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# Fermented Foods as Experimentally Tractable Microbial Ecosystems

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**Microbial communities of fermented foods have provided humans with tools for preservation and flavor development for thousands of years. These simple, reproducible, accessible, culturable, and easy-to-manipulate systems also provide opportunities for dissecting the mechanisms of microbial community formation. Fermented foods can be valuable models for processes in less tractable microbiota.**

## Introduction

The study of microbial communities currently faces a difficult impasse. As we continue to amass terabytes of sequencing data that describe the phylogenetic diversity of microbes around the world, we are faced with the challenge of dissecting the assembly, organization, and functions of these multi-species communities. Major questions remain about the nature, extent, mechanisms, and impact of species-species and species-environment interactions within microbial communities.

There are a number of barriers to understanding microbial ecosystems. First and foremost is the enormous diversity and complexity of most microbial communities. DNA sequencing-based surveys have now been applied to many habitats and provide a picture of the microbial diversity within and across environments (Lozupone and Knight, 2007). Although there is substantial variation from one environment to the next, the number of species in most habitats can reach into the hundreds or thousands. The inability to isolate the vast majority of species from natural systems by culturing is another significant barrier to characterizing the role of any given species in an ecosystem. A related constraint is the difficulty in recreating experimental conditions in an in vitro setting such that processes can be studied under controlled conditions.

One way to overcome these challenges is to move toward the development and analysis of simpler and experimentally tractable model microbial communities. An ideal model system should be simpler than natural communities yet still exhibit patterns of community formation and dynamics that are representative of those observed in more complex systems. The microbial communities involved should form under defined, reproducible, and easily accessible spatial and temporal scales to allow for predictable and straight-forward sampling procedures. The conditions for community formation and substrates of microbial growth should be measurable and possible to recreate in an in vitro setting. Finally, the individual members of the community should be culturable to facilitate application of the full range of genetic and omics-enabled tools, experimental analysis, and in vitro community manipulation.

Model microbial ecosystems have already emerged that have some of these properties (Jessup et al., 2004). These systems range from synthetic mixtures of model microbial strains (Harcombe et al., 2014; Hom and Murray, 2014), to model systems composed of a subset of culturable strains in complex free-living or host-associated communities (Lawrence et al., 2012; Peay et al., 2012; Goodman et al., 2011), to naturally occurring communities that are intensively sampled or perturbed in situ (Tyson et al., 2004). Studies across this spectrum have provided incredible opportunities to dissect the biology of microbial communities. However, systems that fall in the middle of the spectrum of simplified synthetic to irreducibly complex are needed help us to move toward a mechanistic understanding of microbial communities.

## Fermented Foods as Experimentally Tractable Ecosystems

Fermentation is an ancient method for preserving foods that depends on reproducible formation of multi-species microbial communities. Over thousands of years, humans have optimized the conditions that promote the growth of certain types of microbial communities. The metabolic activity of these communities is key to the safety, flavor, texture, and aroma of fermented foods (Hutkins, 2006). Manipulation of microbial growth variables such as temperature, salinity, and moisture results in a wide spectrum of fermented foods, including cheese, beer, wine, chocolate, sourdough, sauerkraut, kimchi, and miso (Figure 1 and Table 1). The distinct microbial communities involved in fermenting these foods have a number of properties that make them ideal candidates for development as experimentally tractable model ecosystems.

Because the microbial communities of fermented foods (MCoFFs) offer a wide range of paradigms for community formation, it is possible to address experimental questions across many different types of ecosystems (Table 1). These communities take many forms: multi-species biofilms associated with surfaces (e.g., cheese rinds), suspended biofilms in liquid (e.g., kombucha, kefir, and vinegar), dispersed growth in liquid (e.g., lambic beers, natural wines, and yogurt), or in semi-solid substrates (e.g., kimchi and miso).

