeling the evolution; this quantity is interpreted as an amount of information left to learn before reaching an evolutionary stable state (Baez and Pollard 2016). (Notice that a notion of evolutionary stable state is a specific manifestation of the broad paradigm of Nash equilibrium applied in to the context of EGT.) This point of view provides a rigorous framework for treating the evolution as learning and natural selection as an evolutionary game. Moreover, there is a precise mathematical analogy between evolutionary games and Bayesian inference, where a probabilistic hypothesis about the state of environment is gradually refined by repeated experiments (Suchow et al. 2017, Czegel et al. 2022).

This talk is a brief overview of some old paradigms and new results that establish bridges between EGT, evolutionary optimization, Bayesian learning, decision making and cognition and stochastic thermodynamics, through the lenses of information theory,

I also point out limitations of the presented approach, and (try to) identify mathematical and physical paradigms that might help to overcome them, thus making further steps towards the unified mathematical view on biological evolution. Most important, one needs tools to explain phase transitions and pattern formation in emergence of life. The most obvious tools for this goal are mathematical bifurcation theory and physics of complex systems. Furthermore, one has to take into account also developmental biology, where the theory of PDE's plays an important role (Baker et al. 2008). Finally, classical information theory seems to be insufficient for deeper understanding of biological systems, motivating recent research efforts on quantum computing in living organisms (Baez and Biamonte 2018, Basieva et al. 2021).

Keywords

Evolutionary game theory, Bayesian learning, maxent, open Markov processes, potential information, phase transition.

Reference

Baez JC, Pollard BS. **2016.** Relative entropy in biological systems. *Entropy* 18(2):46.

Baez JC, Biamonte JD. **2018.** *Quantum Techniques in Stochastic Mechanics*. World Scientific.

Baker RE, Gaffney EA, Maini PK. **2008.** PDE's for cell organization in cellular and developmental biology. *Nonlinearity* 21:251-290.

Basieva I. Khrennikov A. Ozawa M. **2021.** Quantum-like modeling in biology with open quantum systems and instruments. *BioSystems* 201:104328.

Czegel D, Giaffar H, Tenenbaum JB, Szathmary E. **2022.** Bayes and Darwin: How replicator populations implement Bayesian computations. *BioEssays* 44(4):2100255.

England JL. **2013.** Statistical physics of self-replication. *J. Chem. Phys.* 139:121923.

Harte J. **2011.** *Maximum Entropy and Ecology: A Theory of Abundance, Distribution and Energetics*. Oxford University Press.

Hofbauer J, Sigmund K. **1998.** *Evolutionary Games and Population Dynamics*. Cambridge University Press.

Komarova NL, Niyogi P, Nowak MA. **2001.** The evolutionary dynamics of grammar acquisition. *J. Theor. Biol.* 223(4):43-59.

Leinster T. **2021.** *Entropy and Diversity: The Axiomatic Approach*. Cambridge University Press.

Maynard Smith J. **1972.** Game Theory and Evolution of Fighting. In: *On Evolution*. Edinburgh University Press.

Suchow JW, Bourgin DD, Griffiths TL. **2017.** Evolution in Mind: Evolution Dynamics, Cognitive Processes and Bayesian Inference. *Trends Cogn. Sci.* 21(7):522-530.

Plenary Lecture

Is the Emergence of Life an Expected Phase Transition in the Evolving Universe?

Stuart A. KAUFFMAN[1,*], Niles LEHMAN[2,3] and Andrea ROLI[4]

*Corresponding author e-mail: stukauffman@gmail.com

[1]*Institute for Systems Biology, Seattle, Washington, United States*
[2]*Department of Chemistry, Portland State University, Portland, United States*
[3]*Department of Computer Science and Engineering, University of Bologna, Campus of Cesena, Cesena, Italy*
[4]*European Centre for Living Technology, Venezia, Italy*

Medical Diagnostics with Quantum Potential Extracted from Dendrogram Representation for EEG-data

Andrei KHRENNIKOV[1,*], Oded SHOR[2,3] and Felix BENNINGER[2,3]

*Corresponding author e-mail: Andrei.Khrennikov@lnu.se

[1]*International Center for Mathematical Modeling\in Physics and Cognitive Sciences, Linnaeus University, Växjö, SE-351 95, Sweden*
[2]*Felsenstein Medical Research Center, Petach Tikva, Israel*
[3]*Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel*

Abstract

Disorders of the brain, such as schizophrenia, epilepsy, depression, and dementia, constitute approximately 27% of the global disease burden in terms of disability-adjusted life-years (DALYs) and that surpasses cardiovascular diseases and cancer combined. For most brain disorders no single accurate, diagnostic tool is available as yet. Electroencephalography (EEG) is an inexpensive and well-established tool used for resting-state power, spectral and functional connectivity analyses as well as microstate analysis, which may assist in diagnosing these disorders with variable success and little use in clinical practice. We suggested (Shor et al. 2021) the novel diagnostics based on analysis of the EEG-data via its representation by dendrograms – finite trees and then applying the quantum-like Bohmian mechanics on such trees. The simplest trees are homogeneous p-adic trees with p branches leaving each vertex. In this way our method of p-adic quantum-like medical diagnostic is coupled to p-adic theoretical physics (established by Vladimirov, Volovich, Parisi, Dragovich, Khrennikov,...) and quantum-like models of decision making and cognition (Khrennikov, Aerts, Haven, Bagarello, Busemeyer, Bruza,...).

So, we start with collection of EEG signals from a family of electrodes coupled to the brain. Then we apply one of clustering algorithms to extract the treelike hierarchic structure in this data and construct a dendrogram. Each dendrogram corresponds to time interval. In this way, by splitting the EEG data into blocks we generate an ensemble of dendrograms and their probability distribution that is used to construct the quantum potential. This potential is the basic tool of Bohmian mechanics, a special mathematical representation of quantum theory. We proceed in quantum-like approach: we do not refer to genuine quantum physical processes in the brain. The latter is treated as a black box processing mental information in the accordance with the laws of quantum information theory and theory of open quantum systems. So, the methodology and mathematical formalism of quantum theory are applied to model information processing in macroscopic biosystems.

