Environmental Microbiology

ENVIRONMENTAL MICROBIOLOGY

MINI REVIEW OPEN ACCESS

Paradox of the Sub-Plankton: Plausible Mechanisms and Open Problems Underlying Strain-Level Diversity in Microbial Communities

Akshit Goyal[1] | Griffin Chure[2]

[1]International Centre for Theoretical Sciences, Tata Institute of Fundamental Research, Bengaluru, India | [2]Department of Biology, Stanford University, Stanford, California, USA

Correspondence: Akshit Goyal (akshitg@icts.res.in) | Griffin Chure (griffinchure@gmail.com)

Received: 25 November 2024 | **Revised:** 15 February 2025 | **Accepted:** 25 March 2025

Keywords: community assembly | evolution/evolutionary processes/gene transfer/mutation | microbe:microbe interactions | microbial communities | microbial ecology | modelling and system analysis | theoretical ecology

ABSTRACT

Microbial communities are often complex and highly diverse, typically with dozens of species sharing spatially-restricted environments. Within these species, genetic and ecological variation often exists at a much finer scale, with closely related strains coexisting and competing. While the coexistence of strains in communities has been heavily explored over the past two decades, we have no self-consistent theory of how this diversity is maintained. This question challenges our conventional understanding of ecological coexistence, typically framed around species with clear phenotypic and ecological differences. In this review, we synthesise plausible mechanisms underlying strain-level diversity (termed microdiversity), focusing on niche-based mechanisms such as nutrient competition, neutral mechanisms such as migration, and evolutionary mechanisms such as horizontal gene transfer. We critically assess the strengths and caveats of these mechanisms, acknowledging key gaps that persist in linking genetic similarity to ecological divergence. Finally, we highlight how the origin and maintenance of microdiversity could pose a major challenge to conventional ecological thinking. We articulate a call-to-arms for a dialogue between well-designed experiments and new theoretical frameworks to address this grand conceptual challenge in understanding microbial biodiversity.

1 | Introduction

Natural ecosystems are remarkably complex, often encompassing organisms spanning the tree of life that directly and indirectly interact through their dynamic environments. The past century of technological and theoretical advancements have allowed us to probe the 'invisible' community members–the protists, microbes, and their associated viruses–revealing perplexing ecological phenomena. Studying these phenomena in natural environments has revealed a 'paradox of the plankton' (Hutchinson 1961). How do hundreds to thousands of species (Hong et al. 2006; Tran and Boedicker 2017; Hoshino et al. 2020; Shu and Huang 2022) coexist across long timescales (Goldford et al. 2018) despite the comparatively low diversity of available nutrients (tens to hundreds) they use to grow (Figure 1A)? Many studies have since proposed possible resolutions to this paradox (Roy and Chattopadhyay 2007; Record et al. 2014; Menden-Deuer and Rowlett 2014; Flynn et al. 2022). Each of these proposals provide new mechanisms by which species may be able to coexist on a limited pool of nutrients, thereby providing new ecological 'niches' that these species can occupy in order to coexist. Although species may coexist by occupying distinct niches, it is reasonable to hypothesise that competition *within* species (between strains, as defined in Box 1) is so intense that only one

---

Akshit Goyal and Griffin Chure contributed equally to this study.

Environmental Microbiology, 2025; 27:e70094
https://doi.org/10.1111/1462-2920.70094

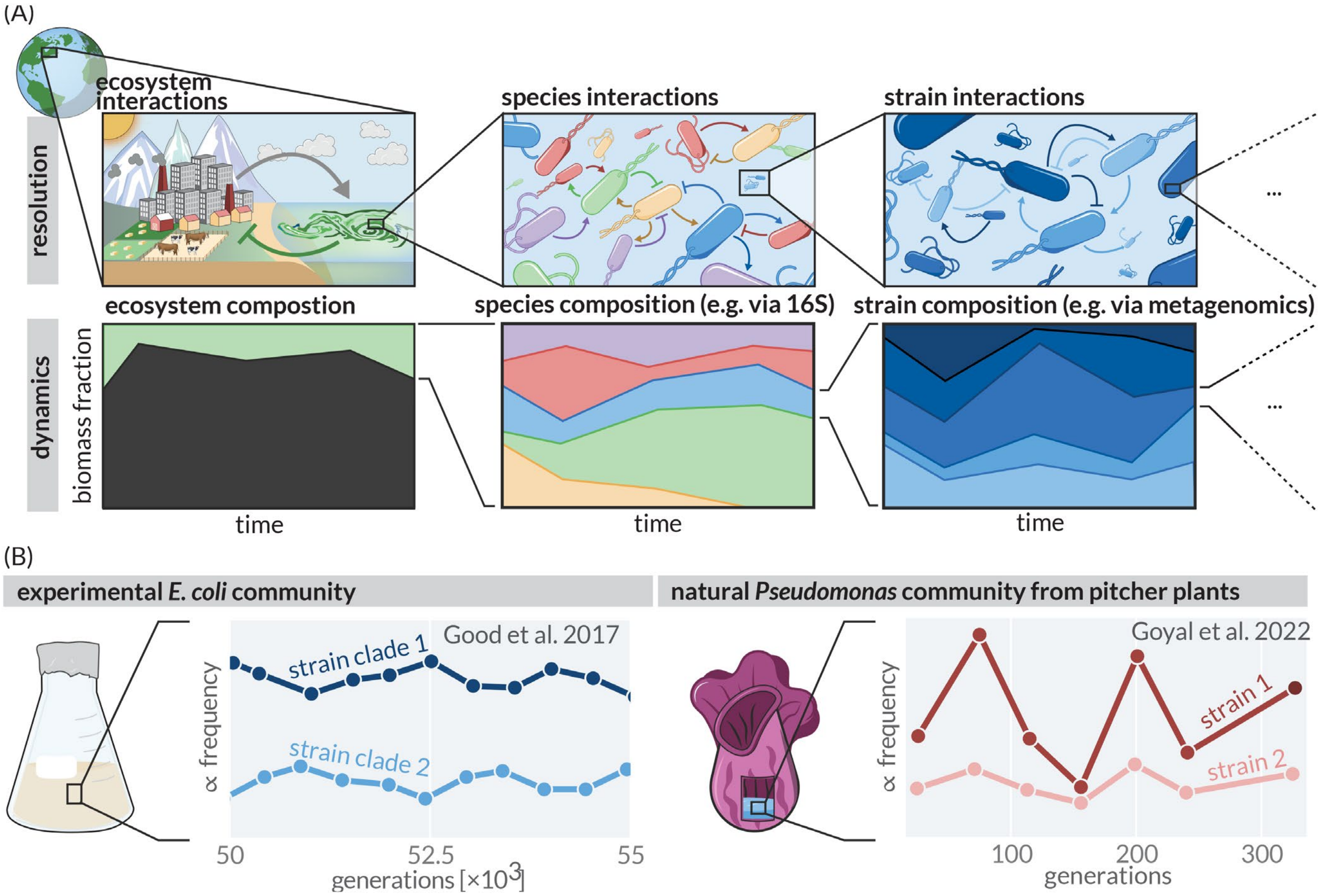


FIGURE 1 | Coexistence of organisms across scales. (A) Top row schematizes different levels of taxonomic resolution with hypothesized interactions between community members depicted using sharp- and blunted-arrows. Bottom row diagrams temporal dynamics of community biomass composition at each taxonomic level. (B, left) Observed coexistence of strain clades in an experimental *Escherichia coli* community (Good et al. 2017) and (B, right) observed coexistence of *Pseudomonas* strains in a natural community from pitcher plants (Goyal et al. 2022).

strain could dominate. How, then, can strains with nearly identical genomes occupy distinct niches?

Recent advances in DNA sequencing and genome reconstruction have permitted a deeper understanding of microbial diversity, allowing us to identify and track the dynamics of individual strains within these populations. In both natural and experimental settings, we see diversity at the strain level, where multiple distinct strains not only coexist but also display unique ecological dynamics (Figure 1B). On a genetic level, coexisting strains differ on the order of hundreds of base pair differences (or less) (Goyal et al. 2022; Garud and Pollard 2020; Garud et al. 2019), raising several key questions that make strain coexistence a qualitatively distinct problem from species coexistence: How can closely related strains coexist even when they are likely competing for the same nutrient sources? How do new strains emerge and compete in this environment? How do strains exhibit impressive physiological diversity when their genetic diversity is minimal? What is the structure of the genotype–phenotype maps in highly similar strains, and is it sufficient to yield the physiological diversity necessary for strains to coexist?

