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Université Claude Bernard (Lyon 1)

Activity Report 2019

Project-Team BEAGLE

Artificial Evolution and Computational Biology

IN COLLABORATION WITH: Laboratoire d'InfoRmatique en Image et Systèmes d'information (LIRIS)

RESEARCH CENTER
Grenoble - Rhône-Alpes

THEME
Computational Biology

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Project-Team BEAGLE

Creation of the Team: 2011 June 17, updated into Project-Team: 2013 January 01

Keywords:

Computer Science and Digital Science:

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A6.1.1. - Continuous Modeling (PDE, ODE)
A6.1.3. - Discrete Modeling (multi-agent, people centered)
A6.1.4. - Multiscale modeling
A6.2.7. - High performance computing
A8.1. - Discrete mathematics, combinatorics

Other Research Topics and Application Domains:

B1. - Life sciences
B1.1.2. - Molecular and cellular biology
B1.1.6. - Evolutionnary biology
B1.1.7. - Bioinformatics
B1.1.10. - Systems and synthetic biology
B1.2.1. - Understanding and simulation of the brain and the nervous system
B9.2.1. - Music, sound
B9.2.4. - Theater

1. Team, Visitors, External Collaborators

Research Scientists

Hugues Berry [Inria, Senior Researcher, HDR]
Anton Crombach [Inria, Researcher]
Eric Tannier [Inria, Senior Researcher, HDR]
Leonardo Trujillo Lugo [Inria, Advanced Research Position, from Nov 2019]

Faculty Members

Guillaume Beslon [Team leader, INSA Lyon, Full Professor, HDR]
Carole Knibbe [INSA Lyon, Associate Professor]
Christophe Rigotti [INSA Lyon, Associate Professor, HDR]
Jonathan Rouzaud-Cornabas [INSA Lyon, Associate Professor]

Post-Doctoral Fellow

Charles Rocabert [Inria, Post-Doctoral Fellow, from May 2019]

PhD Students

Audrey Denizot [INSA Lyon, PhD Student]
Julie Etienne [INSERM, PhD Student, from Oct 2019]
Marco Foley [Inria, PhD Student, from Nov 2019]
Théotime Grohens [INSA Lyon, PhD Student, from Sep 2019]
Vincent Liard [INSA Lyon, PhD Student]

Interns and Apprentices

Justine Antoine [Inria, from Apr 2019 until Aug 2019]
Paul Banse [Inria, from Feb 2019]

Ella Beaumann [Inria, from Feb 2019 until Jul 2019]
Julie Etienne [INSA Lyon, from Feb 2019 until Jul 2019]
Marco Foley [Inria, until Jun 2019]
Sujin Hyun [Inria, from Feb 2019 until Jul 2019]
Juliette Luiselli [Inria, from Jun 2019 until Jul 2019]
Hamza Mabrouk [Inria, from Jun 2019 until Sep 2019]
Tymofii Prokopenko [Ecole Normale Supérieure Lyon, from Feb 2019 until Jun 2019]

Visiting Scientist

Leonardo Trujillo Lugo [INSA Lyon, until Sep 2019]

External Collaborator

Hedi Soula [Univ Pierre et Marie Curie]

2. Overall Objectives

2.1. An interface between biology and computer science

The expanded name for the BEAGLE research group is "Artificial Evolution and Computational Biology". Our aim is to position our research at the interface between biology and computer science and to contribute new results in biology by modeling biological systems. In other words we are making artifacts – from the Latin *artis factum* (an entity made by human art rather than by Nature) – and we explore them in order to understand Nature. The team is an Inria Project-Team since January, 2014. It gathers researchers from Inria, INSA, UCBL, who are members of three different labs, the LIRIS [1], the LBBE [2], and CARMEN [3]. It is led by Prof. Guillaume Beslon (INSA-Lyon, LIRIS, Computer Science Dept.).

Our research program requires the team members to have skills in computer science but also in life sciences: they must have or develop a strong knowledge in biosciences to interact efficiently with biologists or, ideally, to directly interpret the results given by the models they develop. A direct consequence of this claim is that it is mandatory to restrict the domain of expertise in life sciences. This is why we focus on a specific scale, central in biology: the cellular scale. Indeed, we restrict our investigations on the cell, viewed as a dynamical system made of molecular elements. This specific scale is rich in open questions that deserve modeling and simulation approaches. We also focus on two different kinds of constraints that structure the cellular level: biophysical constraints and historical constraints. The cell is a system composed of molecules that physically interact and the spatio-temporal nature of these interactions is likely to strongly influence its dynamics. But the cell is also the result of an evolutionary process that imposes its own limits on what can evolve (or is the most likely to evolve) and what cannot (or is the less likely to evolve). A better understanding of what kind of systems evolution is the most likely to lead to in a given context could give us important clues for the analysis of extant biological systems.

2.2. An organization into two tools and four main axes

To study these two kinds of constraints we mainly rely on two specific tools: computational cellular biochemistry and evolution models. We use these tools to develop our "artifacts" and we compare their output with real data, either direct measurements collected by experimentalists or ancestral properties computationally inferred from their extant descendants. The team research is currently organized in four main research axes. The first two ones are methodologically-oriented: we develop general formalisms and tools for computational cellular biochemistry (research axis 1) and families of models to study the evolutionary process (research axis 2). The

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[2] Laboratoire de Biometrie et Biologie Evolutive: UMR CNRS 5558, Univ. Claude Bernard Lyon 1.

[3] Laboratoire de Recherche en Cardiovasculaire, Métabolisme, Diabétologie et Nutrition: UMR U1060 INSERM, INSA-Lyon, INRA 1235, Univ. Claude Bernard Lyon 1.

third “NeuroCell” axis (research axis 3) is the one in which biochemical models are specifically applied on brain cells (neurons and glia). Eventually the last axis aims at integrating the two tools, computational biochemistry and evolution, in what we call "Evolutionary Systems Biology" (research axis 4). The next four sections describe these four axes in more details. The biological questions described are not the sole topics tackled by the team. They are the ones that mobilize a substantial fraction of the researchers on the long run. Many other questions are tackled by individual researchers or even small groups. In the following these ones will be briefly described in their methodological context, *i.e.* in the two sections devoted to research axes 1 and 2.

