

Coalescence of cohesive microbial communities

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Abstract

Community assembly, the process whereby species come together and interact to form functioning and coherent aggregations, is an old-age unsolved problem in ecology. In the microbial world, it is common that whole communities come into contact with each other and reassemble into a new community. This process has been termed community coalescence. The mechanisms that govern these events are poorly understood, partly because theoretical work in community coalescence rarely considers communities with mutualistic interactions, which are pervasive in microbial consortia. In this work, I use a new consumer-resource model to simulate communities harbouring competitive and mutualistic interactions, and propose a measure of community cohesion that predicts the outcome of microbial community coalescence. The proposed metric explicitly quantifies the so-called *cohesiveness* exhibited by microbial communities. It reproduces an important previous result, i.e., that more cohesive communities are more successful in community coalescence events while pinning it down to more realistic assumptions about the interactions in the community. The consistency of my results with previous works demonstrates that the collective coherence exhibited by coalescing communities is a general consequence of ecological interactions, resource partitioning, and the community shaping its environment. The proposed cohesion measure can be used to guide coalescence experiments in which different communities are successively combined until a desired beneficial functioning is reached.

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1 Introduction notes

- State my aims/hypotheses/questions by the end of the introduction.

- Why is it interesting? Why don't we know the answer?

Following, what I want to talk about

- Will a coalesced community be more perssistent than a naive one upon a event if it has a history of coalescence?

- How cohesive a community is when we analyze it in terms of cohord and dominant species?

- say at some point how many possible networks there are.

- measure community productivity and check that the correlation breaks down because there is co-selection.

- microbial ensamblages

13 2 Introduction

14 Microbial communities are widespread throughout our planet, from the deep
15 ocean to the human gut, and they play a critical role in natural processes
16 ranging from animal development and host health (Huttenhower et al. 2012)
17 to biogeochemical cycles (Falkowski et al. 2008). These communities are very
18 complex, often harbouring hundreds of species (Gilbert et al. 2014), making
19 them hard to characterize. Recently, DNA sequencing has facilitated a high-
20 resolution mapping of these consortia, opening a niche for ambitious theorists
21 and experimentalists to collaboratively disentangle the complexity of these sys-
22 tems (Marsland et al. 2019, Goldford et al. 2018, Goyal & Maslov 2018, Fried-
23 man et al. 2017, Costello et al. 2012). One of the problems yet to be solved is
24 community assembly – the process by which species come together and inter-
25 act to establish a community. Contrary to what is found in the macroscopic
26 world, in microbial ecology, it is common that whole communities move to a
27 region where they encounter another community. The process by which two
28 or more communities that were previously separated join and reassemble into a
29 new community has been termed *community coalescence* (Rillig et al. 2015). This
30 type of event repeatedly happens in nature due to abiotic (wind, tides or river
31 flow), biotic (animal courtship, parent-offspring interactions or leaves falling),
32 and anthropogenic (industrial anaerobic digestion, agriculture, between-human
33 contact) factors (Castledine et al. 2020). Despite the frequency and importance
34 of microbial community coalescence, the mechanisms responsible for the com-
35 munity structure and function resulting from coalescence events remain poorly
36 understood.

37 Early mathematical models of community-community invasion revealed that
38 when two communities previously separated by a barrier merge due to its re-
39 moval, asymmetrical dominance of one community over the other one is likely to
40 occur (Gilpin 1994, Toquenaga 1997). As an explanation for this observation, it
41 was argued that, because communities have been assembled through a history of
42 competitive exclusion, they are likely to compete with each other as coordinated
43 entities, rather than as a random collection of species. This result is also shown
44 in new theoretical work, where consumer-resource models are used to show that
45 coalescing microbial communities exhibit an emergent cohesiveness (Tikhonov
46 2016, Tikhonov & Monasson 2017). These findings suggest that communities
47 arising from the struggle for existence of its members display a certain level of
48 coherence. These communities have been termed Metabolically Cohesive [micro-
49 bial] Consortium (MeCoCos) by Pascual-García et al. (2020) and suggested to
50 be pervasive.

51 Recent results from coalescence experiments of methanogenic communities sug-
52 gest that during a coalescence event between two communities, multiple taxa
53 from the same community act as cohesive units and are selected together (eco-
54 logical co-selection) (Sierocinski et al. 2017). Further experimental evidence of
55 co-selection in community coalescence has been reported in Lu et al. (2018),
56 where it was shown that the invasion success of a given taxon is determined
57 by its community members. The microbial communities used in these exper-
58 iments are characterized by complex cross-feeding interactions (Hansen et al.
59 2007, Lawrence et al. 2012, Embree et al. 2015), where the metabolic by-products
60 of one species are substrates for others. Furthermore, the type of interactions

present in a community has been suggested as a factor that might affect the outcome of community coalescence (Castledine et al. 2020). Yet, theoretical models used in community coalescence studies so far have considered competition between species as the only force driving community assembly. In this work, I explore the combined role of other types of interactions, namely, competition and mutualism, which appear to be ubiquitous in microbial communities. First, I use a new consumer-resource model that includes both facilitation of metabolites via by-product secretion, and competition for substrates, to simulate many instances of community assembly. Second, I propose a metric of community cohesion that accounts for both competitive and mutualistic interactions, and I measure the cohesion level in the simulated communities. Third, I apply the proposed metric to predict the outcome of microbial community coalescence events.

3 Methods and Results

3.1 Consumer resource model with cross feeding interactions

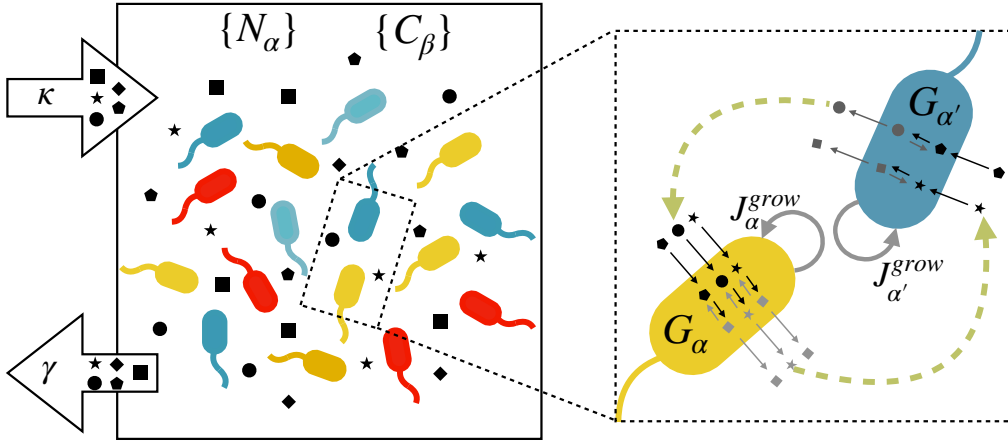


Figure 1: **Schematic of the model.** (left) Consider a chemostat where m metabolites are steadily supplied at rate κ and diluted at rate γ . Different bacterial strains coexist in the chemostat, and they consume the metabolites in the environment, C_β through their reaction networks G_α (right), to obtain the necessary power J_α^{grow} to increase their abundance N_α . The green arrows in the magnified portion emphasize that species α (yellow) facilitates metabolites to species α' (blue) and viceversa. The double arrows shown within the cells denote the fact that I am considering reversible reactions, so the reaction rate depends on both substrate and product concentrations.

