Final report on the OTKA K140164 project
“Dynamical models in the origin of life”

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In the course of the research project, we have achieved most of the tasks set out in the work plan, in one area (strand separation problem of RNA) we have not achieved any results, while in all other areas we have achieved the research tasks set out; in some areas we have even extended the scope of the studies. During the duration of the project, 17 peer-reviewed publications were published on the research topic, mostly in Q1 and D1 journals. We have contributed 32 conference presentations and posters. We put great emphasis on the presentation of our results to the public, and our results were published in several high readership media (telex.hu, 24.hu, valaszonline.hu, etc.).

Below, in chronological order, we briefly present our published results. We wrote a review on dynamical modelling of the RNA world as an invited contribution to the special issue "The RNA World and the Origin of Life" of the journal Life [1]. We developed a model for the evolutionary origin of mitochondria. We presented dynamical models to directly simulate the origin of mitochondria in an eco-evolutionary context. Our results show that regulated cultivation of prey bacteria and delayed digestion can facilitate the establishment of a stable endosymbiosis when prey-rich and prey-poor periods alternate [2,3]. We have shown that, using the laboratory as a simple environment, populations are able to move towards the same phenotypic adaptive peak, but the genetic paths they take to get there are complex and unpredictable. Even in populations with high levels of genetic variation, the predictability of evolution depends on the biological level analysed [4].

We published an editorial overview of systems ecology and evolution [5] and a review article on mathematical models of early evolution, with particular emphasis on the ability to maintain ecological and evolutionary stability and diversity [6]. We used the Stochastic Corrector Model (SCM) as a model framework to analyse the amount of maintainable information (genetic diversity) in early evolution, the maximum maintainable gene number in protocells, and possible evolutionary pathways to the complexity of group selection in compartmentalised replicator systems in the RNA world era. We have also investigated the effect of fusion (horizontal gene transfer) on maintainable diversity, and the effect of different metabolic topologies and explicit handling of waste [7]. We have made progress with the Metabolically Coupled Replicator System (MCRS) model by introducing explicit replicators and extending the it with biologically plausible complementary strand replication and physicochemical details. Preliminary studies show that the resulting models remain stable in an ecological and evolutionary sense and can maintain moderate genetic diversity [8]. We have written a detailed review on the possible evolutionary pathways of infrabiological systems [9]. We demonstrated the important effect of catalytic promiscuity on the ability to maintain diversity in a physicochemically realistic version of the Metabolically Coupled Replicator System (MCRS) [10]. We proposed a possible detailed evolutionary pathway from unlinked genes to chromosomes in the context of the Stochastic Corrector Model (SCM) [11].

We wrote a review article on the possible essential role of mineral surfaces in prebiotic evolution and early living systems [12] and a review article on the information integration capacity of ribocell-like systems [13]. We have analysed the robustness of the genetic code to mutation. The results suggest that the genetic code performs better under non-extremophilic conditions [14]. We investigated the emergence of the genetic code and human language (the codes of life) as possible major evolutionary transitions. The results suggest that the emergence of the codes of life are not major evolutionary transitions, but are required for major evolutionary transitions to occur [15]. We showed that the genetic code works best with mesophilic codon usage, strengthening the view that LUCA or its ancestors preferred lower temperature environments [16]. Finally, in collaboration with a French group we have created and analysed an infrabiological construct of considerable prebiotic relevance consisting of the autocatalytic formose reaction enclosed in growing water-in-oil droplets. The compartments can be divided by shearing forces thus a population of reproducing vesicles was shown to arise with some degree of competition and inheritance [17].

Articles

[1] **A. Szilágyi**, **I. Zachar**, I. Scheuring, **Á. Kun**, **B. Könnyű**, **T. Czárán**: Ecology and evolution in the RNA World. - Dynamics and stability of prebiotic replicator systems. *Life* **7**(4):48 https://doi.org/10.3390/life7040048 (2017)

[2]. **I. Zachar**, **A. Szilágyi**, S. Számadó, **E. Szathmáry**: Farming the mitochondrial ancestor as a model of endosymbiotic establishment by natural selection. *Proceedings of the National Academy of Sciences* **115**(7):E1504-E1510; https://doi.org/10.1073/pnas.1718707115 (2018)

[3] **I. Zachar**, **A. Szilágyi**, S. Számadó, **E. Szathmáry**: Reply to Garg and Martin: The mechanism works. *Proceedings of the National Academy of Sciences* 201805021; https://doi.org/10.1073/pnas.1805021115 (2018)

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[5] **E. Szathmáry**, F. Jordán: Systems ecology and evolution—editorial overview *Current Opinion in Systems Biology* **13**:vii-ix (2019) https://doi.org/10.1016/j.coisb.2019.02.004

