An Evolutionary Approach to Behavioural Morphometrics

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ABSTRACT

In this short paper, we briefly outline the design of a new framework, BOODLE (BiOlOgical DeveLopment Environment), that empowers biologists to retrace developmental processes at the intercellular level. This framework allows one to import volumetric data as retrieved by micro-CT scanners. Meta-information such as labels of specific regions can be imported or annotated interactively in the virtual simulation environment. Consistently labelled series of multiple embryonic scans that have been recorded at different times capture developmental processes. In order to generate models to retrace the underlying dynamics, we deploy a Genetic Algorithm (GA). The GA optimises the parameters of physics-based virtual cells to retrace the captured processes in a simulation. In particular, the fitness of a set of parameters is calculated based on comparisons between the emerging geometric shapes and the real-world information. The real-world data is provided by said annotations or inferred from grey values captured by the CT scans. To support effective evolutionary optimisation, the user interface supports the user during the import and refinement of CT-data sets, the editing of landmarks, the popluating of imported volumetric data with virtual cells, and the configuration of the Genetic Algorithm.

CCS CONCEPTS

•Computing methodologies → Genetic algorithms; •Applied computing → Computational biology;

KEYWORDS

Genetic Algorithm, Developmental Biology

1 INTRODUCTION

In this paper, we provide a quick overview of a Biologist-in-the-Loop modelling and simulation system called BOODLE (BiOlOgical DeveLopment Environment) and we present early results that demonstrate its comprehensive functionality. More specifically, we show that BOODLE can import recorded micro-CT-data alongside some metadata, harness the grey values of the CT-scan to initialise a virtual cell population and utilise a Genetic Algorithm (GA) to optimise the model's parameters. BOODLE not only provides a vast array of functionality but it also provides user interfaces for each stage of the involved data processing processes. For instance, meta-data, e.g. markings of certain anatomic regions of an embryo, cannot only be imported but also added and adjusted manually. These informations are the foundation for calculating the fitness values of any of the GA's solutions. In particular, after importing the volumetric data of the embryonic body, we populate the geometric structures with virtual cells—either automatically based on grey values of the CT-scans or manually by means of according 3D user interaction widgets that we have designed. The cells, configured by means of the GA, change themselves and each other over time. In case their changes correspond closely to the recorded data, the parameter model is considered better.

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2 RELATED WORK

The emphasis of BOODLE lies in the interactivity of the system—in terms of realtime simulation (similar to [1]), in terms of configuration (similar to [6]), but also with respect to various optimisation criteria. The challenge is multifaceted: Build on empirical data, allow the user to define constraints, let the system automatically close model gaps. Thus, BOODLE needs to approximate globally emerging developmental structures based on cellular behaviours. This top-down-challenge coined the term guided self-organisation (GSO). GSO implies that a process of self-organising results in desirable global changes of a system without having been given clear instructions on how to get there. There are formal approaches to GSO which are based on the theory of complex systems. An exemplary result based on formal work is the quantification of parameters' influences on state changes of in complex systems [3]. Complementarily, formal deliberations could help one to infer the extent to which individual agents of self-organising systems are capable to handle a range of situations [5]. In this paper, the self-organised process of organismal development based on intercellular interactions is guided by means of a GA.

3 BOODLE OVERVIEW

We employ a particle-based soft body representation of the cells exterior based on the FLEX physics engine [2], providing control over the cells' individual shape and their physical interactions. The cell model is further designed in accordance with [4]. The main parameterization categories are cohesion, division and substance diffusion. By means of a visual programming interface, the user can define cells with individual behaviours and parameter sets. He can also define certain categories of cell types that the GA can deploy and fine tune to maximise a cell population's fitness. To support empirical research, BOODLE allows to import CT scan data and meta data into the simulation contexts, to mark surfaces and volumes, to populate specific areas with virtual cells, and to observe, measure and log simulated model alterations.