Here, we provide a concise overview of the plausible mechanisms that allow for the maintenance of strain-level diversity (which we refer to as 'microdiversity') in microbial communities, emphasising their caveats and open questions (Figures 2 and 3), and highlight that we lack a rigorous practical definition of what coexistence means across environmental and evolutionary contexts. We highlight both the potential explanatory power of these mechanisms and their pitfalls, while acknowledging the significant gaps in our understanding that remain. Finally, we issue an interdisciplinary call-to-arms for new experiments and theoretical tools to address the simple reality that, the closer we look, the more diversity and coexistence we find.

2 | Niche-Based Mechanisms

Niche-based mechanisms are among the most common ways to explain coexistence across diverse ecosystems. The central idea of niche theory (Chase and Leibold 2009) is that different resources provide different opportunities for growth and survival, and species vary in how they utilise these resources (Martiny et al. 2015; Monod 1949; Gralka et al. 2023; MacLean and Gudelj 2006; Kehe et al. 2021; Dal Bello et al. 2021; Goyal et al. 2021). However, coexisting species must differ sufficiently in utilising these resources, with each species typically being the 'best' among the others at utilising a specific resource or combination of resources. Each such combination is said to be a specific 'niche', and species are such to 'fill' or 'pack' niches.

BOX 1 | Candidate definitions of a 'strain'.

The taxonomic classification of life has been undeniably useful in piecing together evolutionary history. However, the genomic flexibility of microbes poses unique challenges to these classifications, often making species designations difficult. This problem is even more pronounced for microdiversity—how do we distinguish between microbes of the same species that have distinct traits and ecological behaviour, yet highly similar genomic sequences?

In this work, we use the term 'strain' to describe such differences, but a more quantitative and concrete definition would be incredibly useful. In our view, there are several ways one could define different strains, each with benefits and caveats. *Any two microbes are considered different strains if…*

- *…they descended from a clonal culture yet exhibit different physiological or ecological behaviours*. This definition is particularly useful in ecological contexts, where functional traits determine interactions and fitness. Indeed, grouping microbes into groups with similar traits–termed ecotypes–has allowed for near-real-time monitoring of microbial evolution in diverse environments (Good et al. 2017; Chase et al. 2018, 2021; Behringer et al. 2022). However, the practical limitations are significant as distinct traits or physiological differences are often difficult to quantify, highly context-dependent, and are not always easily mapped onto genetic variation, which is more easily measurable. Moreover, in natural environments, we rarely have access to complete life histories, making it impossible to verify clonal descent in most (but not all (Good et al. 2017)) cases. Finally, the stochastic nature of gene expression (Sanchez et al. 2013) and epigenetic regulation (Riber and Hansen 2021) means that genetically identical individuals can exhibit different phenotypes (e.g., spore formation (Tan and Ramamurthi 2014) and antibiotic susceptibility (Akiyama and Kim 2021)). As a result, this definition, while conceptually appealing, is difficult to operationalise in nature.
- *…a certain percentage of their DNA is identical, averaged across the entire genome*. This approach, termed genome-wide Average Nucleotide Identity (ANI), has been widely adopted for delineating microbial species ($<90\%$ identity) and has been proposed for defining strains at $>99.5\%$ identity (Rodriguez-R et al. 2023). The appeal of this definition lies in its precision and ease of measurement with modern sequencing technologies. However, the choice of a 99.5% threshold is ultimately arbitrary—why not 99.4% or 99.6%? Furthermore, it is unlikely that a single universal threshold applies across all microbial species, as genome divergence rates and recombination frequencies vary widely. This inherent subjectivity means that while ANI provides a useful operational definition, it does not necessarily capture meaningful ecological or functional differences between strains.
- *…they have identical 16S/18S rRNA sequences but differ elsewhere in their genomes*. This definition provides a simple and operationally convenient way to distinguish strains from more distantly related taxa, as rRNA sequences are widely used for broad taxonomic classification. However, it is unclear how much genomic divergence is permissible before two organisms should no longer be considered the same strain—differences could range from a single nucleotide polymorphism to substantial genomic rearrangements.

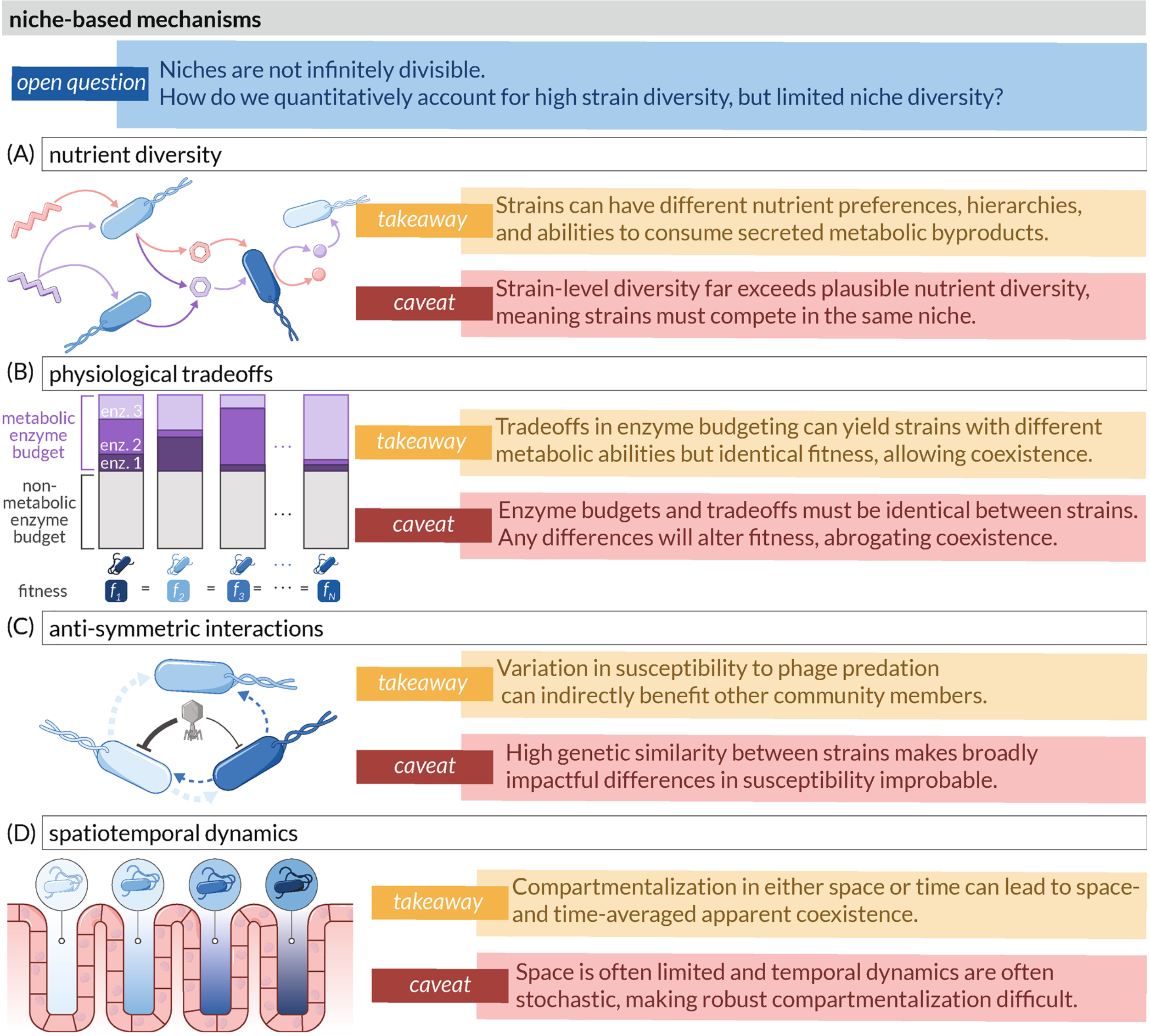
This is by no means an exhaustive list of definitions, but regardless of which definition one adopts, the framework explored in this review can help assess and contextualise microbial diversity at the strain level.

While this may be intuitive, rigorously quantifying and defining what makes a niche remains an unsolved problem in ecology. We have no general way to identify which resources can contribute to niches and how many niches are present in a particular environment (Martiny et al. 2015; Holt 2009) and, as a result, we cannot predict a priori how much coexistence we expect in a given environment due only to niche diversity. Nevertheless, recent studies have invoked various niche-based mechanisms that attempt to quantitatively explain strain coexistence. These mechanisms can be classified based on the three broad categories of resources that provide niches: nutrients, time, and space.

