



## EVOLUTIONARY ECOLOGY

### EVOLUTION, BEHAVIOUR, ADAPTATION GROUP

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## News

### **Seeking a postdoc – Modeling the evolution of enzymes along complex metabolic networks**

The postdoc is funded until the end of 2024. Please send an email to [etienne.rajon@univ-lyon1.fr](mailto:etienne.rajon@univ-lyon1.fr) for details / informal inquiries, or to apply (then include a CV, a short description of your research interest / ideas about the project, and the names / emails of 2 references). Evaluation will start in mid-September and continue until the position is filled. Net salary: 1864 euros per month, including health insurance – ideal start date: ASAP.

Research

The living world is spectacularly complex, but the theory of evolution makes it possible to understand, step by step, its intricacies. Modeling is a powerful tool to overcome the limits of our intuition and understand how complex phenomena emerge from simple ingredients. Obviously, when changing the list of ingredients, the outcome can change, making their knowledge essential.

My goal is to integrate information about the mechanisms that underlie phenotypes – the genotype-phenotype map – in order to build realistic evolutionary models. This approach avoids making (many) arbitrary choices, in particular on the distribution of mutational effects, and on the constraints that may govern evolution: there may be pleiotropy, robustness, trade-offs, and these descriptors of the distribution of mutational effects may themselves evolve.

Remarkably, these mechanisms that underlie the phenotypes form networks, the evolution of which (or in which) I study. Three currently occupy me: gene networks, endocrine networks and metabolic networks.

Gene networks are formed by the relationships governing gene expression. Some genes code for regulators (for example transcription factors) that interact with certain small sequences surrounding other genes and modify their transcription. Notice that this is a good example of the interest of mechanistic modeling; we can make simple models where these relationships appear or disappear, with certain probabilities, but in reality the regulatory sequence(s) can be more or less distant to the “right” sequence, so that these probabilities themselves change over time, which cannot be accounted for without explicitly modeling changes in regulatory sequences.

Gene networks are at the origin of many (all?) phenotypes. But their functioning is subject to noise, the number of copies of elements produced by each of these genes (RNA and proteins) necessarily varying from one cell to another. I take into account the presence of this noise (thesis of Florian Labourel) to model its exploitation in generating strategies of diversifying bet-hedging (the random expression of various phenotypes by a single genotype) and of multicellularity (several cell types by a single genotype).

My current projects on this theme (still) concern the evolution of bet-hedging and multicellularity. I am also interested in the emergence and evolution of non-genetic inheritance systems (Rajon and Charlat, 2019), for which these networks seem to be an ideal breeding ground: oddly enough, a vast majority of the mechanisms of non-genetic inheritance described take part in gene networks (small RNAs, methylation, etc.).

Physical pairings between hormones and receptors are at the origin of many phenotypes observed in multicellular organisms, and especially of the relationships between these phenotypes. It is in this context that I became interested in their evolution (thesis by Salomé Bourg), in order to model the evolution of the form of trade-offs (Bourg et al, 2019).

On this theme, my current project is to build a model to understand the evolution of temporal dynamics (over the course of life) of energy allocation to life history traits.

Without enzymes, life cannot be sustained: the biochemical reactions that provide living beings with energy and building materials, from what is in their environment, would be much too slow to sustain the life of self-replicating organisms. However, the archetype of hyper-efficient enzymes, operating at the limits of their physical limits, does not stand up to the analysis of their kinetic constants.

To understand this, we (thesis by Florian Labourel) have built models of enzyme evolution integrating an essential characteristic of living beings based on enzymatic efficiency (competition for resources) and details of the environment of a enzyme (catalyzed reaction, characteristics of the metabolite produced, etc.). This work has shown that the observed inefficiency can be understood by a plateau beyond which increasing efficiency does not increase fitness much (Labourel and Rajon, 2021).

On the other hand, the integration of the cellular constraints underlying the (expensive) expression of these enzymes has made it possible to understand why, sometimes, organisms release metabolites which still make it possible to generate energy, for the benefit of others, making thus shedding light on the evolution of common crossover interactions in microbial communities (Labourel et al, 2021).