In order to simulate communities with cross-feeding interactions, I use a consumer-resource model based on the the work of Marsland et al. (2019). Consider an environment with m resources present in different concentrations C_β , where $\beta \in \{1 \dots m\}$. Let now N_α denote the abundance of each bacterial strain α , present in the environment, where $\alpha \in \{1 \dots s\}$. Each species is uniquely characterized by the metabolic strategy it uses to harvest resources. This strategy is encoded in its reaction network G_α , a collection of chemical

reactions between the metabolites in the environment that produce energy that is used by bacteria for survival and replication (see Figure 1). If we now allow the dynamics of this system to unfold, the concentration of each metabolite C_β determines the dynamics of the abundances N_α of each species, which harvest resources through their different metabolic strategies. The changes in species abundance therefore translate into changes in the total supply and demand of resources. In turn, resource concentrations C_β are depleted until equilibrium is reached. A more rigorous description of the model, along with its mathematical form will now be presented.

Consider the population dynamics of s consumers (eg. bacterial strains) that feed on m resources. In this model, a species is defined by the metabolic strategy it uses to harvest energy from the environment. Let $G_\alpha(\mathcal{M}, \mathcal{N})$ be the metabolic network of species α (in the network theory sense), where \mathcal{M} is a set of nodes $\mathcal{M} = \{x : x \text{ is an integer from the interval } [1, m] \text{ labeling the metabolite}\}$ and \mathcal{N} a set of uni-directed edges $\mathcal{N} = \{(x, y) : x \in \mathcal{M}, y \in \mathcal{M} \text{ and } x < y \text{ (} x \text{ and } y \text{ are the product and the substrate of a chemical reaction, respectively)}\}$. The growth power of species α , J_α^{grow} will be given by the product of the amount of generated energy per reaction event η_i and rate q_i of each reaction, summed across all reactions in \mathcal{N} .

$$J_\alpha^{grow} = \sum_{i=1}^{|\mathcal{N}|} q_i \eta_i \quad (1)$$

where $|\cdot|$ denotes cardinality of a set. Refer to subsection 7.1 for specifications on q and η .

Every species has a maintenance cost χ_α that represents the required energy to sustain life, which is assumed to take the form

$$\chi_\alpha = \chi_0 \sum_{\mathcal{N}} (y - x) \quad (2)$$

where χ_0 is the average cost per reaction, x and y are the substrate and the product of the reaction, respectively, and the summatory term adds up the metabolite gap of all reactions. Therefore, the maintenance cost of one species increases if one or both of the following quantities increases: (1) the amount of enzymes a species is able to produce, and (2) the energy yielded by the reactions in which these enzymes are involved. Intuitively, the more enzymes a species is capable to express, the higher is the probability that at least two of them require starkly different conditions for optimal function. Therefore, expressing those enzymes simultaneously would imply maintaining two separate compartments, and incur in extra cost (see Supplementary material in Tikhonov & Monasson (2017)). The effect of the cost function (Eq. 2) is to ensure that neither generalists, nor specialists, are systematically favored during the community assembly.

Under this parametrization, the time evolution of the population of species α can be written as

$$\frac{dN_\alpha}{dt} = g_\alpha N_\alpha [J_\alpha^{grow} - \chi_\alpha] \quad (3)$$

where g_α is a proportionality constant relating energy to abundance of strain α . The dynamics of the resources depend on the incoming and outgoing resource fluxes due to the biochemical reactions taking place inside bacteria, as well as the resource external dynamics. The incoming resource flux of metabolite β

127 generated by strain α is its rate of consumption due to all the biochemical reac-
 128 tions possessed by α in which β is a substrate. The outgoing flux is that due to
 129 reactions in which β is a product.

$$\begin{aligned}
 v_{\alpha\beta}^{in} &= \sum_{\mathcal{S}} q & \text{with } \mathcal{S} &\equiv N \cap \{(x = \beta, y)\} \\
 v_{\alpha\beta}^{out} &= \sum_{\mathcal{P}} q, & \text{with } \mathcal{P} &\equiv N \cap \{(x, y = \beta)\}
 \end{aligned}
 \tag{4}$$

132 The external resource dynamics are modelled as a supply rate minus a dilution
 133 rate that depends on the resource concentration to ensure convergent dynamics.

$$h_{\beta} = \kappa - \gamma C_{\beta} \tag{5}$$

135 Therefore, the variation with time of the concentration of metabolite β has the
 136 form

$$\frac{dC_{\beta}}{dt} = h_{\beta} + \sum_{\alpha=1}^s (v_{\alpha\beta}^{in} - v_{\alpha\beta}^{out}) N_{\alpha} \tag{6}$$

138 Thus, the model is a system of $s + m$ coupled differential equations completely
 139 specified by Eqs. 3 & 6.

140
 141 In the following section, I characterize the communities that assemble after
 142 integrating a collection of these systems, where each system has 10 bacterial
 143 strains ($s = 10$) in an environment with 15 different resources ($m = 15$). For
 144 each system, species are assigned metabolic strategies drawn at random.

146 3.2 Community Assembly

147 Armed with this model I now simulate $n_s = 2 \cdot 10^3$ community assembly events
 148 of $s = 10$ species that interact in an environment with $m = 15$ substrates that
 149 are steadily supplied.

150 The values of the parameters of the model remain constant throughout all sim-
 151 ulations, and have been chosen motivated by biological processes (total free en-
 152 ergy of photosynthesis or glucose respiration) and to avoid pathological situations
 153 (species always being saturated or maintenance higher than the maximal amount
 154 of energy that can be harvested) (subsection 7.2, table 1). The reason for this
 155 is that, my aim is not to parametrize the model to reveal large-scale patterns
 156 found in experiments (although that would be a fruitful endeavour because of
 157 the rich parameter space of this model). Rather, I use it to simulate a set of
 158 microbial communities with cross-feeding interactions that will be later used in
 159 the community coalescence experiments.

