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The results of our research supported by this OTKA project have been published in 14 papers, of which 8 are in high-ranking international journals, 3 are textbook chapters and 3 are summaries of our work, intended either for the professional or the general public, in Hungarian. Below we give some details of the results:

We have published 5 papers within the framework of the sub-project on the microbial evolution of cooperation:

Czárán, T. & Hoekstra, R. (2007) A spatial model of the evolution of quorum sensing. Behavioral Ecology 18: 866-873.

Background: Like any form of cooperative behaviour, QS in bacteria is potentially vulnerable to cheating, the occurrence of individuals that contribute less but still profit from the benefits provided by others. We explore the evolutionary stability of QS in a spatially structured population, using Cellular Automaton modelling. QS is supposed to regulate the excretion of a bacteriocin (anti-competitor toxin) in a population of bacteria polymorphic for the ability to produce and to be immune to the bacteriocin. Both the social interactions resulting from QS and the competitive interactions resulting from the bacteriocin excretion are supposed to be only effective at the local scale, i.e. restricted to the immediately neighbouring cells. This implies a rather diffuse kind of group selection. The Cellular Automaton model is contrasted to a model assuming no spatial structure but with otherwise identical assumptions.

Results: Our analysis predicts that QS as a regulatory mechanism of bacteriocin excretion is evolutionarily unstable. Therefore, although bacteriocin excretion is frequently regulated by QS, it is likely qourum sensing has evolved for other reasons and has been involved later in the regulation of bacteriocin excretion. Moreover, the way group selection works appears to be crucial for the evolutionary stability of QS.

Habets, M.G.J.L., T. Czárán, R.F. Hoekstra and J.A.G.M. de Visser. 2007. Spatial structure inhibits the rate of invasion of beneficial mutations in asexual populations. *Proc. R. Soc. London B*, **274**: 2139-2143.

Background: Populations in spatially structured environments may be divided into a number of (semi-) isolated subpopulations due to limited offspring dispersal. Limited dispersal and, as a consequence, local competition could slow down the invasion of fitter mutants, allowing the short-term coexistence of ancestral genotypes and mutants. We determined the rate of invasion of beneficial mutants of *Escherichia coli*, dispersed to different degrees in a spatially structured environment during 40 generations, experimentally and theoretically.

Results: Simulations as well as experimental data show a decrease in the rate of invasion with increasingly constrained dispersal. When a beneficial mutant invades from a single spot,

competition with the ancestral genotype takes place only along the edges of the growing colony patch. As the colony grows, the fitness of the mutant will decrease due to a decrease in the mutant's fraction that effectively competes with the surrounding ancestor. Despite its inherently higher competitive ability, increased intragenotype competition prevents the beneficial mutant from rapidly taking over, causing short-term coexistence of superior and inferior genotypes.

Czárán, T. & Hoekstra, R.F. 2009. Microbial Communication, Cooperation and Cheating: Quorum sensing drives the evolution of cooperation in bacteria. *PLoS ONE* **4**(8): e6655. doi:10.1371/journal.pone.0006655

Background: An increasing body of empirical evidence suggests that cooperation among clone-mates is common in bacteria. Bacterial cooperation may take the form of the excretion of „public goods": exoproducts such as virulence factors, exoenzymes or components of the matrix in biofilms, to yield significant benefit for individuals joining in the common effort of producing them. Supposedly in order to spare unnecessary costs when the population is too sparse to supply the sufficient exoproduct level, many bacteria have evolved a simple chemical communication system called quorum sensing (QS), to "measure" the population density of clone-mates in their close neighborhood. Cooperation genes are expressed only above a threshold rate of QS signal molecule re-capture, i.e., above the local quorum of cooperators.The cooperative population is exposed to exploitation by cheaters, i.e., mutants who contribute less or nil to the effort but fully enjoy the benefits of cooperation. The communication system is also vulnerable to a different type of cheaters ("Liars") who may produce the QS signal but not the exoproduct, thus ruining the reliability of the signal. Since there is no reason to assume that such cheaters cannot evolve and invade the populations of honestly signaling cooperators, the empirical fact of the existence of both bacterial cooperation and the associated QS communication system seems puzzling.
Results: Using a stochastic cellular automaton approach and allowing mutations in an initially non-cooperating, non-communicating strain we show that both cooperation and the associated communication system can evolve, spread and remain persistent. The QS genes help cooperative behavior to invade the population, and *vice versa*; cooperation and communication might have evolved synergistically in bacteria. Moreover, in good agreement with the empirical data recently available, this synergism opens up a remarkably rich repertoire of social interactions in which cheating and exploitation are commonplace.

