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In Silico Evolution Dynamics of Quorum Sensing

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Introduction

Quorum sensing is the concept that bacteria in high densities exhibit behavior that is not seen in lower densities [4]. This behavior was first seen in bacteria in a mutualistic relationship with squid, where at high enough density in the pores of the squid, they will become bioluminescent, helping the squid avoid predation [1]. The dynamics of quorum sensing are well studied with many diving into the genetic and proteomic pathways involved [4]. The evolutionary dynamics have not been examined as extensively. Wang et al. modeled the evolutionary dynamics using thresholds [3]. However, some new research suggests a more graded response rather than strict thresholds [2].

Simulation of Bacteria

We adapted the simulation regime of Wang et al. to incorporate a graded response. The following describes the general logic of the simulation.

$$F_i = \overbrace{B_0}^{\text{Baseline Payoff}} + \underbrace{B_{coop}\sum_{N_j} I\left(N_j \cdot \underset{g\in G}{AVG}\left(Sn_g S_{N_j}\right) > N_{Th}\right)}_{\substack{\text{Benefit of cooperation}\\ \uparrow \text{average response} \Rightarrow \uparrow \text{benefit}}} - \underbrace{C_{coop}\sum_{N_j} Sn_i S_{N_j}}_{\substack{\text{Net Cooperation Impact}\\ \uparrow \text{response} \Rightarrow \uparrow \text{cost}}} - \overbrace{C_{sig}P_i}^{\text{Cost of Signaling}}$$

1. Initialize the population: 5000 individuals with the same initial sensitivity (Sn_i), production rate (p_i), and in auto-regulation, the auto-regulation ratio (r_i).
2. For ith individual, form the testing environment G. The size of G is generated from a zero truncated Poisson and is filled with random individuals including i.
3. Test each individual for fitness: for the ith individual evaluate the fitness, F_i, with respect to G.
4. Use the normalized fitness vector as a probability distribution to select the next generation of 5000 individuals.
5. Randomly select a subset of individuals to mutate p_i, Sn_i, and r_i based on a truncated normal distribution suited to each trait.
6. Repeat items 2 through 5 until the desired number of generations is reached.

