Environmental Microbiology

ENVIRONMENTAL MICROBIOLOGY

PERSPECTIVE OPEN ACCESS

Wine Fermentation as a Model System for Microbial Ecology and Evolution

Ignacio Belda[1] | Sergio Izquierdo-Gea[1] | Belen Benitez-Dominguez[1,2] | Javier Ruiz[1] | Jean C. C. Vila[3]

[1]Department of Genetics, Physiology and Microbiology, Biology Faculty, Complutense University of Madrid, Madrid, Spain | [2]Institute of Functional Biology & Genomics, IBFG - CSIC, Universidad de Salamanca, Salamanca, Spain | [3]Department of Biology, Stanford University, Stanford, USA

Correspondence: Ignacio Belda (ignaciobelda@ucm.es) | Jean C. C. Vila (jccvila@stanford.edu)

Received: 8 October 2024 | **Revised:** 11 March 2025 | **Accepted:** 24 March 2025

Funding: supported by grants PID2019-105834GA-I00 (acronym Wineteractions) and PID2022-138343NB-I00 (acronym INDUSYNCON) funded by the Spanish State Research Agency/Science and Research Ministry (https://doi.org/10.13039/501100011033) and by ERDF/EU. Sergio Izquierdo-Gea acknowledges his predoctoral grant FPU21/06830 funded by the Spanish Ministry of Science, Innovation and Universities. Belen Benítez-Dominguez acknowledges her predoctoral grant PRE2022-103063 funded by MICIU/AEI/10.13039/501100011033 and by ESF+. JCC Vila was partially funded by a Center for Computational (CEHG), Evolutionary and Human Genomics postdoctoral fellowship at Stanford.

Keywords: evolution/evolutionary processes/gene transfer/mutation | functional diversity | microbe: Microbe interactions | microbial communities | microbial ecology | synthetic microbial communities | yeasts

ABSTRACT

In vitro microbial communities have proven to be invaluable model systems for studying ecological and evolutionary processes experimentally. However, it remains unclear whether quantitative insights obtained from these laboratory systems can be applied to complex communities assembling and evolving in their natural ecological context. To bridge the gap between the lab and the 'real-world', there is a need for laboratory model systems that better approximate natural and semi-natural ecosystems. Wine fermentation presents an ideal system for this purpose, balancing experimental tractability with rich ecological and evolutionary dynamics. In this perspective piece we outline the key features that make wine fermentation a fruitful model system for ecologists and evolutionary biologists. We highlight the diversity of environmentally mediated interactions that shape community dynamics during fermentation, the complex evolutionary history of wine microbial populations, and the opportunity to study the impact of complex ecologies on evolutionary dynamics. By integrating knowledge from both wine research and microbial ecology and evolution we aim to enhance understanding and foster collaboration between these fields.

1 | Introduction

Most biological research has progressed using a few model systems. The unique biological and technological features of these systems have been instrumental in formulating research questions or, at the very least, in determining how these questions are addressed. Consequently, the peculiarities of our chosen model can profoundly influence our understanding of nature (Duffy et al. 2021). Ecologists and evolutionary biologists have traditionally relied on a relatively narrow range of model systems to investigate questions concerning the assembly and evolution of complex communities, particularly when aiming to achieve mechanistic insight. For example, community ecologists have endeavoured to test causal hypotheses by manipulating natural communities of plants and animals or simplified versions of them as microcosms in controlled environments (Lawton 1995; Srivastava et al. 2004). Meanwhile, evolutionary biologists have often focused on well characterised model organisms or clades in isolation in order to obtain general insights about evolutionary processes (Donoghue and Edwards 2019).

Ignacio Belda and Sergio Izquierdo-Gea contributed equally to this work.

Over the past few decades in vitro microbial communities have increasingly served as model systems to explore the dynamic relationship between ecology and evolution, as well as the processes that generate and sustain biological diversity (Shayanthan et al. 2022; Estrela et al. 2021; Jessup et al. 2004). In vitro microcosms have several advantages over macrobial systems, especially concerning the spatial and temporal scales required to experimentally study the population dynamics of communities across generations (Lenski and Travisano 1994; Meroz et al. 2021). Moreover, microbial communities display many unique attributes requiring new theory which builds on the core principles of ecology and evolutionary biology (Koskella et al. 2017). Despite the ever-expanding number of studies which test ecological and evolutionary theory using in vitro microcosms, it is often unclear how these insights translate to 'real world' communities. This has largely been by design, experimental microbial communities are typically assembled in the same laboratory environments that have been used to cultures model microbes in isolation, allowing researchers to quantitatively connect known biology at the cellular, metabolic and molecular level to emergent population and community-level dynamics (Estrela et al. 2022; Gowda et al. 2022; Pontrelli et al. 2022). Whilst immensely powerful, this approach comes at a cost, by studying microbes in novel environments we risk focusing on 'spandrels', phenotypic characteristics critical in the lab environment but irrelevant to the ecological function and evolutionary history of microbes in their natural context (Bergelson et al. 2021; Amir 2017).

For microbial ecology and evolution to progress as a field, there is a need to develop experimentally tractable model laboratory systems that can approximate the natural ecology of their 'real-world' counterpart. We are not the first to make this point. For example, in a recent editorial, George A. O'Toole (2024) states that "we have a community problem," highlighting the need for model systems of complex communities whose dynamics and functional output better approximates the 'real world' environment (O'Toole 2024). Similarly in the 2017 Winogradsky review, Richard E. Lenski called for the field of experimental evolution to move beyond experiments involving a small number of species evolving in isolation, towards 'Embedded species evolving in natural community experiments' (ESSENCE) (Lenski 2017). Both these pieces highlight the importance of developing and describing model community systems as the way to advance the field and bridge the gap between applied and fundamental microbiological research.

Inspired by these calls to action, here we set out to describe the key aspects which make wine fermentation an ideal model system for ecology and evolution. The central idea of this piece is that "wine has as much to contribute to ecology and evolution as ecology and evolution have to contribute to wine." Therefore, it is essential to connect wine researchers with community ecologists and evolutionary biologists. We recognise that these groups are separated by technical and theoretical backgrounds, but we believe they pursue common objectives, even if they express them using different vocabularies. Reconciling these differences and merging the knowledge and interests of both groups is the first step we aim to achieve with the simultaneous publication of this article and its companion piece in *Microbial Biotechnology* (Belda et al. 2025).

2 | Wine Fermentation as a Model System for Ecology

Like other fermented foods (B. E. Wolfe and Dutton 2015), wine fermentation is a highly tractable system, serving as a middle ground between highly complex but challenging environments like soil or freshwater microbiomes, and more simplistic set-ups like monocultures or pairwise combinations of species in laboratory culture mediums. Building on O'Toole's perspective (2024), Figure 1 summarises how wine fermentations embody the ideal characteristics of a model system: (i) A substantial knowledge of community features in the real world; (ii) a balance between complexity and feasibility; (iii) the existence of a functional measurable output; (iv) benchmarking and high reproducibility of community performance; (v) the genetic tractability of key community members. Despite these favourable methodological features, only a handful of studies have utilised wine yeast communities as model systems to explore fundamental questions in community ecology (Ponomarova et al. 2017; Bagheri et al. 2020; Lax and Gore 2023; Ruiz et al. 2023; Leale et al. 2024) and even fewer for experimental evolution (Ghiaci et al. 2024).

An extensive literature documents the microbial diversity found in grapes, grape musts, and wine fermentations (Belda, Zarraonaindia, et al. 2017a). While hundreds to thousands of fungal and bacterial genera can be detected on grape surfaces (de Celis et al. 2022; Bokulich et al. 2014), about fifty yeast genera have been isolated directly from grape musts, and most experimental studies focus on the 2–10 most abundant yeast species (repeatedly reaching $>1\%$ abundance during fermentation) (Drumonde-Neves et al. 2021; Ruiz et al. 2023; Conacher et al. 2020; Lax and Gore 2023). For this first section of our perspective, we will focus on the yeast community dynamics since they are the drivers of alcoholic fermentation and have been the main focus of ecological study. We will return to other microbial kingdoms in the following section.

Following grape crushing, wine fermentation proceeds as a highly repeatable microbial succession involving a number of different yeast species but culminating in the dominance of *Saccharomyces cerevisiae*. Initially, the grape must exerts a strong selective pressure due to its high osmolarity, which, together with the reduction in oxygen availability, acts as a significant environmental filter (Morales et al. 2015). These selection pressures cause a drastic change in the original community structure found on the grape surfaces, as almost all filamentous fungi and most basidiomycetous yeasts rapidly disappear, leaving communities dominated by ascomycetous yeast and yeast-like fungi (such as *Aureobasidium pullulans* or *Starmerella bacillaris*) (Conacher et al. 2021).

Shortly after grape crushing, these initially dominant osmophilic species are gradually replaced by weakly fermentative species (such as *Hanseniaspora uvarum* or *Torulaspora delbrueckii*), further reducing the fungal diversity (Conacher et al. 2021). These fermenters transform the environment by consuming nutrients and releasing ethanol as the main byproduct of fermentation. Between the initial phase dominated by osmotic pressure and the later phase dominated by ethanol, there exists a brief temporal window with a high diversity of fast-growing yeast