2.3. A strategy

The scientific objective of the BEAGLE team is to develop a consistent set of concepts and tools – mainly based on computational science – to *in fine* contribute to knowledge discovery in systems biology. Our strategy is to develop strong interactions with life science researchers to become active partners of the biological discovery process. Thus, our aim as a team is not to be a computer science team interacting with biologists, nor to be a team of biologists using computer science tools, but rather to stay in the middle and to become a *trading zone* [27] between biology and computer science. Our very scientific identity is thus fuzzy, melting components from both sciences. Indeed, one of the central claims of the team is that interdisciplinarity involves permanent exchanges between the disciplines. Such exchanges can hardly be maintained between distant teams. That’s why the BEAGLE team tries to develop local collaborations with local scientists. That’s also why BEAGLE also tries to organize itself as an intrinsically interdisciplinary group, gathering different sensitivities between biology and computer science inside the group. Our ultimate objective is to develop interdisciplinarity at the individual level, all members of the team being able to interact efficiently with specialists from both fields.

3. Research Program

3.1. Introduction

As stated above, the research topics of the BEAGLE Team are centered on the modelization and simulation of cellular processes. More specifically, we focus on two specific processes that govern cell dynamics and behavior: Biophysics and Evolution. We are strongly engaged into the integration of these level of biological understanding.

3.2. Research axis 1: Computational cellular biochemistry

Biochemical kinetics developed as an extension of chemical kinetics in the early 20th century and inherited the main hypotheses underlying Van’t Hoff’s law of mass action : a perfectly-stirred homogeneous medium with deterministic kinetics. This classical view is however challenged by recent experimental results regarding both the movement and the metabolic fate of biomolecules. First, it is now known that the diffusive motion of many proteins in cellular media exhibits deviations from the ideal case of Brownian motion, in the form of position-dependent diffusion or anomalous diffusion, a hallmark of poorly mixing media. Second, several lines of evidence indicate that the metabolic fate of molecules in the organism not only depends on their chemical nature, but also on their spatial organisation – for example, the fate of dietary lipids depends on whether they are organized into many small or a few large droplets (see e.g. [28]). In this modern-day framework, cellular media appear as heterogeneous collections of contiguous spatial domains with different characteristics, thus providing spatial organization of the reactants. Moreover, the number of implicated reactants is often small enough that stochasticity cannot be ignored. To improve our understanding of intracellular biochemistry, we study spatiotemporal biochemical kinetics using computer simulations (particle-based spatially explicit stochastic simulations) and mathematical models (age-structured PDEs).

3.3. Research axis 2: Models for Molecular Evolution

We study the processes of genome evolution, with a focus on large-scale genomic events (rearrangements, duplications, transfers). We are interested in deciphering general laws which explain the organization of the genomes we observe today, as well as using the knowledge of these processes to reconstruct some aspects of the history of life. To do so, we construct mathematical models and apply them either in a "forward" way, *i.e.* observing the course of evolution from known ancestors and parameters, by simulation (*in silico experimental evolution*) or mathematical analysis (*theoretical biology*), or in a "backward" way, *i.e.* reconstructing ancestral states and parameters from known extant states (*phylogeny, comparative genomics*). Moreover we often mix the two approaches either by validating backwards reconstruction methods on forward simulations, or by using the forward method to test evolutionary hypotheses on biological data.

3.4. Research axis 3: Computational systems biology of neurons and astrocytes

Brain cells are rarely considered by computational systems biologists, though they are especially well suited for the field: their major signaling pathways are well characterized, the cellular properties they support are well identified (e.g. synaptic plasticity) and eventually give rise to well known functions at the organ scale (learning, memory). Moreover, electro-physiology measurements provide us with an experimental monitoring of signaling at the single cell level (sometimes at the sub-cellular scale) with unrivaled temporal resolution (milliseconds) over durations up to an hour. In this research axis, we develop modeling approaches for systems biology of both neuronal cells and glial cells, in particular astrocytes. We are mostly interested in understanding how the pathways implicated in the signaling between neurons, astrocytes and neurons-astrocytes interactions implement and regulate synaptic plasticity.

3.5. Research axis 4: Evolutionary Systems Biology

This axis, consisting in integrating the two main biological levels we study, is a long-standing and long-term objective in the team. These last years we did not make significant advances in this direction and we even removed this objective from last year's report. However the evolution of the team staff and projects allows us to give it back its central place. We now have the forces and ideas to progress. We have several short and middle term projects to integrate biochemical data and evolution. In particular we are analysing with an evolutionary perspective the 3D conformation of chromosomes, the regulatory landscape of genomes, the chromatin-associated proteins.

4. Application Domains

4.1. Functional and Evolutionary Biology

We do not distinguish our research and its application domains. Our shared idea is that the research is oriented by a scientific question, which is a multidisciplinary one, most often of biological nature. We do not develop methodologies independently from this question and then look for applications. Instead we collectively work with other disciplines to solve a question, with our competencies.

In consequence the application domains are already listed in the description of our projects and goals. They concern functional and evolutionary biology, related to critical social questions as human and plant health.

4.2. Social and Environmental Responsibility (Implication domains)

These last years we have maintained a frequent team discussion on the social and environmental responsibility of researchers. It has become more frequent this year, with the announcements of serious environmental issues by many governmental or non governmental organizations.

We are engaged in many actions regarding this responsibility. A constant ethics questioning, directing our research projects according to our values, teaching and popularization of ethical values. In particular we are engaged in several research projects on health and environment, and one of us has been a member of the institutional workgroup on environmental issues at Inria.

Regarding the functioning of research activities, we attempted a measure of the environmental footprint of our activities, regardless of their aims. It has the shape of a carbon footprint analysis, gathering the carbon footprint of travels, computer usage, computer equipment. We are aware of the incompleteness of this analysis, as well by not including many activities (nutrition, homeplace-workplace trips), and not taking other environmental issues than carbon emissions.

However it is a starting point, that we presented to many colleagues who were interested in reproducing the computation, so we give the headlines here. We used the unitary costs given by a website we constructed: https://ferme.yeswiki.net/Empreinte. The data was collected on an average taken over 3 years, 2016-2018 (we cannot yet at this stage make the analysis for 2019). Travels by members of the team or invited researchers emitted 39.86tCO2. Computing hours on local clusters emitted 17.46tCO2. The acquisition of computers accounts for the emission of 4.53tCO2. The total is 61.85tCO2.

Based on this lower bound of our CO2 emissions, the total per person is around 3 tons per person. Probably this number is highly underevaluated since it accounts for only part of our professional activities.

Whether it is too high or acceptable, and the establishment of a carbon budget is a difficult question. If we refer to the goals of the COP21 conclusions, we should emit less than 2 tons of CO2 per person in 2050 to reach carbon neutrality. This includes professional and personal life, and all the services we benefit from. We did not arrive yet at a consensus on the objective we should reach to consider we have a sutainable activity, but we in majority recognize that we are anyway far above what would be a consensus objective. We are still in a discussion to engage in a reduction.