Surprisingly the form of this potential characterizes with high precision the mental state of a patient. This novel method accurately identified participants with mild cognitive impairment (MCI), AD, schizophrenia, or depression, by routine EEG records analysed by this novel approach. Why does it work? Dendrograms reflect the complex hierarchy in information processing by the brain and the quantum potential is the integral nonlocal characteristic of cognitive information collected be electrodes located at the different points. The theoretical basis of this method was established in monograph (Khrennikov 2004).

Keywords
Dendrograms, p-adics, hierarchical structure, mental state, medical diagnostic, schizophrenia, EEG.

References

Khrennikov A. **2004.** *Information Dynamics in Cognitive, Psychological, Social, and Anomalous Phenomena*. Kluwer, Dordrecht.

Shor O, Glik A, Yaniv-Rosenfeld A, Valevski A, Weizman A, Khrennikov A, Benninger F. **2021.** EEG p-adic quantum potential accurately identifies depression, schizophrenia and cognitive decline. *PLoS ONE* 16(8): e0255529; https://doi.org/10.1371/journal.pone.0255529.

Simulation of Base Excision Repair in the Calculus of Covalent Bonding

Stefan KUHN[1,*] and Irek ULIDOWSKI[2]

*Corresponding author e-mail: stefan.kuhn@ut.ee

[1]*Department of Computer Science, Tartu University, Tartu, Estonia*
[2]*Department of Informatics, University of Leicester, Leicester, United Kingdom*

Abstract

Process calculi are a family of formalisms to model processes and their behavior. Originating in computer science and the field of distributed computing, they have also been used to model biological processes, e.g., BioPepa (Ciocchetta, Hillston 2009). These models use similarities in the behavior of computer processes and biological entities. For example, message passing between separate processes can be compared to chemical interaction between biomacromolecules. Reversibility is an aspect of chemical and biological processes, which is an area of ongoing research in computer science. In the area of process calculi, CCS-K (Phillips, Ulidowski, Yuen 2013) is an attempt to include reversibility in a forward calculus.

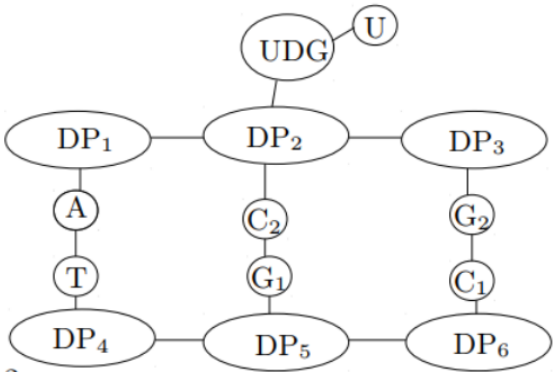


Figure 1. Visualisation of the modelling of Base Excision Repair in CCB.

We have developed a new process calculus inspired by chemical reactions, called the Calculus of Covalent Bonding or CCB (Kuhn 2018). The key feature of the calculus was a new prefix operator of the form (s; b), where doing of action b triggers undoing of one of the actions in s. Because of this connection between doing and undoing of actions (or forming and breaking of bonds in a chemical modelling) we called this local reversibility. We have shown that our calculus enables out-of-causal order reversibility. In this paper we demonstrate the Base Excision Repair of DNA, a high-level biological example, using our calculus. We also introduce a software which allows us to check the syntax of processes and to simulate their execution.

CCB could be used as a starting point for new ways to model biological processes. Inclusion of rates and probabilities is one option here. Also, the software could be extended to be used for simulating a range of processes. We are interested in collaborations also with respect to other applications of computer science in biology, in particular modelling and simulation.

Keywords

Process calculi, base excision repair, calculus of covalent bonding, distributed computing.

Reference

Ciocchetta F, Hillston J. **2009.** Bio-PEPA: a Framework for the Modelling and Analysis of Biochemical Networks. *Theoretical Computer Science* 410(33-34):3065-3084; https://doi.org/10.1016/j.tcs.2009.02.037.

Kuhn S. **2018.** Simulation of base excision repair in the calculus of covalent bonding. In: Kari, J., Ulidowski, I. (eds) *Reversible Computation. RC 2018. Lecture Notes in Computer Science*, vol 11106, pp 123–129, Springer, Cham; https://doi.org/10.1007/978-3-319-99498-7_8.

Phillips I, Ulidowski I, Yuen S. **2013.** A reversible process calculus and the modelling of the ERK signalling pathway. In: Glück, R., Yokoyama, T. (eds) *Reversible Computation. RC 2012. Lecture Notes in Computer Science*, vol 7581, pp 218–232, Springer, Berlin, Heidelberg; https://doi.org/10.1007/978-3-642-36315-3_18.

Life's Genesis, Consciousness and the Fabric of Reality: Shifting Perspectives on Spacetime

Iván MARQUÉS CAMPILLO[1,*]

*Corresponding author e-mail: iwmarquescampillo197@gmail.com

[1]*Department of Physics, University of the Balearic Islands, Palma de Mallorca, Spain*

Abstract

From the mainstream classical-materialist point of view, spacetime is considered fundamental. This paradigm asserts that the Big Bang marked the beginning of the physical universe and that all complex structures, included life and conscious beings, arise from the interaction of irreducible, fundamental and independent to the observer elements. According to this reductionist perspective, all the processes occurring in spacetime can be explained based on these basic elements. However, the limits of modern theories, such as quantum field theory, suggest that spacetime may not be fundamental:

- At Planck scale, neither space nor time possesses intrinsic meaning, as matter starts to collapse into black holes.

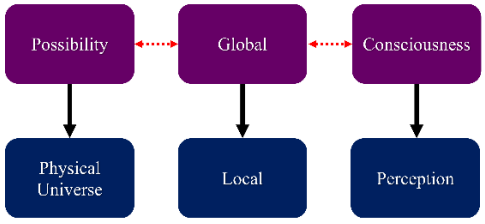
- Bell's theorem stablishes that neither realism nor locality holds true.

- The outcomes of experiments, and thus the degrees of freedom in the physical universe, depend on how the observer measures them.