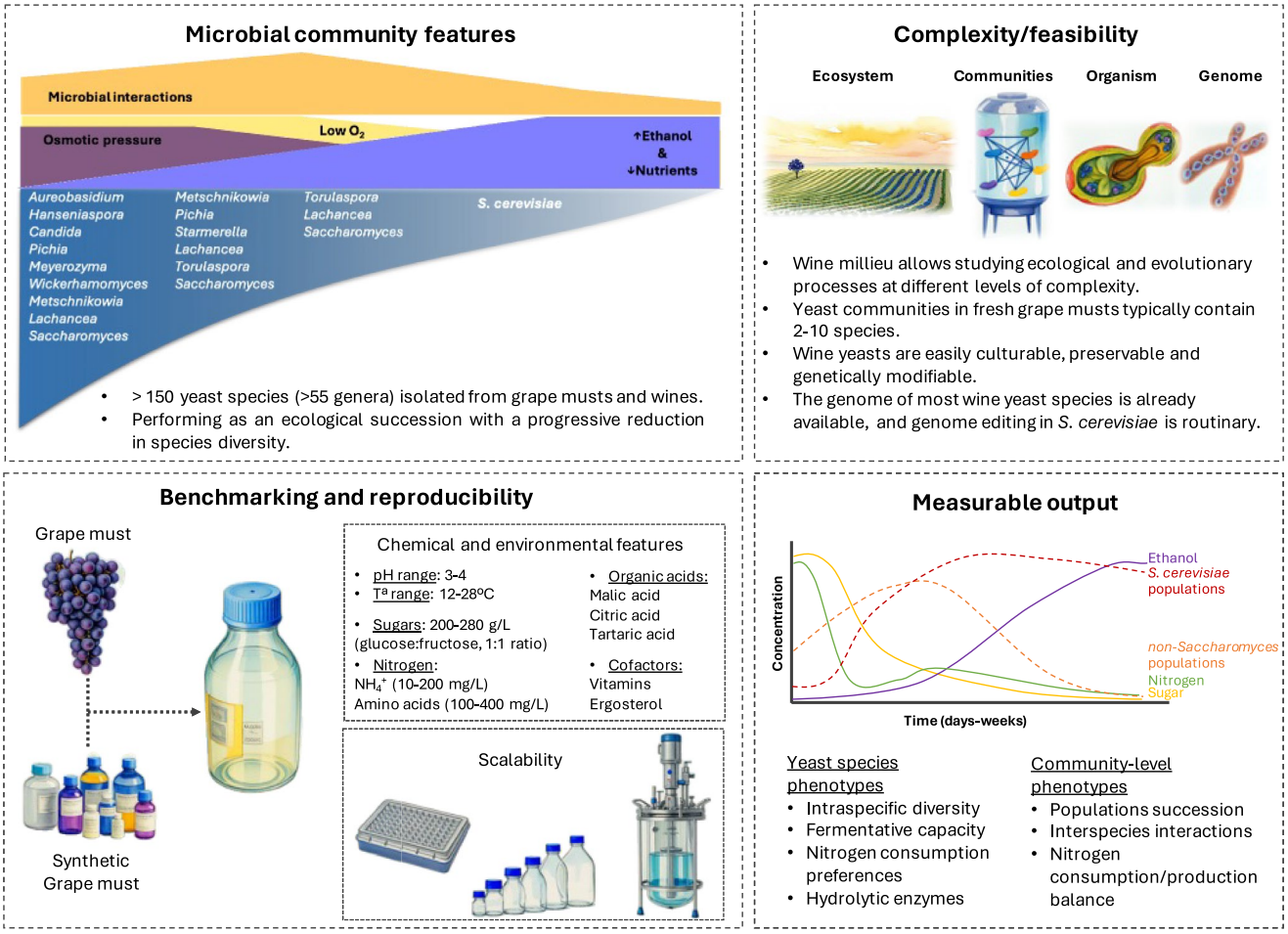

FIGURE 1 | Main features of wine fermentations as a model system. The population dynamics during spontaneous wine fermentations result in a gradual decline in yeast species diversity, primarily due to the selective pressure exerted by rising ethanol levels in the environment. Additional environmental factors, such as osmotic pressure, pH, limited oxygen availability, and nutrient scarcity, along with biotic factors like interspecies interactions, also shape the diversity patterns in wine yeast communities. As a model system, wine fermentation provides a unique opportunity to investigate biological questions across different levels of complexity, ranging from molecular to ecological studies. It also allows for the study of biological processes in both natural and fully controlled experimental conditions. Moreover, a broad range of ecological and metabolic traits can be measured to assess yeast performance, from fermentation kinetics to the consumption and production of flavour-impacting compounds.

species and in which biotic interactions can play a crucial role in determining population dynamics and, consequently, in the ecological and industrial performance of the community (Bagheri et al. 2020) (Figure 2).

To characterise the diversity of ecological interactions between microbial species during this phase of fermentation, we will adopt the categorization of environmentally mediated social interactions proposed by Estrela et al. (2019). In this work, the authors laid out a four-way classification of interaction, as individuals produce/consume an environmental factor which can either help (enrich/detox) or harm (deplete/pollute) co-occurring individuals. Intuitively, depletion may seem to be the most important behaviour for the success of individual species in the wine environment, particularly at the start of fermentation. While sugars are highly abundant as a carbon source (200–280 g/L of glucose: fructose in 1:1 ratio), the yeast assimilable nitrogen (i.e., ammonium and amino acids yielding 50–500 mg N/L) is limiting and will eventually be depleted by the most efficient consumers. Nitrogen consumption efficiency is therefore a key trait determining population dynamics during the early stages of fermentation. Substantial evidence indicates that different wine yeast strains exhibit varying preferences for nitrogen sources available in grape musts (Gobert et al. 2017). To date, this has been mainly studied from an industrial perspective—certain amino acids are key precursors for aroma-impact compounds in wines and ammonium exerts strong nitrogen catabolite repression on aroma-related genes (Subileau et al. 2008). Understanding how specialisation on different nitrogen sources impacts population dynamics is a major unresolved question with important implications for predicting the outcome of fermentation.

In addition to depleting the initial nitrogen pool, different microbial species can also enrich the environment through the release of organic nitrogen supporting the growth of

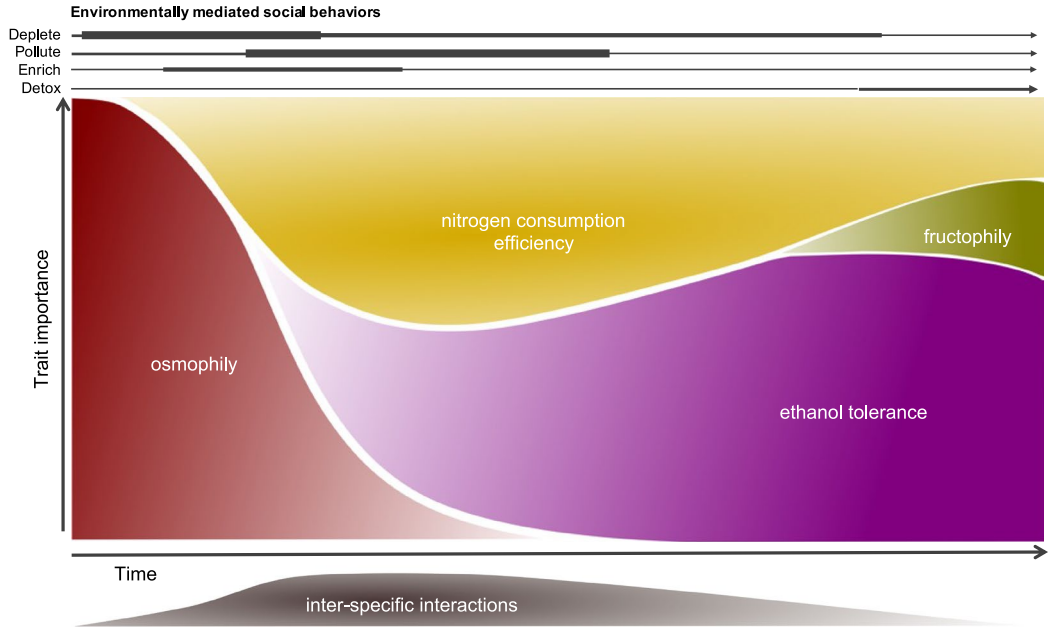

FIGURE 2 | Schematic illustrating how, over the course of a typical spontaneous fermentation, environmentally mediated ecological interactions lead to shifts in the traits under selection.

co-occurring species. In many cases, this may be a direct consequence of individual cellular metabolism. For example, Ponomarova et al. (2017) demonstrated that an active release of amino acid by *S. cerevisiae* creates a niche that facilitates the later growth of lactic acid bacteria. We speculate that there may also be an important ecological role for lysis and cell death in releasing nitrogen similar to the vitamin recycling that has recently been observed in marine particles (Gregor et al. 2024). For example, Becerra-Rodríguez et al. (2020) outline how the complex proteins released by dying cells can be transformed into utilisable sources of organic nitrogen (oligopeptides and amino acids) with the protease activities of different species determining the concentration and composition of these assimilable nitrogen sources. Since the initial nitrogen sources in grape must are often depleted during the first half of wine fermentation, the nitrogen released by these processes may significantly impact later population dynamics and fermentation kinetics (Marsit et al. 2016).

After the initial competition for nitrogen, the next critical trait determining the success of wine yeast populations is their capacity to produce and tolerate ethanol. *S. cerevisiae* alongside other fermenters pollute the environment by producing ethanol, which gradually kills the majority of yeast species as the concentration increases (Conacher et al. 2020). *S. cerevisiae* is the expectable winner of this competition, as it engineers the environment by fermentation (Goddard 2008) being the only yeast species capable of surviving the highest alcohol concentration needed for complete consumption of fermentable sugars (9%–14%). However, the population density achieved by different community members during the initial stages of fermentation can influence the time it takes for *S. cerevisiae* to outcompete and dominate the community in the later stages (Lax and Gore 2023). Since *S. cerevisiae* is a minority yeast species in vineyards and grape musts, since the mid-20th century, the practice of adding high doses of selected *S. cerevisiae* yeast strains as industrial seed inoculum has become the standard approach in winemaking. Pioneered by researchers such as Martinus Beijerinck and Jean-Marie Cantacuzène, this method has the advantage of reducing uncertainty, increasing reproducibility and predictability in wine fermentations. However, this approach diminishes (though does not eliminate) the importance of biotic interactions and results in lower microbial complexity during fermentation, leading to wines with less metabolite diversity and, consequently, reduced sensory complexity (Liu et al. 2020). To reconcile spontaneous and inoculated fermentations, the wine industry has, in the last decade, begun commercialising multi-species consortia. These consortia combine *S. cerevisiae* with non-*Saccharomyces* species, which possess desirable industrial traits that complement the fermentative performance of *S. cerevisiae* (Mateo and Maicas 2016).

During the final phase of wine-making, the dominant *S. cerevisiae* continues to convert sugars into ethanol until either the sugar has been depleted or ethanol concentration exceeds its maximum tolerance (12%–14%) (Ghareib et al. 1988). Because *S. cerevisiae* has a higher preference for glucose over fructose, fructose is typically the main sugar during this stage (Tronchoni et al. 2009). High ethanol concentration has been shown to inhibit fructose utilisation by *S. cerevisiae* populations, preventing the complete depletion of fermentable sugars (Berthels et al. 2004). Consequently, fructophily (preference for fructose over glucose) may be a critical metabolic trait in the final phase of fermentation (Figure 1). While strict fructophily is a rare trait among yeasts of the subphylum Saccharomycotina (Opulente et al. 2024), there is substantial variability in the degree of glucose-fructose preference among *S. cerevisiae* (Berthels et al. 2004). Furthermore, it is known that some wine strains harbour an allelic variant of the hexose transporter *HXT3* (Guillaume et al. 2007), while others contain a horizontally transferred *FSY1* gene (Galeote et al. 2010), both enhancing fructose utilisation during fermentation. How this phenotypic variability impacts ecological

dynamics during the final phase of fermentation is unclear, in part because we do not yet know whether wine fermentation is dominated by a single *S. cerevisiae* or a diverse consortium of co-occurring strains occupying different sugar niches. Resolving this discrepancy will require the development of new strain-resolved fungal metagenomic approaches, similar to those that have been successfully developed for bacterial communities (Roodgar et al. 2021; Olm et al. 2021; Garud et al. 2019).

