Evolutionary dynamics of a selfishly spreading gene that stimulates sexual reproduction in a partially sexual population

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Abstract

The ability of selfishly spreading DNA sequences to invade host populations is intimately bound up with sex. In the absence of sexual reproduction, an element that lowers the fitness of its host and which is initially found in only some of the population will inevitably be lost by natural selection. This will occur even if the element can spread selfishly in the genomes of those individuals which initially possessed it. Here, we create a model in which such a gene is introduced into a population in which individuals sometimes reproduce sexually and sometimes asexually. The element can raise the level of sexuality in its bearers. There is selection against those individuals with the gene (i.e. it is selfish), and a further selective cost to sexual reproduction. The dynamics of the model that arises from these simple assumptions are remarkably complex, with fixation or loss of the selfish gene, unstable and stable equilibria, and effective neutrality all being possible dependent on the parameter values. A selfish gene that increases the level of sexuality of its bearers will tend to have a higher likelihood of invading a host population, and faster spread, but a lower likelihood of spreading to fixation, than an equivalent gene with no effect on sex.

Keywords:
facultative sex;
population genetics;
selfish DNA.

Introduction

Many types of DNA elements seem to be present in genomes not because of the improvement that they create in the fitness of the organism, but rather because they undergo a process which causes them to over-replicate relative to the rest of the genome. The ability of such elements to spread is very strongly dependent upon sexual reproduction (Hickey, 1992). In the absence of sex, any clonal individuals which lack selfish elements altogether will have an advantage relative to individuals which possess the elements, and this advantage will cause the elimination of the clones with selfish elements from the population. This elimination will be speeded up, rather than diminished, by the selfish spread of the elements through the genomes of individuals which initially possessed them.

The spread of a selfish element requires that there be at least a low level of sex in individuals lacking the element. In a totally asexual population, the element could never invade and selection against its bearers would eliminate it. Because the spread of a selfish element which invades the homologue is conditional upon it being found in the heterozygous state in a diploid, then the lower the level of sexuality, the less effective the selfish element will be in spreading through the population (Burt & Trivers, 1998).

In many organisms, particularly single celled eukaryotes, only a fraction of the reproduction is sexual; indeed, the common ancestor of the eukaryotes may well have been a facultative sexual (Dacks & Roger, 1999). As much of the benefit of sex can be gained even if sex is only occasional, the rarity of facultative sex is a conundrum (Green & Noakes, 1995). Facultative sex may be unstable, and liable to collapse into asex or obligate sex (Peck & Waxman, 2000).

Here, we consider a non-Mendelian element, such as a cytoplasmic gene or a homing endonuclease, in a partially sexual population. We modelled the spread of
a selfish element that can stimulate sexual reproduction in its host, and find that the dynamics of spread of the element are complex. As expected, the selfish element can spread to fixation or be lost from the population depending on the parameters of rates of sexuality and of selection. However, we also find that, depending on the parameter values, such a gene can create a stable polymorphism, or an unstable polymorphism, or can be effectively neutral.

The model

We imagine that there exists a polymorphism with regard to the presence or absence of a selfish element. The frequency of the selfish element is \( p \). Individuals lacking the selfish element have a probability \( t \) of reproducing sexually, whereas individuals with the selfish element have a probability \( x + t \) of reproducing sexually. \( x \) thus must fall in the range from 0 to \( 1 - t \).

We assume that there is a cost of sex, such that sexual individuals have a fitness of \( 1 - c \) relative to the fitness of nonsexual individuals. There is also assumed to be a metabolic cost for the selfish element which is independent of sex, such that individuals with the element have a fitness of \( 1 - s \) relative to those that lack it.

Mating is at random, between the gametes of sexual individuals, and diploids are formed. If a diploid is either homozygous or heterozygous for the selfish element, all its offspring have the selfish element. There are no degrees of selfish element effect. The element is assumed to have complete efficiency of transfer to all offspring and is never spontaneously lost from any host.

The proportion of the population that is sexual is \( xp + t \). Only matings between two sexual individuals which lack the selfish element will produce offspring without the element. Thus, among those individuals that are sexually produced, the proportion that have the selfish element is

\[
\frac{[(xp + t)^2 - (1 - p)^2t^2]/(xp + t)^2}.
\]

The proportion of all cells in the population that are both sexually produced and emerge having the selfish element is \( [(xp + t)^2 - (1 - p)^2t^2]/(xp + t) \).

However, these cells will suffer a selection of \( c \) (experienced by all sexually produced offspring), whereas a proportion of \( p(1 - x - t) \) of the population after reproduction will have the element but will not be sexual.