Maximizing the Benefits of Cooperation

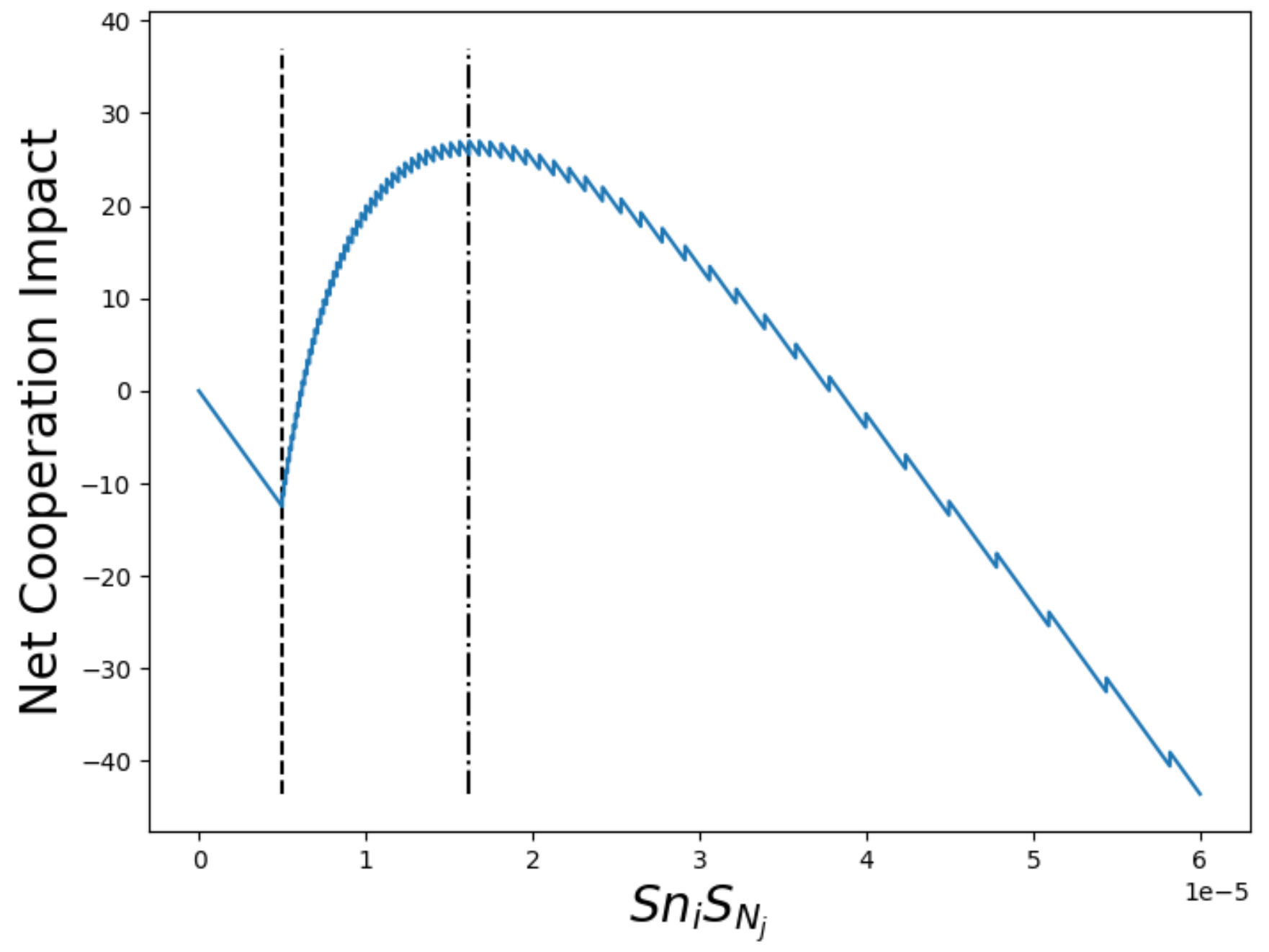

Figure 1. Net Cooperation over the response in the clonal case. Dashed black lines will represent the local minimum and dot-dashed lines will represent the relative maximum in future plots. This shows that there are two evolutionary outcomes: 1) Quorum sensing is stable and $Sn_iS_{N_j} \approx 1.620 \cdot 10^{-5}$, or 2) Quorum sensing is not stable and both Sn_i and S_{N_j} go to zero.

Without Auto-Regulation

Without auto-regulation, we get the following:

$$S_{N_j} = \underset{g\in G}{AVG}\left(\frac{p_g N_j}{u}\right) \qquad P_i = p_i$$

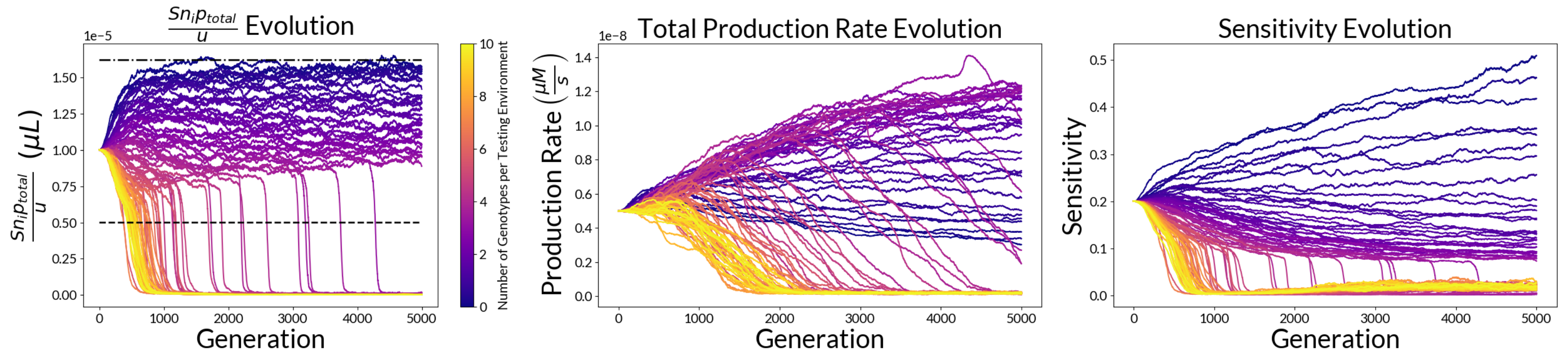

Figure 2. The results of the *in silico* evolution over 5000 generations at a variety of average genotypes per testing environment without auto-regulation.