2.1 | Nutrients as Niches

Competition between organisms for nutrients–whether it be carbon-containing compounds (Machado et al. 2021; Ho et al. 2024), nitrogen sources (Zhou et al. 2017; Jones et al. 2018), or even wavelengths of light (Stomp et al. 2007; Chen and Blankenship 2011; Holtrop et al. 2021)—is amongst the most widely studied components of niche theory. Variation in nutrient preferences and utilisation strategies is necessary to enable coexistence, since niche theories place strict limits on how similar the metabolic abilities and growth behaviours can be for species to coexist (MacArthur and Levins 1967). Microbial species with completely non-overlapping nutrient requirements can easily coexist, whereas nearly identical requirements will force the slightly more competitive species to competitively exclude the others. Between these two extremes may lie a threshold of 'limiting similarity' (MacArthur and Levins 1967) where the minimal differences in nutrient preferences exist to allow coexistence, though the threshold is not strict (Abrams 1975; Roughgarden 1974). This is related to the idea of stabilising mechanisms in modern coexistence theory, where reducing niche overlap promotes coexistence (Letten et al. 2017; Chesson 2000). However, how can different nutrient consumption preferences emerge from organisms that are almost genetically identical? Recent work has highlighted that nutrient-based competition may indeed be an important force enabling coexistence between strains, with three key mechanisms promoting coexistence: diversity in metabolic abilities, shared physiological constraints, and anti-symmetric interactions via, for example, phage predation.

Recent work suggests that despite strong genetic similarities, closely related strains might indeed have different nutrient



Niches are not infinitely divisible.
How do we quantitatively account for high strain diversity, but limited niche diversity?

Strains can have different nutrient preferences, hierarchies, and abilities to consume secreted metabolic byproducts.

Strain-level diversity far exceeds plausible nutrient diversity, meaning strains must compete in the same niche.

Tradeoffs in enzyme budgeting can yield strains with different metabolic abilities but identical fitness, allowing coexistence.

Enzyme budgets and tradeoffs must be identical between strains. Any differences will alter fitness, abrogating coexistence.

Variation in susceptibility to phage predation can indirectly benefit other community members.

High genetic similarity between strains makes broadly impactful differences in susceptibility improbable.

Compartmentalization in either space or time can lead to space- and time-averaged apparent coexistence.

Space is often limited and temporal dynamics are often stochastic, making robust compartmentalization difficult.

FIGURE 2 | Niche-based mechanisms of strain-level coexistence. Through schematics, we highlight the four key niche-based mechanisms that have been suggested to contribute to strain coexistence in microbial communities. For each mechanism, we provide the major takeaway and caveat that may spur future work.

preferences and metabolic abilities (Figure 2A). For example, lab-domesticated microbial communities isolated from pitcher plants show patterns where strains with genomes differing by only 100 bases (99.99% genomic similarity) coexist over hundreds of generations with nearly uncorrelated dynamics (Goyal et al. 2022). At a genomic level, these strains primarily differ through mutations in transporters and metabolic enzymes/regulators, supporting the idea that strains can diversify in nutrient preferences. Similar behaviour has been observed in the Long-Term Evolution Experiment (LTEE (Lenski 2023)) where clonal *Escherichia coli* populations have been evolving in a fixed environment for 75,000 generations (and counting). At a genetic level, different *E. coli* variants have routinely lost the ability to metabolise a variety of substrates they never encounter (Leiby and Marx 2014; Favate et al. 2022), typically by the deletion or significantly reduced expression of different transporters. As each variant has evolved from a single ancestor, it is reasonable to assume that at any time, different lineages possess different metabolic abilities, and that this can affect the evolution of the population (Balakrishnan and Cremer 2023). There is a limit, however, to *how* different these abilities can be, considering they maintain nearly identical genomes and it is difficult to rationalise how this limited variation in metabolic abilities and preferences can explain more than a handful of strains coexisting at any given time (Fridman et al. 2022). Addressing this question rigorously requires quantifying genotype–phenotype maps for natural strains in community contexts—something that is challenging and can only be achieved via a combination of high-throughput measurements and physiological modelling.

The likelihood of coexistence may be increased when accounting for cross-feeding: the utilisation of metabolic waste products secreted by other community members (Fritts et al. 2021; Mee et al. 2014). At the strain level, this requires diversification into metabolically complementary types. The de novo emergence of cross-feeding from an isogenic population has emerged in the LTEE system (Rozen and Lenski 2000) where two major clades of strains coexist over at least 50,000 generations

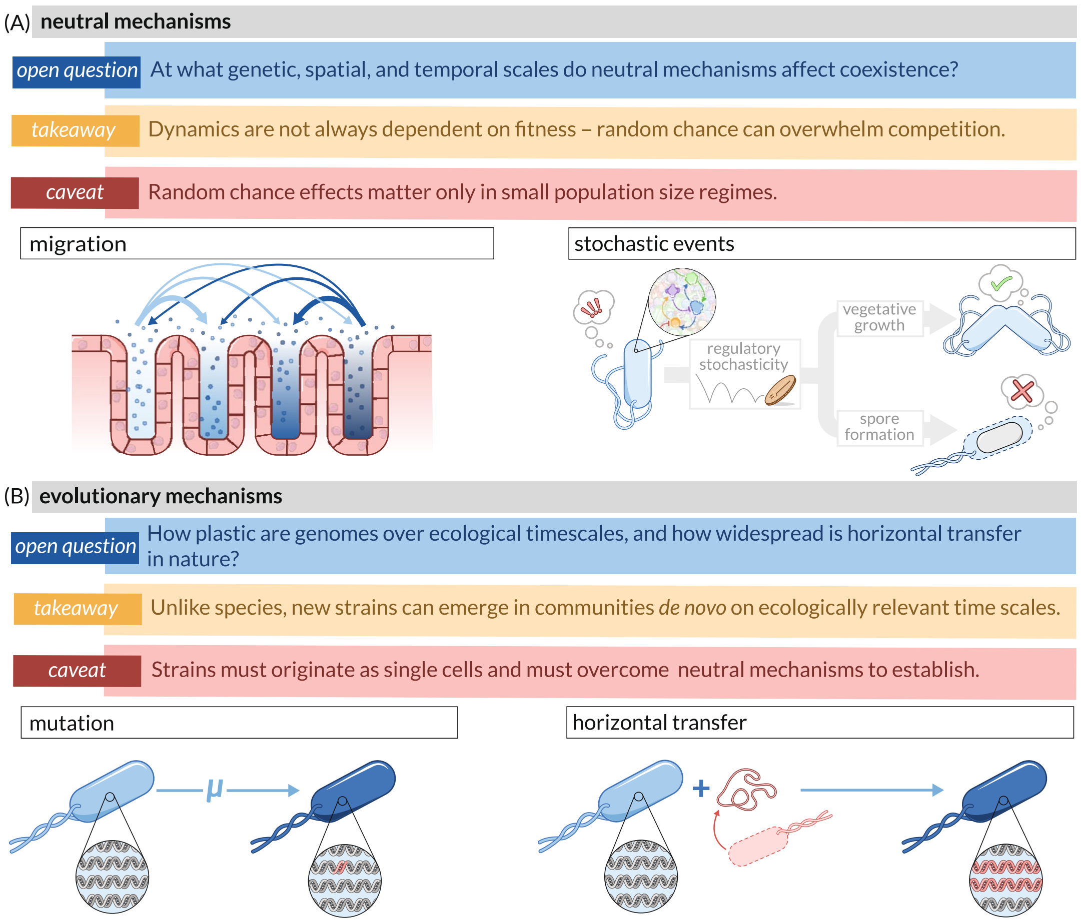


FIGURE 3 | Neutral and evolutionary mechanisms of strain-level coexistence. Through schematics, we highlight the two key neutral-based and two key evolutionary mechanisms that have been suggested to contribute to strain coexistence in microbial communities. For each mechanism, we provide a major open question, takeaway and caveat that may spur future work.

(Figure 1B, left). One clade consumes glucose in the environment and secretes acetate as a metabolic byproduct. A second clade then consumes this acetate to grow. This produces negative frequency-dependent stabilising selection between the two clades, permitting coexistence. Recent theory and genomic studies suggest that cross-feeding should be common (Goldford et al. 2018; Marsland et al. 2019; Goyal and Maslov 2018; Goyal and Krishna 2022; D'Souza et al. 2014; Kost et al. 2023) and its effect has been inferred in experimental studies (Sung et al. 2017; Culp et al. 2024; Pande et al. 2014). This is perhaps not too surprising given the molecular complexity within microbial metabolomes, yet it is difficult to imagine each metabolite producing a new niche for another strain. As of this writing, we only have a quantitative picture of the extracellular metabolite pools in a handful of contexts (Douglas 2020). Expanding our understanding of these pools in more contexts is crucial to understand the role that cross-feeding plays in promoting coexistence in natural environments. The widespread use of metabolic byproducts as nutrients would also, presumably, require systems to be spatially mixed, which is not the case in many natural systems.