Unlike other microbial systems with industrial relevance, such as those involved in wastewater treatment or the degradation of metalworking fluids (Piccardi et al. 2019), we did not find clear empirical examples of a wine yeast species detoxifying the environment. Nevertheless, several metabolites with inhibitory capabilities are consumed by wine yeast, and thus we suspect that such interactions do exist. For example, freshly pressed grape must contains significant concentrations of organic acids (such as tartaric, malic, lactic, and citric acids) which different non-*Saccharomyces* species consume to varying degrees (Ruiz et al. 2023). Growth and ethanol production by *S. cerevisiae* are highly influenced by pH, and we speculate that consumption of these different metabolites by non-*Saccharomyces* species can serve as a form of detoxification for *S. cerevisiae*, especially when the initial pH is lower (<3.2) or higher (>4.0) than the typical range found in grape musts. On the other hand, many of these same species produce organic acids that acidify the environment, and so these could be considered a form of enrichment (or even pollution if the initial pH is low (<3.0)) (Vicente et al. 2022). Another indirect form of detoxification could be sugar respiration during the early phase of fermentation (such as by *Metschnikowia pulcherrima*) which, by redirecting sugars away from stronger fermenters, leads to reductions in the final ethanol concentrations (Gonzalez et al. 2021). These more nuanced examples help illustrate the complexity of categorising environmentally mediated interactions and the benefit of describing them explicitly (Momeni et al. 2017; Niehaus et al. 2019).

In summary, in this section we have outlined how over the course of a typical fermentation, interactions, both positive and negative, can shape community dynamics, ultimately determining the aromatic profile of the final wine (Belda, Ruiz, et al. 2017b). Despite the reproducibility of this process at a coarse-grain level, we would be remiss not to highlight the variability that exists across fermentations contributing to the uniqueness of any given wine. Wine-makers have long known that differences in grape varietals can play a significant role in fermentation dynamics by changing the physio-chemical features of the grape-must. More recently, high-throughput genomic techniques have allowed us to identify unique geographically isolated microbial communities (microbial terroir) with distinctive metabolic profiles (Knight et al. 2015; Bokulich et al. 2016). Furthermore, during wine fermentation, the ecological processes at play can be directly manipulated by wine-makers using traditional methods such as sulfite addition to eliminate spoilage yeast, stirring to increase the degree of oxygen availability, and nitrogen supplementation to prevent stuck fermentations (Bagheri et al. 2020; Morales et al. 2015; Morgan et al. 2019; Varela et al. 2021). We consider this variability to be a feature, and not a bug, of wine fermentation as a model system. In fact, wine-makers have been performing natural microbial ecology experiments for centuries. By bringing these experiments into the lab, microbial ecologists have a unique opportunity to explore how these different environmental factors quantitatively shape interspecies interactions and ultimately determine community dynamics and function.

3 | Wine Fermentation as a Model System for Cross-Kingdom Interactions

Most ecological studies of wine fermentation have primarily focused on yeast for several key reasons: first, yeast drives the bulk of alcoholic fermentation; second, their taxonomic diversity can be readily characterised using a single marker gene; and third, most taxa are easily culturable, allowing for high-throughput and quantitative in vitro experiments. Nonetheless, a diverse array of other microorganisms—including bacteria and viruses—are also present and can significantly influence the final aromatic profile of wine (Bubeck et al. 2020; Liu et al. 2019). Incorporating this additional layer of complexity offers ecologists an opportunity to explore interkingdom ecological interactions and community dynamics across multiple trophic levels.

Compared to the predictable succession of yeast, bacterial community dynamics during wine fermentation are typically more variable. Freshly pressed grape musts are often dominated by multiple classes of Pseudomonadota (formerly Proteobacteria), including Gammaproteobacteria, Alphaproteobacteria, and Betaproteobacteria (Pinto et al. 2015; Piao et al. 2015; Stefanini et al. 2016; Del Portillo and Mas 2016). Within the Alphaproteobacteria, acetic acid bacteria such as *Gluconobacter* and *Acetobacter* are frequently present and have been linked to wine spoilage due to their secretion of acetic acid, which alters wine flavour and can inhibit *S. cerevisiae* fermentation by inducing apoptosis (Vilela-Moura et al. 2011). At the same time, ethanol production by *S. cerevisiae* can inhibit acetic acid bacteria, suggesting a potential role for priority effects in shaping the early stages of fermentation—a phenomenon observed in other yeast–bacteria communities as well (Chappell et al. 2022).

Over the course of fermentation, the abundance of Proteobacteria typically declines, while Bacillota—including various lactic acid bacteria—become more dominant (Bokulich et al. 2014; Pinto et al. 2015; Piao et al. 2015). One of the most well-studied metabolic functions of lactic acid bacteria is malolactic fermentation, a secondary process in which malic acid is converted to lactic acid after alcoholic fermentation is complete. Several bacterial species can perform malolactic fermentation, though the most abundant is usually *Oenococcus oeni*, which is sometimes introduced as a starter culture to modulate pH and promote the production of secondary flavour compounds (e.g., diacetyl) (Yang et al. 2024). Interestingly, malolactic fermentation is notoriously unpredictable, in stark contrast to the more consistent progression of alcoholic fermentation (Fu et al. 2022). The causes of this variability remain unclear, but we speculate that the yeast-bacteria interactions highlighted earlier may create priority effects that drive divergent functional outcomes

(Bittleston et al. 2020). Supporting this idea, a 2005 study found that some yeast produce a proteinaceous factor that inhibits *O. oeni* (Comitini et al. 2005). Additionally, Balmaseda et al. (2021) demonstrated that ethanol produced by yeast exerts strong selective pressure on *O. oeni* populations, drastically reducing strain-level diversity between the start of alcoholic fermentation and the initiation of malolactic fermentation (Balmaseda et al. 2021). Future studies tracking both alcoholic and malolactic fermentation across diverse microbial community compositions could provide broader insights into how ecological interactions shape patterns of functional divergence and redundancy in microbial ecosystems.

Beyond bacteria, several studies have examined the role of viruses—both eukaryotic and prokaryotic—in wine fermentation. It has long been known that many yeast species harbour non-lethal double-stranded RNA viruses that encode toxins, allowing them to kill susceptible yeast that lack the corresponding viral sequence (see Marquina et al. 2002 for a review) (Bevan et al. 1973). *S. cerevisiae* wine strains are often "killer" strains, carrying these viruses and outcompeting non-killer *S. cerevisiae* strains during fermentation (Boynton 2019). Similar killer-yeast systems have also been described in non-*Saccharomyces* wine yeasts. For example, *Torulaspora delbrueckii* harbours a killer virus with an exceptionally broad killing spectrum, capable of inhibiting *S. cerevisiae* and disrupting fermentation (Ramírez et al. 2015). To date, all known myco-viruses are thought to lack an extracellular transmission route, with these viruses spreading through populations via mating (Billerbeck et al. 2024). Since yeast sporulation occurs as a starvation response, horizontal viral transmission during fermentation is likely minimal. However, the long-term persistence and spread of these viruses within populations, as well as their potential impact on the dynamics of spontaneous fermentations, remain an open question that warrants further investigation.

Despite the growing use of next-generation sequencing to study wine fermentation, the wine virome remains poorly characterised and lags behind other fermented food systems such as cheese and dairy products (Paillet et al. 2024; Dugat-Bony et al. 2020). Metagenomic sequencing of these other systems has revealed a diverse array of both temperate and virulent bacteriophages, with phage community dynamics closely tracking bacterial community composition. There is little reason to think that similar dynamics will not be observed during spontaneous wine fermentation despite the lack of comprehensive metagenomic studies. Indeed, several individual phages have already been isolated from wine fermentations that can infect key lactic acid and acetic acid bacteria, and some have even been proposed as natural biocontrol agents (Cordero-Bueso et al. 2020). For example, Philippe et al. (2018) identified a phage that infects *Gluconobacter cerinus*, an acetic acid bacterium linked to wine spoilage (Philippe et al. 2018). Interestingly, recent studies have identified multiple phages infecting *Oenococcus oeni*, and it has been suggested that these phages may be a common cause of malolactic fermentation failure (Chaïb et al. 2022). As the field of viral community ecology continues to grow, wine fermentation could present a tractable system to study phage community dynamics—both in terms of how phage communities assemble in a relatively simple environment and how they shape bacterial and yeast community dynamics (Pyenson et al. 2024).

4 | Wine Fermentation as a Model System for Evolution

For the majority of yeast and bacterial species, each batch fermentation represents an evolutionary dead-end, with the stressful environmental conditions either killing cells or rendering them non-viable (Bagheri et al. 2017). In *S. cerevisiae*, however, wine-adapted strains have been shown to maintain > 90% viability at the end of fermentation, and yeast cells can persist in cellars for years before seeding future fermentations (Rosini 1984; Le Jeune et al. 2006). At the start of spontaneous fermentation, the genetic diversity of *S. cerevisiae* appears to be exceedingly high, with a recent screen of 289 strains isolated from 7 cellars identifying 225 unique microsatellite profiles (using only 17 loci) (Börlin et al. 2020). This genetic diversity means that selection can act on a population of *S. cerevisiae* strains through successive fermentations, which, combined with *de novo* mutations, leads to locally adapted cellar populations with unique aromatic profiles (Knight et al. 2015; Granchi et al. 2019) In some cases, these locally adapted strains will be descendants of an initial commercial starter originally isolated from other wineries but propagated in the lab (Chalvantzi et al. 2020). In other cases, these strains originate from natural sources and may hybridise with wild strains of *S. cerevisiae* as well as closely related yeast species such as *S. uvarum* and *S. kudriavzevii* (Dunn et al. 2012; González et al. 2006; Dunn et al. 2013). Thus, while at the genome-wide level wine-adapted *S. cerevisiae* form a clear mono-phyletic group within the species (Peter et al. 2018), individual genes exhibit a broader range of evolutionary histories thanks to the combination of hybridization, gene duplications, and complex genomic rearrangements (García-Ríos and Guillamón 2022).

In spite of the complex evolutionary history of individual genes, members of the Wine/European clade of *S. cerevisiae* are all believed to have descended from a single domestication event in the Mediterranean around 5000 BC, coinciding with the origin of viticulture (Almeida et al. 2015). Compared to their closest wild relatives in the mediterranean oak clade, the wine clade displays numerous genomic signatures of domestication, such as extensive loss of heterozygosity and a high dN/dS ratio (Peter et al. 2018; Almeida et al. 2015). Some of the most notable adaptations are highlighted in Table 1. These adaptations are underpinned by various different genetic modifications, ranging from simple codon substitutions (Guillaume et al. 2007) to more complex structural rearrangements (Goto-Yamamoto et al. 1998). Because genome editing tools are readily available for *S. cerevisiae*, the adaptive benefits of individual genetic changes can be tested experimentally across different genetic backgrounds and in environments that mimic the conditions in which these adaptations originally evolved. For example, in a recent study, Kessi-Pérez and colleagues used CRISPR-Cas9 editing to confirm that several SNPs identified via GWAS as improving growth under nitrogen limitation enhanced growth in nitrogen-limited micro-vinifications when introduced into a laboratory strain (Kessi-Pérez et al. 2023). We argue that the ability to bring this

TABLE 1 | Table highlighting some of the key phenotypic and genomic adaptations to the wine environment observed in *S. cerevisiae*. See (Marsit and Dequin 2015) and (García-Ríos and Guillamón 2022) for more comprehensive reviews.