5. Highlights of the Year

5.1. Highlights of the Year

Last year our highlights were focused on remarkable publications. This year the main events are on organizations and grants applications.

- We have been in charge of organizing the Scientific Days of Inria in July 2019 https://project.inria.fr/journeesscientifiques2019/
- We were awarded two exploratory actions by Inria in 2019, one on high performance computing, the other in agro-ecology
- We were auditioned for an ERC synergy grant call (very last step in the many steps for the grant obtention)
- We organized MMEE https://mmee2019lyon.sciencesconf.org/ in Lyon

6. New Software and Platforms

6.1. aevol

Artificial Evolution

KEYWORDS: Bioinformatics - Genomics - Evolution

FUNCTIONAL DESCRIPTION: Aevol is a digital genetics model: populations of digital organisms are subjected to a process of selection and variation, which creates a Darwinian dynamics. By modifying the characteristics of selection (e.g. population size, type of environment, environmental variations) or variation (e.g. mutation rates, chromosomal rearrangement rates, types of rearrangements, horizontal transfer), one can study experimentally the impact of these parameters on the structure of the evolved organisms. In particular, since Aevol integrates a precise and realistic model of the genome, it allows for the study of structural variations of the genome (e.g. number of genes, synteny, proportion of coding sequences).

The simulation platform comes along with a set of tools for analysing phylogenies and measuring many characteristics of the organisms and populations along evolution.

An extension of the model (R-Aevol), integrates an explicit model of the regulation of gene expression, thus allowing for the study of the evolution of gene regulation networks.

RELEASE FUNCTIONAL DESCRIPTION: Fix compilation error on Mac (tr1 included in std). The new mac compiler includes the tr1 directly in std which caused a compilation error. This issue was specific to aevol-4.4.1

- Participants: Antoine Frénoy, Bérénice Batut, Carole Knibbe, David P. Parsons, Dusan Misevic, Guillaume Beslon, Jonathan Rouzaud-Cornabas and Vincent Liard
- Partners: UCBL Lyon 1 - INSERM - Université Paris-Descartes - Insa de Lyon
- Contact: Guillaume Beslon
- URL: http://www.aevol.fr/

6.2. Treerecs

KEYWORDS: Bioinformatics - Biology - Computational biology

SCIENTIFIC DESCRIPTION: The reconciliation between gene trees and species trees is a modern method of molecular phylogeny, which does not yet have its standard software, as for example phylogeny from DNA or amino acid sequences. Treerecs has this ambition, incorporating the classic functionalities of reconciliation: annotating the vertices of a gene tree with the tops of a species tree, rooting and correcting the gene tree. Rooting and correction are calculated to minimize the number of duplications and losses in reconciliation. Medium-sized solutions are randomly sampled according to a uniform law. A likelihood can then be calculated using probabilistic methods. In addition, Treerecs is integrated into a standard software ecosystem of phylogeny, bio ++, ALE, Seaview, and has a graphical interface. Some original features are implemented, such as the possibility of combining two types of likelihoods, the one calculated from the sequences and the one calculated from the reconciliations, the possibility of estimating the costs of the evolutionary events, the possibility of exploring the space of trees according to a joined likelihood.

FUNCTIONAL DESCRIPTION: Treerecs takes as minimum input a gene tree and a species tree. It "reconciles" them, that is, it annotates gene tree nodes with events and assign them to species tree nodes. Biologically, it is a reconstruction of the gene history, given the species history, in terms of duplications, speciations, losses.

With the appropriate options Treerecs can root and correct the gene tree.

NEWS OF THE YEAR: Release of a 0.1 stable version

- Participants: Nicolas Comte, David P. Parsons, Eric Tannier and Benoît Morel
- Partner: Laboratoire de Biométrie et Biologie Evolutive (LBBE) - UMR CNRS 5558
- Contact: Eric Tannier

7. New Results

7.1. Computational Glioscience: A book to review the existing mathematical models of the glial cells

[participant: H. Berry]

Over the last two decades, the recognition that astrocytes - the predominant type of cortical glial cells - could sense neighboring neuronal activity and release neuroactive agents, has been instrumental in the uncovering of many roles that these cells could play in brain processing and the storage of information. These findings initiated a conceptual revolution that leads to rethinking how brain communication works since they imply that information travels and is processed not just in the neuronal circuitry but in an expanded neuron-glial network. On the other hand the physiological need for astrocyte signaling in brain information processing and the modes of action of these cells in computational tasks remain largely undefined. This is due, to a large extent, both to the lack of conclusive experimental evidence, and to a substantial lack of a theoretical framework to address modeling and characterization of the many possible astrocyte functions. This book [https://hal.inria.fr/hal-01995842] aims at filling this gap, providing the first systematic computational approach to the complex, wide subject of neuron-glia interactions. The organization of the book is unique insofar as it considers a selection of "hot topics" in glia research that ideally brings together both the novelty of the recent experimental findings in the field and the modelling challenge that they bear. A chapter written by experimentalists, possibly in collaboration with theoreticians, will introduce each topic. The aim of this chapter, that we foresee less technical in its style than in conventional reviews, will be to provide a review as clear as possible, of what is "established" and what remains speculative (i.e. the open questions). Each topic will then be presented in its possible different aspects, by 2-3 chapters by theoreticians. These chapters will be edited in order to provide a "priming" reference for modeling neuron-glia interactions, suitable both for the graduate student and the professional researcher.

7.2. The impact of tracers on lipid digestion kinetics

[Participant: Carole Knibbe]

Dietary fats are present in the diet under different types of structures, such as spread vs emulsions (notably in processed foods and enteral formula), and interest is growing regarding their digestion and intestinal absorption. In clinical trials, there is often a need to add stable isotope-labeled triacylglycerols (TAGs) as tracers to the ingested fat in order to track its intestinal absorption and further metabolic fate. Because most TAG tracers contain saturated fatty acids, they may modify the physicochemical properties of the ingested labeled fat and thereby its digestion. However, the actual impact of tracer addition on fat crystalline properties and lipolysis by digestive lipases still deserves to be explored. In this context, we monitored the thermal and polymorphic behavior of anhydrous milk fat (AMF) enriched in homogeneous TAGs tracers and further compared it with the native AMF using differential scanning calorimetry and power X-ray diffraction. As tracers, we used a mixture of tripalmitin, triolein and tricaprylin at 2 different concentrations (1.5 and 5.7wt%, which have been used in clinical trials). The addition of TAG tracers modified the AMF melting profile, especially at the highest tested concentration (5.7 wt%). Both AMF and AMF enriched with 1.5wt% tracers were completely melted around 37°C, i.e. close to the body temperature, while the AMF enriched with 5.7wt% tracers remained partially crystallized at this temperature. Similar trends were observed in both bulk and emulsified systems. Moreover, the kinetics of AMF polymorphic transformation was modified in the presence of tracers. While only β' form was observed in the native AMF, the β-form was clearly detected in the AMF containing 5.7wt% tracers. We further tested the impact of tracers on the lipolysis of AMF in bulk using a static in vitro model of duodenal digestion. Lipolysis of AMF enriched with 5.7wt% tracers was delayed compared with that of AMF and AMF enriched with 1.5wt% tracers. Therefore, low amounts of TAG tracers including tripalmitin do not have a high impact on fat digestion, but one has to be cautious when using higher amounts of these tracers.

