Notes on the simple non spatial model

A consumer-resource model for the simulation of well-mixed communities dynamics

1. Introduction

The model is intended to perform simulations of the dynamics of microbial communities in a well-mixed setting. The focus is on interactions between different species, which are mediated by the exchange of chemicals.

2. Mathematical model

The model includes both positive and negative interactions, and couples the dynamic of chemicals to the one of populations through the conversion of chemicals absorption into energy, and through the modulation effect that net energy fluxes have on the growth rate of species.

2.1. Assumptions

- Energy is (locally) conserved
- Populations shrink and grow as an effect of the net energy fluxes
- Energy fluxes represent interactions between species
- The interaction between species is mediated by chemicals they exchange, which are characterized by an intrinsic energy contribution
- Species consume chemicals produced by others or themselves
- Chemicals production by a species is a result of metabolic processes that depend on the type of chemicals consumed: if metabolism of chemical A results in the production of chemical B, then all species consuming chemical A should produce chemical B
- There are two different types of chemicals, that have respectively a positive and negative contribution to the net energy flux available to populations: nutrients and toxins
- Nutrients and toxins can either follow the same dynamics, or different ones (user's choiche)
- Chemicals' dynamics is much faster than population dynamics
- Chemicals can be replenished from the outside
- Chemicals and populations can be diluted from the outside

2.2. Species dynamics

$$\frac{dN_i}{dt} = g_i N_i \left[\sum_\alpha E_\alpha^{in} - \sum_t E_t^{out} - M_i - \frac{1}{\tau_{dil}} \right] \tag{1}$$

In equation 1 the basal growth rate g_i of species i is modulate by uptake of nutrients and toxins. Energy for growth is supplied by nutrients E_α^{in} and withdrawn by toxins E_t^{out}; the term M_i accounts for the maintenance energy of the species. If the term in the square brackets is greater than 1 (i.e. the energy absorbed from nutrients is greater than the maintenance and toxins withdrawal) the basal growth rate in enhanced.

- $\mathbf{M_i}$ is an intrinsic parameter of species i
- $\mathbf{g_i}$ is an intrinsic parameter of species i
- $\mathbf{E_\alpha^{in}} = (\mathbf{1} - \mathbf{l}_\alpha)\mathbf{w}_\alpha \sigma(\mathbf{u_{i,\alpha}} \mathbf{R}_\alpha) = (\mathbf{1} - \mathbf{l}_\alpha)\mathbf{w}_\alpha \frac{\mathbf{u_{i\alpha}} \mathbf{R}_\alpha}{\mathbf{1} + \frac{\mathbf{u_{i\alpha}} \mathbf{R}_\alpha}{\sigma_{\mathbf{max}}}}$ is the up-taken energy available to use for growth, given by the product of a conversion factor w_α (converts nutrient quantity in energy) and the up-take function, of Monod form; σ_{max} can be related to the usual K_{max} parameter of the Monod function trough $K_{max_{i,\alpha}} = \frac{\sigma_{max}}{u_{i,\alpha}}$ and it is a parameter accounting for the steepness of the uptake curve; $u_{i,\alpha}$ is the uptake rate of species i for nutrient α, and R_α its abundance in the well-mixed environment [2]; l_α is the fraction of up-taken energy used for metabolism and not growth (local energy conservation implies that $(1 - l_\alpha)$ fraction is used for growth)
- $\mathbf{E_t^{out}} = \tilde{\mathbf{u}}_{\mathbf{i,t}} \frac{\mathbf{R_t}}{\mathbf{K_t}}$ is the energy withdrawal caused by toxins, and it depends again on the uptake rate of species i for toxin t, on the toxin concentration R_t and on the toxin-intrinsic parameter K_t that governs how strongly uptake depends on concentration [1]
- $\frac{\mathbf{1}}{\tau_{\mathbf{dil}}}$ is the term governing how often the well-mixed solution gets diluted

2.3. Chemicals dynamics option 1

All chemicals follow the same dynamics, regardless of their nature, and their concentration results form the combined effects of external reinsertion, uptake by individuals and production by individuals, where production of a chemical depends on both the number of individuals producing it and on the allocation strategy that the individual follows. (Add second option which follows the same rules of the first one for nutrients, but toxin production is independent from the metabolic allocation of the species, but is rather only influenced by the number of individuals that produce it.)

$$\frac{dR_c}{dt} = e(R_c) - \sum_i N_i \sigma(u_{i,c} R_c) - \frac{1}{\tau_{dil}} R_c + \sum_{i,c'} N_i \frac{\sigma(u_{i,c'} R_{c'})}{w_c} \left[D_{c,c'} w_{c'} l_{c'} \right] \tag{2}$$

In equation 2 the dynamics of chemicals abundance is determined by the external reinsertion, the consumption by individuals, and the production, mediated by the metabolic allocations.