Selection pressure	Phenotypic adaptation	Genomic basic	References
Sulfite toxicity	Increased expression of plasma membrane sulfite pump	Chromosomal rearrangements and promoter: SSU1	(Goto-Yamamoto et al. 1998; Pérez-Ortín et al. 2002; Zimmer et al. 2014; García-Ríos et al. 2019)
Copper toxicity	Increased expression of copper binding metallothioneins	Copy Number Increase: CUP1	(Crosato et al. 2020)
High osmolarity	Loss of aquaporins (water transporters)	Frame-Shifting deletion: AQY2 Nonsense mutation: AQY1	(Will et al. 2010)
High ethanol concentration	Increased Ethanol Tolerance	Aneuploidy: Chromosome III	(Voordeckers et al. 2015; Morard et al. 2019)
Low nitrogen availability	Uptake of more diverse oligopeptides due to increase transporter number	Gene transfer: FOT1-2	(Novo et al. 2009; Damon et al. 2011; Marsit et al. 2015)
High fructose availability	Increase fructose affinity by hexose transporters: acquisition of novel fructose symporter	Missense Mutation: HXT3 Horizontal Gene Transfer: FSY1	(Guillaume et al. 2007; Galeote et al. 2010)

natural genetic variation into the lab represents a unique and currently under-exploited feature of wine fermentation as a model system. It could allow evolutionary biologists to reconstruct the history of different innovations in vitro and perform counter-factual evolution experiments with subtly different starting conditions (Blount 2016; Karageorgi et al. 2019). Such an approach could help disentangle the roles of epistasis, fluctuating selection pressures, and ecological context in generating observed patterns of genomic diversity, linking micro-evolutionary processes with macro-evolutionary patterns.

Compared to adaptations to wine fermentation as a whole, adaptation to different wine making practices or conditions has been relatively under-explored. The best-known example of a specialised wine sub-clade is the flor yeast, responsible for the aging of sherry and sherry-like wines. In sherry making, flor yeast forms a biofilm (or velum) on the surface of wine, preventing excessive exposure to oxygen and allowing sherry to age, developing its unique aromatic profile (Ibeas and Jimenez 1997). The key adaptations underlying this evolutionary innovation are the increased expression of the *FLO11* gene (encoding hydrophobic cell wall glycoproteins) which evolved due to a deletion within a repression region of the *FLO11* promoter (Fidalgo et al. 2006; Legras et al. 2016). We note with interest that the *FLO11* gene is under the control of the Ras/cAMP/PKA and the MAP-kinase pathways, both of which have been recurrent targets of adaptation both within the flor yeast clade (Coi et al. 2017) and also in laboratory evolution experiments (Kinsler et al. 2020; Venkataram et al. 2016; Kvitek and Sherlock 2013).

Outside of the wine-clade, *S. cerevisiae* has been found in a wide range of other fermentation environments such as bread, beer and sake. The prominence of *S. cerevisiae* in fermentation environments is typically attributed to its unique metabolic strategy: the Crabtree effect (the ability to convert simple sugars into ethanol even under fully aerobic conditions) and the evolved "make-accumulate-consume ethanol" strategy (efficient catabolism of ethanol) (Hagman et al. 2013). A whole-genome duplication that arose at the base of *Saccharomyces* genus is thought to have 'primed' (or potentiated) yeast to evolve this key innovation by generating a repertoire of duplicate metabolic genes capable of handling increased glycolytic flux (Wolfe and Shields 1997; Conant and Wolfe 2007; Blount et al. 2012).

The exact adaptive benefits of the Crabtree effect remain in dispute and multiple non-mutually exclusive hypotheses have been proposed. Some authors have suggested that the crabtree effect evolved as a consequence of physiological constraints on growth optimisation (Thomas Pfeiffer and Morley 2014; Pfeiffer et al. 2001; Molenaar et al. 2009); others suggest that ethanol production evolved as an ecological weapon in highly competitive environments (Piskur et al. 2006; Rozpędowska et al. 2011); and still other suggest that ethanol production is a 'spandrel' or by-product of growing *S. cerevisiae* in a high sugar environment when it has adapted to low sugar concentrations (Goddard and Greig 2015). While all *S. cerevisiae* strains are crabtree-positive, the quantitative details of this effect vary across the phylogeny, with wine strains typically producing the highest levels of ethanol in lab fermentations (Camarasa et al. 2011; Barbosa et al. 2014). As well as varying by strain, levels of ethanol production can also vary substantially depending on the carbon/nitrogen source a strain chooses to consume as determined by the carbon/nitrogen catabolite repression system (Beltran et al. 2004; Simpson-Lavy and Kupiec 2019). Ecological interactions may therefore play a significant and currently under-appreciated role in the evolution of ethanol production as non-*Saccharomyces* species indirectly modify levels of ethanol production in *S. cerevisiae* by changing the resource environment (Jouhten et al. 2016).

Undoubtedly, *S. cerevisiae* will continue to be the primary focal species for genetic and evolutionary studies in wine-related yeasts. However, over the past decade, genomic signatures of adaptation to wine environments have been identified in other *Saccharomyces* species, such as introgression events from undomesticated *S. eubayanus* into *S. uvarum* (Almeida et al. 2015). Additionally, phylogenetically distinct clades from wine environments have been discovered among non-*Saccharomyces* yeasts, including *Brettanomyces bruxellensis, Torulaspora delbrueckii*, and *Lachancea thermotolerans*. Interestingly, the adaptation signatures of these species to wine-related environments mirror those described in *S. cerevisiae*, such as increased efficiency when consuming alternative nitrogen sources, suggesting that repeatable adaptive outcomes may be observed even when evolving from very different genetic backgrounds (Avramova et al. 2018; Silva et al. 2023; Vicente et al. 2024). How non-*S. cerevisiae* species are able to adapt to the wine environment when the populations are presumably killed off by *S. cerevisiae* during fermentation remains unclear. One possibility is that non-*Saccharomyces* yeasts are able to evolve and adapt to other high-sugar, low-nitrogen environments (such as rotting fruit) or nectar where *S. cerevisiae* do not have as large a competitive advantage (Chappell and Fukami 2018). We speculate that non-*Saccharomyces* yeast adaptations in these environments may end up being beneficial during the early stage of wine fermentation, similar to other forms of metabolic exaptation that have been observed in computational and experimental studies (Barve and Wagner 2013; Szappanos et al. 2016; Hosseini and Wagner 2016).

How the diverse bacterial species present on grape-must evolve and adapt to the wine fermentation niche is also unexplored and could be the target of future evolutionary studies. *O. oeni* is an especially interesting focal species for experimental evolution since alcoholic fermentation by *S. cerevisiae* has been shown to impose strong selective pressure on *O. oeni* favouring strains with higher ethanol tolerance (Balmaseda et al. 2021). Moreover, different non-*Saccharomyces* yeasts have markedly different physiological impacts on *O. oeni*, which presumably lead to different biotic selection pressures and divergent evolutionary adaptations (Balmaseda et al. 2021). Experimental evolution of *O. oeni* in different yeast communities could therefore be a rich system to explore the impact of biotic selection pressures on evolutionary adaptation and the impact of evolutionary adaptation on ecological interactions. For example, experimental evolution with *O. oeni* and *S. cerevisiae* could be used to test whether coevolution leads to increasing interdependence (in line with the Black Queen Hypothesis; (Morris et al. 2012)) or whether it results in an evolutionary arms race (Niehus et al. 2021). Furthermore, the presence and culturability of *O. oeni* specific bacteriophages in wine fermentation environments (Philippe et al. 2021) offers an additional opportunity to explore phage-bacteria co-evolution in an experimentally tractable multi-trophic ecosystem.

5 | Conclusion

In addition to being economically important, we have outlined how wine fermentation is a tractable model system for addressing key questions in microbial population biology. The 'simple' chemical composition of grape-must enables the reproduction of complex ecological dynamics in vitro using synthetic habitats where external sources of variation are carefully controlled. At the same time, the keystone species *S. cerevisiae* has undergone thousands of years of adaptation to the biotic and abiotic challenges of wine fermentation, resulting in a diverse clade with unique genomic and phenotypic adaptations.

Wine fermentation complements other fermented food microbial systems that have previously been studied as model systems, including the microbial communities associated with cheese rind, sourdough, kimchi, and beer, as well as other traditionally fermented products (Wolfe and Dutton 2015; Louw et al. 2023; Alekseeva et al. 2021). Many of these systems rely on chemically and spatially complex substrates, such as milk or grains, which contrasts with the relatively simple chemical composition of grape must, where sugars serve as the primary carbon source and ammonium and amino acids serve as the primary nitrogen sources (Ruiz et al. 2023). The 'simple' and 'well-mixed' nature of wine fermentation provides a major advantage for mechanistic ecological and evolutionary studies, as microbial physiology and environmentally mediated interactions can be explicitly tracked and accounted for. However, this comes at the cost of excluding key ecological dynamics that emerge in spatially structured communities, such as surface-attached biofilms (e.g., cheese rind; (Wolfe et al. 2014)) or in semi-solid substrates containing complex polysaccharides (e.g., sourdough starters or kimchi; (Landis et al. 2021; Jung et al. 2011)). Additionally, few other fermented products have as global a distribution as wine, which is produced in more than 50 countries and dates back to at least 5000 B.C. (Marsit and Dequin 2015). The widespread distribution and long history makes wine fermentation particularly valuable for evolutionary studies, as the vast number of evolving microbial populations across wineries provides a unique opportunity to examine the ecological drivers of repeatable and divergent adaptive outcomes (Blount et al. 2018; Lenski 2017).

As with other fermented food systems, wine fermentation lacks a dedicated host, meaning that the influence of host-associated factors, such as innate and adaptive immunity, on microbial community composition is largely absent. However, a potential exception could be Drosophila fruit flies, which are commonly found in vineyards and wineries and are often associated with several key wine-associated yeast species, including *Saccharomyces cerevisiae, Metschnikowia pulcherrima*, *Hanseniaspora uvarum*, and *Torulaspora delbrueckii* (Lam and Howell 2015; Hoang et al. 2015). Several studies suggest that fruit flies aid wine yeast dispersal and persistence, both in a species-specific and general manner, with ongoing debate about whether a coevolved mutualism exists (Quan and Eisen 2018; Buser et al. 2014; Günther and Goddard 2019). While a deeper exploration of this phenomenon is beyond the scope of this perspective, further investigation into host–microbe interactions in wine-attracted flies may yield valuable eco-evolutionary insights.