7.3. The control of synaptic plasticity by external factors

[participant: H. Berry]

The dorsal striatum exhibits bidirectional corticostriatal synaptic plasticity, NMDAR- and endocannabinoids-(eCB)-mediated, necessary for the encoding of procedural learning. Therefore, characterizing factors controlling corticostriatal plasticity is of crucial importance. Brain-derived neurotrophic factor (BDNF) and its receptor, the tropomyosine receptor kinase- B (TrkB), shape striatal functions and their dysfunction deeply

affects basal ganglia. BDNF/TrkB signaling controls NMDAR-plasticity in various brain structures including the striatum. However, despite cross-talk between BDNF and eCBs, the role of BDNF in eCB- plasticity remains unknown. In https://hal.inria.fr/hal-02076121, we show that BDNF/TrkB signaling promotes eCB-plasticity (LTD and LTP) induced by rate-based (low-frequency stimulation) or spike-timing- based (spike-timing-dependent plasticity, STDP) paradigm in striatum. We show that TrkB activation is required for the expression and the scaling of both eCB-LTD and eCB-LTP. Using two-photon imaging of dendritic spines combined with patch-clamp recordings, we show that TrkB activation prolongs intracellular calcium transients, thus increasing eCB synthesis and release. We provide a mathematical model for the dynamics of the signaling pathways involved in corticostriatal plasticity. Finally, we show that TrkB activation enlarges the domain of expression of eCB-STDP. Our results reveal a novel role for BDNF/TrkB signaling in governing eCB-plasticity expression in striatum, and thus the engram of procedural learning.

7.4. A new model for calcium signals in tiny sub-cellular domains

[participants: A. Denizot, H. Soula, H. Berry]

Astrocytes, a glial cell type of the central nervous system, have emerged as detectors and regulators of neuronal information processing. Astrocyte excitability resides in transient variations of free cytosolic calcium concentration over a range of temporal and spatial scales, from sub-microdomains to waves propagating throughout the cell. Despite extensive experimental approaches, it is not clear how these signals are transmitted to and integrated within an astrocyte. The localization of the main molecular actors and the geometry of the system, including the spatial organization of calcium channels IP3R, are deemed essential. However, as most calcium signals occur in astrocytic ramifications that are too fine to be resolved by conventional light microscopy, most of those spatial data are unknown and computational modeling remains the only methodology to study this issue. In https://hal.inria.fr/hal-02184344v2, we propose an IP3R-mediated calcium signaling model for dynamics in such small sub-cellular volumes. To account for the expected stochasticity and low copy numbers, our model is both spatially explicit and particle-based. Extensive simulations show that spontaneous calcium signals arise in the model via the interplay between excitability and stochasticity. The model reproduces the main forms of calcium signals and indicates that their frequency crucially depends on the spatial organization of the IP3R channels. Importantly, we show that two processes expressing exactly the same calcium channels can display different types of calcium signals depending on the spatial organization of the channels. Our model with realistic process volume and calcium concentrations successfully reproduces spontaneous calcium signals that we measured in calcium micro-domains with confocal microscopy and predicts that local variations of calcium indicators might contribute to the diversity of calcium signals observed in astrocytes. To our knowledge, this model is the first model suited to investigate calcium dynamics in fine astrocytic processes and to propose plausible mechanisms responsible for their variability.

7.5. Evolution of genome size

Using the Aevol software, we investigated the dynamics of genome size under different evolutionary pressures (variation of mutation rates and variation of population sizes). The dynamics of the model enabled us to identify a new mutational pressure on genome size that spontaneously increase the fraction of non-coding sequences. We showed that this mutational pressure interact with the selective pressure for robustness (knibbe et al., 2007), resulting in an equilibrium of genome size and non-coding proportion. Moreover, we showed that this equilibrium can change depending on the size of the population due to the resulting effect on selection intensity. A paper has been published in the proceedings of the ALife 2019 conference (cardes et al, 2019) and an article in in preparation.

7.6. Dynamics of evolutionary innovation

Using a combination of mathematical and computational models (NK-Fitness-Landscapes and Aevol), we investigated the dynamics of innovation in evolving systems. We showed that innovation is often triggered by specific mutational events, typically structural variation of the genome (e.g. duplications, inversions, ...).

We further studied this effect and showed that innovation is due to the differences of time scale between the different kinds of mutations: fast mutations (typically point mutations) are rapidly exhausted, resulting in a fitness plateau. However, slow mutations (typically structural variations) can open new evolutionary paths, resulting in the population escaping from the fitness plateau. An article is in preparation in collaboration with Santiago F. Elena (CSIC, Spain).

7.7. Evolution of biological complexity

Using a modified version of the Aevol platform, we studied the evolution of complex features. By evolving population of organisms in conditions where complexity is counter-selected, we showed that complexity accumulates even in these conditions, i.e. even when complex organisms are less fit than simple ones. Moreover we showed that complex organisms are not more robust and not more evolvable than simple ones. This shows that evolution spontaneously initiate a "complexity ratchet" that forces complexity to grow. An article is in press in the Artificial Life Journal (to be published in 2020).

7.8. Dynamics of mutator strains

In a long-lasting collaboration with Utrecht University, we studied the dynamics of mutator strains in constant environments (mutator strains being individuals which mutation rate is increased by several orders of magnitude). Contrary to what is generally admitted, we showed that, although mutators initially suffer from a mutational burden (in coherence with the theory), they are able to quickly recover and avoid the burden. Moreover, we showed that they do so by contracting their coding genome compartment and expanding their non-coding compartment. This result show that mutators can thrive even in a constant environment (rutten et al., 2019).