Clonal Case

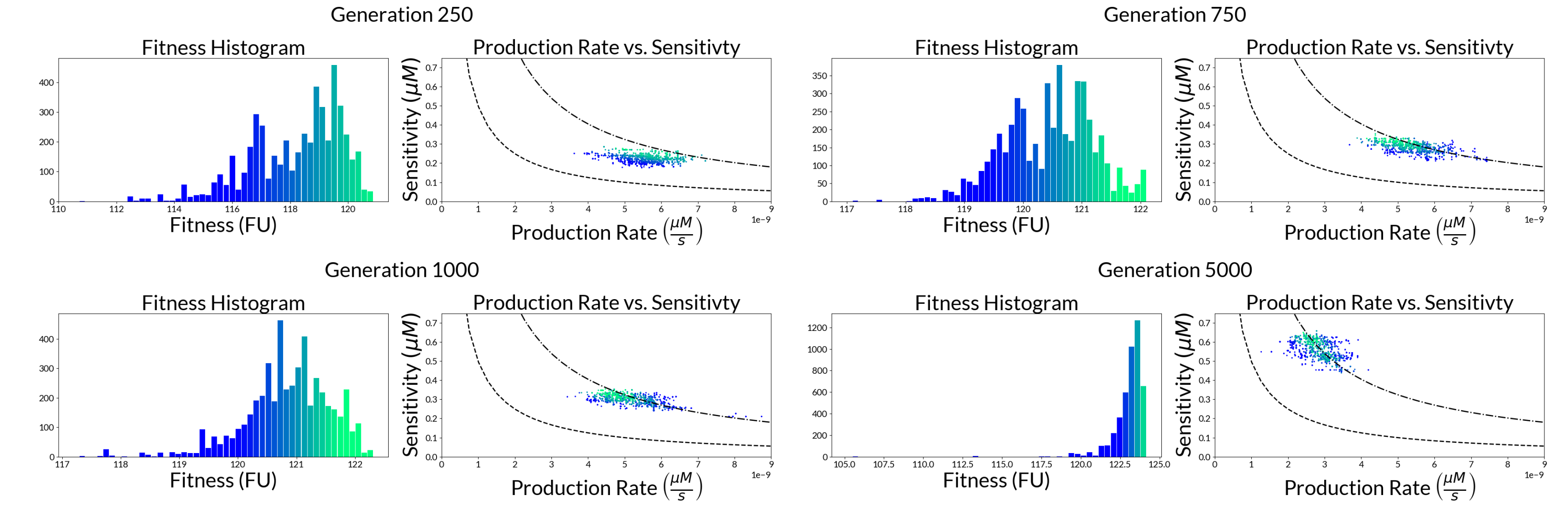

Figure 3. Fitness Histogram and Production Rate vs Sensitivity graph for generations 250, 750, 1000, 5000. In the clonal case, quorum sensing is a relatively stable outcome. In fact, the population can start below the dashed curve threshold and still achieve stable quorum sensing.

