OVERVIEW, DESIGN CONCEPTS AND DETAILS (ODD) - Structured Habitat

The model description follows the Overview, Design concepts and Details protocol for describing individual and agent-based and other computation models (Grimm et al., 2006, 2010; Railsback and Grimm, 2019).

1. Purpose

The purpose of our model is to analyse if the cost experienced by transconjugant cells may be evolutionarily advantageous to donor cells and that plasmid transfer constitutes spiteful behaviour in a **structured habitat**. The model aims to identify the role of the frequency of plasmid donor bacteria relative to recipient bacteria, the conjugation rate, and the costs associated with the plasmid, in the ability of the donor bacteria to exert a harmful behaviour.

2. Entities, state variables and scales

The entities included in this model are **empty spaces** and bacteria.

The empty spaces are characterized by their coordinates.

Bacteria are characterized by: **coordinates**, type ([1-6]), plasmid fitness cost ([0, 0.05, 0.2, 0.2, 0.4, 0.6]), adaptation period [(70, 400)], **local neighbourhood, and nutrient neighbourhood**.

The coordinates represent the location of each bacterium in a grid of 1000 x 1000 sites with periodic boundaries - that is, the upper margin is linked to the lower margin, and the left margin is linked to the right margin.

The parameter type defines whether the bacterium is recipient (1), donor (2), transconjugant (3), adapted transconjugant that lost the plasmid (4), non-adapted transconjugant that lost the plasmid (5), or donor that lost the plasmid (6).

The plasmid fitness cost is the cost associated with the presence of the plasmid. Transconjugant cells pay a fitness cost for some generations, after which the cost ameliorates to the same value as that of the original donor cells.

The adaptation period is the number of generations during which the conjugants pay the fitness cost.

The local neighbourhood is defined by the 3x3 squares centred on a focal bacterium, and represents the places where it can duplicate and the available neighbours for conjugation.
The nutrient neighbourhood is defined by the 7x7 squares centred on the focal bacterium, and allows estimating the available nutrients (C) for that bacterium. The C value is also the proportion of empty spaces in the nutrient neighbourhood.

In this model, a time step corresponds to a possibility for a bacterium to duplicate and/or conjugate (in case it has a plasmid).
Having our grid 1000x1000 sites in which each site can have a single cell, assuming the average size of a cell is 1 μm^2, the lattice size corresponds to an area of approximately 1 mm^2.

3. Process overview and scheduling

In each simulation cycle of the structured habitat**, a location on the grid containing a bacterium** is randomly chosen to verify whether the "bacterial_growth" submodel is performed. If the bacterium has a plasmid, it is verified if the submodel "conjugation" is performed.

If the “bacterial_growth” submodel is activated, **an empty space is updated to a bacterium**, with the corresponding characteristics of the originating bacterium. If the “conjugation” submodel is activated, the characteristics of the bacterium receiving the plasmid are updated accordingly. At the end of each time step**, it is checked whether the number of bacteria present in the grid is at least 95% of the total capacity (950,000 bacteria)**. If this condition is met, the number of each type of bacteria present is stored in a variable, and then bacteria are randomly eliminated so that **only 50% of the grid is filled.**

This process is repeated **until the grid has reached its maximum capacity** 1073 times. After that, the data with the number of each type of bacteria at each time is written to a .csv-file in the submodel “files_writing”.

4. Design concepts

We took the following design concepts into account:

Basic principles**.** This model is derived from the model developed by Krone et al. (2007). However, we consider that the grid can reach the total capacity several times, and each time this happens, we simulate a serial dilution with 47% of the population dying. Furthermore, we added a segregation rate to the bacterial_growth submodel. To be conservative, we used the highest value described in the literature (10^-3) (Lau et al., 2013; Loftie-Eaton et al., 2017).

Emergence**. The growth of each bacterium depends on the type of bacteria in the nutrient neighbourhood and their interactions. Therefore, the final result of the ratio of original plasmid donor bacteria to the remaining bacteria will depend on this growth as well as on the conjugation rate values.**

Adaptation**.** The bacteria grow **to a new randomly selected position within the available ones**, according to the percentage of empty spaces **in the nutrient neighbourhood**. Transconjugant bacteria have a decrease in the plasmid cost based on the number of duplications.

Interaction**.** Plasmid donor cells interact directly with plasmid recipient cells and can transfer the plasmid to them. This action directly imposes a fitness cost on the plasmid-receiving bacterium. **This only happens when the bacteria are in the same neighbourhood.** On the other hand, the model contemplates mediated interactions since bacteria interact with each other, competing for available nutrients during growth.

Stochasticity**. The model is initialised stochastically in such a way that the bacteria are distributed over the grid with their coordinates randomly obtained from a range between 0 and 1000 (grid edge). This means that from simulation to simulation the interactions between the different types of bacteria are different.** In addition, the bacterium to be analysed in each cycle of the programme is chosen randomly from the currently existing bacteria, to make the model asynchronous. Stochasticity is also used to impose variability in bacterial growth, segregation and conjugation (see the "bacterial_growth" and "conjugation" submodels, below). Finally, the bacteria that are eliminated whenever the grid reaches its maximum capacity are also chosen randomly, so that each bacterium has the same probability of dying.

