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Microbial secretor–cheater dynamics

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Microbial secretions manipulate the environment and communicate information to neighbours. The secretions of an individual microbe typically act externally and benefit all members of the local group. Secreting imposes a cost in terms of growth, so that cheaters that do not secrete gain by sharing the benefits without paying the costs. Cheaters have been observed in several experimental and natural settings. Given that cheaters grow faster than secretors when in direct competition, what maintains the widely observed patterns of secretion? Recent theory has emphasized the genetic structure of populations, in which secretors tend to associate spatially with other secretors, reducing direct competition and allowing highly secreting groups to share mutual benefits. Such kin selection can be a powerful force favouring cooperative traits. Here, I argue that, although kin selection is a factor, the combination of mutation and demographic processes dominate in determining the relative fitness of secretors versus cheaters when measured over the full cycle of microbial life history. Key demographic factors include the local density of microbes at which secretion significantly alters the environment, the extent to which secretion enhances microbial growth and maximum local density, and the ways in which secretion alters colony survival and dispersal.

Keywords: cycle fitness; demography; life history; mutation; population dynamics; social evolution

1. INTRODUCTION

Microbes secrete molecules to alter their local environment. Pathogens secrete signals that sabotage host immunity; bacteria secrete substances that form protective biofilms; various species secrete molecules that scavenge scarce resources such as iron (West *et al.* 2007). Single microbes often cannot secrete a sufficient quantity to alter the environment in a beneficial way. Only the social cooperation of a population can achieve the benefits of environmental engineering. But, as in all social traits, the need for group coordination contains the seeds of social collapse (Crespi 2001).

An individual that does not secrete its share still gains the same benefit as its neighbours. Such cheaters often outcompete neighbours, because they do not pay the costs of secretion. As the frequency of cheaters rises, group efficiency declines, decreasing the reproductive success of all group members, including the cheaters (Diggle *et al.* 2007; Sandoz *et al.* 2007).

Many recent studies have documented the existence of cheaters in a wide diversity of socially cooperative microbes (Foster *et al.* 2007; West *et al.* 2007; Nadell *et al.* 2009). Several papers have analysed how population structure influences the balance between social cooperation and competition (Buckling *et al.* 2007). Here, population structure means the patterns of genetic variability within and between groups. Genetic similarity within groups associates non-cheaters with other non-cheaters, promoting social traits by a process often referred to as kin selection.

The current literature emphasizes kin selection, often using game theory to understand the conditions under which secretors or cheaters dominate. Game theory provides a simple way to analyse this conflict. However, game theory analyses commonly make very simple assumptions about the fitnesses of secretors and cheaters, without regard to the demographic and dynamical processes that influence fitness (Frank 1998).

With regard to demography, the rise of cheaters depends on how much the secretions can enhance local opportunities for growth and how long resource patches last (Brown & Johnstone 2001; Brockhurst *et al.* 2007; Gardner *et al.* 2007; Nadell *et al.* 2008; Ross-Gillespie *et al.* 2009). Such demographic factors must be analysed in a dynamical context, because the quantitative relations between characters and fitness often change dramatically in relation to the scaling of various rate processes. These demographic rate processes strongly influence the costs and benefits of secretion in competition with the inevitable rise of cheaters.

In this paper, I analyse the relative importance of various demographic factors in secretor–cheater dynamics. I conclude that too much emphasis on kin selection and game theory analysis is misleading. Although genetic structuring and kin selection influence the evolution of secretion, demographic processes often dominate in determining secretor–cheater dynamics.

I propose an alternative to thinking about secretors and cheaters as competitors in a game. Instead, a

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microbial population of secretors may start out as a nearly homogeneous multicellular aggregation. As the population grows, it inevitably produces, by loss of function mutations, cheaters that do not secrete. Those 'somatic' mutants often grow faster than their secreting progenitors, reducing the aggregate secretion rate and the ability of the aggregate to control its environment. The ultimate benefits of secretion depend on how the inevitable internal competition from somatic mutants affects the birth and death components of fitness, how rapidly a population sends out successful dispersers to colonize new locations, and how long a population survives in its current location.

By this view, cheaters that arise by mutation impose an inevitable tax on multicellular cooperation. The problem concerns how the magnitude of this tax grows over time in relation to the multicellular aggregate's rates of birth and death.

