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Natural selection for imprecise vertical transmission in host–microbiota systems

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How and when the microbiome modulates host adaptation remains an evolutionary puzzle, despite evidence that the extended genetic repertoire of the microbiome can shape host phenotypes and fitness. One complicating factor is that the microbiome is often transmitted imperfectly across host generations, leading to questions about the degree to which the microbiome contributes to host adaptation. Here, using an evolutionary model, we demonstrate that decreasing vertical transmission fidelity can increase microbiome variation, and thus phenotypic variation, across hosts. When the most beneficial microbial genotypes change unpredictably from one generation to the next (for example, in variable environments), hosts can maximize fitness by increasing the microbiome variation among offspring, as this improves the chance of there being an offspring with the right microbial combination for the next generation. Imperfect vertical transmission can therefore be adaptive in varying environments. We characterize how selection on vertical transmission is shaped by environmental conditions, microbiome changes during host development and the contribution of other factors to trait variation. We illustrate how environmentally dependent microbial effects can favour intermediate transmission and set our results in the context of examples from natural systems. We also suggest research avenues to empirically test our predictions. Our model provides a basis to understand the evolutionary pathways that potentially led to the wide diversity of microbe transmission patterns found in nature.

Microbial life occupies almost every habitat on Earth. Increasingly, there is evidence that microbial communities living in and on eukaryotic hosts can strongly affect host phenotypes, shaping features including behaviour[1–3], development[4,5], illness[6], pathogen resistance[7–9] and life span[10]. Such strong effects on host traits indicate that the microbiome can affect host fitness. Moreover, the composition of microbiome communities often varies greatly between hosts within a population, explaining a substantial proportion of host phenotypic variation[11,12]. The importance of the microbiome for host fitness, together with the considerable variation between hosts, implies that the microbiome has the potential to impact host adaptive evolution. However, it is largely unknown how much the microbiome contributes to host adaptation[13,14].

The importance of the microbiome for host fitness implies that hosts will be under selection to 'manage' their microbiome communities[15]: adaptations that enable hosts to control their microbiome composition have clear potential to increase fitness. Such adaptations could act on different stages during microbe acquisition and establishment[15]. Our focus here is on hosts controlling their microbe composition by controlling the transmission of microbes from parents to offspring (that is, vertical transmission). There exists a wide variety of mechanisms for transmission, producing a broad range of transmission fidelity across systems (Fig. 1). Some host species have faithful microbial transmission (Fig. 1a), leading to high concordance between the microbiomes of parents and offspring, ultimately echoing the inheritance of host genetic material. The most faithful transmission method is through intracellular infection of oocytes, epitomized in obligate nutritional symbiosis observed in many sap-feeding insects[16]. For example, aphids are nearly all infected with *Buchnera* bacteria, enabling these insects to feed on phloem sap, an otherwise unbalanced diet[17]. Other forms of vertical transmission occur through 'intimate neighbourhood transmission' during seed formation, egg laying or passage through the birth canal[18]. For instance, to transmit bacteria from parents to offspring, stinkbugs can attach special symbiont capsules to their eggs[19] or cover their eggs with symbiont-supplemented jelly[20]. Faeces consumption (coprophagy) is an important mechanism by which early-stage cockroaches acquire their gut bacteria, increasing their fitness compared with individuals reared under sterile conditions[21]. In dung beetles, vertical transmission is ensured through a brood ball, which results in remarkably faithful microbial transmission[22]. Recent modelling studies suggest that whenever transmission is faithful, as in these examples, the microbiome has the potential to contribute to host adaptation[23,24].

However, despite these intriguing examples of tightly linked host–microbe associations, most host populations have microbiomes that vary through time and across hosts, leading to hosts associating with variable microbial communities (Fig. 1b–d). For instance, vertical transmission in marine sponges is highly unfaithful; they are no more likely to share symbionts between parents and offspring than they are between species[25]. This generally low transmission fidelity has led some studies to suggest that selection at the level of the host and microbiome together is unlikely to drive adaptive changes in most natural host systems[13,26].

While a low transmission fidelity could indeed reflect a relatively small role of the microbiome in host adaptation, it could also be that current models lack relevant elements. One of these elements might be environmental variation. There is some empirical evidence suggesting that loose host–microbiome associations might be beneficial under changing environmental conditions. In animals that undergo metamorphosis, such as holometabolous insects, flexibility in the microbiome may optimize phenotypes for different environments at different life stages[27]. Furthermore, the microbiome potentially

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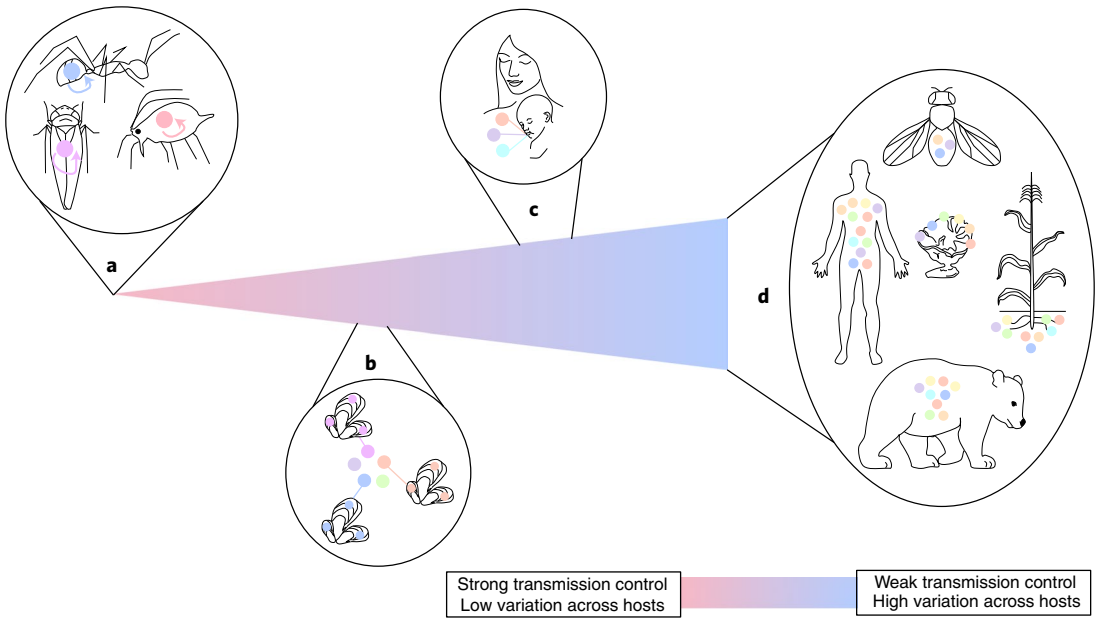

Fig. 1 | Natural variation in microbiome transmission fidelity across the eukaryotic kingdom, resulting in variation in microbiome composition across hosts in a population. a, Obligate intracellular symbionts represent strong control over microbial transmission. Across insects, such as carpenter ant–*Blochmannia*[85], aphid–*Buchnera*[86] and leafhopper–*Sulcia* associations[87], both host and microbe have intricate molecular mechanisms whereby symbionts are transovarially transmitted from mother to offspring, limiting symbiont diversity. **b**, Hosts may exert strong control over which microbes may infect, but maintain flexible associations with a broader diversity of microbes than in the scenarios illustrated in **a**. For example, deep-sea mussels restrict acquisition to a single bacterial species, but this bacterial species may vary across individuals and populations[88]. Bacterial diversity is reduced within hosts but variable across hosts. **c**, Some hosts have behavioural mechanisms that transmit only some portions of the microbiome. In humans, mothers transmit a distinct subset of microbes to their infants that probably help with lactose digestion and immune development[56–58]. However, the homogenization of microbiota between mother and infant disappears over the next few years[89,90]. **d**, For many hosts, microbiome transmission is thought to be unfaithful, leading to high variance among individuals. In *Drosophila* and maize, only a small percentage of the microbiome is faithfully transmitted[91,92]. Sponges harbour specific microbial communities but are no more likely to share symbionts between parents and offspring than they are between species; rather, sponge microbiomes are environment-specific[25]. For some hosts, such as bears, flexibility in the microbiome may enable microbes associated with increased nutrient acquisition in preparation for hibernation[93]. This flexibility may also happen in humans[94], but drivers of microbial diversity in humans (and in these other systems) are not well understood.

plays a role in the variance in timing of important life history events, which could help hosts hedge their bets in unpredictable environments or when in competition[28]. Finally, a study on wild marine sponges suggested that the observed unfaithful vertical transmission rates might benefit larvae facing variable environments[25]. However, such fluctuating selection has not been incorporated in models of how faithful microbial transmission should be to optimize host fitness.

We explore how vertical microbiome transmission fidelity (here defined as the expected fraction of the parental microbiome that gets transmitted to offspring at birth) could affect long-term host fitness, and how this interacts with constant versus fluctuating selection. Can the microbiome contribute to host adaptation even if heritability is low, or perhaps because heritability is low? To tackle this question, we model host phenotypes as a function of their microbiome and map host phenotypes to fitness in interaction with the environment. We vary vertical transmission fidelity, assuming that this is a heritable trait of the hosts, and assess how this fidelity affects phenotypic distributions and long-term fitness of a population of hosts. We show that the microbiome has the potential to contribute to host adaptation, not only by altering the mean phenotype to one that maps to higher fitness but also potentially by adjusting the variance in phenotypes to increase fitness[29,30]. Under sufficiently large fluctuating selection, a low microbiome transmission fidelity, increasing host phenotypic variation, can benefit host fitness. Our findings provide a new lens to interpret a fast-growing body of literature suggesting that the microbiome has the potential to contribute to host adaptation.

Results

Microbiome transmission fidelity shapes host phenotypic distributions and fitness. More faithful vertical microbe transmission decreases host phenotypic variance (Fig. 2a): when all microbes are faithfully transmitted from parents to offspring (vertical transmission fidelity $\tau = 1$), all phenotypic variance disappears due to a combination of selective (loss of hosts that are maladapted in that time step) and stochastic (loss of hosts by chance) events. This is analogous to a population in which, in the absence of new mutations, all genetic variation eventually disappears (Supplementary Information 1). In contrast, under no vertical transmission ($\tau = 0$), each host starts with a completely random set of microbial species every host generation, resulting in maximal phenotypic variance among hosts (analogous to a biologically unrealistic scenario where each allele mutates every generation; Supplementary Information 1). Here we assume that microbial composition does not change during a host's life and that there are no other sources of phenotypic variation among hosts than microbiome variation; below we show the consequences of relaxing these assumptions.

A non-zero transmission fidelity not only reduces the amount of variation but also has the potential to shift the population-level mean phenotype from one generation to the next. This, under constant selection, results in the average phenotype matching the long-term