In sum, we have suggested that evolutionary biologists and ecologists can use wine fermentation to study: (i) The contributions of different ecological processes in shaping community dynamics; (ii) the connection between the microevolutionary processes of mutation and selection and macroevolutionary processes shaping genetic diversity in nature; and (iii) the impact of biotic

and genomic context on adaptation and evolutionary innovations. Thus, wine fermentation provides the perfect playground for building and testing predictive models of complex community ecology, evolution, and function.

Author Contributions

Ignacio Belda: conceptualization, investigation, supervision, funding acquisition, resources, writing – original draft, writing – review and editing. **Sergio Izquierdo-Gea:** investigation, writing – original draft. **Belen Benitez-Dominguez:** investigation, writing – original draft. **Javier Ruiz:** writing – original draft, writing – review and editing, supervision. **Jean C. C. Vila:** conceptualization, writing – original draft, writing – review and editing, supervision.

Acknowledgements

We thank members of Sanchez, Petrov and Microbial Interactions and Ecology Lab for helpful discussion. In particular, we thank Dmitri Petrov, Clare Abreau and Marianna Karageorgi for providing insightful comments on this piece. Recent research by Ignacio Belda's lab has been supported by grants PID2019-105834GA-I00 (acronym Wineteractions) and PID2022-138343NB-I00 (acronym INDUSYNCON) funded by the Spanish State Research Agency/Science and Research Ministry (https://doi.org/10.13039/501100011033) and by ERDF/EU. Sergio Izquierdo-Gea acknowledges his predoctoral grant FPU21/06830 funded by the Spanish Ministry of Science, Innovation and Universities. Belen Benítez-Dominguez acknowledges her predoctoral grant PRE2022-103063 funded by MICIU/AEI/10.13039/501100011033 and by ESF+. JCC Vila was partially funded by a Center for Computational (CEHG), Evolutionary and Human Genomics postdoctoral fellowship at Stanford.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

There is no new data included in this work.

References

Alekseeva, A. Y., A. E. Groenenboom, E. J. Smid, and S. E. Schoustra. 2021. "Eco-Evolutionary Dynamics in Microbial Communities From Spontaneous Fermented Foods." *International Journal of Environmental Research and Public Health* 18, no. 19: 10093. https://doi.org/10.3390/ijerph181910093.

Almeida, P., R. Barbosa, P. Zalar, et al. 2015. "A Population Genomics Insight Into the Mediterranean Origins of Wine Yeast Domestication." *Molecular Ecology* 24, no. 21: 5412–5427. https://doi.org/10.1111/mec.13341.

Amir, A. 2017. "Is Cell Size a Spandrel?" *eLife* 6: e22186. https://doi.org/10.7554/eLife.22186.

Avramova, M., A. Cibrario, E. Peltier, et al. 2018. "Brettanomyces Bruxellensis Population Survey Reveals a Diploid-Triploid Complex Structured According to Substrate of Isolation and Geographical Distribution." *Scientific Reports* 8: 4136. https://doi.org/10.1038/s41598-018-22580-7.

Bagheri, B., F. F. Bauer, and M. E. Setati. 2017. "The Impact of *Saccharomyces Cerevisiae* on a Wine Yeast Consortium in Natural and Inoculated Fermentations." *Frontiers in Microbiology* 8, no. October: 1988.

Bagheri, B., F. F. Bauer, G. Cardinali, and M. E. Setati. 2020. "Ecological Interactions Are a Primary Driver of Population Dynamics in Wine Yeast Microbiota During Fermentation." *Scientific Reports* 10, no. 1: 4911.

Balmaseda, A., M. Lorentzen, L. Dutilh, et al. 2021. "Alcoholic Fermentation Drives the Selection of *Oenococcus Oeni* Strains in Wine but Not in Cider." *International Journal of Food Microbiology* 400: 110276. https://doi.org/10.1016/j.ijfoodmicro.2023.110276.

Barbosa, C., P. Lage, A. Vilela, A. Mendes-Faia, and A. Mendes-Ferreira. 2014. "Phenotypic and Metabolic Traits of Commercial *Saccharomyces Cerevisiae* Yeasts." *AMB Express* 4: 39.

Barve, A., and A. Wagner. 2013. "A Latent Capacity for Evolutionary Innovation Through Exaptation in Metabolic Systems." *Nature* 500, no. 7461: 203–206. https://doi.org/10.1038/nature12301.

Becerra-Rodríguez, C., S. Marsit, and V. Galeote. 2020. "Diversity of Oligopeptide Transport in Yeast and Its Impact on Adaptation to Winemaking Conditions." *Frontiers in Genetics* 11: 602.

Belda, I., B. Benitez-Dominguez, S. Izquierdo-Gea, C. C. J. Vila, and J. Ruiz. 2025. "Ecology and Evolutionary Biology as Frameworks to Study Wine Fermentations." *Microbial Biotechnology* 18: e70078. https://doi.org/10.1111/1751-7915.70078.

Belda, I., I. Zarraonaindia, M. Perisin, A. Palacios, and A. Acedo. 2017a. "From Vineyard Soil to Wine Fermentation: Microbiome Approximations to Explain the 'Terroir' Concept." *Frontiers in Microbiology* 8: 821.

Beltran, G., M. Novo, N. Rozès, A. Mas, and J. M. Guillamón. 2004. "Nitrogen Catabolite Repression in *Saccharomyces Cerevisiae* During Wine Fermentations." *FEMS Yeast Research* 4, no. 6: 625–632.

Bergelson, J., M. Kreitman, D. A. Petrov, A. Sanchez, and M. Tikhonov. 2021. "Functional Biology in Its Natural Context: A Search for Emergent Simplicity." *eLife* 10: e67646. https://doi.org/10.7554/eLife.67646.

Berthels, N. J., R. R. Cordero Otero, F. F. Bauer, J. M. Thevelein, and I. S. Pretorius. 2004. "Discrepancy in Glucose and Fructose Utilisation During Fermentation by *Saccharomyces Cerevisiae* Wine Yeast Strains." *FEMS Yeast Research* 4, no. 7: 683–689.

Bevan, E. A., A. J. Herring, and D. J. Mitchell. 1973. "Preliminary Characterization of Two Species of dsRNA in Yeast and Their Relationship to the Killer Character." *Nature* 245, no. 5420: 81–86. https://doi.org/10.1038/245081b0.

Billerbeck, S., R. S. K. Walker, and I. S. Pretorius. 2024. "Killer Yeasts: Expanding Frontiers in the Age of Synthetic Biology." *Trends in Biotechnology* 42, no. 9: 1081–1096. https://doi.org/10.1016/j.tibtech.2024.03.003.

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: 1440. https://doi.org/10.1038/s41467-020-15169-0.

Blount, Z. D. 2016. "History's Windings in a Flask: Microbial Experiments Into Evolutionary Contingency." In *Chance in Evolution*, edited by G. Ramsay, and C. H, Pence, 244–263. University of Chicago Press.

Blount, Z. D., J. E. Barrick, C. J. Davidson, and R. E. Lenski. 2012. "Genomic Analysis of a Key Innovation in an Experimental *Escherichia Coli* Population." *Nature* 489, no. 7417: 513–518.

Blount, Z. D., R. E. Lenski, and J. B. Losos. 2018. "Contingency and Determinism in Evolution: Replaying Life's Tape." *Science* 362, no. 6415: eaam5979. https://doi.org/10.1126/science.aam5979.

Bokulich, N. A., J. H. Thorngate, P. M. Richardson, and D. A. Mills. 2014. "Microbial Biogeography of Wine Grapes Is Conditioned by Cultivar, Vintage, and Climate." *Proceedings of the National Academy of Sciences of the United States of America* 111, no. 1: E139–E148.

Bokulich, N. A., T. S. Collins, C. Masarweh, et al. 2016. "Associations Among Wine Grape Microbiome, Metabolome, and Fermentation

Behavior Suggest Microbial Contribution to Regional Wine Characteristics." *MBio* 7, no. 3: e00631-16. https://doi.org/10.1128/mBio.00631-16.

Börlin, M., O. Claisse, W. Albertin, F. Salin, J. L. Legras, and I. Masneuf-Pomarede. 2020. "Quantifying the Effect of Human Practices on *S. Cerevisiae* Vineyard Metapopulation Diversity." *Scientific Reports* 10, no. 1: 16214. https://doi.org/10.1038/s41598-020-73279-7.

Boynton, P. J. 2019. "The Ecology of Killer Yeasts: Interference Competition in Natural Habitats." *Yeast* 36, no. 8: 473–485. https://doi.org/10.1002/yea.3398.

Bubeck, A. M., L. Preiss, A. Jung, et al. 2020. "Bacterial Microbiota Diversity and Composition in Red and White Wines Correlate With Plant-Derived DNA Contributions and Botrytis Infection." *Scientific Reports* 10: 13828. https://doi.org/10.1038/s41598-020-70535-8.

Buser, C. C., R. D. Newcomb, A. C. Gaskett, and M. R. Goddard. 2014. "Niche Construction Initiates the Evolution of Mutualistic Interactions." *Ecology Letters* 17, no. 10: 1257–1264. https://doi.org/10.1111/ele.12331.

Camarasa, C., I. Sanchez, P. Brial, F. Bigey, and S. Dequin. 2011. "Phenotypic Landscape of *Saccharomyces Cerevisiae* During Wine Fermentation: Evidence for Origin-Dependent Metabolic Traits." *PLoS One* 6, no. 9: e25147.

Chaïb, A., C. Philippe, F. Jaomanjaka, et al. 2022. "Phage-Host Interactions as a Driver of Population Dynamics During Wine Fermentation: Betting on Underdogs." *International Journal of Food Microbiology* 383: 109936. https://doi.org/10.1016/j.ijfoodmicro.2022.109936.

Chalvantzi, I., G. Banilas, C. Tassou, and A. Nisiotou. 2020. "Patterns of Genetic Diversity and the Invasion of Commercial Starters in *Saccharomyces Cerevisiae* Vineyard Populations of Santorini Island." *Foods (Basel, Switzerland)* 9, no. 5: 561. https://doi.org/10.3390/foods9050561.

Chappell, C. R., and T. Fukami. 2018. "Nectar Yeasts: A Natural Microcosm for Ecology." *Yeast* 35, no. 6: 417–423. https://doi.org/10.1002/yea.3311.

Chappell, C. R., M. K. Dhami, M. C. Bitter, et al. 2022. "Wide-Ranging Consequences of Priority Effects Governed by an Overarching Factor." *eLife* 11: e79647.