Average of 6 Genotypes

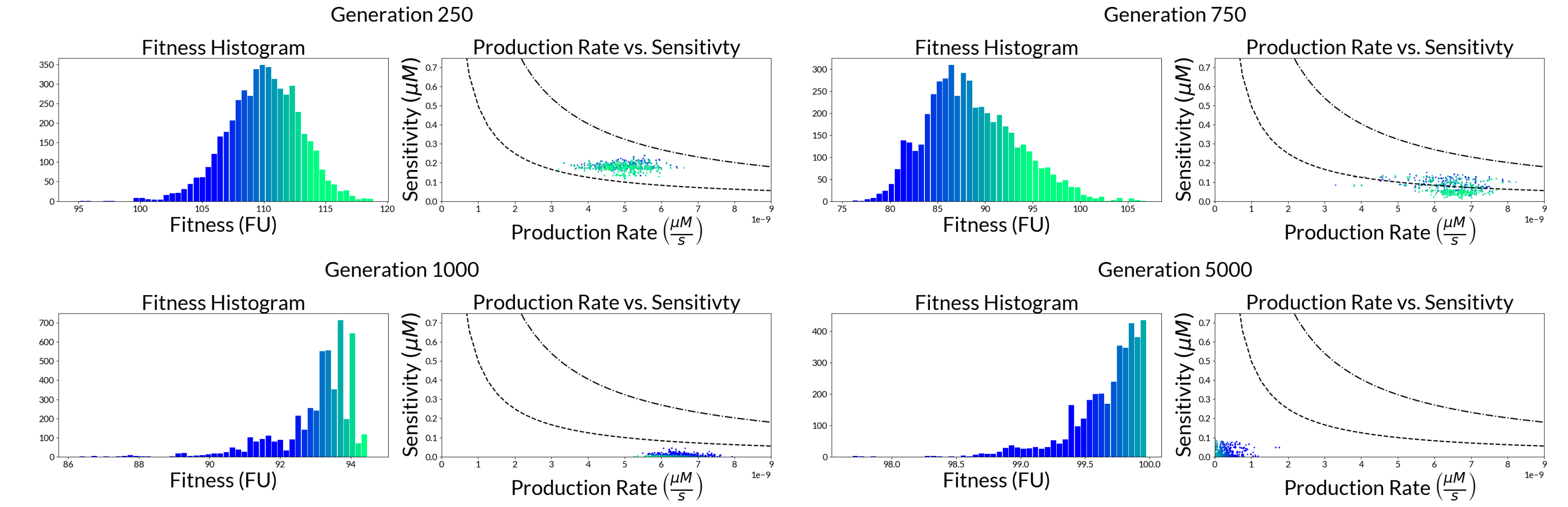

Figure 4. Fitness Histogram and Production Rate vs Sensitivity graph for generations 250, 750, 1000, 5000 for 6 average genotypes per testing environment. We can see that as soon as they average around the dashed line, they crash out as a few bacteria can lessen production while still getting some cooperation benefit from their neighbors, which will lead to no production.

With Auto-Regulation

With auto-regulation, we get the following:

$$S_{N_j} = \underset{g\in G}{AVG}\left(\frac{\sqrt{(Ku - N_jp_g(1+r_g))^2 + 4KN_jp_gu} - Ku + N_jp_g(1+r_g)}{2u}\right) \qquad P_i = p_i + \frac{r_ip_iS_{N_j}}{S_{N_j} + K}$$

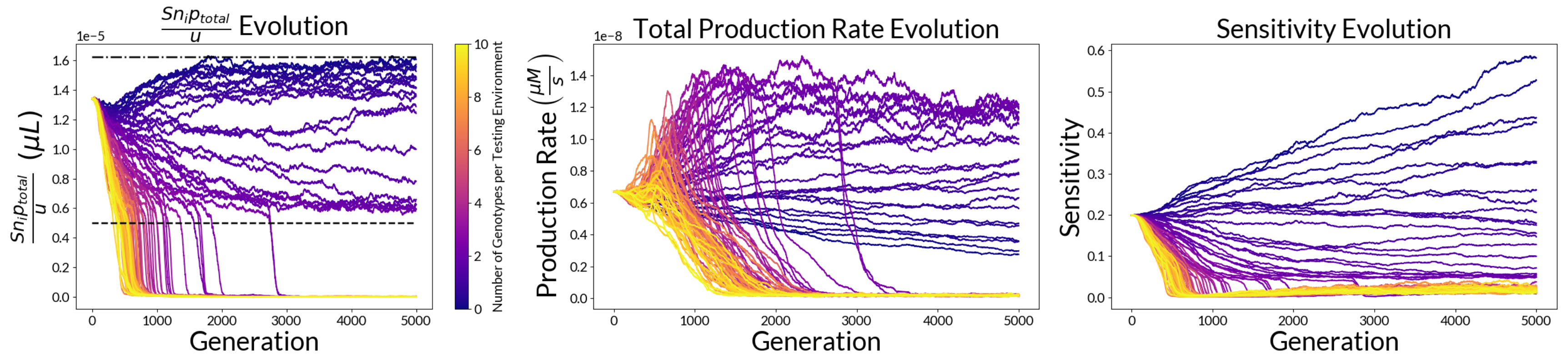

Figure 5. The results of the *in silico* evolution over 5000 generations at a variety of average genotypes per testing environment with auto-regulation.