2. SECRETOR–CHEATER DYNAMICS

Secretion provides benefits by changing the environment to enhance growth or survival. Against these benefits, secretors can be outcompeted by cheaters that do not secrete. In addition, we must consider the rate of secretion: presumably, faster secretion may, up to a point, confer greater benefits, but faster secretion may also impose higher costs in terms of growth or survival. Thus, I consider secretion as a quantitative trait, and consider how different rates of secretion may be favoured in various environments. Cheaters are just the endpoint of a continuum at which the secretion rate goes to zero.

A full model of secretor–cheater dynamics can become overwhelmingly complex if we take into account all possible factors. Thus, we must seek an intermediate level of complexity: enough detail to provide insight, but not so much that the complexity overwhelms our ability to extract the main qualitative insights.

I build the model in two steps. Developing the model in steps makes it easier to read the equations and highlight the main points.

The first step uses the classical logistic equations for the growth of two populations in competition. In this case, the competition is between secretors and cheaters. In the second step, I add the consequences of secretion for growth. In particular, secretion alters the environment to allow a higher population size of microbes. I also include a mutation rate that transforms a small fraction of secretors into loss of function cheaters.

The basic logistic equation for the dynamics of the cheater (non-secretor) type growing by itself is

$$\dot{C} = \alpha C\left[1 - \frac{C}{K}\right],$$

where $\dot{C}$ is the change in the abundance of the cheater type per unit time, α the maximum growth rate per unit time, C the abundance at time t and K the carrying capacity of the environment. Given low initial abundance, logistic growth leads to standard 'S'-shaped dynamics, in which abundance first rises at a slow rate during the lag phase, then rises rapidly in the middle exponential phase, and finally levels off during the plateau phase as the population grows to the maximum, K, that can be supported by the environment.

Similarly, we write the logistic growth of a secretor growing by itself, when secretion reduces growth by a factor $1 - \gamma$ and secretion does not have any other effect on the environment with regard to growth, as

$$\dot{S} = \alpha S\left[(1-\gamma) - \frac{(1-\gamma)S}{K}\right].$$

The combined logistic equations for the dynamics of secretors, S, and cheaters, C, are

$$\dot{S} = \alpha S\left[(1-\gamma) - \frac{(1-\gamma)S + C}{K}\right]$$

and

$$\dot{C} = \alpha C\left[1 - \frac{(1-\gamma)S + C}{K}\right],$$

where the last term in each equation accounts for the combined intensity at which the secretors, S, and cheaters, C, extract resources in relation to the carrying capacity, K. Note that secretors extract resources relatively slowly, reduced by $1 - \gamma$.

I add two additional factors to get the final equations for this section

$$\dot{S} = \alpha S\left[(1-\gamma) - \frac{(1-\gamma)S + C}{K + sK}\right] - \mu S \tag{2.1}$$

and

$$\dot{C} = \alpha C\left[1 - \frac{(1-\gamma)S + C}{K + sK}\right] + \mu S. \tag{2.2}$$

First, secretors become cheaters by losing the ability to secrete, at a rate μ, which, with proper scaling, can be thought of as the mutation rate. Second, secretion enhances the environment for the growth of the microbes, expressed by the additional component of the carrying capacity, sK, which is given by

$$sK = eK\left(\frac{\gamma S}{\phi + \gamma S}\right), \tag{2.3}$$

where eK is the maximum enhancement of the environment, γS is proportional to the amount of secreted molecules, and ϕ is the value of γS at which secretion achieves one-half of its maximal effect.

3. ANALYSIS

What conditions favour secretion? I will analyse equations (2.1) and (2.2) to gain insight into this question.

I start by summarizing the parameters of the model. I then give some examples to illustrate the dynamics. With that background, I turn to the first main analysis, in which I make some assumptions about how the dynamics of secretor–cheater abundances translates into the relative fitnesses of the types. From the relative fitnesses, I infer the conditions that can maintain secretion in the face of competition from cheaters, and I describe the magnitude of secretion that would be favoured under various conditions.