Thus, the proportion of cells which have the selfish element, after the sexual phase, or \( p' \), is equal to

\[
p' = \frac{p(1 - x - t)(xp + t) + [(xp + t)^2 - (1 - p)^2t^2] }{(1 - c)}/[1 - c(xp + t)](xp + t)\].
\]

But, there will also be selection of strength \( s \) against individuals with the selfish element. The value of \( p \) after this selection, or \( p'' \) is given by

\[
p'' = \frac{p'(1 - s)}{(1 - p')s}.
\]

and the change in \( p \) over one generation, \( p'' - p = \delta p \) is given by

\[
\delta p = \frac{[p'(1 - s) - p(1 - p')s]}{(1 - p')s}.
\]

Substituting the value of \( p' \) given in (1) in (2), and re-arranging gives

\[
\delta p = \frac{p(1 - p)[ct^2(2s - 1) + xt(1 - s) + t^2(1 - s) + 2ctx(s - 1) - ts - p(x^2c + xs + sc^2 - stx - s^2 - scx^2)]/[t(1 - tc) + p(x + 2ctx^2 + 2ctx - 2tcx - xs - st^2 - st)}
\]

\[
- p^2(x^2c + xs + sc^2 - stx - s^2 - scx^2)]
\]

(3)

An equilibrium value for \( p \) would be one which gives \( \delta p = 0 \). The formula also allows the calculation of the rate of spread of the selfish element.

The denominator of (3) will almost always be positive. Equation (1) gives a formula for \( p' \), which will be a positive number in the range from 0 to 1. The denominator of this \([1 - c(xp + t)](xp + t), \) cannot be negative, and will be zero only if \( xp + t \) is zero (i.e. no sex takes place), or \( c(xp + t) \) is one (i.e. all individuals are sexual, and the cost of sex is 100%). Thus, given that neither of these situations hold, \( p' \) can be represented by the ratio of two positive numbers \( a/b \) and \( a \leq b \). The denominator in (2) is \( (b - as)/b \) and that in (3) is \( b - as \). Thus, provided that \( s < 1 \), and/or \( p' < 1 \), the denominator in (3) will be positive.

Results

This unexpectedly complicated formula (3) implies that there are three values of \( p \) which give \( \delta p = 0 \). An equilibrium value for \( p \) is one that makes the numerator zero. These include, as expected, \( p = 0 \), and \( p = 1 \), corresponding to the absence and the fixation of the selfish element, respectively. In addition, \( \delta p = 0 \) when

\[
p = \frac{[ct^2(2s - 1) + xt(1 - s) + t^2(1 - s) + 2ctx(s - 1) - ts]}{[(x^2c + xs + sc^2 - stx - s^2 - scx^2)/t]}.
\]

(4)

Clearly, there can be many combinations of \( c, t, s, \) and \( x \) which will give a value of \( p \) in (4) which falls in the range from 0 to 1. This then corresponds to a third equilibrium value for \( p \), in addition to 0 and 1. Given that the denominator of (3) is positive, the sign of \( x^2c + xs + sc^2 - stx - s^2 - scx^2 \) determines whether an equilibrium value of \( p \) is stable or unstable, with a positive sign generating a stable equilibrium and a negative sign generating an unstable equilibrium. This is because, if \( x^2c + xs + sc^2 - stx - s^2 - scx^2 \) has a positive sign, increasing \( p \) will be decreasing \( \delta p \). Thus, if \( p \) is greater than its equilibrium value, \( \delta p \) will be negative, and \( p \) will be returning to its equilibrium value with time, i.e. the equilibrium will be stable. Conversely, for a negative value of \( x^2c + xs + sc^2 - stx - s^2 - scx^2 \), then, if \( p \) is greater than its equilibrium value, \( \delta p \) will be positive,
and \( p \) will be moving further away from its equilibrium value the equilibrium is unstable. For example, if \( x = 0.1, t = 0.1, c = 0.1 \) and \( s = 0.12 \), the equilibrium value of \( p \) is 0.291, and the equilibrium is stable. If \( x = 0.1, t = 0.7, c = 0.0 \), and \( s = 0.55 \) the equilibrium value of \( p \) is 0.5257 and the equilibrium is unstable.

