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Review

Microbial Invasions: The Process, Patterns, and Mechanisms

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There has recently been a surge of literature examining microbial invasions into a variety of environments. These studies often include a component of biological diversity as a major factor determining an invader's fate, yet common results are rarely cross-compared. Since many studies only present a snapshot of the entire invasion process, a bird's eye view is required to piece together the entire continuum, which we find consists of introduction, establishment, spread, and impact phases. We further examine the patterns and mechanisms associated with invasion resistance and create a mechanistic synthesis governed by the species richness, species evenness, and resource availability of resident communities. We conclude by exploring the advantages of using a theoretical invasion framework across different fields.

Trends

Microbial invasions are widespread in nature and resemble a process of (i) introduction, (ii) establishment, (iii) growth and spread, and (iv) impact. This process is crucial in determining the diversity and distribution of microbes across the Earth.

Invasion resistance is a product of microbial community diversity. More diverse communities are better able to exploit available resources than less diverse communities. This limits any sustenance for an invading population and ultimately leads to its elimination.

The addition of resources to even a highly diverse community can temporarily uncouple the relationship between diversity and invasion.

The ecological principles that govern microbial invasions can be used to advance practical applications, such as biocontrol, biofertilization, and probiotic use.

Microbial Invasions

Invasive microbes run the gamut of microbial life, from viruses and bacteria to fungi and protozoa [1]. Although older work has addressed the survivability of bacteria released into soil [2,3], envisioning microorganisms as invaders is a poorly studied phenomenon in microbiology. It is preceded by the way the dispersal and biogeography of microbes have traditionally been viewed. In fact, the very idea of a **microbial invasion** (see Glossary) was until only recently inconceivable. A previous leading principle in microbial community ecology postulated that, in terms of incidence, microbes are homogeneously distributed on Earth and lack clear biogeographic patterns due to their high dispersability and large population sizes [4,5]. This consideration of ubiquity rendered any exploration of invasion behavior moot, because an invader could not invade a region where it already existed. Yet, the adage that "everything is everywhere but the environment selects" [6] has been challenged with the advent of direct high-throughput sequencing from environmental samples. These recent research efforts helped to reveal that microbes do, in many cases, exhibit biogeographic patterns and are also, albeit dependent on scale, dispersal-limited [5,7,8]. Although some studies report the existence of homogeneous distributions of microbes across certain ecosystems, such as the bacterial community in oceans [9], it is important to note that such conclusions are usually based on data originating from a small portion of the 16S rRNA taxonomic marker gene and not whole genomes. While the debate on microbial biogeography is not yet resolved, the high rates of horizontal gene transfer in microbial communities [10]; the great number of **ecotypes** with different physiological adaptations [11,12]; and the existing evidence of biogeographic patterns [13], especially when using multilocus sequence typing [14], reveals that microbial communities and ecosystems alike are mosaics of genetically and phenotypically distinct organisms that are susceptible to invasion by fitter forms. Accordingly, the past 5 years has brought a surge of literature that documents the invasion of various ecological systems by microbes and the mechanisms that control this

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process [15–27]. A synthesis of these recent conclusions and their eventual merging into existing ecological and microbiological theory will enhance our understanding of the fundamental processes that govern microbial life.

The recent advent of microbial invasion research spans several fields of microbiology, including agricultural, medical, and environmental. Despite the fact that the entrance of a foreign microorganism into a resident community of microbes (a microbial invasion) is a common phenomenon across these fields, there is a scarcity of general principles to foster cross-comparisons that can enhance the understanding, interpretation, and future research of this phenomenon. In fact, a major shortcoming is the failure of researchers to recognize a microbial invasion as a process rather than a mere snapshot of a longer frame. In the first part of this review, we examine different examples of invasion and fuse these into a unified framework. As dispersal is a key process in invasion, we highlight that the establishment of microbes in and throughout environments is a process mediated by passive and active dispersal, adaptability of the organism, and the biotic 'resistance to invasion' of the habitat. Once biotic resistance is breached, an invader will likely grow and spread, potentially leading to large impacts on the functioning of native communities. The second part of this review delves deeper into the patterns and mechanisms of invasion resistance, revealing a direct relationship with microbial diversity. We provide a mechanistic synthesis of how microbial diversity mediates invasion resistance and, in doing so, address another major shortcoming of microbial invasion research: the disconnect between short-term invasion experiments performed *in vitro* and long-term experiments usually performed *in vivo* or *in situ.* The former experiments most often utilize small diversity gradients with simulated invasions lasting anywhere from 24 to 48 hours, while the latter often employ larger diversity gradients and can last from weeks to months. This leaves us to wonder if the same patterns and mechanisms govern each scenario.

