JOURNAL OF Evolutionary Biology

doi: 10.1111/jeb.12222

Multicoloured greenbeards, bacteriocin diversity and the rock-paper-scissors game

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Keywords:

beard chromodynamics;
chloropogonology;
genetic kin recognition;
kind discrimination;
local resource competition;
marker diversity;
nontransitive competition;
spite.

Abstract

Greenbeard genes identify copies of themselves in other individuals and cause their bearer to behave nepotistically towards those individuals. Bacterial toxins (bacteriocins) exemplify the greenbeard effect because producer strains carry closely linked genes for immunity, such that toxicity is limited to nonproducer strains. Bacteriocin producers can be maintained in a dynamic polymorphism, known as rock-paper-scissors (RPS) dynamics, with immune and susceptible strains. However, it is unclear whether and how such dynamics will be maintained in the presence of multiple toxin types (multiple beard 'colours'). Here, we analyse strain dynamics using models of recurrent patch colonization and population growth. We find that (i) polymorphism is promoted by a small number of founding lineages per patch, strong local resource competition and the occurrence of mutations; (ii) polymorphism can be static or dynamic, depending on the intensity of local interactions and the costs of toxins and immunity; (iii) the occurrence of multiple toxins can promote RPS dynamics; and (iv) strain diversity can be maintained even when toxins differ in toxicity or lineages can exhibit multitoxicity/multi-immunity. Overall, the factors that maintain simple RPS dynamics can also promote the coexistence of multiple toxin types (multiple beard colours), thus helping to explain the remarkable levels of bacteriocin diversity in nature. More generally, we contrast these results with the maintenance of marker diversity in genetic kin recognition.

Introduction

A greenbeard is a gene, or a cluster of tightly linked genes, that can identify copies of itself in other individuals and cause its bearer to behave nepotistically towards those individuals (Hamilton, 1964; Dawkins, 1976). Dawkins (1976) illustrated this with an example of a gene that caused individuals to both display a phenotypic marker (e.g. a green beard) and help other individuals with identical markers. More generally, the greenbeard effect does not require a phenotypic marker but rather an assortment mechanism that directs help towards other carriers of the gene or harm towards noncarriers (Hamilton, 1975; Gardner & West, 2010; Strassmann *et al.*, 2011). This is similar to but distinct from genetic kin recognition, in which the genes for recognition and behaviour need not be tightly linked (Dawkins, 1982; Rousset & Roze, 2007; Gardner & West, 2010).

Although real-world examples of greenbeard genes have been found – several in microbes and two in animals – they are thought to be relatively scarce in nature (reviewed by Gardner & West, 2010). There are two major reasons for this scarcity. First, greenbeard effects may be hard to identify once the greenbeard gene approaches fixation, thereby eliminating the diversity necessary for discrimination (Crozier, 1986). Second, greenbeards can be outcompeted by cheating 'false-beards' that retain the beard (the marker or assortment mechanism) but avoid the cost of performing the behaviour themselves (Dawkins, 1976; Gardner & West, 2010).

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One way that greenbeards could be maintained is in a dynamic polymorphism with falsebeards and individuals that lack the greenbeard ('nonbeards'). Although this possibility has been rarely considered in a greenbeard context, it has been examined in detail in the specific context of bacteriocins (see also Axelrod *et al.*, 2004; Jansen & van Baalen, 2006; Rousset & Roze, 2007 for dynamic polymorphisms in kin recognition markers). Bacteriocins are compounds produced by bacteria to kill other bacteria (Riley & Gordon, 1999; Riley & Wertz, 2002). Bacteriocin-producing strains carry closely linked genes for the corresponding immunity factors, and so their toxins are preferentially directed to noncarriers, making them a type of harming greenbeard (Gardner & West, 2010). Furthermore, both the production of bacteriocins and the immunity to bacteriocins are costly. This means that producer strains (greenbeards) can be outcompeted by immune strains that do not produce bacteriocins (falsebeards), immune strains can be outcompeted by susceptible strains that do not produce bacteriocins or carry immunity (nonbeards), and producers can outcompete susceptibles (Chao & Levin, 1981; Kerr *et al.*, 2002). This can lead to cycling among the three strains, analogous to the dynamics of the classic rock-paper-scissors (RPS) game (Durrett & Levin, 1997; Kerr *et al.*, 2002; Kirkup & Riley, 2004; see also Sinervo & Lively, 1996).

However, it is not clear whether such dynamics, and the resulting diversity, will be maintained when multiple beard types, or 'colours', can exist. Theoretical models have shown that it is generally difficult to maintain diversity in genetic recognition markers, especially when markers are tightly linked to a social behaviour, as in the greenbeard effect (Jansen & van Baalen, 2006; Rousset & Roze, 2007). Yet genotypic and phenotypic surveys of bacteria have found that several types of producer and immune strains usually coexist (i.e. several beard colours can coexist), and lineages may carry multitoxicity and multi-immunity (i.e. individuals can have multiple beards; Riley & Gordon, 1999; Riley & Wertz, 2002; Gordon & O'Brien, 2006; Hawlena *et al.*, 2010a). The coexistence of multiple strains has been predicted by lattice-based simulations of bacteriocin warfare (Pagie & Hogeweg, 1999; Szabó & Czárán, 2001; Czárán *et al.*, 2002), but whether and how such diversity is maintained by RPS dynamics remains unclear. For example, the presence of multiple toxins could make it harder for susceptibles or immunes to invade (thus inhibiting RPS dynamics), and the possibility of variation among strains could make it impossible for less-toxic strains to coexist with more-toxic strains.

Here, we use a population genetic approach to determine how greenbeard dynamics and diversity are influenced by the occurrence of multiple beard colours. Although our model can be applied more broadly to other forms of greenbeards, here we frame it in terms of bacteriocins, with multiple toxin-producing and immune strains, in order to provide a concrete biological context. Our specific aims are to determine whether and how bacteriocin diversity is maintained when there can be multiple toxin types in the population, toxin types differ in toxicity, and lineages can exhibit multitoxicity/multi-immunity. More generally, we clarify links between studies that have examined bacteriocins from the perspective of the RPS game, genealogical kin selection and greenbeard dynamics, and we compare our results with studies of marker diversity in genetic kin recognition (e.g. Crozier, 1986; Axelrod *et al.*, 2004; Jansen & van Baalen, 2006; Rousset & Roze, 2007).

Models and results

We use mathematical models to study the dynamics of multiple bacterial strains, where strains are analogous to fixed 'strategies' in an evolutionary game. We first describe and analyse the basic model – the single-toxin case, in which three strains can exist (producer, immune and susceptible). This allows us to derive the conditions for maintaining polymorphism in our population structure and to examine the possible dynamics that can arise. We then use these results as a baseline for comparison to three extensions: (i) adding a second and third toxin type in the population, allowing individual lineages to carry only one toxin and/or immunity factor; (ii) adding a second toxin type (as above) but assuming that it is less toxic than the existing type; and (iii) adding a second toxin type, allowing lineages to carry both toxins and/or both immunity factors.

Basic model – description

We consider an arbitrarily large (effectively infinite) population of clonal lineages. The population is subdivided into homogeneous patches of n lineages, where a patch defines the arena in which all bacteriocin-mediated interactions occur. We assign each patch and each lineage in the population a unique index $i \in I$ and $l \in L$, respectively, and we assume that each lineage belongs to a strain of type $j \in J$. Hence, in the basic model, we have $J = \{G, F, N\}$, where G is a toxin producer with the corresponding immunity (greenbeard), F is immune (falsebeard), and N is susceptible (nonbeard). We do not consider strains that produce toxin but do not have immunity, given that such strains would be toxic to themselves. Furthermore, most of our analyses consider populations with a patch size of at least two ($n \geq 2$). This is because no bacteriocin-mediated killing can occur in single-lineage patches ($n = 1$), so in this case, the susceptible strain (N) will always be favoured (Inglis *et al.*, 2011).