Even if strains have the same set of metabolic genes, trade-offs in how they are expressed can be sufficient to permit coexistence (Figure 2B) by equalising fitness differences between them (Letten et al. 2017; Chesson 2000) These trade-offs can manifest due to a fixed cellular budget allocated towards metabolic enzymes (Posfai et al. 2017; Taillefumier et al. 2017). Increasing consumption of a nutrient requires expressing more metabolic components (such as specific enzymes or transporters), yet at the cost of making less of another. Such resource allocation has been deeply explored at theoretical and experimental levels (Scott et al. 2010, 2014; Sheng et al. 2015; Mori et al. 2021; Chure and Cremer 2023), making such tight control of enzymes budgets physiologically plausible. Modelling the collective dynamics of strains with different metabolic capabilities, but the same enzyme budget, has revealed that an infinite number of strains can coexist on a finite number of nutrients held at particular ratiometric values (Goyal et al. 2022; Posfai et al. 2017; Tikhonov and Monasson 2017). While such balancing of the environment and the strain-level metabolic budgets permits broad coexistence, it is incredibly fragile; if even one strain increases its fixed enzyme budget, the neutrality is broken and the coexistent community shatters (Posfai et al. 2017; Tikhonov and Monasson 2017). This can occur from stochastic physiological variation in gene expression (Sanchez et al. 2013), meaning that genetic variation is not necessarily needed to surpass this fragile barrier.

Finally, differences in susceptibility to viral (phage) predation can create the anti-symmetric interactions between strains necessary for coexistence (Figure 2C). A modality common to all microbial viruses is the extracellular attachment to specific proteins, permitting injection of genetic material into the cell. Bacterial strains can rapidly diversify in these receptors, leading to different phage binding affinities even with a single mutation. A strain that 'absorbs' a phage predator better than a closely related cousin will thus effectively promote its cousin's growth but hinder its own. Modelling the dynamics of a large number of these rapidly evolving strains leads to their coexistence that is maintained by huge fluctuations in strain populations across space and time (Pearce et al. 2020; Mahadevan et al. 2023). The growth of one strain comes with the death of another, but as a growing strain becomes more abundant, it is more likely to be infected even with a lower binding affinity. This leads to a continuous cycle of growth and death that can maintain several closely related strains. These dynamics are intriguing, but tracking and confirming them experimentally has remained an enormous challenge. It also remains quantitatively unclear how strong anti-symmetric interactions must be to yield broad coexistence between many strains.

2.2 | Space and Time as Niches

Most models of nutrient-based niche competition examine a steady-state regime where the environment is static and the community members grow at a rate comparable to the rate of nutrient inflow, similar to a chemostat (Goldford et al. 2018; Marsland et al. 2019; Goyal 2018). While this has been a remarkably powerful regime to explore experimental systems, they are hardly reflective of natural systems which almost always experience fluctuations in both space and time. In a steady-state environment, resource concentrations stay pinned to specific values and strains that cannot grow at these concentrations go extinct (Tilman 1982). In time-varying environments, however, resource concentrations are dynamic and, in essence, provide new niches for microbes to occupy and exploit (Wang et al. 2021). Time variation can thus create 'satellite niches' that can allow closely related strains to coexist (Fridman et al. 2022; Wang et al. 2021). Indeed, if strains have a trade-off between their growth rates at high and low resource concentrations, they are more likely to coexist. Even in the absence of such a trade-off (Fink et al. 2023), these computational studies show that coexistence is still possible, and a trade-off between surviving strains still emerges (Wang et al. 2021), but the number of strains that can coexist significantly diminishes, typically limited to only a few of the same species.

Changes in nutrient concentrations can either be systematic and predictable, as in a serially diluted batch culture (Lenski 2023), or stochastic and uncertain, as in naturalistic environments with feast-and-famine cycles (Madsen 2011; Sokol et al. 2022). In the former, nutrient concentrations decrease over a dilution cycle as strains grow by depleting the initially supplied nutrients. Such time variation typically allows the linear scaling of the number of coexisting species with the number of nutrients. Models of the latter scenario, however, suggest a quadratic scaling—a significant increase in the number of coexisting species per nutrient (Bloxham et al. 2024). It remains unclear whether these scaling relationships hold at the level of strains where physiological differences and nutrient preferences are less divergent. In general, one would expect more environmental variability to promote coexistence since it would allow otherwise dying strain populations to transiently grow in periods of time that favour their growth, delaying their time to extinction.

Time-varying environments can also promote strain coexistence not just via changing nutrient concentrations, but also dynamic environmental stressors such as toxins (Culp et al. 2024), pH (Ratzke et al. 2020), temperature (Abreu et al. 2023) or salinity (Talley 2002). Changes in these stressors, either due to extrinsic factors or intrinsic community metabolism, can induce periods of growth, no growth and even death for strains. If closely related strains respond differently to these stressors due to rapidly evolving physiological responses, their net growth may be balanced on average, enabling coexistence. Observations from pairs of marine microbial species act as a proof of concept for this mechanism (Yawata et al. 2014), however, similar evidence for closely related strains is absent. Confounding this detection is dormancy—the ability for strains to enter non-growing yet non-dead quiescent states that can persist for very long periods of time. Recent game-theoretic work (Nevermann et al. 2024) has shown that nucleation of dormant states can yield elevated and temporally stable states of diversity. While the formation of endospores and 'persister' cells has been studied extensively at the molecular and physiological levels, quantifying the role they may play in ecological diversity remains poorly understood.

Strains may also coexist by self-organising in space, creating spatial refuges to avoid competition or patterns to enhance cooperation. Studies that domesticate communities in microfluidic chambers show that obligately cross-feeding *E. coli* strains exchange metabolites over short distances (a few microns), and self-organise to maintain inter-strain distances within this range (Dal Co et al. 2020). Similar self-organisation is seen with yeast strains in petri dishes (Varahan et al. 2019). Here, yeast strains are isogenic, but show two switchable phenotypes: a glycolytic and a gluconeogenic one, which cross-feeds sugars to the former efficiently due to specific spatial structuring. These two strains may thus continue to coexist due to this spatial structure, and diversify along other genomic axes. Furthermore, spatially separated bacterial communities have been shown to coexist by sharing resources in time (Liu et al. 2017).

In addition to nutrients, spatially structured environments can enable coexistence due to trade-offs between competition and colonisation ability (Miller et al. 2024; Ebrahimi et al. 2022). *E. coli* strains from the human gut that cannot coexist in well-mixed test tubes can nevertheless coexist on agar plates since the slower-growing strain can evade competition due to faster motility (Gude et al. 2020). Similarly, modelling shows that strains varying only in their foraging ability—their detachment rates from sinking organic particles in the oceans—can also coexist due to a trade-off between growth and death (Ebrahimi et al. 2022). Slower-detaching strains would grow better on each particle, but also suffer more death due to nutrient exhaustion or predation by phases. Faster-detaching strains would grow more slowly since they would leave particles early (therefore giving up nutrients), but suffer less death from predators or starvation. The distribution of organic particles in the oceans could thus provide the patchy spatial structure necessary for coexistence of even closely related strains with slightly different foraging strategies.

3 | Neutral Mechanisms

The mechanisms proposed in Figure 2 assume that coexistence emerges from strong, selectable differences in physiology. However, how much coexistence can be explained by neutral mechanisms such as migration and stochasticity alone (Azaele et al. 2016; Hubbell 2011; Grilli 2020; Kimura 1979) (Figure 3A)? Phenotypically identical strains could show random, uncorrelated population fluctuations simply if their dynamics were subject only to stochasticity in birth and death rates, or due to sampling noise. However, such neutrality would leave behind testable signatures in the statistics of abundance fluctuations, with the strength (variance) of population fluctuations scaling linearly with the population size (Hubbell 2011; Good et al. 2018). Large populations would thus be expected to show only weak fluctuations due to neutrality, which is testable from dynamical data. Furthermore, any apparent strain coexistence arising from neutrality would be transient, with no stabilising selection acting to counterbalance a strain on the brink of extinction. Thus, co-occurring strains at low abundances would be far more likely to go extinct at long times than more abundant strains. This could also create testable patterns in data about divergence times of coexisting strains. In addition to transient dynamics, strains in different communities might be able to better establish if they arise or arrive earlier than others (Fukami 2015; Bittleston et al. 2020). Such effects of historical contingencies, known as priority effects, have been widely studied in ecology, but have remained unexplored for closely related strains.

Such signatures serve as null models to rule out neutral coexistence. Strain dynamics data have indeed been used to rule out neutral coexistence in several cases such as in the human gut microbiome (Garud et al. 2019), and in microbial mats (Rosen et al. 2015). Data from facial skin pores, however, provide one of the few known pieces of evidence consistent with neutrality. Co-occurrence patterns from lineages of *Cutibacterium acnes* and *Staphylococcus epidermidis* suggest that these strains coexist neutrally (Conwill et al. 2022), painting a picture of phenotypically indistinguishable strains migrating across a large network of skin pores and potentially coexisting via stochastic dynamics.