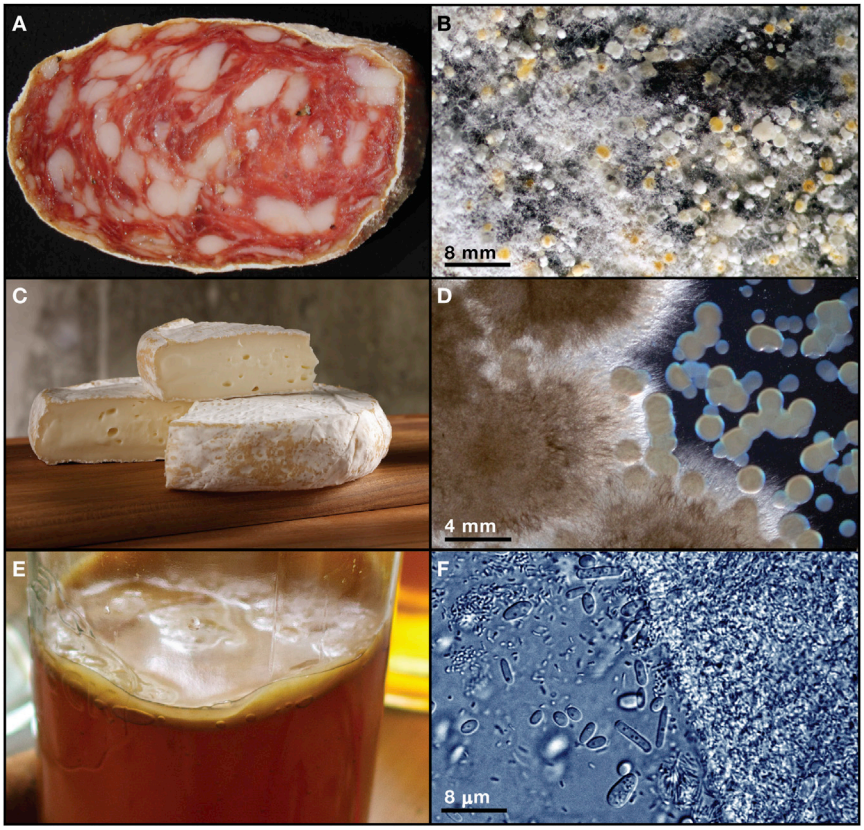


**Figure 1. Multi-species Microbial Communities Form during the Production of Fermented Foods**

(A) Fermented meats, such as salami, are produced by fermentation of meat by lactic acid bacteria.

(B) During the aging process, the salami surface is colonized by a mixture of yeast and bacteria, visible as white and yellow colonies, and filamentous fungi (diffuse white filaments) such as *Penicillium*.

(C) Cheeses, such as the Camembert-style cheese shown, are made through the fermentation of milk by lactic acid bacteria. During aging, a biofilm, commonly called a rind, develops on the surface and contributes to the flavor, texture, and aroma of the cheese.

(D) A rind biofilm plated on standard lab medium shows a subset of the mixed eukaryotic (filamentous fungi on the left) and prokaryotic (Proteobacteria on the right) members of these microbial communities.

(E and F) (E) Visible microbial communities also form in liquid fermentations, such as this fermented tea, commonly known as kombucha. The microbial cells within the pellicle (floating biofilm) can be seen in the micrograph (F). Kombucha is typically composed of yeasts (larger cells) and acetic acid bacteria (smaller cells). The yeasts are involved in the fermentation of sugar to produce ethanol and carbon dioxide. The acetic acid bacteria then ferment the ethanol and produce acetic acid. The intact biofilm is on the right, and yeast and bacterial cells are sloughing off on the left.

All photos by Benjamin Wolfe, except (C) (Jasper Hill Farm) and (E) (Adam DeTour).

Recent advances in genomic and metagenomic sequencing are providing researchers with catalogs of the bacterial, fungal, and viral diversity in many traditionally produced fermented foods (Table 1; reviewed in Bokulich and Mills, 2012). These communities range in composition from those dominated by bacterial species to those dominated by fungal species, with some communities containing a mix of both bacteria and fungi. Certain bacterial groups such as the lactic acid bacteria (LAB) and acetic acid bacteria (AAB), as well as fungal species such as *Saccharomyces cerevisae*, have well-established roles in fermentation. However, the increasingly detailed analysis of the microbial diversity of fermented foods is revealing many additional species whose roles have not been characterized extensively, if at all. For example, marine-associated *Pseudoalteromonas* are dominant members of some cheese rinds (Wolfe et al., 2014) (in Table 1, these and all non-LAB/AAB fall under "other bacterial groups").

After characterizing the diversity of a microbial community, one of the biggest challenges in the study of microbial ecosystems is the difficulty in culturing community members in the laboratory. Because MCoFFs have defined starting materials as growth substrates (e.g., milk, grapes, and wheat flour) and known incubation conditions, these same conditions can be replicated in the lab and used as starting conditions for isolation of community members. Indeed, some food-associated microbes are already well-established model organisms, such as *Saccharomyces cerevisiae* and *Lactococcus lactis*.