Czárán T. & Hoekstra R.F. 2010. Janus-headed communication promotes bacterial cooperation and cheating: Is quorum sensing useful against infections? *Virulence* **1**(5): 1-2.

This paper was invited by the journal (*Virulence*) as an addendum to the previous one (Czárán & Hoekstra, 2009). It summarizes the results of the model and presents an outlook to possible medical applications of the results.

Czárán T. 2010. Együttműködés, kommunikáció és csalás a mikrobák világában: A quorum sensing és a kooperáció együttes evolúciója baktériumokban. *Magyar Tudomány* **171/4**: 396-406. (in Hungarian)

This is a Hungarian summary of our results obtained by modelling microbial evolution, intended for the „educated laymen", i.e., for scientists of diverse fields.

4 publications on the "prebiotic evolution" subtopic:

Szabó, P., Czárán, T. and Szabó, Gy. 2007. Competing associations in bacterial warfare with two toxins. *Journal of Theoretical Biology* **248**: 736-744.

Background: Simple combinations of common competitive mechanisms can easily result in cyclic competitive dominance relationships between species. The topological features of such competitive networks allow for complex spatial coexistence patterns. We investigate self-organization and coexistence in a lattice model, describing the spatial population dynamics of competing bacterial strains.

Results: With increasing diffusion rate the community of the nine possible toxicity/resistance types undergoes two phase transitions. Below a critical level of diffusion, the system exhibits expanding domains of three different defensive alliances, each consisting of three cyclically dominant species. Due to the neutral relationship between these alliances and the finite system size effect, ultimately only one of them remains. At large diffusion rates the system admits three coexisting domains, each containing mutually neutral species. Because of the cyclical dominance between these domains, a long term stable coexistence of all species is ensured. In the third phase at intermediate diffusion the spatial structure becomes even more complicated with domains of mutually neutral species persisting along the borders of defensive alliances. The study reveals that cyclic competitive relationships may produce a large variety of complex coexistence patterns, exhibiting common features of natural ecosystems, like hierarchical organization, phase transitions and sudden, large-scale fluctuations.

Könnyű, B., Czárán, T. & Szathmáry, E. 2008. Prebiotic replicase evolution in a surface-bound metabolic system: parasites as a source of adaptive evolution. *BMC Evolutionary Biology* **8**:267.

Background: The remarkable potential of recent forms of life for reliably passing on genetic information through many generations now depends on the coordinated action of thousands of specialized biochemical “machines” (enzymes) that were obviously absent in prebiotic times. Thus the question how a complicated system like the living cell could have assembled on Earth seems puzzling. In seeking for a scientific explanation one has to search for step-by-step evolutionary changes from prebiotic chemistry to the emergence of the first proto-cell.

Results: We try to sketch a plausible scenario in the first half of the story by exploring the ecological feasibility of a mineral surface-bound prebiotic replicator system that facilitates a primitive metabolism. Metabolism is a hypothetical network of simple chemical reactions producing monomers for the template-copying of RNA-like replicators, which in turn catalyse metabolic reactions. Using stochastic cellular automata (SCA) simulations we show that the surface-bound metabolic replicator system is viable despite internal competition among the genes and that it also maintains a set of mild “parasitic” sequences which occasionally evolve functions such as that of a replicase. Replicase activity is shown to increase even at the expense of slowing down the replication of the evolving ribozyme itself, due to indirect mutualistic benefits in a diffuse form of group selection among neighbouring replicators. Finally we suggest possible paths for further evolutionary changes in the metabolic replicator system leading to increased metabolic efficiency, improved replicase functionality, and membrane production.