These observations indicate that the physical universe may not be governed solely by fundamental laws describing the dynamics of elementary particles on a fixed spacetime framework. Upon closer examination of the implications of these fundamental laws, it becomes apparent that the physicality of reality is not fundamental, and space and time are not genuine but rather emergent phenomena. Therefore, a shift in perspective is necessary to address the problem of life and consciousness.

To understand the origin of life, we must first grasp the foundation of reality, as life is a manifestation of reality's capabilities. If we do not approach reality from the correct perspective, we cannot expect to explain life in its fundamental terms. Our current understanding of life posits that its essence lies in patterns of information expressed in inert matter, such as atoms and molecules.

However, how did these organized patterns initially emerge?



By applying critical thinking, we realize that even the objects we perceive in spacetime are not only defined in form but also in relevance by biological evolution. Natural selection enabled us to solve the problem of survival, which involved compressing and simplifying reality. Evolution does not seek truth but utility: spacetime is an emergent interface that facilitated the survival and functioning of life as we know it.

As carriers of life, we should take perceptions seriously but not interpret them as literally. If spacetime is not fundamental, then what is? Drawing inspiration from the observer's significance in quantum mechanics, this work assumes that consciousness is the transcendental reality.

We are the first link from which reality is experimented, and then described. The intrinsic ability of conscious beings (or reality itself) to acknowledge its internal reality and conceive spaces of possibility in their imagination is often overlooked. We propose a teleological approach to reality, where a space of purposes is fundamental and change (spacetime) emerges from it. In this new perspective, we hypothesize that survival is the only stable purpose when examined within a spacetime framework like our own, and therefore life is possible. Finally, we explore the emergence of knowledge (resilient information) or complexity for a given purpose.

Keywords

Spacetime, emergent, reality, life, consciousness, fundamental.

Deterministic and Stochastic Modelling of Protocells

Fabio MAVELLI[1,*] and Emiliano ALTAMURA[1]

*Corresponding author e-mail: fabio.mavelli@uniba.it

[1]*Chemistry Department, University of Bari Aldo Moro, Bari, Italy*

Abstract

Protocells are micro-compartmentalized structures that share their unique static and dynamic organization with primitive cells or modern living cells, gaining increasing attention in an interdisciplinary field that embraces both studies of the origins of life and modern synthetic biology. Therefore, the term protocells can refer to both primitive cell models and artificial cell-like systems of minimal complexity. In both cases, they consist of chemically reactive compartmentalized systems that can exhibit a very broad distribution of sizes and compositions. Therefore, modeling the time behavior of a protocell population can be very difficult and challenging. In this contribution we will review our previous attempts to describe the dynamics of protocell populations following deterministic, stochastic or semi-deterministic approaches (Mavelli et al. 2014). In particular, the general problem of describing the time behavior of chemically reacting compartments will be introduced by considering the polydispersity in size and composition of the whole set of compartmentalized reactors and the low number of reacting molecules.

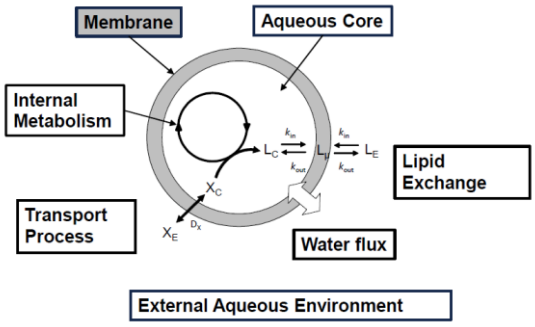


Figure1. Schematic draw of a reacting protocell.

First, the results of the stochastic simulation of a Ribocell population will be presented and discussed. Ribocell is a hypothetical minimal cell model, proposed by Szostak and collaborators (Szostak et al. 2001), which predicted that a minimal cell could be implemented by encapsulating in lipid vesicles a pair of ribozymes capable of self-replicating and catalyzing membrane conversion lipids of the available molecular precursors. The aim of the theoretical study was to verify the feasibility of this hypothetical model in terms of spontaneous synchronization of the replication of the genetic code and of the reproduction of the vesicles (Mavelli 2012). Next, the kinetics of protein expression within lipid vesicles will be considered using the PURE system, a purified cell-free transcription and translation kit. A simplified deterministic model for protein expression kinetics was developed in a bulk solution and validated with experimental data (Mavelli et al. 2015). Thus, this model has been used to predict the protein synthesis taking place in the aqueous core of lipid vesicles by assuming two alternative probability density functions: the Gaussian or the power law, to describe the distribution of DNA and enzymes within the vesicle population (Mavelli and Stano 2015). The results obtained were compared with the available experimental data confirming that the power law can better describe the encapsulation of protein complexes during the formation of lipid vesicles. Finally, the kinetics of photogeneration of the pH gradient across the lipid membrane of protocells will be introduced and discussed (Altamura et al. 2017).

Keywords

Protocell, lipid vesicles, pure system, stochastic kinetics, ribozyme, transcription-translation.

Reference

Altamura E et al. **2017.** Highly oriented photosynthetic reaction centers generate a proton gradient in synthetic protocells. PNAS 114(15):3837-3842, https://doi.org/10.1073/pnas.161759311.

Mavelli F. **2012.** Stochastic simulations of minimal cells: the Ribocell model. *BMC Bioinformatics* 13(4):S10; https://doi.org/10.1186/1471-2105-13-S4-S10.

Mavelli F et al. **2014.** Recent Theoretical Approaches to Minimal Artificial Cells. *Entropy* 16(5):2488-2511; https://doi.org/10.3390/e16052488.

Mavelli F et al. **2015.** A Simple Protein Synthesis Model for the PURE System Operation. *Bull. Math. Biol.* 77(6):1185-1212.

Mavelli F, Stano P. **2015.** Experiments and numerical modelling on the capture and concentration of transcription-translation machinery inside vesicles. A. *Life* 21:1–19; https://doi.org/10.1162/ARTL_a_00187.

Szostak et al. **2001.** Synthesizing life. *Nature* 409:387-390; https://doi.org/10.1038/35053176.