Experimentation using MCoFFs is also greatly facilitated by the fact that they are extremely accessible microbial ecosystems. The production of fermented foods happens at regular intervals (from daily to seasonally), and communities develop on short timescales (from days to months), allowing for predictable access to many replicated samples over relatively short time periods. Fermented foods are often produced across multiple geographic regions, also increasing the accessibility of samples. These communities form as part of discrete entities (e.g., a wheel of cheese), which allows well-defined spatial and temporal sampling.

MCoFFs have some potential limitations as model systems. Given the short timescales required to form communities, there may be fewer opportunities for species to coevolve. However, horizontal gene transfer between species that co-occur in MCoFFs suggests that at least some members of these communities have coexisted long enough to allow for gene exchange (Cheeseman et al., 2014; Rossi et al., 2014). In fact, some MCoFFs are maintained for many years through serial transfer (Table 1), providing ample opportunities for long-term coevolution within communities. For example, fermented teas such as kombucha consist of a pellicle that contains bacteria and yeasts in a mixed biofilm (Figures 1E and 1F). These pellicles have been spread all around the world (Marsh et al., 2014), leading to geographically separated communities that potentially started from initially identical species and genetic backgrounds.

Because MCoFFs grow on raw food materials, such as grains, meat, or milk, most nutrients are not limited. This high resource

**Table 1. Diverse Fermented Foods Provide Ample Opportunities to Study Microbial Communities**

| Type of Food | Fermented Product | Main Ingredients | Major Microbial Groups | Opportunities to Study | References |
|---|---|---|---|---|---|
| Fruit | wine | pressed grapes | Y (natural styles: LAB) | biogeography, population biology due to wide geographical distribution | Bokulich et al. (2014a); Knight and Goddard (2015) |
| | chocolate | cacao pods | FF, Y, LAB, AAB, OBG | community interactions and dynamics due to successional development and broad phylogenetic diversity | Meersman et al. (2013) |
| | coffee | coffee cherries | FF, Y, OBG | community interactions and dynamics due to successional development and broad phylogenetic diversity | Vilela et al. (2010) |
| Dairy | yogurt | milk | LAB | co-evolution and adaptation due to serial transfer over long time periods | Sieuwerts et al. (2008) |
| | cheese | milk, salt | FF, Y, LAB, AAB, OBG | biogeography, community interactions and dynamics, and abiotic selection due to wide geographical distribution, broad phylogenetic diversity, and strong abiotic filters | Wolfe et al. (2014); Montel et al. (2014) |
| | kefir | milk | Y, LAB, AAB, OBG | co-evolution, adaptation, and biofilm formation due to self-replicating, highly organized biofilm and serial transfer over long time periods | Marsh et al. (2013) |
| Grains | beer | barley, hops, water | Y (lambic styles: AAB, LAB, OBG) | adaptation, community interactions and dynamics in lambic styles: accumulation of species in facility, successional development | Bokulich et al. (2012) |
| | sake, soy sauce, miso | rice, water (soy beans added for soy sauce and miso) | FF, Y, LAB, AAB, OBG | community interactions and dynamics due to successional development, adaptation due to domestication of Aspergillus oryzae | Bokulich et al. (2014b); Gibbons et al. (2012) |
| | sourdough | wheat flour, water | Y, LAB | biogeography, co-evolution, adaptation due to wide geographical distribution and serial transfer over long time periods | Minervini et al. (2014) |
| Meat | salami | ground meat, salt | FF, Y, LAB, OBG | community interactions and dynamics due to broad phylogenetic diversity | Cocolin et al. (2011) |
| Plants | kimchi | cabbage, spices, salt | Y, LAB | community interactions and dynamics, abiotic selection due to successional development and strong abiotic filters | Jung et al. (2011) |
| | sauerkraut | cabbage, salt | LAB | community interactions and dynamics, abiotic selection due to successional development, abiotic filters | Plengvidhya et al. (2007) |
| | kombucha | tea, sugar | Y, LAB, AAB, OBG | co-evolution, adaptation, biofilm formation due to self-replicating, highly organized biofilm and serial transfer over long time periods | Marsh et al. (2014) |
| | | | | Key: FF = filamentous fungi; Y = yeast; LAB = lactic acid bacteria; AAB = acetic acid bacteria; OBG = other bacterial groups | |

availability may be one reason why productivity is high in these systems and diversity can be low (Mittelbach et al., 2001). However, certain micronutrients such as iron, which has been shown to be a crucial factor in microbial interactions and coevolution in other environments (Cordero et al., 2012), is also limited in some MCoFFs, such as cheese rinds (Monnet et al., 2012). Finally, MCoFFs are not host-associated communities. Although this may simplify many aspects of experimental analysis, the impact of host innate and adaptive immune responses in dictating microbial community composition will be missing. An exception is the presence of biologically active host-derived products in milk, such as lactoferrin, oligosaccharides, and peptides (German et al., 2002).