160 In order to do so, I first create $s \cdot n_s$ random reaction networks, $G_{\alpha}(\mathcal{M}, \mathcal{N})$ (one
 161 for each strain) using the following procedure. Consider, the $m \times m$ adjacency
 162 matrix A_{ij}^{α} , whose elements; the edges (i, j) of G_{α} , represent chemical reactions.
 163 Since the reaction network is hierarchical ($i < j$, subsection 7.1), the adjacency
 164 matrix is an upper triangular matrix with zeros in the main diagonal (see figure
 165 **2B**), and the reactions possessed by strain α can be expressed as $(i, i + k)$, where
 166 k represents the k^{th} diagonal of A ($k \in \{1, \dots, m - 1\}$ with $k = 0$ being the
 167 main diagonal), and i is the row number of one of its elements ($i = 1 \dots m$). The

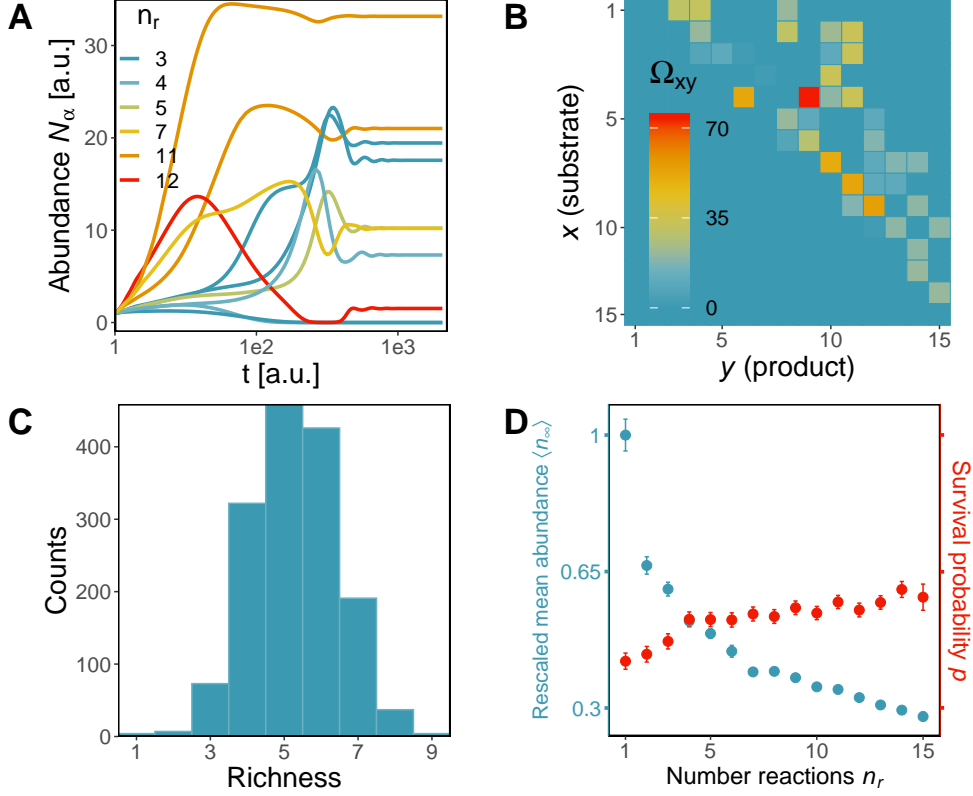


Figure 2: **Results from community assembly simulations.** Plots (A) and (B) exemplify one community assembly event and (C) and (D) convey results across simulations. (A) Time variation of species' abundance for one instance of community assembly with $m = 15$, $s = 10$, and a set of s randomly generated reaction networks. Time (x-axis) and population (y-axis) are measured in arbitrary units. Each time series is coloured according to n_r , the number of reactions possessed by the reaction network of each strain. (B) Community reaction network, obtained by summing the reaction network adjacency matrices of all species weighted by their respective carrying capacity: $\Omega = \sum_{k=1}^s N_\infty^k A_k$. The community reaction network is unique for each community, and it constitutes a blueprint of how that community depletes resources in the environment. Note that, according to the imposed constraints, reactions where $x > y$ are absent, and those where $y \gg x$, are rare. (C) Histogram of richness of the n_s simulations. (D). In blue, mean value of carrying capacity rescaled to 1 against the number of reactions n_r . In red, survival probability against number of reactions n_r . Species with less reactions (specialists) tend to be present at higher abundances than those with higher n_r (generalists), but they have a lower surviving probability.

168 reaction network G_α is constructed by sampling n_r reactions from different diag-
 169 onals, with decreasing probability as the order of the diagonal increases. Thus, I
 170 choose n_r pairs of integers (i, k) according to the algorithm summarized below.

- 171 1. Choose n_r by sampling it from a uniform distribution $U(1, m)$
- 172 2. Choose k by sampling one value from a truncated normal distribution
 173 $N(1, \sqrt{m-1})$ with limits $[1, m-1]$, and rounding it to the closest integer.
- 174 3. Sample i from a uniform distribution of integers $U(0, m-k)$.
- 175 4. The reaction $(i, i+k)$ is stored, and the process is repeated until n_r reac-
 176 tions have been sampled.

177 Several things are important to note about this algorithm. Firstly, sampling k
 178 from a truncated normal distribution ensures that high metabolite gaps (very
 179 energetic reactions) are not likely to happen. This introduces a bias against the
 180 presence of organisms with few and very energetic reactions, which are rare in
 181 microbial communities. Second, the truncation limits in step 2 have been chosen
 182 to respect the imposed constraint that reactions can only be of the form $i < j$.
 183 Third, the upper limit of the uniform distribution from which i is sampled is
 184 bounded by k , the diagonal we are sampling from.

185 When the sampling of reaction networks is completed, Eqs. 6 and 3 are in-
 186 tegrated using a Runge Kutta method (Dormand & Prince 1980) with initial
 187 conditions $N_\alpha(t=0) = 2$ and $C_\beta(t=0) = 0$.

188
 189 Relevant results stemming from the simulations of community assembly events
 190 are plotted in figure 2. The first two figures convey information about the
 191 dynamics and the resource consumption map of one particular community. In
 192 figure (2A), all abundances start increasing because all resources are present and
 193 steadily supplied. As the dynamics evolve, the community engineers its own envi-
 194 ronment by consumption of metabolites and secretion of by-products, causing the
 195 creation of ecological niches. During this process, species sorting results in com-
 196 petitive exclusion of species whose niches overlap. Alternatively, species whose
 197 niches are separate may engage in mutualistic relationships through metabolic
 198 complementarity (see figure 1), resulting in a net benefit to the interacting part-
 199 ners (Pascual-García et al. 2020). Figure (2B), shows that all metabolites are
 200 being consumed (all rows have at least one non-zero element), which is to say,
 201 that all vacant niches are being occupied.