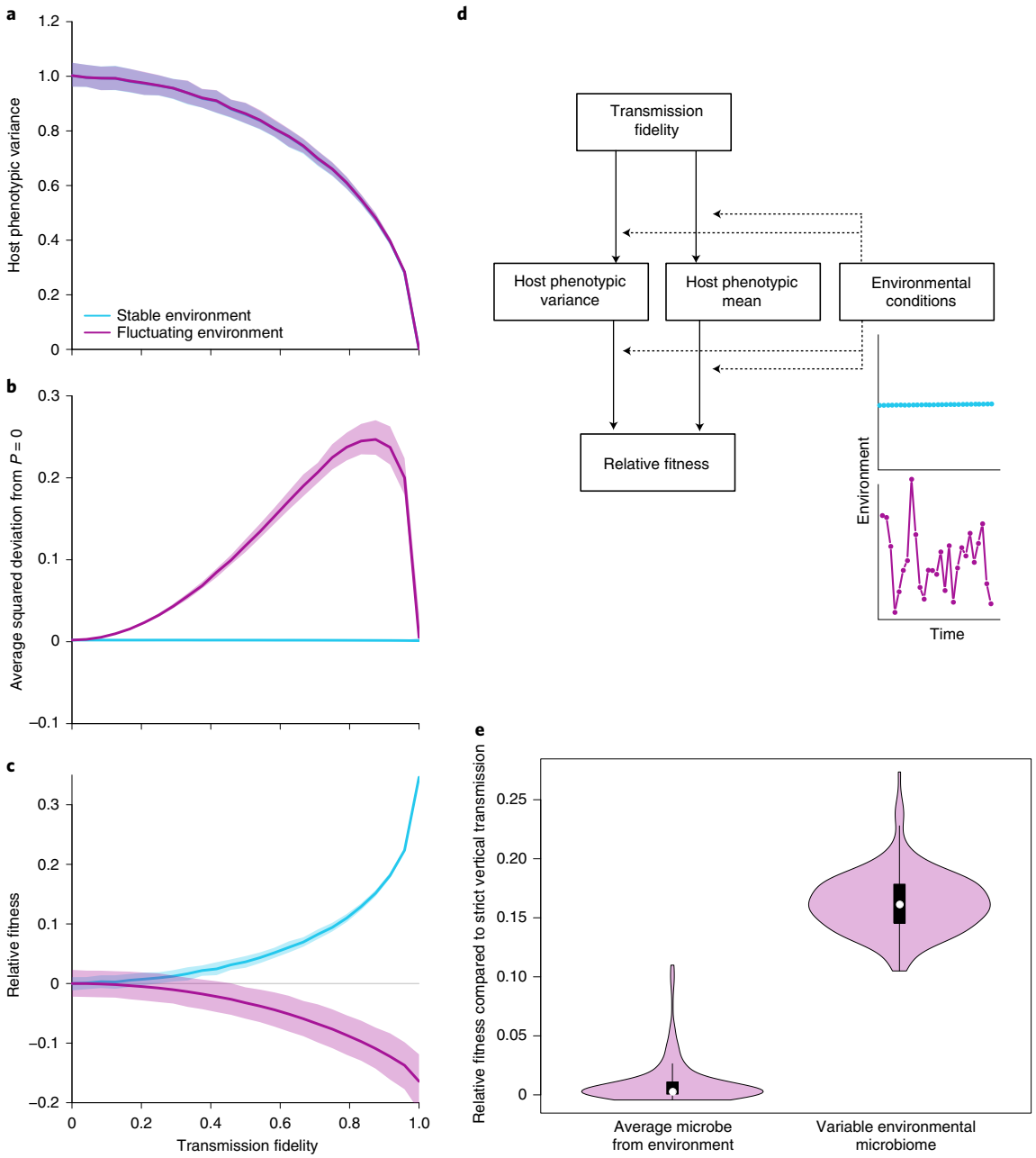

Fig. 2 | Interactions among transmission fidelity, host phenotypes and fitness, and the environment. a–**c**, Vertical microbiome transmission fidelity affects both host phenotypic variance (**a**) and the deviation from the optimal mean (**b**), which together shape long-term fitness (**c**). The environment shapes these relations (blue indicates a stable environment, and purple indicates a fluctuating environment; note that the lines completely overlap in **a**). **d**, Conceptual overview of these results. **e**, As shown in **c**, under fluctuating environments, hosts benefit from not vertically transmitting their microbiome. This is not only because the average environmental microbe is more beneficial than what is inherited due to a slight deviation from the optimal phenotype but also because the existence of variation among offspring increases long-term fitness. In **b**, the squared deviation is calculated by comparing host phenotypes with the long-term optimum phenotype of 0. In **c**, relative fitness is calculated as the difference in log fitness, comparing each strategy with the strategy without vertical transmission ($\tau = 0$). The lines show median values based on 250 replicate simulations. The shaded regions indicate the 68% ranges of the simulations. Transmission fidelity (x axis) is defined as the expected proportion of microbes that is faithfully transmitted from parents to offspring. Selection strength toward the optimum phenotype, $\omega^2 = 1$; degree of environmental fluctuations, $\sigma_\varphi^2 = 0$ (blue) or $\sigma_\varphi^2 = 2$ (purple); variance in microbial effects on host phenotype, $V_\alpha = 0.01$.

phenotype optimum (Fig. 2b). However, under selection that fluctuates unpredictably (that is, no temporal autocorrelation, extended below), faithful transmission increases the average deviation (per time step) from the long-term phenotype optimum (Fig. 2b), up to when transmission fidelity is almost 100%. We note that we simulated a large host population, consisting of 500 individuals. Reducing the population size makes the population more sensitive to stochastic processes, leading to an increase in the number of maladapted populations that deviate from the optimum of 0 (Extended Data Fig. 1).

These effects of transmission fidelity on host phenotypic variance and mean translate into effects on long-term host fitness

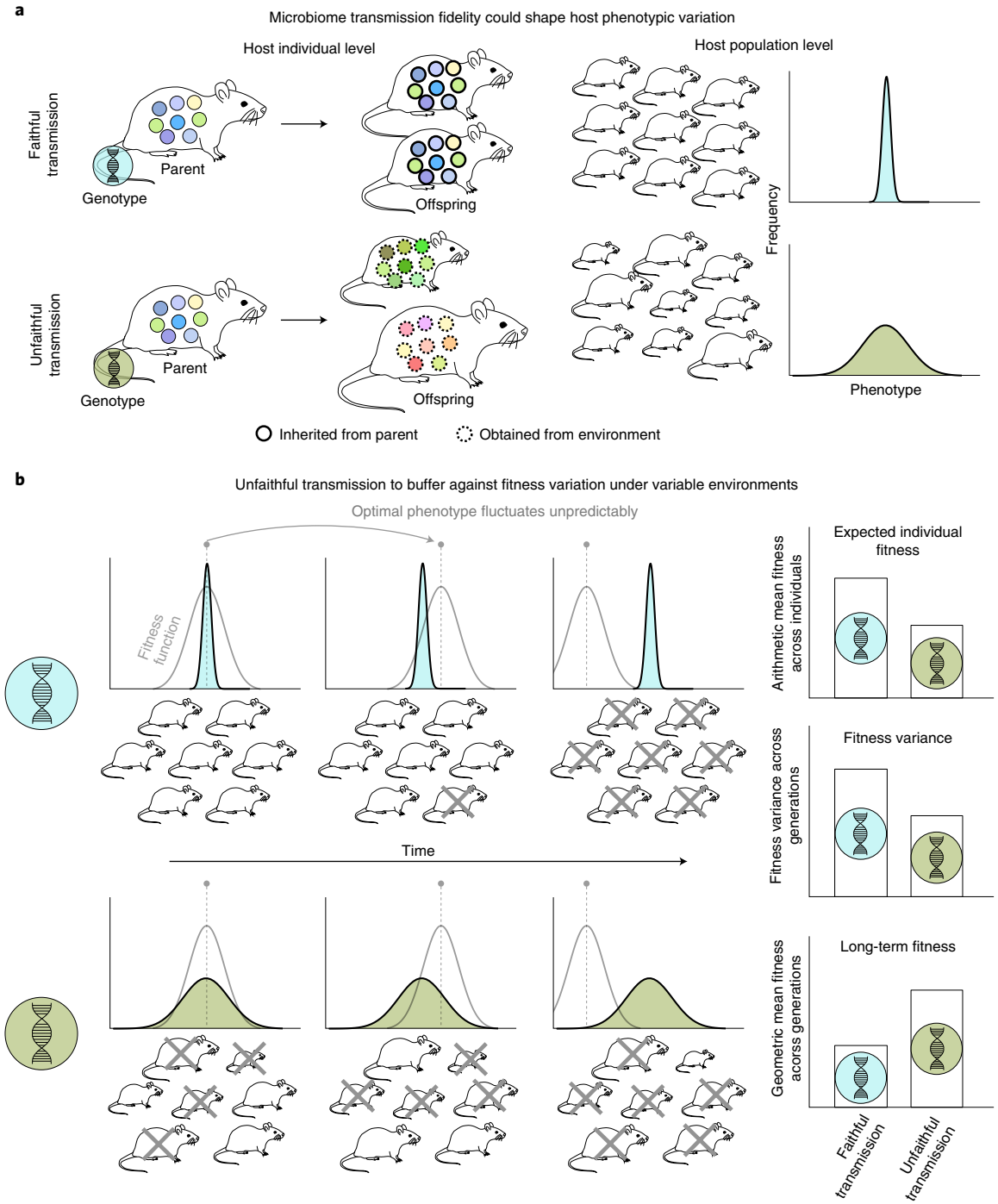

Fig. 3 | Conceptual overview of how microbiome transmission could shape host phenotypic variance and when phenotypic variation among genetically similar individuals might be beneficial. a, Hosts are represented as mice and are characterized by their microbiomes (circles). Microbes differ in their host effects (colours), and their combined effects determine their host's phenotype (body size in this case). A population of hosts with faithful microbiome transmission will eventually result in the loss of variation, due to stochasticity and selection. In a host population with unfaithful transmission, new variation is introduced every generation, resulting in maximal phenotypic variation across hosts. **b**, Such increased phenotypic variation can be beneficial under variable environments, by increasing the chance that at least some individuals match the most beneficial phenotype in any given environment. Increased phenotypic variation by imperfect transmission reflects a diversified bet-hedging strategy: a reduction in fitness variance across generations may optimize long-term fitness, despite a reduction in the expected year-to-year individual fitness. Host genotypes with low transmission fidelity could therefore be favoured by natural selection under fluctuating selection.

(Fig. 2c). As expected, in a stable environment, strict faithful transmission maximizes fitness by reducing phenotypic variance while ensuring that the average phenotype matches the optimum (blue lines in Fig. 2a–c). In contrast, under sufficiently large fluctuating selection, fitness decreases with an increasing transmission fidelity (purple line in Fig. 2c).

These effects on long-term fitness are driven by the effects of transmission fidelity on both the amount of phenotypic variation

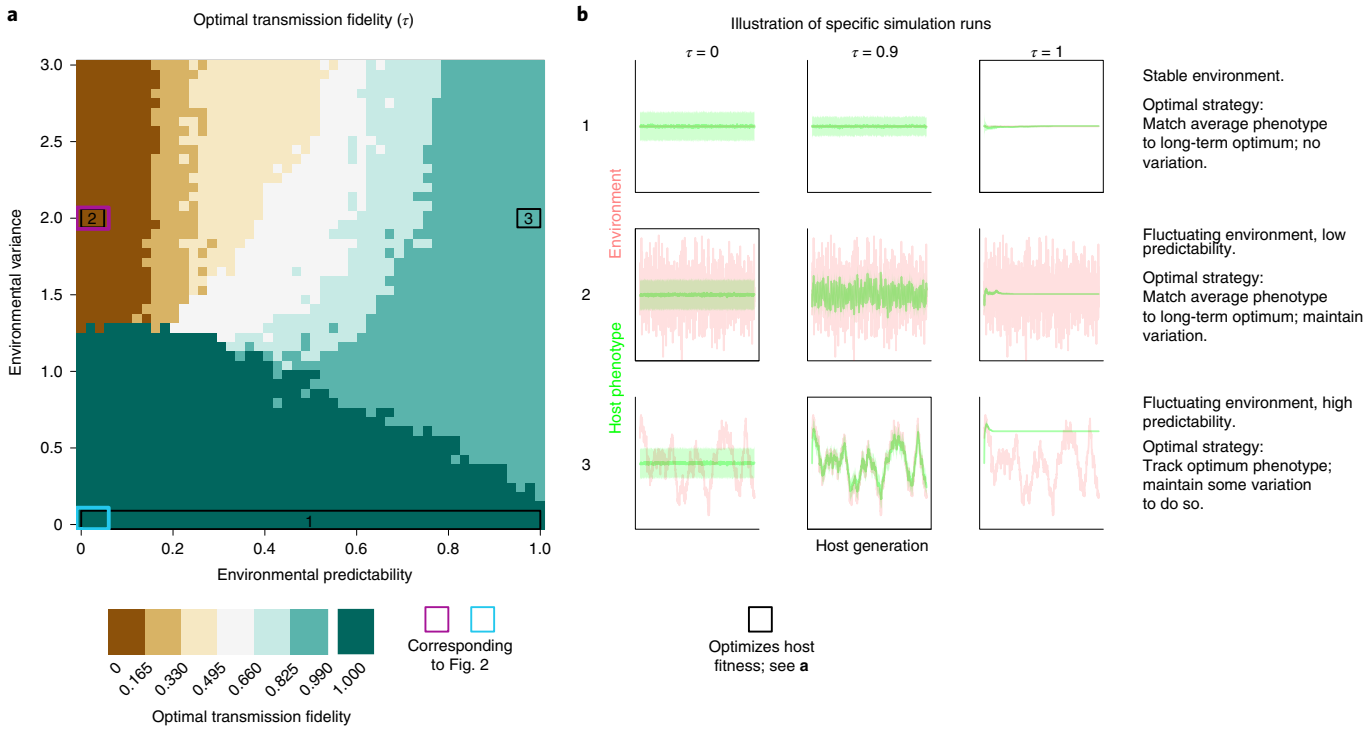

Fig. 4 | Environmental predictability and variance together shape the optimal transmission fidelity. a, Optimal transmission fidelity for 50 × 50 combinations of environmental variance and predictability (that is, temporal autocorrelation) (brown indicates low optimal transmission fidelity; teal indicates high optimal transmission fidelity). The coloured rectangles correspond to the scenarios depicted in Fig. 2 (blue represents a stable environment; purple represents a fluctuating environment). The black rectangles with labels 1–3 indicate combinations that are further illustrated in **b**. **b**, Output of specific simulation runs. The green lines indicate population-level average phenotypes, and the shading indicates one standard deviation below and above the average. Note that when the environment is stable (scenario 1), the flat red line is not visible in the graphs. Each set of graphs shows the results when τ is set at 0, 0.9 and 1, and the black rectangles indicate the transmission fidelity that maximizes fitness. $\omega^2 = 1$; $V_\alpha = 0.01$.

and deviations from the optimal phenotype (Fig. 2d). This implies that under fluctuating selection, even when the average phenotype is kept at its long-term optimum, hosts benefit from not (or only partly) transmitting their microbiome as a means to increase phenotypic variation (see Extended Data Fig. 2 for the results when the mean is kept at its optimum). In other words, under fluctuating environments, host genotypes that produce offspring with randomly assembled microbiomes attain a higher long-term fitness than hosts that faithfully transmit their microbiomes or that take up only the 'average' (long-term optimal) microbial genotype from the environment (Fig. 2e). These benefits of random variation arise because long-term fitness, as it is a multiplicative process, is very sensitive to occasional low values: only one year with a fitness of 0 is enough to reduce long-term fitness to 0. The result is that a strategy that buffers against (occasional) low fitness values—for example, by creating offspring with variable microbiomes, so that some offspring will do well whatever the generation-specific conditions are—can be selected for in the long term. Such variation in offspring ensures that at least some individuals are able to maintain a non-zero fitness in any given time step, despite a reduction in expected individual fitness; this is the concept of diversified bet-hedging[29,31]. We here show that host genotypes can express such a bet-hedging strategy by lowering their microbiome transmission fidelity (see Fig. 3 for a conceptual overview).

