Project: Evolution of a non-lethal pathogen

In the lectures, we have studied the evolution of the infectivity of a pathogen. We have seen that spatial self-organisation strongly influences the evolutionary outcome. In the model in the lecture, we assumed that the pathogen caused a severe disease that was lethal: once infected, individuals could only die from the disease, they could not recover. This might be a good model for some infections (like Ebola), but fortunately many other infectious diseases don't lead to the death of infected hosts, but rather to recovered individuals that are immune for some time (think for instance of the flu). In this project, you will extend the SI-model (Susceptible-Infected) from the lecture to an SIR-model (Susceptible-Infected-Recovered). You will use this model to study how such recovery of infected individuals influences the spatial self-organisation of the system and the evolution of the pathogen.

The report of your project should be approximately 4 pages of text (excluding figures etc). To guide your project, below some questions are given for you to answer in the report. The report should however be a stand-alone document, meaning that readers can understand it without reading the assignment. The target audience are your classmates that did not do this project. Your report should have the following sections:

Introduction: Briefly describe the background of the project, your research question(s) and how you will tackle these questions.

Models: Describe the models used. If you want, you could integrate this section with the next to make one continuous story.

Results: Describe your results. You may also already provide some interpretation of your results here, to make clear why you take the next step in your analysis.

Conclusion and discussion: Summarise and explain your results. Link your results to observations from the course (SI-model) and from other studies (*i.e.*, last question below).

Deadline: Friday April 15th, 17:00.

As a starting point of your project, download the directory `SImodel`. This directory contains a Mesa version of the SI-model that was discussed in the lectures. In this model, evolution of the infectivity is deliberately left out. You will need to implement a different type of mutations for this project.

When we consider non-lethal infectious diseases, the spread of the disease usually occurs on a much faster time scale than the natural reproduction and death of the host. For instance, flu spreads through human populations within weeks, while the generation time of humans is approximately 25 years. This allows us to make a simplifying assumption:

- When considering the spread of a non-lethal infection, we ignore the natural reproduction and death dynamics of the host. Hosts are therefore only affected by the disease.

(a) Remove all non-infection dynamics from the SI-model. Then change the SI-model to an SIR-model by making the following assumptions:

- When an infected individual has been ill for `infection_duration` time steps, it does not die. Instead, it becomes "recovered" (new type of cell: R).
- Recovered individuals are immune to the infection for a fixed time `immunity_duration`. After that, they revert to the susceptible state.
- There are no empty cells, all cells represent individuals that are of type S, I or R.
- To avoid problems with extreme initial synchronisation of the infection, initialise the type I and R individuals at a random stage in their infection or immunity (i.e. some R individuals will lose their immunity quicker than others).

(b) Run the simulation for different values of `immunity_duration`: `immunity_duration` < `infection_duration`, `immunity_duration` = `infection_duration`, and `immunity_duration` > `infection_duration`. Make sure to run the simulations for a relatively long time, so you can truly study their dynamics. Describe your results. Do you see different patterns for the three cases? Can you explain these differences?

The duration of the infection is a property of the pathogen: because of its interactions with the host, it can either stay in the host for a long time or is quickly cleared by the host's immune system. We will now study the evolution of this infection duration, both in a non-spatial and in a spatial context. Note that evolutionary simulations take time! Make sure to let your computer run the model for sufficient time (you could for instance start writing your report while the code is running...).

(c) To study the system in a non-spatial context, derive the Mean-Field Approximation (MFA) of the spatial SIR-model. In your report, explain how you derived the MFA. To model the infection duration and immunity duration, use the following simplifying approach:

- Model the fixed infection duration T_{inf} with a probability of leaving the infectious state per time step: $p_{I\to R} = \frac{1}{T_{inf}}$. This keeps the average duration of infection

the same, although it does lead to more variation in the duration of infection.

(d) Simulate the dynamics of the MFA-model (see example code of the MFA of the predator-prey exercise). Compare your results to your results in the spatial model.

(e) Add a second type of infected individuals to the MFA-model, that are the same to the other I-type individuals except that they have a slightly longer infection duration ($T_{inf1} < T_{inf2}$). Assume that these new infections are caused by a mutant pathogen, that otherwise yields the same recovered individuals. Simulate the dynamics. Which pathogen wins the competition?

(f) Determine the *per capita* growth rate of the infection in the MFA-model. How does this depend on the infection duration? Does this agree with your competition experiment above? Predict which values of the infection duration will evolve in the MFA-model.

(g) Next, add mutations of the infection duration to the CA model. Study the evolution of the infection duration (If your computer can handle it, set the grid size to $150x150$ for more reliable results. Make sure to give evolution some time). Do you find the same results as in the MFA?

(h) Repeat your evolutionary experiment for several values of the disease infectivity. Plot the evolved infection duration vs the disease infectivity. What do you see? Can you explain this result?

(i) Read the paper by van Ballegooijen and Boerlijst [1]. Compare your results to the results presented in this paper.

Literature:

[1] van Ballegooijen and Boerlijst, Emergent trade-offs and selection for outbreak frequency in spatial epidemics, PNAS, 2004.