- $\mathbf{e}(\mathbf{R_c}) = \frac{\mathbf{1}}{\tau_{\mathbf{c}}} (\mathbf{R_c} - \mathbf{R_c^0})$ is the external reinsertion of chemical c, and depend on the fixable parameter τ_c, which accounts for temporal delays in the reinsertion compared to the timescale of the chemicals dynamics (i.e. $\tau = 1$ corresponds to bringing the chemicals back to the initial concentration at every step)

- the second term describes depletion of the chemical caused by uptake from the individuals
- $\sum_{\mathbf{c'}} \mathbf{N_i}\sigma(\mathbf{u_{i,c'}R_{c'}})\left[\mathbf{D_{c,c'}}\frac{\mathbf{w_{c'}}}{\mathbf{w_c}}\mathbf{l_{c'}}\right]$ is the term describing the production of toxins: $\sigma(u_{i,c'})w_{c'}l_{c'}$ returns the amount of up-taken c' that is used for metabolism by individuals of species i, converted into energy by multiplication by $w_{c'}$, this is then multiplied by the matrix element $D_{c,c'}$, which describes how much of this energy is allocated for the production of c, finally re-converted in energy flux dividing by w_c; the effect is summed over all c' such that their metabolism yields c
- $\frac{\mathbf{1}}{\tau_{\mathbf{dil}}}$ is the term governing how often the well-mixed solution gets diluted

2.4. Chemicals dynamics option 2

In this second option, the dynamics presented in the previous paragraph is used for nutrients, but toxins production is decoupled from metabolism to only depend on the number of present individuals producing them and on the rate of production.

$$\frac{dT_\alpha}{dt} = -\sum_i N_i\sigma(u_{i,\alpha}R_\alpha) - \frac{1}{\tau_{dil}}R_\alpha + \sum_i \frac{N_i p_{i,\alpha}}{1+N_i p_{i,\alpha}} \quad (3)$$

- $\sum_{\mathbf{i}} \frac{\mathbf{N_i p_{i,\alpha}}}{\mathbf{1+N_i p_{i,\alpha}}}$ is the term accounting for toxins production, depends on the number of producers N_i and on the production rate $p_{i,\alpha}$ and has a saturating form

3. Workflow

We start with the definition of two networks, where nodes represent species and edges represent the chemical-mediated interactions (facilitation for the first network and inhibition for the second). From these, two matrices are created: the consumer preference matrix, with species as rows, nutrients as columns and uptake rates $u_{i,\alpha}$ as entries; and the inhibition matrix, with species as rows, toxins as columns, and the uptake rates $\tilde{u}_{i,t}$ as entries. From this, the combined matrix with species as rows and all chemicals as column is also created. Then the metabolic matrix is created, with all the chemicals on both rows and columns, and the $D_{c,c'}$ allocation rates as entries; this matrix is created by looking at the combined facilitation and inhibition network, and assigning a random value between 0 and 1 to entry c, c' if there exists, in the combined network, a node such that an incoming edge is labeled c' and an outgoing edge is labeled c; the columns are then normalized to sum to 1, meaning that the energy available for metabolism after the consumption of c' is allocated to the different products that metabolism of c' yields (again follows from local energy conservation). After assigning fixed parameters and initial state, a choice between to possible chemicals dynamics is made and the model is run by looking for the steady state of the chemicals dynamics (by direct solution and not by integration), and using these equilibrium concentrations to integrate one step of the population dynamics; the two steps are repeated until the population stabilizes. Solving for the chemicals steady state follows from the assumption that chemicals and populations evolve on two very different time scales, the first reaching equilibrium much faster than the second.

3.1. A note on external carbon sources

Given how the workflow is set up, external carbon sources can be included in the networks by adding a species with only outgoing edges, connecting it to the other nodes that are meant to consume the resource and with basal growth rate equal to 0. The only parameter concerning such species that will have an influence on the dynamics will therefore be the initial amount of resource that it produces, the initial number of individuals not playing any role on the simulation.

