Morphogen-Based Self-Generation of Evolving Artificial Multicellular Structures with Millions of Cells

Alessandro Fontana
Evolving Systems Laboratory, Faculty of Biology,
Adam Mickiewicz University, Umultowska 89,
PL61614 Poznań, Poland
fontana@evosys.org

Borys Wrobel
Evolving Systems Laboratory, Faculty of Biology,
Adam Mickiewicz University, Umultowska 89,
PL61614 Poznań, Poland
wrobel@evosys.org

ABSTRACT

Epigenetic Tracking is a model of Artificial Embryology whose central feature is separation of cells into normal cells and driver cells. Drivers are much fewer in number than normal cells and orchestrate developmental events. This separation allows for generation of structures with much more complexity and much higher number of cells (in the order of millions) than in other Artificial Embryology models. We introduce in this paper a new mechanism for the generation of driver cells, based on diffusing morphogens. We show that this change preserves the evolvability of very large complex structures, provided that the density of the drivers is sufficiently high. We than draw the outline of the future work that will build on this mechanism towards evolution of structures robust to damage and developmental noise in our system.

Categories and Subject Descriptors

I.2.11 [**Artificial Intelligence**]: Distributed Artificial Intelligence—*coherence and coordination, intelligent agents, multiagent systems*

General Terms

Theory, experimentation

Keywords

artificial embryology, evo-devo, regeneration

1. INTRODUCTION

Artificial Embryology is a sub-field of Artificial Life which aims to mimic "in silico" the biological process of embryogenesis. Artificial Embryology aims at modelling biological life, and building artificial systems with "bio-like" properties. These properties include self-generation, self-maintenance, and self-repair. The issue of self-repair has been investigated in several Artificial Embryology models [1, 2, 6]. In these models multicellular development is regulated by diffusible artificial substances, inspired by biological morphogens. In the work presented here, we introduce morphogens into another Artificial Embryology system, Epigenetic Tracking. This model, whose first version was presented in [3], allows, in comparison to other Artificial Embryology models, for the generation of 3-dimensional structures with much higher complexity. We have previously demonstrated how cancer growth, ageing, and other biological phenomena can be modelled in Epigenetic Tracking [4, 5]. In this paper, we introduce morphogens to our system, as a first step towards self-regeneration.

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2. EPIGENETIC TRACKING: A MODEL OF EVOLUTION OF MULTICELLULAR DEVELOPMENT

In Epigenetic Tracking genomes are relatively compact compared with the size of the structure whose self-generation they allow (for example, 113 genes specify the shape of the Egyptian God Anubis, patterned with the colours of the Dutch flag; Fig. 1). The structure consists of cube-shaped cells arranged on a 3-dimensional grid. The growth of the embryo starts from a single cell and unfolds in a prespecified number of developmental stages. Cells in Epigenetic Tracking belong to two categories: *normal cells* and *driver cells*. Driver cells have a variable called *mobile code*, but the genome – organised as an array of developmental genes – is identical for all cells. Mobile code may be understood as a differentiation state of a driver cell: cells with different codes behave differently despite sharing the same genome. The genomes are sequences of digits and evolve using a genetic algorithm with a fitness function measuring proximity to a target structure [4].

Developmental genes are composed of a left part and of a right part. The left part contains a field called *switch* which specifies if a gene is active or inactive, a field called *mobile sequence*, and a field called *timer*. At each developmental stage, the mobile sequence of each developmental gene is compared with the mobile code of each driver cell, and the timer value is compared with the clock value. If a match occurs, the right part of the gene is executed. The right part of the gene determines the type of event (proliferation or apoptosis), the shape of the local structure created or deleted (an ellipsoid), and the colour of the normal cells created in case of proliferation. In case of proliferation, both normal cells and driver cells are generated. Each new driver cell is assigned a new and unique mobile code, and drivers are much less numerous then normal cells.