The development of model systems based on fermented foods is already in progress. For a number of systems, the catalogs of microbial diversity within and across foods, temporal dynamics of community formation, and cultured community members are already established (Table 1). As an example of the characterization and development of such a system, we have recently focused on the microbial communities that form on the surface of cheese as it ages, also known as the rind (Figures 1C and D) (Wolfe et al., 2014). We cataloged the diversity of bacteria and fungi of cheese rinds across broad geographic regions, and measured the temporal dynamics of community formation. We cultured representatives of all dominant microbial groups and then reconstructed in vitro communities, which displayed many of the properties of natural communities. The ability to move quickly from observations of microbial diversity to the establishment of highly manipulable in vitro systems makes model systems based on MCoFFs excellent starting points for studying the mechanisms and principles of microbial community formation.

## Using Fermented Foods to Link Patterns, Processes, and Mechanisms of Microbial Community Assembly

One of the current challenges in microbiology is linking patterns of microbial diversity within communities with the ecological processes that generate those patterns. What determines the composition of a microbial community? When and how do new species successfully invade communities? What causes shifts in composition of established microbial communities? To address such questions, microbiologists have begun to adopt community assembly frameworks developed for plant and animal communities to explain ecological processes underlying patterns of diversity (Costello et al., 2012; Hanson et al., 2012; Nemergut et al., 2013). Community assembly approaches usually consider contributions from the amount and timing of microbial propagules colonizing a habitat (dispersal), interactions between species (biotic selection), interactions between a species and the environment (abiotic selection), stochastic changes in the relative abundances of species within communities (drift), and evolution of new species within communities (diversification).

MCoFFs provide many opportunities for quantifying the relative roles of each of these ecological processes because microbial community dynamics can be easily measured, monitored, and controlled. For example, dispersal can be manipulated by controlling the openness of system (e.g. by simulating a highly controlled and sterilized environment versus a rustic production facility open to migration), using pasteurization of raw materials, or by incorporating known starter cultures. Biotic selection can be manipulated through the addition of specific combinations of species that are known to have strong species interactions. Abiotic selection can be controlled through the same selections that food producers use, including the manipulation of salt, moisture, temperature, and pH. These systems offer the ability to alter inputs and known ecological filters and allow testing of the relative impacts of each process on the composition of communities.

MCoFFs are particularly ripe with opportunities to link pattern, process, and mechanism in the study of microbial interactions (Mounier et al., 2008; Sieuwerts et al., 2008). For example, most fermented foods go through a clear and relatively consistent process of ecological succession with early colonizing microbes being replaced with one or more succeeding microbial groups. In some systems, such as the fermentation of cocoa pods (Meersman et al., 2013) and sourdough fermentations (Minervini et al., 2014), changes in the environment caused by early colonizing species and metabolic cooperation between functional groups are underlying drivers of these successions.

In vitro community reconstructions and the ever-growing suite of microbial "-omics" tools can help uncover the molecular mechanisms driving succession and identify how species interactions play a role in these temporal changes in community composition. Approaches such as RNA-seq can be used to winnow many potential mechanisms down to a short list of molecular mechanisms underlying microbial interactions. The application of sequencing-enabled transposon mutagenesis (TnSeq and INseq) has been successful in elucidating key microbial interactions in complex microbial communities such as the human gut microbiome (Goodman et al., 2009) and could be an extremely powerful tool for the analysis of microbial interactions in MCoFFs. In addition, new approaches in the identification of molecules responsible for species interactions, such as imaging mass spectrometry (Watrous and Dorrestein, 2011), could enrich our understanding of the chemical cross-talk in MCoFFs.

## Taste of Place? Microbial Biogeography of Fermented Foods

Similar types of MCoFFs are produced in many locations around the world (Table 1), making it possible to address basic questions in microbial biogeography. Because microbial diversity can have an important impact on the flavor of fermented foods, such as wine or cheese (Ciani et al., 2010; Montel et al., 2014), MCoFFs can help link patterns in microbial diversity from place to place to the functional consequences of this diversity. As with plant and animal communities, microbial communities have clear species abundance distributions, with a few microbial taxa that are locally abundant within and across communities, while many tend to be relatively low abundance (Nemergut et al., 2013). This pattern has also been observed in high-throughput sequencing surveys of MCoFFs (e.g., Jung et al., 2011; Wolfe et al., 2014), although the typical long tail of low-abundance species tends to be shorter due to the lower diversity in MCoFFs. Thus, MCoFFs can be used to compare the patterns of community diversity over both regional scales, such as in wine

(Bokulich et al., 2014a), and over global scales, such as with cheese (Wolfe et al., 2014).