7.9. Mutiscale phylogenetics models

[Participant: Eric Tannier]

We progressed in the modeling of multi-scale phylogenetic events: we gave an algorithm to infer gene conversions according to a phylogeny [7], a complexity result and an algorithm for transfers with replacements [6], and we devised a simulation tool integrating extinct species and horizontal inheritance [3].

7.10. Evolution of the Drosophila melanogaster Chromatin Landscape and Its Associated Proteins

[participant: A. Crombach]

In the nucleus of eukaryotic cells, genomic DNA associates with numerous protein complexes and RNAs, forming the chromatin landscape. Through a genome-wide study of chromatin-associated proteins in Drosophila cells, five major chromatin types were identified as a refinement of the traditional binary division into hetero- and euchromatin. These five types were given color names in reference to the Greek word chroma. They are defined by distinct but overlapping combinations of proteins and differ in biological and biochemical properties, including transcriptional activity, replication timing, and histone modifications. We assessed the evolutionary relationships of chromatin-associated proteins and presented an integrated view of the evolution and conservation of the fruit fly Drosophila melanogaster chromatin landscape. We combined homology prediction across a wide range of species with gene age inference methods to determine the origin of each chromatin-associated protein. This provided insight into the evolution of the different chromatin types. Our results indicate that for the euchromatic types, YELLOW and RED, young associated proteins are more specialized than old ones; and for genes found in either chromatin type, intron/exon structure is lineage-specific. Next, we provide evidence that a subset of GREEN-associated proteins is involved in a centromere drive in D. melanogaster. Our results on BLUE chromatin support the hypothesis that the emergence of Polycomb Group proteins is linked to eukaryotic multicellularity. In light of these results, we discuss how the regulatory complexification of chromatin links to the origins of eukaryotic multicellularity.

8. Partnerships and Cooperations

8.1. Regional Initiatives

- CPER LECO++: Parallel HPC architectures evolve and the calculation codes are naturally bound to vary over time. Indeed, the architectures change every 2-3 years while the lifespan of a scientific code is much longer (at least 10 years). Knowing how to control the impacts of these changes in order to automatically adapt the digital simulation codes to maintain a high level of performance is a necessity to guarantee a certain sustainability of the developed code. Currently, these variations are manually managed by programmers which require a high level of expertise as well as time.

  A collaboration between the AVALON teams from LIP and BEAGLE from LIRIS on this subject involved one master trainees this year (funding from Federation Informatique de Lyon – PMSISEE project). More specifically, BEAGLE is interested in designing AEVOL a high performance parallel code for simulating the evolution of a population of bacteria. The different parts of the code have been adapted to the hardware characteristics of current architectures (multicore, vector computing, etc.) for which certain operations have several implementations (CPU or vector) or several parallel variants. Designing the assembly of the right versions and choosing the right parameters remains a difficult problem. In this issue, the AVALON team brings its expertise in the development and exploitation of component models, in parallel programming models and in the expertise of executive supports for HPC.

  A PhD thesis between Avalon and Beagle (Laurent Turpin) linked to the CPER LECO++ project (coordinator: T. Gautier, AVALON) has started with the aim of studying the robustness of computer codes on modern parallel architectures and their evolution. Thus, the targeted hardware is that being acquired through the LECO++ project (ARM machine, massively multi-GPU (10)).

  The work of this thesis aims to study the methods and approaches allowing to contribute to a solution to the problems of composition, choice of parameters and efficient execution on a parallel architecture in HPC. The problem addressed in the thesis concerns the portability of the performance of a parallel application for managing code variants and variations at runtime. The solutions that will be studied will be those at the interface between a programming model and its exploitation by executive support. In order to exploit the performance of a class of machines in a portable manner, the candidate will propose the necessary adaptations, whether to the existing component-based programming model (typically Comet) and to executive support (OpenMP type or an executive engine with task base). A major constraint of this work is the performance at execution: the evaluation will be based on an experimental methodology with AEVol as target application. The target hardware is that of an HPC computing node of tomorrow: a multi-core server coupled with a large number of hardware accelerators - GPUs - allowing to have a significant computing density (approximately from 30 to 128 TFlops double precision for 4 to 16 GPUs).

8.2. National Initiatives

8.2.1. ANR

- Evoluthon (2019-2022): Artificial Life as a benchmark for evolutionary studies, a 4-year project leaded by E Tannier with 2 partners, Beale Inria and Le Cocon, LBBE.
- Dopaciumcity (2014-2018): Dopamine modulation of calcium influx underlying synaptic plasticity, a 4-year project funded by a grant from the ANR-NSF-NIH Call for French-US Projects in Computational Neuroscience. With L. Venance, College de France, CIRB, CNRS/UMR 7241 - INSERM U1050, Paris, France and K Blackwell, Krasnow Institute of Advanced Studies, George Mason University, Fairfax, VA, USA. Supervisor: L Venance (for France) and K.L. Blackwell (for US). Participants: H Berry, I Prokin, A Foncelle

- Dallish (2016-2020): Data Assimilation and Lattice LIght SHeet imaging for endocytosis/exocytosis pathway modeling in the whole cell, Call AAPG ANR 2016. With C. Kervrann (Inria Rennes), J. Salamero (Institute Curie, Paris), B. Laroche (INRA, Jouy-en-Josas). Participants: H. Berry.
- Storiz (2018-2020): Horizontal transfers as documents from extinct or unknown species. Call ANR JCJC 2018. Leaded by Damien de Vienne (LBBE, Lyon) Participant: Eric Tannier
- LncEvoSys (2017-2019): An evolutionary systems approach to understand long non-coding RNA functionality, Call ANR JCJC 2017. Leaded by Anamaria Necsulea (LBBE, Lyon). Participant: Eric Tannier