A mathematical framework to calculate the optimal amount of phenotypic variation as a function of the strength of stabilizing selection and how much it fluctuates through time is proposed by Bull[30] (Supplementary Information 2). When keeping the average phenotype at its optimum, our results match Bull's predictions (Extended Data Fig. 2).

High transmission fidelity enables adaptive tracking in predictable environments. Up to this point, we considered no temporal autocorrelation—that is, the environment at time t was not predictive of the environment at time $t+1$. In nature, however, many environmental conditions are temporally autocorrelated[32,33], and the combination of environmental predictability and variation could shape host evolutionary responses[34]. We increase the temporal autocorrelation (predictability ρ), adding directional selection on the mean phenotype. We assess the optimal transmission fidelity for combinations of environmental variance and predictability, keeping the average environment at 0 (Fig. 4) and still assuming no microbial changes during host development and no other sources of phenotypic variation. Optimal transmission fidelity is assessed by comparing the long-term fitness of populations that differ in their transmission fidelity. When there is considerable environmental variation and a low environmental predictability (labelled 2 in Fig. 4; see also Fig. 2), selection favours a low transmission fidelity, as this ensures that phenotypic variation across hosts is maintained and that the mean phenotype remains at its long-term optimum of 0. In contrast, a highly predictable environment with the same environmental variance (labelled 3 in Fig. 4) favours a transmission fidelity close to 1, as this allows hosts to follow changes in the mean environment through adaptive tracking. Note that even though the environment changes in a highly predictable way, strict faithful transmission ($\tau = 1$) again quickly results in the loss of all variation, hampering the population's ability to track these changes, and strongly reduces fitness.

Other sources of phenotypic variation among hosts. Until now, phenotypic variation among hosts was solely determined by variation in their microbiome composition—that is, we focused only on

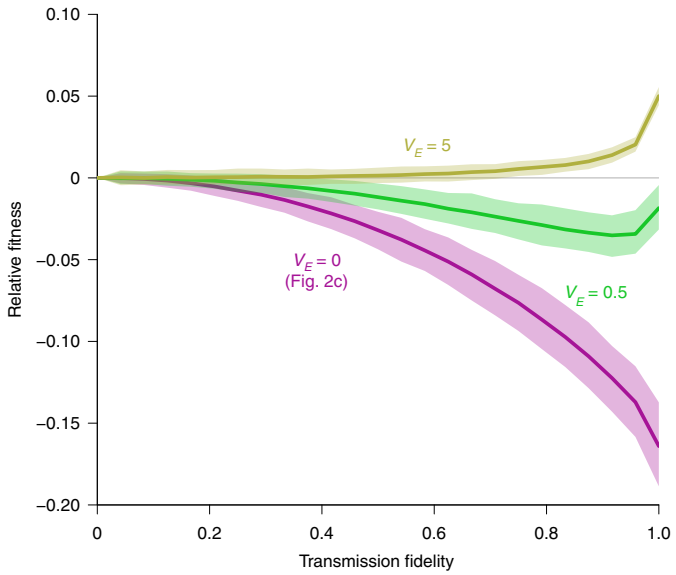

Fig. 5 | Including other sources of phenotypic variation among hosts changes selection on transmission fidelity. The colours show the results for different values of the environmental (residual) contribution (V_E) to host phenotypic variance. Larger V_E values weaken selection on vertical transmission and select for more faithful microbe transmission. In accordance with Fig. 2, we set $\omega^2 = 1$; $\sigma_\varphi^2 = 2$; $V_a = 0.01$; and relative fitness is the difference in log fitness compared with $\tau = 0$. The lines show the median predictions based on 250 simulations; the shaded regions indicate the 68% ranges of the simulations.

determinants and consequences of phenotypic variance associated with the microbiome. However, phenotypic variation in natural populations is evidently not only caused by variation in microbiome composition. According to a quantitative genetic framework, phenotypes can be described as the sum of one or more genetic and non-genetic components. We recently proposed an approach to framing how a microbiome contribution can be incorporated[14]. Assuming no interactions, host phenotypes can be written as:

$$P = G + \gamma + E \quad (1)$$

where G is a host's genetic value (assuming only additive effects), γ is its microbiome contribution (where we also assume only additive effects; Methods) and E is a residual component. The total host phenotypic variance (V_P) can now be written as:

$$V_P = V_G + V_\gamma + V_E \quad (2)$$

Up to this point, we have assumed that all G and E values are zero, resulting in $V_G = V_E = 0$, and hence $V_P = V_\gamma$. Thus, the microbiome variance required to optimize phenotypic variance is $\tilde{V}_\gamma = \tilde{V}_P$. Equation (2) illustrates that a non-zero contribution of other variance components affects the optimal microbiome variance, as now $\tilde{V}_\gamma = \tilde{V}_P - V_G - V_E$. The optimal microbiome variance thus decreases with larger contributions of other sources of variation, which can be achieved by increasing τ (Fig. 2a). Indeed, starting from an unpredictably fluctuating environment (Fig. 2a), varying V_E changes the selection on transmission fidelity: larger values of V_E increase the optimal transmission fidelity while weakening selection on vertical microbe transmission in general (Fig. 5). Here we consider one focal host genotype (or strategy), such that $V_G = 0$. By the same logic as above, increasing V_G (due to sexual reproduction, for example) will decrease the optimal microbiome variance, therefore increasing the optimal transmission fidelity.

These findings illustrate that selection on microbiome transmission fidelity is shaped by how inherently stochastic host phenotypes are. Hosts with phenotypes with a strong stochastic component might, even under fluctuating selection, benefit from strict microbiome control, to avoid increasing phenotypic variance even more. In contrast, host with phenotypes that show little inherent variation (for example, in the absence of environmental or genetic variation) might, under sufficiently large fluctuating selection, benefit from extra variance induced by noisy transmission.

Changes in microbiome composition during host development. As the generation time of microbes is generally orders of magnitude shorter than that of their host, microbiome composition generally changes over the course of a host's life[35,36]. To account for this, we allow neutral dynamics to affect microbiome composition between the moment hosts are born and the moment they reproduce. We do so by varying the number of microbial generations (T_m), as a measure of the relative host generation time, and varying the balance between the acquiring of new microbes from the environment (with probability c) and within-host proliferation (with probability $1-c$). The parameter c is a measure of how much the microbiome composition changes due to horizontal transmission during host development, and empirical estimates of c vary within the full 0 to 1 range[37].

More microbial generations within one host generation (that is, higher T_m values) increase phenotypic variation among hosts (Fig. 6a–c) (we here simulate host dynamics in an unpredictable environment and do not include other sources of phenotypic variation). Increasing colonization from the environment reduces the effects of T_m and τ and creates a more homogeneous phenotypic variance landscape (Fig. 6c). Environmental colonization c thus has the ability to both increase and decrease phenotypic variance (Fig. 6d), depending on the transmission fidelity and the number of microbial generations occurring within a host (coloured dots in Fig. 6a–c mapping onto curves in Fig. 6d). Both increasing the number of microbial generations and increasing colonization can strongly reduce microbiome heritability, even under strict vertical transmission, illustrating the difference between inheritance and heritability (Extended Data Fig. 3).

These neutral dynamics within one host generation result in patterns as expected from ecological metacommunity theory: increased microbe (that is, species) migration from the source pool to individual hosts (that is, communities) decreases variation among hosts (that is, β-diversity) (Extended Data Fig. 4). This is in line with empirical studies showing that dispersal among hosts leads to more similar microbial communities[38,39]. However, as our focus is on the long-term evolutionary consequences for a population of hosts, we additionally model stochastic and selective host reproduction. This has no analogue in a metacommunity framework, where communities do not duplicate or disappear (see also ref. [40]). Our extended framework, including these host dynamics, shows that even though environmental transmission generally reduces variation within one host generation (Extended Data Fig. 4 and Fig. 6d), it is required to maintain variation on host evolutionary timescales.

Discussion

We developed a general model to evaluate how vertical transmission fidelity could affect long-term host fitness, accounting for the important but often neglected feature of fluctuating environmental conditions. We found that transmission fidelity affects the amount of microbiome variation across hosts: strong control over transmission reduces variation in microbial composition across hosts, while weak control increases microbial variation (Figs. 2 and 3). We found that there are conditions under which lower transmission fidelity is beneficial, and we showed that both external properties (such as the strength of phenotypic selection (Supplementary Information 2), how selection fluctuates through time (Figs. 2 and 4) and the importance

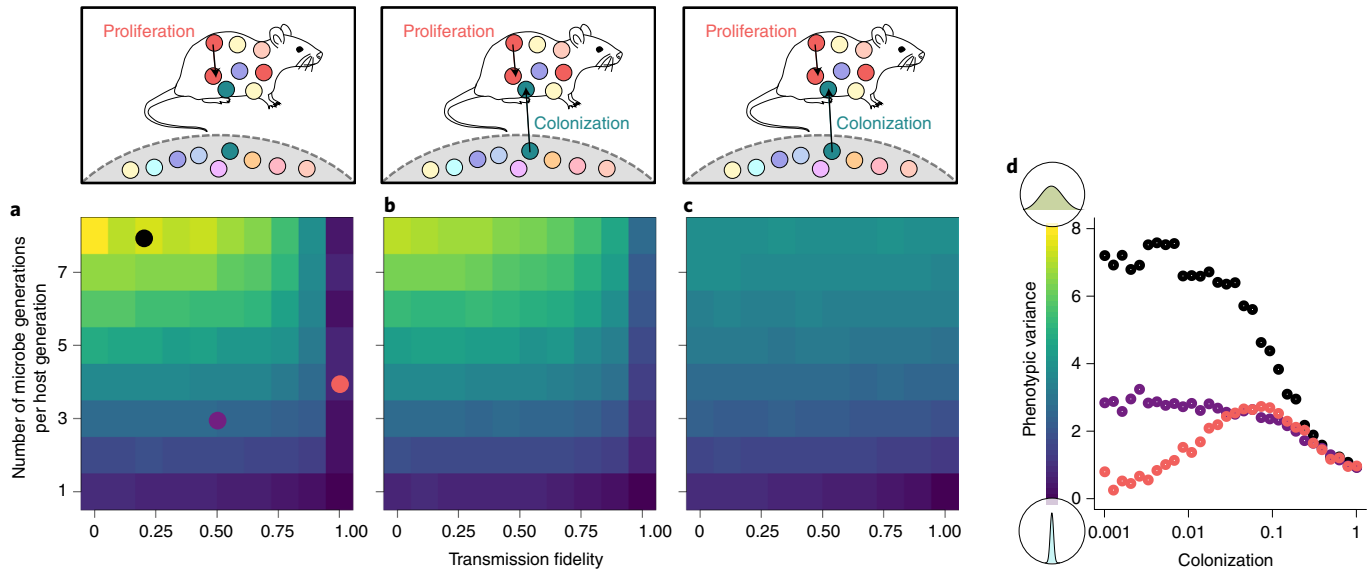

Fig. 6 | Environmental colonization and within-host proliferation alter host phenotypic variance. a–c, Effects of changes in microbiome composition during host development on host phenotypic variance (yellow indicates high variance; dark blue indicates low variance), for different colonization probabilities of 0 (**a**), 0.01 (**b**) and 0.1 (**c**). **d**, Phenotypic variance as a function of colonization probabilities (note the log scale on the *x* axis). The coloured dots correspond to combinations of T_m and τ, shown in **a**. $\omega^2 = 1$; $\sigma_\varphi^2 = 2$; $V_a = 0.01$.

of microbial transmission from the environment (Fig. 6)) and host properties (such as relative generation time (Fig. 6) and the relative contribution of microbiome variation to host phenotypic variation (Fig. 5)) can shape selection on microbiome transmission fidelity. Our results suggest that, under unpredictable environmental conditions, imperfect transmission can be adaptive, not only by affecting the mean host phenotype (Fig. 2b) but also by tuning phenotypic variability among hosts (Fig. 2a,e). This is because under imperfect transmission, each offspring obtains a random set of microbes from the environment, resulting in more variation among offspring than when each offspring inherits the same microbes from their parent (Fig. 3). In fluctuating environments, a strategy (that is, genotype) that creates such random variation in phenotypes can be selected for (this is the concept of diversified bet-hedging[29,31]; Fig. 3).