202 The community assembly simulations generated communities with richness span-
 203 ning from 1 to 9 species (figure 2C), where specialists are, on average, more abun-
 204 dant than generalists (figure 2D, blue points). This can be attributed to several
 205 specialists being able to deplete all resources through their combined action more
 206 efficiently than one generalist (Pascual-García et al. 2020), thus, dominating the
 207 community at equilibrium. Note that in the simulated communities, while spe-
 208 cialists tend to be present at higher abundances than generalists, their survival
 209 probability is lower (figure 2D, red points). Upon competition, generalists have
 210 more alternatives to obtain energy, while specialists do not, and thus are more
 211 vulnerable to extinctions.

212
 213 Following the assembly of many synthetic communities, I propose a metric
 214 of community cohesion that takes into account all the interactions, mutualistic

and competitive, between the species in the community. The cohesion of the communities is then tracked during and after the process of community assembly. This measure is later used to predict the outcome of community coalescence events.

3.3 A metric of community cohesion

The cohesion of a community is ultimately determined by the nature of the interactions between its members. Since I am considering two types of interactions, namely, competition, and mutualism, the simplest way to render them into a mathematical expression is to subtract them.

$$Cohesion = Facilitation - Competition \quad (7)$$

Measuring levels of facilitation and competition within a microbial community is experimentally challenging. However, the metabolic strategies of each species are well determined in this theoretical framework. Therefore, I use the reaction network of each bacterial strain to compute their competition and facilitation indices with the rest of the species in the community.

Let s_1 and s_2 be two sequences of integers labeling metabolites. I am interested in measuring their *overlapping degree* $\xi(s_1, s_2)$, ie, the proportion of metabolites of s_1 that intersect with s_2 summed with the proportion of metabolites of s_2 that intersect with s_1 , normalized to 1.

$$\xi(s_1, s_2) = \frac{1}{2} \sum_{k \in s_1 \cap s_2} \left(\frac{D_{s_1}(k)}{|s_1|} + \frac{D_{s_2}(k)}{|s_2|} \right) \quad (8)$$

Here, k takes the values in the set that result from intersecting s_1 and s_2 . $D_s(k)$ is the number of elements from the sequence s that are equal to k . Vertical bars $| \cdot |$ express cardinality of a sequence. The purpose of all denominators in equation 8 is to normalize ξ to 1.

One way to capture the facilitation of a community is by calculating its facilitation matrix F , which is composed of the facilitation indices of all possible ordered pairs i, j of species in the community. Precisely, the facilitation index f_{ij} of species i towards species j , is given by the overlapping degree of the sequence of products y_i of species i , with the sequence of substrates x_j of species j . Equivalently, the competition matrix C gathers the competition level of the community. The competition index between species i and j , c_{ij} is given by the overlapping degree of the sequence of substrates x_i of species i , and the sequence of substrates x_j of species j . Thus,

$$F_{ij} = \begin{cases} \xi(y_i, x_j) & \text{if } i \neq j \\ 0 & \text{if } i = j \end{cases} \quad C_{ij} = \begin{cases} \xi(x_i, x_j) & \text{if } i \neq j \\ 0 & \text{if } i = j \end{cases} \quad (9)$$

Note that facilitation is directional but competition is not. This implies that $F_{ij} \neq F_{ji}$ and F is not symmetric, but $C_{ij} = C_{ji}$ and C is symmetric. Following the idea sketched in equation 7, a cohesion matrix Ψ can be defined using equations in 9, as an upper triangular $s \times s$ matrix whose elements are

253 given by

$$254 \quad \Psi_{ij} = \begin{cases} \frac{1}{2} (F_{ij} + F_{ji}) - C_{ij} & \text{if } i < j \\ 0 & \text{if } i \geq j \end{cases} \quad (10)$$

255 I choose to define Ψ as an upper triangular matrix because cohesion is not a
 256 directional measure; two species are not more cohesive if measured from i to j ,
 257 than from j to i . Instead, cohesion is a pairwise estimate independent of the
 258 direction of measure, so its matrix representation should be either symmetric
 259 or triangular. The triangular definition of Ψ allows me to interpret it as the
 260 adjacency matrix of a directed weighted network of cohesion between species. An
 261 example of this network, corresponding to the instance of community assembly
 262 shown in figures **2A** and **2B**, is illustrated before and after assembly in figures
 263 **3A** and **3B**, respectively. Nodes represent species and edges are weighted by
 264 their corresponding element in the cohesion matrix (represented in the figures
 265 by line thickness and color). Each species has a different node size and color.
 266 The size of the species encodes the number of reactions in its reaction network.
 267 The color encodes the node strength s_α , which is the sum of the edge weights
 268 connected to node α . This represents the total cohesion level of species α with
 269 the rest of species in the community, and it is calculated as

$$270 \quad s_\alpha = \sum_{j \neq \alpha} \Psi_{\alpha j} \quad (11)$$

271 The cohesion network is a powerful tool to fully track the changes in interac-
 272 tions between members in the community during its assembly. The two networks
 273 illustrated in figures **3A** and **3B** show that the top 4 species (s3, s0, s8 and s7)
 274 with higher total cohesion levels s_α remain extant after the community assem-
 275 bles. Additionally, the bottom 3 species (s1, s9 and s6) with lower s_α have more
 276 reactions in their reaction networks than the average. To test the generality
 277 of these observations I calculate the median survival probability after commu-
 278 nity assembly for each s_α rank position in the random community, across all
 279 instances of community assembly. Figure **3C** shows a clear correlation between
 280 these two measures, indicating that species with lower s_α go extinct more easily
 281 than more cohesive species. The survival probability is plotted also as a function
 282 of individual performance rank in figure **3C** (see subsection 7.4 for details on the
 283 calculation of the proxy of individual performance). The individual performance
 284 of a species is calculated here by measuring its equilibrium abundance in isola-
 285 tion. Interestingly, individual performance does not predict survival probability
 286 as well as total cohesion level, suggesting that in these experiments, the individ-
 287 ual fitness of a species becomes decoupled from its probability of success. This
 288 observation reflects the well-known fact that the success of a species is context-
 289 dependent, and observing a species in isolation does not measure its performance
 290 in the relevant environment (McGill et al. 2006, McIntire & Fajardo 2014).
 291 The stabilization of the system is normally accompanied by a cascade of extinc-
 292 tions. The effect of these extinctions in the cohesion at a community level can
 293 be conveyed by averaging the cohesion network