We model strain dynamics over recurrent cycles of patch colonization and population growth, where each cycle consists of the following stages:

Colonization

We assume that patches are colonized by n founding lineages that start as single cells (note that in experimental settings, this is approximated by founding patches (tubes) with n clonal lineages; e.g. Griffin *et al.*, 2004). Founders are a random selection of lineages in the population as a whole, where the frequency of strain j is p_j and $\sum_J p_j = 1$. Hence, we assign lineages to each patch according to a multinomial distribution with parameters n and $\mathbf{p}$, where patch size n is the number of 'trials' and $\mathbf{p}$ is a vector of the population frequencies of each strain [in the basic model, $\mathbf{p} = (p_G, p_F, p_N)$]. Picking a patch at random, the number of lineages of strain j in that patch defines a random variable N_j, and the frequency of strain j in that patch defines a random variable $P_j = N_j/n$.

Bacteriocin warfare and subsequent growth

We assume that founder lineages initially grow independently (and at an equal rate) to a critical density at which bacteriocin production is initiated. This is consistent with real populations, where bacteriocins are produced only when competition among colonies is sufficiently strong (Riley & Wertz, 2002). Once bacteriocin interactions occur, we assign a relative growth factor g_j to a randomly selected, focal lineage of strain j. We assume that toxin production incurs a growth cost c to the producer lineage, that toxins inflict a growth cost d on susceptible lineages (where $d > c$) and that immunity incurs a growth cost k. Hence, in the basic model, the relative growth factors are as follows: $g_G = g_0 - c - k$; $g_F = g_0 - k$; and $g_N = g_0 - P_G d$, where g_0 is a baseline value.

Resource competition

The focal lineage may compete for resources in its own patch, where the average growth factor is $g' = \sum_J P_j g_j$, or in the global population, where the average growth factor, taken over the distribution of patch compositions, is $\bar{g} = \mathrm{E}_I(g')$. The fitness of a focal lineage is then given by its growth factor relative to that of its competitors:

$$w_j = \frac{g_j}{ag' + (1-a)\bar{g}} \qquad (1)$$

where a is the 'scale of competition' (Frank, 1998; Gardner *et al.*, 2004). Bacteriocin interaction and competition may occur at the same local scale ($a = 1$), or some proportion of competition may occur less locally than bacteriocin interaction ($a < 1$). For example, in the context of pathogenic bacteria, density regulation of the bacterial population could occur mostly within hosts, before the dispersal/transmission stage (large a), or mostly between hosts, after dispersal (small a). Hence, the scale of competition parameter is a simple way of capturing a range of bacterial life histories, and it has the benefit of being easily translated to experimental settings (Griffin *et al.*, 2004; Inglis *et al.*, 2011).

Selection

Population strain frequencies will change according to the average fitness W_j among all lineages of strain j. Recalling that the fitness w_j of a focal lineage is a random variable (with a distribution that depends on the frequency of different group compositions), W_j can be expressed as $\sum_L \wp_{lj} w_j / \sum_L \wp_{lj}$, where $\wp_{lj} = 1$ if lineage l is of type j and 0 otherwise. Given the normalization in eqn 1, strain j is favoured when $W_j > 1$, and its frequency in the population after selection is $p'_j = W_j p_j$.

Mutation

We assume that the final frequency of strain j in the next cycle, denoted by p''_j, depends on mutations that occur at a rate μ per cycle. We treat 'mutation' as a general mechanism for introducing strain diversity, which in real populations could include large-effect mutations, plasmid infections or immigration (Czárán *et al.*, 2002; Riley & Wertz, 2002). Specifically, we consider mutations that act just before cells disperse to colonize new patches (although additional mutations may also occur within patches, we assume that their effect is negligible). Furthermore, to simplify the analysis, we consider only those mutational steps that would allow a potentially superior competitor to invade a monomorphic population (as in Czárán *et al.*, 2002). Hence, in the basic model, mutations convert susceptibles to producers (N → G), producers to immunes (G → F) and immunes to susceptibles (F → N). We have checked that including all possible mutational steps, or assuming that some transitions are more common than others, does not make a qualitative difference to the results below.

Dispersal

Descendant cells disperse and compete globally to colonize empty patches of size n, thereby starting a new cycle. Note that global dispersal implies that the average genealogical relationship ('kinship') between lineages in a patch is zero. Alternatively, from the perspective of a focal bacterium, its kinship to all other bacteria in the patch is approximately $1/n$ (given that $1/n$th of the bacteria in a patch will be clonemates). In Appendix 1, we also calculate the relatedness (genetic similarity, regardless of kinship) between a focal toxin-producing bacterium and its potential victims, measured with respect to the scale of competition. We show that this relatedness is always negative when some proportion of competition is local ($a > 0$).

Basic model – invasion analyses

We first use invasion analyses to predict the conditions in which all three strains (G, F and N) can be maintained in a polymorphism. A necessary condition for this to occur is that all three possible monomorphic populations ($p_G = 1$, $p_F = 1$ and $p_N = 1$) must be invasible by a

potentially superior competitor (i.e. F beats G, N beats F, G kills N).

Result 1 – for polymorphism to be maintained, toxin production and immunity must be costly, patches must be founded by a sufficiently small number of lineages, and resource competition must be sufficiently local

1.1 If toxin production is costly ($c > 0$), then a rare immune lineage, which saves the cost of toxin production, always invades a monomorphic population of toxin producers (eqn. A2).

1.2 If immunity is costly ($k > 0$), then a rare susceptible lineage, which saves the cost of immunity, always invades a monomorphic population of immunes (eqn. A3).

1.3 If patches are founded by a sufficiently small number of lineages (small n) and resource competition is sufficiently local (large a), then a rare producer lineage can invade a monomorphic population of susceptibles (eqns A4–A6). This occurs because (i) an invading toxin producer can sufficiently harm the other lineages in its patch only when it makes up a significant fraction of the patch and (ii) harming other lineages in the patch is beneficial only when the producer competes for resources with the lineages that it harms. Accordingly, Fig. 1 shows that the ability of a toxin producer to invade is maximized when patches contain two lineages ($n = 2$ or $P_G = 0.5$) and competition is entirely local ($a = 1$).

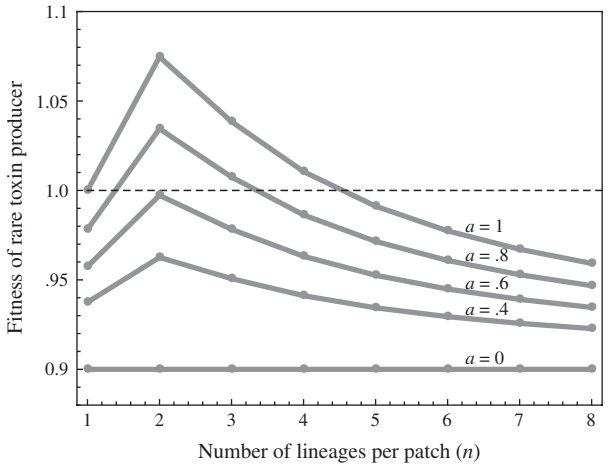

Fig. 1 Invasion conditions for toxin producers (greenbeards). We plot the fitness of a rare producer lineage in a monomorphic population of susceptibles as a function of the number of founding lineages per patch (n) and the spatial scale of competition over resources (a). A lineage is favoured when fitness is larger than one; hence, toxin producers can invade when the number of founding lineages is small (small n, but at least $n = 2$) and resource competition is mostly local (large a). Other parameters used: $g_0 = 2$, $d = 0.9$, $c = 0.1$, $k = 0.1$.

Basic model – dynamics

We now examine the dynamics of the three different strains under the influence of selection and mutation, using numerical simulations of the complete recursion equations (eqns A7). We first consider the effect of mutations on the predicted dynamics. We then choose an intermediate mutation rate ($\mu = 10^{-3}$) to focus on the dynamics that can arise depending on the number of founding lineages n and the scale of competition a (all other parameters as in Fig. 1, unless stated otherwise). Finally, we consider whether the results differ with a minimal cost for toxin production and immunity (small c and k, respectively).

