

Syntrophy reduces the effective competition and increases dynamical stability of microbial communities

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Abstract

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Introduction

The importance of microbial communities (MCs) is increasingly recognized. For instance, its control may have enormous benefits for human health [1], land use [2] or biofuel production [3]. However, our understanding of the complexity of the ecological and evolutionary mechanisms governing assembly and functioning of MCs is still in its infancy. Many important functions in which MCs are involved occur in time-scales much longer than bacterial generation times and, hence, it is of great interest to understand which are the determinants of MC stability.

In macroscopic organisms, a large body of theoretical research has been developed around Lotka-Volterra (LV) models, aimed at understanding the relative influence of ecological interactions on the stability of ecosystems. With these models, new concepts have emerged explicitly linking ecological interactions with the determinants of coexistence, such as the storage effects [Chesson], the connection between the effective competition in the system and its global stability [Ferrerá], or the influence of interaction patterns such as nestedness [Bascompte] or modularity [Ref]. Also novel angles to study the stability of ecosystems beyond dynamical stability were developed, such as structural stability [Rohr, Bastolla] or permanence [Schreiber],

The dynamics of microbial communities, however, is strongly influenced by the available nutrients in the environment which may fluctuate in very short-time scales. As a consequence, although some agreement with experimental data under laboratory conditions have been achieved by using LV models [Gore], under natural conditions it is expected that an explicit modelling of the resources dynamics is needed to achieve predictions [LV vs cons res]. Following the seminal work of MacArthur [Ref] or Tilman [], the surge of experiments involving microbes has prompted renewed interest in consumer-resources models.

Recent theoretical work showed that microbial communities can shape their own environment to achieve coexistence even if no syntrophy is present in the system [Tikhonov] or if there are more species than resources [Posfai], under the assumption that resources equilibrate in timescales shorter than the population dynamics. Moreover, analysis of these cohesive communities led to the identification of optimal metabolic classes and how their combination explain stable strategies [Taillefumier]. Extending these results to models in which the dynamics of resources is not at a steady-state, and in which feedbacks between microbes and the environment exist through the release of by-products, represents a challenge [Marsland MEE]. The release of by-products of some species that can be consumed by others is a form of mutualism, termed syntrophy, widespread in the microbial world

[DSouza]. Also, from a theoretical point of view, LV models predict an important role for mutualistic interactions in biodiversity maintenance [Ref], and a complex interplay with competitive interactions [Pascual]. For these reasons, gathering a deeper understanding of the relative role of competitive and mutualistic interactions in consumer-resources models is an important question.

In this work, we considered a consumers-resources model with syntrophy, to show that it is possible to find a sufficient condition for dynamical stability, which has so far remained elusive [Dwyer]. The condition allowed us to propose an optimization algorithm to design interaction matrices maximizing the likelihood of being dynamically stable. By studying the feasibility and dynamical stability of this system for different parameters, we found that syntrophy hinders feasibility but enhances dynamical stability. Moreover, the optimized matrices have a higher feasibility and dynamical stability than their random counterparts. Finally, we gather deeper ecological insight transforming a system into an effective competition LV model, finding that the results can be rationalized in terms of an increase (decrease) of the ratio between the intra-specific and the interspecific competition.

We considered that the dynamics of population densities S_i of N_S species and of the resources N_R consumed and secreted by microbes, R_μ , are governed by the following set of differential equations [Dwyer]:

$$\begin{aligned}\frac{dR_\mu}{dt} &= l_\mu - \sum_j \gamma_{j\mu} S_j R_\mu + \sum_j \alpha_{\mu j} S_j - m_\mu R_\mu \\ \frac{dS_i}{dt} &= \sum_\nu \sigma_{i\nu} \gamma_{i\nu} R_\nu S_i - \sum_\nu \alpha_{\nu i} S_i - d_i S_i,\end{aligned}\tag{1}$$