$$294 \quad \Theta = \frac{1}{T_s} \sum_{i < j} \Psi_{ij} \quad (12)$$

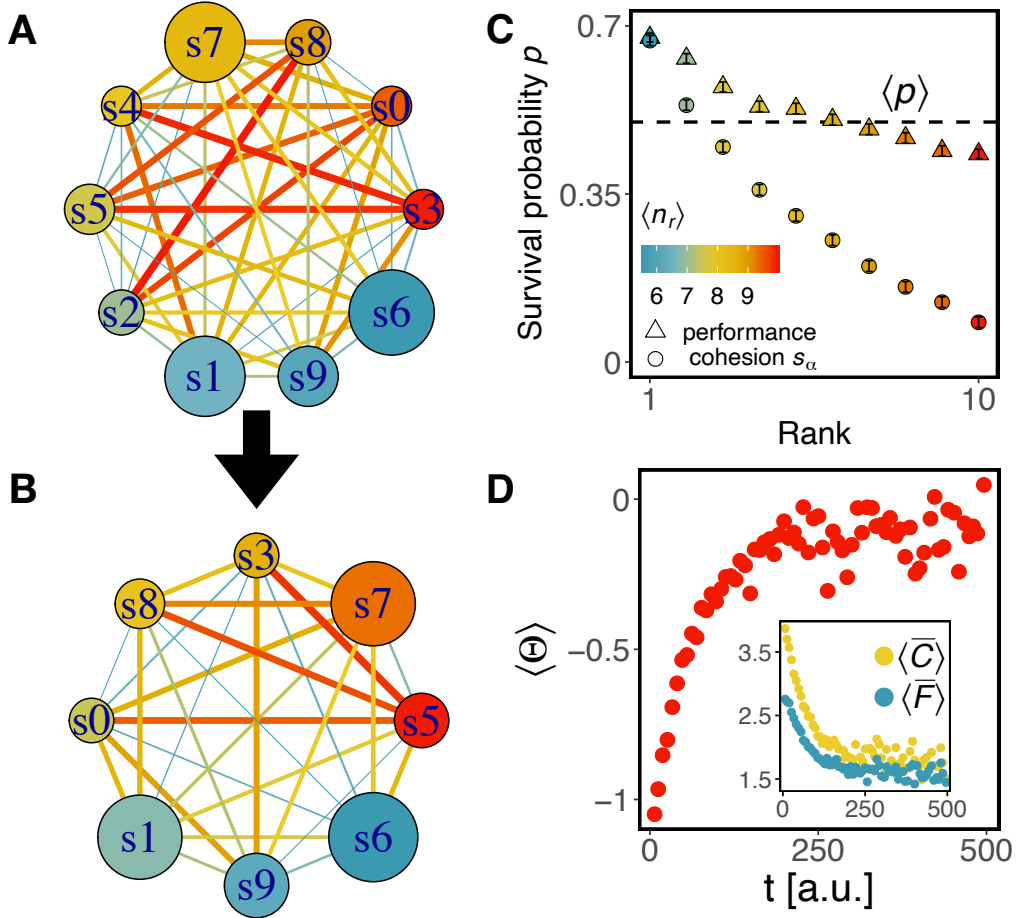


Figure 3: Cohesion metric across community assembly events. Cohesion network before (A) and after (B) community assembly. Thicker and red edges represent higher cohesion coefficient Ψ_{ij} between its nodes, species i and j . The color of the nodes changes from red to blue in anti-clockwise direction indicating decreasing total cohesion level s_α . The size of the node represents the number of reactions possessed by that species. (C) Median survival probability after community assembly as a function of cohesion rank (circles) and individual performance rank (triangles) of species in the random community (before assembly) across all simulations. Circles are weighted by the cohesion rank measured in the assembled community, e.g., weight is maximum when the first ranked species in the random community remains first ranked after assembly. The dashed line is the average number of extinctions across simulations. Species with higher cohesion and individual performance are less likely to go extinct during community assembly. However, cohesion predicts survival probability better than individual performance. The color of the points reflects the mean number of reactions of species in each rank. There is a slight correlation between the number of reactions and the survival probability. (D) Community-level cohesion averaged across all community assembly events, $\langle \Theta \rangle$, as a function of time. Every time a species goes extinct during community assembly, the community cohesion is recalculated with the remaining species. On average, community assembly follows trajectories where community cohesion increases. (D, inset) Community competition and facilitation levels averaged across all simulations. Both decrease during community assembly, but competition decreases faster. Decrease of facilitation is explained by the positive correlation between $\langle C \rangle$ and $\langle F \rangle$ (see Figure 4, A).

Where $T_s = \binom{s+1}{2}$ is the number of elements being summed: those in the upper diagonal of Ψ (the triangular number of order s). To investigate how the community-level cohesion changes over the course of community assembly, I measure Θ after the occurrence of every extinction across all simulations. This variation can be seen in figure **3D**, where the binned averaged value of all measures of Θ is represented during the first 500 units of time for all simulations. A systematic increase of community-level cohesion during the first half of measured time, and following stabilization near $\Theta = 0$ is observed. This increase is due to a faster decrease in community competition and facilitation levels, $\langle \bar{C} \rangle$, and $\langle \bar{F} \rangle$, averaged across simulations. (**3D, inset**).

This section presented a measure of cohesion, Ψ , that proved to be a useful tool to capture relevant insights of the dynamics of community assembly when mutualistic interactions are present. In the next section, I perform community coalescence experiments to test the predictive power of my metric, finding that communities with higher community cohesion are more successful upon coalescence.

3.4 Community-level cohesion predicts the outcome of community coalescence experiments.

Consider a coalescence event, whereby two communities previously separated come into sudden contact. In general, monodominance of one community after the mix reaches stable state is not guaranteed. Instead, both communities will contribute species to the final equilibrium. Can we predict which community will do so more successfully?

To answer this question I firstly, use all the simulated communities to populate a facilitation-competition (F-C) diagram where the axes are $\langle F \rangle$ and $\langle C \rangle$; community-level facilitation and competition respectively. They are calculated by averaging the non-diagonal elements of facilitation and competition matrices. Communities are scattered across the plot, bringing out two regimes: a mutualistic regime where $\langle F \rangle > \langle C \rangle$, and a competitive regime where $\langle F \rangle < \langle C \rangle$. The former case has a community-level cohesion Θ satisfying, $\Theta > 0$ whereas the latter has $\Theta < 0$ for the former (see subsection 7.3 for a rigorous description of the relationships between these variables). I then select communities with 4 species from the extremes of the two regimes, $\Theta \gg 0$ and $\Theta \ll 0$. This puts at my disposal two groups of communities with higher and lower levels of cohesion (blue and red strips in figure **4A**). I now perform coalescence experiments where a resident community \mathcal{C}_R from one group is mixed with an invading one \mathcal{C}_I from the other group. One would expect that communities from the mutualistic regime are more successful on average than those from the competitive regime. To confirm this, results from an 'elimination assay' competing pairs of communities from each group is presented in figure **4C**. Near five hundred pairs of communities are mixed, and correspond to the columns in figure **4C**. For each pair, species from both communities are equilibrated together. The rows in figure **4C** correspond to these species, and are ordered increasingly according to their total cohesion level s_α . For each species that goes extinct during the coalescent event, its provenance is identified (i.e. does it come from the blue or the red community?), and the corresponding tile in figure **4C** is coloured accordingly.