Result 2 – mutation stabilizes strain dynamics over time

Figure 2 shows that relatively low and intermediate mutation rates ($\mu = 10^{-4}$ and $\mu = 10^{-3}$, respectively) can lead to stable, (quasi-)periodic cycles involving all three strains (herein 'dynamic polymorphism'), whereas a relatively high mutation rate ($\mu = 10^{-2}$) can lead to a stable equilibrium point (herein 'static polymorphism'; see also Rousset & Roze, 2007). On the other hand, when mutations do not occur ($\mu = 0$), the dynamics are characterized by cycling between populations that are nearly monomorphic for a particular strain (as in a 'heteroclinic' cycle; e.g. May & Leonard, 1975; Jansen & van Baalen, 2006). Biologically, this

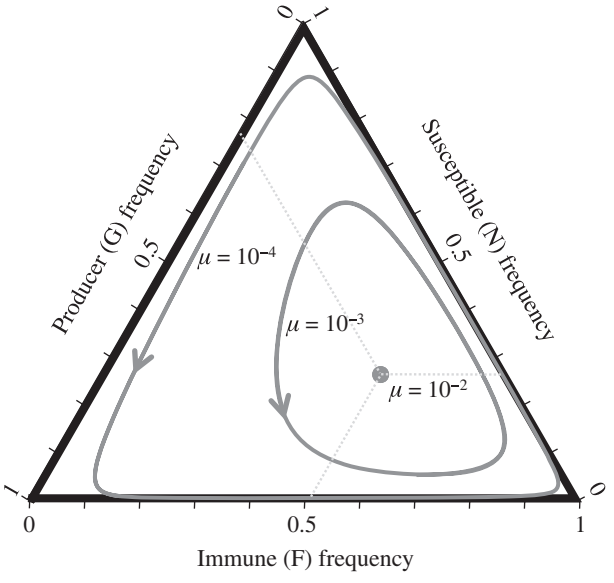

Fig. 2 Effect of mutation on rock-paper-scissors dynamics. We plot the predicted dynamics of the basic model with producer (greenbeard), immune (falsebeard) and susceptible (nonbeard) strains, using a mutation rate of $\mu = 10^{-4}$ (outer stable cycle), $\mu = 10^{-3}$ (inner stable cycle) or $\mu = 10^{-2}$ (stable equilibrium point, where strain frequencies are indicated by the dotted lines). Other parameters used: $n = 3$, $a = 1$, $g_0 = 2$, $d = 0.9$, $c = 0.1$, $k = 0.1$.

implies that all but one of the strains will eventually be lost; hence, mutation (in addition to the conditions of Result 1) will be necessary for the maintenance of polymorphism. (From here on, we will use 'RPS dynamics' to refer to cycles that are either periodic or heteroclinic).

Result 3 – when mutations occur, simulations confirm a region of three-strain polymorphism

Figure 3 (left panel, regions I and II) shows that all three strains are maintained in a polymorphism when patches are founded by a small number lineages (small n) and resource competition is mostly local (large a). This is consistent with Result 1, although mutations slightly expand the predicted region of polymorphism.

Result 4 – polymorphism can be either static or dynamic

4.1 If patches are founded by exactly two lineages ($n = 2$) and resource competition is highly local ($a > 0.8$), then all three strains eventually coexist in a static polymorphism (Fig. 3a, region I). In this scenario, bacteriocin and resource interactions are mainly pairwise, and so lineages are often paired with a superior competitor. This inhibits the growth of favoured strains, thereby dampening the amplitude of cycles and allowing strains to settle to their equilibrium frequency.

4.2 If interactions are moderately local (the remaining region of polymorphism from Result 3), then all three strains are eventually maintained in periodic cycles (Fig. 3a, region II).

4.3 If the costs of toxin production and immunity are minimal, then a second type of static polymorphism can arise (Fig. S1a, using $c = k = 0.03$). In this scenario, the growth of the susceptible strain is inhibited by its weak advantage over the immune strain, and this allows strains to settle to a stable equilibrium. These examples also show that low costs (small c and k) lead to an expanded region of

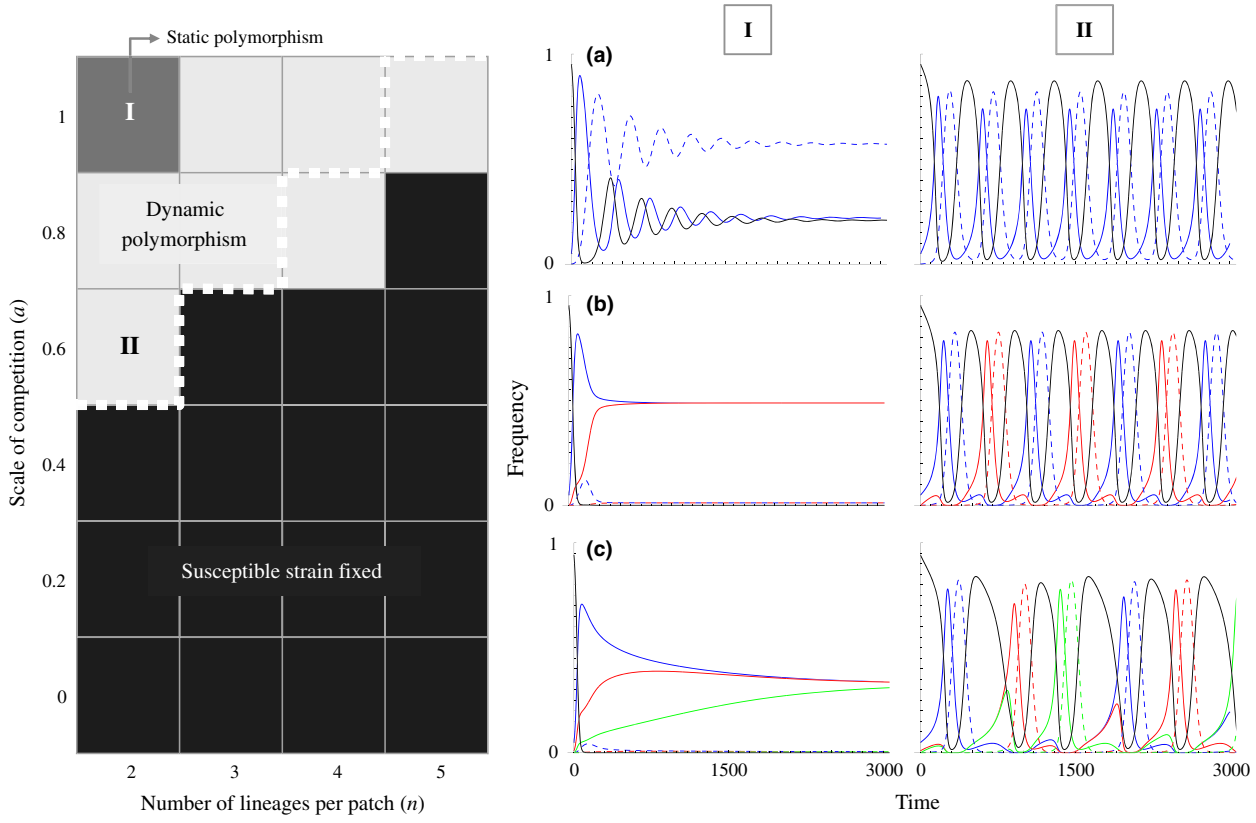

Fig. 3 Predicted strain dynamics with one, two or three toxin types in the population (several beard colours can exist). Depending on the scale of competition (a) and the number of founding lineages per patch (n), three outcomes can occur (left panel): a static polymorphism (region I, grey), a dynamic polymorphism (region II, white) or fixation of the susceptible strain (region III, black). The dashed white line (left panel) indicates the predicted threshold for polymorphism to arise in the analytical model with no mutation (from Result 1.3 of the main text). In the right panels (a–c), we plot numerical examples from regions I and II. In (a), the strains are producer (G, solid blue), immune (F, dotted blue) and susceptible (N, solid black). In (b), we add producer 2 (G2, solid red) and immune 2 (F2, dotted red). In (c), we add producer 3 (G3, solid green) and immune 3 (F3, dotted green). Other parameters and starting frequencies used: $g_0 = 2$; $d = 0.9$; $c = 0.1$; $k = 0.1$; $\mu = 10^{-3}$; $p_{G,t=0} = 0.05$; $p_{G2,t=0} = 0.01$; $p_{G3,t=0} = 0.02$; $p_{F,t=0} = 0$; $p_{F2,t=0} = 0$; $p_{F3,t=0} = 0$.

polymorphism, as predicted by the invasion analyses (eqn. A4).

Extension 1 – adding a second and third toxin type

We now extend the basic model to examine the consequences of having additional toxin types (additional beard colours) in the population. In this section, we assume that multiple toxins exist but each lineage can carry only one toxin and/or immunity factor. Furthermore, we assume that although strains differ in their harming and immune specificity, they are otherwise equivalent.

