OVERVIEW, DESIGN CONCEPTS AND DETAILS (ODD) – Unstructured 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 an **unstructured 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 bacteria.

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

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.

In this model, a time step corresponds to a possibility for a bacterium to duplicate and/or conjugate (in case it has a plasmid).

3. Process overview and scheduling

In each simulation cycle of the unstructured habitat, **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, **is added a new 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 is at least 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 bacteria remains.**

This process is repeated 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 results emerge from the relationship between the values of the conjugation rate and the values of the plasmid cost.**

Adaptation**.** The bacteria grow randomly according to the percentage of **total empty spaces**. 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 a donor bacterium meets a recipient bacterium.** On the other hand, the model contemplates mediated interactions since bacteria interact with each other, competing for available nutrients during growth.

Stochasticity**.** The bacterium to be analysed in each cycle of the program 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 **creates the initial bacterial lists** 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: **type, plasmid fitness cost, and adaptation period.**

6. Input data

There is no external input of data.

7. Submodels

Table 1 – Model parameters.		
Entities	**Parameter range**	**Description**
maximum_number_bacteria	**950 000 [constant]**	**Maximum number of bacteria**
remaining_proportion_bacteria	**0.5 [constant]**	**Proportion of bacteria remaining when bacteria are randomly removed**
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

Bacterial growth depends 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 $\psi^{max} = 1$ for plasmid-free cells and that $\psi^{max} = 1 - cost$ 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 existing bacteria over the maximum capacity (1 000 000).**

If a random number is equal to or less than the growth rate, we add a new 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

Conjugation depends on the encounter probability and the conjugation rate (γ). Therefore, for each plasmid carrying bacterium selected, we check the encounter

probability given by: PBC/N*PFC/N, where PBC is plasmid-bearing cell, PFC is plasmid-free cell, and N is the total number of cells in the system. If a random number is less or equal to the encounter probability, 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. **Once again, the C value is the proportion of existing bacteria over the maximum capacity (1 000 000).**