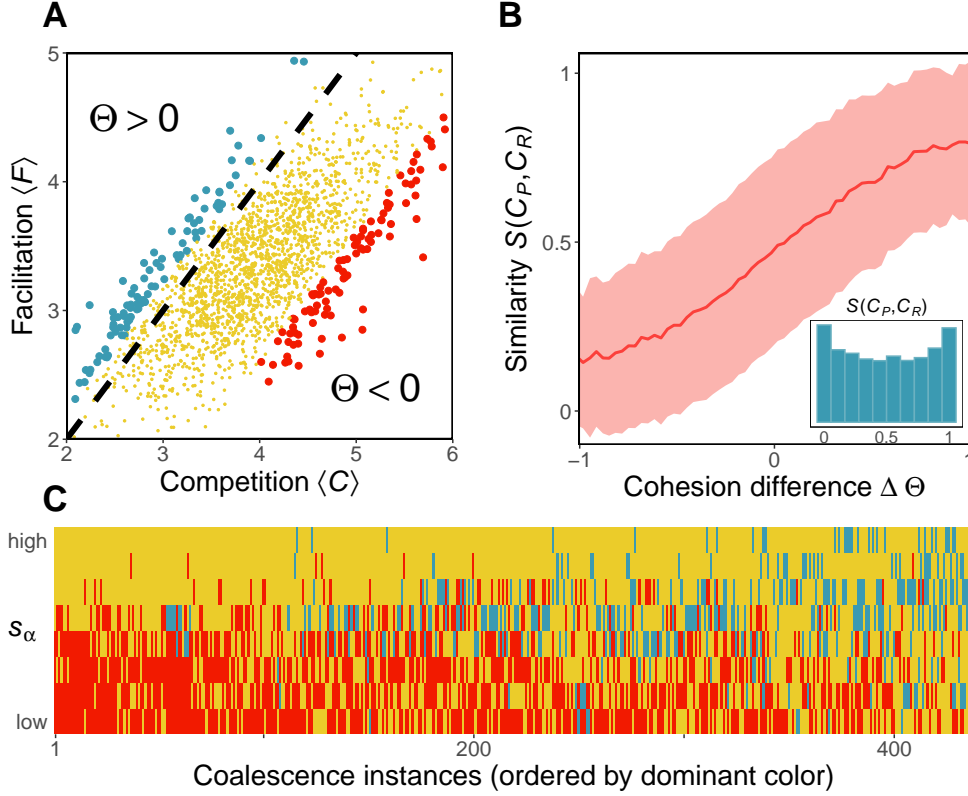


Figure 4: **Results from community coalescence experiments.** (A) Each simulated community is plotted in a competition-facilitation diagram. Communities above the dashed line $\langle C \rangle = \langle F \rangle$ have $\Theta > 0$, and thus they are in the facilitation-dominated regime. Communities below the dashed line have $\Theta < 0$, and therefore they belong to the competition-dominated regime. The extremes of each regime are selected (blue and red dots), and coalescence experiments where one community from the blue group mixes with one community from the red group are performed, only for communities of richness 4. (C) Altruistic communities ($\Theta > 0$) outperform competitive communities ($\Theta < 0$) in the latter experiments. In this elimination assay, each column represents one coalescence instance, and each element in a column is a species. Extinctions are coloured to match the group in plot A to which the extinct species belonged. There is a higher proportion of extinct species from the red group (more red tiles than blue tiles). (B) The outcome of community coalescence is predicted by community-level cohesion. The similarity between the post-coalescence community and the resident community, $S(C_P, C_R)$ is plotted as a function of the community cohesion difference $\Delta \Theta$ between them, for all possible coalescence events between 2 communities of richness 5. Shown is binned mean (100 bins) over communities with similar $\Delta \Theta$ (solid line) $\pm \sigma$ (shaded) (B, inset) Histogram of similarity showing that monodominance of one community after coalescence ($S = 0$, $S = 1$) is more frequent than a perfect mixing ($S = 0.5$)

342 The dominant colour is red, confirming that communities in the competitive
 343 regime experiment more extinctions, and thus, are worse at contributing with
 344 their members to the final equilibrium.
 345 Finally, I select the N communities with 5 species (figure **2B**), and perform
 346 all $\binom{N}{2}$ possible community coalescence events in which a resident community
 347 \mathcal{C}_R is mixed with an invading one \mathcal{C}_I . At each event, I calculate the similarity
 348 of between post-coalescence and resident communities as the normalized scalar
 349 product of their species abundance vector at stable state.

$$350 \quad S(\mathcal{C}_R, \mathcal{C}_P) = \frac{\vec{N}_\infty^R \cdot \vec{N}_\infty^P}{\sqrt{|\vec{N}_\infty^R|} \sqrt{|\vec{N}_\infty^P|}} \quad (13)$$

351 Additionally, I calculate the community-level cohesion difference $\Delta\Theta$ between
 352 the two coalescing communities. A clear non-linear correlation emerges when I
 353 plot similarity versus cohesion difference (figure **4B**). The larger the difference
 354 between community cohesion, the more similar is the post-coalescent community
 355 to its more cohesive parent. The non-linearity of this curve is a manifestation
 356 of the asymmetrical dominance reported in the first works of community coa-
 357 lescence (Gilpin 1994). This is more evident when looking at the histogram of
 358 similarities (**4B, inset**) for the coalescence experiments performed, where mon-
 359 odominance of one community ($S = 1, S = 0$) is more frequent than a perfect
 360 mixing ($S = 0.5$)

361 4 Discussion

362 A frequent way in which microbial communities come to be is through the mix of
 363 two or more communities, an event that has been termed community coalescence
 364 (Rillig et al. 2015). Numerous theoretical and experimental studies suggest that
 365 coalescing communities behave as 'coherent wholes', and compete against each
 366 other like coordinated armies (Gilpin 1994, Toquenaga 1997, Livingston et al.
 367 2013, Tikhonov 2016, Tikhonov & Monasson 2017, Sierocinski et al. 2017, Lu
 368 et al. 2018). To date, competition in coalescence is the most studied interaction,
 369 but more work is needed to understand how other types of interactions lead to
 370 different coalescence outcomes (Castledine et al. 2020). In this work, I investi-
 371 gated the behaviour of pairs of coalescent communities that harboured organism
 372 interdependence through metabolic complementarity (i.e., cross-feeding). How
 373 does including mutualistic interactions affect the outcome of community coales-
 374 cence?