4. Modules organization

The model is written in python over different interdependent modules, structured in the following way:

- **__init__.py** is the main file, where all other modules are imported and the simulations can be run, here a network is chosen from the ones defined in the **specifications.py** file; if one prefers to start from the matrices instead of the networks, pre-created matrices can be loaded in this step, otherwise they are created from the selected network; after defining the initial state vector, the model is thus run
- **models.py** is the file containing the function for running the model and plotting the populations and nutrients dynamics
- **aux.py** is the file containing all the auxiliary functions the model uses, such as the uptake function, the replenishment function and the dynamics of chemicals and populations
- **specifications.py** is the file where the networks are defined and the parameters fixed; a Community class is defined to facilitate the running of the model; the networks are defined through 3 dictionaries: the species dictionary (keys=letters, values=name of species), the nutrients dictionary (keys=nutrient, values=couples of nodes it connects and strength of the connection i.e. uptake rate) and the toxins dictionary (keys=toxin, values=couples of nodes it connects and strength of the connection i.e. uptake rate)
- **make_network.py** is the file where functions to create network and matrices starting from the dictionaries is defined

4.1. Parameters ranges

We propose in table 1 all the parameters the user needs to fix when defining the network, their biological meaning and reasonable values for each of them.

5. Examples

We provide here two examples, ready to be selected from the **specifications.py** file, of how the model can be used.

5.1. Two species competing for one resource

For this specific network, the construction and parameters would look like this:

```python
# nodes dictionary (species)
species_dict_cfr = {'A' : 'specialist1',
                    'B' : 'specialist2',
                    'M' : 'source1',
}
# edges dictionary (nutrients)
# for each nutrients who produces it and all the
    species that use it
nutrients_dict_cfr = {'x' : ['MA,MB', 0.5, 0.5]
}
# define toxins dictionary
# for each nutrients who produces it and all the
    species that use it
toxins_dict_cfr = {
}

# fix parameters
parameters_dict_cfr = { # initial resource
    availability
                        'R_0_cfr' : np.array([300])
    ,
                        # initial toxins
    concentration
                        'T_0_cfr' : np.array([]),
                        # initial species abundance
                        'N_0_cfr' : np.array
    ([100,100,1]),
                        # inverse reinsertion rate
                        'tau_cfr' : np.array([1]),
                        # toxins inverse insetrion
    rate
                        'tau_t_cfr' : np.array([]),
                        # dilution time
                        'tau_dil_cfr' : 100,
                        # intrinsic growth rates
                        'g_cfr' : np.array
    ([1,0.8,0.1]),
                        # maintainance energy
    requirements
                        'm_cfr' : np.array
    ([0.1,0.1,0.]),
                        # external leakage of
    nutrients
                        'l_cfr' : np.array([0.8]),
                        # toxins leakage
                        'l_t_cfr' : np.array([]),
                        # energy content of
    resources
                        'w_cfr' : np.array([1]),
                        # energy content (negative)
     in toxins i.e. toxicity (?
                        'w_t_cfr' : np.array([]),
                        # maximal absorption for
    Monod function
                        'sig_max_cfr' : 1,
                        # vector with toxins
    maximal absorption
                        'k_cfr' : np.array([]),
}
```

