Mathematical Modelling of Bacterial Resistance to Anti-microbial Treatment by Bet-hedging

By

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Introduction

Bet-hedging is a strategy whereby some physical fitness of a species will be reserved for later use when it suffers a decrease in the future.

The Method

In this research, we considered three different species of bacteria and two different environments, one with high amount of nutrients for their growth. The bacterial growth rate is giving as;

$$\beta\ (r\ ,\ \alpha) = 1 + re^{\frac{-r}{\alpha}}$$

r is the enzymes and α as the environment. The model equation for the bet-hedging based on the aforementioned is given by;

$$s_0' = s_0\ (\beta\ (r_0\ ,\ \alpha_t)\ -\ S)$$
$$s_1' = s_1\ (\beta\ (r_1\ ,\ \alpha_t)\ -\ \epsilon_1\ -S) +\ \epsilon_2 s_2$$
$$s_2' = s_2\ (\beta\ (r_2\ ,\ \alpha_t)\ -\ \epsilon_2\ -S) +\ \epsilon_1 s_1$$

where; $\mathrm{S} = s_0 + s_1 + s_2$,
$-s_0$ is the species that grows at a constant rate in any of the environments.
- s_1 and s_2 are effectively the same strain but can perform better or worse in different environments.
- ϵ_i is the transition rate from one species to different ones [1].

- Fluctuating environment:
  Due to some factors the environments fluctuates and the growth rate of the species fluctuates too, which is modeled by;

$$\beta\ (r\ ,\ \alpha) = 1\ +\ r\ e^{\frac{-r}{0.25*\sin(\omega t)\ +\ 1}}$$

- Adding treatment to the model:
  We include an antibiotic drug with the respective death rates of the species in our model as;

$$s_0' = s_0(\beta(r_0, \alpha_t) - S) - k_0 D s_0$$
$$s_1' = s_1(\beta(r_1, \alpha_t) - \epsilon_1 - S) + \epsilon_2 s_2 - k_1 D s_1$$
$$s_2' = s_2(\beta(r_2, \alpha_t) - \epsilon_2 - S) + \epsilon_1 s_1 - k_2 D s_2$$

where; $S = s_0 + s_1 + s_2$ as above,
D is the antibiotic drug,
k_i, as $i = 0, 1$ and 2 are the respective death rates of the species [2].

