Genomic data-guided mathematical modeling of cancer

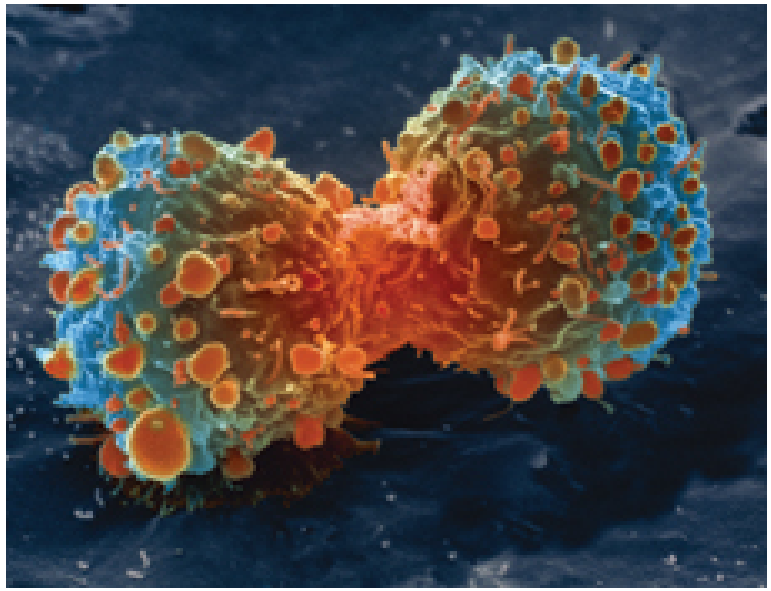
Andrew Brettin

University of Minnesota
DIMACS REU

June 4, 2018

Introduction

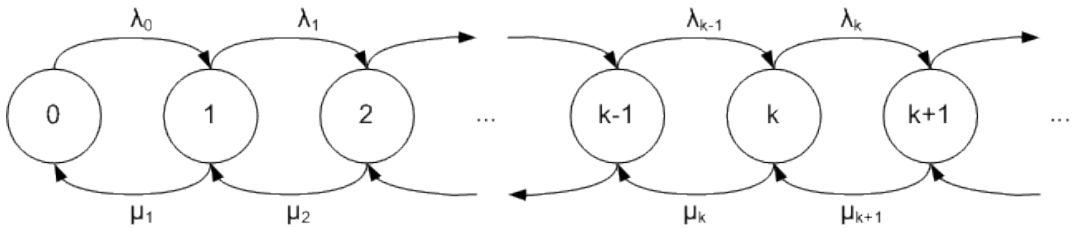
- Cancer is a type of disease characterized by abnormal and uncontrollable cell growth
- In the United States, cancer is the second leading cause of death, with around 40% of Americans developing cancer in their lifetimes [3]



Stochastic models of cell growth

Cell proliferation can be modeled as a *birth-death process*:

- Number of cells at any time is a nonnegative integer:



- Have some probability distribution which describes the next time when a cell will either divide or die
- Given the time until the next population change, compute whether the cell divides or dies