Standard Genetic Code Model that Supports De Duve's Idea of an Evolutionary Game Written into the Fabric of the Universe

Nataša Ž. MIŠIĆ[1,*]

*Corresponding author e-mail: natasa.misic@li.rs, nmisic@rcub.bg.ac.rs

[1]*Computational Bioengineering, R&D Institute Lola Ltd, Belgrade, Serbia*

Abstract

Scientific efforts to obtain "minimal" cells by removing as much complexity as possible have resulted in organisms that are simple by biological standards, but still extremely complex by chemical ones. Living systems, even in their minimal form, are arranged in many different ways at many scales, either in terms of composition, spatial configuration or dynamics. This complex behavior of a system is controlled by the interaction of top-down and bottom-up processes, whereby smaller processes, structures and states are optimally aggregated into larger scales in a robust manner.

More recent research goes beyond the usual perspective of emergent complexity through a mechanistic process of different outcomes that simply occur as a result of different environmental influences. Rather, it is proposed that the flexible and adaptive behavior of an individual organism is the result of morphogenetic mechanisms that exist on a continuum of problem-solving capacities at different scales within the biosphere (Smith 2013, Levin 2019). This problem-solving driven evolution is increasingly viewed within the framework of teleonomy – "evolved purposiveness" (Corning et al. 2023), or Cognition-Based Evolution in which biological and evolutionary development represents a continuous autopoietic defense of self-referential basal cellular states of homeostatic preference, achieved and maintained through self-referential measurement of information and its communication (Miller et al. 2021).

The information-centered origin and evolution of life brings into focus the problem of biological and thus natural coding and computation, actualizing De Duve's famous idea that an evolutionary game is to some extent written into the fabric of the universe. Here we will present the standard genetic code model, which is based on the invariant nucleon packing quantum and the corresponding mass balances and where this fine-tuning of the nucleon distribution can be related to mathematical structures characterized by self-referentiality and the scale-free property (Mišić 2011, 2014, 2016).

Keywords

Origin of life, information-based evolution, standard genetic code, self-referentiality, scale-free property.

Reference

Corning PA, Kauffman SA, Noble D et al., Eds. **2023.** *Evolution "On Purpose": Teleonomy in Living Systems*. Cambridge: MIT Press.

Levin M. **2019.** The Computational Boundary of a "Self": Developmental Bioelectricity Drives Multicellularity and Scale-Free Cognition. Front. Psychol. 10:2688; https://doi.org/10.3389/fpsyg.2019.02688.

Miller WB, Enguita FJ, Leitão AL. **2021.** Non-Random Genome Editing and Natural Cellular Engineering in Cognition-Based Evolution. *Cells* 10:1125; https://doi.org/10.3390/cells10051125.

Mišić NŽ. **2011.** Nested Numeric/Geometric/Arithmetic Properties of shCherbak's Prime Quantum 037 as a Base of (Biological) Coding/Computing. *NeuroQuantology* 9(4):702-715; https://doi.org/10.14704/nq.2011.9.4.489.

Mišić NŽ. **2014.** From genetic code toward spacetime geometry. Proc. TABIS.2013 Conf.: *Theoretical Approaches to BioInformation Systems*, Institute of Physics, Belgrade, pp. 101-123.

Mišić NŽ. **2016.** Standard genetic code: p-Adic modelling, nucleon balances and selfsimilarity. *FU Phys. Chem. Tech.* 14:275–298; https://doi.org/10.2298/FUPCT1603275M.

Smith E. **2013.** Emergent order in processes: The interplay of complexity, robustness, correlation, and hierarchy in the biosphere. In: *Complexity and the Arrow of Time* (Lineweaver C, Davies P, Ruse M, Eds.), Cambridge University Press, pp. 191-223; https://doi.org/10.1017/CBO9781139225700.012.

Acknowledgment

This research was supported by Ministry of Education, Science and Technological Development of the Republic of Serbia, Grant No. 451-03-68/2023-14/200066, and partly by the COST Action DYNALIFE CA21169.

A Rudimentary Genetic Code Supports Darwinian Evolution in Protocells

Raquel NUNES PALMEIRA[1,2,*], Marco COLNAGHI[1,2], Andrew POMIANKOWSKI[1,2] and Nick LANE[1]

*Corresponding author e-mail: raquel.palmeira.13@ucl.ac.uk

[1]*Genetics Evolution and Environment, University College London, London, United Kingdom*
[2]*Centre for Computation, Mathematics and Physics in the Life Sciences and Experimental Biology, University College London, London, United Kingdom*

Abstract
Widely known patterns in the genetic code point to an era of early coding based on biophysical interactions (Harrison et al. 2022). The strongest amongst those patterns relates the hydrophobicity of anticodons to the relative hydrophobicity of their cognate amino acids. This is of particular interest because relative hydrophobicity could both inform stereochemical relationships between nucleotides and peptides, culminating in rudimentary translation; but also, loosely dictate the type of function a peptide might have in a cell, because of how they might bind to metal ions and cofactors or interact with a membrane.

We use population genetics modelling to investigate a population of growing autotrophic protocells containing nucleotide and peptide polymers. These have two basic functions: carbon fixation (or monomer addition) and templated polymerisation; and can undergo simple copying and translation based on the loose biophysical interactions described above.

In our model information is not reliant on a specific sequence, so we can circumvent the problem of error catastrophe (Eigen 1992). Further, we find that even the slight bias in the polymer populations caused by this simple mode of coding can, in theory, support growth and evolution. Different topologies of the model support more or less robust evolution, giving us clues about what the early translational system might have looked like.

Keywords
Origin of life, genetic code, protocells, autotrophy.

Reference
Harrison SA, Palmeira RN, Halpern A, Lane N. **2022.** A biophysical basis for the emergence of the genetic code in protocells. *Biochim Biophys Acta Bioenerg*. 1863(8):148597; https://doi.org/10.1016/j.bbabio.2022.148597.

Eigen M. **1992.** *Steps Towards Life: A Perspective on Evolution*. Oxford University Press.