8.2.2. Inria

- Naviscope (Inria Project Lab, 2018-2022): image-guided Navigation and VIsualization of large data sets in live cell imaging and microSCOPy. Nowadays, the detection and visualization of important localized events and process in multidimensional and multi-valued images, especially in cell and tissue imaging, is tedious and inefficient. Specialized scientists can miss key events due to complexity of the data and the lack of computer guidance. In Naviscope we develop original and cutting-edge visualization and navigation methods to assist scientists, enabling semi-automatic analysis, manipulation, and investigation of temporal series of multi-valued volumetric images, with a strong focus on live cell imaging and microscopy application domains. We build Naviscope upon the strength of scientific visualization and machine learning methods in order to provide systems capable to assist the scientist to obtain a better understanding of massive amounts of information. Such systems will be able to recognize and highlight the most informative regions of the dataset by reducing the amount of information displayed and guiding the observer attention. Head: C. Kervrann (Serpico), other EPIs: Aviz, Beagle, Hybrid, Morpheme, Mosaic, Parietal, and MaIage (INRA unit).
- Action Exploratoire "Community Garden Book": IPBES's recent report on declining biodiversity calls for generalization of agroecological, productive, biodiversity and environmental friendly methods, oriented towards participatory action research. This exploratory action is a proposal to develop tools from open science, evolution science and algorithmics for the co-construction and use of an agroecological network of interactions between groups, species, varieties found in fields and gardens.
- Action Exploratoire ExODE: In biology, the vast majority of systems can be modeled as ordinary differential equations (ODEs). Modeling more finely biological objects leads to increase the number of equations. Simulating ever larger systems also leads to increasing the number of equations. Therefore, we observe a large increase in the size of the ODE systems to be solved. A major lock is the limitation of ODE numerical resolution so ware (ODE solver) to a few thousand equations due to prohibitive calculation time. The AEx ExODE tackles this lock via 1) the introduction of new numerical methods that will take advantage of the mixed precision that mixes several floating number precisions within numerical methods, 2) the adaptation of these new methods for next generation highly hierarchical and heterogeneous computers composed of a large number of CPUs and GPUs. For the past year, a new approach to Deep Learning has been proposed to replace the Recurrent Neural Network (RNN) with ODE systems. The numerical and parallel methods of ExODE will be evaluated and adapted in this framework in order to improve the performance and accuracy of these new approaches.

8.3. International Initiatives

8.3.1. Inria International Partners

8.3.1.1. Declared Inria International Partners

- Beagle is a member of the CNRS Laboratoire International Associé "EvoAct" (Evolution in Action). Other members of EvoAct are the TIMC-IMAG (Grenoble) and the Beacon Center (Michigan State University, USA).

8.3.1.2. Informal International Partners

- Collaboration with Alexander Fleischmann at Brown University (USA) on neuro-evo-devo.
- Collaboration with Cedric Chauve, SFU, Vancouver (Canada) on phylogeny and rearrangements.
- Collaboration with Tom Williams, Bristol (UK) on phylogeny.

8.4. International Research Visitors

8.4.1. Visits of International Scientists

- We welcomed Leonardo Trujillo (Venezuela) as a visiting professor from January 2019 to July 2019. Leonardo Trujillo worked on the innovation dynamics in evolution using NK Fitness-Landscapes.
- Corrado Cali, BESE Division, KAUST University, Saudi Arabia, 1 week in november

8.4.1.1. Internships

- Barbara Genocchi (PhD candidate, Tampere University of Technology, Tampere, Finland) visited us for 16 days (Sept 9 - Sept 24).

9. Dissemination

9.1. Promoting Scientific Activities

9.1.1. Scientific Events: Organisation

9.1.1.1. General Chair, Scientific Chair

- Eric Tannier was the organizing committee chair of the Inria scientific days, July 2019.

9.1.1.2. Member of the Organizing Committees

- Guillaume Beslon and Anton Crombach, members of the organizing committee of MMEE 2019 (Mathematical Modeling in Ecology and Evolution, Lyon, July 2019)
- Guillaume Beslon : member of the organizing committee of the EvoLyon Day (Lyon, November 2019)
- Guillaume Beslon : member of the organizing committee of BDA 2019 (Bases de Données Avancées, Lyon, October 2019)
- Anton Crombach was part of the organizing and scientific committees of the winter course "Advanced Lectures in Computational Systems Biology" in Aussois.
- Hugues Berry was a member of the Local Organising Committee for conference MedInfo 2019 (https://www.medinfo-lyon.org/en/)
- Eric Tannier is a member of the organizing committee of "SEMOVI", séminaire de modélisation du vivant, a local scientifica animation in systems biology.

9.1.2. Scientific Events: Selection

9.1.2.1. Chair of Conference Program Committees

- Eric Tannier was the program committee chair of the Inria scientific days, July 2019.

9.1.2.2. Member of the Conference Program Committees

- Anton Crombach, involved in the selection of talks and posters for MMEE (Mathematical models in ecology and evolution, Lyon, July)
- Christophe Rigotti, member of the program committee of the 19th IEEE International Conference on Data Mining (ICDM).

- Christophe Rigotti, member of the program committee of the 34rd ACM Symposium On Applied Computing (SAC).
- Guillaume Beslon and Jonathan Rouzaud-Cornabas, members of the program committee of ALife 2019 (2019 Conference on Artificial Life. Newcastle. United Kingdom)
- Eric Tannier, member of the program committee of Jobim 2020
- Eric Tannier, member of the program committee of RECOMB Comparative Genomics 2019
- Eric Tannier, member of the program committee of ISBM/ECCB 2019

9.1.2.3. Reviewer

- Eric Tannier reviewed for RECOMB 2020

9.1.3. Journal

9.1.3.1. Member of the Editorial Boards

- Hugues Berry is Associate Editor for PLoS Computational Biology
- Eric Tannier is a guest editor for the epijournal DMTCS, and edited a special issue in 2019
- Eric Tannier is an editor of "Peer Community in Evolutionary Biology"
- Eric Tannier is a founding editor of "Peer Community in Mathematical and Computational Biology"

9.1.3.2. Reviewer - Reviewing Activities

- Bioinformatics, Journal of Experimental Zoology Part B...

9.1.4. Invited Talks

- Carole Knibbe, 2019 Gordon Conference on "Organismal, Cellular, Molecular and Theoretical Approaches to Understanding Evolution", Easton, MA, USA, June 9-14 2019.
- Anton Crombach, lab seminar at LBMC
- Anton Crombach, lab seminar at LBBE
- Anton Crombach, invited speaker at the EvoLyon conference in november 2019
- Hugues Berry, Artificial Intelligence and Health: the ambition of the French Plan, Aviesan Meeting, Brussels Belgium, Dec. 2019
- Hugues Berry, An introduction to the theoretical models for passive molecule movements in living cells, Action Nationale de Formation du CNRS, Measurement of Molecular Dynamics in Living Cells, Lille, France, Oct. 2019
- Hugues Berry, Searching for deterministic chaos in biological data,Dynamical Systems and Applications to Biology, CIMPA School, Dhaka, Bangladesh, June 2019
- Hugues Berry, Anomalous diffusion in living cells : bridging the gap between experiments and models through collaborative challenges, Random Walks and Intracellular Transport, School of Mathematics, University of Manchester, Manchester, UK, April 2019
- Hugues Berry, Investigating the effect of the nanoscale architecture of astrocytic processes on the propagation of calcium signals, Tampere University of Technology, Tampere, Finland, April 2019
- Hugues Berry, Inria research at the forefront of digital sciences for medicine, 2019 French-American Innovation Day (FAID2019), Houston, Texas, USA, march 2019
- Carole Knibbe, Eric Tannier, Which social and environmental responsibility for researchers, lab seminar at LBMC
- Eric Tannier, open science as an institutional response to the editorial crisis in research, "open science day" of the research biology federation, Lyon.
- Guillaume Beslon, invited talk at UGA (séminaire "Translation et Innovation en Médecine et Complexité") in November 2019