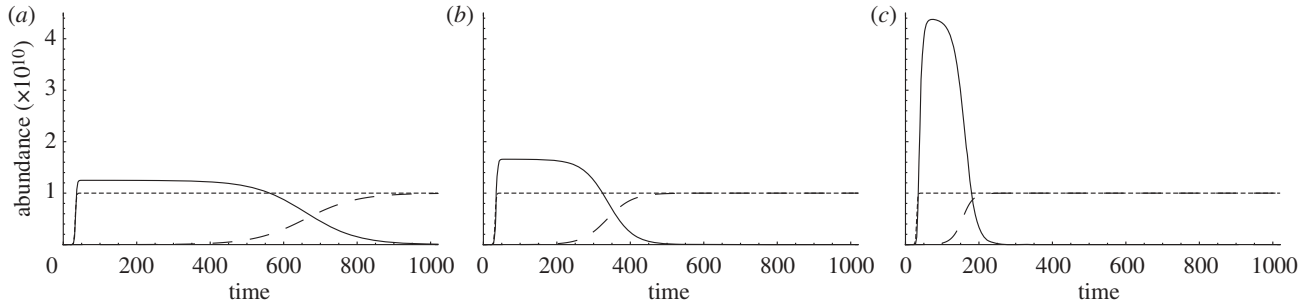

Figure 1. Dynamics of secretors (solid line) and cheaters (long-dash line) from equations (2.1)–(2.3). Initial abundances $S_0 = 1$ and $C_0 = 0$ and parameters $\alpha = \ln(2)$, $\mu = 10^{-6}$, $K = 10^{10}$, $eK = \theta K$, $\theta = 100$, and $\phi = eK/10$. The values of γ vary ((*a*) $\gamma = 0.02$; (*b*) $\gamma = 0.04$ and (*c*) $\gamma = 0.08$). The short-dash line shows that the cheater rises and holds to the carrying capacity, K, when the initial abundances do not include any secretors: $S_0 = 0$ and $C_0 = 1$. Time is measured by the number of doublings that would be achieved in the absence of competition for resources in the local patch and in the absence of a cost of secretion.

That first analysis assumes that secretion enhances the success of dispersal to new locations (birth rate), but assumes that secretion does not affect survival in the current location. In the second analysis, I assume that secretion enhances survival in the current location, but does not affect dispersal success.

The first two analyses assume that, at each location, all initial colonists are of the same type—either all secretors or all cheaters. If the initial colonists are secretors, then cheaters will arise by mutation during the growth phase. In the last analysis, I consider the consequences of mixtures during the colonization phase.

(a) *Parameters*

In equations (2.1)–(2.3), the parameter α is the maximal rate of growth. For convenience, I set $\alpha = \ln(2)$. This assumption means that time units measure the number of doublings at the maximal growth rate. By transforming the measure of time in this way, we do not lose any generality by fixing α.

The parameter μ describes the rate at which loss of function mutations change a secretor into a cheater. I use $\mu = 10^{-6}$ as a standard assumption about mutation rate. Because time is given in maximal doublings, the mutation rate is measured per maximal doubling. Mutation has significant consequence only when cheaters are absent in the initial population, because the mutation rate is so small compared with maximal growth. If cheaters are absent in the initial population, mutation quickly seeds the population with a relatively small fraction of cheaters. After that initial seeding, further mutation has almost no effect on the relative ratio of secretors and cheaters.

The parameter K sets the maximal total population size supported by the environment in the absence of secretion.

The parameter γ describes the two consequences of secretion. First, greater secretion increases γ and reduces maximal growth rate. Second, secretion enhances the environment to allow a greater total population, as described next.

The enhancement of total population size by secretion is expressed in equation (2.3). The term γS quantifies the total amount of secretion given the abundance of secretors, S. The parameter ϕ is the value of γS at which secretion has one-half of its maximal effect. Thus, the ratio $\gamma S/(\phi + \gamma S)$ gives the consequences of secretion as a saturating function of secretor abundance, S, with the ratio ranging between zero and one. The parameter eK quantifies the maximal enhancement to total population size caused by secretion. I express eK as a multiple of K, given by $eK = \theta K$. With this formulation, $\theta > 1$ is the key parameter for maximal enhancement, as long as K is sufficiently large relative to the initial population size. I use $K = 10^{10}$.

In summary, there are three key parameters: γ, ϕ, and θ. In addition, the initial abundances of secretors and cheaters, S_0 and C_0, also play an important role.

(b) *Basic dynamics*

Figure 1 illustrates some examples of the dynamics. In each case, the solid and long-dash lines show the abundances of the secretors and cheaters, respectively, when a colony is seeded with one secretor and no cheaters. The secretors grow rapidly towards the maximum sustainable population—an increased level of secretion, γ, raises the maximum by enhancing the environment. The secretors mutate to cheaters at the low rate of 10^{-6}. Those few cheaters slowly increase and eventually outcompete the secretors, because the cheaters do not pay the cost of secretion but gain the same benefit as the secretors. Higher secretion level, γ, imposes greater costs on the secretors and so allows the cheaters to increase in frequency more rapidly.

