Gene-regulated multicellular morphogenesis and behavior

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Duration: 6 months, starting from May 2025 (with flexibility)

Level: Master 2 research internship

Keywords: *Artificial Life, Computational Biology, Cellular Automata, Particle Simulation, Gene Regulation, Morphogenesis, Multicellular Coordination, Artifical Evolution*

How to apply: Contact clement.moulin-frier@inria.fr with a CV and letter of motivation. We also recommend sending documents or reports describingprevious projects you have been working on (even if they are not directly related to the topic), as well as your grades and links to code repositories.

Requirements: We are looking for highly motivated MSc students (Master II). Programming skills and prior experience with Python and large-scale numerical simulation, e.g. in JAX, are expected (or at least a strong interest in learning it).

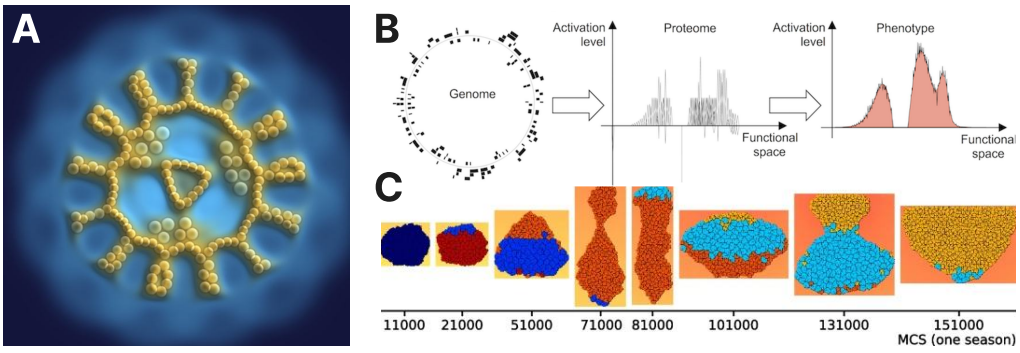

Figure 1: The project aims at integrating a particule-based model of morphogenesis (A, from Mordvintsev et al., 2022) with a genome model as nucleotide sequences (B, from Liard et al., 2020) to study the self-organization of complex morphologies and behaviors (C, from Vroomans and Colizzi, 2023).

The fields of Computational Biology and Artificial Life both seek to simulate *in silico* the fundamental principles of life (with a focus on "life as we know it" in the former, vs. "life as it could be" in the latter). This project aims at integrating computational models from both fields to investigate how complex multicellular morphologies and behaviors can evolve from gene-regulated cell replication, metabolism, and migration.

In both fields, Cellular Automata (CA) have proven to be a particularly relevant framework for studying how complex macro-level forms can self-organize from simple local interactions at the micro level (i.e., morphogenesis). For instance, the famous Game of Life has been used to explore fundamental principles of autopoiesis (Beer, 2014), while the Cellular Potts Model has been employed to investigate morphogenesis and the evolution of multicellular organisms (Vroomans and Colizzi, 2023).

Novel classes of CA have been recently proposed in the Artificial Life community. Lenia (Chan, 2020) is a class of parametrizable CA that generalizes the Game of Life to continuous multidimentional state spaces with parameterizable update fonctions operating on an arbitrarily large neighborhood. It is able to generate a wide diversity of self-organizing patterns, some of them ressembling artificial life forms (Hamon et al., 2024; Plantec et al., 2023. Recently, Lenia has been extended to a particle-based framework (Particle Lenia, Fig. 1.A), which we believe is particularly relevant to study the evolution and morphogenesis of multicellular organisms.

In parallel, contributions in Computational Biology have proposed detailed and realistic models of the genome as nucleotide sequences characterized by potentially varying number of genes, genetic architecture, and coding/non-coding sequence proportion (Fig. 1.B). Such models can capture relevant features of the complexity and evolvability of the genotype-to-phenotype mapping in biology (Liard et al., 2020). However, they have not yet been applied to the morphogenesis of multicellular structures whose fitness depends on their resulting form or function. Other contributions have instead focused on this latter aspect (Fig. 1.C), but using less expressive models of the genotype-to-phenotype mapping.

The objective of this project is to integrate realistic models of genome representations in a particle-based automata framework to study the evolution of complex multicellular morphologies and behaviors (Fig. 1). For this aim, we will formalize, implement and evaluate a computational model based on the following principles.

- Each cell is represented by a particle localized in space (see Mordvintsev et al., 2022; Schoenholz and Cubuk, 2020, for related particle-based simulation frameworks).
- A cell has a genome, represented as a set of genes that encode information on their phenotypic effects (as e.g. in Hindré et al., 2012; Liard et al., 2020).
- Gene (de)activation is regulated as a function of the cell state (as e.g. in Hintze et al., 2024; Vroomans and Colizzi, 2023). The form and parameters of this activation function is encoded in the gene.
- A gene encodes information specifying its phenotypic action on the cell when activated. Depending on this information, the activation of a gene triggers either cell replication (producing an identical daughter cell with small somatic mutations of its genome), cell death, cell migration (driven by the minimization of an energy function, as in Mordvintsev et al., 2022 or Schoenholz and Cubuk, 2020) or cell metabolism (the modulation of the cell state according to the state of neighbor cells).

We will first formalize this model and implement it, potentially using the JAX library for its ability to perform efficient numerical computations on GPUs.

We will then study how we can optimize a single embryonic cell genome to give rise to diverse morphologies (e.g. a segment, a star shape, etc), using evolutionary strategies as black box optimization (see e.g. Steiner et al., 2008 for earlier attempts).

Then we will study optimization toward behaviors requiring multicellular coordination (e.g. collecting or moving large elements of the environment). This might require more advanced methods than mere optimization, e.g. based on diversity search (as e.g. in Hamon et al., 2024).

Finally, if time allows, we will explore how to introduce builtin conservation laws in the entire system (e.g. constant total mass or energy) and study the resulting ecosystem dynamics of cell collectives cooperating or competing for shared resources (as in Plantec et al., 2023; Vroomans and Colizzi, 2023).

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