Tutorial on ecological dynamics

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1 Introduction

1.1 The generalized Lotka-Volterra model

Historically, the first mathematical model introduce to describe the dynamics of an ecological system was put forward in the 1920s by Lotka [16] and Volterra [28] for a predator-prey system. In the case of one predator and one prey this well-known model prescribes that

$$\dot{x} = x(\alpha - \beta y) \tag{1a}$$

$$\dot{y} = y(\gamma x - \delta) \ , \tag{1b}$$

where $x(t)$ is the prey population at time t and $y(t)$ is the predator population. The equations are written making the (unreasonable) assumption that preys grow exponentially with rate α for an unlimited amount of time when there are no predators; furthermore, in absence of preys the population of predators decays exponentially with rate δ, and β and γ are the parameters representing the effect of predators on preys and vice versa. The model assumes the law of mass actions, i.e. that these effects are proportional to the product of the two populations.

Eqs (1) can be easily generalized to a system of k preys and k predators:

$$\dot{x}_i = x_i \left(\alpha_i - \sum_{j=1}^{k} \beta_{ij} y_j \right) \tag{2a}$$

$$\dot{y}_i = y_i \left(\sum_{j=1}^{k} \gamma_{ij} x_j - \delta_i \right) \ . \tag{2b}$$

The dynamics of this system has been studied extensively (see, e.g., [24, chpt. 3]), and can either exhibit unstable fixed points or oscillating solutions.

It is possible to generalize equations like (1) and (2) for systems with any type of interaction, for example competition and mutualism. The starting point

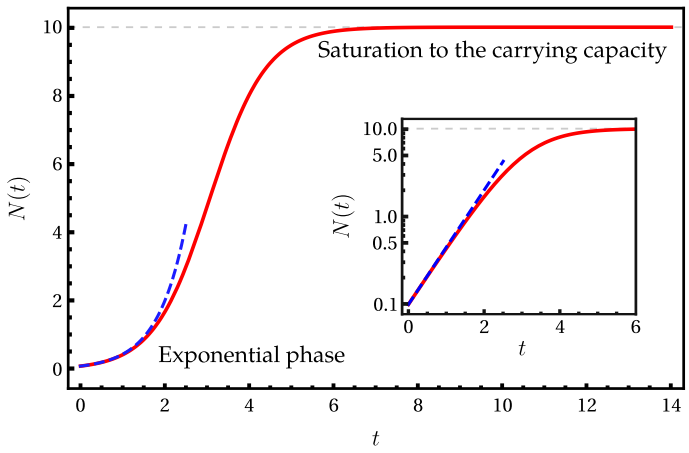

Figure 1: Solution of the logistic growth equation (3) (red curve) with $N(0) = 0.1$, $r = 1.5$ and $K = 10$. When it is small, the population grows exponentially (for comparison, the blue dashed curve is $N(t) = N(0)\exp(rt)$), and in the end it saturates to the carrying capacity K (grey dashed line). INSET: Same plot with logarithmic scale on the y-axis

is assuming that each species' population, in absence of other species, follows a *logistic growth equation*, i.e.:

$$\dot{N} = rN\left(1 - \frac{N}{K}\right) \ , \tag{3}$$

where $N(t)$ is the population. Any role played by the resources is absorbed by the parameters r and K, which are respectively the *intrinsic growth rate* and the *carrying capacity* of the species, i.e. the maximum population that the species can reach in the system. The behavior of the nontrivial (i.e., $N(t) \neq 0$) growing solution of Eq (3) is shown in Figure 1: after an initial quasi-exponential growth phase, the population saturates to the carrying capacity K. In fact, when the population N is small ($N \ll K$) the second term in the parentheses in Eq (3) is negligible ($N/K \approx 0$), and thus $\dot{N} \sim rN \ \Rightarrow \ N(t) \sim \exp(rt)$. On the other hand, when $N \approx K$ the term in the parentheses is small ($1 - N/K \approx 0$) and $\dot{N} \sim 0$, i.e. the population saturates to K. If the initial condition was larger than the carrying capacity, i.e. $N(0) > K$, the term in the parenthesis in Eq (3) would be negative, and the population would decay towards K.

If we generalize Eq (3) to a system of S species, each population N_i will have its own intrinsic growth rate r_i and its own carrying capacity K_i. We can then include inter-species interactions in the picture using an approach similar to the one used in the Lotka-Volterra equations for predator-prey systems, i.e. Eqs (2). This means that we assume that the effect of species i on species j is proportional to the product of the two populations. In other words, we can

write:

$$\dot{N}_i = r_i N_i \left(1 - \frac{N_i}{K_i} + \sum_{j \neq i} \alpha_{ij} N_j \right) \ , \tag{4}$$

where α_{ij} are called *competition coefficients* (with $\alpha_{ii} = 0$) and the matrix $A = (\alpha_{ij})_{i,j \in \{1,\dots,S\}}$ is called *interaction matrix*. The sign of the competition coefficients $\alpha_{i,j}$ determines the nature of the interaction between species i and j:

- If $\alpha_{i,j} < 0$, then if one species' population grows considerably it will decrease the other species' growth. This is the case, for example, of competition for common resources: when a species grows a lot, it will consume more resources and therefore limit the growth of other species
- If $\alpha_{i,j} > 0$ the interaction is cooperative: if one species' population grows considerably, it will produce more metabolic by-products that can help other species grow

In general the interaction coefficients do not need to be symmetric (i.e., $\alpha_{i,j} = \alpha_{j,i}$); when that happens and their sign is positive, the interaction between species i and j is called *mutualistic* (i.e., both species benefit from the interaction), while if they are not symmetric the interaction is called *commensalistic*.