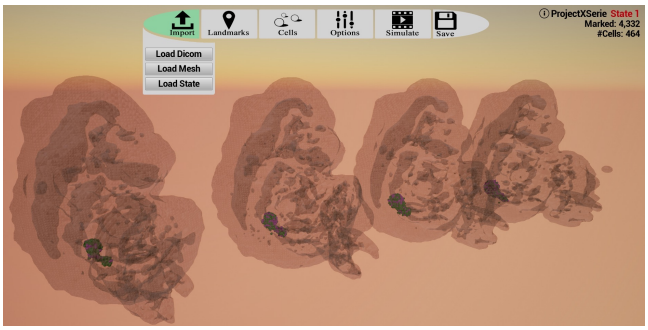
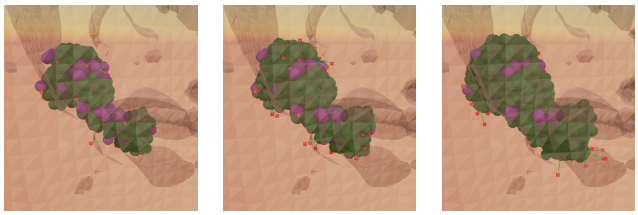


Figure 1: Four volumetric scans of embryos with different markers (light green) represent four simulation states.



$F(t_1) = 0.25$ $F(t_2) = 0.18$ $F(t_3) = 0.19$

Figure 2: An average performing phenotype, yielding a total fitness values of 0.62.

4 EVOLUTIONARY OPTIMISATION

Due to potentially large search spaces, we have chosen evolutionary optimisation approaches to close model gaps and tweak parameters. We extended a standard GA to consider time series of target states [7]. For each target state, we calculate a distance measure between the target volume's convex hull and the convex hull of the volume of the cell population emerging from a given solution. We calculate the morphological fitness F_M of the solution's phenotype and a specific target state i as the inverse of the distance measure. Factors such as structural properties of emerging tissues, the ordering of cells, or a multitude of additional constraints could define additional fitness criteria. In terms of fitness criteria, this demonstration is rather specific. We also only target a very small part of the embryo. The genotype of the cells specifies the following behavioural parameters of a cell: its stiffness, its maximal distance for adhesion and maximal number of adhering cells, division based on physical stresses due to other cells, stress thresholds, and whether only a single involved cell divides, division based on chemical signals and the respective threshold, reaction to morphogens, its morphogen emission rate, and how it is affected by morphogen gradients. We created a small mock-up example based on embryonic chick CT-data sets. For each of four target states, we introduced changes in the shape and the spatial dimensions. Next, we populated the initial surfaces with two types of virtual cells. The genetic algorithm was configured to feature a population of ten solutions of 80 bits at a time, deploy probabilities of bitwise mutation $p_m = 0.05$ and one-point crossover recombination $p_r = 0.3$, and to select descendants based on roulette-wheel selection. Figure 2 shows an example of an average performing solution. It can be observed how one cell type dominates the other, how the number of cells grows, and how the morphology evolves and differentiates its shape.

5 CONCLUSION

We presented the concept of BOODLE, an interactive simulation framework for developmental biologists. It represents a Biologist-in-the-Loop simulation for the exploration of developmental processes. It features import and annotation of volumetric CT-data sets and morphometrically relevant data and automatic preprocessing necessary for real time model building, simulation, and optimisation. Data preparation is modelled closely along the workflow of developmental biologists, for example by using morphological landmark information. A genetic algorithm was used to optimise cell behaviour on annotated CT-data time series, allowing to successfully approximate tissue formation in limited areas.

The development of the user interface needs to be continuously evaluated and optimized with respects to usability and user experience, and specifically with egards to the target audience. Also, an in-depth analysis of the features of the physical cell model, especially its parameterisation, is needed.

As an important next step, we need to identify and adapt a rather generic but equally performant variant of an evolutionary algorithm. The evolutionary optimization we realized is still very limited in scope and capability. A more thorough and demanding experiment, making use of time series data of chick development, is planned to be performed as soon as we receive the corresponding data. It will emphasize the high dimensionality of the interacting factors and put the scalability of our system, in terms of voxel data handling, the simulated cell count, and the efficiency of the optimization algorithms to a test. The evolutionary algorithm may be adapted to an island model, improving the speed of optimization. Once the full processing loop for parametric optimisation based on genetic algorithms is set up, genetic programming techniques may help in more aptly capturing the complex facets of cellular behaviour.

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