4 | Evolutionary Mechanisms

We have focused on the ecological dynamics of extant strains in a community, but where do they come from? Unlike different species—whose presence necessarily results from immigration into a community—strains have a much larger probability of emerging de novo within the community. Evolutionary forces, namely mutation and recombination through horizontal gene transfer (Figure 3B), very likely command strain-level diversity visible within communities (Frazão et al. 2022). Though mutation rates are small (~10^{-11}–10^{-8} per bp per generation; Wielgoss et al. 2011; Drake et al. 1998), the short generation times and large population sizes of microbes makes rapid diversification through mutation a reality. Recently, it has been empirically demonstrated that genome-wide differences as few as 100 SNPs can be sufficient for strains to exhibit independent ecological dynamics in natural environments (Goyal et al. 2022). With genomes on the order of a few million bases, such diversity can emerge within a few hundred to a thousand generations, on the order of a few months assuming modest growth rates.

However, mutation via single base pair substitutions is often not rapid or severe enough to permanently alter the gene content, gene dosage, or functional landscape of strain-level diversity. While microbes are typically asexual, genome content can be recombined through the horizontal transfer of genetic material ranging from entire gene cassettes and operons to short, regulatory regions. There are many routes by which this can occur–such as conjugation, phage-mediated transduction and others–with varying degrees of rarity (Arnold et al. 2022). Of key interest is natural transformation through competence, the direct uptake of DNA from the environment. Species that can do so are termed 'competent' and express a bevy of proteins that facilitate the direct binding of DNA in the environment, its translocation into the cytoplasm and its integration into the chromosome. This mechanism is widespread across the bacterial domain (Johnston et al. 2014) but requires the presence of specialised macromolecular structures. Many competent bacteria integrate the exogenously acquired DNA into their own genomes, either through random or homologous recombination. This may play a critical role in the sharing and swapping of genomic content between strains as the vast majority of their genomic sequences will be identical. This, however, makes its detection and quantification in natural communities much more difficult, though not theoretically impossible (Adato et al. 2015). Doing so will likely require new bioinformatic tools to detect statistical differences between mutation and horizontal transfer in highly similar genomes.

It is important to note that all of these mechanisms are not limited solely to strain–strain transfer. Horizontal transfer can happen between species and even further up the tree of life. As a consequence, whether recombination can diversify a community rather than homogenise it is dependent on the diversity of the DNA content in the environment that can be passed around. For example, recent work within cyanobacterial communities of geothermal hotsprings has shown that strain diversity has been strongly reduced through the constant swapping of genome content through Horizontal Gene Transfer (HGT) (Birzu et al. 2023). This is likely due to the remarkably narrow spatial thermal niches present in these environments, resulting in free DNA that is already highly similar. Conversely, HGT within less spatially restricted environments has been shown to yield highly diverse genomes (Woods et al. 2020).

5 | Conclusion

How and why different types of organisms coexist in a shared ecosystem has long been a central question in ecology. There are varied mechanisms by which biodiversity is maintained across taxonomic levels, many of which rely on the occupation of different niches. However, these mechanisms begin to break down when we probe the microbial world, where there is abundant, temporally stable diversity even at the level of individual strains with marginal genetic diversity. Here, we have highlighted some ideas for how closely related strains could coexist via niche-based mechanisms (metabolic diversity, physiological trade-offs, anti-symmetric interactions, and spatiotemporal dynamics), neutral mechanisms (migration and stochasticity) and evolutionary mechanisms (mutation and HGT). We stress that these mechanisms should be considered proposals which are lacking concrete demonstration for strain-level coexistence in natural or laboratory communities. Experimentally demonstrating these mechanisms as forces behind the coexistence of closely related strains is absolutely critical. Moreover, these mechanisms should be considered *collectively* to explain coexistence—anyone in isolation is likely insufficient to quantitatively match observation. Doing so opens a variety of fascinating questions: How important are dynamics versus steady states for coexistence? Can communities with population fluctuations due to time-varying environments or strong community interactions promote strain coexistence when averaged over time? What are the rates of HGT and generation of microdiversity in natural microbial communities, and how do they balance the rates at which diversity is lost? Are there robust generic mechanisms that can make closely related strains effectively neutral? If so, how can they be tested? Answering these questions not only demands novel theory and experiments; it demands their dialogue.

At a theoretical level, we must have a pragmatic view of what encompasses coexistence in natural ecosystems, delineating between the 'hard' mathematical definition and the 'soft' definition which is applicable to realistic conditions. This applies to all ecological subjects—from forests to grasslands to tide pools—but is even more relevant for the microbial world where physiological differences are often small and generation times are short. At a theoretical level, coexistence can be defined as the continual presence of at least two distinguishable organisms across an infinite time span. While mathematically rigorous, this is hardly applicable to reality. For example, say there exists an ecosystem where two strains compete with a vanishingly small, but non-zero, fitness difference between them. While it may take longer than the age of the universe for one species to outcompete the other (i.e., failing the 'hard' definition), we can say that the two strains *effectively* coexist, at least over the ecologically and evolutionary relevant time scales (i.e., satisfying the 'soft' definition) (Louca and Doebeli 2016; Martiny et al. 2023). Unlike 'hard' coexistence, there is no one definition for 'soft' coexistence, and the relevant temporal regimes will be highly contextual to the particular ecosystem of study, encompassing the timescales of both the environmental fluctuations and the tempo of evolution in the community. Finding this definition therefore requires a holistic knowledge of the various relevant timescales, knowledge that can only come from direct measurement.

On the experimental side, we need targeted observations of strain dynamics at higher temporal and genetic resolution. While current metagenomic snapshots have revealed tremendous diversity, several key experiments could quantitatively test predictions about these coexistence mechanisms. First, introducing known strains (with known or engineered phenotypes) into natural or synthetic communities as 'tracer particles' may reveal the relative strength of neutral versus competitive mechanisms in maintaining microdiversity. Doing so may allow us to infer ecological dynamics within specific microbial demographics without requiring high-cost deep metagenomic sequencing. Second, deep metagenomic long-read sequencing of natural communities over time would enable estimation of distributions of strain interactions, testing whether observed interactions are more stabilising than predicted by random community assembly. Third, systematic measurements of physiological parameters across strains—including growth rates, half-saturation constants and yield coefficients—coupled with modern genomic sequencing methods would allow direct comparison with the diversity bounds predicted by resource competition theory. Importantly, this will permit us to construct meaningful maps between genotype and metabolic phenotype, which can be integrated with measurements of environmental contexts to better understand the expected levels of strain-level coexistence. Fourth, experiments applying controlled environmental perturbations (e.g., temperature shocks, antibiotic pressures, or nutrient fluctuations) could reveal correlations in strain abundances before and after community collapse, helping understand the intricate networks of ecological interactions between strains. Any clustering in such networks would reflect underlying competition, metabolic dependencies or cross-feeding relationships between strains in communities. Finally, quantification of horizontal gene transfer rates in nature would significantly aid in our understanding of its ecological importance. These experimental advances, combined with theoretical developments in modelling genotype–phenotype relationships, will be essential for understanding the mechanisms enabling the remarkable strain-level diversity observed in microbial communities.

6 | Outlook

At first, strain coexistence might seem an incremental problem, one that is qualitatively similar to species coexistence. This was indeed our viewpoint when we started to collect the current state of the field on mechanisms of strain coexistence. Writing it, however, forced our viewpoint to drastically change. Strain coexistence is in fact a qualitatively distinct problem that severely challenges current ecological theory. The dominant frameworks to explain coexistence, when put together, are either fragile or numerically insufficient. For instance, a general conceptual prediction of niche theory is that the finer the differences between species get, the harder it is for them to coexist. However, with strains we seem to be in the opposite regime: the finer we look, the more coexistence we see. One could expect that all of these mechanisms are independent, meaning that they multiply to numerically explain the observed diversity. However, decades of ecological theory and experimental dissection reveals that mechanisms are rarely independent (Fridman et al. 2022; Marsland et al. 2019; Tilman 1982; Feng et al. 2024; Dubinkina et al. 2019), and, as a consequence, their explanatory powers sum rather than multiply. This leaves a quantitative mismatch between the amount of diversity we see and the theoretical maximum we can compute, making the problem of microdiversity much more pronounced. Incremental improvements—such as finding or counting a few more niches here and there—will not solve this issue and we can either accept this as a challenge never to be overcome, or acknowledge the urgent need for a new theoretical framework to explain microdiversity. Such new frameworks might for instance allow distinct, orthogonal mechanisms to multiply their contributions to diversity, providing new insights and opportunities to greatly promote coexistence. In our opinion, this is the first time since the formulation of the problem of diversity that we have a grand conceptual challenge. The answer to microdiversity is unlikely to be finding ways to ‘count niches better’. There need to be new frameworks for thinking about coexistence. Beyond new theory, quantitatively accounting for coexistence demands new, creative microbiological experiments and field work to test them. A truly interdisciplinary effort is required to solve this problem. Otherwise, we will remain in a tennis match between making new observations and inventing new niches to explain them away.

