

## Spotlight

# Horizontal Gene Transfer and Ecosystem Function Dynamics

Maarten van de Guchte<sup>1,\*</sup>

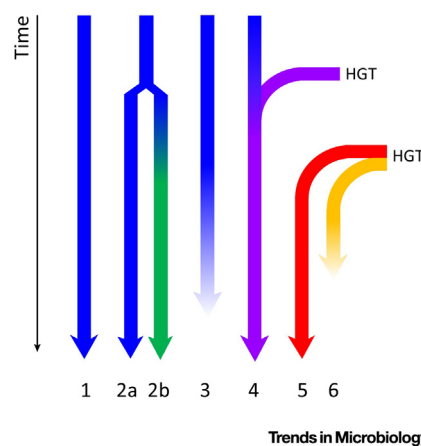
**Horizontal gene transfer can provide bacteria with new functions that confer an important competitive advantage, and is therefore likely to affect the dynamics of bacterial ecosystems. Two studies by Wolfe *et al.* and Bonham *et al.* prepare the way to study this hypothesis in a model ecosystem with reproducible properties.**

Horizontal, or lateral, gene transfer (HGT) is commonly known for its role in the alarming spread of antibiotic resistance. For the past two decades, HGT has been recognized to play a more general role as an important force in the evolution of bacterial genomes [1,2], taking part in a continuous succession of function enrichment and, sometimes extreme, loss of functions that have become superfluous [3] (Figure 1). The acquisition of genetic information from closely related or more distant bacterial species, from archaea, or even from eukaryotes, permits bacteria to explore new (niche) environments. Numerous examples document the horizontal influx of metabolic capacities that allow the exploitation of new resources, and of other functions mediating environmental adaptation. HGT may also serve to optimize existing abilities, as exemplified by the replacement of ancestral (vertically transmitted) genes for lactose transport and metabolism in the yogurt bacterium *Lactobacillus delbrueckii* ssp. *bulgaricus* by genes that specify a transport system and a lactose-degrading enzyme of completely different types, and that most probably originate from the second yogurt bacterium,

*Streptococcus thermophilus* [4]. Even genes from the conserved core genome of bacterial species appear to be subject to (sometimes very frequent) substitution by orthologues from closely related species [5]. Substitution can also be partial, and yield hybrid 'mosaic' genes [6]. These observations may again be interpreted as the results of a stepwise optimization of the gene repertoire. In addition, HGT may have a direct effect on interbacterial relationships and promote cooperation [7]. HGT can thus provide a competitive edge to receiving bacteria and directly influence interactions between bacteria, and is therefore likely to affect community structure and dynamics of ecosystems, and possibly ecosystem function. These aspects have hardly or not been studied due to the complexity of most natural ecosystems and the associated difficulty in reproducibly reconstituting them in an experimental setup.

With this idea in mind, Bonham *et al.* in a recent study [8] looked at HGT in bacteria found in cheese rinds, the biofilms that form on the surface of traditional cheeses as they age. Why cheese rinds? In fact,

this study builds on a previous study by the same group [9] where they characterized the microbial communities (bacteria and fungi) from cheese rinds and found that patterns of succession were highly reproducible. Representative species from six (three bacterial and three fungal) dominant genera were then used to constitute a simplified *in vitro* rind community, again with highly reproducible succession patterns, while species from another 11 bacterial and seven fungal dominant genera could be individually cultured for future use. This simplified ecosystem could thus be used as a model to study community assembly and dynamics in response to potentially perturbing factors, such as HGT (with bacteria or fungi containing specific horizontally acquired DNA sequences or not), and provide important insight into microbial community ecology. Besides the two-(bacterial)-species yogurt ecosystem, the six-(bacterial and fungal)-species cheese rind-derived ecosystem, and complete cheese rind ecosystems, many other fermented food (derived) ecosystems with different degrees of complexity could probably be used for this kind of research as they