[6] A Scheuring, **A. Szilágyi**: Diversity, stability, and evolvability in models of early evolution *Current Opinion in Systems Biology* **13**:115-121 (2019) https://doi.org/10.1016/j.coisb.2018.12.007

[7] **Zs. Vig-Milkovics**, **I. Zachar**, **Á. Kun**, **A. Szilágyi**, *E. Szathmáry*: Moderate sex between protocells can balance between a decrease in assortment load and an increase in parasite spread. *Journal of Theoretical Biology* **462**:304-310 (2019) https://doi.org/10.1016/j.jtbi.2018.11.020

[8] **A. Szilágyi**, **B. Könnyű**, **T. Czárán**: Dynamics and stability in prebiotic information integration: an RNA World model from first principles *Scientific Reports* **10**:51 (2020). https://doi.org/10.1038/s41598-019-56986-8

[9] P. Adamski, M. Eleveld, A. Sood, **Á. Kun**, **A. Szilágyi**, **T. Czárán**, **E. Szathmáry**, S. Otto: From self-replication to replicator systems en route to de novo life. *Nature Reviews Chemistry* **4:**386–403 (2020) https://doi.org/10.1038/s41570-020-0196-x

[10] **D. Vörös**, **B, Könnyű**, **T. Czárán**: Catalytic promiscuity in the RNA World may have aided the evolution of prebiotic metabolism. *PLoS Computational Biology* **17**(1):e1008634. (2021) https://doi.org/10.1371/journal.pcbi.1008634

[11**] A. Szilágyi**, V.P. Kovács, **E. Szathmáry**, M. Santos: Evolution of linkage and genome expansion in protocells: The origin of chromosomes. *PLOS Genetics* **16**(10):e1009155. (2020) https://doi.org/10.1371/journal.pgen.1009155

[12] **B. Könnyű**, **Á. Kun**: Surfaces, the missing link in the Origins of Life. *Journal of Systems Chemistry* **8**:95-106 (2020) https://www.nls-publishers.com/shop/journal/journal+of+systems+chemistry+2020,+volume+8

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[17] H. Lu, A. Blokhuis, R. Turk-MacLeod, J. Karuppusamy, A. Franconi, G. Woronoff, C. Jeancolas, A. Abrishamkar, E. Loire, F. Ferrage, P. Pelupessy, L. Jullien, **E. Szathmáry,** P. Nghe, A D. Griffiths: Small-molecule autocatalysis drives compartment growth, competition and reproduction. *Nature Chemistry,* accepted. (2023).

Presentations, posters

E. Szathmáry: Replication in space and time – evolution in structured replicator populations /SysChem 2017/ COST CM1304 meeting 11–15 Sept 2017, Sopron, Hungary (presentation)

A. Hubai, **Á. Kun**: Three conjectures on the possible role of group selection at the origins of life. /SysChem 2017/ COST CM1304 meeting 11–15 Sept 2017, Sopron, Hungary (presentation)

Á. Radványi, **Á. Kun**: Getting from RNA world to proteins: A notional scenario. /SysChem 2017/ COST CM1304 meeting 11–15 Sept 2017, Sopron, Hungary (presentation)

Á. Kun: The coexistence of RNA replicators and parasites in compartmentalized systems. /SysChem 2017/ COST CM1304 meeting 11–15 Sept 2017, Sopron, Hungary

Á. Kun: Compartmentalization as a prerequisite for the origin of life. /Dynamics Days Europe International Conference/ 5–9 Jun 2017, Szeged, Hungary (presentation)

Á. Radványi, **Á. Kun**: When two worlds collide: A prequel to proteins, and a sequel to RNAs. /4th International Conference in Code Biology/ May 22–26 2017, Kőszeg, Hungary (presentation)

Á. Kun, **E. Szathmáry**: The “code of the codes”: a classification and evaluation of approaches to the origins of the genetic code. /4th International Conference in Code Biology/ 22–26 May 2017, Kőszeg, Hungary (presentation)

A. Hubai, **Á. Kun**: The coexistence of independent genes is aided by multilevel selection, but only to a limited extent. /Modelling Biological Evolution 2017: Developing Novel Approaches/. 4–7 Apr 2017, Leicester, England (presentation)

Á. Kun: The coexistence of RNA replicators and parasites in compartmentalized systems. COST CM1304 WG1 Meeting on Systems Chemistry 2-3 Febr 2017, Paris, France (presentation)

Á. Kun: The ecology of compartmentalized RNA replicators – The second error threshold. /Minisymposium on Theoretical Biology/ 21 Dec 2016, Utrecht, The Netherlands (presentation)

T. Czárán, **B. Könnyű**, **E. Szathmáry**: Metabolically Coupled Replicator System (MCRS), overview of an RNA-world model concept of prebiotic evolution on mineral surfaces. XVIIIth ISSOL Conference 16–21 July 2017, San Diego, California, USA Conference publication: https://www.hou.usra.edu/meetings/issol2017/pdf/sess603.pdf. (presentation)

