Specification and Simulation of Multi-celled Behaviors

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***Short Abstract* — Recently the design and construction of synthetic multi-celled systems in *E. coli* and *S. cerevisiae* suggest that it may be possible to implement sophisticated distributed algorithms with these relatively simple organisms. Existing design frameworks for synthetic biology do not account for the unique morphologies of growing micro-colonies or the relationship between multi-celled systems and parallel algorithms. We introduce a framework for the specification and simulation of multi-celled behaviors that combines a simple simulation of micro-colony growth and molecular signaling with a new specification language called gro.**

***Keywords* — Multi-celled behaviors, specification language, pattern formation, synthetic biology, software tool.**

I. Introduction

THE ability to engineer complex, synthetic, multi-celled systems could revolutionize tissue engineering, biomass production, biosensing, and biodetection. Combining small genetic networks with cell-to-cell signaling has produced synthetic coupled oscillators [1], multi-cell logic [2], pattern formation [3], and population control [4]. These examples explore some of the basic mechanisms that synthetic biologists must harness to make further progress: environmental response, signaling, genetic network design, and control of growth and apoptosis.

Design tools developed for synthetic biology are generally focused on the behavior single genetic circuits, expressed using chemical reactions, enzyme kinetics, and gene network models [5]. Interactions induced by signaling and their effects on geometry have been examined in simulations of plant morphogenesis [6] which combine reaction-diffusion models with geometrical models of cell growth and division. However, such simulations are geared toward modeling existing systems, not designing new ones. Separately, research in computer networks, distributed systems, multi-robot systems, and stochastic self-organization has become quite advanced. The theoretical foundation for distributed systems [7] and parallel algorithms [8] has enabled new algorithms and also described the inherent limitations of distributed computation. However, most of the approaches in the distributed systems literature rely on various assumptions that do not hold in biological multi-celled systems.

Here we introduce a gro [9], a tool intended to assist in the design and exploration of possible of multi-celled behaviors that combines a distributed systems and parallel computing approach with biological modeling and simulation.

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II. Results

The gro simulation environment accounts for cell growth, division, noise, crowding, cell-cell forces, and the production, diffusion, and sensing of molecular signals. We illustrate how gro can be used to both model and specify systems via several examples: transcription and translation in a growing micro-colony; an edge detection behavior that uses diffusing molecular signals; a class of developmental programs that use finite state machines to determine micro-colony morphology; and a comparison of gro output with experimental data. Finally, we describe how gro can be used to model a system at several levels of abstraction, by specifying, modeling, and simulating a bacterial population control system in the literature [4] using an informal refinement process to increase the fidelity of the model.

III. Conclusion

gro allows researchers to explore the collective behaviors induced by high level descriptions of individual cell behaviors. Specifications written in gro can be refined to include increasingly detailed descriptions of their molecular implementations. Whether and how gro specifications can be implemented remains an open question; however gro is a useful design tool, simultaneously guiding the exploration of reliable multi-celled behaviors and their composition into increasingly complex multi-celled behaviors.

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