Trait-based approaches have also emerged to address questions of microbial abundance across these larger spatial scales. Trait-based approaches attempt to use either directly measured microbial life-history traits, such as growth rate or predicted traits from genomic data (Fierer et al., 2014), to explain distributions or functions of microbial species. Unlike many microbial communities dominated by unculturable taxa, it is fairly straightforward to measure phenotypic and genomic traits of species within MCoFFs (Bayjanov et al., 2013; Almeida et al., 2014; Douillard and de Vos, 2014). MCoFFs that are open to dispersal, widely distributed, and are not heavily inoculated with starter cultures, including naturally fermented wines, unpasteurized rind cheeses, and sourdough breads (Table 1), could be ideal MCoFFs for linking the genetic basis of interspecific trait variation with geographic distributions.

## Microbial Evolution in a Community Context

MCoFFs have ideal properties for dissecting ecological processes, but they can also serve as models for understanding mechanisms of microbial evolution. Beer and wine yeasts, lactic acid bacteria used in dairy fermentations, and the filamentous fungus *Aspergillus oryzae* used to make sake, soy sauce, and miso have all served as models of microbial domestication (Douglas and Klaenhammer, 2010; Gibbons et al., 2012; Steensels and Verstrepen, 2014). Comparisons of genomic and phenotypic traits across the large diversity of fermentation and wild strains provided clear evidence for consistent loss of genes unnecessary in the nutrient-rich fermentation environment, acquisition of new traits through horizontal gene transfer, and metabolic remodeling associated with adaptation to the fermentation niche and artificial selection by humans. Experimental evolution of wild strains to the fermentation environment has been used to confirm potential genetic mechanisms involved with the transition to domestication (Bachmann et al., 2012).

One exciting future direction is to link ecological processes described above with the study of evolutionary processes in MCoFFs. Recent work from other model microbial ecosystems has highlighted the importance of eco-evolutionary feedbacks, where the presence and composition of neighboring species can alter evolution of community-level traits, such as species composition (Celiker and Core, 2014), and ecosystem-level traits, such as productivity (Lawrence et al., 2012). MCoFFs that have experienced long periods of serial passage or co-culture could serve as powerful model systems in this emerging field. Future studies could experimentally test for coevolution within these communities by swapping identical species from across geographically isolated communities. Applying experimental evolution approaches in the lab would allow for real-time monitoring of community coevolution within MCoFFs.

## Translation to Other Microbial Communities and Potential Applications

The study of community assembly in MCoFFs has the potential to have direct impacts on the quality and safety of traditional fermented foods. But how might basic ecological and evolutionary principles discovered in these semi-natural microbial ecosystems be applied to other types of microbial communities such as the human microbiome or soil microbial communities? Certain MCoFFs share compositional similarity with less tractable systems, so pattern-process-mechanism relationships identified in MCoFFs may be readily translatable to other microbiomes. One example is the recently characterized molecular mechanism of competitiveness in *Lactobacillus reuteri*, a species found in both sourdough and human gut microbiomes (Lin and Gänzle, 2014). In sourdough fermentations, glycerol metabolism explained the competitive advantage of human-associated strains and potentially could explain how these species compete in human gut microbiomes.

Looking at cheese rind microbial community diversity revealed a diversity of bacteria and fungi with similarity at the genus level to the human skin microbiome (Wolfe et al., 2014). Data from both cheese rinds and the human skin microbiome (Grice et al., 2009) suggest that moisture is a major driver of these surface biofilms, suggesting that ecological selection could play similar roles in both. Thus, although the exact species may not be the same between MCoFFs and other microbial communities, community-level processes will likely be conserved.

MCoFFs have the potential to directly impact human health because they are edible communities. Although the probiotic effects of highly simplified MCoFFs from yogurt have been the topic of intense study (McNulty et al., 2001), the wider microbial diversity across MCoFFs could be a source of many additional microbes and metabolites with direct access to the human digestive tract and gut microbiome. The potential for direct interaction with the human microbiome is evidenced by the findings that MCoFFs can remain viable during passage through the human digestive tract (David et al., 2014).