We consider examples with two and three toxin types in the population, which give similar results. In the first case with two toxins, there are five possible strains: $J = \{G1, G2, F1, F2, N\}$, where G1 and G2 are the two different toxin producers, and F1 and F2 are the corresponding immune strains. All strains are susceptible to at least one toxin: G1 and F1 are susceptible to toxins from G2; G2 and F2 are susceptible to toxins from G1; and N is susceptible to both toxins. Accordingly, the relative growth factors are as follows: $g_{G1} = g_0 - c - k - P_{G2}d$; $g_{G2} = g_0 - c - k - P_{G1}d$; $g_{F1} = g_0 - k - P_{G2}d$; $g_{F2} = g_0 - k - P_{G1}d$; $g_N = g_0 - (P_{G1} + P_{G2})d$, and the corresponding system of recursions is given in Appendix 3 (eqns A9). Also in Appendix 3, we list the analogous payoffs and recursions for the three-toxin case ($J = \{G1, G2, G3, F1, F2, F3, N\}$; eqns A10).

Result 5 – multiple producer strains can coexist in a static polymorphism

Static polymorphism arises under extremely local interactions (same parameters as Result 4.1), but here, the polymorphism consists of producer strains only (Fig. 3b,c; region I). This is because bacteriocin and resource interactions are mainly pairwise ($n = 2$, $a > 0.8$), and so immune lineages often share a patch with a toxin producer to which they are susceptible. Hence, in this scenario, the occurrence of multiple toxin types inhibits immune strains, and as a result, susceptible strains are inhibited as well. We have checked that this result does not depend on the occurrence of mutations.

Result 6 – multiple toxin and immunity types can be maintained in a dynamic polymorphism

6.1 When mutations occur ($\mu > 0$), dynamic polymorphism arises under moderately local interactions (same parameters as Result 4.2). In this case, however, periodic cycles involve alternating toxin and immunity types (alternating beard colours; Fig. 3b,c; region II). Hence, although both toxin/immunity types are maintained, only one type (a single beard colour) dominates the population at once.

6.2 If mutations do not occur ($\mu = 0$), then RPS dynamics eventually involve only one toxin/immunity type (a single beard colour; not shown).

Result 7 – the presence of multiple toxins can promote RPS dynamics

We show in the Supporting Information (Fig. S1b) that dynamic polymorphism also arises when the costs of toxin production and immunity are minimal (same parameters as Result 4.3) and interactions are not extremely local (as in Result 5). This is because, whereas in the basic model the immune strain reaches its equilibrium frequency (Fig. S1a), a second toxin producer in the population (G2) can displace the original immune strain (F1). This leads to cycles of alternating toxin and immunity types (as in Result 6.1) and the maintenance of much higher levels of toxin production than in the basic model (compare Fig. S1a and S1b).

Extension 2 – adding a second toxin type with different toxicity

We now examine the consequences of adding a second toxin-producing strain with a lower toxicity (smaller d) than the existing producer strain. Although this new strain is less toxic, we assume that it pays the same cost of toxin production (c) as its competing producer strain, thereby giving it a basic disadvantage.

We first consider a scenario in which no immune strains can exist. In this case, there are three possible strains: $J = \{G1, G2, N\}$, and we denote the toxicity of strains G1 and G2 by d_1 and d_2, respectively. The relative growth factors are as follows: $g_{G1} = g_0 - c - k - P_{G2}d_2$; $g_{G2} = g_0 - c - k - P_{G1}d_1$; and $g_N = g_0 - P_{G1}d_1 - P_{G2}d_2$, and the corresponding system of recursions is in Appendix 3 (eqns A8). We examine a case in which G1 is more toxic than G2 ($d_1 > d_2$).

Result 8 – in the absence of immune strains, producer strains that differ in toxicity cannot coexist

8.1 If both producer strains invade from rarity, then the more-toxic strain (G1) is always fixed when patches are founded by a small number of lineages (small n) and resource competition is mostly local (large a; Fig. 4a, region I). Moreover, if producer strains invade from equal but intermediate frequencies, then the more-toxic strain is fixed under an even wider range of parameters (Fig. S2).

8.2 If the less-toxic strain (G2) starts at a higher frequency than the more-toxic strain (G1), then G2 can be fixed, as long interactions are not extremely local (Fig. S2).

8.3 In all other conditions, the susceptible strain (N) is fixed (Fig. 4a, region II; Fig. S2).

Next, we consider the same scenario while allowing immune strains to occur. In this case, there are five possible strains: $J = \{G1, G2, F1, F2, N\}$, where the

toxicity of strains G1 and G2 differs, as above. The new growth factors in this scenario are as follows: $g_{F1} = g_0 - k - P_{G2}d_2$ and $g_{F2} = g_0 - k - P_{G1}d_1$, and the full system of recursions is in Appendix 3 (eqns A9). As above, we consider an example in which G1 is more toxic than G2 ($d_1 > d_2$), but here, we focus on the invasion of producer strains from rarity.

Result 9 – the presence of immune strains promotes the coexistence of producer strains that differ in toxicity

9.1 Static polymorphism arises under extremely local interactions (same parameters as Result 4.1), but here, only three strains coexist (Fig. 4b, region I). This is because the less-toxic strain (G2) is maintained at lower frequency than the more-toxic strain (G1), and this in turn maintains the strain that is immune to the most common producer (F1).

9.2 Dynamic polymorphism arises under moderately local interactions (same parameters as Result 4.2), but here cycles involve only four strains (Fig. 4b, region II). This is because cycles become dominated by the more-toxic strain (G1), its corresponding immune strain (F1) and the susceptible strain (N). Although the less-toxic strain (G2) cycles at low frequency, it is always outcompeted by the more-toxic strain, and so the remaining immune strain (F2) remains at negligible frequency.

Extension 3 – adding a second toxin type, allowing multitoxicity and multi-immunity

Finally, we consider the consequences of allowing individual lineages to produce multiple toxins and carry multiple immunity factors.