Coded Interneural Communication via Chaotically Spiking Neurons

Oreste PIRO[1,2,*]

*Corresponding author e-mail: oreste.piro@uib.es

[1]*Department of Physics, University of Balearic Islands, Carretera de Valldemossa, km 7.5, Palma de Mallorca, Spain*
[2]*Department of Ecology and Marine Resources, Mediterranean Institute for Advanced Studies, IMEDEA (CSIC–UIB), Esporles, Spain*

Abstract
The van der Pol–FitzHugh–Nagumo neuron model with inertia was shown to exhibit a chaotic mixed-mode dynamic composed of large-amplitude spikes separated by an irregular number of small-amplitude chaotic oscillations. In contrast to the standard 2D van der Pol–FitzHugh Nagumo model driven by noise, the interspike intervals distribution displays a complex arrangement of sharp peaks related to the unstable periodic orbits of the chaotic attractor. For many ranges of parameters controlling the excitability of the system, we observe that chaotic mixed-mode states consist of lapses of nearly regular spiking interleaved by others of highly irregular one. We explore here the emergence of these structures and show their correspondence to the intermittent transitions to chaos. In fact, the average residence times in the nearly-periodic firing state, obey the same scaling law – as a function of the control parameter – than the one at the onset of type I intermittency for dynamical systems in the vicinity of a saddle node bifurcation. We hypothesize that this scenario is also present in a variety of slow-fast neuron models characterized by the coexistence of a two-dimensional fast manifold and a one- dimensional slow one. We also show experimental evidence that the behaviour described above is present in a class of neurons and we finally speculate on the possible functional role that these complex temporal patterns of the neuron firing might have on the codification of interneural communication through shared nerve bundles.

Keywords
Chaotic firings, interneural communication, intermittence.

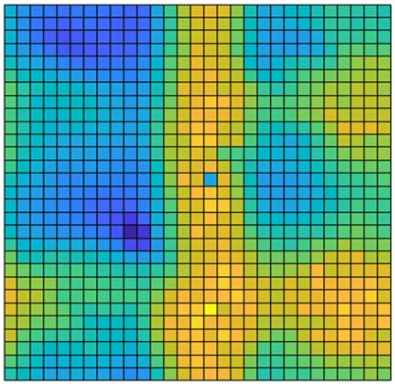
Meaningful Representations of Protein Sequences

Stefano PIOTTO[1,2,*], Lucia SESSA[1,2] and Simona CONCILIO[1,2]

*Corresponding author e-mail: piotto@unisa.it

[1]*Department of Pharmacy, University of Salerno, Fisciano (SA), Italy*
[2]*Bionam center for biomaterials, University of Salerno, Fisciano (SA), Italy*

Abstract
Protein encoding plays a crucial role in understanding the intricate relationship between protein sequences and their functions. Traditional approaches to protein encoding have relied on established methods such as one-hot encoding or position-specific scoring matrices (PSSMs) (Sevgen et al. 2023). However, the introduction of new protein descriptors has opened up novel avenues for capturing more comprehensive and meaningful information from protein sequences.
In this study, we propose the utilization of protein transmembrane analysis as a means to derive enhanced protein descriptors (Piotto et al. 2018). Transmembrane proteins play critical roles in various cellular processes and exhibit unique characteristics that can be exploited for encoding purposes. By considering the amino acid sequences of transmembrane peptides, we extract valuable insights into the structural and functional properties of proteins.



To accomplish this, we employ advanced computational techniques to analyze the composition, physicochemical properties, and evolutionary patterns of transmembrane peptides. Through this analysis, we derive a set of novel descriptors that encapsulate crucial information about the protein's transmembrane regions. These descriptors provide a more comprehensive representation of protein sequences, capturing both global and local features that are relevant to their function.

Overall, this study introduces a novel approach to protein encoding by incorporating transmembrane analysis to derive enhanced protein descriptors. By capturing crucial information from transmembrane regions, we provide a more comprehensive representation of protein sequences, leading to improved performance in various protein-related tasks. These findings have significant implications for advancing our understanding of protein structure, function, and evolution

Keywords
Protein sequence, 3d structure, motif, encoding, molecular dynamics.

Reference
Sevgen E, Moller J, Lange A, Parker J, Quigley S, Mayer J, Srivastava P, Gayatri S, Hosfield D, Korshunova M, Livne M, Gill M, Ranganathan R, Costa AB, Ferguson AL. **2023.** ProT-VAE: Protein Transformer Variational AutoEncoder for Functional Protein Design. *BioRxiv* https://doi.org/10.1101/2023.01.23.525232.

Piotto S, Di Biasi L, Sessa L, Concilio S. **2018.** Transmembrane peptides as sensors of the membrane physical state. *Frontiers in Physics* 6:48, https://doi.org/10.3389/fphy.2018.00048.

Modified Optimal Homotopy Asymptotic Method for Study of Thermal Radiative Convective Nanofluid Flow

Nicolina POP[1,*], Remus Daniel ENE[2] and Rodica BADARAU[3]

*Corresponding author e-mail: nicolina.pop@upt.ro

[1]*Department of Physical Foundations of Engineering, Politehnica University of Timisoara, Timisoara, Romania*
[2]*Department of Mathematics, Politehnica University of Timisoara, Timisoara, Romania*
[3]*Department of Mechanical Machines, Equipment and Transportation, Politehnica University of Timisoara, Timisoara, Romania*

Abstract

The aim of using nanofluids is to significantly improve heat transfer by increasing the thermal conductivity of base fluids (ethylene glycol, water, motor oil, acetone, etc.). Solving the equations that characterize nanofluids is important because they govern a very important class of common physical processes. Computational techniques and new approximation methods have made it possible to solve these equations with increasing accuracy, confirming experimental results in broad engineering fields.

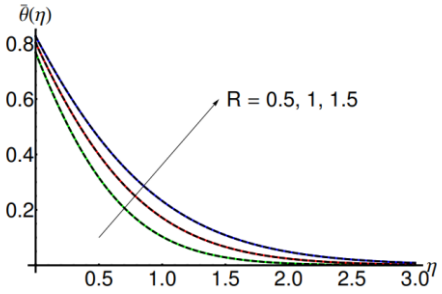


Figure 1. Profile of the temperature $\bar{\theta}(\eta)$ with increasing of the radiation parameter R for fixed others physical parameters: n = 0.5, Pr = 6, δ_2 = 0.2, γ = 0.25, δ_1 = 0.5.