B. Könnyű, **A. Szilágyi**, **T. Czárán**: In silico rybozym evolution in a metabolically coupled RNA population. XVIII ISSOL Conference 16-21 July, 2017, San Diego, California, USA. Conference publication: https://www.hou.usra.edu/meetings/issol2017/pdf/sess714.pdf

B. Könnyű, **A. Szilágyi**, **T. Czárán**: In silico ribozyme evolution in a metabolically coupled RNA population. Czech Chemical Society Symposium Series 3 & CMST COST Action CM1304 Conference /SysChem/ 8–12 May 2016 Valtice Chateau, Czech Republic (presentation)

B. Könnyű, **A. Szilágyi**, **T. Czárán**: In silico ribozyme evolution in a metabolically coupled RNA population. XVIII ISSOL Conference 16–21 July 2017, San Diego, California, USA. (poster)

B. Könnyű, **A. Szilágyi**, **T. Czárán**: In silico ribozyme evolution in a metabolically coupled RNA population. SysChem 2017 Conference 11–15 Sept 2017, Sopron, Hungary (presentation)

Á. Kun: The coexistence of RNA replicators and parasites in compartmentalized systems. II. Joint Conference on Evolutionary Biology, Montpellier, France, 18-22 August 2018 18–22. (presentation)

Á. Radványi, **Á. Kun**: From RNA world to proteins: A transient era of amino acid coenzymes inferred from protein catalytic centres. II. Joint Conference on Evolutionary Biology, Montpellier, France, 18-22 August 2018 18–22. (presentation)

Á. Kun: Biological codes and the major evolutionary transitions. Fifth International Conference in Code Biology. Granada, Spain 5-9 July 2018 (presentation)

Á. Kun: Key steps in the development of the RNA world. Evolutionary Biology Day 2018. Budapest, 28. március 2018 (presentation)

Á. Kun: A korai replikátorok ökológiája. Integratív ökológia: járványoktól a tájhasználatig Magyar Tudomány Ünnepe, Budapest, 16 November 2017 (presentation in Hungarian)

B. Könnyű: Prebiotic evolution of RNA molecules on mineral surface. 1 st EvolBiolDay 28. March 2018, Eötvös Loránd University, Budapest, Hungary (presentation)

B. Könnyű, **A. Szilágyi**, **T. Czárán**: The role of enzymatic promiscuity in the evolution of RNA molecules. Science of Early Life Conference 24-17 June, 2018, Hamilton, Canada. Conference publication p.11. (poster)

D. Vörös, **B. Könnyű**, **T. Czárán**: The role of catalytic promiscuity in prebiotic evolution. Evolution Montpellier 18-22 August 2018, Montpellier, France. Conference publication (p-0171) p. 69. (poster)

Á. Kun, Á. Radványi: Changing the genetic code – Is it possible? 6th International Conference in Code Biology, Friedrichsdorf, Germany 3-7 June 2019 (presentation)

Á. Radványi, **Á. Kun**: On the origin of translation and the possible habitat of LUCA based on a simple neutral model of amino acid composition. 6th International Conference in Code Biology, Friedrichsdorf, Germany, 3-7 June 2019 (presentation)

Á. Kun: The role of peptides and the evolution of translation. 2nd EvolBiol Day, Szeged, Hungary 17-18 April 2019 (presentation)

D. Vörös, **B. Könnyű**, **T. Czárán**: The role of catalytic promiscuity in the evolution of prebiotic replicators. 2nd EvolBiolDay, Szeged, Hungary 17-18 April 2019 (presentation)

A. Szilágyi, **B. Könnyű**, **T. Czárán**: Dynamics and stability in prebiotic information integration: an RNA World model from first principles. Molecular Origin Of Life 2020. 8-10 July 2020, Munich, Germany. Conference publication (p-48) p. 94.

A. Szilágyi, **B. Könnyű**, **T. Czárán**: Dynamics and stability in prebiotic information integration: an RNA World model from first principles. Molecular Origin Of Life 2021. 25-27 August 2021, Munich, Germany. (poster)

A.Szilágyi, **B. Könnyű**, **T. Czárán**: Dynamics and stability in prebiotic information integration: an RNA World model from first principles. XIX ISSOL Meeting 2021. 18-22 October 2021, Munich, Germany. Conference publication p.41.

B. Könnyű: Coexistence and evolution of replicators in Metabolically Coupled Replicator System. Molecular Origins of Life 2022. 16-17 June 2022, Munich, Germany. (poster)

B. Könnyű: Coexistence and evolution of replicators in Metabolically Coupled Replicator System. Molecular Latsis Symposium 2022, The Origin and Prevalence of Life, August 30 – September 2 ETH Zurich, Switzerland. (online presentation)