Observation**.** Cell density of each type of bacteria, whenever the grid reaches its maximum capacity, is the observation of this model.

5. Initialisation

The “bacteria_distribution” submodel **initially distributes plasmid donor and recipient bacteria randomly across the grid**. **This distribution is done** according to the number of donor cells [10, 99, 5000, 9901] and the number of recipient cells [9990, 9901, 5000, 99]. In this way, the initial cell number is always 10 000 cells.

In the submodel “bacteria_distribution”, each of the bacteria is assigned inherent characteristics, namely: **coordinates, type, plasmid fitness cost, adaptation period, local neighbourhood, and nutrient neighbourhood.**

6. Input data

There is no external input of data.

7. Submodels

Table 1 – Model parameters.		
Entities	**Parameter range**	**Description**
grid_edge	**1000 [constant]**	**Size of x and y-dimension**
maximum_proportion_full_grid	**0.95 [constant]**	**Maximum proportion of bacteria that the grid can contain**
remaining_proportion_grid	**0.5 [constant]**	**Proportion of bacteria remaining in the grid when bacteria are randomly removed when the grid reaches 95% capacity**
number_plasmid_free_bacteria	9990, 9901, 5000, 99	Initial number of bacteria not carrying plasmid
donor_bacteria	10, 99, 5000, 9901	Initial number of bacteria that carry plasmid
maximum_growth_rate (ψ^{max})	1 [constant]	Maximum bacterial growth rate
maximum_conjugation_rate (γ^{max})	1 [constant]	Maximum bacterial conjugation rate
theta (θ)	0.6, 0.8, 1	Value of theta (bacterial growth)
theta_1 (θ_1)	0.2 [constant]	Value of theta 1 (conjugation)
theta_2 (θ_2)	0.3 [constant]	Value of theta 2 (conjugation)
initial_plasmid_cost	0.2, 0.4, 0.6	Cost that bacterium have when receiving the plasmid
permanent_plasmid_cost	0, 0.05, 0.1	Cost associated with the presence of the plasmid in donors and adapted transconjugants
adaptation_time	70, 400	Number of duplications that bacteria need until the initial plasmid cost changes to permanent plasmid cost

segregation_probability	0.001	Probability of a bacterium losing the plasmid at the moment of its duplication

Bacterial_growth

Following Krone et al. (2017), bacterial growth depends on the existence of an empty space in the local neighbourhood and on the growth rate (ψ). Therefore, for each selected bacterium, we obtain the growth probability according to the following function:

$$\psi(C) = \begin{cases} \psi^{max}, if\ C \geq \theta \\ \psi^{max}\ \frac{C}{\theta}, if\ 0 \leq C < \theta \end{cases}$$

Note that ψ^{max} = 1 for plasmid-free cells and that ψ^{max} = 1 – *cost* for plasmid donor cells, with "*cost*" being the plasmid cost (note that, in our model, the fitness cost differs between bacteria and can even evolve). **The C value is the proportion of empty spaces in the nutrient neighbourhood.**

If a random number is equal to or less than the growth rate, we check for empty spaces in the local neighbourhood. If there is at least one empty space, that space is updated to contain a bacterium. If the original bacterium has plasmid, and if a random number is less than the segregation probability, the resulting bacterium will have no plasmid, retaining the remaining characteristics of the original bacterium. Otherwise, the new bacterium will have all the characteristics of the original bacterium. If it is an unadapted bacterium, the adaptation time of the original bacterium and the new bacterium will decrease by one. If the adaptation time is zero, the plasmid cost of both bacteria is updated to the permanent cost.

Conjugation

Following Krone et al. (2017), conjugation depends on the existence of a plasmid-free bacterium in the local neighbourhood and the conjugation rate (γ). Therefore, for each plasmid carrying bacterium selected, we check if there is a plasmid-free bacterium in the local neighbourhood. If there is, we obtain the conjugation rate according to the following function:

$$\gamma(\mathrm{C}) = \begin{cases} \gamma^{max}, & if\ C \geq\ \theta_2 \\ \gamma^{max}\ \dfrac{C-\theta_1}{\theta_2-\theta_1} & ,if\ \theta_1 \leq C < \theta_2 \\ 0, & if\ C < \theta_1 \end{cases}$$

If a random number is equal to or less than the conjugation rate, the characteristics bacterial type, plasmid cost and adaptation time are updated in the plasmid-free bacterium. Note that, a segregant bacterium may have become segregant due to: (i) a donor bacterium that lost the plasmid; (ii) an adapted transconjugant bacterium that lost the plasmid; or (iii) an unadapted transconjugant bacterium that lost the plasmid. Thus, if the plasmid-free bacterium is segregant, when it receives the plasmid, it will have the same characteristics as the originating bacterium.