Coi, A. L., F. Bigey, S. Mallet, et al. 2017. "Genomic Signatures of Adaptation to Wine Biological Ageing Conditions in Biofilm-Forming Flor Yeasts." *Molecular Ecology* 26, no. 7: 2150–2166.

Comitini, F., R. Ferretti, F. Clementi, I. Mannazzu, and M. Ciani. 2005. "Interactions Between Saccharomyces Cerevisiae and Malolactic Bacteria: Preliminary Characterization of a Yeast Proteinaceous Compound(s) Active Against *Oenococcus oeni*." *Journal of Applied Microbiology* 99, no. 1: 105–111. https://doi.org/10.1111/j.1365-2672.2005.02579.x.

Conacher, C. G., N. A. Luyt, R. K. Naidoo-Blassoples, D. Rossouw, M. E. Setati, and F. F. Bauer. 2021. "The Ecology of Wine Fermentation: A Model for the Study of Complex Microbial Ecosystems." *Applied Microbiology and Biotechnology* 105, no. 8: 3027–3043.

Conacher, C. G., R. K. Naidoo-Blassoples, D. Rossouw, and F. F. Bauer. 2020. "Real-Time Monitoring of Population Dynamics and Physical Interactions in a Synthetic Yeast Ecosystem by Use of Multicolour Flow Cytometry." *Applied Microbiology and Biotechnology* 104, no. 12: 5547–5562.

Conant, G. C., and K. H. Wolfe. 2007. "Increased Glycolytic Flux as an Outcome of Whole-Genome Duplication in Yeast." *Molecular Systems Biology* 3: 129.

Cordero-Bueso, G., J. Moraga, M. Ríos-Carrasco, M. Ruiz-Muñoz, and J. M. Cantoral. 2020. "Bacteriophages as an Up-and-Coming Alternative to the Use of Sulfur Dioxide in Winemaking." *Frontiers in Microbiology* 10: 2931. https://doi.org/10.3389/fmicb.2019.02931.

Crosato, G., C. Nadai, M. Carlot, et al. 2020. "The Impact of CUP1 Gene Copy-Number and XVI-VIII/XV-XVI Translocations on Copper and Sulfite Tolerance in Vineyard *Saccharomyces Cerevisiae* Strain Populations." *FEMS Yeast Research* 20, no. 4: foaa028. https://doi.org/10.1093/femsyr/foaa028.

Damon, C., L. Vallon, S. Zimmermann, et al. 2011. "A Novel Fungal Family of Oligopeptide Transporters Identified by Functional Metatranscriptomics of Soil Eukaryotes." *ISME Journal* 5, no. 12: 1871–1880.

de Celis, M., J. Ruiz, J. Vicente, et al. 2022. "Expectable Diversity Patterns in Wine Yeast Communities." *FEMS Yeast Research* 22, no. 1: foac034. https://doi.org/10.1093/femsyr/foac034.

Del Portillo, M. C., and A. Mas. 2016. "Analysis of Microbial Diversity and Dynamics During Wine Fermentation of Grenache Grape Variety by High- Throughput Barcoding Sequencing." *LWT - Food Science and Technology* 72: 317–321. https://doi.org/10.1016/j.lwt.2016.05.009.

Donoghue, M. J., and E. J. Edwards. 2019. "Model Clades Are Vital for Comparative Biology, and Ascertainment Bias Is Not a Problem in Practice: A Response to Beaulieu and O'Meara (2018)." *American Journal of Botany* 106, no. 3: 327–330.

Drumonde-Neves, J., T. Fernandes, T. Lima, C. Pais, and R. Franco-Duarte. 2021. "Learning From 80 Years of Studies: A Comprehensive Catalogue of Non-Saccharomyces Yeasts Associated With Viticulture and Winemaking." *FEMS Yeast Research* 21, no. 3: foab017. https://doi.org/10.1093/femsyr/foab017.

Duffy, M. A., C. García-Robledo, S. P. Gordon, et al. 2021. "Model Systems in Ecology, Evolution, and Behavior: A Call for Diversity in Our Model Systems and Discipline." *American Naturalist* 198, no. 1: 53–68.

Dugat-Bony, E., J. Lossouarn, M. De Paepe, et al. 2020. "Viral Metagenomic Analysis of the Cheese Surface: A Comparative Study of Rapid Procedures for Extracting Viral Particles." *Food Microbiology* 85: 103278. https://doi.org/10.1016/j.fm.2019.103278.

Dunn, B., C. Richter, D. J. Kvitek, T. Pugh, and G. Sherlock. 2012. "Analysis of the *Saccharomyces Cerevisiae* Pan-Genome Reveals a Pool of Copy Number Variants Distributed in Diverse Yeast Strains From Differing Industrial Environments." *Genome Research* 22, no. 5: 908–924.

Dunn, B., T. Paulish, A. Stanbery, et al. 2013. "Recurrent Rearrangement During Adaptive Evolution in an Interspecific Yeast Hybrid Suggests a Model for Rapid Introgression." *PLoS Genetics* 9, no. 3: e1003366.

Estrela, S., Á. Sánchez, and M. Rebolleda-Gómez. 2021. "Multi-Replicated Enrichment Communities as a Model System in Microbial Ecology." *Frontiers in Microbiology* 12: 657467.

Estrela, S., E. Libby, J. Van Cleve, et al. 2019. "Environmentally Mediated Social Dilemmas." *Trends in Ecology & Evolution* 34, no. 1: 6–18.

Estrela, S., J. C. C. Vila, N. Lu, et al. 2022. "Functional Attractors in Microbial Community Assembly." *Cell Systems* 13, no. 1: 29–42.

Fidalgo, M., R. R. Barrales, J. I. Ibeas, and J. Jimenez. 2006. "Adaptive Evolution by Mutations in the *FLO11* Gene." *Proceedings of the National Academy of Sciences of the United States of America* 103, no. 30: 11228–11233.

Fu, J., L. Wang, J. Sun, N. Ju, and G. Jin. 2022. "Malolactic Fermentation: New Approaches to Old Problems." *Microorganisms* 10, no. 12: 2363. https://doi.org/10.3390/microorganisms10122363.

Galeote, V., M. Novo, M. Salema-Oom, et al. 2010. "FSY1, a Horizontally Transferred Gene in the *Saccharomyces Cerevisiae* EC1118 Wine Yeast Strain, Encodes a High-Affinity Fructose/H+ Symporter." *Microbiology* 156, no. Pt 12: 3754–3761.

García-Ríos, E., and J. M. Guillamón. 2022. "Genomic Adaptations of Saccharomyces Genus to Wine Niche." *Microorganisms* 10, no. 9: 1811. https://doi.org/10.3390/microorganisms10091811.

García-Ríos, E., M. Nuévalos, E. Barrio, S. Puig, and J. M. Guillamón. 2019. "A New Chromosomal Rearrangement Improves the Adaptation of Wine Yeasts to Sulfite." *Environmental Microbiology* 21, no. 5: 1771–1781.

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.

Ghareib, M., K. A. Youssef, and A. A. Khalil. 1988. "Ethanol Tolerance of Saccharomyces Cerevisiae and Its Relationship to Lipid Content and Composition." *Folia Microbiologica* 33, no. 6: 447–452.

Ghiaci, P., P. Jouhten, N. Martyushenko, et al. 2024. "Highly Parallelized Laboratory Evolution of Wine Yeasts for Enhanced Metabolic Phenotypes." *Molecular Systems Biology* 1: 1–25.

Gobert, A., R. Tourdot-Maréchal, C. Morge, et al. 2017. "Non-Saccharomyces Yeasts Nitrogen Source Preferences: Impact on Sequential Fermentation and Wine Volatile Compounds Profile." *Frontiers in Microbiology* 8: 2175.

Goddard, M. R. 2008. "Quantifying the Complexities of *Saccharomyces cerevisiae*'s Ecosystem Engineering via Fermentation." *Ecology* 89: 2077–2082.

Goddard, M. R., and D. Greig. 2015. "*Saccharomyces Cerevisiae*: A Nomadic Yeast With no Niche?" *FEMS Yeast Research* 15, no. 3: fov009. https://doi.org/10.1093/femsyr/fov009.

Gonzalez, R., A. M. Guindal, J. Tronchoni, and P. Morales. 2021. "Biotechnological Approaches to Lowering the Ethanol Yield During Wine Fermentation." *Biomolecules* 11: 1569. https://doi.org/10.3390/biom11111569.

González, S. S., E. Barrio, J. Gafner, and A. Querol. 2006. "Natural Hybrids From *Saccharomyces Cerevisiae*, Saccharomyces Bayanus and Saccharomyces Kudriavzevii in Wine Fermentations." *FEMS Yeast Research* 6, no. 8: 1221–1234.

Goto-Yamamoto, N., K. Kitano, K. Shiki, et al. 1998. "SSU1-R, a Sulfite Resistance Gene of Wine Yeast, Is an Allele of SSU1 With a Different Upstream Sequence." *Journal of Fermentation and Bioengineering* 86, no. 5: 427–433.

Gowda, K., D. Ping, M. Mani, and S. Kuehn. 2022. "Genomic Structure Predicts Metabolite Dynamics in Microbial Communities." *Cell* 185, no. 3: 530–546.

Granchi, L., D. Ganucci, G. Buscioni, S. Mangani, and S. Guerrini. 2019. "The Biodiversity of *Saccharomyces Cerevisiae* in Spontaneous Wine Fermentation: The Occurrence and Persistence of Winery-Strains." *Fermentation* 5, no. 4: 86.

Gregor, R., G. T. Vercelli, R. E. Szabo, et al. 2024. "Widespread B-Vitamin Auxotrophy in Marine Particle-Associated Bacteria." *bioRxiv*: 1–49. https://doi.org/10.1101/2023.10.16.562604.

Guillaume, C., P. Delobel, J.-M. Sablayrolles, and B. Blondin. 2007. "Molecular Basis of Fructose Utilization by the Wine Yeast *Saccharomyces Cerevisiae*: A Mutated HXT3 Allele Enhances Fructose Fermentation." *Applied and Environmental Microbiology* 73, no. 8: 2432–2439.

Günther, C. S., and M. R. Goddard. 2019. "Do Yeasts and Drosophila Interact Just by Chance?" *Fungal Ecology* 38: 37–43. https://doi.org/10.1016/J.FUNECO.2018.04.005.

Hagman, A., T. Säll, C. Compagno, and J. Piskur. 2013. "Yeast "Make-Accumulate-Consume" Life Strategy Evolved as a Multi-Step Process That Predates the Whole Genome Duplication." *PLoS One* 8, no. 7: e68734. https://doi.org/10.1371/journal.pone.0068734.