MCoFFs may also provide opportunities to understand how to better design synthetic microbial communities for medicine, industry, and agriculture. Just as synthetic biologists rely on understanding regulatory networks and other interactions within cells to deconstruct and then reconstruct new metabolic pathways, synthetic microbial community ecologists will need to be able to first understand mechanisms underlying interactions within communities before piecing together synthetic microbial communities (Grosskopf and Soyer, 2014). Because MCoFFs have been designed—although in many cases unintentionally—for specific functions, can we use the pre-existing communities to teach us about design principles? Can we take microbes from disparate MCoFFs and combine them into new compositions not already found in food systems? What ecological or evolutionary constraints will prevent the construction of synthetic microbial communities, and can we use experimental community coevolution to overcome these constraints? Answering these questions with food microbial communities could lead to safer and more delicious foods while also developing much-needed principles of microbial community design.

## REFERENCES

Almeida, M., Hébert, A., Abraham, A.L., Rasmussen, S., Monnet, C., Pons, N., Delbès, C., Loux, V., Batto, J.M., Leonard, P., et al. (2014). Construction of a dairy microbial genome catalog opens new perspectives for the metagenomic analysis of dairy fermented products. BMC Genomics *15*, 1101.

Bachmann, H., Starrenburg, M.J., Molenaar, D., Kleerebezem, M., and van Hylckama Vlieg, J.E. (2012). Microbial domestication signatures of Lactococcus lactis can be reproduced by experimental evolution. Genome Res. *22*, 115–124.

Bayjanov, J.R., Starrenburg, M.J., van der Sijde, M.R., Siezen, R.J., and van Hijum, S.A. (2013). Genotype-phenotype matching analysis of 38 Lactococcus lactis strains using random forest methods. BMC Microbiol. *13*, 68.

Bokulich, N.A., and Mills, D.A. (2012). Next-generation approaches to the microbial ecology of food fermentations. BMB Rep. *45*, 377–389.

Bokulich, N.A., Bamforth, C.W., and Mills, D.A. (2012). Brewhouse-resident microbiota are responsible for multi-stage fermentation of American coolship ale. PLoS ONE *7*, e35507.

Bokulich, N.A., Thorngate, J.H., Richardson, P.M., and Mills, D.A. (2014a). Microbial biogeography of wine grapes is conditioned by cultivar, vintage, and climate. Proc. Natl. Acad. Sci. USA. *111*, E139–E148.

Bokulich, N.A., Ohta, M., Lee, M., and Mills, D.A. (2014b). Indigenous bacteria and fungi drive traditional kimoto sake fermentations. Appl. Environ. Microbiol. *80*, 5522–5529.

Celiker, H., and Gore, J. (2014). Clustering in community structure across replicate ecosystems following a long-term bacterial evolution experiment. Nat. Commun. *5*, 4643.

Cheeseman, K., Ropars, J., Renault, P., Dupont, J., Gouzy, J., Branca, A., Abraham, A.L., Ceppi, M., Conseiller, E., Debuchy, R., et al. (2014). Multiple recent horizontal transfers of a large genomic region in cheese making fungi. Nat. Commun. *5*, 2876.

Ciani, M., Comitini, F., Mannazzu, I., and Domizio, P. (2010). Controlled mixed culture fermentation: a new perspective on the use of non-*Saccharomyces* yeasts in winemaking. FEMS Yeast Res. *10*, 123–133.

Cocolin, L., Dolci, P., and Rantsiou, K. (2011). Biodiversity and dynamics of meat fermentations: the contribution of molecular methods for a better comprehension of a complex ecosystem. Meat Sci. *89*, 296–302.

Cordero, O.X., Ventouras, L.A., DeLong, E.F., and Polz, M.F. (2012). Public good dynamics drive evolution of iron acquisition strategies in natural bacterioplankton populations. Proc. Natl. Acad. Sci. USA *109*, 20059–20064.

Costello, E.K., Stagaman, K., Dethlefsen, L., Bohannan, B.J., and Relman, D.A. (2012). The application of ecological theory toward an understanding of the human microbiome. Science *336*, 1255–1262.

David, L.A., Maurice, C.F., Carmody, R.N., Gootenberg, D.B., Button, J.E., Wolfe, B.E., Ling, A.V., Devlin, A.S., Varma, Y., Fischbach, M.A., et al. (2014). Diet rapidly and reproducibly alters the human gut microbiome. Nature *505*, 559–563.

Douglas, G.L., and Klaenhammer, T.R. (2010). Genomic evolution of domesticated microorganisms. Annu. Rev. Food Sci. Technol. *1*, 397–414.

Douillard, F.P., and de Vos, W.M. (2014). Functional genomics of lactic acid bacteria: from food to health. Microb. Cell Fact *13*(1), S8.

