

CCBM Summer Internship Program (C-SIP)

Evolutionary Adaptation Depends on the Way a Biological Population Spreads Its Territory

Giancarlo Garcia Deleon, Madhuvanthi Athani, Daniel Beller, PhD
School of Natural Sciences, University of California, Merced

Introduction

Antimicrobial resistance is an immense problem for humans, and these problems exist in environments that are not always perfectly well mixed. The dynamics of evolving antibiotic resistance should be investigated in more realistic models of changing environments, such as in the human immune system. Simulations are used to model how evolution changes when the environment is varying spatially rather than temporally. The stepping-stone model is employed to model adaptations in bacterial range expansions in the presence of antibiotics. As the population encounters a higher concentration of antibiotics after growing some distance, the relative growth rates of the subpopulations change.

Summer Research Overview

Our investigation tests whether adaptive mutations are less prominent in spatially heterogeneous environments because it is much easier for populations to be lost to the front where all the growth of populations occurs. **Figure 1** is a microbial evolution and growth arena (MEGA) plate for studying microbial evolution in a spatially structured environment designed by Baym et al. We drew on the MEGA plate model as inspiration for our investigation.

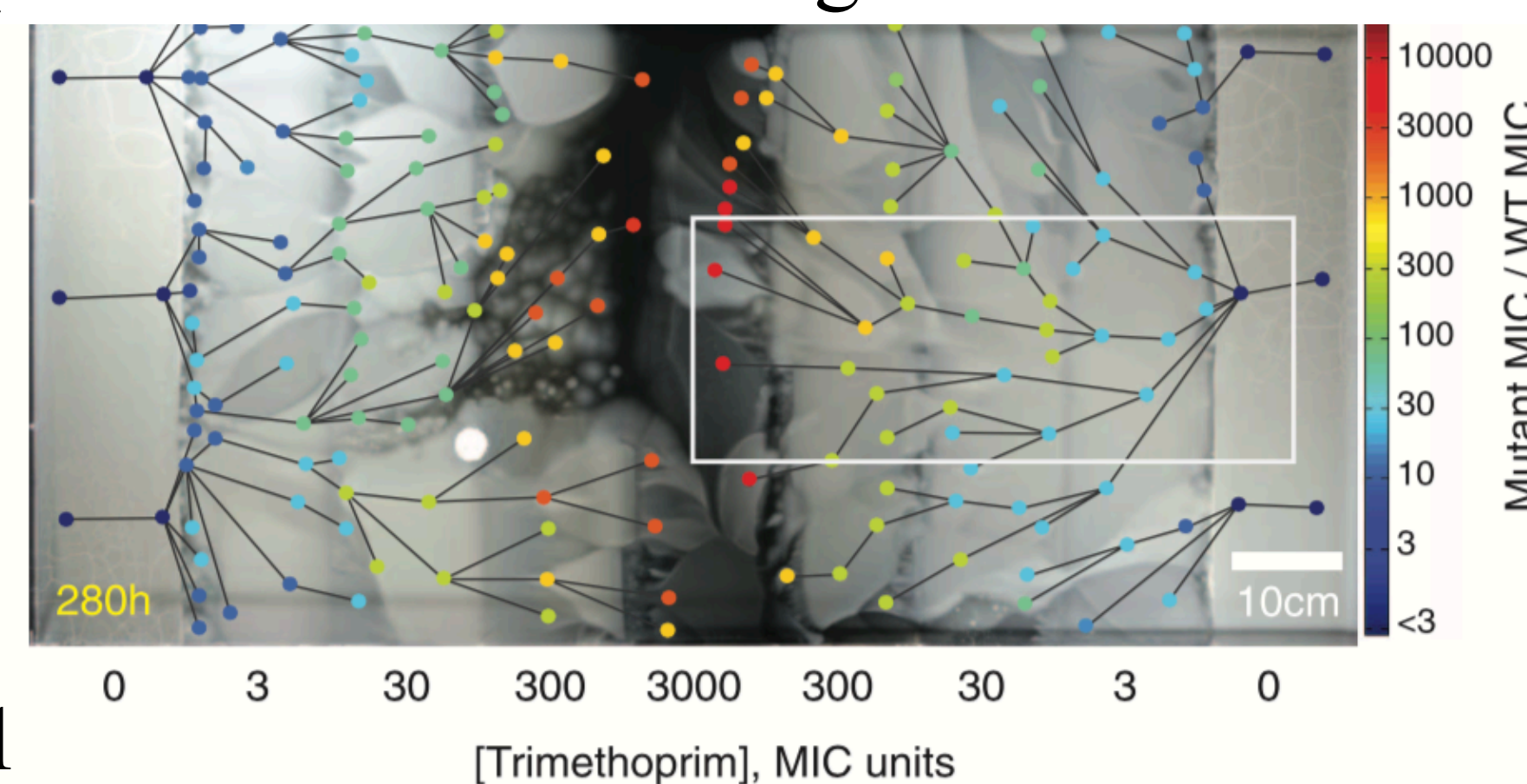


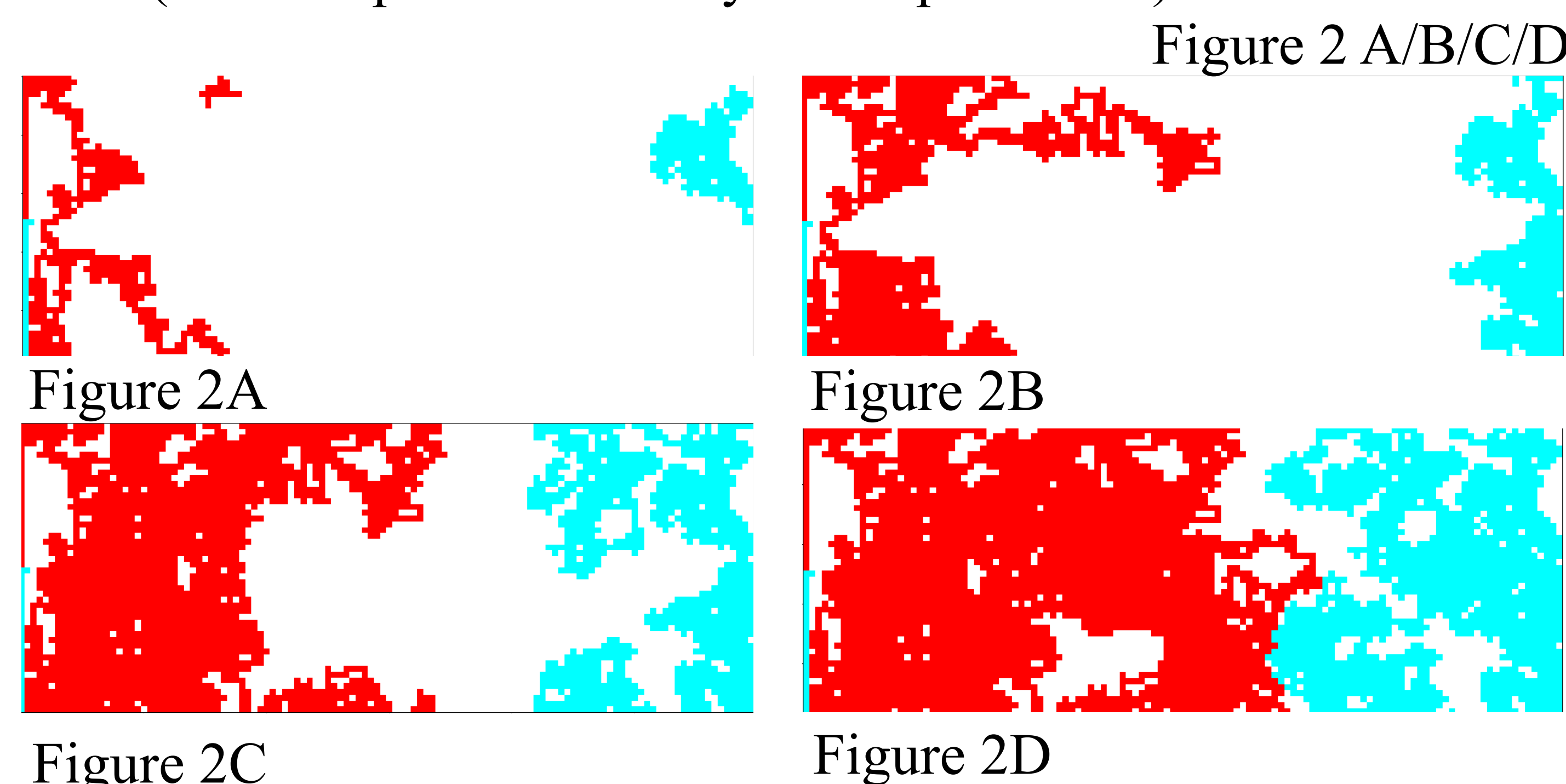
Figure 1

References

- Baym, M., Chait, R., Yelin, I., Gross, R., Kelsic, E. D., Kishony, R., & Lieberman, T. D. Spatiotemporal microbial evolution on antibiotic landscapes. *Science*, 353(6304), 1147–1151, (2016).
- Gillespie, Daniel T. Exact stochastic simulation of coupled chemical reactions. *The Journal of Physical Chemistry*, 81(25):2340–2361, (1977).