Author Contributions

Akshit Goyal: conceptualization, formal analysis (equal), investigation (equal), resources (equal), validation (equal), writing – original draft (equal), writing – review and editing (equal). **Griffin Chure:** formal analysis (equal), investigation (equal), resources (equal), validation (equal), visualization, writing – original draft (equal), writing – review and editing (equal).

Acknowledgements

We thank Jonas Cremer, Avi Flamholz, Karna Gowda, Pankaj Mehta, Manuel Razo-Mejia, Xin Sun and Liang Xu for comments on drafts of the manuscript. We also thank Daniel S. Fisher for many fruitful discussions about the role of microdiversity and the problem of infinitely divisible niches.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

No data associated with this manuscript.

References

Abrams, P. 1975. “Limiting Similarity and the Form of the Competition Coefficient.” *Theoretical Population Biology* 8, no. 3: 356–375.

Abreu, C. I., M. Dal Bello, C. Bunse, J. Pinhassi, and J. Gore. 2023. “Warmer Temperatures Favor Slower-Growing Bacteria in Natural Marine Communities.” *Science Advances* 9, no. 19: eade8352.

Adato, O., N. Ninyo, U. Gophna, and S. Snir. 2015. “Detecting Horizontal Gene Transfer Between Closely Related Taxa.” *PLoS Computational Biology* 11, no. 10: e1004408. https://doi.org/10.1371/journal.pcbi.1004408.

Akiyama, T., and M. Kim. 2021. “Stochastic Response of Bacterial Cells to Antibiotics: Its Mechanisms and Implications for Population and Evolutionary Dynamics.” *Current Opinion in Microbiology* 63: 104–108.

Arnold, B. J., I.-T. Huang, and W. P. Hanage. 2022. “Horizontal Gene Transfer and Adaptive Evolution in Bacteria.” *Nature Reviews Microbiology* 20, no. 4: 206–218. https://doi.org/10.1038/s41579-021-00650-4.

Azaele, S., S. Suweis, J. Grilli, I. Volkov, J. R. Banavar, and A. Maritan. 2016. “Statistical Mechanics of Ecological Systems: Neutral Theory and Beyond.” *Reviews of Modern Physics* 88, no. 3: 035003.

Balakrishnan, R., and J. Cremer. 2023. “Conditionally Unutilized Proteins and Their Profound Effects on Growth and Adaptation Across Microbial Species.” *Current Opinion in Microbiology* 75: 102366.

Behringer, M. G., W.-C. Ho, J. C. Meraz, et al. 2022. “Complex Ecotype Dynamics Evolve in Response to Fluctuating Resources.” *MBio* 13, no. 3: e03467-21.

Birzu, G., H. S. Muralidharan, D. Goudeau, R. R. Malmstrom, D. S. Fisher, and D. Bhaya. 2023. “Hybridization Breaks Species Barriers in Long-Term Coevolution of a Cyanobacterial Population.” *eLife* 12: RP90849.

Bittleston, L. S., M. Gralka, G. E. Leventhal, I. Mizrahi, and O. X. Cordero. 2020. “Context-Dependent Dynamics Lead to the Assembly of Functionally Distinct Microbial Communities.” *Nature Communications* 11, no. 1: 1440.

Bloxham, B., H. Lee, and J. Gore. 2024. “Biodiversity Is Enhanced by Sequential Resource Utilization and Environmental Fluctuations via Emergent Temporal Niches.” *PLoS Computational Biology* 20, no. 5: e1012049.

Chase, A. B., C. Weihe, and J. B. H. Martiny. 2021. “Adaptive Differentiation and Rapid Evolution of a Soil Bacterium Along a Climate Gradient.” *Proceedings of the National Academy of Sciences* 118, no. 18: e2101254118.

Chase, A. B., Z. Gomez-Lunar, A. E. Lopez, et al. 2018. “Emergence of Soil Bacterial Ecotypes Along a Climate Gradient.” *Environmental Microbiology* 20, no. 11: 4112–4126. https://doi.org/10.1111/1462-2920.14405.

Chase, J. M., and M. A. Leibold. 2009. *Ecological Niches: Linking Classical and Contemporary Approaches*. University of Chicago Press.

Chen, M., and R. E. Blankenship. 2011. “Expanding the Solar Spectrum Used by Photosynthesis.” *Trends in Plant Science* 16, no. 8: 427–431.

Chesson, P. 2000. “Mechanisms of Maintenance of Species Diversity.” *Annual Review of Ecology and Systematics* 31, no. 1: 343–366. https://doi.org/10.1146/annurev.ecolsys.31.1.343.

Chure, G., and J. Cremer. 2023. “An Optimal Regulation of Fluxes Dictates Microbial Growth In and Out of Steady State.” *eLife* 12: e84878.

Conwill, A., A. C. Kuan, R. Damerla, et al. 2022. “Anatomy Promotes Neutral Coexistence of Strains in the Human Skin Microbiome.” *Cell Host & Microbe* 30, no. 2: 171–182.

Culp, E. J., N. T. Nelson, A. A. Verdegaal, and A. L. Goodman. 2024. “Microbial Transformation of Dietary Xenobiotics Shapes Gut Microbiome Composition.” *Cell* 187: 6327–6345.e20.

Dal Bello, M., H. Lee, A. Goyal, and J. Gore. 2021. “Resource–Diversity Relationships in Bacterial Communities Reflect the Network Structure of Microbial Metabolism.” *Nature Ecology & Evolution* 5, no. 10: 1424–1434.

Dal Co, A., S. van Vliet, D. J. Kiviet, S. Schlegel, and M. Ackermann. 2020. “Short-Range Interactions Govern the Dynamics and Functions of Microbial Communities.” *Nature Ecology & Evolution* 4, no. 3: 366–375.

Douglas, A. E. 2020. “The Microbial Exometabolome: Ecological Resource and Architect of Microbial Communities.” *Philosophical Transactions of the Royal Society, B: Biological Sciences* 375, no. 1798: 20190250.

Drake, J. W., B. Charlesworth, D. Charlesworth, and J. F. Crow. 1998. “Rates of Spontaneous Mutation.” *Genetics* 148, no. 4: 1667–1686.

D'Souza, G., S. Waschina, S. Pande, K. Bohl, C. Kaleta, and C. Kost. 2014. “Less Is More: Selective Advantages Can Explain the Prevalent Loss of Biosynthetic Genes in Bacteria.” *Evolution* 68, no. 9: 2559–2570.

Dubinkina, V., Y. Fridman, P. P. Pandey, and S. Maslov. 2019. “Multistability and Regime Shifts in Microbial Communities Explained by Competition for Essential Nutrients.” *eLife* 8: e49720.

Ebrahimi, A., A. Goyal, and O. X. Cordero. 2022. “Particle Foraging Strategies Promote Microbial Diversity in Marine Environments.” *eLife* 11: e73948.

Favate, J. S., S. Liang, A. L. Cope, S. S. Yadavalli, and P. Shah. 2022. “The Landscape of Transcriptional and Translational Changes Over

22 Years of Bacterial Adaptation." *eLife* 11: e81979. https://doi.org/10.7554/eLife.81979.

Feng, Z., R. Marsland III, J. W. Rocks, and P. Mehta. 2024. "Emergent Competition Shapes Top-Down Versus Bottom-Up Control in Multi-Trophic Ecosystems." *PLoS Computational Biology* 20, no. 2: e1011675. https://doi.org/10.1371/journal.pcbi.1011675.

Fink, J. W., N. A. Held, and M. Manhart. 2023. "Microbial Population Dynamics Decouple Growth Response From Environmental Nutrient Concentration." *Proceedings of the National Academy of Sciences* 120, no. 2: e2207295120.

Flynn, K. J., A. Mitra, W. H. Wilson, et al. 2022. "'Boom-and-Busted' Dynamics of Phytoplankton–Virus Interactions Explain the Paradox of the Plankton." *New Phytologist* 234, no. 3: 990–1002. https://doi.org/10.1111/nph.18042.

Frazão, N., A. Konrad, M. Amicone, et al. 2022. "Two Modes of Evolution Shape Bacterial Strain Diversity in the Mammalian Gut for Thousands of Generations." *Nature Communications* 13, no. 1: 5604.

Fridman, Y., Z. Wang, S. Maslov, and A. Goyal. 2022. "Fine-Scale Diversity of Microbial Communities due to Satellite Niches in Boom and Bust Environments." *PLoS Computational Biology* 18, no. 12: e1010244.