It is possible to find values of \( c, t, x \) and \( s \) which leave \( x^2c + xs + sc^2 - stx - st^2 - scx^2 \) equal to zero, which means that the ‘fitness’ of the selfish element is frequency independent. It is also possible to find combinations of values of \( c, t, x \) and \( s \) which not only leave \( x^2c + xs + sc^2 - stx - st^2 - scx^2 \) equal to zero, but \([x^2(2s-1) + xt(1-s) + t^2(1-s) + 2ctx(s-1) - s]\) [the numerator in (4)] equal to zero also. An example of such a set of values is \( x = 0.1, t = 0.5, c = 0.6667 \) and \( s = 0.1667 \). This set of parameter values will ensure that any \( P \)-value is a neutral equilibrium. Thus, remarkably, given the strength of the forces involved (e.g. selection against sexual individuals of 66.7% and selection against individuals with the selfish element of 16.7%), the polymorphism will be subject to random drift only.

In order to clarify why there is this unexpected range of outcomes, we have explored the areas of parameter space which result in stable and unstable equilibria, and fixation and loss of the element.

Figure 1 shows the outcomes expected for different values of \( t \) (the underlying rate of sexuality), but in each case with a cost to sexuality, \( c \), of 0.1. Figure 1a shows the situation when \( t = 0.1 \). Depending on the \( x \) (elevation of sexuality) and \( s \) (selection) values of an introduced selfish element, there can be different outcomes. For low \( s \) and low \( x \), the element will spread to fixation. However, with higher values of \( x \) and of \( s \) there will be a stable equilibrium, where the selfish element can invade a
population, but cannot go to fixation. Finally, when \( s \) is high and \( x \) is low, the element will be lost: it can neither invade nor go to fixation.

Figure 1b shows the corresponding outcomes when \( t = 0.5 \). Now, with this higher underlying level of sexuality, all \( s \) values under 0.3 will result in the spread to fixation of the element, whatever the value of \( x \). Then, for low \( x \), as \( s \) increases, an unstable equilibrium will be generated, in which the selfish element cannot invade but will be fixed if it starts at a high frequency in the population. For similar values of \( s \) but high \( x \) there will be a stable equilibrium, where the element can invade but not be fixed. Finally, when \( s \) is very high, the element will always be lost. It cannot invade when rare, and cannot be fixed when common.

At first sight, Figs 1a & b are very different, but their similarities are more important than their differences. In Fig. 1a, the two lines do not cross on the \( x \)-axis, but at a point where \( x = 0.0099 \), and \( s = 0.09 \). For \( s = 0.09 \) and \( x < 0.0099 \), there is an unstable equilibrium. In each graph there is a pair of \( s \) and \( x \)-values at which the two lines cross, and this point will give a neutral equilibrium. Above this point (higher \( x \)) there is a stable equilibrium. Below this point (lower \( x \)) there is an unstable equilibrium. To the left of the point (lower \( s \)) there will be fixation of the selfish element. To the right of this point (higher \( s \)) there will be the loss of the selfish element.

Invasion and fixation of the element

Given the unexpected complexity of the complete model, it is useful to investigate the behaviour of the element at the extremes of invasion and fixation, where some simplifying assumptions can be made.

When the element is extremely rare, the chances of its meeting another infected host are negligible, and the chances of any one uninfected individual meeting an element are also negligible. The uninfected hosts pay only the cost of sex \( \alpha \). Carriers of the element pay both the cost of the element, \( s \), and a higher cost of sex, \( c(t + x) \), but gain \( (1 - s)(1 - c)(t + x) \) new hosts per generation.

The element will therefore invade if

\[
1 - \alpha t < (1 - s)[1 - t - x + (1 - c)(t + x)],
\]

which rearranges to \( s < \frac{\alpha t + (t + x)(1-2c)}{1 + (t + x)(1-2c)} \).

Increasing \( x \) at this stage always makes the threshold level of \( s \) lower, allowing an element to spread that would otherwise be lost. It will always favour the invasion of the element to stimulate sexual reproduction in the host.

When the element is extremely common, any uninfected host that is sexual will be infected. Uninfected hosts are therefore lost at a rate equal to their level of sexuality \( t \). The infection of new hosts per element is now negligible, and the infected hosts now suffer selection against the element at level \( s \) plus the higher cost of sex. The element can spread all the way to fixation only if:

\[
1 - t < (1 - s)[1 - t - x + (1 - c)(t + x)],
\]

which is equivalent to

\[
s < \frac{[t - c(t + x)]}{[1 - c(t + x)]}.
\]

Increasing sex at this stage will always be deleterious to the spread of the element.

Fate of the element around the neutral point

Figure 2 shows the dynamics of element frequency at and around the point of effective neutrality in Fig. 1b. At this point \((x = 0.40909, s = 0.45)\), element frequency is constant, whatever the starting value of \( p \) (centre). Rapid fixation (left) or loss (right) of the element occur if the value of \( s \) changes. If \( x \) is increased to 0.42909 (top), the element can reach a stable equilibrium from an initial frequency of \( 10^{-6} \) within 4000 generations, and takes around 9000 to fall from \( 1 - 10^{-6} \) to the same level. There is a similar equilibrium level of \( p \) when \( x \) is lower than the neutral point (bottom), but this equilibrium is unstable: the element is lost if \( p \) is lower than 0.81814, and fixed if \( p \) is higher than this critical value.