If we redefine the interaction matrix so that $\alpha_{ii} = 1/K_i$, Eqs (4) can be simplified to:

$$\dot{N}_i = r_i N_i \left(1 + \sum_{i=1}^{S} \alpha_{ij} N_j \right) \ , \tag{5}$$

which are the *generalized Lotka-Volterra equations* in the literature. Similarly to logistic growth in Eq (3), this model only describes the dynamics of the species' populations and it contains no explicit information about resource dynamics: any role played by the resources is again absorbed by the parameters (in this case r_i and α_{ij}). This makes the model relatively easy to study mathematically (especially if the interaction coefficients are symmetric), and in fact the mathematical properties of Eqs (5) have been explored extensively in the literature, and they are still commonly used to describe microbial ecosystems. It has been shown that any system described by the generalized Lotka-Volterra equations has very rich dynamics, exhibiting from fixed points to limit cycles and attractors [27, 14, 10, 15, 11, 12, 13].

The mathematical tractability of Eqs (5), however, is balanced by the very limited predictive power of the model. In fact, while r_i and K_i can be measured by observing each species growing in isolation[1], the interaction coefficients α_{ij} are completely unknown, i.e. there is no way of knowing their value but fitting them against data *after* an observation is made. The model would gain in

[1] In principle, however, there is nothing that guarantees that a species' r_i or K_i remains unaltered when it interacts with other species.

predictive power if there were some additional hypotheses relating the competition coefficients α_{ij} with some measurable quantities, but this does not always happen.

Even if we neglect this last point, there is still a bigger issue with Eqs (5): the generalized Lotka-Volterra equations model inter-specific interactions as *pairwise*, i.e. species interact with each other *only* in couples. This means that this model cannot describe higher order interactions [3], which have been extensively studied in the past and are known to occur ubiquitously in ecosystems [2, 5, 29]. It is now known that including higher-order interactions into models of ecological communities can improve our ability to predict experimental data [20], and that they have a stabilizing effect on systems that would otherwise be unstable [9]. Since microbes have numerous different ways with which they can interact with each other, a model that can only describe pairwise interactions is *destined* to miss many crucial aspects of such systems, and therefore will be unable to correctly describe them [21].

For a comprehensive discussion of the assumptions and limitations of the generalized Lotka-Volterra equations, see Gonze *et al.* [8].

1.2 The consumer-resource model

The inability to use the generalized Lotka-Volterra equations to satisfactorily describe experimental data on competition between species encouraged scientists to find different ways to model competitive systems. A new approach in this direction was pioneered by Robert MacArthur [17, 19, 18], who introduced what would be later known as the *consumer-resource model* [6].

The main difference between the generalized Lotka-Volterra and this approach is that the consumer-resource model does not only describe the dynamics of the species' populations, but also of the resources' abundances. In other words, the main idea of the consumer-resource model is to write two coupled systems of differential equations:

$$\dot{n}_\sigma = f_n(n_\sigma, \{c_i\}) \qquad \sigma = 1, \dots, N_S \tag{6a}$$

$$\dot{c}_i = f_c(\{n_\sigma\}, c_i) \qquad i = 1, \dots, N_R \ , \tag{6b}$$

where n_σ is the population of species σ, c_i is the abundance[2] of resource i, N_S is the number of species present in the system and N_R the number of resources. In this case, therefore, we are writing explicitly that the interaction between different species is not direct as in Eq (5), but is "mediated" by the resources.

What we need now are assumptions and hypotheses so that we can write explicitly the right hand sides of Eqs (6). We assume that species σ uptakes resource i with a given rate[3] $n_\sigma J_{\sigma i}$, and that this uptake rate contributes with a

[2] Alternatively, n_σ and c_i can be interpreted, respectively, as the population *density* of species σ and the *concentration* of resource i.

[3] From our definition, $J_{\sigma i}$ is the resource uptake rate per unit population (or population density).

term ${g_\sigma}^{(i)} = v_i J_{\sigma i}$ to the total growth rate[4] $g_\sigma = \sum_i {g_\sigma}^{(i)}$ of species σ. We also assume that the (abiotic) resources are being supplied with constant rates[5] s_i and that all species have an intrinsic mortality rate δ_σ. This way the equations of the consumer-resource model are written as:

$$\dot{n}_\sigma = n_\sigma \left(\sum_{i=1}^{N_R} v_i J_{\sigma i} - \delta_\sigma \right) \tag{7a}$$

$$\dot{c}_i = s_i - \sum_{\sigma=1}^{N_S} n_\sigma J_{\sigma i} \ . \tag{7b}$$

The parameters v_i are generally called *resource values*, because they measure how efficiently the uptake of each resource is translated into growth and therefore how "valuable" they are.

The simplest approach to write explicitly the expression of $J_{\sigma i}$ could be to assume that it is proportional to the resource concentration, i.e. $J_{\sigma i} \propto c_i$. This is certainly a reasonable assumption if the resource is scarce, but becomes unreasonable when its concentration becomes high, since no living being can eat or uptake an unlimited amount of nutrients. Therefore, we need to write $J_{\sigma i} \propto r_i(c_i)$, where $r_i(c_i)$ is a function that is linear for small values of c_i and saturates at high c_i, and that is also monotonically increasing. The choice that is generally made when describing microbial populations is to use the so-called *Monod function*:

$$r_i(c_i) = \frac{c_i}{K_i + c_i} \ , \tag{8}$$

which was introduced by Jacques Monod in the 1940s from his studies on microbial growth [22, 23]. The parameter K_i is called *half-saturation constant* or *affinity constant* for resource i, and represents the resource abundance (or concentration) at which the growth rate of the microbial species is half the maximum one.

[4]Notice that the way we are writing g_σ implies that the N_R resources are *substitutable*, i.e. the uptake of *either* one of them is *sufficient* for growth. In general, microbes need several different *essential* resources to thrive, i.e. the uptake of *all* of them is *necessary* for growth (and in this case we would have written g_σ, for example, as the *product* of the ${g_\sigma}^{(i)}$ instead of their sum). In particular, bacteria like *Escherichia coli* need supplies of carbon, nitrogen, phosphorus and other substrates in order to be cultured in the lab. What is normally done in experiments, however, is that all essential resources except one are supplied in excess, and the effects of the limiting resource on microbial systems are studied. Generally speaking, the limiting resource in experiments involving bacteria is the carbon source: in this case, microbes are cultured in media with high concentrations of compounds containing nitrogen (e.g., ammonium salts), phosphorus (e.g., phosphates) etc., and then different sugars or carbohydrates (i.e., the carbon sources) are added to assess their effect on the system.