Code 1. *Example of Python code*

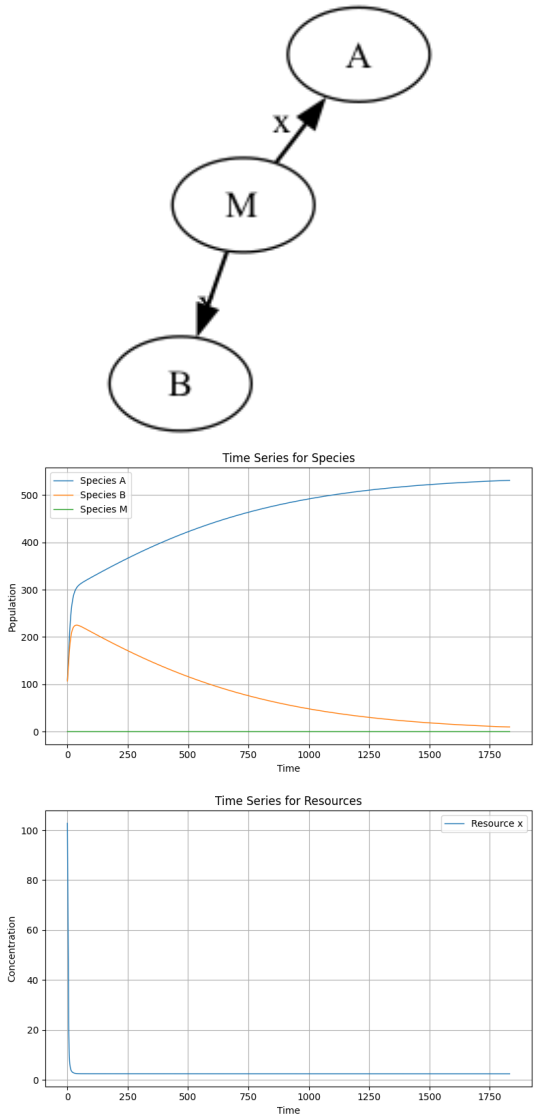

Figure 1. *From top to bottom: the network structure, the dynamics of the population and the dynamics of the resource.*

So that the generated network and dynamics are the ones in figure 1

5.2. Two cross-feeding species

All parameters here are kept the same, a part form growth rate: $g_A = 1, g_b = 0.8$ (Fig 2)

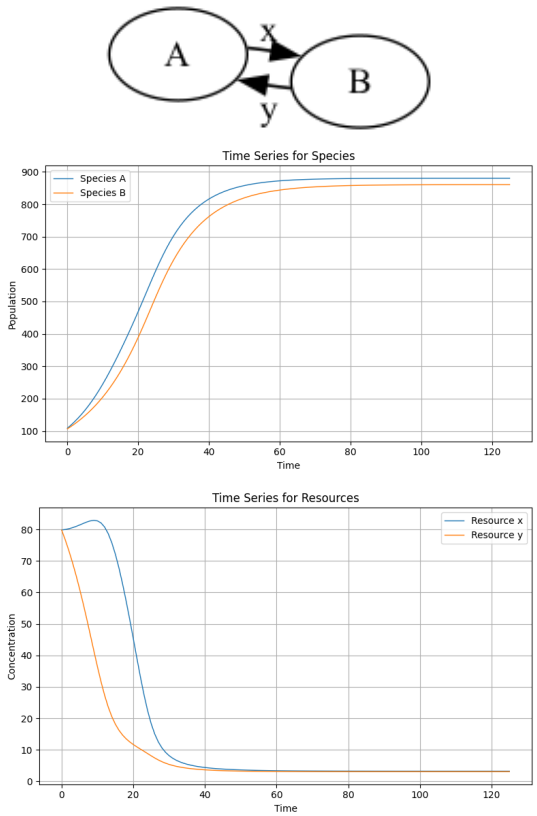

Figure 2. *From top to bottom: the network structure, the dynamics of the population and the dynamics of the resource.*

References

[1] L. Niehaus, I. Boland, M. Liu, *et al.*, "Microbial coexistence through chemical-mediated interactions", *Nature Communications*, vol. 10, no. 2052, p. 2052, 2019. DOI: 10.1038/s41467-019-10062-x.

[2] R. Marsland, W. Cui, J. Goldford, and P. Mehta, "The community simulator: A python package for microbial ecology", *PLoS ONE*, vol. 15, no. 3, e0230430, 2020. DOI: 10.1371/journal.pone.0230430.

Par.	Meaning	Values
$m\left[\frac{energy}{time}\right]$	energy requirements for maintenance	strong effect on the dynamics, keep ≤ 0.8
$g\left[\frac{1}{energy}\right]$	intrinsic growth rate	influences weakly the dynamics, reasonable to keep =1
$w\left[\frac{energy}{mass}\right]$	energy conversion factor	influences the dynamics, reasonable to keep =1
$u\left[\frac{volume}{time}\right]$	uptake rate	influences weakly the dynamics, reasonable to keep ≥ 0.3
$l\,[adim.]$	leakage rate (fraction of up-taken nutrient that is used for metabolism)	influences the dynamics, reasonable to keep ≤ 0.3
$\sigma_{max}\left[\frac{mass}{time}\right]$	steepness of the Monod curve	very strong effect on dynamics, keep below 1
$\tau\,[time]$	reinsertion frequency	connected to initial concentration of chemicals, keep ≤ 1 (1 is chemostat)
$\tau_{dil}\,[time]$	dilution frequency	only influences velocity of convergence, and slightly the dynamics, can be any order of magnitude
N_0, R_0, T_0 $\left[\frac{1}{volume}\right], \left[\frac{mass}{volume}\right]$	initial populations and concentrations	keep 2 orders of magnitude higher than the rest of the parameters i.e. 10^2

Table 1