- Guillaume Beslon, invited talk at the I4ID 2019 conference (Immunotherapies & Innovations for Infectious Diseases Congress, Lyon, December 2019)

9.1.5. Leadership within the Scientific Community

- Anton Crombach is the lead editor of book "Evolutionary Systems Biology, 2nd edition" (ongoing work).
- Hugues Berry organised the 1st Singapore-France Joint Workshop on AI in Health, in association with the international conference MedInfo (https://medinfo-lyon.org/en/), Lyon, France, August 27-29, 2019.
- Hugues Berry co-organized the INSERM Workshop “Intracellular dynamics of molecules: analysis and models” (https://research.pasteur.fr/en/event/intracellular-dynamics-of-molecules-analysis-and-models/). The workshop combined a 3-day critical assessment phase (in Bordeaux, France, June 24-26 2019) and a 3-day technical worskshop (in Lyon, France, July 1-3 2019). This workshop addressed a biologist audience and covered the main experimental methods to quantify the mobility and trajectories of biomolecules in living cells, with an emphasis on the quantification methods for individual trajectories and the interest of computer simulations for analysis and interpretation.
- Carole Knibbe and Guillaume Beslon (together with Dusan Misevic from the Center for Research and Interdisciplinarity in Paris) edited a special issue of the Artificial Life journal (vol25 issue 4, nov 2019), with extended versions of the best papers of ECAL 2017. Link : https://www.mitpressjournals.org/doi/abs/10.1162/artl_a_00298?af=R

9.1.6. Scientific Expertise

- Hugues Berry, Reviewer for the Fond National de la Recherche Scientifique (FNRS, Belgium) for the call "FRQ-FNRS Québec - Communauté française de Belgique"

9.1.7. Research Administration

- Christophe Rigotti, elected member of Insa Scientific board (Conseil scientifique)
- Eric Tannier, elected member of the Inria Administration Council
- Eric Tannier, member of the open science committee of the French Ministry of research
- Eric Tannier, member of the ethics platform of the university of Lyon
- Eric Tannier, member of the "Sciences Environments Societies" workgroup of Inria
- Eric Tannier, member of the Environmental responsibility workgroup of LBBE
- Eric Tannier, scientific responsible of the "cours colloques" committee of Inria
- Eric Tannier, member of the scientific committee of the science shop, univ Lyon
- Hugues Berry, Deputy scientific director of Inria for digital biology and health
- Guillaume Beslon, member of the ANR CE45 committee (Mathématiques et sciences du numérique pour la biologie et la santé)
- Guillaume Beslon, member of the IRD CSS5 committee (Science des données et des modèles)

9.2. Teaching - Supervision - Juries

9.2.1. Teaching

License: Jonathan Rouzaud-Cornabas, Object-Oriented Programming, 120h, L3, Computer Science Department, INSA de Lyon

Master: Jonathan Rouzaud-Cornabas, System Programming, 60h, M1, Computer Science Department, INSA de Lyon

Master: Jonathan Rouzaud-Cornabas, Network Programming, 20h, M1, Computer Science Department, INSA de Lyon

Master: Jonathan Rouzaud-Cornabas, High Performance Computing, 60h, M2, Computer Science Department, INSA de Lyon

Master: Jonathan Rouzaud-Cornabas, High Performance Computing, 12h, M2, Bioinformatics and Modeling Department, INSA de Lyon

Licence: C. Knibbe, Fundamentals of algorithmics and programming, 80 heqTD, L3, Bioinformatics and Modelling program of INSA-Lyon

Licence: C. Knibbe, Architecture of computer systems, 19 heqTD, L3, Bioinformatics and Modelling program of INSA-Lyon

Licence: C. Knibbe, Software development, 32 heqTD, L3, Bioinformatics and Modelling program of INSA-Lyon

Licence: C. Knibbe, HTML/CSS, 4 heqTD, L3, Bioinformatics and Modelling program of INSA-Lyon

Master: C. Knibbe, Careers in bioinformatics and modelling, 20 heqTD, M1, Bioinformatics and Modelling program of INSA-Lyon

Licence: Christophe Rigotti, Object-Oriented Programming and Graphical User Interfaces, 86h, L2, Department 1er cycle of INSA-Lyon.

Licence: Christophe Rigotti, Simulation of Chemical Reactions, 26h, L2, Department 1er cycle of INSA-Lyon.

Licence: Christophe Rigotti, Numerical Modelling for Engineering, 60h, L2, Department 1er cycle of INSA-Lyon.

Master: Christophe Rigotti, Data Mining, 25h, M1, Bioinformatics and Modeling Department of INSA-Lyon.

Master: Eric Tannier, Comparative Genomics, 8h, M1, Bioinformatics and Modeling Department of INSA-Lyon.

Master: Eric Tannier, String algorithmics, 12h, M1, Bioinformatics and Modeling Department of INSA-Lyon.

Master: Eric Tannier, String algorithmics, 12h, M1, Bioinformatics UCBL.

Master: Eric Tannier, Research Ethics, 6h, M2, Bioinformatics UCBL

Doctorat: Eric Tannier, Environmental responsibility of research activities, NGS formation, Lyon

Doctorat: Eric Tannier, Research Ethics, 12h, all specialities, Université de Lyon

Doctorat: Eric Tannier, Research Ethics, 6h, Inria PhD students

Master: Audey Denizot, 64h de cours en enzymologie (M1, INSA Lyon) et biologie cellulaire (M2, ENS Lyon).

E-learning

MOOC: Eric Tannier, Research Ethics, FUN, Ph-D candidates, 3000 registered participants

9.2.2. Supervision

PhD in progress: Julie Etienne, "Modélisation et simulation du flux de triglycérides alimentaires, de l'absorption entérocytaire à la sécrétion des chylomicrons", INSA-Lyon, co-supervised by Carole Knibbe and Marie-Caroline michalski (CarMeN laboratory), started in October 2019.