Fierer, N., Barberán, A., and Laughlin, D.C. (2014). Seeing the forest for the genes: using metagenomics to infer the aggregated traits of microbial communities. Front. Microbiol. *5*, 614.

German, J.B., Dillard, C.J., and Ward, R.E. (2002). Bioactive components in milk. Curr. Opin. Clin. Nutr. Metab. Care *5*, 653–658.

Gibbons, J.G., Salichos, L., Slot, J.C., Rinker, D.C., McGary, K.L., King, J.G., Klich, M.A., Tabb, D.L., McDonald, W.H., and Rokas, A. (2012). The evolutionary imprint of domestication on genome variation and function of the filamentous fungus Aspergillus oryzae. Curr. Biol. *22*, 1403–1409.

Goodman, A.L., McNulty, N.P., Zhao, Y., Leip, D., Mitra, R.D., Lozupone, C.A., Knight, R., and Gordon, J.I. (2009). Identifying genetic determinants needed to establish a human gut symbiont in its habitat. Cell Host Microbe *6*, 279–289.

Goodman, A.L., Kallstrom, G., Faith, J.J., Reyes, A., Moore, A., Dantas, G., and Gordon, J.I. (2011). Extensive personal human gut microbiota culture collections characterized and manipulated in gnotobiotic mice. Proc. Natl. Acad. Sci. USA *108*, 6252–6257.

Grice, E.A., Kong, H.H., Conlan, S., Deming, C.B., Davis, J., Young, A.C., NISC Comparative Sequencing Program, Bouffard, G.G., Blakesley, R.W., Murray, P.R., et al. (2009). Topographical and temporal diversity of the human skin microbiome. Science *324*, 1190–1192.

Grosskopf, T., and Soyer, O.S. (2014). Synthetic microbial communities. Curr. Opin. Microbiol. *18*, 72–77.

Hanson, C.A., Fuhrman, J.A., Horner-Devine, M.C., and Martiny, J.B. (2012). Beyond biogeographic patterns: processes shaping the microbial landscape. Nat. Rev. Microbiol. *10*, 497–506.

Harcombe, W.R., Riehl, W.J., Dukovski, I., Granger, B.R., Betts, A., Lang, A.H., Bonilla, G., Kar, A., Leiby, N., Mehta, P., et al. (2014). Metabolic resource allocation in individual microbes determines ecosystem interactions and spatial dynamics. Cell Rep *7*, 1104–1115.

Hom, E.F., and Murray, A.W. (2014). Plant-fungal ecology. Niche engineering demonstrates a latent capacity for fungal-algal mutualism. Science *345*, 94–98.

Hutkins, R. (2006). Microbiology and Technology of Fermented Foods (Wiley-Blackwell).

Jessup, C.M., Kassen, R., Forde, S.E., Kerr, B., Buckling, A., Rainey, P.B., and Bohannan, B.J. (2004). Big questions, small worlds: microbial model systems in ecology. Trends Ecol. Evol. *19*, 189–197.

Jung, J.Y., Lee, S.H., Kim, J.M., Park, M.S., Bae, J.W., Hahn, Y., Madsen, E.L., and Jeon, C.O. (2011). Metagenomic analysis of kimchi, a traditional Korean fermented food. Appl. Environ. Microbiol. *77*, 2264–2274.

Knight, S., and Goddard, M.R. (2015). Quantifying separation and similarity in a Saccharomyces cerevisiae metapopulation. ISME J *9*, 361–370.

Lawrence, D., Fiegna, F., Behrends, V., Bundy, J.G., Phillimore, A.B., Bell, T., and Barraclough, T.G. (2012). Species interactions alter evolutionary responses to a novel environment. PLoS Biol. *10*, e1001330.

Lin, X.B., and Gänzle, M.G. (2014). Effect of lineage-specific metabolic traits of Lactobacillus reuteri on sourdough microbial ecology. Appl. Environ. Microbiol. *80*, 5782–5789.

Lozupone, C.A., and Knight, R. (2007). Global patterns in bacterial diversity. Proc. Natl. Acad. Sci. USA *104*, 11436–11440.

Marsh, A.J., O'Sullivan, O., Hill, C., Ross, R.P., and Cotter, P.D. (2013). Sequencing-based analysis of the bacterial and fungal composition of kefir grains and milks from multiple sources. PLoS ONE *8*, e69371.

Marsh, A.J., O'Sullivan, O., Hill, C., Ross, R.P., and Cotter, P.D. (2014). Sequence-based analysis of the bacterial and fungal compositions of multiple kombucha (tea fungus) samples. Food Microbiol. *38*, 171–178.