Fritts, R. K., A. L. McCully, and J. B. McKinlay. 2021. "Extracellular Metabolism Sets the Table for Microbial Cross-Feeding." *Microbiology and Molecular Biology Reviews* 85, no. 1: e00135-20. https://doi.org/10.1128/mmbr.00135–20.

Fukami, T. 2015. "Historical Contingency in Community Assembly: Integrating Niches, Species Pools, and Priority Effects." *Annual Review of Ecology, Evolution, and Systematics* 46, no. 1: 1–23.

Garud, N. R., B. H. Good, O. Hallatschek, and K. S. Pollard. 2019. "Evolutionary Dynamics of Bacteria in the Gut Microbiome Within and Across Hosts." *PLoS Biology* 17, no. 1: e3000102. https://doi.org/10.1371/journal.pbio.3000102.

Garud, N. R., and K. S. Pollard. 2020. "Population Genetics in the Human Microbiome." *Trends in Genetics* 36, no. 1: 53–67.

Goldford, J. E., N. Lu, D. Baji, et al. 2018. "Emergent Simplicity in Microbial Community Assembly." *Science* 361, no. 6401: 469–474.

Good, B. H., S. Martis, and O. Hallatschek. 2018. "Adaptation Limits Ecological Diversification and Promotes Ecological Tinkering During the Competition for Substitutable Resources." *Proceedings of the National Academy of Sciences* 115, no. 44: E10407–E10416.

Good, B. H., M. J. McDonald, J. E. Barrick, R. E. Lenski, and M. M. Desai. 2017. "The Dynamics of Molecular Evolution Over 60,000 Generations." *Nature* 551, no. 7678: 45–50. https://doi.org/10.1038/nature24287.

Goyal, A. 2018. "Metabolic Adaptations Underlying Genome Flexibility in Prokaryotes." *PLoS Genetics* 14, no. 10: e1007763.

Goyal, A., L. S. Bittleston, G. E. Leventhal, L. Lu, and O. X. Cordero. 2022. "Interactions Between Strains Govern the Eco-Evolutionary Dynamics of Microbial Communities." *eLife* 11: e74987. https://doi.org/10.7554/eLife.74987.

Goyal, A., and S. Krishna. 2022. "The Chemical Basis of Metabolic Interdependence in Microbial Communities." *bioRxiv*, 2022-03.

Goyal, A., and S. Maslov. 2018. "Diversity, Stability, and Reproducibility in Stochastically Assembled Microbial Ecosystems." *Physical Review Letters* 120, no. 15: 158102.

Goyal, A., T. Wang, V. Dubinkina, and S. Maslov. 2021. "Ecology-Guided Prediction of Cross-Feeding Interactions in the Human Gut Microbiome." *Nature Communications* 12, no. 1: 1335.

Gralka, M., S. Pollak, and O. X. Cordero. 2023. "Genome Content Predicts the Carbon Catabolic Preferences of Heterotrophic Bacteria." *Nature Microbiology* 8, no. 10: 1799–1808.

Grilli, J. 2020. "Macroecological Laws Describe Variation and Diversity in Microbial Communities." *Nature Communications* 11, no. 1: 4743.

Gude, S., E. Pinçe, K. M. Taute, A.-B. Seinen, T. S. Shimizu, and S. J. Tans. 2020. "Bacterial Coexistence Driven by Motility and Spatial Competition." *Nature* 578, no. 7796: 588–592.

Ho, P.-Y., T. H. Nguyen, J. M. Sanchez, B. C. DeFelice, and K. C. Huang. 2024. "Resource Competition Predicts Assembly of Gut Bacterial Communities In Vitro." *Nature Microbiology* 9, no. 4: 1036–1048.

Holt, R. D. 2009. "Bringing the Hutchinsonian Niche Into the 21st Century: Ecological and Evolutionary Perspectives." *Proceedings of the National Academy of Sciences* 106, no. supplement_2: 19659–19665.

Holtrop, T., J. Huisman, M. Stomp, et al. 2021. "Vibrational Modes of Water Predict Spectral Niches for Photosynthesis in Lakes and Oceans." *Nature Ecology & Evolution* 5, no. 1: 55–66.

Hong, S.-H., J. Bunge, S.-O. Jeon, and S. S. Epstein. 2006. "Predicting Microbial Species Richness." *Proceedings of the National Academy of Sciences* 103, no. 1: 117–122. https://doi.org/10.1073/pnas.0507245102.

Hoshino, T., H. Doi, G.-I. Uramoto, et al. 2020. "Global Diversity of Microbial Communities in Marine Sediment." *Proceedings of the National Academy of Sciences* 117, no. 44: 27587–27597.

Hubbell, S. P. 2011. *The Unified Neutral Theory of Biodiversity and Biogeography* (MPB-32). Princeton University Press.

Hutchinson, G. E. 1961. "The Paradox of the Plankton." *American Naturalist* 95, no. 882: 137–145. https://doi.org/10.1086/282171.

Johnston, C., B. Martin, G. Fichant, P. Polard, and J.-P. Claverys. 2014. "Bacterial Transformation: Distribution, Shared Mechanisms and Divergent Control." *Nature Reviews Microbiology* 12, no. 3: 181–196. https://doi.org/10.1038/nrmicro3199.

Jones, D. L., E. A. Magthab, D. B. Gleeson, et al. 2018. "Microbial Competition for Nitrogen and Carbon Is as Intense in the Subsoil as in the Topsoil." *Soil Biology and Biochemistry* 117: 72–82. https://doi.org/10.1016/j.soilbio.2017.10.024.

Kehe, J., A. Ortiz, A. Kulesa, J. Gore, P. C. Blainey, and J. Friedman. 2021. "Positive Interactions Are Common Among Culturable Bacteria." *Science Advances* 7, no. 45: eabi7159.

Kimura, M. 1979. "The Neutral Theory of Molecular Evolution." *Scientific American* 241, no. 5: 98–129.

Kost, C., K. R. Patil, J. Friedman, S. L. Garcia, and M. Ralser. 2023. "Metabolic Exchanges Are Ubiquitous in Natural Microbial Communities." *Nature Microbiology* 8, no. 12: 2244–2252.

Leiby, N., and C. J. Marx. 2014. "Metabolic Erosion Primarily Through Mutation Accumulation, and Not Tradeoffs, Drives Limited Evolution of Substrate Specificity in *Escherichia coli*." *PLoS Biology* 12, no. 2: e1001789 Publisher: Public Library of Science.

Lenski, R. E. 2023. "Revisiting the Design of the Long-Term Evolution Experiment With *Escherichia coli*." *Journal of Molecular Evolution* 91, no. 3: 241–253.

Letten, A. D., P.-J. Ke, and T. Fukami. 2017. "Linking Modern Coexistence Theory and Contemporary Niche Theory." *Ecological Monographs* 87, no. 2: 161–177.

Liu, J., R. Martinez-Corral, A. Prindle, et al. 2017. "Coupling Between Distant Biofilms and Emergence of Nutrient Time-Sharing." *Science* 356, no. 6338: 638–642.

Louca, S., and M. Doebeli. 2016. "Transient Dynamics of Competitive Exclusion in Microbial Communities." *Environmental Microbiology* 18, no. 6: 1863–1874.

MacArthur, R., and R. Levins. 1967. "The Limiting Similarity, Convergence, and Divergence of Coexisting Species." *American Naturalist* 101, no. 921: 377–385.

Machado, D., O. M. Maistrenko, S. Andrejev, et al. 2021. “Polarization of Microbial Communities Between Competitive and Cooperative Metabolism.” *Nature Ecology & Evolution* 5, no. 2: 195–203.

MacLean, R. C., and I. Gudelj. 2006. “Resource Competition and Social Conflict in Experimental Populations of Yeast.” *Nature* 441, no. 7092: 498–501.

Madsen, E. L. 2011. “Microorganisms and Their Roles in Fundamental Biogeochemical Cycles.” *Current Opinion in Biotechnology* 22, no. 3: 456–464.

Mahadevan, A., M. T. Pearce, and D. S. Fisher. 2023. “Spatiotemporal Ecological Chaos Enables Gradual Evolutionary Diversification Without Niches or Tradeoffs.” *eLife* 12: e82734.

Marsland, R., W. Cui, J. Goldford, A. Sanchez, K. Korolev, and P. Mehta. 2019. “Available Energy Fluxes Drive a Transition in the Diversity, Stability, and Functional Structure of Microbial Communities.” *PLoS Computational Biology* 15, no. 2: e1006793. https://doi.org/10.1371/journal.pcbi.1006793.

Martiny, J. B. H., S. E. Jones, J. T. Lennon, and A. C. Martiny. 2015. “Microbiomes in Light of Traits: A Phylogenetic Perspective.” *Science* 350, no. 6261: aac9323.

Martiny, J. B. H., A. C. Martiny, E. Brodie, et al. 2023. “Investigating the Eco-Evolutionary Response of Microbiomes to Environmental Change.” *Ecology Letters* 26: S81–S90.