Methods/Results

Simulations written in C++ used the stepping stone model to simulate the duplication of the cells and ultimately, the filling of the environment given the spatial parameters. The simulation consisted of two microbial populations competing in a spatially varying environment when one population was selectively more advantageous than the other. Additionally, Gillespie's Algorithm of the generation of a statistically correct trajectory of a stochastic equation, allowed for the model of a much more adept use to simulate the creation of cells, and their birth rates are measured in fitness. **Figure 2** is an illustration of our simulation of two spatially spreading populations when the red population had a growth rate of two. (Red - Population 1 & Cyan - Population 2)



Observations indicate that adaptive mutations are typically less prominent in spatially varying environments because it is much easier for populations to be lost to the front (where all the growth of populations occur).

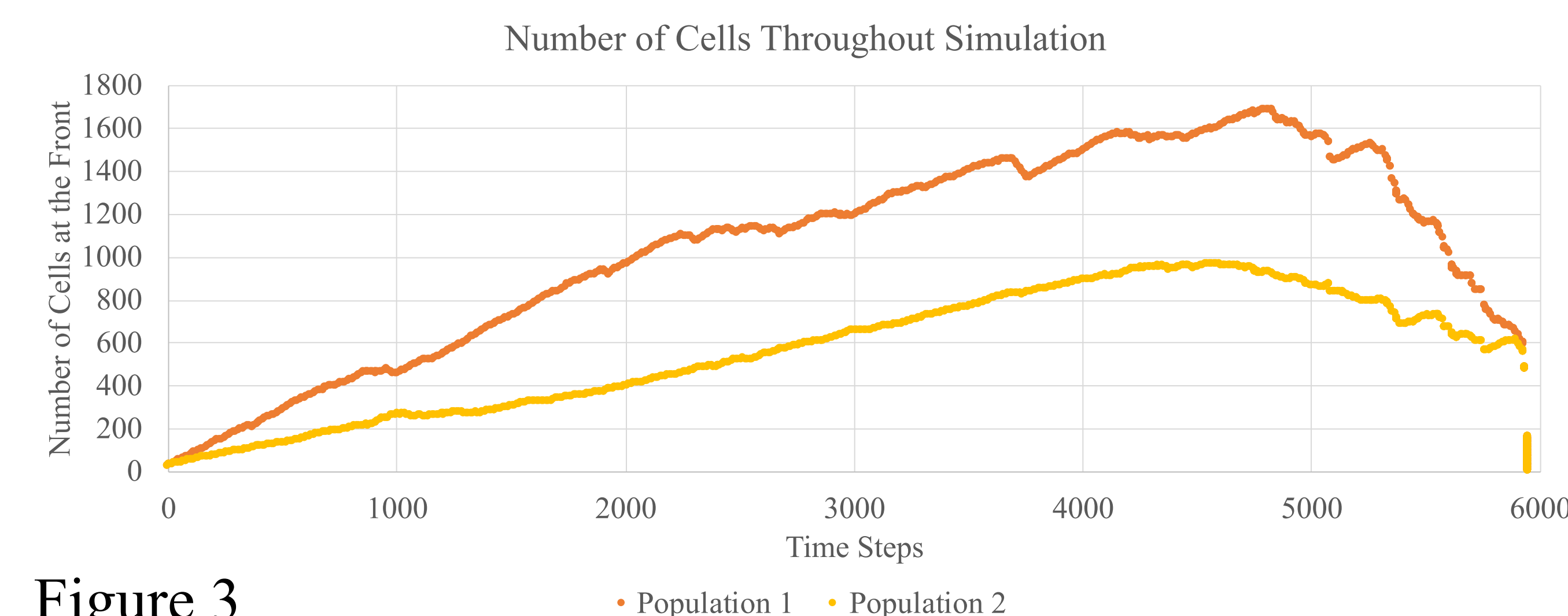


Figure 3

Figure 3 illustrates an instance where adaptive mutations are more more likely to be duplicated for the first 6000 times steps.

Discussion/Conclusion

In the presence of antibiotics, the resistant population, will be far more prominent than the other. However, if the fitter population is not in an antimicrobial environment, then the faster population is the non-resistant population because there is a metabolic cost to have the mutation. In this instance, non-resistant subpopulations would be far more prominent. Spatially heterogeneous environments are the cause for adaptive mutations to be less prominent since it is much easier for populations to be lost to the front, and since their growth rates are reduced.

Acknowledgements

The Science and Technology Enrichment Program (STEP) at the University of California, Merced is supported by NSF-CREST: Center for Cellular and Biomolecular Machines (CCBM) at the University of California, Merced (NSF-HRD-1547848).

The STEP program is managed and organized by the NSF-CREST Center for Cellular and Biomolecular Machines (CCBM) at the University of California, Merced: <http://ccbm.ucmerced.edu>

Future Work

Experiments can go back and quantitatively research an instance where a mutant grows slower than in general, but is antibiotic resistant. We hoped to introduce a well-mixed system in which heterogenous populations were spontaneously introduced into the system. Based on this work, future simulations can work on further investigating our question and design simulations with various concentrations of antibiotics.