[5]If we were considering *biotic* resources, the supply rates would not be constant and would describe how resources grow. For example, we could use a logistic growth term, i.e. $s_i \propto c_i(1 - c_i/\kappa)$.

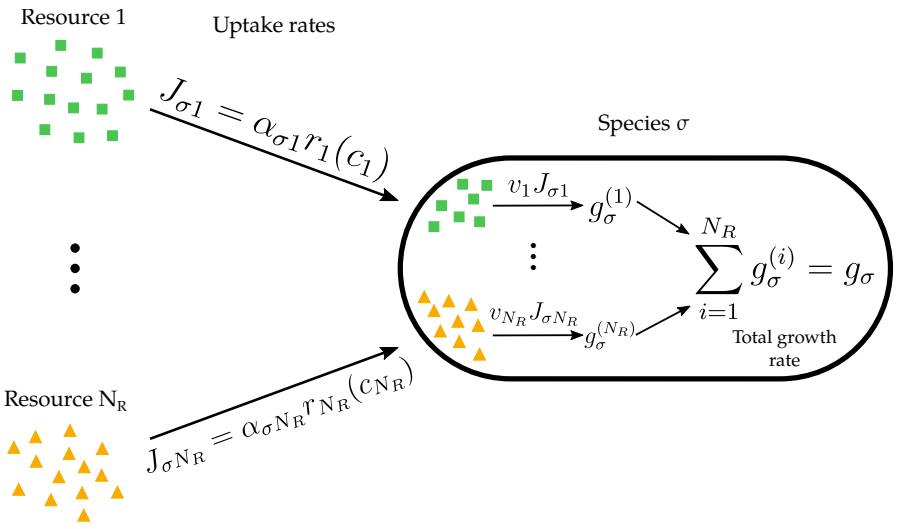

Figure 2: Assumptions that we have used to write the consumer-resource model, i.e. Eqs (9). The specific resource uptake rates $J_{\sigma i}$ are proportional to the Monod function $r_i(c_i) = c_i/(K_i + c_i)$ through the metabolic strategies $\alpha_{\sigma i}$. Every resource uptake rate is then converted into a growth term ${g_\sigma}^{(i)}$ that contributes linearly to the overall growth rate $g_\sigma = \sum_i {g_\sigma}^{(i)}$

Therefore, we can write the equations of the consumer-resource model as follows:

$$\dot{n}_\sigma = n_\sigma \left(\sum_{i=1}^{N_R} v_i \alpha_{\sigma i} r_i(c_i) - \delta_\sigma \right) \tag{9a}$$

$$\dot{c}_i = s_i - \sum_{\sigma=1}^{N_S} n_\sigma \alpha_{\sigma i} r_i(c_i) \ . \tag{9b}$$

The parameters $\alpha_{\sigma i}$ are called *metabolic strategies*, and each one measures how much species σ is using resource i for growth. The main assumptions used to write these equations are sketched in Fig. 2, while a schematic representation of the model is given in Fig. 3.

The consumer-resource model has two main differences with the generalized Lotka-Volterra approach. The first one is the fact that we can now express the growth rate of each species as a function of resource availability: while in Eqs (5) we are assuming that every species has a fixed intrinsic growth rate, in Eqs (9) the growth of species σ does not happen at a *fixed* rate, but depends *explicitly* on how abundant resources are in the system. The second one, as already stated, is the fact that resource dynamics is explicitly modeled in this case. This makes Eqs (9) less easy to study mathematically, but with the advantage that now the mechanism of competition between species is modeled

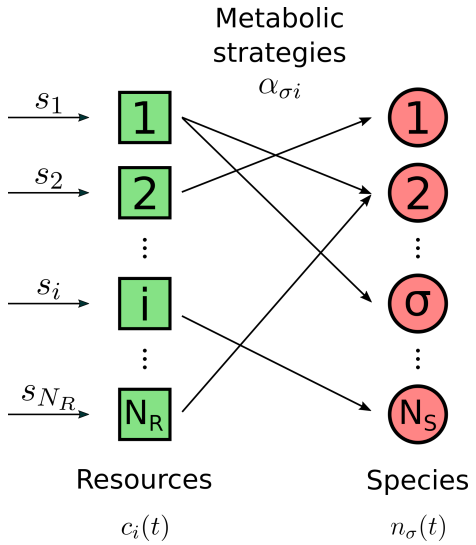

Figure 3: Schematic representation of the consumer-resource model as written in Eqs (9).

correctly: if the population of one species increases, the uptake term in Eq (9b) decreases the amount of available resources, and therefore the other species will be limited in their growth (since $r_i(c_i)$ is monotonic). Notice that this means that the inter-specific interactions in consumer-resource systems are naturally of the highest possible order (i.e., all species interact simultaneously with all the others) and not just pairwise, since an increase in only one species' population will have repercussions on the whole system.

2 Middle half-hour of consumer-resource tutorial

- Use one species one resource to introduce the idea that CR models provide mechanistic definitions to phenomenological models

- Repeat procedure for two species to resources, arrive at LV and look at competition vs. co-existence (Tillman)

- Many species many resources

2.1 One species one resource

Start with a chemostat model, one species one resource

$$\frac{dn}{dt} = \underbrace{r(c)n}_{\text{Growth}} - \underbrace{\delta n}_{\text{Dilution}} \tag{10a}$$

$$\frac{dc}{dt} = \underbrace{\delta c_0}_{\text{Input}} - \underbrace{\delta c}_{\text{Dilution}} - \underbrace{r(c)\frac{n}{Y}}_{\text{Consumption}} \tag{10b}$$

- δ = dilution factor, fraction of volume that flows in and out per unit time
- Y = Yield, # cells per unit resource
- $r(c) = r_{max}\frac{c}{c+K}$, Monod equation

At steady-state, $r(c^*) = \delta$, effective generation time $\tau^* = \delta^{-1}$. No dependence on c_0!