Average of 3 Genotypes

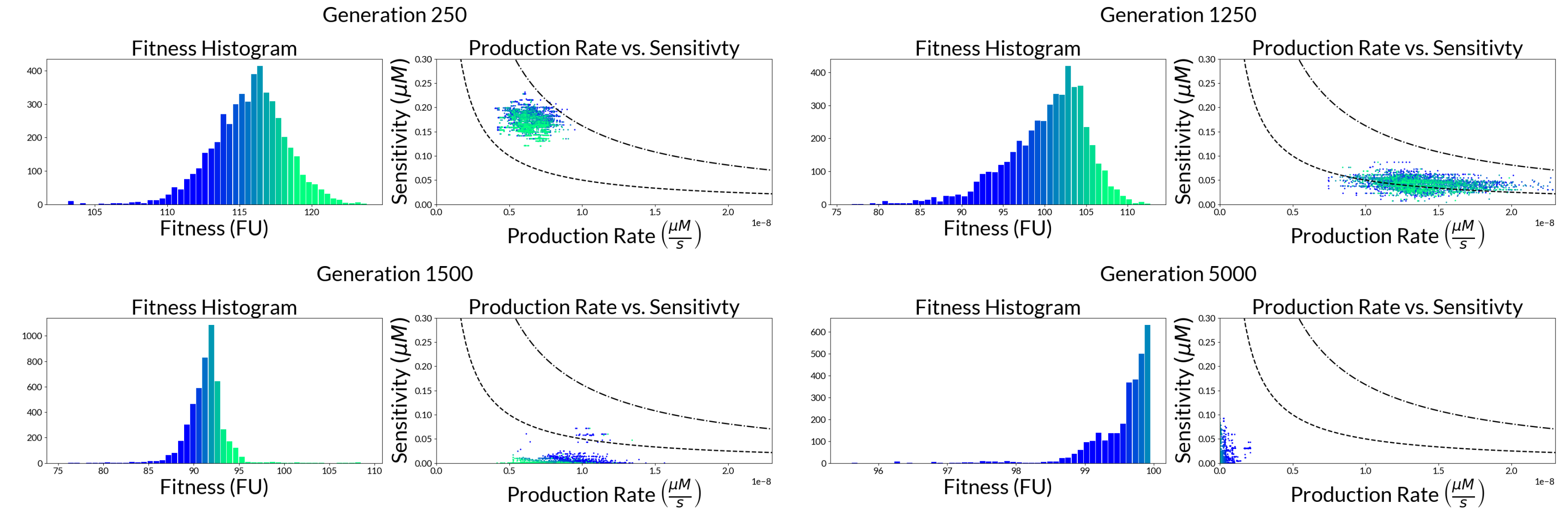

Figure 6. Fitness Histogram and Production Rate vs Sensitivity graph for generations 250, 1250, 1500, 5000 for 3 average genotypes per testing environment. The clonal case is similar to the clonal case without auto-regulation.

Conclusion

Overall, auto-regulation produces less stable communication in this regime than no auto-regulation. However, since we know that quorum sensing is a desired evolutionary outcome, it suggests that there are some other forces governing its evolution. Incorporating spatial dynamics and differing fitness assessments will provide more insight into the evolutionary dynamics. Early experiments, which examined the bacteria population rather than the individual, have yielded results closer to those found in Rattray et at. [2].

Acknowledgements/ References

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[2] J. B. Rattray, S. A. Thomas, Y. Wang, E. Molotkova, J. Gurney, J. J. Varga, and S. P. Brown. Bacterial quorum sensing allows graded and bimodal cellular responses to variations in population density. *mBio*, 13(3):e00745–22, 2022.

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Parameters and Default Values: walloch.xyz/parameters

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