The short-dash lines illustrate the dynamics when cheaters colonize a location without any secretors. In that case, the cheaters grow quickly to the baseline carrying capacity, K, and hold that level.

Secretors always do best when they colonize a patch without cheaters. The eventual production of cheaters in an initially pure patch of secretors can be thought of as somatic mutation. Thus, we can think of the fitness of the secretors when colonizing alone as the somatic fitness of the multicellular aggregation. That somatic fitness is degraded by the somatic mutation to cheaters and the eventual dominance of the cheaters.

The extent to which cheaters degrade fitness depends on the timing of dispersal from the patch to new locations. If those dispersals—births—primarily happen early, then the tax is low for competition imposed by somatic mutation to cheaters. If births

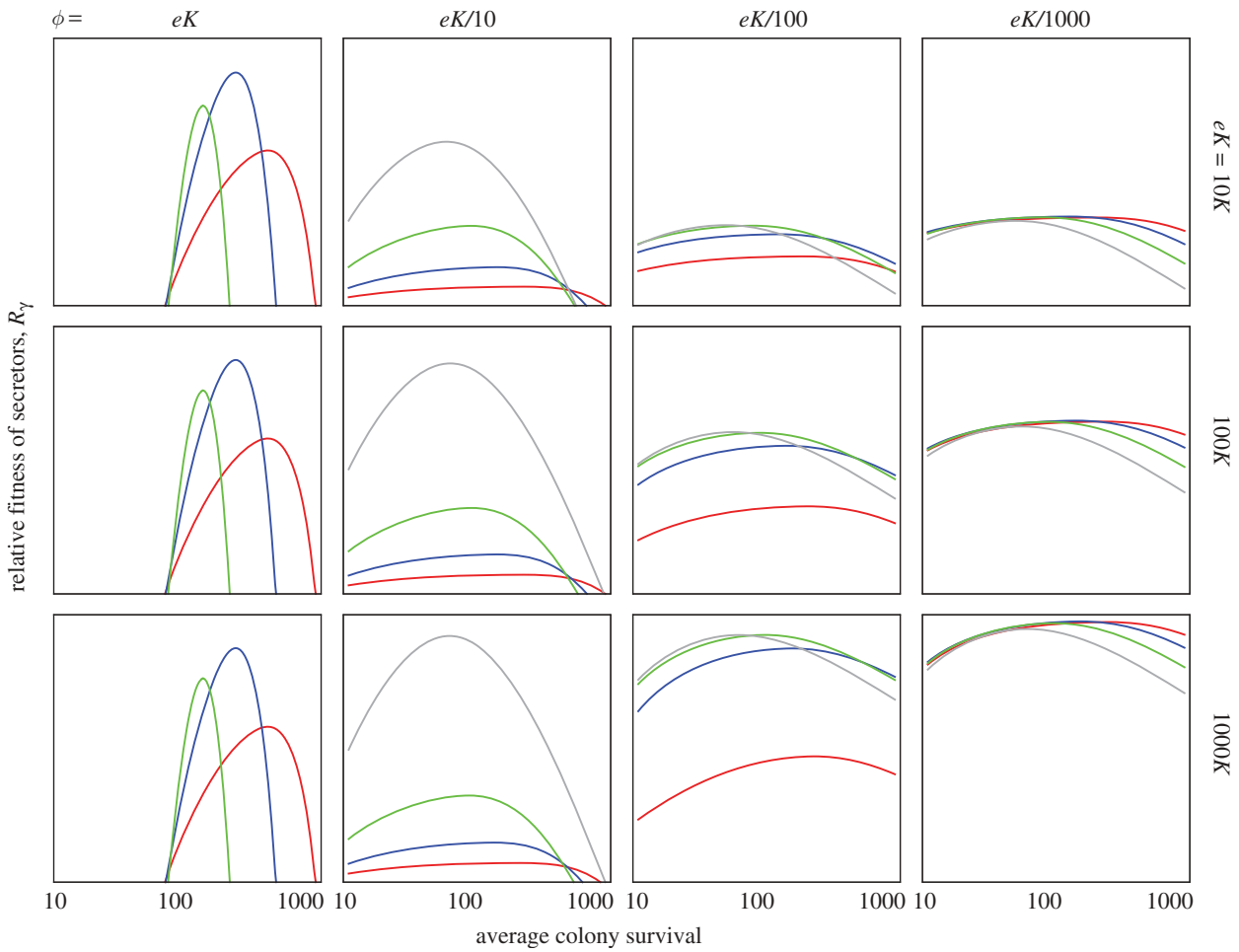

Figure 2. Fitness of secretors compared with cheaters when the rate of colony survival is constant and the benefits of secretion accrue to dispersal (birth). Average colony survival, $1/\delta$, is scaled logarithmically along the x-axis. The height of each curve measures the relative fitness of secretors compared with cheaters, R_γ, according to equation (3.1). The low point in each panel is $R_\gamma = 0$, at which the fitnesses of secretors and cheaters are equal. The colours red, blue, green and grey correspond, respectively, to secretion levels, γ, of 0.01, 0.02, 0.04 and 0.08. The columns show different levels of ϕ, the amount of secreted substance at which one-half of the maximal benefit is obtained, expressed in relation to the maximum enhancement caused by secretion, eK. The rows show different levels of eK. The highest curve at each colony survival level indicates the level of secretion, γ, favoured by natural selection among the alternatives shown. When no curve appears at a particular x value, secretion cannot be maintained for the values of γ examined, and cheaters may dominate the population. The scaling of height, R_γ, varies across columns, with maximum values from left to right of 0.016, 2, 10 and 10.