Steady-state when strain is eating most of the resource $c^* \ll c_0$ (often the case)

$$0 = \delta c_0 - \delta c^* - r(c^*)\frac{n^*}{Y} \tag{11a}$$

$$= \delta c_0 - \delta c^* - \delta\frac{n^*}{Y} \tag{11b}$$

Gives us $n = Yc_0 - c^* \approx Yc_0$

No growth rate dependence! Because c^* adjusts until $r(c^*) = \delta$

We can get back phenomenological models of growth using 1) the principle of *mass conservation* $\frac{n}{Y} + c = c_0$ 2) and in the limit where dilution rate limit $\delta \ll r_{max}$

1) Take the derivative of the mass conservation equation for total biomass B

$$\frac{1}{Y}\frac{dn}{dt} + \frac{dc}{dt} = \delta(c_0 - c - \frac{n}{Y}) \equiv \frac{dB}{dt} \tag{12}$$

The dynamics of the system are fast (adiabatic limit), so we can treat the derivative $\frac{dB}{dt}$ as ≈ 0 and solve the remainder to identify the constraint $c = c_0 - \frac{n}{Y}$

2) Next, if we set $\delta \ll r_{max}$, we decrease c^*. If we can push c^* down we can reduce it so that $c^* \ll K$, allowing for the growth rate to be linearized $r(c^*) = \frac{r_{max}c^*}{K}$, giving us

$$\frac{dn}{dt} = n\frac{r_{max}}{K}c_0(1 - \frac{n}{Yc_0}) - \delta n \tag{13}$$

Rearranging terms, we can define the growth rate and carrying capacity of Verhulst's logistic growth equation

$$\tilde{r} = \frac{r_{max}}{K} c_0 - \delta \tag{14a}$$

$$\tilde{K} = \left(\frac{r_{max}}{K} c_0 - \delta\right) \cdot \frac{YK}{r_{max}} = \tilde{r} \frac{YK}{r_{max}} \tag{14b}$$

$$\frac{dn}{dt} = n\tilde{r}\left(1 - \frac{n}{\tilde{K}}\right) \tag{14c}$$

This equation defines the phenomenological parameters of the logistic growth equation in mechanistic terms!

2.2 Many species

Let's find a mechanistic view of the Lotka-Volterra equation. What we examined above is a version of what's known as a consumer-resource model. Introduced through a series of papers

- Mechanistic competition coefficients via heuristic arguments. MacArthur and Levins 1967, Amer. Nat. - Mechanistic competition coefficients via analytic methods. MacArthur 1969, PNAS - Fully introduced. MacArthur 1970, Theoretical Population Biology

and

- summarized by Chesson, 1990, Theoretical Population Biology

Two main features we will discuss

1) Derive mechanistic competition coefficients using separation of timescales (adiabatic approximation)

2) Demonstrating global stability via Lyapunov functions

2.3 Many species one resource

When we have two species and one resource only one species can survive at steady-state. This is because steady-state solutions $\delta = r_1(c^*) = r_2(c^*)$ cannot be **simultaneously satisfied** unless species have equal growth rates. Which, in the context of this model would mean there are no meaningful differences. Instead, the species with the lowest steady-state resource requirement, $\min[c_i^*]$ wins out.

If species 1 wins, species 2 goes extinct, so at steady-state

$$\frac{dn_1}{dt} = n_1^*(r_1(c^*) - \delta) \tag{15a}$$

$$= 0 \tag{15b}$$

$$\rightarrow c_1^* = K_1\left(\frac{\delta}{r_{max,1} - \delta}\right) \tag{15c}$$

If we use this c_1^* value in our requirement that $\frac{dn_2}{dt} < 0$, we get the following inequality.

$$\frac{dn_2}{dt} = n_2 \left(\frac{r_{max,2} c_1^*}{K_2} - \delta \right) < 0 \tag{16a}$$

$$\rightarrow c_1^* < c_2^* \tag{16b}$$

This is known as Tilman's c^* rule.

2.4 Many species many resources

It is easier to show how you get the Lotka-Volterra equation from the CR when resources are formulated as self-renewing as opposed to the chemostat formulation. All important results for this tutorial (e.g., stability) are equivalent for these two formulations. But differences exist and you can learn more in

- Cui, Marsland, and Mehta, PRL, 2020 - Supplement: Marsland, Cui, and Mehta, Am. Nat., 2020

We have N_S species and N_R resources.

$$\frac{dn_\sigma}{dt} = \underbrace{\sum_{i=1}^{N_R} r_{\sigma,i} c_i n_\sigma}_{\text{Growth}} - \underbrace{\delta_\sigma n_\sigma}_{\text{Maintenance/death}} \tag{17a}$$

$$\frac{dc_i}{dt} = \underbrace{\mu_i c_i \left(1 - \frac{c_i}{\kappa_i}\right)}_{\text{Self-renewing growth}} - \underbrace{\frac{c_i}{Y_i} \sum_{\sigma=1}^{N_S} r_{\sigma,i} n_\sigma}_{\text{Consumption}} \tag{17b}$$

