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Investigating Artificial Cells' Spatial Proliferation with a Gene Regulatory Network

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Abstract

This paper discusses the combination of a Gene Regulatory Network (GRN) with a Genetic Algorithm (GA) in the context of spatial proliferation of artificial and dynamical cells. It gives the first steps in constructing and investigating simple ways of self-adaptation to furnish lifelike behaving cells. We are thus interested in growing an adaptive cells population in respect to environmental conditions. From a single cell, evolving on some nutriment field, we obtain relatively complex shapes, and functions, acquired with a GA. In a previous work, the artificial cells have been implemented with physical primitives for motion (in order to move correctly in space by convection and diffusion dynamics). The main goal of this current work is therefore to implement, for these physically moving cells, an embedded mechanism providing them with decisions capacities when it comes to choose the suitable "biological" routines (mitosis, apoptosis, migration…) depending on nutriment conjuncture. To that end, we use a "protein-based" GRN, "easily" evolvable to achieve adequate behavior in response to environment inputs. In order to build such a GRN, we start from random GRNs, train them using a GA with a generic nutriment field and different fitness functions, and finally we run the obtained evolved GRN in different nutriment fields to test the robustness of our self-adaption structure.

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Keywords: Artificial ontogeny; Dynamical Systems; Particle Systems; Genetic programming; Evolutionary algorithm; Adaptive systems.

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1. Introduction

Computational tools are more and more suitable for understanding complex phenomena, specially those occurring in biological systems. Many efforts are indeed made in computational intelligence to deal with complex biological dynamics; diseases like cancer, questions like angiogenesis or organogenesis are of great interest and involve more and more computer scientists willing to offer tools in order to build "virtual laboratories", especially in cell dynamics. Indeed, there is a significant number of computational models for cells, using different formalisms [1] (compartment-based, agent-based, lattice-based) and tools [2]. Some platforms are also available and provide different functionalities; CompuCell [3], Virtual Cell [4], Smoldyn [5], etc.

The work, presented in this paper, is meant to bring a contribution in this multidisciplinary area. It tries to combine a physical model of motion/transport and a biological one with self-adaptation capabilities. Evolutionary algorithms, genetic programming and dynamical systems are therefore used within the same framework to provide a generic tool that can be apply to specific dynamics. Consequently, the purpose of this paper is not to make comparison to others existing platforms, but to give the first architecture of our own.

To that end, we briefly present in section 2.1, the physical model that have already been built in a previous work. Artificial cells are implemented with physical primitives for motion, allowing them to move correctly in space by convection and diffusion. Then, in section 2.2 and 2.3, we run the first naïve simulation with some basic biological routines. In these sections, no GRN is used, just an execution diagram is implemented into cells.

Section 3.1 displays the structure of the GRN. It is an object-oriented one, made of input, regulatory and output proteins. Such structure will be the embedded mechanism into cells, providing them with decisions capacities when it comes to choose the suitable biological "routines" (mitosis, apoptosis, migration, keeping or releasing nutriment…) depending on nutriment and vicinity conjuncture.

In Section 3.2, a genetic algorithm is introduced to evolve our protein-based GRN, in order to achieve adequate cells behaviors in response to their environment inputs. The evolution process starts from randomly generated GRNs. With a fitness function a selection is made to keep the best GRNs, and so on until reaching suitable fitness values.

Section 3.3, finally runs different scenarios, with a single initial field. The achieved GRN is then used in different nutriment fields to test the robustness of our structure.

Section 4 discusses the results, the drawbacks and the perspectives of the model.

2. The cell development model

The model we are presenting here relies on some physical principles of motions induced by spatial forces. It is therefore important to first present the formalism that allows us to handle physical constraints for cells motion. Therefore, before giving the biological behaviors that are implemented, let us briefly present the motion and transport routines in our individual-based our agent-based context. With other words, let us see how we consider cells as "physical particles".

2.1. Physical basis for motion and transport

Smoothed Particle Hydrodynamics (SPH) is the calculation groundwork of our cells motion. It has been defined for proto-stars and galaxies dynamics [6]. Hence, SPH can numerically describe a flow of Lagrangian particles. Afterward, many specifications and ameliorations came through [7], [8]. SPH uses particles positions x as quadrature points in order to approximate any given field function f (density, pressure, viscosity…) and its spatial derivative.

$$< f(x) >= \int_{\Omega} f(y)W(x-y,h)dy \tag{1}$$

$$< f_i > \approx \sum_{j=1}^{N} f_j . \frac{m_j}{\varphi_j} W(x_i - x_j, h) \tag{2}$$

$$(\nabla f)_i \approx \sum_{j=1}^{N} f_j . \frac{m_j}{\varphi_j} \nabla_i W(x_i - x_j, h) \tag{3}$$