mostly happen late, then the tax on secretion is high, and the global population may not maintain secretors. For secretors to be maintained in the global population, they must have a higher fitness when they colonize by themselves than the cheaters have when they colonize a patch by themselves. Otherwise, initially purely cheating patches outcompete initially purely secreting patches, and the secretors would inevitably decline to extinction in the global population.

To make the comparison between the fitnesses of initially pure secretor patches and initially pure cheater patches, we have to make some additional assumptions about how the dynamics within a patch translates into fitness. The next two sections compare alternative assumptions about fitness.

(c) *Secretion enhances birth rate*

To translate the dynamics within patches into fitness, we have to make assumptions about birth and death rates. Fitness is the sum, over each point in time, of the product of surviving to that point in time multiplied by the births produced at that time (Fisher 1958). I define birth as the number of dispersers from the focal patch that colonize new patches. Death is the probability of extinction of the local patch.

Combining terms, fitness is

$$w = \int_0^\infty L(t)M(t)\mathrm{e}^{-\lambda t}\,\mathrm{d}t,$$

where $L(t)$ is survival to time t, and $M(t)$ is the number of births per unit time at time t. The term $\mathrm{e}^{-\lambda t}$ discounts births at time t by the amount of global population growth, because a single birth in a larger population has less consequence. Here, the population grows at rate λ, so population size is proportional to $\mathrm{e}^{\lambda t}$, and the discount is the reciprocal of that measure of population size (Fisher 1958).

In this section, I assume a constant death rate, δ, so that $L(t) = \mathrm{e}^{-\delta t}$ and $L(t)\mathrm{e}^{-\lambda t} = \mathrm{e}^{-(\delta+\lambda)t}$, showing that