Environmentally dependent microbial effects. Our model provides some general predictions regarding selection on control over microbiome transmission. Importantly, we illustrate that environmentally dependent microbial effects are crucial for selection to favour intermediate transmission fidelity: selection in the case of consistently beneficial microbes always favours fully faithful transmission, whereas host selection favours no transmission for consistently detrimental microbes. Indeed, such environmentally dependent microbial effects on hosts are found in a range of systems, suggesting that mixed modes of inheritance might indeed be favoured in nature. For example, in thrips, the effects of *Erwinia* bacteria depend on host diet[41], proposed as an explanation for why thrips did not evolve strict vertical transmission[41]. Mycorrhizal effects in plants can depend on environmental conditions[42], and in damselfish, the benefits of cleaning gobies depend on the presence of ectoparasites[43]. Finally, in aphids, fitness effects of multiple symbionts (and their environmental interaction), as well as transmission patterns, are relatively well understood[44,45]. For instance, the maternally transmitted facultative symbiont *Hamiltonella defensa* provides protection against endoparasitoid wasps[46] but comes with an apparent fitness cost in parasitism-free environments[47]. Indeed, variation in selection can maintain hosts both with and without this symbiont[48]. *Serratia symbiotica*, another facultative aphid symbiont, increases host heat tolerance[44,49,50] but can decrease host fitness under lower temperatures[49].

Understanding the lack of faithful transmission of beneficial microbes. Despite the numerous examples of microbes with environmentally dependent effects, there are also microbes with seemingly consistent benefits for their hosts, irrespective of the environment, but lacking faithful transmission. For instance, *Burkholderia* bacteria provide insecticide resistance to their host bean bugs[51], and we are not aware of any study reporting negative host effects of this symbiont. On the basis of our model, we predict that, in such cases, host-level selection should favour perfect vertical transmission—but *Burkholderia* bacteria are not vertically transmitted, and hosts have to reacquire their symbiont from the soil every generation[52]. We have the following four explanations for the lack of faithful transmission of consistently beneficial microbes.

First, developmental or physiological constraints can make it difficult to ensure full concordance between parent and offspring microbiome composition. It might be difficult to faithfully transmit all microbial species from parents to offspring, and furthermore, microbial dynamics often have ample opportunity to change microbiome composition during host development[35,36], due to stochastic processes or competition among microbes. This is especially true for hosts with longer generation times (Fig. 6).

Second, there could be hidden fitness costs of the microbe—that is, decreasing host fitness components in certain life stages or in certain environments. For instance, *Drosophila* individuals with their microbiomes removed suffer from reduced fecundity (implying beneficial microbial effects); however, their life span is increased[53]. Future studies that combine our inference with demographic models, such as matrix population models or integral projection models[54,55], could help us better understand selection patterns on microbiome transmission in species with more complex demography.

Third, weak selection on the optimal vertical transmission fidelity could explain the lack of faithful transmission. This could be due to different reasons. In humans, mothers and newborn babies share similar microbiomes; however, this similarity breaks down

over the first few years[56–58]. This may partly reflect constraints due to the long host development time (see the first explanation), but it may additionally be that these maternally transmitted microbes are particularly important early in life, with the importance disappearing in later life stages, weakening selection on parent–offspring microbiome resemblance later in life (although it might result in within-host selection on maintaining microbes—an intriguing but different question). Selection on transmission also becomes weaker with a lower contribution of microbial variation to host phenotypic variation (Fig. 5). Finally, the broader demographic context of a species can affect selection on the optimal amount of variation in one phenotypic trait[29].

Fourth, hosts could exert control to maintain specific host–microbe associations through controlling environmental transmission instead of vertical transmission. Bobtail squid–*Vibrio*[59], bean bug–*Burkholderia*[60] and legume–rhizobia[61] systems are examples where hosts have evolved mechanisms to efficiently limit environmental acquisition to their particular microbial associations.

Understanding faithful transmission of detrimental microbes. Similarly puzzling is why hosts would faithfully transmit microbes that seem consistently disadvantageous (or neutral) for host fitness. For instance, *Wolbachia* infections are very common in insects, and *Wolbachia* is transmitted through strict vertical maternal transmission. By manipulating host reproduction, many *Wolbachia* groups are considered to be parasites[62]. Why would hosts transmit such harmful microbes? Using the same reasoning as above, there could be hidden benefits of the microbe, benefiting certain life stages or fitness components, or under certain environmental conditions. For example, in flies, *Wolbachia* can block the establishment of viral pathogens[63], where a higher *Wolbachia* density leads to better protection[64]. However, in the absence of viral pressure, high densities lead to earlier death in flies[65]. This again illustrates the potential complexity in environmentally dependent fitness effects, affecting multiple components of fitness.

An alternative explanation is selection at the level of the microbe. Especially if host-level selection on transmission fidelity is low (see above), microbe-level selection might efficiently increase transmission rates up to a certain extent. A recent modelling study illustrates this idea, although their focus was not on transmission fidelity: weaker host-level selection increased the success of faster-growing neutral microbes[23]. Expanding our model to include different microbe strategies, instead of the neutral microbial dynamics that we included, could provide insights into how strong microbe-level versus host-level selection must be for non-zero transmission rates of pathogenic microbes to evolve.

Going forward. Developing approaches that balance realistic complexity with tractable simplicity is a crucial challenge in advancing our theoretical understanding of microbiome–host dynamics. The conceptual similarity between microbiome transmission fidelity and genetic mutations outlined here resulted in a close match between our simulation results and quantitative genetic predictions (Supplementary Information 2; see also ref. [66]). This illustrates the potential power of leveraging the wealth of theory existing in the field of quantitative genetics. For instance, could we use developed theory on epistatic variance (for example, ref. [64]) to inform how host–microbe interactions affect selection on transmission? What are the consequences of such interactions for the coevolution of host and microbes? Evaluating where the conceptual similarity between the transmission of microbes and genetic material breaks down, and where we thus need to develop new theory, will be crucial.

Our model simplifies many important biological features. This simplicity is warranted as it yields insight into the core processes at play; and added biological realism or a different model structure is unlikely to alter our main conclusion: in unpredictable environments, host selection can favour unfaithful microbe transmission to increase variation among offspring, leading to a bet-hedging strategy. Moreover, we show that even the limited range of biological processes that we explore here are sufficient to result in optimal transmission fidelities encompassing the wide range observed in nature. Our simple model thereby provides a starting point for generating testable predictions.

It is important to note that some of our simplifying assumptions may not hold in natural populations. For instance, we assumed that the host genotype with the highest fitness is expected to increase in frequency, so that the genotype with the highest long-term fitness will eventually dominate. By construction, our model did not incorporate processes such as frequency-dependent selection, interference competition or non-transitivity. Such processes add complexity to the evolution of transmission fidelity (or any trait, for that matter), so that a strategy that has the highest long-term fitness might not always evolve in a population[67]. Evolutionary invasion analysis, which accounts for frequency dependence, could yield additional counterintuitive results, building beyond our approach of identifying the strategy with the highest long-term fitness. Furthermore, in finite populations, short-term selection against the strategy with the highest long-term fitness may impede its evolution (for example, this has been proposed as a mechanism that maintains lower mutation rates than would be optimal for long-term adaptation[68]). Indeed, a bet-hedging strategy (here through a low transmission fidelity) may not always establish in a finite population, even if beneficial in the long run, due to drift or short-term selection against the strategy[69]. Finally, we simplified many properties of the microbes and basically assumed microbes to be static entities that do not interact, while there exist interactions between microbes[53], interactions between hosts and microbes[70,71], microbe- or environment-dependent transmission rates[70,72–74] and microbe-level selection[35,39]. While neutral dynamics are able to capture observed dynamics quite well in some systems[35,37] (but see ref. [75]), within-host microbial interactions are probably an important factor shaping microbiome communities[76–78], with consequences for host fitness[53,79]. We assumed an unchanging microbial source pool that did not depend on host dynamics. The environmental microbial pool could, however, also be a function of what is present in each host, thereby responding to host selection. Due to this 'collective inheritance', horizontal transmission could also lead to host population-level changes in microbiome composition, increasing host fitness[80].

To test our theoretical predictions and further develop our model, carefully designed experiments could be used. With empirical data in hand to motivate such refinement, it will be straightforward to extend the model and build in more realism for particular systems. First and foremost, this requires a host system where microbiome variation translates into variation in a fitness-related host phenotype (or in a measure of fitness directly). This could be done either with entire microbiome communities (Extended Data Fig. 5a) or with specific host-associated microbes (Extended Data Fig. 5b). Second, there must be some environmental interaction with this phenotypic trait or with fitness, so that by varying environmental conditions, fluctuating selection can be imposed. Alternatively, artificial selection could be used—for example, alternately selecting for small versus large host body sizes. Third, one must be able to control microbiome transmission fidelity from parents to offspring, and possibly the importance of microbial colonization from the environment. When these criteria are met, this will allow testing of how vertical microbial transmission fidelity affects long-term host fitness under different selection regimes (Extended Data Fig. 5).

The low microbiome heritability in many host systems has led to a lively and ongoing discussion on the importance of the microbiome for host evolution[13,14,26,81]. We propose that a low microbiome heritability resulting from imperfect transmission may actually benefit hosts under certain conditions. These conditions include

environmentally dependent microbial effects, where the effects change over time. We explain that this is because microbiome transmission fidelity shapes phenotypic distributions in a population of hosts. The phenotypic mean and variance optimizing fitness depend on various host and environmental properties. Using a simple model, we have generated some general predictions on how faithful microbiome transmission should be, given these properties. We believe that the way forward is to test these predictions under controlled conditions, in combination with continuing the development of theory. This will provide new insights into the wide diversity of transmission modes that we observe in nature, contributing to our understanding of the role of the microbiome in host evolution.

Methods

General overview. We use a modelling approach to assess how different factors shape host selection on vertical microbe transmission fidelity (Extended Data Fig. 6). To do so, we run simulations for a range of parameters, reflecting different biological scenarios. In each scenario, we simulate individual hosts in a population, where a host's microbiome composition affects its phenotype, which then shapes reproduction, upon which the next host generation takes place (Extended Data Fig. 6a). These relations are governed and modified by different processes that vary across scenarios, such as the transmission fidelity, environmental conditions and microbial dynamics (see the coloured boxes in Extended Data Fig. 6a; this is explained in detail in the following sections). For each simulation, we keep track of population-level outcomes: phenotypic distributions (both mean and variance) and fitness (Extended Data Fig. 6b), averaged across time steps.

Our model is conceptually and mathematically similar to quantitative genetic mutation–drift–selection models (see also Ravel et al.[66] for the case of a single symbiont), which describe how the balance between drift, selection and new mutations determines the amount of additive genetic variance in a population (Supplementary Information 1).

In short, the simulation procedure is as follows. We simulate a microbial 'source pool', assumed to be present in the host environment, consisting of 1,000 different microbial species, where each microbial species is equally abundant. Microbial species are characterized by their (additive) effects on host phenotypes. The effect m that microbial species j has on its host phenotype is drawn from a normal distribution:

$$m_j \approx \text{Normal}\,(0, V_\alpha) \tag{3}$$

where V_α is the variance in microbial effects on host phenotype. We start by assuming that hosts do not differ in any other aspect. Phenotypic variation among hosts thus results from variation in microbiome composition only. We simulate the dynamics of N hosts, where each host carries 100 microbes. We thus assume a constant microbial population size within each host. At the start of a simulation, we assign 100 randomly sampled (with replacement) microbes from the source pool to each host. Throughout the simulations, both the number of microbes within each host and the number of hosts are kept constant, so that responses are due to changes in composition (of both hosts and microbes) and not due to changes in numbers. We follow dynamics across T_h host generations. Within each host generation, T_m microbial generations take place to capture changes in microbiome composition during host development ('Within-host microbial dynamics'). To explore the impact of temporal variability in the environment, the relationship between phenotypes and fitness ('Host selection and transmission of microbes') can change in every host generation. This is captured by drawing from a normal distribution defined by:

$$\varphi_t \approx \text{Normal}\left(0, \sigma_\varphi^2\right) \tag{4}$$

where φ_t represents the environment at time t and σ_φ^2 controls the degree of environmental fluctuations (when set at 0, the environment is stable). Equation (4) simulates environments without any autocorrelation ($\rho = 0$)—that is, the environment at time t is not predictive of the environment at time $t+1$. Below, we extend this by simulating environments using an autoregressive model with specified autocorrelation.

Within-host microbial dynamics. To simulate microbial dynamics within a host generation, we use a metacommunity model. In each microbial generation, all microbes are replaced either by colonization (by immigration from the source pool outside the host) with probability c or by proliferation (the replication of a microbe within the host microbe community) with probability $1-c$ (green box in Extended Data Fig. 6a). We assume that all microbe species have equal colonization and proliferation probabilities and that each microbial species is equally represented in the source pool. Such neutral dynamics have been shown to adequately describe microbial community composition in different systems[35,37,82]. We note, however, that the model could easily be extended to allow for variation in these rates to model different microbe strategies, such as trade-offs between colonization and proliferation rates, pathogenic strains with high proliferation rates, or variation in microbial abundance. For each host, this random colonization and proliferation is repeated for T_m time steps, allowing for changes in microbiome composition during host development. All hosts survive during this period.