375 To answer this question, I proposed to quantify the coherence of these consor-
 376 tia through a metric of community cohesion, Ψ , which computes the level of
 377 positive feedback between every pair of species in the community. I found that
 378 Ψ increased on average during community formation (see Figure **2D**). Tracking
 379 cohesion in coalescence events revealed a non-linear relationship between cohe-
 380 siveness and post-coalescence success, that is, more cohesive communities were
 381 coherently favoured during species sorting, and therefore dominated at equi-
 382 librium. This result constitutes strong evidence supporting that a community
 383 undergoing a coalescence event behaves as a 'coherent whole'. It is expected that
 384 members of cohesive communities have been ecologically co-selected; those indi-
 385 viduals from a key taxon whose presence provides an advantage for individuals

from other taxa are positively selected (Sierocinski et al. 2017). This contrasts with the alternative hypothesis suggesting that those communities harbouring species with higher individual performance are the ones that would dominate in the formation of communities. Only weak support was found for this hypothesis (see Figure 2C). These two hypotheses are two extremes of a continuum. Although it certainly seems an exaggeration to view the community as a *super-organism*, it is also a perilous simplification to consider it as a mere collection of individuals, ignoring the fact that coevolutionary processes can play an important role in it (Rillig & Mansour 2017).

A recent idea that smoothly interpolates between these two extremes has been proposed in (Pascual-García et al. 2020). Metabolically Cohesive microbial Consortium (MeCoCos) are groups of microbes that exhibit a positive feedback loop, whereby they engineer their environment by both creating and using resources. They constitute an intermediate level of organization between the community and the individual. These groups have been hypothesized to be resistant against invasions because no other species would be able to harvest resources rapidly enough to compete with the established members. My finding that more metabolically cohesive consortia are more successful in community coalescence experiments confirms their hypothesis. A possible line for future research would be to use the metric of cohesion to identify MeCoCos in the synthetic communities, and track their behaviour to try to answer the following question: can we understand microbial community assembly as a succession of MeCoCos coalescence events?

Another prediction of Pascual-García et al. (2020) is that MeCoCos efficiently deplete resources to the lowest concentration. This result was obtained in the absence of mutualistic interactions by Tikhonov (2016), who showed that when two communities compete, the one that is more efficient at simultaneously depleting all substrates will dominate. Intuitively, the more efficient community (higher community-level fitness) succeeds because it is able to engineer an environment suitable for its members. In his model, the dynamics conveniently took the form of optimizing a community level function (MacArthur 1969). In this more general model, collective dynamics were not reducible to solving an optimization problem, yet, the results here are consistent with Dr. Tikhonov's work. Specifically, the cohesive communities of my work behave in the same way as the more efficient (or more fit) communities in his work when it comes to community coalescence (see figure 4). This confirms that more cohesive communities are also more efficient at depleting resources simultaneously.

The results obtained in theoretical works of community-community competition up to date have been consistent across different models, and types of interactions. Therefore, the coherence exhibited by microbial communities seems to be a general consequence of ecological interactions, resource partitioning, and the community shaping its own environment (niche construction).

4.1 Empirical relevance

Measuring cohesion in the synthetic communities used in this work was possible because the theoretical framework of the model provided readily usable reaction networks. The aim of these is to resemble bacterial metabolic pathways, and

433 thus lay out the foundations for the formulation of consumer-resource models
434 that characterize more realistic microbial communities. A promising direction of
435 research would be to focus on parametrizing the model based on available high-
436 resolution metabolic networks in the literature and then attempting to use it
437 to predict the outcome of community coalescence events. This could be applied
438 then to drive the community in question, through successive coalescence events,
439 towards states where certain functions are optimized (e.g. methane production,
440 as in Rillig et al. (2016), crops disease resistance as suggested in Calderón et al.
441 (2017) or the abundance of a healthy donor community in the gut microbiome,
442 reviewed in Wilson et al. (2019) and Wang et al. (2019)).

443 4.2 Caveats

444 5 Discussion notes

- 445 • This thesis addresses the question of what are truly the mechanisms ex-
446 plaining what experiments show? An alternative measure of cohesiveness
447 that stems from more realistic modelling of microbial ecosystems is able
448 to reproduce these results and thus is closer to uncover what are the real
449 mechanisms behind community cohesion.
- 450 • community coalescence is a way to explicitly show and test the cohesiveness
451 of microbial communities while asking questions about how these commu-
452 nities came to be.
- 453 • discuss why I chose m as the upper limit for the number of reactions that
454 a strain can possess.
- 455 • Discuss why the traditional fitness (how fast resources are consumed) doesn't
456 correlate with what I call fitness: community cohesion. Show that in the
457 case of pure competition, it does (Tikhonov 2016), but in the case of purely
458 facilitation, it doesn't
- 459 • My measure of cohesion is an approximate one. Does facilitation help the
460 same degree that competition bothers?
- 461 • talk about environment engineering, and reference
- 462 • Maybe facilitation is actually not that important, But competition, and
463 functional groups, the ones that drive cohesion..
- 464 • There is no allusion to individual species fitness, because here it's more
465 important the cohesion between them.
- 466 • Talk about innovation rather than improvement when it comes to facilita-
467 tion.
- 468 • One species can change the whole community because it affects all of it!
469 (all the elements in the matrix, or a good portion of them.)

470 6 Things to do in the future

- 471 • Ask Emma about papers of hierarchy of metabolites
- 472 • Find a paper that says that organisms with few and very energetic reactions
473 are rare.
- 474 • Should I include a page at the end specifying what things did I do, and
475 what things didn't I do, and that way I don't have to do it during the
476 paper?
- 477 • make a nice looking table of the paramters of the model.
- 478 • Revise the cohesion of my thesis as a whole: are sections well separated?
479 Do they link well with each other? For example, at the end of the model
480 presentation section, I can introduce the next one by saying that I will
481 investigate the dynamics of community assembly, and then just start with
482 that right away. Additionally, at the end of the cohesion section, I can
483 specify what is the type of coalescence events I am going to study next,
484 namely, those in which the environmet remains constant.
- 485 • Turn to my dictionary of cool words, and use them.
- 486 • Find a reference for the claim: The cohesion of a community is ultimately
487 determined by the nature of the interactions of its members.
- 488 • The cost of the model This cost model corresponds to the assumption of
489 approximate neutrality.
- 490 • change color and lables of nodes in figure 3
- 491 • add a concluding paragraph to each section.
- 492 • Consider transforming figure **3C** into a barplot, it seems more sensible.
- 493 • In the presentation of the model, talka bout the number of possible net-
494 works that it has (efectively random), and also that different choice of
495 initial biomass of each species would only alter the transient dynamics,
496 but not the outcome of assembly,: the equilibrium state where $\frac{dN_\alpha}{dt} = 0$
- 497 • Talk about simplifications of the model: deterministic dynamics and well-
498 mixed environment (acknowledge their importance).
- 499 • When talking about the fitness, mention that the success of a species is
500 context dependent, and that organisms modify their own environment.
- 501 • Talk about avoiding priority effects and species sorting in the methods,
502 when I say that the resources when mixing two communities are reset back
503 to 2 equiabundant concentrations.
- 504 • Talk about diversifying selection when saying that specialists are more
505 abundant.
- 506 • Talk about species sorting when describing the model in biological terms:
- 507 • synonym for mutualism metabolic complementarity.