An Ecological Blueprint of Microbial Invasions: A Four-Step Process

To properly identify and understand the invasion of a system by a microorganism, it is important to comprehend the entire process leading to the success of an invader. Part of the difficulty in understanding the process lies in the fact that invasions are only rarely tracked from start to finish. Simply identifying studies pertaining to microbial invasions and collating them by phases reveals the emergence of a universal and stepwise invasion process that contains several barriers to a successful invasion. Although several variants of the invasion process have been concocted [28], our synthesis indicates that microbial invasions most closely follow a sequential process entailing (i) introduction, (ii) establishment, (iii) growth and spread, and (iv) impact (as hypothesized in [29]; Figure 1, Key Figure; see Box 1 for an *Escherichia coli* case study). Within each phase there are salient aspects that emerge, which provide insight into the ecological and evolutionary characteristics that define **microbial invaders** and their respective invasions.

Invasive microbes must first be transported from a source to foreign environment in order to commence the first invasion phase: introduction (Figure 1A). This is mediated by passive and active dispersal. Ocean currents passively transport and introduce endospores of bacilli over long distances throughout the world's seas and oceans [30]. This has resulted in the creation of communities of 'kin', whose networks stretch from Svalbard in the Arctic, the Baltic sea in Northern Europe, and even to the gulf of California in North America [30]. Several other types of marine bacteria are also circulated through regions of the Earth's oceans, forming distinct populations that are subject to invasion by neighboring taxa [31]. High above ocean waters, air samples collected from the Northwestern United States have been found to contain an average of 4.94×10^{-5} and 4.77×10^{-3} ng of microbial DNA m^{-3}, representing cells of bacteria and fungi, respectively [32]; these organisms were hypothesized to originate from the Gobi desert, being transported via transatlantic wind patterns that pushed the microbe-carrying, air-suspended matter [32,33]. Across large spatial scales, microbial dispersal rates are expected to be

Glossary

Biofilm: communities of microorganisms attached to a surface [77].

Community niche: a metric to estimate the resource use and functioning of an ecological community, which is based on the sum of the best performances of individuals on an array of different resources [78].

Competition-colonization tradeoff: refers to the ecological theory that species coexistence is mediated by the ability of some individuals to be better competitors while others are better colonizers [79].

Diversity–invasion effect: a common relationship witnessed between microbial community diversity (often measured in species richness or evenness) and the survival of an invading microbe, where more diverse communities better resist invasion than less diverse communities.

Ecotype: a genetically distinct form among a species, which may be adapted to a certain environmental condition.

Functional dissimilarity: the differential ability of species in a community to perform certain functions, such as the ability to use different resources.

Keystone species: a species that plays a disproportionately large role in maintaining the balance of an ecosystem or ecological community.

Microbial invader: any microorganism that is transported into a new environment or community where it has never before existed. Even if the invasion is not successful, it is still considered an invader.

Microbial invasion: a four-step process consisting of the (i) introduction, (ii) establishment, (iii) growth and spread, and (iv) impact of a microbial invader. While a successful invasion passes all four steps, reference to the term 'microbial invasion' could imply any one of the phases. Many variants of the invasion process exist; see [28] for an exhaustive list.

Microbiostasis: the inability of a microorganism to multiply in a particular environment.

Quorum sensing: the regulation of gene expression in response to cell density via chemical signaling [80].

Remaining niche available to the invader: a measure of the resources