where the non-negative matrices $\gamma_{j\mu}$ ($\alpha_{\mu j}$) describe the uptake (secretion) rate of resource μ by species j , and we consider continuous growth under a constant supply of resources l_μ , and dilution rates m_μ and d_i for resources and species, respectively. We further consider that only a fraction σ_μ of the resources consumed are converted into biomass. Note that the secretion of resources only depends on the densities of species and not on the resources they consume. This has been interpreted in the original formulation of the model as an appropriate choice for by-products of central metabolism, and/or biomass released in the environment upon cell death [Dwyer]. The model also impose conservation of biomass by subtracting the biomass released by the organism from their biomass, and we impose the following conservation of biomass condition to hold

$$\sum_\nu (1 - \sigma_{i\nu}) \gamma_{i\nu} R_\nu^* \geq \sum_\nu \alpha_{\nu i} \quad \forall i,$$

which ensures that the biomass secreted is smaller or equal to the fraction not converted into biomass at steady state R^* . Note that this condition could be relaxed if microbial death is considered.

The characteristic equation of the Jacobian of the system has no explicit solution, as detailed in Supplementary Materials. With the help of the Gerschgoring circle theorem [Ref] it is, however, possible to find a bound (hereafter critical radius r_c) for the modulus of every eigenvalue of the Jacobian, i.e. $|\lambda| \leq R_C \quad \forall \lambda$. This allow us to show that if 0 is not an eigenvalue of the Jacobian at a given equilibrium, and the following condition

$$(\Gamma B)_{\mu\mu} < - \sum_{\nu \neq \mu} |(\Gamma B)_{\mu\nu}| - r_c^2 \quad \forall \mu,\tag{2}$$

holds for every resource, then the system is dynamically stable (see SM for proof and explicit definition of r_c). Note that that the product of the matrices $\Gamma = \gamma \text{diag}((R^*) + \alpha)$ and $B = \text{diag}((S^*) \sigma \gamma)$ impose constraints on the relation between the consumption matrix γ and the secretion matrix α , and that the sufficient condition expresses that the matrix ΓB is diagonally dominant. By working with mean field matrices $\gamma = \gamma_0 G$ and $\alpha = \alpha_0 A$, where γ_0 and α_0 are metaparameters drawn from uniform distributions and G and A are binary matrices, after some simplifications detailed in Supplementary Materials it is possible to find an objective function whose minimization increases the likelihood of finding dynamically stable systems:

$$E(A, G) = \sum_\mu (\alpha_0 A G - \gamma_0 R_0 G^T G)_{\mu\mu} + \sum_{\mu \neq \nu} |(\alpha_0 A G - \gamma_0 R_0 G^T G)_{\mu\nu}|.\tag{3}$$

We studied the topologies obtained by minimizing the condition in Eq. 3, by considering a large set of consumption matrices with $N_R = N_C = 25$ with different connectances and mean ecological overlap. We define the consumption (secretion) overlap of a pair of species i and j counting the fraction of resources consumed in