Mee, M. T., J. J. Collins, G. M. Church, and H. H. Wang. 2014. “Syntrophic Exchange in Synthetic Microbial Communities.” *Proceedings of the National Academy of Sciences* 111, no. 20: E2149–E2156.

Menden-Deuer, S., and J. Rowlett. 2014. “Many Ways to Stay in the Game: Individual Variability Maintains High Biodiversity in Planktonic Micro-Organisms.” *Journal of the Royal Society Interface* 11, no. 95: 20140031.

Miller, Z. R., M. Clenet, K. Della Libera, F. Massol, and S. Allesina. 2024. “Coexistence of Many Species Under a Random Competition–Colonization Trade-Off.” *Proceedings of the National Academy of Sciences* 121, no. 5: e2314215121.

Monod, J. 1949. “The Growth of Bacterial Cultures.” *Annual Review of Microbiology* 3: 371–394.

Mori, M., Z. Zhang, A. Banaei-Esfahani, et al. 2021. “From Coarse to Fine: The Absolute *Escherichia coli* Proteome Under Diverse Growth Conditions.” *Molecular Systems Biology* 17, no. 5: e9536.

Nevermann, D. H., C. Gros, and J. T. Lennon. 2024. “A Game of Life With Dormancy.” *arXiv:2406.13765*.

Pande, S., H. Merker, K. Bohl, et al. 2014. “Fitness and Stability of Obligate Cross-Feeding Interactions That Emerge Upon Gene Loss in Bacteria.” *ISME Journal* 8, no. 5: 953–962.

Pearce, M. T., A. Agarwala, and D. S. Fisher. 2020. “Stabilization of Extensive Fine-Scale Diversity by Ecologically Driven Spatiotemporal Chaos.” *Proceedings of the National Academy of Sciences* 117, no. 25: 14572–14583.

Posfai, A., T. Taillefumier, and N. S. Wingreen. 2017. “Metabolic Trade-Offs Promote Diversity in a Model Ecosystem.” *Physical Review Letters* 118, no. 2: 028103. https://doi.org/10.1103/PhysRevLett.118.028103.

Ratzke, C., J. Barrere, and J. Gore. 2020. “Strength of Species Interactions Determines Biodiversity and Stability in Microbial Communities.” *Nature Ecology & Evolution* 4, no. 3: 376–383.

Record, N. R., A. J. Pershing, and F. Maps. 2014. “The Paradox of the “Paradox of the Plankton”.” *ICES Journal of Marine Science* 71, no. 2: 236–240.

Riber, L., and L. H. Hansen. 2021. “Epigenetic Memories: The Hidden Drivers of Bacterial Persistence?” *Trends in Microbiology* 29, no. 3: 190–194.

Rodriguez-R, L. M., R. E. Conrad, T. Viver, et al. 2023. “An ANI Gap Within Bacterial Species That Advances the Definitions of Intra-Species Units.” *MBio* 15, no. 1: e02696-23.

Rosen, M. J., M. Davison, D. Bhaya, and D. S. Fisher. 2015. “Fine-Scale Diversity and Extensive Recombination in a Quasisexual Bacterial Population Occupying a Broad Niche.” *Science* 348, no. 6238: 1019–1023.

Roughgarden, J. 1974. “Species Packing and the Competition Function With Illustrations From Coral Reef Fish.” *Theoretical Population Biology* 5, no. 2: 163–186.

Roy, S., and J. Chattopadhyay. 2007. “Towards a Resolution of ‘*The Paradox of the Plankton*’: A Brief Overview of the Proposed Mechanisms.” *Ecological Complexity* 4, no. 1: 26–33.

Rozen, D. E., and R. E. Lenski. 2000. “Long-Term Experimental Evolution in *Escherichia coli*. VIII. Dynamics of a Balanced Polymorphism.” *American Naturalist* 155, no. 1: 24–35. https://doi.org/10.1086/303299.

Sanchez, A., S. Choubey, and J. Kondev. 2013. “Regulation of Noise in Gene Expression.” *Annual Review of Biophysics* 42: 469–491.

Scott, M., C. W. Gunderson, E. M. Mateescu, Z. Zhang, and T. Hwa. 2010. “Interdependence of Cell Growth and Gene Expression: Origins and Consequences.” *Science* 330, no. 6007: 1099–1102.

Scott, M., S. Klumpp, E. M. Mateescu, and T. Hwa. 2014. “Emergence of Robust Growth Laws From Optimal Regulation of Ribosome Synthesis.” *Molecular Systems Biology* 10, no. 8: 747.

Sheng, H., J. M. Silverman, S. S. Chen, et al. 2015. “Quantitative Proteomic Analysis Reveals a Simple Strategy of Global Resource Allocation in Bacteria.” *Molecular Systems Biology* 11, no. 2: 784. https://doi.org/10.15252/msb.20145697.

Shu, W.-S., and L.-N. Huang. 2022. “Microbial Diversity in Extreme Environments.” *Nature Reviews Microbiology* 20, no. 4: 219–235.

Sokol, N. W., E. Slessarev, G. L. Marschmann, et al. 2022. “Life and Death in the Soil Microbiome: How Ecological Processes Influence Biogeochemistry.” *Nature Reviews Microbiology* 20, no. 7: 415–430.

Stomp, M., J. Huisman, L. J. Stal, and H. C. P. Matthijs. 2007. “Colorful Niches of Phototrophic Microorganisms Shaped by Vibrations of the Water Molecule.” *ISME Journal* 1, no. 4: 271–282.

Sung, J., S. Kim, J. J. T. Cabatbat, et al. 2017. “Global Metabolic Interaction Network of the Human Gut Microbiota for Context-Specific Community-Scale Analysis.” *Nature Communications* 8, no. 1: 15393.

Taillefumier, T., A. Posfai, Y. Meir, and N. S. Wingreen. 2017. “Microbial Consortia at Steady Supply.” *eLife* 6: e22644. https://doi.org/10.7554/eLife.22644.

Talley, L. D. 2002. “Salinity Patterns in the Ocean.” In *The Earth System: Physical and Chemical Dimensions of Global Environmental Change*, edited by M. C. MacCracken and J. S. Perry, vol. 1, 629–640. John Wiley & Sons, Ltd.

Tan, I. S., and K. S. Ramamurthi. 2014. “Spore Formation in *Bacillus subtilis*.” *Environmental Microbiology Reports* 6, no. 3: 212–225.

Tikhonov, M., and R. Monasson. 2017. “Collective Phase in Resource Competition in a Highly Diverse Ecosystem.” *Physical Review Letters* 118, no. 4: 048103.

Tilman, D. 1982. *Resource Competition and Community Structure*. Vol. 17. Princeton University Press.

Tran, F., and J. Q. Boedicker. 2017. “Genetic Cargo and Bacterial Species Set the Rate of Vesicle-Mediated Horizontal Gene Transfer.” *Scientific Reports* 7, no. 1: 8813. https://doi.org/10.1038/s41598-017-07447-7.

Varahan, S., A. Walvekar, V. Sinha, S. Krishna, and S. Laxman. 2019. “Metabolic Constraints Drive Self-Organization of Specialized Cell Groups.” *eLife* 8: e46735.

Wang, Z., A. Goyal, V. Dubinkina, et al. 2021. "Complementary Resource Preferences Spontaneously Emerge in Diauxic Microbial Communities." *Nature Communications* 12, no. 1: 6661. https://doi.org/10.1038/s41467-021-27023-y.

Wielgoss, S., J. E. Barrick, O. Tenaillon, et al. 2011. "Mutation Rate Inferred From Synonymous Substitutions in a Long-Term Evolution Experiment With *Escherichia coli*." *G3 Genes|Genomes|Genetics* 1, no. 3: 183–186.

Woods, L. C., R. J. Gorrell, F. Taylor, T. Connallon, T. Kwok, and M. J. McDonald. 2020. "Horizontal Gene Transfer Potentiates Adaptation by Reducing Selective Constraints on the Spread of Genetic Variation." *Proceedings of the National Academy of Sciences* 117, no. 43: 26868–26875. https://doi.org/10.1073/pnas.2005331117.

Yawata, Y., O. X. Cordero, F. Menolascina, J.-H. Hehemann, M. F. Polz, and R. Stocker. 2014. "Competition–Dispersal Tradeoff Ecologically Differentiates Recently Speciated Marine Bacterioplankton Populations." *Proceedings of the National Academy of Sciences* 111, no. 15: 5622–5627.

Zhou, Z., C. Wang, M. Zheng, L. Jiang, and Y. Luo. 2017. "Patterns and Mechanisms of Responses by Soil Microbial Communities to Nitrogen Addition." *Soil Biology and Biochemistry* 115: 433–441.