M2 : Julie Etienne, "Analysing and modelling the traffic of triglycerides through enterocytes", co-supervised by Carole Knibbe (80

M2 : Ella Beaumann, "Modélisation compartimentale de cinétiques postprandiales cliniques", co-supervised by Carole Knibbe (70

M2: Hugues Berry and Christophe Rigotti where co-supervisors of the M2 internship of Tymofii Prokopenko (co-supervision with Olivier Pascual of team SynatAc INSERM/CNRS) from 28/01/2019 to 14/06/2019. Title: "Classification and clustering of activity data of microglial cells".

M2 Sujin Hyun, 1 feb 2019 to 31 jul 2019 (6 months), title "Re-assessing the link between splicing and mRNA quality control" (supervised by A Crombach)

PhD: Audrey Denizot, "Simulation de la signalisation calcique dans les prolongements fins astrocytaires", INSA Lyon, 08 Nov. 2019 (co-supervision H. Soula and H. Berry)

PhD: Hugues Berry participated to the PhD Advisory Committee of Barbara Genocchi (BioMediTech, Tampere University of Technology, Finland)

PhD: Eric Tannier participated to the PhD Advisory Committee of Raphael Forquet (UCBLyon)

PhD in progress: Alexandre Laverré, "influence croisée de l'organisation spatiale et des mutations structurales dans les génomes", encadré par Anamaria Necsulea et Eric Tannier, début en septembre 2018

PhD in progress: Théo Tricou, "Détection d'espèces éteintes avec les transferts horizontaux", encadré par Damien de Vienne et Eric Tannier, début en septembre 2018

PhD in progress: Hugo Menet, "Phylogénie multi-échelles des holobiontes", encadré par Eric Tannier et Vincent Daubin, début en septembre 2019

M2: Hugo Menet, "Phylogénie multi-échelles des holobiontes", encadrée par Eric Tannier, 2019

9.2.3. Juries

- HDR: Jérémie Roux,"Integrative single-cell approaches to understanding cancer drug response heterogeneity in tumor cell dynamics" Université Côte d'Azur, Nice, France, September 2019 (Hugues Berry, reviewer)
- HDR: Jean-Baptiste Masson, "Probabilistic induction and physics modelling to probe biological decision making In situ", Sorbonne University, Paris, France, May 2019 (Hugues Berry, reviewer)
- HDR: Celine Scornavacca, "Phylogenetic reconciliations and networks", Univ Montpellier (Eric Tannier, examinateur)
- PhD: Audrey Denizot (Ph-D, INSA-Lyon, October 2019) (Guillaume Beslon was a member of the PhD Committee)
- PhD: Andreas Odorico (Ph-D, Gif-sur-Yvette, December 2019) Guillaume Beslon was reviewer
- PhD: Adrien Legrand (University of Picardie Jules Verne, Amiens, November 2019) Christophe Rigotti was reviewer

9.3. Popularization

9.3.1. Articles and contents

- Hugues Berry participated in popularization activities with the edition of a book, written in French, on the relationships between sex (i.e. a biology concept) and Gender (a sociology approach) (Abou, B. and Berry, H., eds., (2019). Sexe et Genre: de la Biologie a la Sociologie. Editions Materiologiques, Paris, https://materiologiques.com/sciences-philosophie-2275-9948/282-sexe-et-genre-de-la-biologie-a-la-sociologie.html) In recent years, debates about sex and gender concepts between biology and the humanities and social sciences have become more intense, both for scientific reasons and for their societal impacts. Many biologists reject the questioning made by researchers in humanities and social sciences, of what biology considers fundamental, such as sex binarity or sex differences. Humanities and social scientists, on the other hand, often see biology as an academic and institutional source of naturalistic arguments used to oppose gender studies. They denounce biases in the interpretation of biologists as resulting, precisely, from gender-related biases. However, scientific exchanges at the interface between biology and the humanities and social sciences are undoubtedly necessary to overcome these antagonisms. The objective of this book is to implement a dialogue between the two fields, trying to overcome misunderstandings and misconceptions that have gone on for long. The book consists in 12 chapters stemming from biologists and sociologists, organized so as to try and foster dialogue between both communities. The target readership of the

book is composed of non specialist readers (in particular non biologists nor sociologists) with a pre-existing interest on gender issues and their relations to biology. That is why the book was written in French and includes chapters intended to newcomers in the field (e.g. “The determination of sex in the human species and the rest of life” or “Why Gender?”) to more advanced viewpoints (“What we learn from transidentities"). The objective of the publisher was to publish a reference book in French on the relations between sex and gender.

- “Le mouvement est devenu massif”, an interview of Hugues Berry to the French journal L’Usine Nouvelle, Special Edition “A year of simulation”, number 3608, April 25, 2019. https://www.usinenouvelle.com/editorial/le-mouvement-est-devenu-massif.N834680
- Eric Tannier is a co-author of "Quand les branches de l’arbre du vivant s’entremêlent", in *Pour la science*, 2019.

9.3.2. Education

- We have an ongoing collaboration with the Grenoble Rectorat. The aim is to use our computational models to train school professor to evolutionary concepts.

9.3.3. Interventions

- Audrey Denizot participated to activities in the mediation association DéMesures:
  - "Cosmograff" project. This project aims to present the solar system and its scales to the general public, in collaboration with the Musée des Confluences and the collective of street artists Superposition https://bit.ly/35gtYpI. Creation of audio guides in French and English for reuse at the 2019 EWASS international astronomy conference. https://bit.ly/2rQlB5y
  - "ArtScience" project, which aims to present the work of scientists to artists. This project culminated in an artistic exhibition at the ENS Lyon, from April to July 2019, in collaboration with the Taverne Gutenberg https://bit.ly/2OldNR3. Creation of a series of photographs presenting the links between science and art that emerged from this project https://bit.ly/2XqjaCz.
- Eric Tannier co-organized a citizen science event at the Théâtre Nouvelle Génération, Vaise, december 2019
- Eric Tannier organizes a workshop on environmental responibility of researchers in january 2020
- Eric Tannier participated to a "pint of science" evening on the social and environmental responsibility of researchers, May 20, 2019

9.3.4. Internal action

- Eric Tannier and Carole Knibbe gave a lecture on environmental responsibility at the Inria Bio days, 2019
- Eric Tannier gave a training to PhD students on research ethics, 6h, Inria Grenoble Rhône-Alpes, January 2019

9.3.5. Creation of media or tools for science outreach

- We developed the GreenMice game, a small video-game designed to teach the basis of evolutionary biology to young children

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Articles in International Peer-Reviewed Journals

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