PDE Models of Adder Mechanisms in Cellular Proliferation

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***Abstract*— Cell division is a process that involves many biochemical steps and complex biophysical mechanisms. Here, we propose a unified adder-sizer models and investigate some of the properties of different adder processes arising in cellular proliferation. Based on our proposed new adder-sizer model, experimental findings such as a blowup behavior in average cell size are verified through numerical experiments, and we also show that generalizations of our model have the potential to explain and incorporate many experimental hypotheses of cellular division mechanisms.**

***Index Terms*— structured populations, adder-sizer model, PDE, cell size control, initiation adder**

I. Purpose

How cells regulate and maintain their sizes, as well as sizes of their appendages, is a longstanding research topic in cell biology. Besides the growth of an individual cell, the size distributions within a population of cells are also a quantity of interest. When considering proliferating cell populations, individual cell growth is interrupted by cell division events that generate smaller daughter cells. The biological mechanisms that control when and how a cell divides are complex and involve many steps such as metabolism, gene expression, protein production, DNA replication, chromosomal separation (for eukaryotic cells), and fission or cell wall formation [1], [2]. These processes are regulated and may involve intricate biochemical signaling.

To simplify the understanding of what triggers cell division, three basic models that subsume more microscopic cellular processes associated with cell division have been proposed. Cells can divide based on the time elapsed since their birth, their size, and/or the volume added since their birth—the timer, sizer, and adder models, respectively. Here, we propose a unified adder-sizer models and investigate some of the properties of different adder processes arising in cellular proliferation. Although the adder-sizer model provides a direct way to model cell population structure, we illustrate how it is mathematically related to the well-known model in which cell division depends on age and size. Existence and uniqueness of weak solutions to our 2+1-dimensional PDE model are proved, leading to the convergence of the discretized numerical solutions and allowing us to numerically compute the dynamics of cell population densities. We then generalize our PDE model to incorporate recent experimental findings of a system exhibiting mother-daughter correlations in cellular growth rates. Numerical experiments illustrating possible average cell volume blowup and the dynamical behavior of cell populations with mother-daughter correlated growth rates are carried out. Finally, motivated by new experimental findings, we extend our adder model cases where the controlling variable is the added size between DNA replication initiation points in the cell cycle.

II. Conclusion

We proposed a PDE model to describe population dynamical behavior under the adder division mechanism. Numerical studies of this PDE model were implemented to verify certain experimental findings such as a blowup in average cell size. Furthermore, our model could also incorporate some recent hypotheses of cellular growth and division mechanisms such as a correlation between daughter and mother cells' growth rates and a novel added-size-after-initiation (initiation adder) mechanism.

References

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