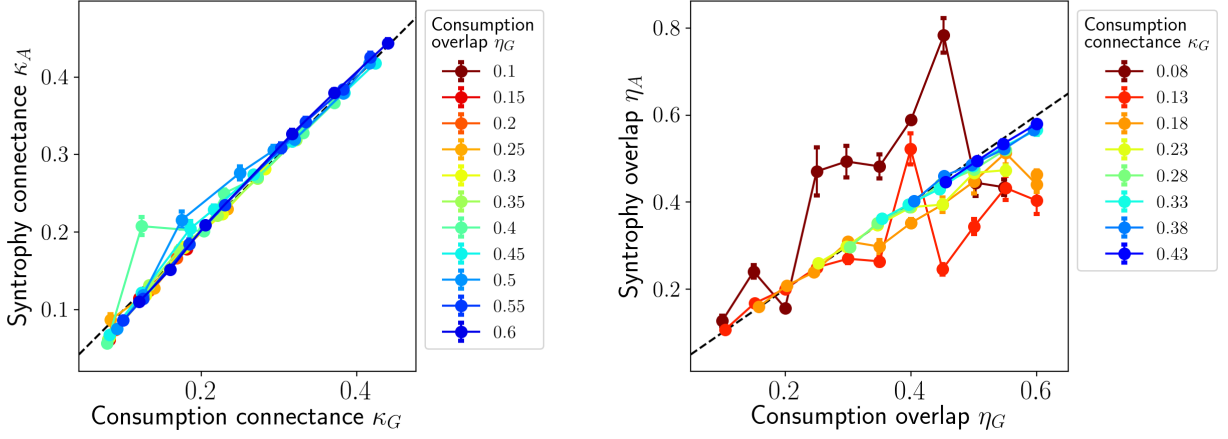


Figure 1: Optimized syntrophy matrices have similar connectance and ecological overlap than their correspondent consumption matrices. (A) Illustration of the optimization procedure. For each consumption matrix, we randomly searched for a syntrophy matrix minimizing the function in Eq. 3. An example of the minimization is displayed. (B) Connectance and (C) ecological overlap of the optimized syntrophy matrices against their correspondent consumption matrices.

matrix $X = G$ (or secreted $X = A$) by both species, i.e. $\sum_{\mu} X_{i\mu} X_{j\mu} / \min(\sum_{\mu} X_{i\mu}, \sum_{\mu} X_{j\mu})$. We then define the mean consumption (secretion) overlap, η_G (η_A) taking the mean across all pairs. We searched with a Monte Carlo algorithm the matrices A minimizing the objective function in Eq. 3 (optimized matrices, OM, Fig. 1A). Strikingly, the OM have a connectance similar to the one of the consumption matrices from which they were derived (Fig. 1C) and their mean secretion overlap is also similar to the correspondent mean consumption overlap (Supplementary Fig. 1).

To understand the consequences of the optimization we studied the feasibility (namely, the volume of parameter space compatible with species coexistence), and the local dynamical stability of model systems with different combinations of G and A matrices. In our computations, we compared each OM with A matrices that are either fully connected, or random matrices (RM) with the same connectance than the OM. To make systems with different A matrices comparable, we set for all systems the same metaparameters (γ_0 , α_0 , l_0 , S_0^* and R_0^*), and we verified the feasibility of each system by solving the ODEs at the fixed point for m_{μ} and d_i , and asking if these parameter were positive. For each combination of metaparameters, we generated 200 realizations by randomly drawing parameters from uniform distributions around the metaparameters, and we considered a combination feasible if all realizations were feasible.

For all pairs of G and A matrices we found that increasing the syntrophy strength α_0 reduced the volume compatible with feasible systems (Fig. 2A). More specifically, systems with no syntrophy ($\alpha_0 = 0$) were more feasible, which was expected since non-zero syntrophy imposes more stringent constraints to solve the ODEs at a fixed point. Consistent with this idea, when A was fully connected feasibility was smaller, and it decayed faster with increasing α_0 . On the other hand, OM led to systems more feasible than fully connected systems and than random systems with the same connectance (XX test Supplementary Fig. 1). We observed in the box-plots, however, that the variance of the OM was also larger, suggesting that the optimization was less effective for some G matrices. To investigate which properties of G matrices influenced feasibility we represented, for $\alpha_0 = 0$, feasibility as a function of connectance and consumption overlap. We found that systems with optimized matrices have a more modest reduction if the connectance of the consumption matrix is small and their consumption overlap is high (Fig. 2B and C). Indeed, it is apparently a trend in which increasing the consumption overlap reduced feasibility (Supplementary Fig. 1), suggesting that increasing competition for the same resources hinders feasibility.