Hoang, D., A. Kopp, and J. A. Chandler. 2015. "Interactions Between Drosophila and Its Natural Yeast Symbionts-Is *Saccharomyces Cerevisiae* a Good Model for Studying the Fly-Yeast Relationship?" *PeerJ* 3: e1116. https://doi.org/10.7717/peerj.1116.

Hosseini, S. R., and A. Wagner. 2016. "The Potential for Non-Adaptive Origins of Evolutionary Innovations in Central Carbon Metabolism." *BMC Systems Biology* 10: 97. https://doi.org/10.1186/s12918-016-0343-7.

Ibeas, J. I., and J. Jimenez. 1997. "Mitochondrial DNA Loss Caused by Ethanol in Saccharomyces Flor Yeasts." *Applied and Environmental Microbiology* 63, no. 1: 7–12.

Jessup, C. M., R. Kassen, S. E. Forde, et al. 2004. "Big Questions, Small Worlds: Microbial Model Systems in Ecology." *Trends in Ecology & Evolution* 19, no. 4: 189–197.

Jouhten, P., O. Ponomarova, R. Gonzalez, and K. R. Patil. 2016. "*Saccharomyces Cerevisiae* Metabolism in Ecological Context." *FEMS Yeast Research* 16, no. 7: fow080. https://doi.org/10.1093/femsyr/fow080.

Jung, J. Y., S. H. Lee, J. M. Kim, et al. 2011. "Metagenomic Analysis of Kimchi, a Traditional Korean Fermented Food." *Applied and Environmental Microbiology* 77, no. 7: 2264–2274. https://doi.org/10.1128/AEM.02157-10.

Karageorgi, M., S. C. Groen, F. Sumbul, et al. 2019. "Genome Editing Retraces the Evolution of Toxin Resistance in the Monarch Butterfly." *Nature* 574, no. 7778: 409–412.

Kessi-Pérez, E. I., E. Acuña, C. Bastías, et al. 2023. "Single Nucleotide Polymorphisms Associated With Wine Fermentation and Adaptation to Nitrogen Limitation in Wild and Domesticated Yeast Strains." *Biological Research* 56, no. 1: 43. https://doi.org/10.1186/s40659-023-00453-2.

Kinsler, G., K. Geiler-Samerotte, and D. A. Petrov. 2020. "Fitness Variation Across Subtle Environmental Perturbations Reveals Local Modularity and Global Pleiotropy of Adaptation." *eLife* 9: e61271. https://doi.org/10.7554/eLife.61271.

Knight, S., S. Klaere, B. Fedrizzi, and M. R. Goddard. 2015. "Regional Microbial Signatures Positively Correlate With Differential Wine Phenotypes: Evidence for a Microbial Aspect to Terroir." *Scientific Reports* 5: 14233.

Koskella, B., L. J. Hall, and C. J. E. Metcalf. 2017. "The Microbiome Beyond the Horizon of Ecological and Evolutionary Theory." *Nature Ecology & Evolution* 1, no. 11: 1606–1615.

Kvitek, D. J., and G. Sherlock. 2013. "Whole Genome, Whole Population Sequencing Reveals That Loss of Signaling Networks Is the Major Adaptive Strategy in a Constant Environment." *PLoS Genetics* 9, no. 11: e1003972.

Lam, S. S., and K. S. Howell. 2015. "Drosophila-Associated Yeast Species in Vineyard Ecosystems." *FEMS Microbiology Letters* 362, no. 20: fnv170. https://doi.org/10.1093/femsle/fnv170.

Landis, E. A., M. Oliverio, E. A. McKenney, et al. 2021. "The Diversity and Function of Sourdough Starter Microbiomes." *eLife* 10: e61644. https://doi.org/10.7554/eLife.61644.

Lawton, J. H. 1995. "Ecological Experiments With Model Systems." *Science* 269, no. 5222: 328–331.

Lax, S., and J. Gore. 2023. "Strong Ethanol- and Frequency-Dependent Ecological Interactions in a Community of Wine-Fermenting Yeasts." *Communications Biology* 6, no. 1: 939.

Le Jeune, C., C. Erny, C. Demuyter, and M. Lollier. 2006. "Evolution of the Population of *Saccharomyces Cerevisiae* From Grape to Wine in a Spontaneous Fermentation." *Food Microbiology* 23, no. 8: 709–716.

Leale, A. M., E. Pourcelot, S. Guezenec, D. Sicard, and T. Nidelet. 2024. "*S. Cerevisiae* Serves as Keystone Species for Spoilage Resistance in Experimental Synthetic Wine Yeast Communities." *bioRxiv*: 1–34. https://doi.org/10.1101/2024.07.04.602080.

Legras, J.-L., J. Moreno-Garcia, S. Zara, et al. 2016. "Flor Yeast: New Perspectives Beyond Wine Aging." *Frontiers in Microbiology* 7: 503. https://doi.org/10.3389/fmicb.2016.00503.

Lenski, R. E. 2017. "Experimental Evolution and the Dynamics of Adaptation and Genome Evolution in Microbial Populations." *ISME Journal* 11, no. 10: 2181–2194. https://doi.org/10.1038/ismej.2017.69.

Lenski, R. E., and M. Travisano. 1994. "Dynamics of Adaptation and Diversification: A 10,000-Generation Experiment With Bacterial Populations." *Proceedings of the National Academy of Sciences of the United States of America* 91, no. 15: 6808–6814.

Liu, D., P. Zhang, D. Chen, and K. Howell. 2019. "From the Vineyard to the Winery: How Microbial Ecology Drives Regional Distinctiveness of Wine." *Frontiers in Microbiology* 10: 2679. https://doi.org/10.3389/fmicb.2019.02679.

Liu, D., Q. Chen, P. Zhang, D. Chen, and K. S. Howell. 2020. "The Fungal Microbiome Is an Important Component of Vineyard Ecosystems and Correlates With Regional Distinctiveness of Wine." *mSphere* 5, no. 4: e00534-20. https://doi.org/10.1128/mSphere.00534-20.

Louw, N. L., K. Lele, R. Ye, C. B. Edwards, and B. E. Wolfe. 2023. "Microbiome Assembly in Fermented Foods." *Annual Review of Microbiology* 77: 381–402. https://doi.org/10.1146/annurev-micro-032521-041956.

Marquina, D., A. Santos, and J. M. Peinado. 2002. "Biology of Killer Yeasts." *International Microbiology* 5, no. 2: 65–71. https://doi.org/10.1007/s10123-002-0066-z.

Marsit, S., A. Mena, F. Bigey, et al. 2015. "Evolutionary Advantage Conferred by an Eukaryote-To-Eukaryote Gene Transfer Event in Wine Yeasts." *Molecular Biology and Evolution* 32, no. 7: 1695–1707.

Marsit, S., and S. Dequin. 2015. "Diversity and Adaptive Evolution of Saccharomyces Wine Yeast: A Review." *FEMS Yeast Research* 15, no. 7: fov067. https://doi.org/10.1093/femsyr/fov067.

Marsit, S., I. Sanchez, V. Galeote, and S. Dequin. 2016. "Horizontally Acquired Oligopeptide Transporters Favour Adaptation of *Saccharomyces Cerevisiae* Wine Yeast to Oenological Environment." *Environmental Microbiology* 18, no. 4: 1148–1161.

Mateo, J. J., and S. Maicas. 2016. "Application of Non-Saccharomyces Yeasts to Wine-Making Process." *Fermentation* 2, no. 3: 14.

Meroz, N., N. Tovi, Y. Sorokin, and J. Friedman. 2021. "Community Composition of Microbial Microcosms Follows Simple Assembly Rules at Evolutionary Timescales." *Nature Communications* 12, no. 1: 2891.

Molenaar, D., R. Van Berlo, D. de Ridr, and B. Teusink. 2009. "Shifts in Growth Strategies Reflect Tradeoffs in Cellular Economics." *Molecular Systems Biology* 5: 323.

Momeni, B., L. Xie, and W. Shou. 2017. "Lotka-Volterra Pairwise Modeling Fails to Capture Diverse Pairwise Microbial Interactions." *eLife* 6: e25051. https://doi.org/10.7554/eLife.25051.

Morales, P., V. Rojas, M. Quirós, and R. Gonzalez. 2015. "The Impact of Oxygen on the Final Alcohol Content of Wine Fermented by a Mixed Starter Culture." *Applied Microbiology and Biotechnology* 99, no. 9: 3993–4003.

Morard, M., L. G. Macías, A. C. Adam, et al. 2019. "Aneuploidy and Ethanol Tolerance in *Saccharomyces Cerevisiae*." *Frontiers in Genetics* 10: 82.

Morgan, S. C., G. C. McCarthy, B. S. Watters, et al. 2019. "Effect of Sulfite Addition and Pied de Cuve Inoculation on the Microbial Communities and Sensory Profiles of Chardonnay Wines: Dominance of Indigenous Saccharomyces Uvarum at a Commercial Winery." *FEMS Yeast Research* 19, no. 5: foz049. https://doi.org/10.1093/femsyr/foz049.

Morris, J. J., R. E. Lenski, and E. R. Zinser. 2012. "The Black Queen Hypothesis: Evolution of Dependencies Through Adaptive Gene Loss." *MBio* 3, no. 2: e00036-12. https://doi.org/10.1128/mBio.00036-12.

Niehaus, L., I. Boland, M. Liu, et al. 2019. "Microbial Coexistence Through Chemical-Mediated Interactions." *Nature Communications* 10, no. 1: 2052. https://doi.org/10.1038/s41467-019-10062-x.

Niehus, R., N. M. Oliveira, L. Aming, A. G. Fletcher, and K. R. Foster. 2021. "The Evolution of Strategy in Bacterial Warfare via the Regulation of Bacteriocins and Antibiotics." *eLife* 10: e69756. https://doi.org/10.7554/eLife.69756.

Novo, M., F. Bigey, E. Beyne, et al. 2009. "Eukaryote-To-Eukaryote Gene Transfer Events Revealed by the Genome Sequence of the Wine Yeast *Saccharomyces Cerevisiae* EC1118." *Proceedings of the National Academy of Sciences of the United States of America* 106, no. 38: 16333–16338.

O'Toole, G. A. 2024. "We Have a Community Problem." *Journal of Bacteriology* 206, no. 4: e0007324.

Olm, M. R., A. Crits-Christoph, K. Bouma-Gregson, B. A. Firek, M. J. Morowitz, and J. F. Banfield. 2021. "inStrain Profiles Population Microdiversity From Metagenomic Data and Sensitively Detects Shared Microbial Strains." *Nature Biotechnology* 39, no. 6: 727–736.

Opulente, D. A., A. L. LaBella, M. C. Harrison, et al. 2024. "Genomic Factors Shape Carbon and Nitrogen Metabolic Niche Breadth Across Saccharomycotina Yeasts." *Science* 384, no. 6694: eadj4503. https://doi.org/10.1126/science.adj4503.