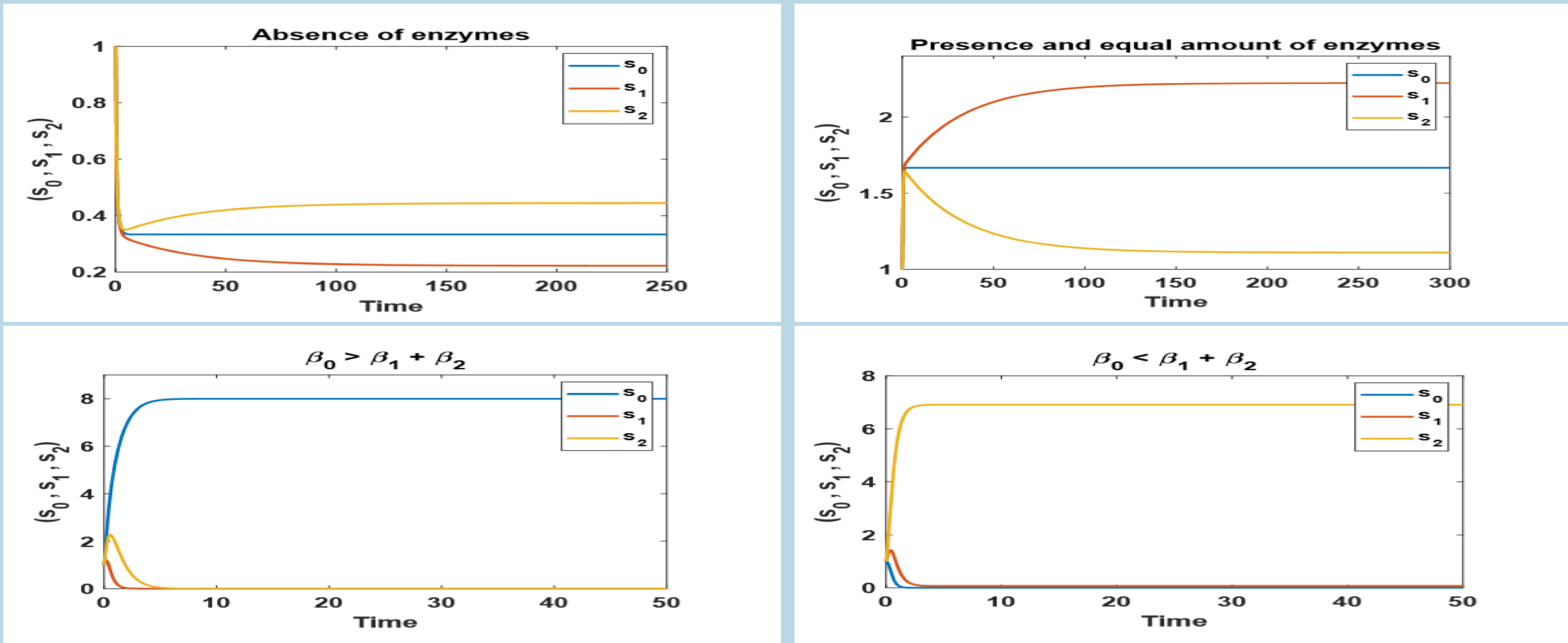
References

[1] Muller J., Hense B. A., Fuch T. M., Utz M., and Potzche Ch., 2013, " Bet-hedging in stochastically switching environments", Elsevier Journal of Theoretical Biology 336, pp 144 - 157.

[2] Ibarguen-Mondragon, E., Mosquera, S., Ceron, M., Burbano-Rosero, E. M., Hidalgo-Bonilla, S. P., Esteva, L., and Romero-Leiton, J. P., 2014, " Mathematical modelling on bacterial resistance to multiple antibiotics caused by spontaneous mutations," Elsevier Journal of Bio-Systems 117, pp 60 - 67.

Absence and presence of enzymes

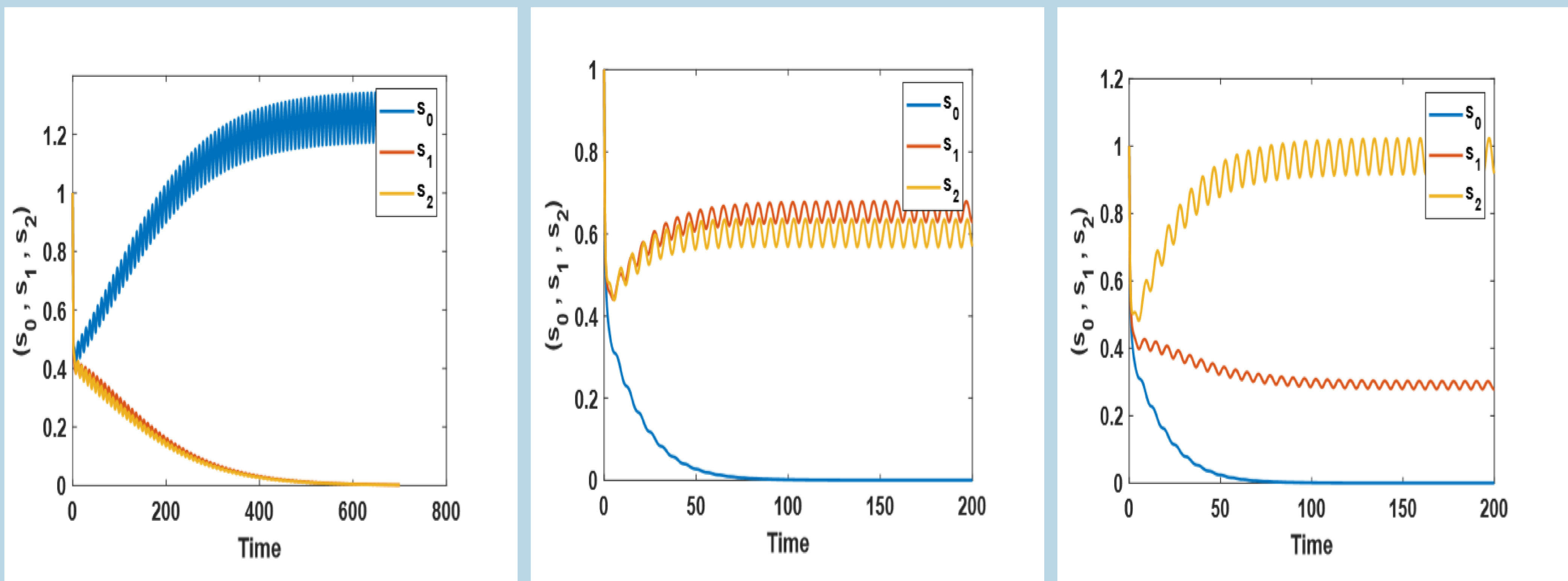
- Existence and extinction of some or all species were noticed for different parameter values.