In the version of Epigenetic Tracking presented here, each driver activated in development produces one specific morphogen (selected from a set of N possible morphogens). The distance from the morphogen-producing drivers determines the morphogen concentrations (using an inverse quadratic function) at a particular grid position. The concentration

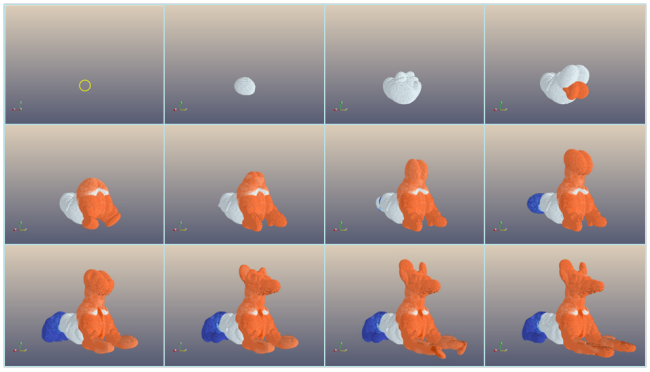

Figure 1: Developmental trajectory of the "Dutch Anubis" composed of 3.3 million cells. The development was evolved with the version of Epigenetic Tracking in which new driver cells are distributed uniformly on the grid.

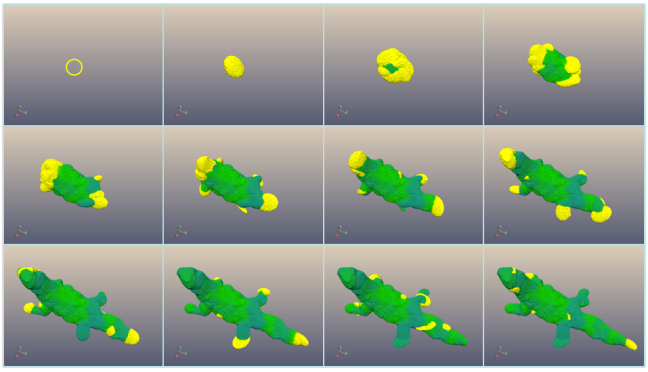

Figure 2: Developmental trajectory of a lizard composed of 500 000 cells. The development was evolved with the version of Epigenetic Tracking introduced in this paper, in which the creation of new driver cells relies on diffusible morphogens.

values are rounded to integer values, dividing the grid into regions which share the same morphogen concentration. In every such region one normal cell is selected (in the middle of the region) and turned into a driver. The new drivers obtain a new and unique mobile code. The code is a N-digit number, composed by juxtaposing the N rounded morphogen concentration values (e.g. 4382) perceived in the region, and N is a parameter of the system (we used $N = 4$ for the simulation in Fig. 2).

3. RESULTS, DISCUSSION, AND FUTURE WORK

Our initial results show that the ability to evolve self-generating very large multicellular structures is not affected by the morphogen-based mechanism introduced to Epigenetic Tracking (Fig. 2). The development of such structures evolves as easily as when the morphogens are not used (and drivers are distributed on the grid using a pre-specified pattern, Fig. 1), provided that the parameters of the system force a sufficiently high density of drivers.

The morphogen-based mechanism for generation of drivers is not the only mechanism that needs to be introduced in Epigenetic Tracking in order to promote self-regeneration. We envision that the system will have this property once the following three additional changes are made (and indeed, our preliminary results, whose discussion is out of the scope of this short paper, validate this claim). The rationale behind these changes stems from the intuition – supported by the evidence from biology – that regeneration relies on developmental mechanisms: a sort of re-setting the system to the state it experienced during development. Firstly, in order for such a re-setting to be possible, the drivers that orchestrated the development need to persist in the final structure, in a quiescent state, waiting to be re-activated once a damage necessitating regeneration occurs. Secondly, we propose that the detection of such damage could be made possible if chemical substances would diffuse from the cells and to be detected by the quiescent driver that produced these cells by proliferation. The driver would re-activate if the concentration of such a substance drops as the result of damage. Thirdly, in order for the regeneration to work properly after the damage, the regenerating portion must ignore the sources of morphogens created after the moment in which the portion was created during development.

In future work we plan to investigate not only if new mechanisms in Epigenetic Tracking promote self-regeneration, but also what will happen when these mechanisms are not working perfectly. Our intuition suggests that we should see a spectrum of regenerative abilities, similar to what happens in biology. We plan to investigate if this intuition will be supported by the results of simulations in future versions of Epigenetic Tracking.

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