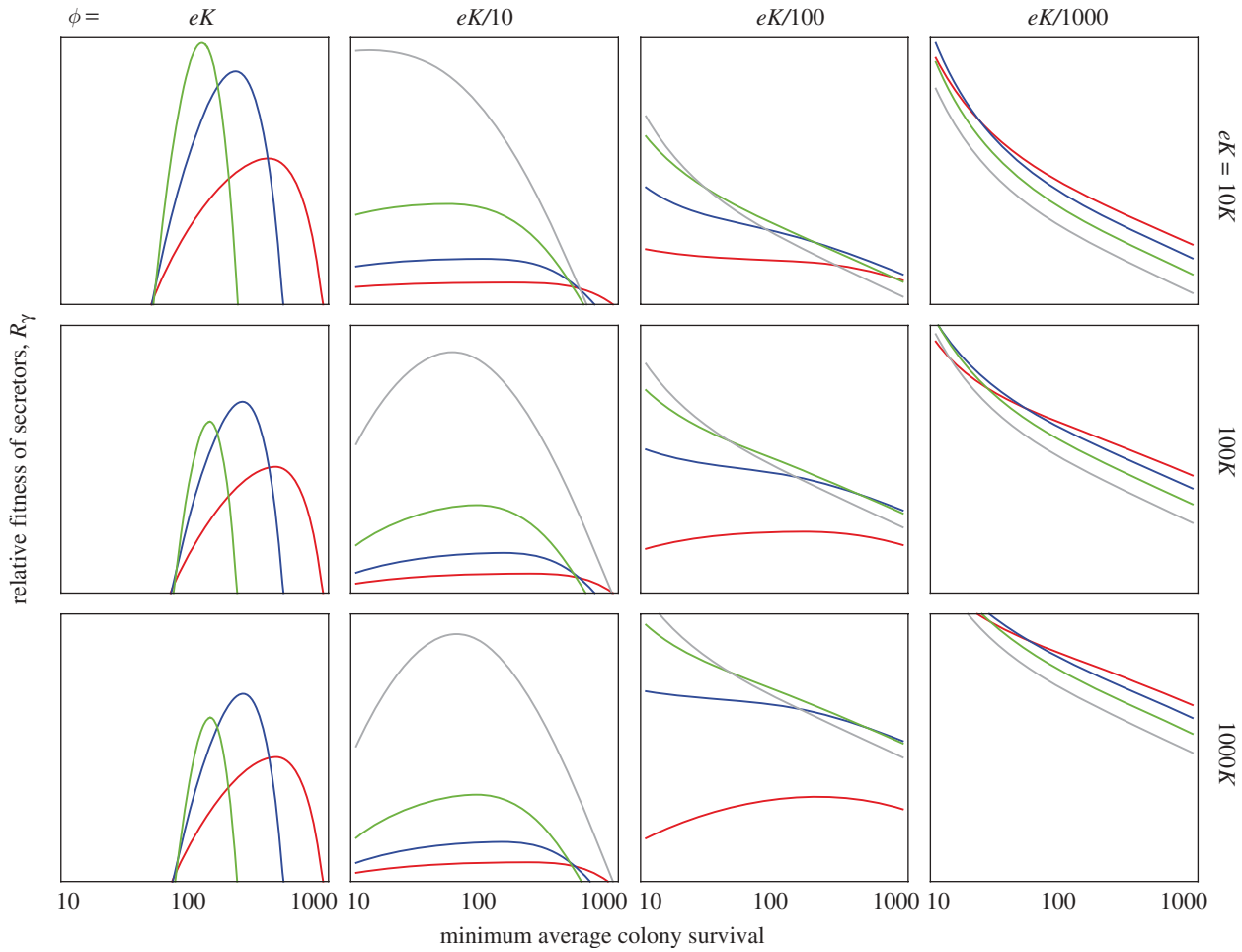

Figure 3. Fitness of secretors compared with cheaters when the dispersal (birth) rate is constant and the benefits of secretion accrue to colony survival. This figure has the same setup as figure 2, except that the x axis shows minimum average colony survival, $\log_{10}(1/\delta)$, whereas actual survival can be enhanced by increased abundance. The scaling of height, R_γ, varies across columns, with maximum values from left to right of 0.02, 2, 15 and 15.

death rate, δ, has the same consequence as a discount for population growth, λ. For convenience, I assume $\lambda = 0$ and ascribe the full effect to death. For birth, I assume $M(t)$ is proportional to abundance, under the assumption that greater abundance leads to a higher probability of successfully colonizing another patch. With these assumptions, total secretor fitness over the full lifetime of a single patch is

$$w_S = \int_0^\infty e^{-\delta t} S(t)\, dt,$$

where $S(t)$ is secretor abundance at time t. When a patch starts with a single secretor, $S_0 = 1$ and $C_0 = 0$, then w_S measures the lifetime somatic fitness of a multicellular secretor colony, accounting for the somatic tax of mutation to cheaters and their eventual dominance.

The magnitude of w_S tells us little by itself. Instead, we need to know the relative value of the lifetime somatic fitness of a multicellular secretor colony, w_S, relative to the lifetime fitness of a colony initiated by a single cheater cell,

$$w_C = \int_0^\infty e^{-\delta t} C(t)\, dt,$$

where $C(t)$ is cheater abundance at time t, and this measure assumes $S_0 = 0$ and $C_0 = 1$.