- κ_i = carrying capacity of resource
- μ_i = growth rate of resource

Using adiabatic approximation, we solve for the stationary resource concentration

$$c_i^* = \kappa_i - \frac{\kappa_i}{\mu_i Y_i} \sum_{\sigma=1}^{N_S} r_{\sigma,i} n_\sigma \tag{18}$$

$$\frac{dn_\sigma}{dt} = \sum_{i=1}^{N_R} r_{\sigma,i} c_i^* n_\sigma - \delta_\sigma n_\sigma \tag{19a}$$

$$= \sum_{i=1}^{N_R} r_{\sigma,i} n_\sigma \left(\kappa_i - \frac{\kappa_i}{\mu_i Y_i} \sum_{\sigma'=1}^{N_S} r_{\sigma',i} n_{\sigma'} \right) - \delta_\sigma n_\sigma \tag{19b}$$

$$= \sum_{i=1}^{N_R} (r_{\sigma,i}\kappa_i - \delta_\sigma) n_\sigma - \sum_{\sigma'}^{N_S} n_\sigma n_{\sigma'} \sum_{i=1}^{N_R} \frac{\kappa_i}{\mu_i Y_i} r_{\sigma,i} r_{\sigma',i} \tag{19c}$$

$$= \tilde{r}_\sigma n_\sigma - \sum_{\sigma'}^{N_S} \alpha_{\sigma,\sigma'} n_\sigma n_{\sigma'} \tag{19d}$$

We now have our generalized Lotka Volterra with mechanistic competition coefficients in the matrix $\mathbf{A}$. If our matrix $\mathbf{A}$ is invertible we can calculate the stationary size of a given species as $n_\sigma^* = \sum_{\sigma'}^{N_S} \alpha_{\sigma,\sigma'}^{-1} \tilde{r}_{\sigma'}$.

This value n_σ^* is the global fixed point of the gLV equation. We can prove this using a Lyapunov function, a scalar function that can be used to establish stability. Lyapunov functions Λ are functions with the following properties

- $\Lambda(n_\sigma) > 0$ for $n_\sigma \neq n_\sigma^*$
- $\Lambda(n_\sigma^*) = 0$
- $\frac{d\Lambda}{dt} \leq 0$

These functions allow us to determine stability without solving the actual equation! (Any other reasons?). Disadvantage: no general method for constructing these function

$$\Lambda = \sum_{\sigma}^{N_S} \left[n_\sigma(t) - n_\sigma^* - n_\sigma^* \ln \frac{n_\sigma(t)}{n_\sigma^*} \right] = \sum_{\sigma}^{N_S} \lambda_\sigma(t) \tag{20}$$

Plot each term $\lambda_s(t)$, demonstrate that $\lambda_s(t)$ has a single minimum at n_σ^*.
Let's look at the derivative

$$\frac{d\Lambda}{dt} = \sum_{\sigma}^{N_S} \left[\frac{dn_\sigma}{dt} - \frac{n_\sigma^*}{n_\sigma} \frac{dn_\sigma}{dt} \right] \tag{21a}$$

$$= \sum_{\sigma}^{N_S} \left[\frac{1}{n_\sigma} \frac{dn_\sigma}{dt} \ (n_\sigma(t) - n_\sigma^*) \right] \tag{21b}$$

$$= \sum_{\sigma}^{N_S} \left[(r_s - \sum_{\sigma'}^{N_S} A_{s,s'} n_{\sigma'}(t))(n_\sigma(t) - n_\sigma^*) \right] \tag{21c}$$

$$= - \sum_{\sigma,\sigma'} A_{\sigma,\sigma'} (n_{\sigma'}(t) - n_{\sigma'}^*)(n_\sigma(t) - n_\sigma^*) \tag{21d}$$

$$= - \sum_{i=1}^{N_R} \frac{\kappa_i}{\mu_i Y_i} \sum_{\sigma,\sigma'} r_{\sigma,i} r_{\sigma',i} (n_{\sigma'}(t) - n_{\sigma'}^*)(n_\sigma(t) - n_\sigma^*) \tag{21e}$$

$$= - \sum_{i=1}^{N_R} \frac{\kappa_i}{\mu_i Y_i} \left(\sum_{\sigma=1}^{N_S} r_{\sigma,i} (n_\sigma(t) - n_\sigma^*) \right)^2 \tag{21f}$$

$$\leq 0 \tag{21g}$$

where we have used the property that the products of all pairs in a matrix is equal to the square of the sum of all entries in the matrix. So Λ decreases until $n_\sigma(t) = n_\sigma^*$, the global attractor, if $n_\sigma^* > 0$.

3 Connecting the consumer-resource model with physiology: the consumer-proteome-resource model

3.1 Generalization of the proteome-growth relationships

Our starting point are the proteomic growth laws [26]. They will be discussed extensively in a separate tutorial, so here is just a *very* quick primer. These laws are simple phenomenological relationships between a species' *steady-state* growth rate and the way its proteome is "allocated" to different functions. In the simplest approach, we can assume that a microbial species (e.g., *E. coli*) is allocating a fraction φ^P of its proteome to nutrient uptake and metabolism, and a fraction φ^R to ribosomes and all the affiliated proteins. In other words, the fraction φ^P contains all the proteins that convert nutrients (like sugars) in amino acids and precursors of protein synthesis, while φ^R contains all the proteins that convert these precursors into proteins. From experiments it turns out that there is also a third fraction φ^Q, is called "housekeeping" fraction, that is responsible for all essential functions that are not covered by φ^P and φ^R. By definition, then, $\varphi^P + \varphi^R + \varphi^Q = 1$ (the sum of these three fractions must be one). Experimentally, it turns out that when we change the growth

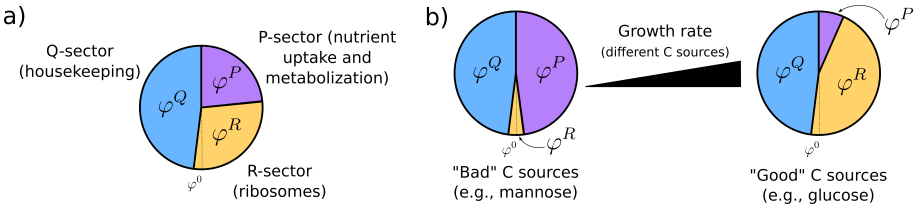

Figure 4: Proteome subdivision introduced by Scott *et al.* [26].

rate of *E. coli* by using different carbon sources (i.e., using mannose or acetate instead of glucose) the proteome fractions φ^P and φ^R change, but φ^Q remains constant; in particular, when the cells are growing on a "bad" carbon source (e.g., mannose for *E. coli*) that yields a slow growth rate, cells upregulate the expression of proteins in the φ^P fraction, while on "good" carbon sources (e.g., glucose for *E. coli*) it's the ribosomal fraction φ^R that is upregulated. Fig. 4 shows a schematic representation of this.