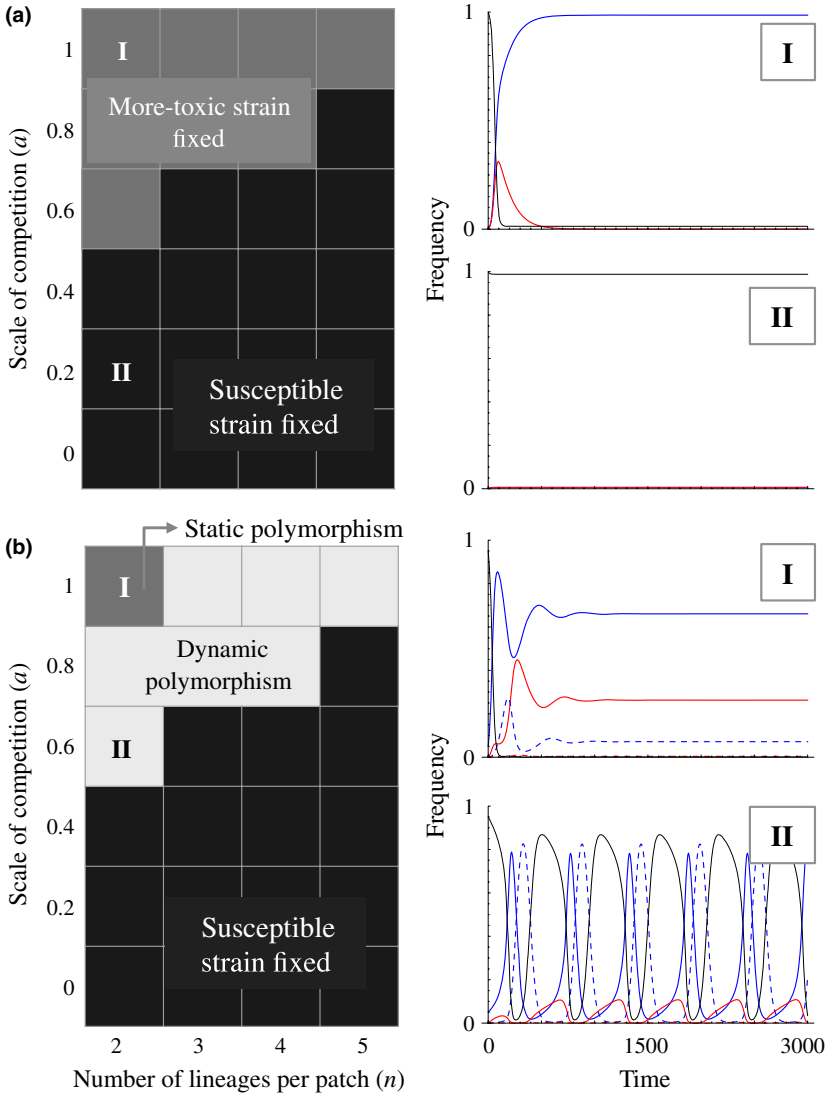

Fig. 4 Predicted strain dynamics when bacteriocins differ in toxicity. If no immune strains can arise, then only two outcomes can occur (a, left panel): either the more-toxic strain is fixed (region I, grey), or the susceptible strain is fixed (region II, black). However, when immunity can arise, three outcomes are possible (b, left panel): a static polymorphism (region I, grey), a dynamic polymorphism (region II, white) or fixation of the susceptible strain (region III, black). We plot numerical examples from regions I and II in the right panel, using the following parameters and starting frequencies: $g_0 = 2$; $d_1 = 0.9$; $d_2 = 0.85$; $c = 0.1$; $k = 0.1$; $\mu = 10^{-3}$; $p_{G1,t=0} = 0.05$; $p_{G2,t=0} = 0.01$; $p_{F1,t=0} = 0$; $p_{F2,t=0} = 0$.

Although only two toxin types exist in this scenario, there can be nine different strains: $J = \{G1, G2, F1, F2, G1G2, G1F2, G2F1, F1F2, N\}$. The novel strains in this scenario are as follows: G1G2, the 'multitoxic' strain; G1F2, a 'mixed' strain that produces toxin 1 and is immune to both toxins; G2F1, a mixed strain that produces toxin 2 and is immune to both toxins; and F1F2, the 'multi-immune' strain, which is immune to both toxins. We assume that (i) the costs of carrying multitoxicity and/or multi-immunity combine additively and (ii) producing two toxins inflicts twice the harm on susceptible strains as does a single toxin (i.e. there is no saturation of toxicity). We list the relative growth factors in Table 1, and the corresponding recursions are in Appendix 3 (eqns A11).

Result 10 – multiple toxin and immunity types can coexist in a static polymorphism

10.1 Static polymorphism arises under extremely local interactions (same parameters as Result 4.1) and is analogous to that in the basic model (compare region I of Figs 5 and 3a). This is because both the basic model and the current scenario involve strains (F and F1F2, respectively) that are immune to all possible toxins. Accordingly, Fig. 5 (region I) shows that the FIF2 strain dominates, followed by the multitoxic (G1G2, analogous to G in the basic model) and susceptible (N) strains, whereas all other strains persist at low frequency.

10.2 Static polymorphism can also arise when the costs of toxin production and immunity are minimal (same parameters as Result 4.3) and resource competition is mostly local (large *a*; Fig. S1c). This result is also analogous to the basic model (Fig. S1a), although here it is the multi-immune strain (F1F2) that dominates.

Result 11 – multiple toxin and immunity types can coexist in a dynamic polymorphism

11.1 When mutations occur, dynamic polymorphism arises under moderately local interactions (same parameters as Result 4.2) and maintains almost all possible strains in a complex form of RPS dynamics (Fig. 5, region II). Specifically, we find that seven strains cycle in a competitive network of five strain 'guilds'. This is because the dynamics of the single toxin producers (G1 and G2) synchronize, becoming a single guild, as do those of the two mixed strains (G1F2 and G2F1). Guilds then fluctuate in the following order of competitive dominance: single toxin producers (G1 and G2) kill susceptibles (N); the multitoxic strain (G1G2) kills G1 and G2; the 'mixed' strains (G1F2 and G2F1) beat G1G2 (by saving the cost of one toxin); multi-immunes (F1F2) beat G1F2 and G2F1 (by saving the cost of another toxin); and finally, susceptibles (N) beat F1F2 (by saving the cost of immunity). This example shows that (i) although cycles are dominated by multitoxic and multi-immune strains, a high diversity of strains can be maintained in the population and (ii) both toxin/immunity types (both beard colours) can coexist at once. This is in contrast to Result 6, where a single beard colour tends to dominate at once.

11.2 If mutations do not occur, then RPS dynamics eventually involve only the susceptible, multitoxic and multi-immune strains (not shown).

11.3 Dynamic polymorphism can also arise when the costs of toxin production and immunity are minimal (same parameters as Result 4.3) and resource competition is mostly global (small *a;* Fig. S1c). In this scenario, the relatively unconstrained growth of the susceptible (N) strain keeps the system from settling to an equilibrium, and this in turn maintains a high diversity of strains in periodic cycles. Hence, as in Result 7, this example shows that the occurrence of multiple toxins can promote RPS dynamics.

Table 1 The relative growth factor g_j of a randomly selected lineage of strain j in model extension 3 (two toxin types, allowing multitoxicity and multi-immunity).

Lineage type	Relative growth factor
G1	$g_0 - c - k - P_{G2}d - P_{G1G2}d - P_{G2F1}d$
G2	$g_0 - c - k - P_{G1}d - P_{G1G2}d - P_{G1F2}d$
F1	$g_0 - k - P_{G2}d - P_{G2F1}d - P_{G1G2}d$
F2	$g_0 - k - P_{G1}d - P_{G1G2}d - P_{G1F2}d$
G1G2	$g_0 - 2c - 2k$
G1F2	$g_0 - c - 2k$
G2F1	$g_0 - c - 2k$
F1F2	$g_0 - 2k$
N	$g_0 - (P_{G1} + P_{G2} + 2\,P_{G1G2} + P_{G1F2} + P_{G2F1})d$

Discussion

We have examined the dynamics of bacteriocin producers (greenbeards), immune strains (falsebeards) and susceptible strains (nonbeards) in increasingly diverse model settings. We found that in all scenarios examined: (i) polymorphism, and hence the maintenance of greenbeard effects, is promoted by a small number of founding lineages per patch (small n, but at least $n = 2$), highly local resource competition (large a) and the occurrence of mutation; and (ii) polymorphism can be static or dynamic, depending on the intensity of local interactions and/or the costs of toxin production and immunity. Furthermore, we found that: (iii) the occurrence of multiple toxins can promote rather than inhibit RPS dynamics; and (iv) such dynamics can maintain strain diversity when there are multiple toxins in the population (Fig. 3b,c), when toxins differ in toxicity (Fig. 4b) and when lineages can exhibit