The figures represent the simulations for the species lacking and possession of enzymes respectively.

Fluctuating environment

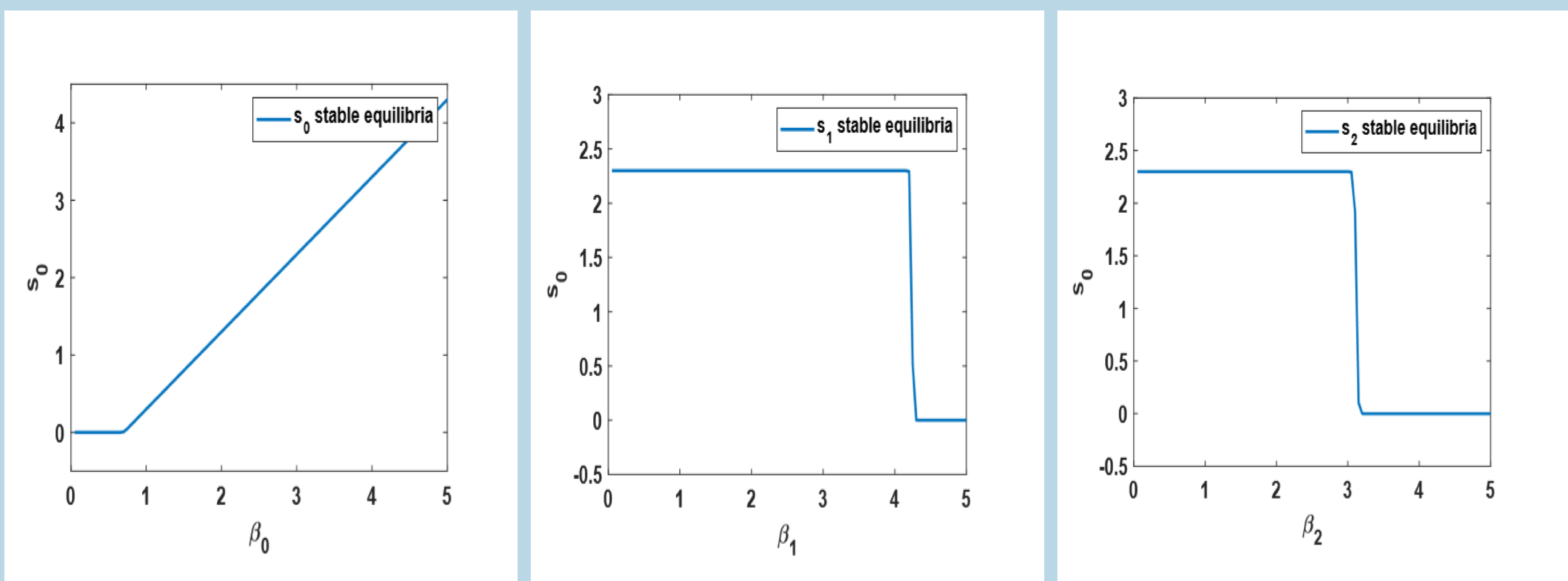
- Species with high level of competition for survival when the environments fluctuates.



The dynamics of the fluctuating environment with different values of enzymes and transition rates.

Adding treatment to the model

- The equilibrium density of each specie within it strain grow/survive and that of others extinct.



Bifurcation technique indicating the switching of stable equililibria with different parameter values.

Conclusion/Summary

- Coexistence of bet-hedgers and non-bet-hedgers is very unlikely.
- Bet-hedgers indicates/demonstrate a very high level of competition for survival in any environment.
- The species are likely very difficult to be eradicated completely by the antibiotic drug in any environment.