Example: Death process

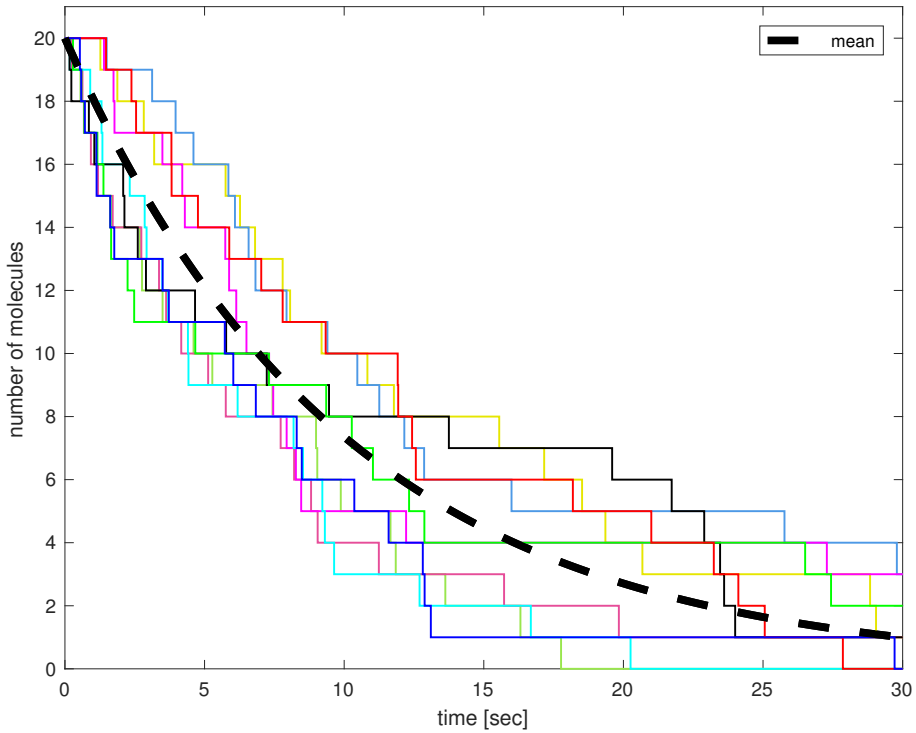


Figure: Ten stochastic simulations of a simple death process, with theoretical mean (dashed line). Simulated using code from Erban, Chapman, and Maini, available at `http://people.maths.ox.ac.uk/erban/Education/`.

Stochastic models of neoplastic growth

- Cells may divide normally, die, or acquire mutations at each time step
- If a cell acquires one mutation yielding a selective advantage, it becomes a *type-1 cell* and begins its own birth-death chain
- Type 1-cells have a selective advantage over type-0 cells, so have for instance a higher birth rate.

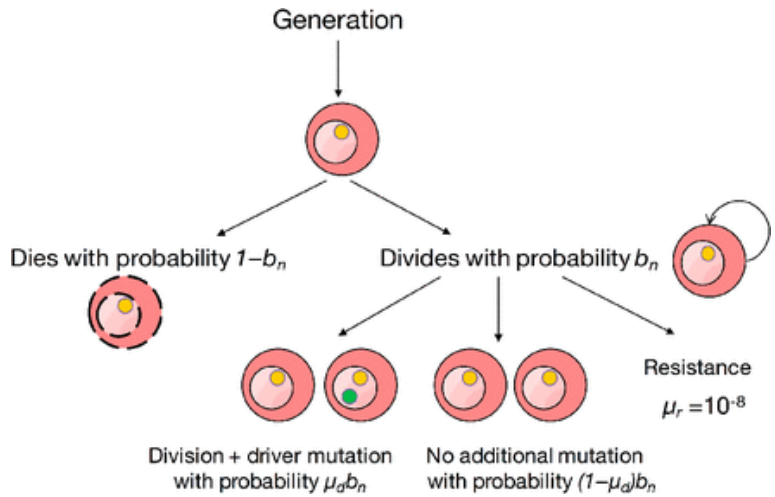


Figure: Diagram of cancer cell division. Taken from Chowell, et al's paper [1].

Objectives

Develop a mathematical framework incorporating spatial constraints for understanding neoplastic evolution.

Issues with current models:

- When cells divide, daughter cells may not inhabit the same space as parent cells
- Cells may grow faster on the outside of a tumor, where there is more room to grow
- Cells may migrate, or diffuse, towards regions of lower cell concentration

Acknowledgements

This research is conducted as part of a Research Experiences for Undergraduates (REU) program held at the Center for Discrete Mathematics and Theoretical Computer Science (DIMACS) and was funded by NSF grant CCF-1559855. Lazaros Gallos, Parker Hund, Peter Korcsok, and many others coordinated the REU program. Special thanks to Dr. Subhajyoti De for his mentorship and guidance.

References

[1] Diego Chowell, James Napier, Rohan Gupta, Karen S. Anderson, Carlo C. Maley, and Melissa A Wilson Sayres.
Modeling the subclonal evolution of cancer cell populations.
Cancer Research, 2017.

[2] R. Erban, J. Chapman, and P. Maini.
A practical guide to stochastic simulations of reaction-diffusion processes.
ArXiv e-prints, April 2007.

[3] American Cancer Society.
Cancer Facts & Figures 2018.