**Figure 1. Gain and Loss of Function in Bacterial Genomes.** Bacterial genomes are dynamic entities. (1) Many functions (genes) are stably maintained, selective pressure allowing no or only minor modifications (mutations). (2) After gene duplication, one copy (2a) is maintained and one copy (2b) can evolve to obtain a new, related, function (e.g., enzyme with altered substrate specificity). (3) Functions that have become superfluous are gradually eliminated. (4) Horizontal gene transfer (HGT) can lead to the (partial) replacement of existing genes by orthologous genes or by functional homologues (different genes with more or less equivalent function). (5) Completely new functions can be acquired through HGT and stably maintained. (6) HGT genes that are, or have become, superfluous are gradually eliminated.

are often reproducibly formed under controlled conditions [9]. Moreover, results of HGT are observed in many of these systems (not necessarily meaning that HGT always took place during the actual process of fermentation). Among the genes acquired by HGT in food-associated bacteria are those encoding substrate utilization, bacteriocin, exopolysaccharide, and biogenic amine production, immunity to bacteriophages, and antibiotic resistance [10].

HGT can be detected using (a combination of) various criteria, such as local unusually high DNA sequence similarity between putative donor and recipient, higher sequence similarity to distant species or taxa than to closely related species, atypical sequence characteristics (e.g., nucleotide composition, codon usage, frequencies of di-, tri- and tetra-nucleotides), or phylogenetic incongruence (i.e., when a gene appears to have a phylogeny different from that of the species). In their study, Bonham *et al.* [8] searched for unusually high DNA sequence similarity between genes from 165 bacterial isolates from diverse cheese rinds and identified 264 putative horizontally transferred genomic regions containing 4733 protein-coding genes. Apart from genes involved in substrate (lactate, peptides, lipids) utilization and antibiotic resistance that are also found among HGT genes in other food ecosystems [10], they identified an unprecedented number of HGT genes from different origins that are involved in iron acquisition (siderophore biosynthesis and acquisition), a trait commonly associated with virulence in pathogens, reflecting the fact that iron is usually a limiting resource in animal hosts as well as in cheese [8] and that efficient means of iron acquisition will thus provide a

competitive advantage or be essential in these environments.

The abovementioned numbers illustrate that genes are often transferred in clusters (genomic regions), containing up to 34 genes (47 kbp) in this study [8] and sometimes much bigger still [2]. This implies that among the transferred genes only some, for instance one operon responsible for the assimilation of a specific substrate, may suffice to establish the transferred region via positive selection, while others are just hitchhiking, but may nonetheless have consequences at the cellular or community level or, in the case of food ecosystems, for human health as they enter the gut ecosystem. As an example, in the study by Bonham *et al.* [8] a single HGT cluster, probably originating from a pathogen, contains genes involved in iron acquisition, which may give a competitive advantage in the cheese environment, and genes encoding the virulence factors hemolysin and fibronectin-binding protein. Another implication is that the selective advantage that leads to the establishment of the transferred region is not necessarily procured by the genes that may seem responsible at first sight, but may also be due to other genes, of known or still unknown function, in the transferred region.

Apart from the consequences for ecosystem dynamics or function, or ecosystem function dynamics for that matter, the presence of horizontally acquired (hitchhiking) genes in food-associated microbial communities can, as mentioned above, have direct implications for human health when they enter the gut ecosystem, where they may reveal properties that were or were not important in the food environment, and further spread through potentially

abundant HGT [5]. Looking at bacteria that contain genes acquired by natural processes of HGT, sometimes originating from very distant organisms, it is difficult not to make a parallel with genetically modified organisms (GMOs). In a certain way, bacteria containing HGT genes can be regarded as GMOs that already existed before even the concept of GMOs was invented, and the same questions and possible concerns apply regarding their propagation and the consequences of their use for health and environment, especially in the context of food-related applications. Experiments in model ecosystems may provide the first answers to some of these questions.

<sup>1</sup>Micalis Institute, INRA, AgroParisTech, Université Paris-Saclay, 78350 Jouy-en-Josas, France

\*Correspondence:

maarten.van-de-guchte@inra.fr (M. van de Guchte).

<http://dx.doi.org/10.1016/j.tim.2017.07.002>

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