Define the lifetime fitnesses of secretors relative to cheaters as

$$R_\gamma = \log_2\left(\frac{w_S}{w_C}\right), \tag{3.1}$$

where the γ subscript denotes the level of secretion for the secretors. For $\gamma = 0$, we obtain $R_0 = 0$, because the fitness of secretors that do not secrete equals the fitness of cheaters. For secreting to evolve at level γ, we must have $R_\gamma > 0$, that is, the secretors must have higher fitness than the cheaters.

The level of γ that maximizes R_γ is favoured by natural selection. With the target of maximizing R_γ, we can now look at the values of R_γ under various assumptions.

In figure 2, each panel illustrates, by different colours, the different levels of secretion in proportion to γ. The highest curve in each panel indicates the evolutionarily favoured level of secretion. When all of the curves dip below the lowest level of $R_\gamma = 0$, then secretion cannot be maintained for the values of γ examined, and cheaters may dominate the population. Overall, the figure shows that the evolutionarily favoured level of secretion depends most strongly on

the interaction between two factors: first, the length of colony survival, given as $1/\delta$ along the x-axis of each panel; second, ϕ, the abundance at which secretion has one-half of its maximum effect, varying along each column of panels.

(d) *Secretion enhances survival*

In this section, I assume that colony survival increases with abundance, expressed by reducing the death rate at any time to

$$\delta\left(1-\frac{A(t)}{eK}\right),$$

where $A(t)$ is abundance at time t. By contrast, dispersal depends only on abundance being above a minimum threshold such that, for abundance $A(t)$, the birth rate is $M(t)=F[A(t)]=1$ if $A(t)>0.1K$, and zero otherwise. Thus, total secretor fitness over the full lifetime of a single patch colonized solely by secretors is

$$w_S=\int_0^\infty e^{-\delta(1-S(t)/eK)t}F[S(t)]\,dt,$$

with corresponding expression for lifetime cheater fitness in patches colonized solely by cheaters as

$$w_C=\int_0^\infty e^{-\delta(1-C(t)/eK)t}F[C(t)]\,dt,$$

using $\lambda=0$ in both cases.

Putting these fitness expressions in equation (3.1), we can calculate the relative fitnesses for different levels of secretion. Figure 3 shows the results. There are two differences compared with figure 2. First, the x-axis shows minimum average colony survival, $1/\delta$; actual survival can be enhanced by increased abundance. Second, the fitness calculations use the new definitions in this section that relate abundance to survival.

The results in figure 3 are roughly similar to figure 2. The main difference is that, when secretion is more effective at lower abundance (smaller ϕ in the right columns), then lower secretion rates are more strongly favoured.

(e) *Mixed colonizations*

My fitness measures quantify the lifetime success of a colony initiated by a pure clone of either a secretor or a cheater type. With no mixing upon initiation, the highest lifetime colony success predicts the level of secretion, in proportion to γ, favoured by natural selection.

Mixed initiation reduces the favoured level of secretion, because earlier competition from cheaters in the inoculum interferes with the benefits of the secretors. The consequences of mixed inoculum are often analysed in terms of kin selection: higher relatedness favours the cooperative secretors, whereas lower relatedness favours the uncooperative cheaters. That contrast is true. But emphasis on kin selection masks the fact that frequency is often a much more potent force than relatedness (Ross-Gillespie *et al.* 2007). The role of frequency is particularly important when one accounts for mutation.

For example, in an initial colony with 10^6 secretors and one cheater, the secretors have essentially the same lifetime fitness as in a pure colony initiated solely by 10^6 secretors. With a mutation rate of 10^{-6}, the pure colony generates the cheater almost immediately. Thus, either initial condition is essentially the same. By contrast, starting a colony with one secretor and one cheater greatly reduces the lifetime fitness of the secretor when compared with a colony started with a lone secretor.

These frequency consequences arise independently from the consequences of kin selection, although relatedness can influence the mixtures of frequencies. Often, the frequency component will overwhelm any consequences of kin selection. This conclusion emphasizes that the direct lifetime fitness over a full life history cycle always provides the most essential measure of success (Charlesworth 1994): one must analyse kin selection within the framework of full cycle fitness (Frank 1998).

In separate papers, I jointly analyse kin selection and demography in models that apply to microbial life history (Frank 2010*a*,*b*). See also Brockhurst *et al.* (2007) for a joint analysis of demography and kin selection applied to microbes.