Host selection and transmission of microbes. After T_m time steps, host selection takes place on the basis of host phenotypes, in interaction with the time-specific environment and the strength of selection (red box in Extended Data Fig. 6a). The phenotype P of host i is calculated as the sum of all the effects of microbes that are present at the moment of host selection:

$$P_i = \sum_{j=1}^{1{,}000} f_{ij} m_j \tag{5}$$

where f_{ij} is the number of times microbe j is present in host i at the moment of selection (note that summing f_{ij} over all j equals 100, the total number of microbes within each host). This procedure implies that microbial composition earlier in life has no effect on the current host phenotype. Furthermore, we model only additive microbial effects (host phenotypes are not affected by, for instance, interactions among microbes or microbial diversity). The fitness R of phenotype i follows a Gaussian distribution and is calculated as:

$$R_i\,(P_i, \varphi_t) = \exp\left(\frac{-(P_i - \varphi_t)^2}{2\omega^2}\right) \tag{6}$$

where ω^2 is the selection strength toward the optimum phenotype, which is defined by the time-specific environment φ_t (see above). The optimum phenotype thus varies through time, and σ_φ^2 determines how much it varies (equation (4)). Note that the average environment is set at 0 (equation (4)), which matches the average microbial effect (equation (3)) and thus the average host phenotype (equation (5)). This implies that hosts with the average microbiome are well adapted in the long term. We thus purposely do not include any directional selection on the mean phenotype. We sample N hosts (with replacement) with probabilities scaled to their fitness, to select hosts that reproduce. This procedure assumes non-overlapping host generations.

Next, microbes of reproducing hosts are vertically transmitted. The parameter τ (ranging between 0 and 1) controls vertical transmission fidelity and is the core parameter that we vary to assess its effects on long-term host fitness. For each microbe that is present in a reproducing host, we sample whether or not it is transmitted to the offspring on the basis of τ (blue box in Extended Data Fig. 6a). We then complement the community with randomly sampled microbes from the source pool to keep the total number of microbes in each host equal to 100. Larger τ values thus indicate more faithful transmission; $\tau = 1$ results in strict vertical transmission, where offspring are born with the same microbiome composition as their parents upon reproducing. In contrast, $\tau = 0$ corresponds to a scenario where offspring are born with a microbiome that is fully sampled from the environmental source pool. We define this process as 'horizontal transmission'. We note that the microbial composition in the environmental source pool does not change over time, differing from the model developed by Roughgarden[80], where the environmental source pool also responds to selection. After this step, microbial dynamics in the next host generation take place as explained above.

Simulations. To evaluate how τ affects phenotype distributions and fitness in a host population (Extended Data Fig. 6b), we ran simulations for 1,000 host generations while following 500 hosts. Including the last 500 host generations, to ensure that these numbers give robust results, we then calculated the average (over all individuals) of the phenotypic squared mean $\left(\frac{\sum_t^{T_\text{h}} (\text{E}(P_t))^2}{T_\text{h}}\right)$, variance $\left(\frac{\sum_t^{T_\text{h}} \text{var}(P_t)}{T_\text{h}}\right)$ and fitness $\left(\exp\left[\frac{\sum_t^{T_\text{h}} \ln(\text{E}(R_t))}{T_\text{h}}\right]\right)$ (calculated as the geometric mean). Assuming competing haploid clones, hosts with those transmission fidelities that result in the highest geometric mean fitness are expected to become the dominant strategy[83] (see Extended Data Fig. 7 for simulations of mixture populations, leading to the same conclusions).

Reporting Summary. Further information on research design is available in the Nature Research Reporting Summary linked to this article.

Data availability

This study uses computer-generated datasets, which can be created using available R code.

Code availability

An interactive tool to run the model can be found at http://marjoleinbruijning.shinyapps.io/simulhostmicrobiome, and example R code is available on Github: http://github.com/marjoleinbruijning/microbiomeTransmission (https://doi.org/10.5281/zenodo.5534317)[84].

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References

1. Bercik, P. et al. The intestinal microbiota affect central levels of brain-derived neurotropic factor and behavior in mice. *Gastroenterology* **141**, 599–609 (2011).
2. Johnson, K. V.-A. & Foster, K. R. Why does the microbiome affect behaviour? *Nat. Rev. Microbiol.* **16**, 647–655 (2018).
3. Sherwin, E., Bordenstein, S. R., Quinn, J. L., Dinan, T. G. & Cryan, J. F. Microbiota and the social brain. *Science* **366**, eaar2016 (2019).
4. Charbonneau, M. R. et al. A microbial perspective of human developmental biology. *Nature* **535**, 48–55 (2016).
5. Blanton, L. V. et al. Gut bacteria that prevent growth impairments transmitted by microbiota from malnourished children. *Science* **351**, aad3311 (2016).
6. Matsuoka, K. & Kanai, T. The gut microbiota and inflammatory bowel disease. *Semin. Immunopathol.* **37**, 47–55 (2015).
7. Niu, B., Paulson, J. N., Zheng, X. & Kolter, R. Simplified and representative bacterial community of maize roots. *Proc. Natl Acad. Sci. USA* **114**, E2450–E2459 (2017).
8. Berg, M. & Koskella, B. Nutrient- and dose-dependent microbiome-mediated protection against a plant pathogen. *Curr. Biol.* **28**, 2487–2492 (2018).
9. Wei, Z. et al. Trophic network architecture of root-associated bacterial communities determines pathogen invasion and plant health. *Nat. Commun.* **6**, 8413 (2015).
10. Keebaugh, E. S., Yamada, R., Obadia, B., Ludington, W. B. & William, W. J. Microbial quantity impacts *Drosophila* nutrition, development, and lifespan. *iScience* **4**, 247–259 (2018).
11. Camarinha-Silva, A. et al. Host genome influence on gut microbial composition and microbial prediction of complex traits in pigs. *Genetics* **206**, 1637–1644 (2017).
12. Difford, G. F. et al. Host genetics and the rumen microbiome jointly associate with methane emissions in dairy cows. *PLoS Genet.* **14**, e1007580 (2018).
13. Moran, N. A. & Sloan, D. B. The hologenome concept: helpful or hollow? *PLoS Biol.* **13**, e1002311 (2015).
14. Henry, L. P., Bruijning, M., Forsberg, S. K. G. & Ayroles, J. F. The microbiome extends host evolutionary potential. *Nat. Commun.* **12**, 5141 (2021).
15. Foster, K. R., Schluter, J., Coyte, K. Z. & Rakoff-Nahoum, S. The evolution of the host microbiome as an ecosystem on a leash. *Nature* **548**, 43–51 (2017).
16. Baumann, P. Biology of bacteriocyte-associated endosymbionts of plant sap-sucking insects. *Annu. Rev. Microbiol.* **59**, 155–189 (2005).
17. Douglas, A. E. Nutritional interactions in insect–microbial symbioses: aphids and their symbiotic bacteria *Buchnera*. *Annu. Rev. Entomol.* **43**, 17–37 (1998).
18. Roughgarden, J., Gilbert, S. F., Rosenberg, E., Zilber-Rosenberg, I. & Lloyd, E. A. Holobionts as units of selection and a model of their population dynamics and evolution. *Biol. Theory* **13**, 44–65 (2018).
19. Fukatsu, T. & Hosokawa, T. Capsule-transmitted gut symbiotic bacterium of the Japanese common plataspid stinkbug, *Megacopta punctatissima*. *Appl. Environ. Microbiol.* **68**, 389–396 (2002).
20. Kaiwa, N. et al. Symbiont-supplemented maternal investment underpinning host's ecological adaptation. *Curr. Biol.* **24**, 2465–2470 (2014).
21. Jahnes, B. C., Herrmann, M. & Sabree, Z. L. Conspecific coprophagy stimulates normal development in a germ-free model invertebrate. *PeerJ* **7**, e6914 (2019).
22. Estes, A. M. et al. Brood ball-mediated transmission of microbiome members in the dung beetle, *Onthophagus taurus* (Coleoptera: Scarabaeidae). *PLoS ONE* **8**, e79061 (2013).
23. van Vliet, S. & Doebeli, M. The role of multilevel selection in host microbiome evolution. *Proc. Natl Acad. Sci. USA* **116**, 20591–20597 (2019).
24. Zeng, Q., Wu, S., Sukumaran, J. & Rodrigo, A. Models of microbiome evolution incorporating host and microbial selection. *Microbiome* **5**, 127 (2017).
25. Björk, J. R., Diez-Vives, C., Astudillo-Garcia, C., Archie, E. A. & Montoya, J. M. Vertical transmission of sponge microbiota is inconsistent and unfaithful. *Nat. Ecol. Evol.* **3**, 1172–1183 (2019).
26. Douglas, A. E. & Werren, J. H. Holes in the hologenome: why host–microbe symbioses are not holobionts. *mBio* **7**, e02099-15 (2016).
27. Hammer, T. J. & Moran, N. A. Links between metamorphosis and symbiosis in holometabolous insects. *Phil. Trans. R. Soc. B* **374**, 20190068 (2019).
28. Metcalf, C. J. E., Henry, L. P., Rebolleda-Gomez, M. & Koskella, B. Why evolve reliance on the microbiome for timing of ontogeny?. *mBio* **10**, e01496-19 (2019).
29. Bruijning, M., Metcalf, C. J. E., Jongejans, E. & Ayroles, J. F. The evolution of variance control. *Trends Ecol. Evol.* **35**, 22–23 (2020).
30. Bull, J. J. Evolution of phenotypic variance. *Evolution* **41**, 303–315 (1987).
31. Philippi, T. & Seger, J. Hedging one's evolutionary bets, revisited. *Trends Ecol. Evol.* **4**, 41–44 (1989).
32. Vasseur, D. A. & Yodzis, P. The color of environmental noise. *Ecology* **85**, 1146–1152 (2004).
33. Halley, J. M. Ecology, evolution and 1f-noise. *Trends Ecol. Evol.* **11**, 33–37 (1996).
34. Botero, C. A., Weissing, F. J., Wright, J. & Rubenstein, D. R. Evolutionary tipping points in the capacity to adapt to environmental change. *Proc. Natl Acad. Sci. USA* **112**, 184–189 (2015).
35. Burns, A. R. et al. Contribution of neutral processes to the assembly of gut microbial communities in the zebrafish over host development. *ISME J.* **10**, 655–664 (2016).
36. Kolodny, O. et al. Coordinated change at the colony level in fruit bat fur microbiomes through time. *Nat. Ecol. Evol.* **3**, 116–124 (2019).
37. Sieber, M. et al. Neutrality in the metaorganism. *PLoS Biol.* **17**, e3000298 (2019).
38. Burns, A. R. et al. Interhost dispersal alters microbiome assembly and can overwhelm host innate immunity in an experimental zebrafish model. *Proc. Natl Acad. Sci. USA* **114**, 11181–11186 (2017).
39. Moeller, A. H., Suzuki, T. A., Phifer-Rixey, M. & Nachman, M. W. Transmission modes of the mammalian gut microbiota. *Science* **362**, 453–457 (2018).
40. Zapién-Campos, R., Sieber, M. & Traulsen, A. Stochastic colonization of hosts with a finite lifespan can drive individual host microbes out of equilibrium. *PLoS Comput. Biol.* **16**, e1008392 (2020).
41. De Vries, E. J., Jacobs, G., Sabelis, M. W., Menken, S. B. J. & Breeuwer, J. A. J. Diet-dependent effects of gut bacteria on their insect host: the symbiosis of *Erwinia* sp. and western flower thrips. *Proc. R. Soc. Lond. B* **271**, 2171–2178 (2004).
42. Johnson, N. C., Graham, J. H. & Smith, F. A. Functioning of mycorrhizal associations along the mutualism–parasitism continuum. *N. Phytol.* **135**, 575–585 (1997).
43. Cheney, K. L. & Côté, I. M. Mutualism or parasitism? The variable outcome of cleaning symbioses. *Biol. Lett.* **1**, 162–165 (2005).
44. Russell, J. A. & Moran, N. A. Costs and benefits of symbiont infection in aphids: variation among symbionts and across temperatures. *Proc. R. Soc. B* **273**, 603–610 (2006).
45. Oliver, K. M., Degnan, P. H., Burke, G. R. & Moran, N. A. Facultative symbionts in aphids and the horizontal transfer of ecologically important traits. *Annu. Rev. Entomol.* **55**, 247–266 (2010).
46. Oliver, K. M., Russell, J. A., Moran, N. A. & Hunter, M. S. Facultative bacterial symbionts in aphids confer resistance to parasitic wasps. *Proc. Natl Acad. Sci. USA* **100**, 1803–1807 (2003).
47. Oliver, K. M., Campos, J., Moran, N. A. & Hunter, M. S. Population dynamics of defensive symbionts in aphids. *Proc. R. Soc. B* **275**, 293–299 (2008).
48. Ives, A. R. et al. Self-perpetuating ecological–evolutionary dynamics in an agricultural host–parasite system. *Nat. Ecol. Evol.* **4**, 702–711 (2020).
49. Chen, D.-Q., Montllor, C. B. & Purcell, A. H. Fitness effects of two facultative endosymbiotic bacteria on the pea aphid, *Acyrthosiphon pisum*, and the blue alfalfa aphid, *A. kondoi*. *Entomol. Exp. Appl.* **95**, 315–323 (2000).
50. Montllor, C. B., Maxmen, A. & Purcell, A. H. Facultative bacterial endosymbionts benefit pea aphids *Acyrthosiphon pisum* under heat stress. *Ecol. Entomol.* **27**, 189–195 (2002).
51. Kikuchi, Y. et al. Symbiont-mediated insecticide resistance. *Proc. Natl Acad. Sci. USA* **109**, 8618–8622 (2012).
52. Kikuchi, Y. & Yumoto, I. Efficient colonization of the bean bug *Riptortus pedestris* by an environmentally transmitted *Burkholderia* symbiont. *Appl. Environ. Microbiol.* **79**, 2088–2091 (2013).
53. Gould, A. L. et al. Microbiome interactions shape host fitness. *Proc. Natl Acad. Sci. USA* **115**, E11951–E11960 (2018).
54. Ellner, S. P. & Rees, M. Integral projection models for species with complex demography. *Am. Nat.* **167**, 410–428 (2006).
55. Caswell, H. *Matrix Population Models: Construction, Analysis and Interpretation* (Sinauer Associates, 2001).
56. Asnicar, F. et al. Studying vertical microbiome transmission from mothers to infants by strain-level metagenomic profiling. *mSystems* **2**, e00164-16 (2017).
57. Yassour, M. et al. Strain-level analysis of mother-to-child bacterial transmission during the first few months of life. *Cell Host Microbe* **24**, 146–154 (2018).
58. Ferretti, P. et al. Mother-to-infant microbial transmission from different body sites shapes the developing infant gut microbiome. *Cell Host Microbe* **24**, 133–145 (2018).
59. Nyholm, S. V. & McFall-Ngai, M. The winnowing: establishing the squid-Vibrio symbiosis. *Nat. Rev. Microbiol.* **2**, 632–642 (2004).
60. Kikuchi, Y., Hosokawa, T. & Fukatsu, T. Insect–microbe mutualism without vertical transmission: a stinkbug acquires a beneficial gut symbiont from the environment every generation. *Appl. Environ. Microbiol.* **73**, 4308–4316 (2007).
61. Ibáñez, F., Tonelli, M. L., Muñoz, V., Figueredo, M. S. & Fabra, A. in *Endophytes: Biology and Biotechnology* (ed. Maheshwari, D.) 25–40 (Springer, 2017).
62. Werren, J. H., Baldo, L. & Clark, M. E. *Wolbachia*: master manipulators of invertebrate biology. *Nat. Rev. Microbiol.* **6**, 741–751 (2008).