These are how the growth laws are written:

$$\varphi^P + \varphi^R + \varphi^Q = 1 \tag{22a}$$

$$\varphi^P = \frac{\rho}{\overline{\kappa}^n(c)} g \tag{22b}$$

$$\varphi^R = \frac{\rho}{\kappa^t} \lambda + \varphi^0 \tag{22c}$$

Here, g is the growth rate, ρ is a conversion factor, κ^t is called "translational capacity" and $\overline{\kappa}^n(c) = \kappa^n \cdot c/(c+K)$, where κ^n is called "nutritional capacity" and K is the Monod constant of resource c (we are assuming that the nutrients are being taken up following Monod's law). For more detailed information, attend Tuesday's tutorial or see [26].

The proteome-growth relationships in Eq (22) have been developed for a *single* microbial species growing on a *single* limiting resource. In order to include these laws in a consumer-resource model, we need to generalize them. The simplest way to do this for a system of N_S consumer species and N_R resources is the following. Considering species σ, we assume that its proteome can be minimally divided in the three aforementioned sectors, respectively φ^P_σ, φ^R_σ and φ^Q_σ. With more than just one resource in the system, we can think of φ^P_σ as being further sub-divided into N_R fractions. In other words, we assume that the proteome of species σ is divided into the fractions φ^Q_σ, φ^R_σ and the N_R fractions $\varphi^P_{\sigma i}$ (with $i = 1, \ldots, N_R$), each one representing the proteome fraction allocated by species σ for the uptake and metabolization of resource i. A schematic representation of this assumption is shown in Figure 5.

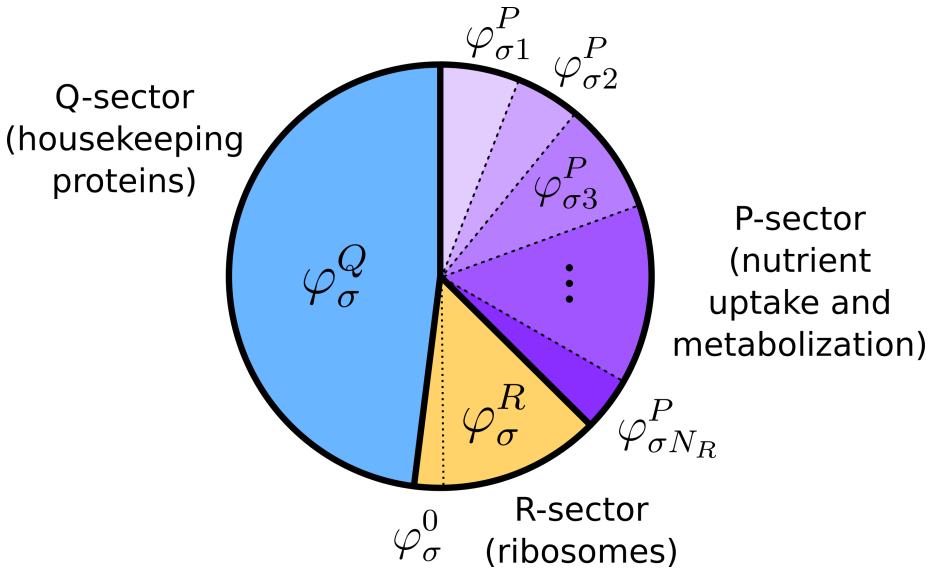

Figure 5: Generalization of the proteome subdivision introduced by Scott *et al.* [26] to the case of multiple resources. We assume that the sector allocated for nutrient uptake and metabolization is subdivided into smaller fractions $\varphi_{\sigma i} = \varphi^P_{\sigma i}$, each one dedicated to a specific resource

Eq (22a) now reads:

$$\varphi^Q_\sigma + \varphi^R_\sigma + \sum_{i=1}^{N_R} \varphi^P_{\sigma i} = 1 \ . \tag{23}$$

Then, we rewrite Eq (22b) as:

$$\varphi^P_{\sigma i} = \frac{\rho_\sigma}{\overline{\kappa}^n_i(c_i)} g^{(i)}_\sigma \ , \tag{24}$$

where ρ is considered to be species-dependent, $\overline{\kappa}^n_i(c_i) = \kappa^n_i \cdot r_i(c_i)$ (with $r_i(c_i) = c_i/(K_i + c_i)$), and ${g_\sigma}^{(i)}$ is the contribution to the growth rate of species σ due to the uptake of resource i. We assume, then, that the uptake of each resource contributes to the growth of species σ independently of the others, i.e. that the total growth rate can be written as the sum of these terms[6]:

$$g_\sigma = \sum_{i=1}^{N_R} g^{(i)}_\sigma \ . \tag{25}$$

[6]This assumption is consistent with previous works that considered the proteome allocation introduced by Scott *et al.* [26] in systems with two substitutable resources (see [1, Eq (3)], [7, Eq (S36)]).