Next, we investigated if feasible systems were dynamically stable. For each combination of matrices and for each of the 200 realizations of the parameters within the feasible region, we computed the eigenvalues of the Jacobian, asking if the real part was negative for all eigenvalues. We considered that a system was linearly stable at each combination of metaparameters if all the realizations were linearly stable. Similar to what we found for feasibility analysis, increasing syntrophy strength reduced the volume of metaparameters compatible with dynamically stable systems (Fig. 2A), with fully connected matrices having the smallest volume. Consistent

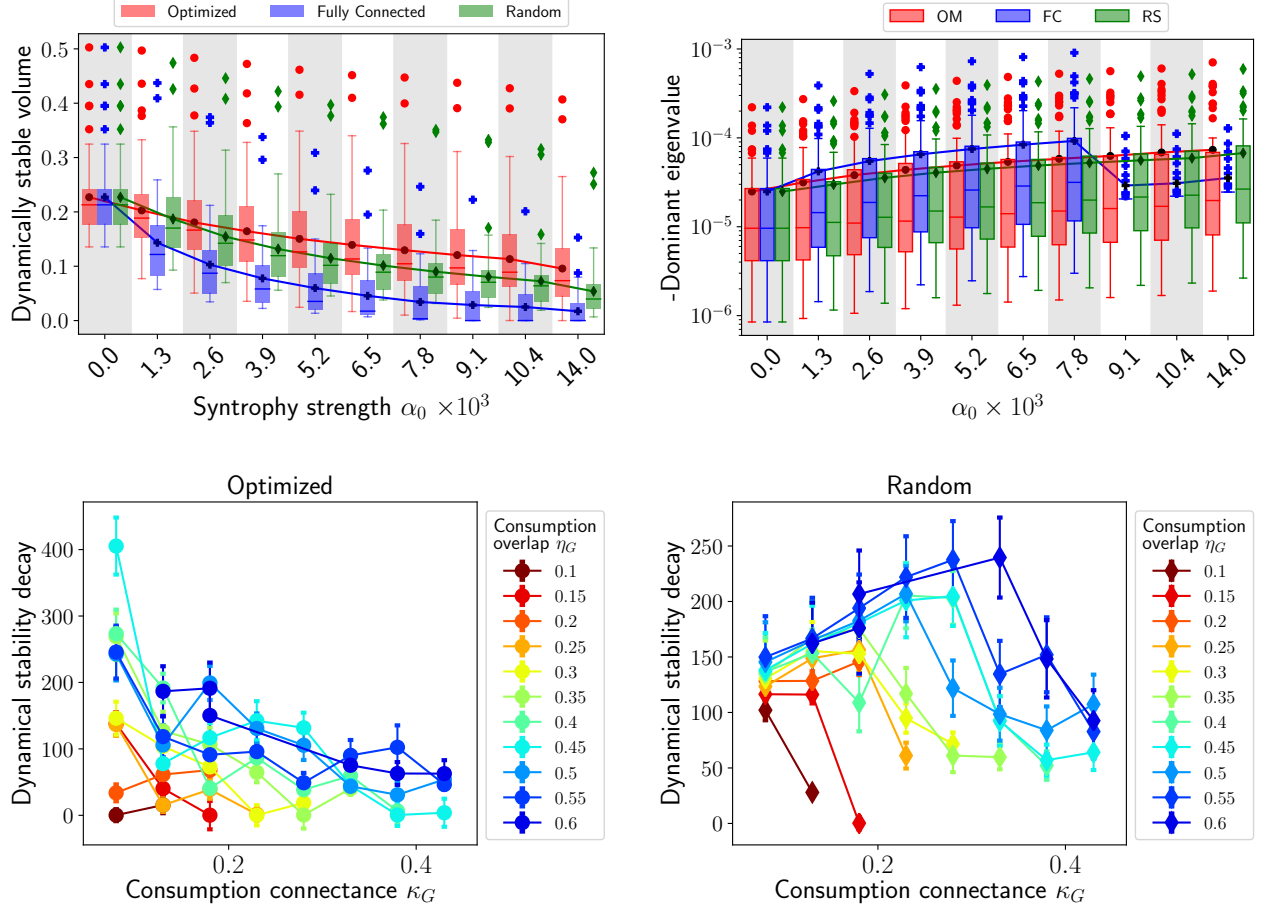


Figure 2: **Analysis of dynamical stability** (A) Decay of the volume of dynamically stable systems for different syntrophy strengths and syntrophy matrix topologies. Each box represents the distribution of consumption networks with the limits of the box being the interquartile region, the line indicating the median. The means are indicated with symbols, connected with continuous lines. (B) Rate of return to equilibrium after a perturbation in the abundances, versus the syntrophy strength for different topologies of the syntrophy matrix.

with our theoretical result, systems with OMs had the largest volume, and the difference with respect to random matrices became more significant for higher syntrophy values.