63. Teixeira, L., Ferreira, Á. & Ashburner, M. The bacterial symbiont *Wolbachia* induces resistance to RNA viral infections in *Drosophila melanogaster*. *PLoS Biol.* **6**, 2753–2763 (2008).
64. Chrostek, E. et al. *Wolbachia* variants induce differential protection to viruses in *Drosophila melanogaster*: a phenotypic and phylogenomic analysis. *PLoS Genet.* **9**, e1003896 (2013).
65. Chrostek, E. & Teixeira, L. Mutualism breakdown by amplification of *Wolbachia* genes. *PLoS Biol.* **13**, e1002065 (2015).
66. Ravel, C., Michalakis, Y. & Charmet, G. The effect of imperfect transmission on the frequency of mutualistic seed-borne endophytes in natural populations of grasses. *Oikos* **80**, 18–24 (1997).
67. Buskirk, S. W., Rokes, A. B. & Lang, G. I. Adaptive evolution of nontransitive fitness in yeast. *eLife* **9**, e62238 (2020).
68. Clune, J. et al. Natural selection fails to optimize mutation rates for long-term adaptation on rugged fitness landscapes. *PLoS Comput. Biol.* **4**, e1000187 (2008).
69. King, O. D. & Masel, J. The evolution of bet-hedging adaptations to rare scenarios. *Theor. Popul. Biol.* **72**, 560–575 (2007).
70. Liu, X.-D., Lei, H.-X. & Chen, F.-F. Infection pattern and negative effects of a facultative endosymbiont on its insect host are environment-dependent. *Sci. Rep.* **9**, 4013 (2019).
71. Oyserman, B. O. et al. Extracting the GEMs: genotype, environment, and microbiome interactions shaping host phenotypes. *Front. Microbiol.* **11**, 3444 (2021).
72. Rock, D. I. et al. Context-dependent vertical transmission shapes strong endosymbiont community structure in the pea aphid, *Acyrthosiphon pisum*. *Mol. Ecol.* **27**, 2039–2056 (2018).
73. Osaka, R., Nomura, M., Watada, M. & Kageyama, D. Negative effects of low temperatures on the vertical transmission and infection density of a *Spiroplasma* endosymbiont in *Drosophila hydei*. *Curr. Microbiol.* **57**, 335–339 (2008).
74. Gundel, P. E. et al. Imperfect vertical transmission of the endophyte *Neotyphodium* in exotic grasses in grasslands of the Flooding Pampa. *Microb. Ecol.* **57**, 740 (2009).
75. Li, L. & Ma, Z. S. Testing the neutral theory of biodiversity with human microbiome datasets. *Sci. Rep.* **6**, 31448 (2016).
76. Foster, K. R. & Bell, T. Competition, not cooperation, dominates interactions among culturable microbial species. *Curr. Biol.* **22**, 1845–1850 (2012).
77. Sprockett, D., Fukami, T. & Relman, D. A. Role of priority effects in the early-life assembly of the gut microbiota. *Nat. Rev. Gastroenterol. Hepatol.* **15**, 197–205 (2018).
78. Stein, R. R. et al. Ecological modeling from time-series inference: insight into dynamics and stability of intestinal microbiota. *PLoS Comput. Biol.* **9**, e1003388 (2013).
79. Scheuring, I. & Yu, D. W. How to assemble a beneficial microbiome in three easy steps. *Ecol. Lett.* **15**, 1300–1307 (2012).
80. Roughgarden, J. Holobiont evolution: Mathematical model with vertical vs. horizontal microbiome transmission. *Phil. Theory Pract. Biol.* **12**, 002 (2020).
81. Theis, K. R. et al. Getting the hologenome concept right: an eco-evolutionary framework for hosts and their microbiomes. *mSystems* **1**, e00028-16 (2016).
82. Sloan, W. T. et al. Quantifying the roles of immigration and chance in shaping prokaryote community structure. *Environ. Microbiol.* **8**, 732–740 (2006).
83. Gillespie, J. Polymorphism in random environments. *Theor. Popul. Biol.* **4**, 193–195 (1973).
84. Bruijning, M. Code for: Natural selection for imprecise vertical transmission in host-microbiota systems. *Zenodo* https://doi.org/10.5281/zenodo.5534317 (2021).
85. Sauer, C., Dudaczek, D., Hölldobler, B. & Gross, R. Tissue localization of the endosymbiotic bacterium "*Candidatus* Blochmannia floridanus" in adults and larvae of the carpenter ant *Camponotus floridanus*. *Appl. Environ. Microbiol.* **68**, 4187–4193 (2002).
86. Koga, R., Meng, X.-Y., Tsuchida, T. & Fukatsu, T. Cellular mechanism for selective vertical transmission of an obligate insect symbiont at the bacteriocyte–embryo interface. *Proc. Natl Acad. Sci. USA* **109**, E1230–E1237 (2012).
87. Brentassi, M. E. et al. Bacteriomes of the corn leafhopper, *Dalbulus maidis* (DeLong & Wolcott, 1923) (Insecta, Hemiptera, Cicadellidae: Deltocephalinae) harbor *Sulcia* symbiont: molecular characterization, ultrastructure, and transovarial transmission. *Protoplasma* **254**, 1421–1429 (2017).
88. Picazo, D. R. et al. Horizontally transmitted symbiont populations in deep-sea mussels are genetically isolated. *ISME J.* **13**, 2954–2968 (2019).
89. Gilbert, J. A. et al. Current understanding of the human microbiome. *Nat. Med.* **24**, 392–400 (2018).
90. Korpela, K. et al. Selective maternal seeding and environment shape the human gut microbiome. *Genome Res.* **28**, 561–568 (2018).
91. Walters, W. A. et al. Large-scale replicated field study of maize rhizosphere identifies heritable microbes. *Proc. Natl Acad. Sci. USA* **115**, 7368–7373 (2018).
92. Douglas, A. E. Simple animal models for microbiome research. *Nat. Rev. Microbiol.* **17**, 764–775 (2019).
93. Sommer, F. et al. The gut microbiota modulates energy metabolism in the hibernating brown bear *Ursus arctos*. *Cell Rep.* **14**, 1655–1661 (2016).
94. David, L. A. et al. Diet rapidly and reproducibly alters the human gut microbiome. *Nature* **505**, 559–563 (2014).

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Author contributions

M.B. and L.P.H. conceived the ideas. M.B. developed the modelling framework with strong input from L.P.H., S.K.G.F., C.J.E.M. and J.F.A. M.B. wrote the first draft, and all authors contributed substantially to revisions.

Competing interests

The authors declare no competing interests.