This implies that we are assuming that the N_R resources are *substitutable* (e.g., different carbon sources), otherwise their contribution to the growth rate may obey an equation with a different form (e.g., their contributions may be multiplicative rather than additive). Finally, we generalize Eqs (22b) and (22c) to:

$$g_\sigma = \sum_{i=1}^{N_R} \frac{\overline{\kappa}_i^n(c_i)}{\rho_\sigma} \varphi_{\sigma i}^P \tag{26a}$$

$$\varphi_\sigma^R = \frac{\rho_\sigma}{\kappa_\sigma^t} g_\sigma + \varphi_\sigma^0 \ . \tag{26b}$$

Now we can use Eq (26a) to write Eq (26b) in terms of the fractions $\varphi_{\sigma i}^P$, and plug it into Eq (23). By doing so we obtain the generalized normalization condition:

$$\sum_{i=1}^{N_R} \varphi_{\sigma i} \left[1 + \frac{\overline{\kappa}_i^n(c_i)}{\kappa_\sigma^t} \right] = 1 - \varphi_\sigma^Q - \varphi_\sigma^0 := \Phi_\sigma \ , \tag{27}$$

where we have written $\varphi_{\sigma i}$ instead of $\varphi_{\sigma i}^P$ for simplicity and Φ_σ is the total proteome fraction that species σ allocates to metabolism and growth (minus φ_σ^0).

3.2 The "consumer-proteome-resource" equations

We now use a slightly different interpretation of the consumer-resource framework. In particular, we write the general structure of the equations as follows:

$$\dot{m}_\sigma = m_\sigma (g_\sigma - q_\sigma) \quad \sigma = 1, \ldots, N_S \tag{28a}$$

$$\dot{c}_i = s_i - \sum_{\sigma=1}^{N_S} J_{\sigma i} m_\sigma \quad i = 1, \ldots, N_R \, , \tag{28b}$$

where m_σ is now the *biomass* density of species σ and g_σ is its growth rate. The parameter q_σ can be interpreted as a maintenance cost, due to the fact that each species requires a minimum amount of energy per unit time to survive without growing. Finally, c_i is the density of resource i, s_i is the (constant) resource supply rate, and $J_{\sigma i}$ is the rate at which species σ uptakes resource i per unit biomass.

Since we now have the expression of g_σ as a function of the proteome fractions $\varphi_{\sigma i}$ (i.e., Eq (26a)), in order to write these equations explicitly we need to introduce some assumptions on the uptake rates $J_{\sigma i}$. In particular, we assume that the uptake rate $J_{\sigma i}$ of resource i per unit biomass is proportional to $\varphi_{\sigma i}$, i.e.:

$$J_{\sigma i} = \xi_i r_i(c_i) \varphi_{\sigma i} \ , \tag{29}$$

where the proportionality constant ξ_i can be interpreted biologically as the

maximum catalytic rate of the enzyme used to metabolize resource i[7]. By comparing Eqs (29) and (24) we can see that the contribution to the growth rate of species σ due to the uptake of resource i is proportional to its uptake rate, i.e. ${g_\sigma}^{(i)} = \chi_{\sigma i} J_{\sigma i}$ with

$$\chi_{\sigma i}\xi_i = \frac{\kappa_i^n}{\rho_\sigma} \ . \tag{30}$$

With all the considerations above, the equations of our model are:

$$\dot{m}_\sigma = m_\sigma \left[\sum_{i=1}^{N_R} \eta_{\sigma i} r_i(c_i) \varphi_{\sigma i} - q_\sigma \right] \tag{31a}$$

$$\dot{c}_i = s_i - \xi_i r_i(c_i) \sum_{\sigma=1}^{N_S} m_\sigma \varphi_{\sigma i} \tag{31b}$$

$$\sum_{i=1}^{N_R} \varphi_{\sigma i} \left[1 + \gamma_{\sigma i} r_i(c_i) \right] = \Phi_\sigma \ , \tag{31c}$$

where we have written explicitly $\overline{\kappa}_i^n(c_i) = \kappa_i^n r_i(c_i)$ with $r_i(c_i) = c_i/(K_i + c_i)$, and we have defined $\eta_{\sigma i} := \kappa_i^n/\rho_\sigma$ and $\gamma_{\sigma i} := \kappa_i^n/\kappa_\sigma^t$ to simplify the notation. A schematic representation of all the assumptions used to write these equations is shown in Figure 6.

Eqs (31a) and (31b) have the traditional structure of a consumer-resource model, but have the added advantage of describing population dynamics using parameters and variables that have a precise biological meaning at the intracellular scale of the system and that can be measured experimentally [26]. In fact, in the "classic" consumer resource model (i.e., Eqs (9)) the way each species grows is determined by the metabolic strategies $\alpha_{\sigma i}$ and by the resources values v_i, which however do not have a clear biological interpretation. Here we can see that their roles are played by, respectively, the proteome fractions $\varphi_{\sigma i}$ and the ratio $\eta_{\sigma i} = \kappa_i^n/\rho_\sigma$, which can be both measured in principle. Therefore, this *consumer-proteome-resource* model describes community dynamics at an intermediate level of complexity between classical consumer-resource models and biochemical models of microbial metabolism [4]. By adopting such an intermediate level of complexity and realism, we can take into account the dynamics of gene expression and microbial metabolism, while preserving analytical

[7] In fact, Scott *et al.* [26, Supporting Online Material] give a microscopic interpretation of the nutritional capacity κ_i^n by stating that the growth rate of a microbial species is given by $g = qJ$, where J is the uptake rate of the (only) resource per unit biomass, and q is a proportionality constant that depends on the properties of the nutrient (e.g., how much energy its metabolization can generate). They then assume that there is only one bottleneck enzyme E for the growth of the microbial species, and write $J = k_E r(c)\varphi_E$, where k_E is the maximal catalytic rate of enzyme E, $r(c)$ is Monod's function, and φ_E is the fraction of the proteome occupied by the enzyme E. Compared to our formalism in the general case of N_S species and N_R resources (so that $J \to J_{\sigma i}$ and $g \to g_\sigma$), we can identify $r(c) \to r_i(c_i)$, $\varphi_E \to \varphi_{\sigma i}$, $q \to \chi_{\sigma i}$ and finally $k_E \to \xi_i$.