We then analysed, for those systems that were dynamically stable, the rate of return to equilibrium of resources and species abundances after a perturbation (Fig. 2B). We found that syntrophy enhanced the rate of return, and that this increase was more marked for systems with fully connected A matrices. Nevertheless, when syntrophy was high, since fully connected systems were less feasible, there was an abrupt drop in the rate of return. On the other hand, the median rate of return for systems with OM was always lower than the one for systems with RM, through the entire range of syntrophy values tested.

These result suggested that the volume of dynamically stable systems was inversely related to the rate of return. We confirmed this extent in Fig. 3A representing the mean rate of return across all dynamically stable systems, against the volume of parameters in which these systems were defined. The linear relation indicated a direct connection between the main eigenvalue of the Jacobian and the volume, which is explained noting that the higher the eigenvalue is the closer it is to zero, and hence the more likely it is that any changes in the parameters shift the eigenvalue to the unstable region ($\lambda_1 > 0$).

We investigated the connection between the rate of return, the dynamically stable volume and the ecological interactions by transforming the full system governed by Eqs. 1, into a LV system. Following previous work [Refs], in Supplementary Materials we show that near equilibrium the indirect interactions between species through resources can be described by a LV effective competition matrix. Specifically, when the input of resources, l_0 are

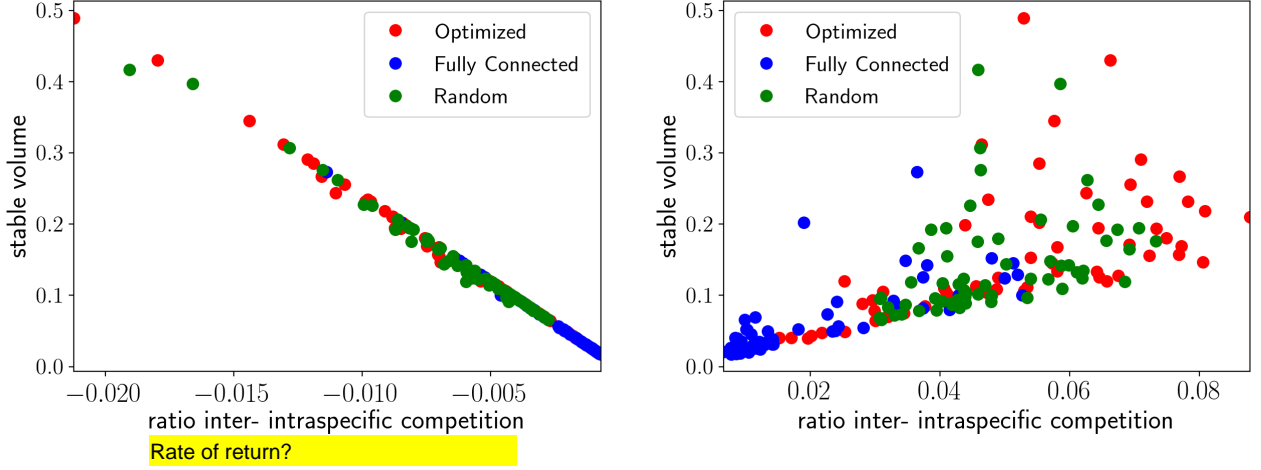


Figure 3: *Effective competition and dynamical stability*

Plot rate of return vs ceff

large or when the equilibrium abundances of species are small, the matrix takes the particularly simple form

$$C_{ij} \approx \sum_{\mu} \frac{\sigma_{i\mu} \gamma_{i\mu} S_i^* R_{\mu}^*}{S_i^* l_{\mu}} (\gamma_{j\mu} R_{\mu}^* - \alpha_{\mu j}). \quad (4)$$