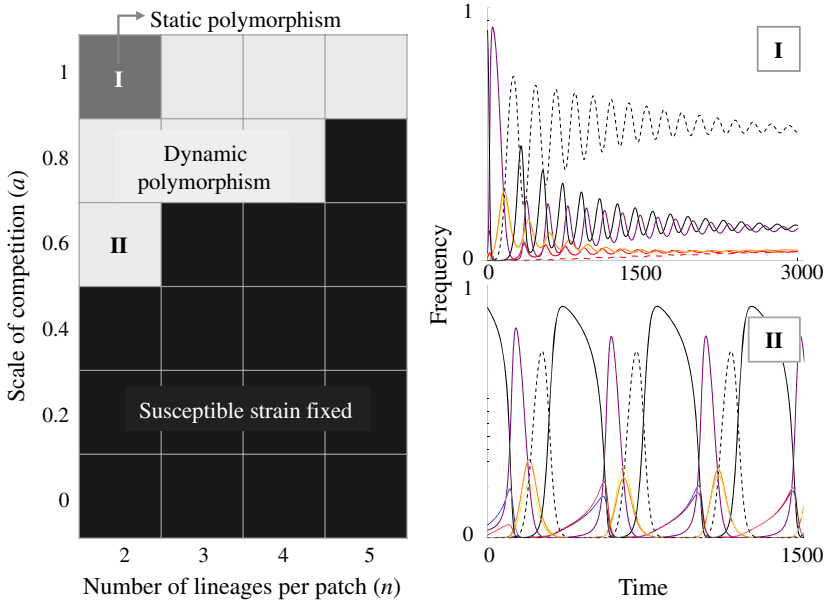

Fig. 5 Predicted strain dynamics when lineages can exhibit multitoxicity and multi-immunity (individuals can have multiple beards). The left panel shows the three possible outcomes: a static polymorphism (region I, grey), a dynamic polymorphism (region II, white) or fixation of the susceptible strain (region III, black). We plot numerical examples from regions I and II in the right panel, where the possible strains are as follows: producer 1 (G1, solid blue), producer 2 (G2, solid red), immune 1 (F1, dotted blue), immune 2 (F2, dotted red), multitoxic (G1G2, solid purple), mixed strain 1 (G1F2, orange), mixed strain 2 (G2F1, yellow), multi-immune (F1F2, dotted black) and susceptible (N, solid black). In the examples shown, all but the single immunity strains (F1 and F2) coexist at non-negligible frequencies. Other parameters and starting frequencies used: $g_0 = 2$; $d = 0.9$; $c = 0.1$; $k = 0.1$; $\mu = 10^{-3}$; $p_{G1,t=0} = 0.05$; $p_{G2,t=0} = 0.03$; $p_{F1,t=0} = 0$; $p_{F2,t=0} = 0$; $p_{G1G2,t=0} = 0.01$; $p_{G1F2,t=0} = 0$; $p_{G2F1,t=0} = 0$; $p_{F1F2,t=0} = 0$.

multitoxicity/multi-immunity (Fig. 5). Overall, the selective factors that promote polymorphism in the simplest scenario can also promote the coexistence of multiple toxin and immunity types (multiple beard colours). This helps to explain the remarkable levels of bacteriocin diversity in natural populations.

Bacteriocin dynamics and diversity

We found that bacteriocin production is promoted when patches are founded by few lineages (small n) and competition is highly localized (large a). This result is generally consistent with previous theoretical and empirical work, which shows that bacteriocin production is favoured in spatially structured populations (Chao & Levin, 1981; Durrett & Levin, 1997; Czárán *et al.*, 2002; Kerr *et al.*, 2002; Tait & Sutherland, 2002; Czárán & Hoekstra, 2003; Hawlena *et al.*, 2010b; Bucci *et al.*, 2011). However, our analysis clarifies why spatial structure is crucial. First, having few lineages per patch ensures that an invading toxin producer makes up a significant fraction of the patch and can therefore sufficiently harm the other lineages in its patch. Second, local resource competition ensures that the toxin-producing lineage actually benefits from harming the other lineages in its patch. Furthermore, whereas simulation models have emphasized the role of limited dispersal (Czárán *et al.*, 2002; Kerr *et al.*, 2002), our analysis illustrates that other forms of local competition (e.g. density regulation before dispersal) also promote bacteriocin production.

Our results also clarify the links between previous kin selection and greenbeard models. Previous kin selection models found that bacteriocins are promoted when the average kinship between bacteria in a patch is intermediate (Gardner *et al.*, 2004; Inglis *et al.*, 2009). Similarly, in our models, bacteriocin production is most advantageous in patches of two lineages ($n = 2$), in which case the average kinship between a focal bacterium and the other bacteria in its patch (clonemates and a 'nonkin' lineage) is approximately 1/2. Our results also agree with relevant greenbeard models, which show that bacteriocins are promoted by negative relatedness between toxin-producing cells (greenbeards) and their potential victims (nonbeards; Gardner & West, 2010; West & Gardner, 2010; Inglis *et al.*, 2011). In our models, this relatedness is most strongly negative when patch size is two ($n = 2$), and resource competition is completely local ($a = 1$; eqn. A1).

Given that bacteriocin production is favoured, we found that two different types of polymorphism with immune and susceptible strains are possible. First,

when bacteriocin and competitive interactions are moderately local and the costs of toxin production and immunity are relatively high, strains can coexist in periodic cycles. Cycling occurs in this case because strains can fluctuate widely in frequency, being strongly favoured when rare but disfavoured when common (negative frequency dependence). Second, when interactions are extremely local ($n = 2$, $a > 0.8$) or the costs of toxin production and immunity are minimal (small c and k), multiple strains can coexist in a static polymorphism. In these cases, the growth of one or more strains is constrained, which inhibits wide fluctuations and allows the system to reach a stable equilibrium (Figs 3, 5; and S1a,c). Previous studies of bacteriocin dynamics have overlooked the possibility of static polymorphism, partly because they focused on toxins that are released by cell lysis, implying a high fitness cost (Durrett & Levin, 1997; Kerr *et al.*, 2002; Kirkup & Riley, 2004). However, in some natural populations, the majority of toxins are released as secretions rather than by cell lysis (Riley & Gordon, 1996). Our results suggest that entirely different dynamics could arise for toxins that are secreted from the cell, if they incur a much smaller fitness cost (Dykes & Hastings, 1997).

We found that two factors are particularly important for explaining bacteriocin diversity in natural populations. First, the occurrence of immune strains (falsebeards) can maintain multiple toxin and immunity types in the population, even when strains differ in toxicity. If immunity cannot arise (and all else is equal), then the less-toxic strain cannot invade from rarity (Fig. 4a, region I). However, if immunity can arise, then multiple strains can be maintained, either in a static polymorphism or in cycles (for the reasons described above; Fig. 4b). Second, a high diversity of strains can be maintained in the population when individual lineages are able to exhibit multiple toxins and/or immunity. In this scenario, dynamic polymorphism tends to be dominated by multitoxic and multi-immune strains (see also Szabó *et al.*, 2007), yet almost all available strains can also be maintained at non-negligible frequencies (Figs. 5, region II; S1c). This result is consistent with lattice-based simulations of multitoxicity and multi-immunity (although these studies focused on spatial patterns rather than strain dynamics; e.g. Pagie & Hogeweg, 1999; Czárán *et al.*, 2002) and also with patterns of bacteriocin diversity in natural populations (Riley & Gordon, 1999; Riley & Wertz, 2002; Gordon & O'Brien, 2006; Hawlena *et al.*, 2010a).

To facilitate our analysis, we ignored some features of natural populations that may be useful to consider in future models. First, we did not explicitly consider space, including spatial variation in habitat quality, which is known to promote diversity (Frank, 1994). Second, we assumed that lineages either produce a standard unit of toxin or none at all whereas, in reality, lineages can produce varying amounts of toxin, and this amount may be subject to natural selection (see models in Gardner *et al.*, 2004; Prado & Kerr, 2008; Nahum *et al.*, 2011). Third, we assumed that toxin production is an obligate strategy, whereas, in reality, toxin production can be induced by the toxins of competing strains (Majeed *et al.*, 2010) and/or mediated by quorum sensing (Van Der Ploeg, 2005). It remains unclear whether and how these effects will affect the maintenance of strain diversity.

Marker diversity: the greenbeard effect vs. genetic kin recognition

More generally, our results help to explain how polymorphism could be maintained at marker loci upon which discrimination is based. The problem arises because selection can favour common markers (beards) over rare ones, thereby eliminating the diversity necessary for discrimination in the first place (Crozier, 1986; Strassmann *et al.*, 2011). For example, if obligate harming greenbeards were to approach fixation, they would continue to express their harming behaviour even though, in the absence of potential victims, this behaviour would have no effect and may therefore go undetected (Gardner & West, 2010). Our results show that the occurrence of falsebeards (cheats) and nonbeards can lead to evolutionary dynamics that prevent greenbeard fixation, therefore making greenbeard effects detectable (Figs 2–5).

Furthermore, our results clarify how selection can maintain diversity in greenbeard markers (multiple beard colours). Previous studies of marker diversity found that the regular appearance of novel types, generated by mutation and/or recombination, is necessary for the maintenance of diversity; otherwise, diversity is eroded by cycles that are dominated by a single type (Axelrod *et al.*, 2004; Jansen & van Baalen, 2006; Rousset & Roze, 2007). Similarly, we found that if mutation is eliminated and/or lineages are able to exhibit only a single toxin or immunity type (a single beard colour), then populations are ultimately dominated by a particular type (Figs 3b,c; region II). One proposed mechanism for the coexistence of greenbeard diversity is via relaxed linkage between marker (beard) and behaviour (Jansen & van Baalen, 2006). However, this is best described as a mechanism for maintaining marker diversity in genetic kin recognition, given that it leads to nepotism among individuals that share any recognition marker (rather than a specific marker; Rousset & Roze, 2007; Gardner & West, 2010). In contrast, our results illustrate a real case in which multiple greenbeards coexist at once, occurring when lineages can exhibit more than one toxin or immunity type (Fig. 5). Hence, motivated by the biology of bacteriocins, we found that the factors that maintain greenbeard effects can also promote the coexistence of greenbeard diversity.