Branciamore, S., Czárán,T., Gallori, E. and Szathmáry, E. 2009. The origin of life – chemical evolution of a metabolic system in a mineral honeycomb? *J Mol Evol* **69**:458–469.

Background: For the RNA-World hypothesis to be ecologically feasible, group selection mechanisms acting on replicator communities need to be invoked, and the corresponding scenarios of molecular evolution specified. Complementing our previous models of chemical evolution on mineral surfaces, in which group selection was the consequence of the limited mobility of macromolecules attached to the surface, here we offer an alternative explanation for prebiotic group-level selection: the physical encapsulation of local replicator communities into the pores of the mineral substrate.

Results: Based on cellular automaton simulations we argue that the effect of group selection in a mineral honeycomb was efficient enough to keep prebiotic ribozymes of different specificities and replication rates coexistent, and their metabolic cooperation protected from extensive molecular parasitism. We suggest that mutants of the mild parasites persistent in the metabolic system can acquire useful functions such as replicase activity or the production of membrane components, thus opening the way for the evolution of the first autonomous protocells on Earth.

Könnyű,B. & Czárán,T. 2011. The Evolution of Enzyme Specificity in the Metabolic Replicator Model of Prebiotic Evolution. *PLoS ONE* **6**(6): e20931. doi:10.1371/journal.pone.0020931

Background: The chemical machinery of life must have been catalytic from the outset. Models of the chemical origins have attempted to explain the ecological mechanisms maintaining a minimum necessary diversity of prebiotic replicator enzymes, but little attention has been paid so far to the evolutionary initiation of that diversity. We propose a possible first step in this direction: based on our previous model of a surface-bound metabolic replicator system we try to explain how the adaptive specialization of enzymatic replicator populations might have led to more diverse and more efficient communities of cooperating replicators with two different enzyme activities. The key assumptions of the model are that mutations in the replicator population can lead towards a) both of the two different enzyme specificities in separate replicators: efficient ‘‘specialists’’ or b) a ‘‘generalist’’ replicator type with both enzyme specificities working at less efficiency, or c) a fastreplicating, non-enzymatic ‘‘parasite’’.

Results: We show that under realistic trade-off constraints on the phenotypic effects of these mutations the evolved replicator community will be usually composed of both types of specialists and of a limited abundance of parasites, provided that the replicators can slowly migrate on the mineral surface. It is only at very weak tradeoffs that generalists take over in a phase-transition-like manner. The parasites do not seriously harm the system but can freely mutate, therefore they can be considered as pre-adaptations to later, useful functions that the metabolic system can adopt to increase its own fitness.

With the acknowledged support of this OTKA project I have contributed (with co-authors) 3 chapters to the Hungarian textbook „Ökológia" (2008, Budapest):

Kalapos, T., Czárán, T., Pásztor, E., Magyar, G., and Hahn, I. 2008. A populációk növekedőképessége. In: Pásztor, E. & Oborny, B. (eds.): ***Ökológia.*** Nemzeti Tankönyvkiadó (in Hungarian)

Pásztor, E., Magyar, G., Czárán, T., Kun, A. & Meszéna, G. 2008. Szabályozott populációnövekedés. In: Pásztor, E. & Oborny, B. (eds.): ***Ökológia.*** Nemzeti Tankönyvkiadó (in Hungarian)

Czárán, T. & Magyar, G. 2008. Együttélés térben és időben. In: Pásztor, E. & Oborny, B. (eds.): ***Ökológia.*** Nemzeti Tankönyvkiadó (in Hungarian)

Based on the material in this textbook and a provisional, contracted OUP book we have published two papers in Hungarian, one for the professionals of different branches of science and another one for the general public:

Pásztor E., Botta-Dukát Z., Czárán T., Magyar G. & Meszéna G. 2009. Darwini őkológia. *Magyar Tudomány* **12**:1434-1443. (in Hungarian)

Pásztor E., Botta-Dukát Z., Czárán T., Magyar G. & Meszéna G. 2009. Darwini fajképződés és modern ökológia. *Természet Világa* **140/12**: 51-55. (in Hungarian)