- 508 • Broadly interacting taxa, taxa with a high level of cohesion, are positively
509 co-selected in community coalescence.
- 510 • cite Inferring metabolic mechanisms of interaction within a defined gut
511 microbiota?
- 512 • talk about how functionally redundant groups *those with similar metabolic
513 capabilities) tend to go extinct because they lead to competitive interac-
514 tions. On the other hand, members from different functional groups may
515 engage in mutualism or comensalism relationships. Members of related
516 through metabolic complementarity tend to occur.
- 517 • Include in the intro that including mutualisms has been suggested as a
518 next step.
- 519 • The same number of species to avoid selection effects.
- 520 • Change labels in nodes so that they are not s, which may be confused with
521 strength of the node.
- 522 • figure, or Figure. equation, Eqs, eq??
- 523 • Should I include any discussion on bottom-up vs top-down assembly?
- 524 • Talk about the upper bound and justify why my communities aren't richer
525 than 9 speces. Read Cui et al. (2020)

526 7 Appendix

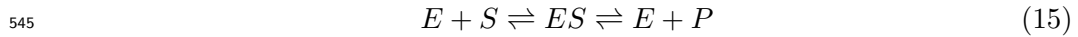
527 7.1 Reversible enzyme kinetics

528 Outside the the bacterial cell, the energy resides in the form of chemical potential
 529 μ held by the metabolites, and biochemical reactions inside the cell produce
 530 energy due to a difference in the chemical potentials of substrate and product. I
 531 assigned chemical potentials to each metabolite according to

$$532 \quad \mu_\beta = E \left(1 - \sqrt{\frac{\beta - 1}{m - 1}} \right) \quad (14)$$

533 where $\beta = 1, \dots, m$ and E is the energy of the most energetic metabolite. I have
 534 chosen this chemical potential function because I hope to find papers where they
 535 explain that there is a hierarchy on the metabolite energetic spectrum. This
 536 means that the energy produced by a reaction of the type $(\beta, \beta + 1)$ decreases as
 537 you go down the hierarchy. Reactions involving metabolites situated higher in
 538 the hierarchy are more energetic than reactions that involve those lower in the
 539 hierarchy.

540 The rate at which a given chemical reaction transforms substrate into product
 541 is modelled using reversible Michaelis-Menten enzyme kinetics. Thus, the model
 542 considers chemical reactions where a substrate S binds to an enzyme E to form
 543 an enzyme-substrate complex ES , which in turn produces a product P and
 544 recovers enzyme E .



546 The choice of fully reversible enzyme kinetics, instead of the traditional assump-
 547 tion of irreversibility in the second reaction, aims to capture more accurately the
 548 nature of biochemical reactions taking place in microbial communities. In these
 549 reactions the Gibbs energy change ΔG is not always big, which implies that the
 550 reaction of product formation can reach equilibrium at a similar time scale as
 551 the formation of the complex (Keener & Sneyd 2008). In this case, the tradi-
 552 tional irreversible Michaelis-Menten scheme breaks down, and more elaborated
 553 frameworks, like the fully reversible one that this model offers, need to be used.
 554 To comply with 2^{nd} law of thermodynamics, the network G_α is completely hier-
 555 archical, ie. the edges are unidirectional ($x < y$), going from the more energetic,
 556 to the less energetic metabolite. Thus, for the reaction scheme in 15 and the
 557 imposed thermodynamic constraint only reactions where $\Delta G^0 = \mu_P - \mu_S < 0$
 558 can take place.

559 With all the above considerations, the expression for the rate of reaction i poss-
 560 esed by strain α is given below. A formal derivation of equation 16 can be found
 561 in Hoh & Cord-Ruwisch (2000)

$$562 \quad q_{\alpha i} = \frac{q_m^{\alpha i} S_\alpha (1 - \theta_\alpha)}{K_S^{\alpha i} + S_\alpha (1 + k_R^{\alpha i} \theta_\alpha)} \quad (16)$$

563 Here, θ_α measures how far is the reaction from equilibrium (0 being the furthest,
 564 and 1 being equilibrium).

$$565 \quad \theta = \frac{[P]}{[S]K_{eq}} \quad (17)$$

566 where $[]$ denote concentration and K_{eq} is the equilibrium constant

$$567 \quad K_{eq} = \exp \left(\frac{-\Delta G^0 - \eta \Delta G_{ATP}}{RT} \right) \quad (18)$$

568 The energy produced by the reaction is then stored in the form of ATP molecules.
 569 In the model, η represents the moles of ATP molecules produced per mole of
 570 reaction. For a given reaction (x, y) eta I calculate eta as

$$571 \quad \eta = \frac{y - x}{m} \quad (19)$$

572 which represents the normalized metabolite gap between substrate and product
 573 of the reaction. Therefore, the higher the gap, the more energy will be stored.
 574

575 7.2 Table of parameter values and meaning

Parameter	Meaning	Value
m	Number of metabolites	100
s	Number of strains	10
ΔG_{ATP}	ATP Gibbs energy	$7.5 \cdot 10^4$
μ_0	Most energetic metabolite	$3 \cdot 10^4$
nATP	$\max \left(\frac{\Delta G_{S \rightarrow P}^0}{\Delta G_{ATP}} \right)$	4
η	Moles of ATP energy per reaction	0.5
q_m	Maximum reaction rate	1
K_S	Saturation constant	0.1
k_r	Reversibility constant	10
g	Growth factor	1
m	Maintenance factor	$0.2 \cdot J_{grow}$
κ	Externally supplied resource	1
γ	Dilution rate	0.5
N_0	Populations initial conditions	(1, 1, ..., 1)
C_0	Concentrations initial condition	(0, 0, ..., 0)

Table 1: Parameter meanings and their values

576 7.3 Relationship between Θ , F , C , and Ψ

577 7.4 Calculation of individual fitness

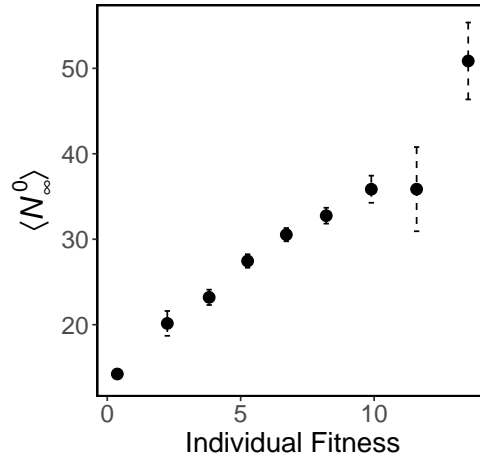


Figure 5: Abundance of 500 random species at isolated equilibrium as a function of proxy of individual fitness. Shown is binned mean (10 bins) over species with similar individual fitness. Errorbars are 1 standard error.

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