Acknowledgments

We thank Ben Kerr, Sean Rice and Minus van Baalen for comments. We are funded by the Natural Sciences and Engineering Research Council of Canada (JMB), The Royal Society and Baliol College (AG) and the European Research Council (SAW).

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Appendix 1

Calculating genetic relatedness (basic model)

Here, we calculate the relatedness (genetic similarity) between a focal toxin-producing bacterium and its potential victims (following Gardner *et al.*, 2004). We use a result from Queller (1994) that the average relatedness between a focal actor and its competitors (including self) is zero. Recalling that patches are made up of n lineages and that the scale of competition a is the proportion of competition that is local, we consider a very large (effectively infinite) pool of competing bacteria in which a proportion a are patchmates, and of these, a proportion $1/n$ are from the same clonal lineage. Choosing a focal toxin-producing bacterium at random, a proportion $a(1/n)$ of its competitors are therefore clonally related by one, a proportion $aP_G(n-1)/n$ are also related by one (owing to identity by state), and the rest (its potential victims) are related by the unknown value r. Altogether, we have $a(1/n + P_G(n-1)/n) + [1-a(1/n + P_G(n-1)/n)]r = 0$, which can be rearranged to give:

$$r = -\frac{a(1+(n-1)P_G)}{n-a(1+(n-1)P_G)}. \tag{A1}$$

The sign of this relatedness is negative for all biologically relevant parameters, and its magnitude is maximized when $n = 2$ and $a = 1$.

Appendix 2

Details of the invasion analyses (basic model)

Here, we derive the conditions for rare mutant lineages to invade populations that are monomorphic for a particular strain. First, we consider the invasion of a rare immune (F) lineage in a population of nearly all toxin producers ($p_G \approx 1$). The relative growth factor for all producer lineages is $g_0 - c - k$, and the invading lineage has a growth factor of $g_0 - k$. Hence, following eqn 1 of the main text, the fitness of a rare immune lineage (its asymptotic growth rate, λ) is:

$$\lambda_F = \frac{(g_0-k)n}{ac+(g_0-c-k)n}. \tag{A2}$$

If toxin production is costly ($c > 0$), then the immune lineage always invades ($\lambda_F > 1$); otherwise, if toxin production is costless ($c = 0$), then toxin-producing and immune lineages are neutrally stable ($\lambda_F = 1$).

Second, we derive the condition for a rare susceptible (N) lineage to invade a population of nearly all immune lineages ($p_F \approx 1$). The relative growth factor for all immune lineages is $g_0 - k$, and the invading lineage has a growth factor of g_0. In this case, the growth rate of the rare susceptible lineage is:

$$\lambda_N = \frac{g_0 n}{ak+(g_0-k)n}. \tag{A3}$$

If immunity is costly ($k > 0$), then the susceptible lineage always invades ($\lambda_N > 1$); otherwise, if immunity is costless ($k = 0$), then immunes and susceptibles are neutrally stable ($\lambda_N = 1$).

Third, we derive the condition for a rare toxin-producing (G) lineage to invade a population of nearly all susceptibles ($p_N \approx 1$). In this case, the susceptible lineages in the greater population have a relative growth factor of g_0, those in the focal patch have a growth factor of $g_0-(1/n)d$, and the invading lineage has a growth factor of g_0-c-k. Hence, the growth rate of the rare producer lineage is:

$$\lambda_G = \frac{(g_0-c-k)n^2}{a\{d-n(c+d+k)\}+g_0n^2}. \tag{A4}$$

This increases with the scale of competition ($D\lambda_G/Da > 0$) when

$$n > \frac{d}{d+c+k}, \tag{A5}$$

which is always satisfied if toxin production and immunity are costly (c, $k > 0$). This implies that the growth rate of a rare toxin-producing lineage always increases with increasing local resource competition (increasing a; Fig. 1). Furthermore, the growth rate of the rare producer lineage increases with an increasing number of lineages per patch ($D\lambda_G/Dn > 0$) when

$$n < \frac{2d}{a+d+k}. \tag{A6}$$

The RHS of this inequality can never exceed two, so although moving from $n = 1$ to $n = 2$ can promote the invasion of a rare toxin-producing lineage, increasing the number of lineages per patch above two always inhibits its invasion (Fig. 1).

Appendix 3

Complete recursion equations (basic model and all extensions)

Basic model

Here, we derive recursive equations for the basic model with three possible strains in the population ($J = \{G, N, F\}$). We assume that mutations, occurring at a rate μ per colonization/growth cycle, convert susceptible lineages to toxin producers (N → G), toxin producers to immunes (G → F) and immunes to susceptibles (F → N). The full system of recursions is as follows:

$$\begin{aligned} p''_{\mathrm{G}} &= (1-\mu)(p_{\mathrm{G}}W_{\mathrm{G}}) + \mu(p_{\mathrm{N}}W_{\mathrm{N}}) \\ p''_{\mathrm{F}} &= (1-\mu)(p_{\mathrm{F}}W_{\mathrm{F}}) + \mu(p_{\mathrm{G}}W_{\mathrm{G}}) \\ p''_{\mathrm{N}} &= (1-\mu)(p_{\mathrm{N}}W_{\mathrm{N}}) + \mu(p_{\mathrm{F}}W_{\mathrm{F}}) \end{aligned} \tag{A7}$$

In this system of equations (and all recursions given below), $W_j = \sum_L \wp_{lj} w_j / \sum_L \wp_{lj}$ is the average fitness among all lineages of strain j, where $\wp_{lj} = 1$ if lineage l is of type j and 0 otherwise, and $w_j = F_j/(aF' + (1-a)\bar{F})$ is a random variable, defined as the fitness of a randomly chosen lineage of the focal strain (eqn. 1 of the main text). Note that in practice, W_j can be calculated as an expectation of w_j over the set of possible patch compositions. For example, in the simplest case of $n = 2$ and where the focal lineage is type G, we would take the expected fitness of the focal lineage with respect to the frequency of the three possible group compositions (G paired with G, F or N). Numerical simulations of eqns A7 are in Figs 2, 3a and S1a.

Adding a second and third toxin type

Two toxins in the population

Here, we derive recursive equations for the case of two toxin types in the population, first assuming that immune strains do not exist (J = {G1, G2, N}). We assume that mutations convert susceptible lineages to toxin producers (N → G1 or G2) and toxin producers to susceptibles (G1 or G2 → N). Hence, the full system of recursions is as follows:

$$\begin{aligned} p''_{\mathrm{G1}} &= (1-\mu)(p_{\mathrm{G1}}W_{\mathrm{G1}}) + (\mu/2)(p_{\mathrm{N}}W_{\mathrm{N}}) \\ p''_{\mathrm{G2}} &= (1-\mu)(p_{\mathrm{G2}}W_{\mathrm{G2}}) + (\mu/2)(p_{\mathrm{N}}W_{\mathrm{N}}) \\ p''_{\mathrm{N}} &= (1-\mu)(p_{\mathrm{N}}W_{\mathrm{N}}) + \mu(p_{\mathrm{G1}}W_{\mathrm{G1}} + p_{\mathrm{G2}}W_{\mathrm{G2}}) \end{aligned} \tag{A8}$$

and simulations of this system are in Fig. 4a.