Additional information

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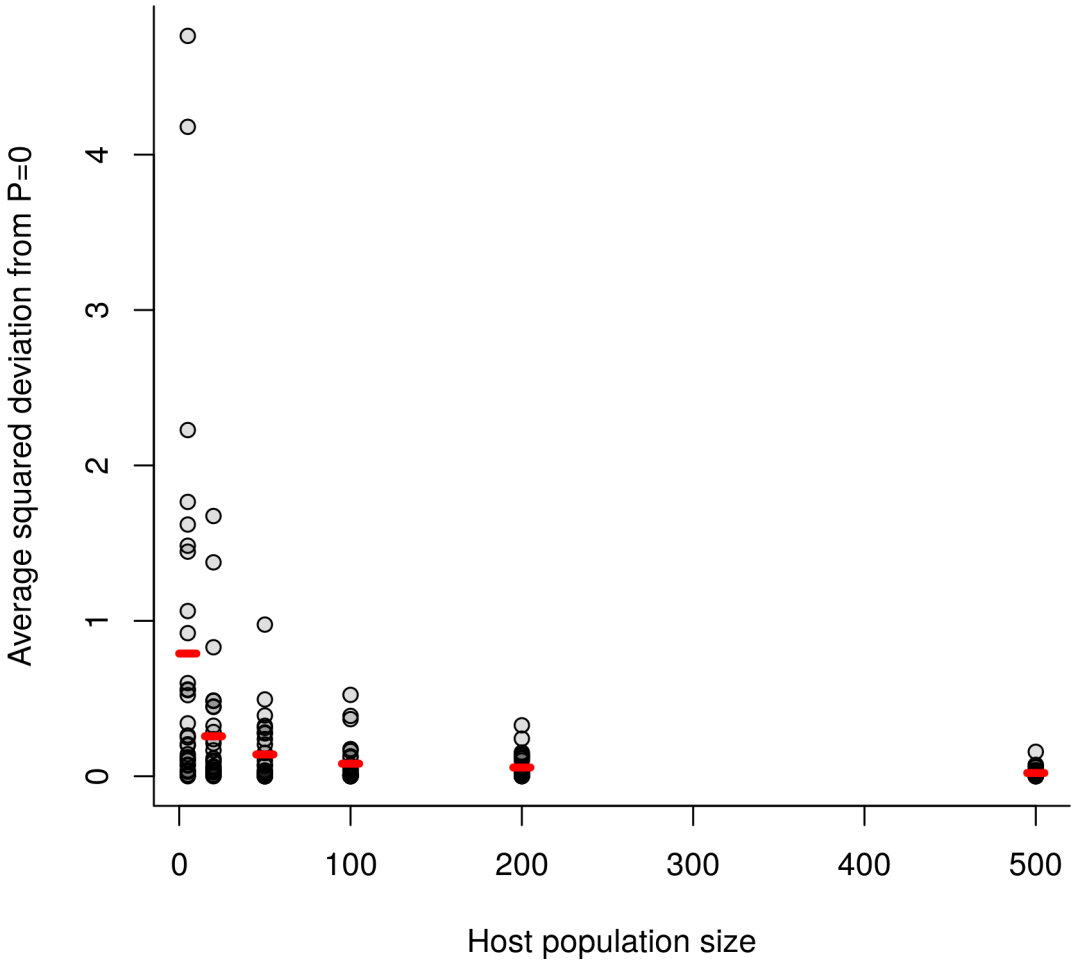
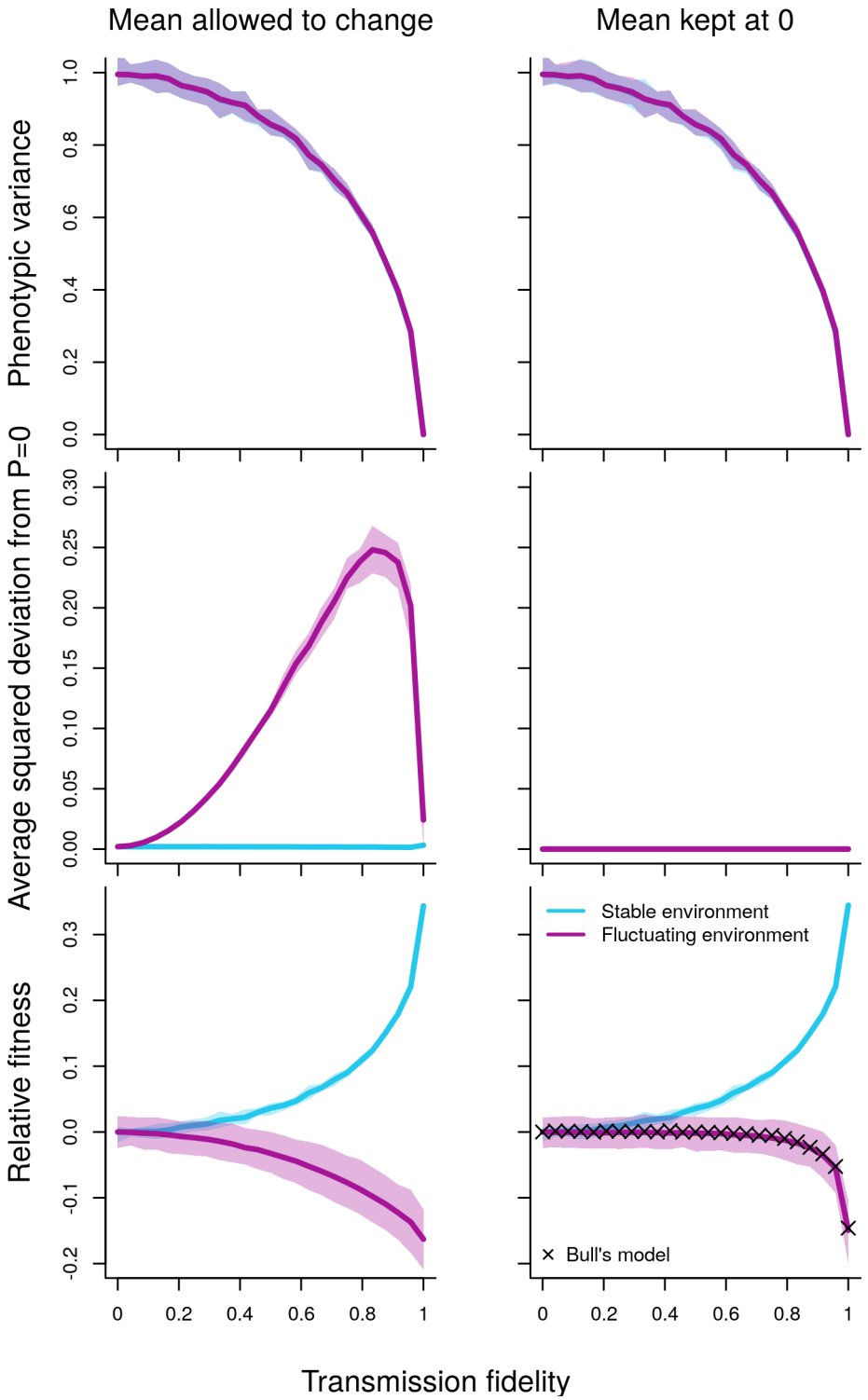
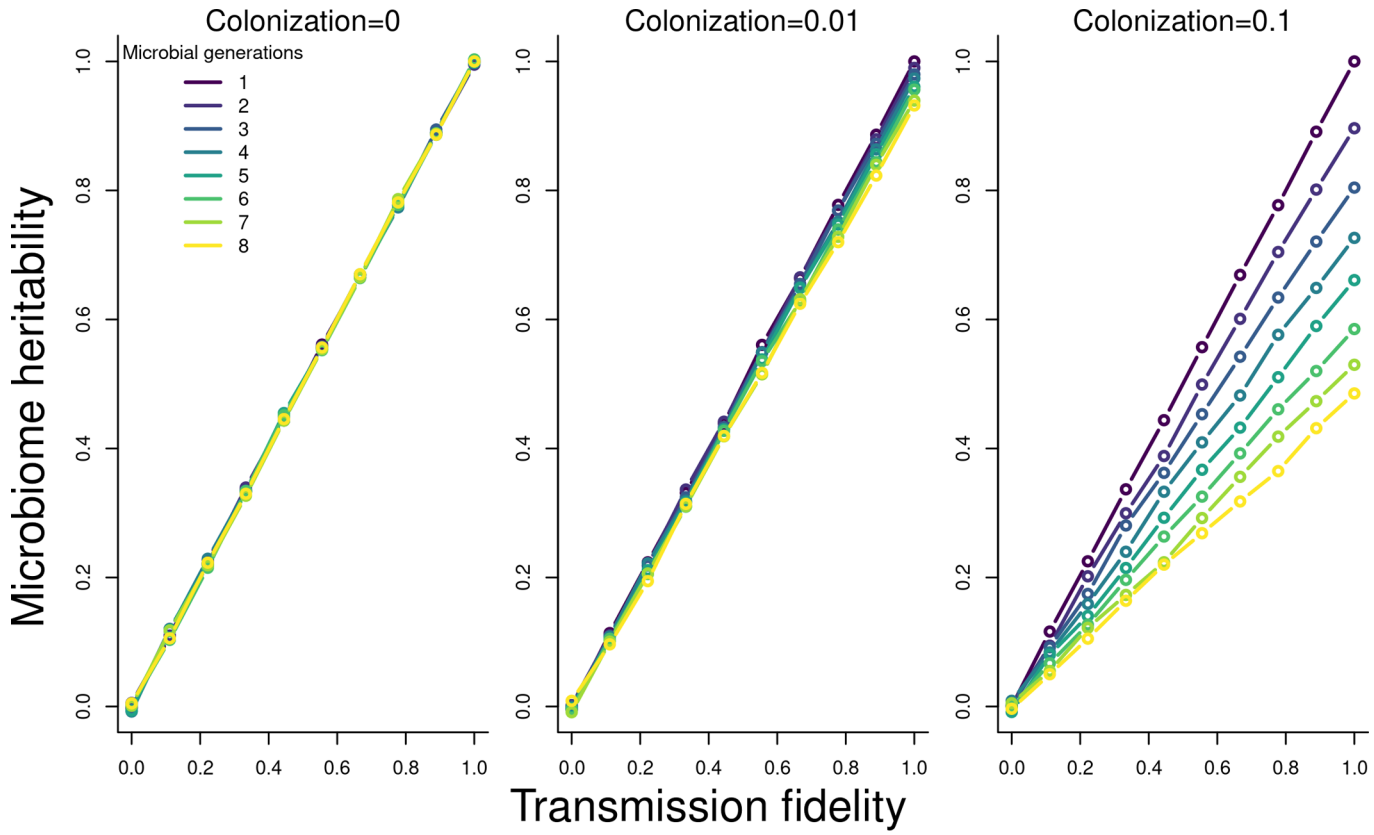


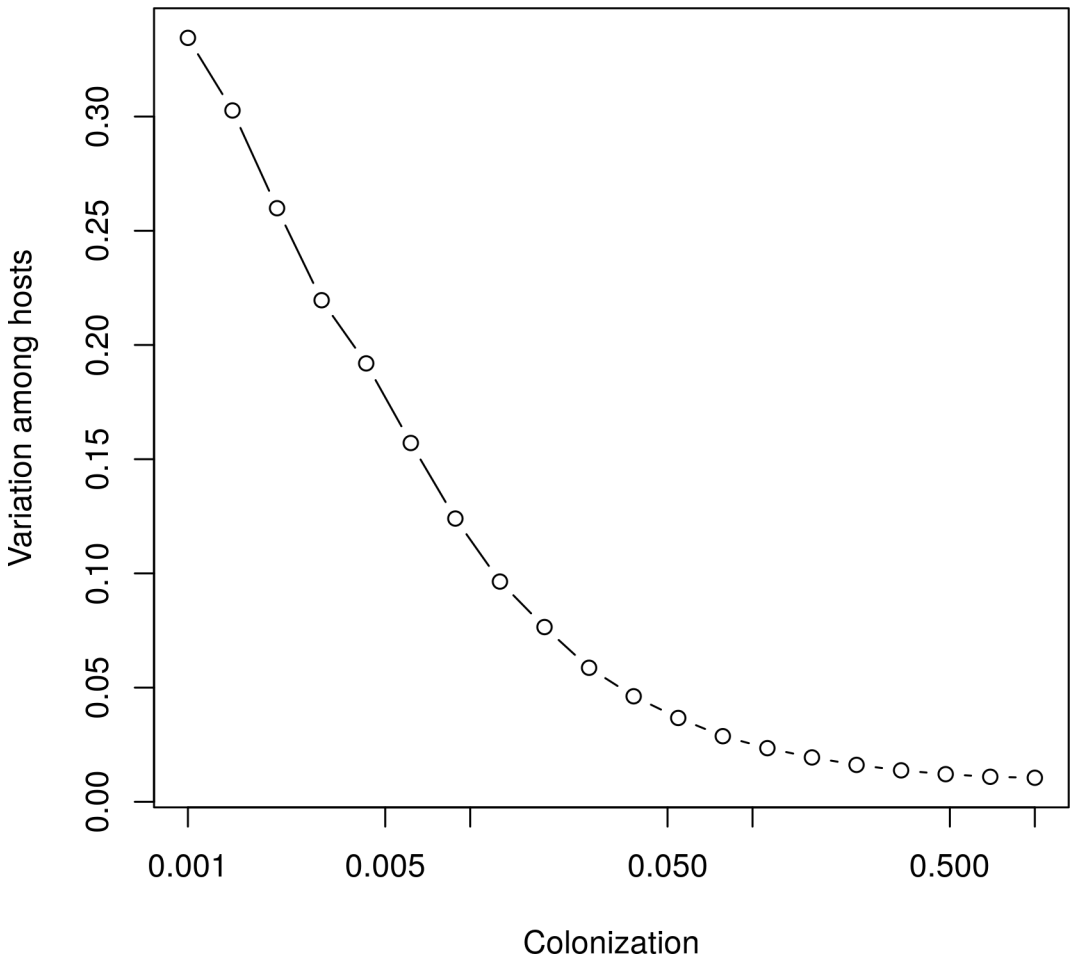
Extended Data Fig. 1 | Increased stochasticity in small host populations. In Fig. 2, we show how the microbiome transmission fidelity shapes host phenotype distributions. In doing so, we simulated large populations, consisting of 500 individuals, in order to obtain robust results. This results in a limited role of stochasticity, explaining the relatively low variation across replicated simulations (see shaded regions in Fig. 2a,b). In smaller populations, however, populations are, unsurprisingly, more sensitive to stochastic processes. Here, we set transmission fidelity τ at 1, implying strict vertical transmission, and assessed the average deviation from P = 0 for varying population sizes. In small populations, there is an increase in the number of maladapted populations (that is a larger deviation from the optimal phenotype). Grey dots indicate individual simulations (30 per population size), red lines indicate median values for each population size. $\tau = 1$; $\omega^2 = 1$; $\sigma_\varphi^2 = 2$; $V_\alpha = 0.01$.