4. DISCUSSION

Suppose one knows the way in which different phenotypes affect reproductive rate. Then one can use the powerful tools of game theory and kin selection to analyse the expected outcome of natural selection. However, the very power of those analytical tools often leads to studies that gloss over the most important aspects of the biology. In particular, I have emphasized that the relationship between phenotype and reproductive rate can be complex. Nearly the whole of the biological puzzle is this relationship between characters, such as microbial secretion, and the dynamical processes that translate those characters into reproductive rate.

To make real progress in understanding microbial life history, one needs to embed microbial characteristics into the full cycle of dynamics over which competition, birth and death play out. The expression of fitness in its full demographic context is crucial, and the very act of trying to lay out a mathematical model for the different components of competition and fitness often leads to a clearer understanding of the key biological processes.

In this paper, I focused on microbial secretion of molecules that alter the external environment. The inherent conflict of secretion systems has been well understood: individuals that do not secrete gain the same benefits from environmental modification as do the secretors, yet those non-secreting cheaters also gain by not paying the cost of secretion (West *et al.* 2007).

The relative success of cheaters versus secretors depends on the relative frequency of the two types (Ross-Gillespie *et al.* 2007). Game theory helps to interpret this frequency dependence. Kin selection tells us how the frequencies of each type sort out into local populations. High relatedness means that

secretors associate with secretors and cheaters associate with cheaters. Such association favours the secretors, because it reduces the competition within groups faced by the secretors.

I showed that these game theory and kin selection processes are often very weak in regard to explaining the relative success of secretors versus cheaters. Instead, the key factors arise from mechanistic aspects of how secretion alters the environment and from demographic processes.

On the mechanistic side, the density of secreted molecules required to cause significant environmental change, ϕ, strongly influences relative success (see figures 2 and 3). The quantification of ϕ's effect scales with the maximum change in population density, eK, that can be accomplished by secretion—which shows the importance of scaling processes in relation to demography.

More directly related to demography, rates of colony survival and reproduction strongly influence the relative benefits of secretion versus cheating (figures 2 and 3). I often expressed those survival and reproduction components of fitness at the colony level, a natural outcome of the fact that the consequence of secretion with regard to environmental modification is a colony attribute.

These ways in which the mechanisms of secretion interact with demography over the full life cycle of the colony led me to emphasize *cycle fitness* (Frank 1998). To obtain a measure of fitness that is useful, one must analyse the characteristics in regard to the full dynamics of the life cycle. From this perspective, I argued that we can usefully think of the full colony life cycle as a multicellular aggregation derived from the small number of colonizing progenitors. Cycle fitness is then the fitness expressed through the 'somatic' and reproductive consequences of the colony. If the full cycle fitness of a colony founded by cheaters is greater than the full cycle fitness of secretors, then secreting cannot be maintained.

The importance of somatic competition from cheaters in an initially purely secreting colony suggests that the secretors would gain by reducing the costs imposed by somatic competitors. Quorum sensing is one mechanism for reducing cost, in which secretion is only expressed when the density of secretors is sufficiently high to have a strongly beneficial effect (Waters & Bassler 2005). This delay in the expression of secretion reduces the cost of secretion, by turning off the secretion pathway until late in the development of the multicellular aggregation. However, quorum sensing itself is subject to cheating by individuals that, on the one hand, do not secrete the signal used to communicate density and, on the other hand, still can take full advantage of the signal (West *et al.* 2007). Perhaps cheaters against quorum sensing impose less cost than do cheaters against secretion to modify the environment.

Another way to reduce the cost imposed by cheaters would be a reduction in the rate at which cheaters arise by mutation. There is, at present, no evidence for such a mechanism. One possibility would be redundant genetic control of secretion, so that loss of secretion would occur only after each of the redundant controls was knocked out by a loss of function mutation. The multiple mutational steps required to create somatic cheaters would greatly help to protect the benefits of multicellular cooperation, in the same way that multiple protections against cancer reduce the costs of somatic mutation (Nunney 1999; Frank 2007).

Waters & Bassler (2005) summarize a few cases of potentially redundant control of quorum sensing. However, complex integration of signalling information probably arose for reasons other than protecting against somatic mutation to cheating. If redundant controls to reduce the cost of somatic mutation do not exist, then we are left with the puzzle of why redundant controls do not arise. Perhaps the tax imposed by somatic mutation is typically not strong enough to favour redundant controls.

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