Paillet, T., Q. Lamy-Besnier, C. Figueroa, M.-A. Petit, and E. Dugat-Bony. 2024. "Dynamics of the Viral Community on the Surface of a French Smear-Ripened Cheese During Maturation and Persistence Across Production Years." *mSystems* 9, no. 7: e00201-24. https://doi.org/10.1128/msystems.00201-24.

Pérez-Ortín, J. E., A. Querol, S. Puig, and E. Barrio. 2002. "Molecular Characterization of a Chromosomal Rearrangement Involved in the Adaptive Evolution of Yeast Strains." *Genome Research* 12, no. 10: 1533–1539. https://doi.org/10.1101/gr.436602.

Peter, J., M. De Chiara, A. Friedrich, et al. 2018. "Genome Evolution Across 1,011 *Saccharomyces Cerevisiae* Isolates." *Nature* 556, no. 7701: 339–344.

Pfeiffer, T., and A. Morley. 2014. "An Evolutionary Perspective on the Crabtree Effect." *Frontiers in Molecular Biosciences* 1, no. October: 17.

Pfeiffer, T., S. Schuster, and S. Bonhoeffer. 2001. "Cooperation and Competition in the Evolution of ATP-Producing Pathways." *Science* 292, no. 5516: 504–507.

Philippe, C., A. Chaïb, F. Jaomanjaka, et al. 2021. "Characterization of the First Virulent Phage Infecting *Oenococcus oeni*, the Queen of the Cellars." *Frontiers in Microbiology* 11: 596541. https://doi.org/10.3389/fmicb.2020.596541.

Philippe, C., M. Krupovic, F. Jaomanjaka, O. Claisse, M. Petrel, and C. le Marrec. 2018. "Bacteriophage GC1, a Novel Tectivirus Infecting *Gluconobacter Cerinus*, an Acetic Acid Bacterium Associated With Wine-Making." *Viruses* 10, no. 1: 39. https://doi.org/10.3390/v10010039.

Piao, H., E. Hawley, S. Kopf, et al. 2015. "Insights Into the Bacterial Community and Its Temporal Succession During the Fermentation of Wine Grapes." *Frontiers in Microbiology* 6: 809. https://doi.org/10.3389/fmicb.2015.00809.

Piccardi, P., B. Vessman, and S. Mitri. 2019. "Toxicity Drives Facilitation Between 4 Bacterial Species." *Proceedings of the National Academy of Sciences of the United States of America* 116, no. 32: 15979–15984. https://doi.org/10.1073/pnas.1906172116.

Pinto, C., D. Pinho, R. Cardoso, et al. 2015. "Wine Fermentation Microbiome: A Landscape From Different Portuguese Wine Appellations." *Frontiers in Microbiology* 6: 905. https://doi.org/10.3389/fmicb.2015.00905.

Piskur, J., E. Rozpedowska, S. Polakova, A. Merico, and C. Compagno. 2006. "How Did Saccharomyces Evolve to Become a Good Brewer?" *Trends in Genetics: TIG* 22, no. 4: 183–186.

Ponomarova, O., N. Gabrielli, D. C. Sévin, et al. 2017. "Yeast Creates a Niche for Symbiotic Lactic Acid Bacteria Through Nitrogen Overflow." *Cell Systems* 5, no. 4: 345–357.

Pontrelli, S., R. Szabo, S. Pollak, et al. 2022. "Metabolic Cross-Feeding Structures the Assembly of Polysaccharide Degrading Communities." *Science Advances* 8, no. 8: eabk3076.

Pyenson, N. C., A. Leeks, O. Nweke, et al. 2024. "Diverse Phage Communities Are Maintained Stably on a Clonal Bacterial Host." *Science* 386, no. 6727: 1294–1300. https://doi.org/10.1126/science.adk1183.

Quan, A. S., and M. B. Eisen. 2018. "The Ecology of the Drosophila-Yeast Mutualism in Wineries." *PLoS One* 13, no. 5: e0196440. https://doi.org/10.1371/journal.pone.0196440.

Ramírez, M., R. Velázquez, M. Maqueda, A. López-Piñeiro, and J. C. Ribas. 2015. "A New Wine Torulaspora Delbrueckii Killer Strain With Broad Antifungal Activity and Its Toxin-Encoding Double-Stranded RNA Virus." *Frontiers in Microbiology* 6: 983. https://doi.org/10.3389/fmicb.2015.00983.

Roodgar, M., B. H. Good, N. R. Garud, et al. 2021. "Longitudinal Linked-Read Sequencing Reveals Ecological and Evolutionary Responses of a Human Gut Microbiome During Antibiotic Treatment." *Genome Research* 31, no. 8: 1433–1446. https://doi.org/10.1101/gr.265058.120.

Rosini, G. 1984. "Assessment of Dominance of Added Yeast in Wine Fermentation and Origin of *Saccharomyces cerevisiae* in Wine-Making." *Journal of General and Applied Microbiology* 30, no. 4: 249–256.

Rozpędowska, E., L. Hellborg, O. P. Ishchuk, et al. 2011. "Parallel Evolution of the Make-Accumulate-Consume Strategy in Saccharomyces and Dekkera Yeasts." *Nature Communications* 2: 302.

Ruiz, J., M. de Celis, J. Diaz-Colunga, et al. 2023. "Predictability of the Community-Function Landscape in Wine Yeast Ecosystems." *Molecular Systems Biology* 19, no. 9: e11613.

Shayanthan, A., P. A. C. Ordoñez, and I. J. Oresnik. 2022. "The Role of Synthetic Microbial Communities (SynCom) in Sustainable Agriculture." *Frontiers in Agronomy* 4: 896307. https://doi.org/10.3389/fagro.2022.896307.

Silva, M., A. Pontes, R. Franco-Duarte, et al. 2023. "A Glimpse at an Early Stage of Microbe Domestication Revealed in the Variable Genome of *Torulaspora Delbrueckii*, an Emergent Industrial Yeast." *Molecular Ecology* 32, no. 10: 2396–2412. https://doi.org/10.1111/mec.16428.

Simpson-Lavy, K., and M. Kupiec. 2019. "Carbon Catabolite Repression in Yeast Is Not Limited to Glucose." *Scientific Reports* 9, no. 1: 6491.

Srivastava, D. S., J. Kolasa, J. Bengtsson, et al. 2004. "Are Natural Microcosms Useful Model Systems for Ecology?" *Trends in Ecology & Evolution* 19, no. 7: 379–384.

Stefanini, I., D. Albanese, A. Cavazza, et al. 2016. "Dynamic Changes in Microbiota and Mycobiota During Spontaneous "Vino Santo Trentino" Fermentation." *Microbial Biotechnology* 9: 195–208. https://doi.org/10.1111/1751-7915.12337.

Subileau, M., R. Schneider, J.-M. Salmon, and E. Degryse. 2008. "Nitrogen Catabolite Repression Modulates the Production of Aromatic Thiols Characteristic of Sauvignon Blanc at the Level of Precursor Transport." *FEMS Yeast Research* 8, no. 5: 771–780.

Szappanos, B., J. Fritzemeier, B. Csörgő, et al. 2016. "Adaptive Evolution of Complex Innovations Through Stepwise Metabolic Niche Expansion." *Nature Communications* 7: 11607. https://doi.org/10.1038/ncomms11607.

Tronchoni, J., A. Gamero, F. N. Arroyo-López, E. Barrio, and A. Querol. 2009. "Differences in the Glucose and Fructose Consumption Profiles in Diverse Saccharomyces Wine Species and Their Hybrids During Grape Juice Fermentation." *International Journal of Food Microbiology* 134, no. 3: 237–243. https://doi.org/10.1016/j.ijfoodmicro.2009.07.004.

Varela, C., F. Pizarro, and E. Agosin. 2021. "Biomass Content Governs Fermentation Rate in Nitrogen-Deficient Wine Musts." *Applied and Environmental Microbiology* 70, no. 6: 3392–3400.

Venkataram, S., B. Dunn, Y. Li, et al. 2016. "Development of a Comprehensive Genotype-To-Fitness map of Adaptation-Driving Mutations in Yeast." *Cell* 166, no. 6: 1585.

Vicente, J., A. Friedrich, J. Schacherer, K. Freel, D. Marquina, and A. Santos. 2024. "Whole-Genome Sequencing and Phenotyping Reveal Specific Adaptations of Lachancea Thermotolerans to the Winemaking Environment." *bioRxiv*: 1–36. https://doi.org/10.1101/2024.05.31.596785.

Vicente, J., Y. Baran, E. Navascués, et al. 2022. "Biological Management of Acidity in Wine Industry: A Review." *International Journal of Food Microbiology* 375: 109726.

Vilela-Moura, A., D. Schuller, A. Mendes-Faia, et al. 2011. "The Impact of Acetate Metabolism on Yeast Fermentative Performance and Wine Quality: Reduction of Volatile Acidity of Grape Musts and Wines." *Applied Microbiology and Biotechnology* 89, no. 2: 271–280.

Voordeckers, K., J. Kominek, A. Das, et al. 2015. "Adaptation to High Ethanol Reveals Complex Evolutionary Pathways." *PLoS Genetics* 11, no. 11: e1005635.

Will, J. L., H. S. Kim, J. Clarke, J. C. Painter, J. C. Fay, and A. P. Gasch. 2010. "Incipient Balancing Selection Through Adaptive Loss of Aquaporins in Natural *Saccharomyces Cerevisiae* Populations." *PLoS Genetics* 6, no. 4: e1000893.

Wolfe, B. E., and R. J. Dutton. 2015. "Fermented Foods as Experimentally Tractable Microbial Ecosystems." *Cell* 161, no. 1: 49–55.

Wolfe, B. E., J. E. Button, M. Santarelli, and R. J. Dutton. 2014. "Cheese Rind Communities Provide Tractable Systems for In Situ and In Vitro Studies of Microbial Diversity." *Cell* 158, no. 2: 422–433. https://doi.org/10.1016/j.cell.2014.05.041.

Wolfe, K. H., and D. C. Shields. 1997. "Molecular Evidence for an Ancient Duplication of the Entire Yeast Genome." *Nature* 387, no. 6634: 708–713.

Yang, L., X. Zhu, Y. Mao, X. Zhang, B. Xu, and X. Yang. 2024. "Effect of Different Inoculation Strategies of Mixed Culture *Saccharomyces cerevisiae*/*Oenococcus oeni* on the Aroma Quality of Chardonnay Wine." *Food Research International* 190: 114636. https://doi.org/10.1016/j.foodres.2024.114636.

Zimmer, A., C. Durand, N. Loira, P. Durrens, D. J. Sherman, and P. Marullo. 2014. "QTL Dissection of Lag Phase in Wine Fermentation Reveals a New Translocation Responsible for *Saccharomyces Cerevisiae* Adaptation to Sulfite." *PLoS One* 9, no. 1: e86298.