Next, we assume that immune strains can exist (J = {G1, G2, F1, F2, N}). We assume that mutations convert susceptible lineages to toxin producers (N → G1 or G2), toxin producers to immunes (G1 → F1, G2 → F2) and immunes to susceptibles (F1 or F2 → N). Hence, the full system of recursions is as follows:

$$\begin{aligned} p''_{\mathrm{G1}} &= (1-\mu)(p_{\mathrm{G1}}W_{\mathrm{G1}}) + (\mu/2)(p_{\mathrm{N}}W_{\mathrm{N}}) \\ p''_{\mathrm{G2}} &= (1-\mu)(p_{\mathrm{G2}}W_{\mathrm{G2}}) + (\mu/2)(p_{\mathrm{N}}W_{\mathrm{N}}) \\ p''_{\mathrm{F1}} &= (1-\mu)(p_{\mathrm{F1}}W_{\mathrm{F1}}) + \mu(p_{\mathrm{G1}}W_{\mathrm{G1}}) \\ p''_{\mathrm{F2}} &= (1-\mu)(p_{\mathrm{F2}}W_{\mathrm{F2}}) + \mu(p_{\mathrm{G2}}W_{\mathrm{G2}}) \\ p''_{\mathrm{N}} &= (1-\mu)(p_{\mathrm{N}}W_{\mathrm{N}}) + \mu(p_{\mathrm{F1}}W_{\mathrm{F1}} + p_{\mathrm{F2}}W_{\mathrm{F2}}) \end{aligned} \tag{A9}$$

Equations A9 apply when strains have the same parameter values (simulations in Figs 3b, S1b) and also when the second producer strain has a different toxicity (simulations in Fig. 4b).

Three toxins in the population

Here, we derive recursions for the analogous case with three toxins in the population (J = {G1, G2, G3, F1, F2, F3, N}). In this case, the relative growth factors are as follows: $g_{\mathrm{G1}} = g_0 - c - k - P_{\mathrm{G2}}d - P_{\mathrm{G3}}d$; $g_{\mathrm{G2}} = g_0 - c - k - P_{\mathrm{G1}}d - P_{\mathrm{G3}}d$; $g_{\mathrm{G3}} = g_0 - c - k - P_{\mathrm{G1}}d - P_{\mathrm{G2}}d$; $g_{\mathrm{F1}} = g_0 - k - P_{\mathrm{G2}}d - P_{\mathrm{G3}}d$; $g_{\mathrm{F2}} = g_0 - k - P_{\mathrm{G1}}d - P_{\mathrm{G3}}d$; $g_{\mathrm{F3}} = g_0 - k - P_{\mathrm{G1}}d - P_{\mathrm{G2}}d$; $g_{\mathrm{N}} = g_0 - (P_{\mathrm{G1}} + P_{\mathrm{G2}} + P_{\mathrm{G3}})d$. We assume that mutations convert susceptible lineages to toxin producers (N → G1, G2 or G3), toxin producers to immunes (G1 → F1, G2 → F2, G3 → F3) and immunes to susceptibles (F1, F2, or F3 → N). Hence, the full system of recursions is as follows:

$$\begin{aligned} p''_{\mathrm{G1}} &= (1-\mu)(p_{\mathrm{G1}}W_{\mathrm{G1}}) + (\mu/3)(p_{\mathrm{N}}W_{\mathrm{N}}) \\ p''_{\mathrm{G2}} &= (1-\mu)(p_{\mathrm{G2}}W_{\mathrm{G2}}) + (\mu/3)(p_{\mathrm{N}}W_{\mathrm{N}}) \\ p''_{\mathrm{G3}} &= (1-\mu)(p_{\mathrm{G3}}W_{\mathrm{G3}}) + (\mu/3)(p_{\mathrm{N}}W_{\mathrm{N}}) \\ p''_{\mathrm{F1}} &= (1-\mu)(p_{\mathrm{F1}}W_{\mathrm{F1}}) + \mu(p_{\mathrm{G1}}W_{\mathrm{G1}}) \\ p''_{\mathrm{F2}} &= (1-\mu)(p_{\mathrm{F2}}W_{\mathrm{F2}}) + \mu(p_{\mathrm{G2}}W_{\mathrm{G2}}) \\ p''_{\mathrm{F3}} &= (1-\mu)(p_{\mathrm{F3}}W_{\mathrm{F3}}) + \mu(p_{\mathrm{G3}}W_{\mathrm{G3}}) \\ p''_{\mathrm{N}} &= (1-\mu)(p_{\mathrm{N}}W_{\mathrm{N}}) + \mu(p_{\mathrm{F1}}W_{\mathrm{F1}} + p_{\mathrm{F2}}W_{\mathrm{F2}} + p_{\mathrm{F3}}W_{\mathrm{F3}}) \end{aligned} \tag{A10}$$

and simulations of this system are in Fig. 3c.

Adding a second toxin type, allowing multitoxicity and multi-immunity

Finally, we derive recursions for the case of two toxin types in the population, where lineages can exhibit multitoxicity and multi-immunity (J = {G1, G2, F1, F2, G1G2, G1F2, G2F1, F1F2, N}). We assume that mutations convert susceptible lineages to single toxin producers (N → G1 or G2), mixed strains to single toxin producers or to multi-immunes (G1F2 → G1, G2F1 → G2, G1F2 or G2F1 → F1F2), single toxin producers to immunes or to multitoxic strains (G1 → F1, G2 → F2, G1 or G2 → G1G2), and immune strains to mixed strains or to susceptibles (F1 → G2F1, F2 → G1F2, F1 or F2 → N). All together, the full system of recursions is as follows:

$$\begin{aligned} p''_{\mathrm{G1}} &= (1-\mu)(p_{\mathrm{G1}}W_{\mathrm{G1}}) + (\mu/2)(p_{\mathrm{N}}W_{\mathrm{N}}) \\ &\quad + (\mu/2)(p_{\mathrm{G1F2}}W_{\mathrm{G1F2}}) \\ p''_{\mathrm{G2}} &= (1-\mu)(p_{\mathrm{G2}}W_{\mathrm{G2}}) + (\mu/2)(p_{\mathrm{N}}W_{\mathrm{N}}) \\ &\quad + (\mu/2)(p_{\mathrm{G2F1}}W_{\mathrm{G2F1}}) \\ p''_{\mathrm{F1}} &= (1-\mu)(p_{\mathrm{F1}}W_{\mathrm{F1}}) + (\mu/2)(p_{\mathrm{G1}}W_{\mathrm{G1}}) \\ p''_{\mathrm{F2}} &= (1-\mu)(p_{\mathrm{F2}}W_{\mathrm{F2}}) + (\mu/2)(p_{\mathrm{G2}}W_{\mathrm{G2}}) \\ p''_{\mathrm{G1G2}} &= (1-\mu)(p_{\mathrm{G1G2}}W_{\mathrm{G1G2}}) + (\mu/2)(p_{\mathrm{G1}}W_{\mathrm{G1}}) \\ &\quad + (\mu/2)(p_{\mathrm{G2}}W_{\mathrm{G2}}) \\ p''_{\mathrm{G1F2}} &= (1-\mu)(p_{\mathrm{G1F2}}W_{\mathrm{G1F2}}) + (\mu/2)(p_{\mathrm{G1G2}}W_{\mathrm{G1G2}}) \\ &\quad + (\mu/2)(p_{\mathrm{F2}}W_{\mathrm{F2}}) \\ p''_{\mathrm{G2F1}} &= (1-\mu)(p_{\mathrm{G2F1}}W_{\mathrm{G2F1}}) + (\mu/2)(p_{\mathrm{G1G2}}W_{\mathrm{G1G2}}) \\ &\quad + (\mu/2)(p_{\mathrm{F1}}W_{\mathrm{F1}}) \\ p''_{\mathrm{F1F2}} &= (1-\mu)(p_{\mathrm{F1F2}}W_{\mathrm{F1F2}}) + (\mu/2)(p_{\mathrm{G1F2}}W_{\mathrm{G1F2}}) \\ &\quad + (\mu/2)(p_{\mathrm{G2F1}}W_{\mathrm{G2F1}}) \\ p''_{\mathrm{N}} &= (1-\mu)(p_{\mathrm{N}}W_{\mathrm{N}}) + (\mu/2)(p_{\mathrm{F1}}W_{\mathrm{F1}} + p_{\mathrm{F2}}W_{\mathrm{F2}}) \end{aligned} \tag{A11}$$

and simulations of this system are in Figs 5 and S1c.

Supporting information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Predicted strain dynamics when the costs of toxin production and immunity are minimal ($c = k = 0.03$).

Figure S2. Predicted strain dynamics in populations with two bacteriocin producers and no immune strains, where one producer (with toxicity $d_1 = 0.9$) is more toxic than other (with toxicity $d_2 = 0.85$).

Received 8 April 2013; revised 3 July 2013; accepted 4 July 2013