McNulty, N.P., Yatsunenko, T., Hsiao, A., Faith, J.J., Muegge, B.D., Goodman, A.L., Henrissat, B., Oozeer, R., Cools-Portier, S., Gobert, G., et al. (2001). The impact of a consortium of fermented milk strains on the gut microbiome of gnotobiotic mice and monozygotic twins. Sci. Transl. Med. *3*, 106ra106.

Meersman, E., Steensels, J., Mathawan, M., Wittocx, P.J., Saels, V., Struyf, N., Bernaert, H., Vrancken, G., and Verstrepen, K.J. (2013). Detailed analysis of the microbial population in Malaysian spontaneous cocoa pulp fermentations reveals a core and variable microbiota. PLoS One *8*, e81559.

Minervini, F., De Angelis, M., Di Cagno, R., and Gobbetti, M. (2014). Ecological parameters influencing microbial diversity and stability of traditional sourdough. Int. J. Food Microbiol. *171*, 136–146.

Mittelbach, G.G., Steiner, C.F., Scheiner, S.M., Gross, K.L., Reynolds, H.L., Waide, R.B., Willig, M.R., Dodson, S.I., and Gough, L. (2001). What is the observed relationship between species richness and productivity? Ecology *82*, 2381–2396.

Monnet, C., Back, A., and Irlinger, F. (2012). Growth of aerobic ripening bacteria at the cheese surface is limited by the availability of iron. Appl. Environ. Microbiol. *78*, 3185–3192.

Montel, M.C., Buchin, S., Mallet, A., Delbes-Paus, C., Vuitton, D.A., Desmasures, N., and Berthier, F. (2014). Traditional cheeses: rich and diverse microbiota with associated benefits. Int. J. Food Microbiol. *177*, 136–154.

Mounier, J., Monnet, C., Vallaeys, T., Arditi, R., Sarthou, A.S., Hélias, A., and Irlinger, F. (2008). Microbial interactions within a cheese microbial community. Appl. Environ. Microbiol. *74*, 172–181.

Nemergut, D.R., Schmidt, S.K., Fukami, T., O'Neill, S.P., Bilinski, T.M., Stanish, L.F., Knelman, J.E., Darcy, J.L., Lynch, R.C., Wickey, P., and Ferrenberg, S. (2013). Patterns and processes of microbial community assembly. Microbiol. Mol. Biol. Rev. *77*, 342–356.

Peay, K.G., Belisle, M., and Fukami, T. (2012). Phylogenetic relatedness predicts priority effects in nectar yeast communities. Proc. Biol. Sci. *279*, 749–758.

Plengvidhya, V., Breidt, F., Jr., Lu, Z., and Fleming, H.P. (2007). DNA fingerprinting of lactic acid bacteria in sauerkraut fermentations. Appl. Environ Microbiol. *73*, 7697–7702.

Rossi, F., Rizzotti, L., Felis, G.E., and Torriani, S. (2014). Horizontal gene transfer among microorganisms in food: current knowledge and future perspectives. Food Microbiol. *42*, 232–243.

Sieuwerts, S., de Bok, F.A., Hugenholtz, J., and van Hylckama Vlieg, J.E. (2008). Unraveling microbial interactions in food fermentations: from classical to genomics approaches. Appl. Environ. Microbiol. *74*, 4997–5007.

Steensels, J., and Verstrepen, K.J. (2014). Taming wild yeast: potential of conventional and nonconventional yeasts in industrial fermentations. Annu. Rev. Microbiol. *68*, 61–80.

Tyson, G.W., Chapman, J., Hugenholtz, P., Allen, E.E., Ram, R.J., Richardson, P.M., Solovyev, V.V., Rubin, E.M., Rokhsar, D.S., and Banfield, J.F. (2004). Community structure and metabolism through reconstruction of microbial genomes from the environment. Nature *428*, 37–43.

Vilela, D.M., Pereira, G.V., Silva, C.F., Batista, L.R., and Schwan, R.F. (2010). Molecular ecology and polyphasic characterization of the microbiota associated with semi-dry processed coffee (Coffea arabica L.). Food Microbiol. *27*, 1128–1135.

Watrous, J.D., and Dorrestein, P.C. (2011). Imaging mass spectrometry in microbiology. Nat. Rev. Microbiol. *9*, 683–694.

Wolfe, B.E., Button, J.E., Santarelli, M., and Dutton, R.J. (2014). Cheese rind communities provide tractable systems for in situ and in vitro studies of microbial diversity. Cell *158*, 422–433.