The partial slip effects for radiative convective flow of a nanofluid over a stretching sheet in porous medium are analytically explored in this work. The Navier-Stokes equations, the momentum and the energy equations are transformed into a set of nonlinear ordinary differential equations by the similarity transformation. Using the modified Optimal Homotopy Asymptotic Method (OHAM), the resulting nonlinear ODEs are analytically approximate solved. The behaviour of the mass and heat transfer depends of the many physical parameters: velocity slip parameter, thermal slip parameter, velocity power's index parameter, wall thickness parameter, the Prandtl number and the radiation parameter. The influence of these parameters is tabular and graphically presented. An excellent agreement between the analytic approximate solution and the corresponding numerical solution is highlighted. The results obtained confirm that the modified OHAM is usefully and competitive mathematical tool for explore a large class of nonlinear problems with applications in different fields of science and engineering.

Keywords

Fluid flow, radiation heat transfer, nanofluid, ordinary differential equations, Optimal Homotopy Asymptotic Method (OHAM).

Reference

Ene RD, Pop N, Badarau R. **2023.** Partial Slip Effects for Thermally Radiative Convective Nanofluid Flow. *Mathematics* 11(9):2199; https://doi.org/10.3390/math11092199.

Ene RD, Pop N, Badarau R. **2023.** Heat and Mass Transfer Analysis for the Viscous Fluid Flow: Dual Approximate Solutions. *Mathematics* 11(7):1648; https://doi.org/10.3390/math11071648.

Origins of Functional Biological Information

Steen RASMUSSEN[1,2,3,*], Kristoffer R. THOMSEN[2] and Marco TUCCIO[4]

*Corresponding author e-mail: steen@sdu.dk

[1]*Department of Physics, Chemistry and Pharmacy, University of Southern Denmark, Odense, Denmark*
[2]*Santa Fe Institute, Santa Fe NM, USA*
[3]*European Centre for Living Technology, Venice, Italy*
[4]*Department of Physics, University of Torino, Torino, Italy*

Abstract
We show how selection between combinatorial co-factors can result in the origin of biological information in a simple protocellular system, if the co-factor modulates an energy transduction process that turns resources into protocellular building blocks. Further, we show that the transition from nonliving to living matter must be discontinuous in protocellular biomass if the free parameter is the protocellular net growth rate. Further, amplification, selection, and evolution of co-factors can only occur once a co-factor is randomly 'discovered' that operates above this critical discontinuous threshold. Thus, this critical point is also the onset of Darwinian evolution.

We have previously experimentally demonstrated that a combinatorial co-factor (including 8-oxo-guanine) and the energy transducer (Ru2+)bpy3 anchored to a fatty acid vesicle surface can transform resources (picolinieum ester and protected DNA oligomers) into building blocks (decanoic acid and functional DNA oligomers) (DeClue et al. 2009, Maurer et al. 2011, Cape et al. 2012). This proto-metabolism enables the vesicle container to grow and divide (Albertsen et al. 2014) as well as oligomers to ligate into a full DNA strand. In simulation we demonstrate that anchored co-factor replication is possible based on lesion induced DNA amplification (LIDA) without the use of enzymes (Bournebush et al. 2020, Engelhardt et al. 2020, Thomsen 2022, Tuccio 2023). Further, we demonstrate in simulation that 8-oxo-guanine integrated within a DNA duplex can still act as an electron donor for the (Ru2+)bpy3 energy transducer due to internal DNA charge (hole) transfer properties (Thomsen 2022), which are sequence dependent. Our simulations also indicate that the (2D) surface anchoring of the involved molecular complexes tends to speed up the reaction rates compared to reactions in bulk (3D) although crowding factors also impact the reaction rates (Tuccio 2023).

Based on our reaction kinetic simulations we can select suitable co-factor DNA strands for optimal metabolic rates as charge transfer is sequence dependent. Our simulations can also estimate optimal sequences dependent replication rates. However, different sequence motifs respectively enhance charge transfer and replication, so it is non-trivial to select optimal co-factors with good, combined charge transfer and replication properties (Thomsen et al. 2023). Thus, the co-factor sequence/composition can be interpreted as primitive biological (functional) information when selection from a combinatorial set of co-factors is possible.

Keywords
Origins, co-factor, functional information, metabolism, protocells, kinetics.

Reference
DeClue et al. **2009.** Nucleobase Mediated, Photocatalytic Vesicle Formation from an Ester Precursor. *Journal of the American Chemical Society* 131(3):931-933; https://doi.org/10.1021/ja808200n.

Maurer et al. **2011.** Interactions between catalysts and amphiphilic structures and their implications for a protocell model. *ChemPhysChem* 12(4):828-835; https://doi.org/10.1002/cphc.201000843.

Cape et al. **2012.** Phototriggered DNA phosphoramidate ligation in a tandem 50-amine deprotection/30-imidazole activated phosphate coupling reaction. *Bioconjugate Chemistry* 23(10):2014-2019; https://doi.org/10.1021/bc300093y.

Albertsen et al. **2014.** Transmission of photo-catalytic function in a self-replicating chemical system: *in situ* amphiphile production over two protocell generations. *Chemical Communications* 50(64):8989-8992; https://doi.org/10.1039/C4CC01543F.

Bornebusch et al. **2020.** Automated replication optimization for protocellular information system. *MIT Press Artificial Life Proceedings*, 219-220; https://doi.org/10.1162/isal_a_00301.

Engelhardt et al. **2020.** Thermodynamics and kinetics of Lesion Induced DNA Amplification (LIDA). *MIT Press Artificial Life Proceedings*, 269-272; https://doi.org/10.1162/isal_a_00312.

Thomsen KR. **2022.** *Master Thesis*, University of Southern Denmark, Denmark.

Tuccio M. **2023.** *Master Thesis*, University of Torino, Italy.

Thomsen et al. **2023.** In preparation.

Why Group Theory in Biology?