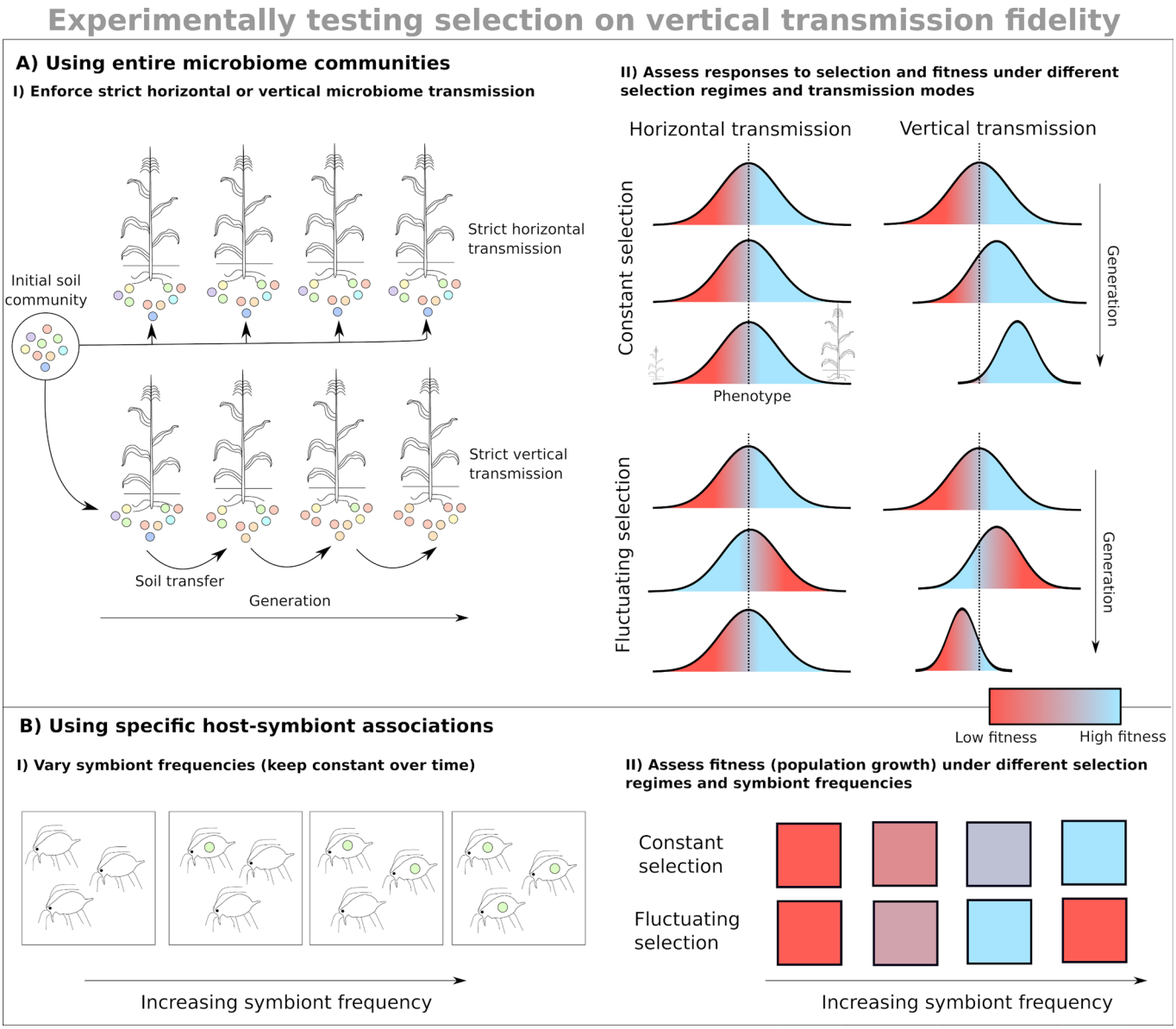
Extended Data Fig. 2 | Results when the average phenotype is kept constant. Plots show relationship between transmission fidelity and phenotypic variance (upper row), deviation from the long-term optimal mean (middle row) and long-term fitness (bottom row) when selection can shift the mean phenotype (left; corresponds to Fig. 2) or when keeping the mean phenotype fixed at 0 (right). This was done by mean-centering phenotypes in each time step, by subtracting each phenotype by the average time-specific phenotype. When we keep the mean host phenotype at 0, we can use Bull's modeling framework[30] to calculate long-term fitness (crosses in bottom right panel), based on the relation between transmission fidelity and phenotypic variance (Appendix S2).



Extended Data Fig. 3 | The difference between heritability and inheritance. Heritability (averaged across 5 replicated simulations) is a function of the transmission fidelity, colonization from the environment, and the number of microbial generations within a host generation. Heritability is measured as the slope of a regression between parent and offspring phenotypes upon the moment of reproduction, averaged across time steps. If there is only one microbial generation within a host generation and/or without colonization, the heritability equals the transmission fidelity. However, when one or both increase, heritability decreases, illustrating the difference between inheritance and heritability.

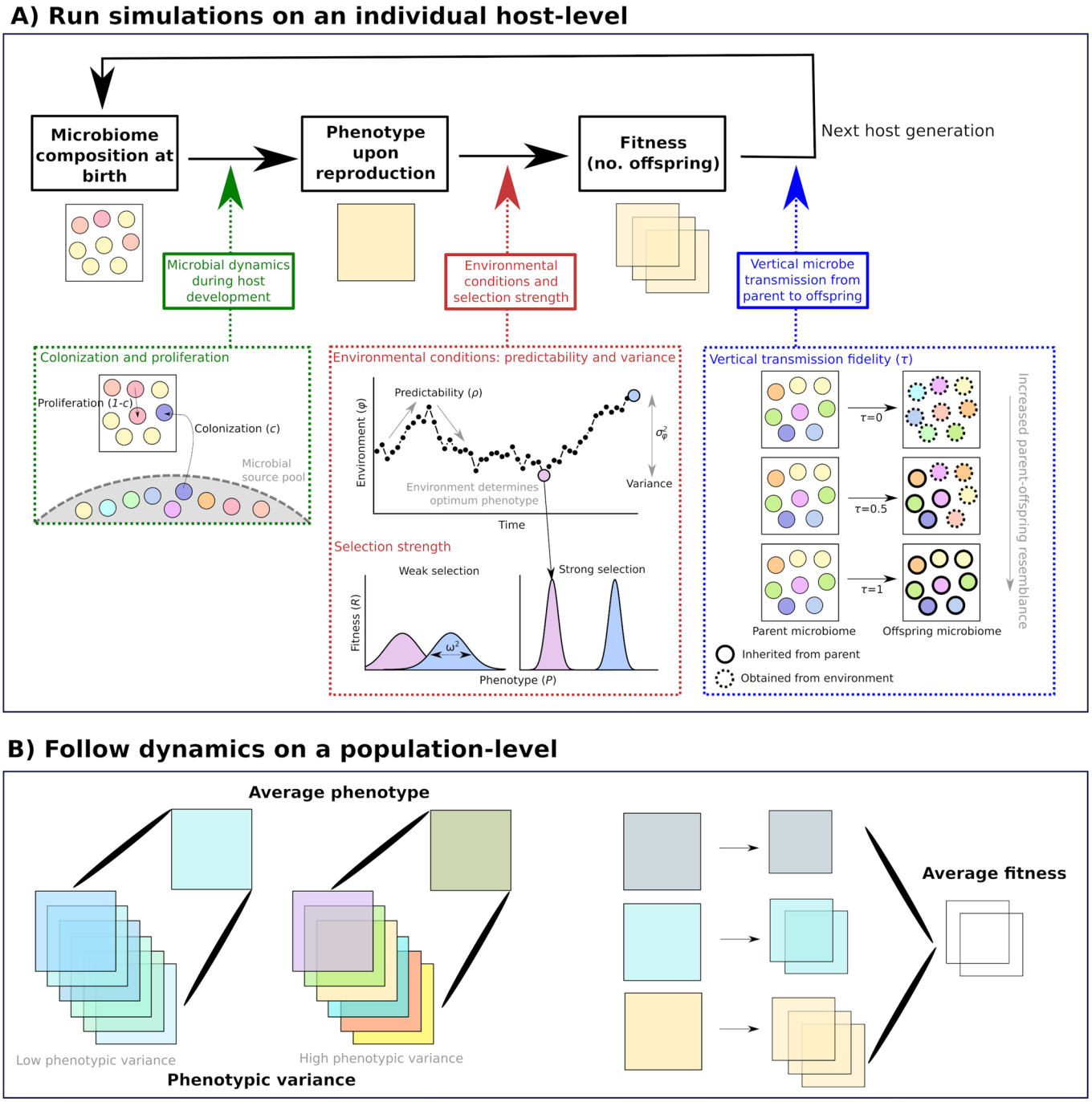


Extended Data Fig. 4 | Microbial variation among hosts within a host generation. Within one host generation, increased colonization from the microbial source pool decreases microbial variation among hosts, as predicted from metacommunity theory. Variation among hosts is calculated as the average microbial diversity within each host, divided by the total microbial diversity across all hosts.

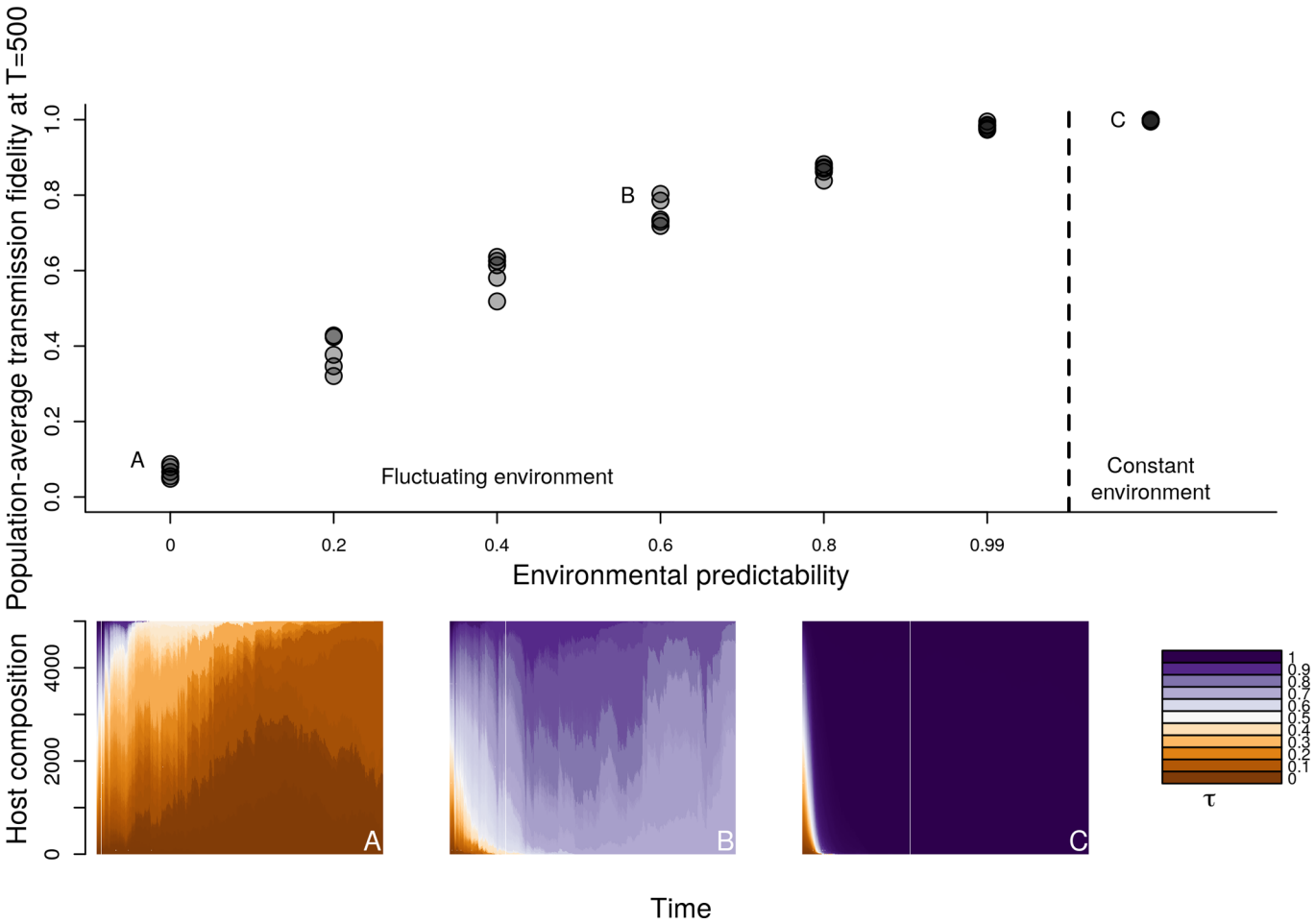


Extended Data Fig. 5 | Empirical approaches to testing how microbiome transmission can affect host fitness. a) Soil transfers in plant microbiomes can be used to enforce strict environmental acquisition or vertical transmission. By either successively inoculating plant generations with their initial starting microbial community (upper row in panel A-i), or passaging the microbial community from the previous to the next generation (bottom row in panel A-i), transmission of microbes can be controlled. Each host generation, artificial selection can be used to select plants based on their phenotype (for example plant size, illustrated here), whereby selection regimes vary (imposing either constant or fluctuating selection). Based on our results, we expect that under constant selection, strict vertical transmission increases fitness compared to strict horizontal transmission, as it allows phenotype distributions to respond to selection. In contrast, under sufficiently large fluctuating selection, vertical transmission reduces phenotypic variation, decreasing long-term fitness. **b**) A single microbe with a clear effect on host performance can also be used to study selection on transmission fidelity. As discussed in the manuscript, aphid fitness effects of several vertically transmitted symbionts, as well as their environmental-dependence, are quite well understood[45]. This makes aphids arguably a suitable system to study selection on vertical transmission fidelity. To do so, one could vary the symbiont frequency in different aphid populations (panel B-i). Populations can be followed through time, while keeping symbiont frequencies constant. Based on our results, we expect that under constant selection, a symbiont frequency of 100% (or 0%) optimizes population growth (panel B-ii), which can be realized by perfect vertical transmission. Under fluctuating selection, some intermediate symbiont frequency might be favored (panel B-ii), which can be achieved by noisy vertical transmission.

Model selection on vertical microbe transmission under varying conditions



Extended Data Fig. 6 | Schematic overview of our model. Upper panel shows the different steps of our simulations, and the parameters that we vary. Bottom panel shows the output that we obtain from each simulation.



Extended Data Fig. 7 | The evolution of transmission fidelity in mixed populations, under different environmental conditions. For the analyses presented in our main text, we assessed long-term fitness of each strategy (transmission fidelity) separately, and take the strategy with the highest long-term fitness (calculated as the geometric mean) for what would evolve in a mixed population. Here, we simulated dynamics of mixed populations (consisting of 5000 individuals), and show that this yield the same outcomes. We assigned to each host a random transmission fidelity at the start of a simulation run, and performed 5 replicated runs for each environmental condition. Three bottom plots show how the composition of transmission fidelities in a host population changes over time in specific simulation runs (letters A-C corresponding to scenarios depicted in upper graph).

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