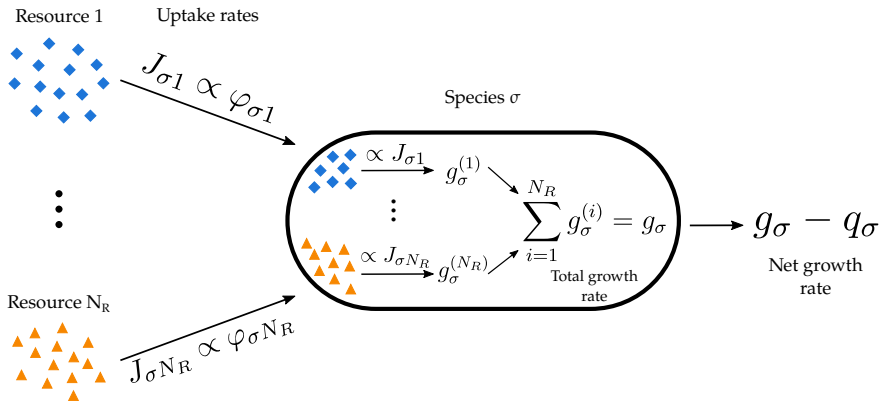

Figure 6: Schematic representation (analogous to Figure 2) of the assumptions used to write our consumer-proteome-resource equations, i.e. Eqs (31)

insights on the microbial community dynamics and identifying the key intracellular properties affecting species coexistence.

Eq (31c), on the other hand, is a constraint that all species have to satisfy at every instant and it is the direct consequence of Eq (23), i.e. the fact that the quantity of proteins expressed by microbes is limited (or, in other words, that the fractions of the three aforementioned proteome sectors must sum to one). In other words, Eq (31c) is the expression of the finiteness of the species' proteomes. This constraint is significantly different from similar ones that have been studied in the consumer-resource framework (see, e.g., [25]).

The first important consequence of this constraint derives from the fact that the coefficients $1 + \gamma_{\sigma i} r_i(c_i)$ in Eq (31c) are *not* fixed, but change with time depending on the system's dynamics through $r_i(c_i)$ (i.e., they are a function of the resources' concentrations). This implies that for the constraint to be satisfied at all times, the proteome fractions $\varphi_{\sigma i}$ *cannot* be fixed but must be, in turn, dynamical variables: an increase (decrease) of $1 + \gamma_{\sigma i} r_i(c_i)$ must be balanced by a decrease (increase) of some of the $\varphi_{\sigma i}$.

3.3 Dynamics of the proteome fractions

The constraint in Eq (31c) has a simple geometrical interpretation: considering species σ, the N_R-dimensional vector $\vec{\varphi}_\sigma = (\varphi_{\sigma 1}, \ldots, \varphi_{\sigma N_R})$ belongs to a hyperplane whose normal vector $\hat{n}_\sigma$ has components $1 + \gamma_{\sigma i} r_i(c_i)$. This means that as the system evolves, the components of $\hat{n}_\sigma$ vary with time and therefore the hyperplane to which $\vec{\varphi}_\sigma$ belongs moves in the N_R-dimensional space and changes orientation. A schematic example for a system with $N_R = 3$ is given in Fig. 7. The fact that the proteome fractions $\varphi_{\sigma i}$ have to change over time

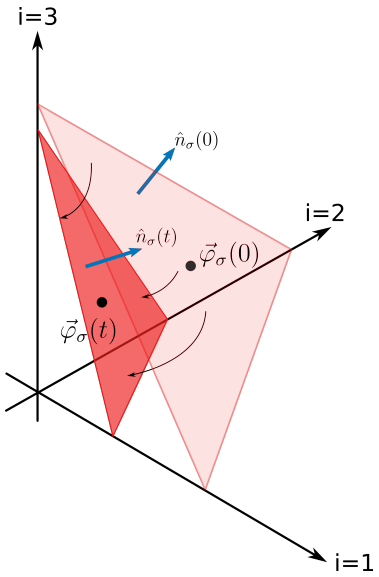

Figure 7: Schematic representation of the geometrical interpretation of the constraint in Eq (31c). The components of the normal vector $\hat{n}_\sigma$ change with time as the system evolves (since they are a function of the resource's concentrations c_i), so the hyperplane on which $\vec{\varphi}_\sigma$ lies moves around as the system evolves.

reflects the ability of microbes to vary their enzyme synthesis with time and switch between nutrients according to environmental conditions.

To write an equation for $\vec{\varphi}_\sigma$ we call $\vec{c} = (c_1, \ldots, c_{N_R})$ the vector of resource concentrations and define

$$F_\sigma(\vec{\varphi}_\sigma, \vec{c}) := \sum_{i=1}^{N_R} \varphi_{\sigma i} \left[1 + \gamma_{\sigma i} r_i(c_i)\right] - \Phi_\sigma \tag{32}$$

so that the constraint given by Eq (31c) can be written more simply as $F_\sigma(\vec{\varphi}_\sigma, \vec{c}) = 0$. Since this constraint must hold at every instant, any equation for $\dot{\vec{\varphi}}_\sigma$ must satisfy

$$\dot{F}_\sigma(\vec{\varphi}_\sigma, \vec{c}) \equiv \dot{\vec{\varphi}}_\sigma \cdot \vec{\nabla}_\varphi F_\sigma + \dot{\vec{c}} \cdot \vec{\nabla}_c F_\sigma = 0 \ , \tag{33}$$

where $\vec{\nabla}_\varphi$ and $\vec{\nabla}_c$ are, respectively, the gradients taken with respect to the components of $\vec{\varphi}_\sigma$ and $\vec{c}$. Therefore, the structure of the "minimal" equation for $\varphi_{\sigma i}$, i.e. the one that simply describes the dynamics of $\vec{\varphi}_\sigma$ as it moves *with* its hyperplane, is:

$$\dot{\vec{\varphi}}_\sigma = -\frac{\vec{\nabla}_\varphi F_\sigma}{(\vec{\nabla}_\varphi F_\sigma)^2} \dot{\vec{c}} \cdot \vec{\nabla}_c F_\sigma \ . \tag{34}$$

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