If there is no syntrophy ($\alpha = 0$) the matrix describes pure competition between resources at steady-state. Interestingly, when there is syntrophy ($\alpha > 0$) we recover previous results for mutualistic systems (e.g. flowering plants and their pollinators) showing that mutualistic interactions effectively reduce the effective competition between species [Refs]. In Supplementary Materials we show that positive definiteness of the effective competition matrix is a necessary condition for dynamical stability of the full system. Moreover, if all terms of C are positive, which is always true when there is no syntrophy and we expect it to be true for dynamically stable systems (note that feasibility imposes that $\alpha < \gamma$), it is possible to derive a parameter encoding the effective competition of the system (see Supplementary Materials):

$$\rho_{\text{eff}} = \frac{1}{N_S - 1} \left(\frac{\lambda_1(C)}{\sum_i C_{ii}/N_S} - 1 \right). \quad (5)$$

The effective competition parameter, ρ_{eff} , represents the ratio between the interspecific competition ($\lambda_1(C) - \sum_i C_{ii}$) and the intraspecific competition ($\sum_i C_{ii}$) and effectively encodes all the properties of the system at the fixed point, including the topologies of G and A .

In Figs. B-C we show that increasing ρ_{eff} increased the volume of dynamically stable systems, and decreased the rate of return to equilibrium (Fig. C). Therefore, for fixed intraspecific competition, the combination of species reducing the most the interspecific competition maximizes dynamical stability (as measured by the rate of return to equilibrium after perturbation).

Our results shed some light on how complex microbial communities could form and maintain when there is syntrophy. In the comparison between systems with and without syntrophy, we chose a conservative scenario in which all resources are externally supplied. This scenario favours purely competitive systems, since those with syntrophy must fulfill more constraints at the fixed point, hence being less feasible. Among those with syntrophy, we observed that random systems were more feasible, which could be an advantage at the first stages in which a set of species encounter.

Then we observed that, once the consortium of species is feasible and dynamically stable, syntrophy enhances dynamical stability, as measured by the rate of return to equilibrium. Importantly, the lower was the effective competition the more the rate of return increased. Since, at equilibrium in the effective system the abundances can be written as $S = C^{-1}p$, with p being the effective species productivities (see Supplementary Material), reducing the effective competition increases species abundances. Therefore, we may expect that, once a feasible community is formed, selection would favour interactions that reduce the effective competition. Indeed, the analysis of some OM having a low effective competition reveals a guild structure, in which groups of species ... This may be seen as a theoretical support for the existence of metabolically cohesive consortia (MeCoCo) [Ref], namely groups of

interacting species through metabolic interactions, that are persistent thanks to their enhanced stability against perturbations, also supported by other theoretical works [Refs]. Moreover, solving in Eq. 5 for the number of species, N_S , results in an inverse relation between diversity and the effective competition $N_S \propto \rho_{\text{eff}}^{-1}$. Therefore, reducing ρ_{eff} increases the number of species that the system can host hence promoting biodiversity, which may help explaining the vast diversity observed in microbial communities.

We didn't consider other possible scenarios such as one in which some resources are not externally supplied but produced by species, which should favour syntrophic systems, in particular for some types of stability not analysed here such as structural stability [Refs]. In structural stability, the parameters of the model (most notably the input of resources, which could be controlled in experiments) and not the abundances are perturbed. Hence, we may expect systems with syntrophy to be more structurally stable, because alternative resources are available when those supplied are perturbed. Indeed, for LV mutualistic systems it was shown that reducing interspecific competition enhanced structural stability, hence promoting biodiversity [Ref]. These scenarios will be studied in future work.

In summary, our results suggest that syntrophy may have an important role in the formation and maintenance of microbial communities by reducing the effective competition, which in turns favours dynamical stability and promotes biodiversity.

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Software availability

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