Paul SORBA[1,*]

*Corresponding author e-mail: paul.sorba@lapth.cnrs.fr

[1]*LAPTH, CNRS, Annecy-le Vieux, France*

"The book of Nature is written in the language of mathematics."
Galileo Galilei

"Mathematics is just a question of groups."
Henri Poincaré

"As far as I can see, all a priori statements in physics have their origin in symmetry."
Hermann Weyl

"Living matter, while not eluding the 'laws of physics' as established up to date, is likely to involve 'other laws of physics' hitherto unknown, which however, once they have been revealed, will form just as integral a part of science as the former."
Erwin Schrödinger

Abstract
Actually, among the mathematical tools which in the second part of the twentieth century have played and are still playing an essential role in theoretical physics, and in particular in particle physics, is the one of Group Theory. This concept is usually called in physics *Symmetry* or *Invariance*. It is this notion which is at the basis of the *Crystal Basis Model* that we are developing for describing the genetic code and studying some biological properties.

It might not be the right one, with its qualities and mainly its limitations, but at least it is an example in a direction among other directions which deserve high interest: cf. several important approaches by other members of COST.

Keywords
Genetic code, group theory, codon-anticodon interaction.

Reference
Sciarrino A, Sorba P. **2017.** Symmetry and Minimum Principle at the Basis of the Genetic Code: A Review. In: *Mathematical Biology and Biological Physics* (RP Mondaini, Ed.), Word Scientific Publishing, pp. 326-362; https://doi.org/10.1142/9789813227880_0019; arXiv:1704.00940 [qbio.OT].

Sciarrino A, Sorba P. 2012. A minimum principle in codon-anticodon interaction. *Biosystems*107(2):113-119; https://doi.org/10.1016/j.biosystems.2011.10.005.

Sciarrino A, Sorba P. 2013. Codon-anticodon interaction and the genetic code evolution. *Biosystems* 111(3):175-180; https://doi.org/10.1016/j.biosystems.2013.02.004.

Sciarrino A, Sorba P. 2016. Codon bias from minimization of codon-anticodon interaction. *Biosystems* 141:20-30; https://doi.org/10.1016/j.biosystems.2015.11.006.

Circular Codes in the Genetic Information

Lutz STRÜNGMANN[1,*] Elena FIMMEL[1] and Christian MICHEL[2]

*Corresponding author e-mail: l.struengmann@hs-mannheim.de

[1]*Institute of Mathematical Biology, Faculty for Computer Sciences Mannheim University of Applied Sciences, Mannheim, Germany*
[2]*Theoretical Bioinformatics, ICube, C.N.R.S., University of Strasbourg, Illkirch, France*

Abstract
Codes are sets of words formed from any given alphabet, characterized by the property of unique decipherability. Among these codes, there exists a special class known as circular codes. Circular codes are sets of words that possess the unique ability to recognize the reading frame of any circularly arranged sequence composed of them. They were originally introduced by Golomb and Gordon in the 1960s under the name "codes with bounded synchronization delay" due to their strong synchronization property. As a result, they play a significant role in error correction problems.

In the mid-1990s, a comprehensive statistical investigation identified a specific circular code, denoted as X, within the genes of bacteria, eukaryotes, plasmids, and viruses. This code, X, consisted of 20 trinucleotides that exhibited a higher preference for the correct reading frame compared to frames 1 and 2. Subsequently, extensive research has been conducted by various authors on circular codes in genetic information and their potential role in maintaining the accurate reading frame during the translation process in the ribosome. Notably, X-motifs, which include the universally conserved nucleotides G530, A1492, and A1493, have been identified in (i) universally present genes, (ii) prokaryotic and eukaryotic tRNAs, (iii) prokaryotic (16S) and eukaryotic (18S) rRNAs, specifically within the ribosome decoding center, and (iv) non-coding regions of eukaryotic genomes. Circular codes exhibit a highly intricate structure, and those found in genes possess additional properties, such as self-complementarity, that reflect their biological nature.

In our talk we give a short introduction to the theory of circular codes and their properties. We then present a new approach to circular sets which offers a new approach to explaining a transition phase during evolution of the genetic code where amino acids were encoded by words of different lengths at the same time.

Keywords
Circular codes, genetic code, frame-shift, translation.

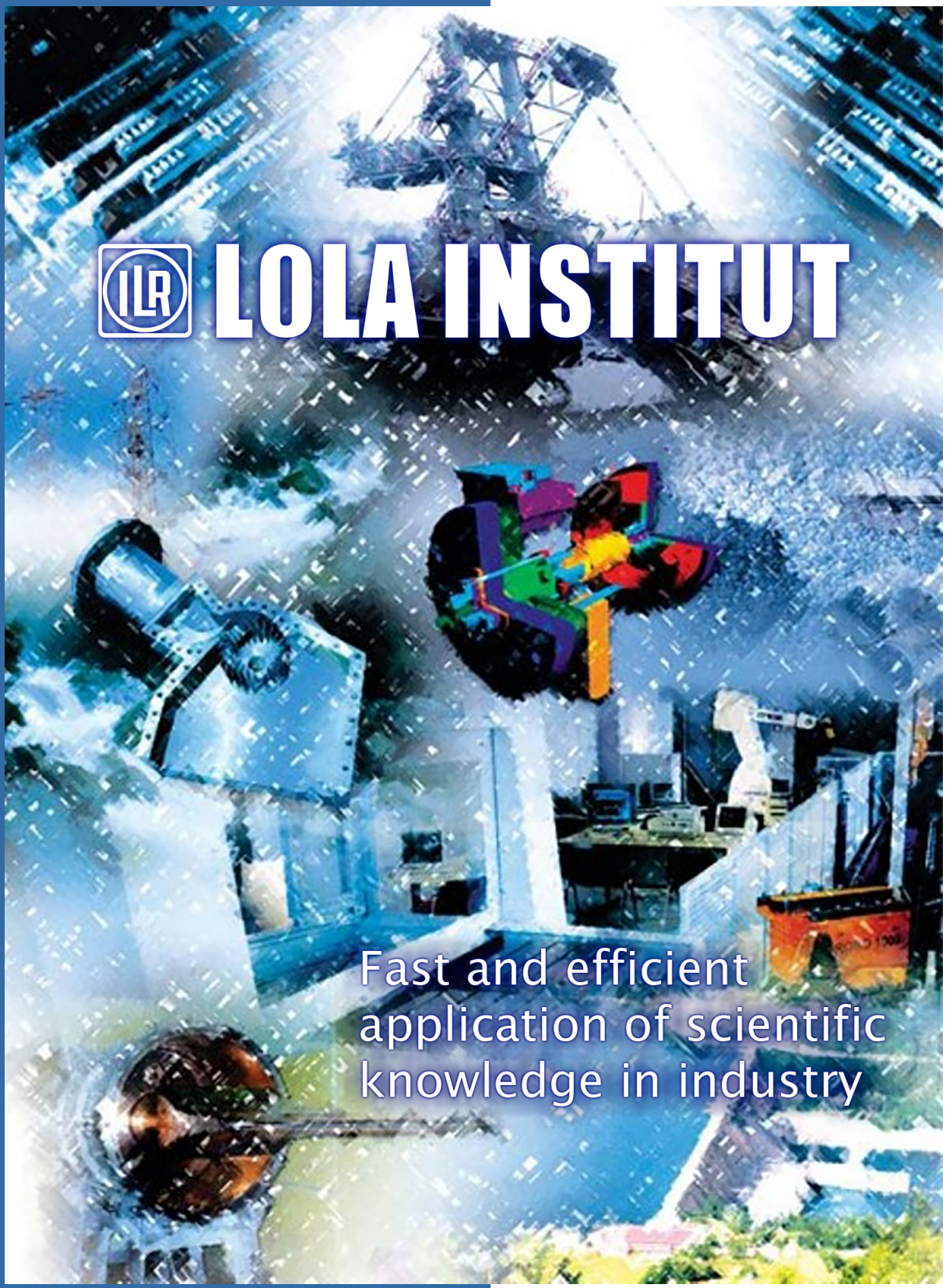
Participants

Emiliano ALTAMURA, University of Bari Aldo Moro, Italy
Utku AVCI, Eskişehir Osmangazi University, Turkiye
Vladan BAJIĆ, University of Belgrade, Serbia
Lilly BARTSCH, University College London, United Kingdom
Paweł BŁAŻEJ, University of Wroclaw, Poland
Ernesto BORRAYO CARBAJAL, University of Guadalajara, México
Selcen ÇELIK UZUNER, Karadeniz Technical University, Turkiye
Dalibor CHEVIZOVICH, University of Belgrade, Serbia
Valentina CIRKOVIC, University of Belgrade, Serbia
Saša CVETKOVIĆ, R&D Institute Lola Ltd, Belgrade, Serbia
Željko ČUPIĆ, University of Belgrade, Serbia
Ozlem DEFTERLİ, Cankaya University, Turkiye
Branko DRAGOVICH, Mathematical Institute SASA, Serbia
Elena FIMMEL, Mannheim University of Applied Sciences, Germany
Aleksej GAJ, Institute of Information Theory and Automation, Czech Republic
Muharrem Tuncay GENÇOĞLU, Fırat University, Turkiye
Diego Luis GONZALEZ, IMM-CNR, Italy
Sonja GRUBISIC, University of Belgrade, Serbia
Tatiana Valentine GUY, Institute of Information Theory and Automation, Czech Republic
Stuart A. HARRISON, University College London, United Kingdom
Jeanine HOUWING-DUISTERMAAT, Radboud University Nijmegen, Netherlands
Vladimir JAĆIMOVIĆ, University of Montenegro, Montenegro
Stuart A. KAUFFMAN, Institute for Systems Biology, United States
Andrei KHRENNIKOV, Linnaeus University, Sweden
Stefan KUHN, University of Tartu, Estonia
Iván MARQUÉS CAMPILLO, University of the Balearic Islands, Spain
Fabio MAVELLI, University of Bari Aldo Moro, Italy
Nataša Ž. MIŠIĆ, R&D Institute Lola Ltd, Serbia
Nenad MITIĆ, University of Belgrade, Serbia
Raquel NUNES PALMEIRA, University College London, United Kingdom
Signem ONEY-BIROL, Burdur Mehmet Akif Ersoy University, Turkiye
Mirko OSTOJIĆ, R&D Institute Lola Ltd, Belgrade, Serbia
Gordana PAVLOVIC LAZETIC, University of Belgrade, Serbia
Stefano PIOTTO, University of Salerno, Italy
Oreste PIRO, University of the Balearic Islands, Spain
Nicolina POP, Politehnica University of Timisoara, Romania
Dragana RANKOVIĆ, University of Belgrade, Serbia
Steen RASMUSSEN, University of Southern Denmark, Denmark
Paul SORBA, LAPTH, CNRS, France
Lutz STRÜNGMANN, University of Applied Sciences Mannheim, Germany
Slobodan ZDRAVKOVIC, University of Belgrade, Serbia

Meeting Notes

Meeting Notes

Meeting Notes


LOLA INSTITUT
Fast and efficient
application of scientific
knowledge in industry

Scientific Committee

Branko Dragovich (MI SASA Belgrade)
Elena Fimmel (University of Mannheim)
Simone Giannerini (University of Bologna)
Diego Luis Gonzalez (CNR-IMM Bologna)
Andrei Khrennikov (Linnaeus University Växjö)
Nataša Mišić (R&D Institute Lola Belgrade)

Local Organizing Committee

Nataša Mišić, Chair (R&D Institute Lola Belgrade)
Branko Dragovich (MI SASA Belgrade)
Srećko Manasijević (R&D Institute Lola Belgrade)
Mirko Ostojić (R&D Institute Lola Belgrade)
Saša Cvetković (R&D Institute Lola Belgrade)

COST Action CA21169 DYNALIFE

cost EUROPEAN COOPERATION IN SCIENCE & TECHNOLOGY

Funded by the European Union

LOLA INSTITUT

unibz Freie Universität Bozen Libera Università di Bolzano Università Liedia de Bulsan

ISBN-978-86-82407-05-8