Equilibrium values of \( p \) and effects on population fitness and sex

The presence of the selfish element will affect the level of sex in the population, and also population fitness, dependent on its frequency. The average fitness of the population, compared with a population lacking the element, is

\[
(1 - tc - sp - pxc)/(1 - tc).
\]

The amount of sex in the population, compared with a population lacking the element, is

\[
(t + xp)/t.
\]

Figure 3 shows the stable and unstable equilibrium values of \( p \), and the effect of the element on the average sexuality and fitness of the population, for the same two values of \( c \) and \( t \) considered in Fig. 1. In both cases, the element is fixed over some of the parameter space. In this region, all members of the population have the element: population sexuality and fitness are simply proportional to \( x \), the amount of extra sex imposed, and the graph shows this slope. Where the element is lost, it can have no effect on the sexuality or fitness of the population and consequently these areas of the graph are flat.

In the areas of stable or unstable equilibria, the situation is more complicated. The extra sex imposed by the element affects the sexuality of the population in two ways: indirectly, by affecting the frequency of the element, and directly, by increasing the sexuality of its bearers. Likewise, the cost of the element affects both the fitness and the frequency of its carriers.
The area of stable equilibrium is seen most clearly in Fig. 3a–c. Figure 3a shows the equilibrium frequency of the element. Without any extra sex imposed by the element (at $x = 0$), there is a sharp cut-off point in the value of the cost of the element $s$, above which the element is lost and below which it is fixed. Introducing extra sex (raising $x$) makes this a shallower curve; some elements that could otherwise become fixed, and many that would otherwise be too costly to persist, can reach stable intermediate frequencies in the population. The equilibrium frequency falls with increasing $s$, and rises with $x$. Extra sex, therefore, makes the element more frequent as well as more powerful, and population sexuality can be raised far above its original level (Fig. 3b). Extra sex here lowers population fitness by increasing the frequency of the costly element. Increasing $s$, the cost of the element, lowers the fitness of carriers, but also lowers the frequency of the element so that population fitness increases with $s$ (Fig. 3c).

In the area of unstable equilibrium (best seen in Fig. 3d–f), the effects of $s$ and $x$ on equilibrium frequency are reversed: the unstable equilibrium frequency of the element increases with $s$ and decreases with $x$. The two effects of $x$ now influence population sexuality (Fig. 3e) in opposite directions: carriers of the element have more sex, but there are less of them. Here, intermediate values of $x$ have the greatest effect on population sexuality for any given value of $s$. Population fitness falls sharply as $s$ increases, because this increases the frequency of the element as well as lowering the fitness of carriers. Increasing $x$ still imposes an extra cost of sex, but decreases the frequency of the element. In the area of unstable equilibrium shown in Fig. 3f, intermediate values of $x$ have the greatest effect on population fitness.

At the point of effective neutrality, population sexuality and fitness would be subject to drift in the same way as element frequency.

**How extra sex affects rates of spread**

Figure 4 shows the spread of the element for different values of $x$ when $c = t = s = 0.1$. Without imposing extra
sex \( (x = 0) \), the element cannot invade the population. With \( x = 0.1 \), the element can spread slowly; where \( x = 0.2 \) it spreads faster and to a higher equilibrium value. For \( x = 0.2 \) and above, further increasing \( x \) now reduces the equilibrium frequency of the element; however, the equilibrium is still being reached more quickly, in around 100 generations for \( x = 0.9 \).

**Discussion**

It seems that, for a selfish element, increasing the level of sexuality of its bearers will increase the probability that it can invade a population. However, it generally decreases the probability that it can spread to fixation in the population once it is established. This makes intuitive sense: a very rare element is guaranteed to infect a new individual if its host is sexual, and its rate of spread will be proportional to the amount of sex it experiences. Imposing extra sex is, therefore, always advantageous to invasion. However, when the element becomes more common, the chance of infecting a new host is less, and eventually may no longer offset the cost of sex.

As a result, this model often allows selfish elements to exist at stable intermediate frequencies. This is in contrast to many previous models of selfish spread in which elements must either fix or be lost. Stable polymorphic levels of selfish element infection are seen in nature: they could be because of population structure or to coevolution between element and host (Hatcher, 2000), but it is also possible that, as in this case, there could be frequency dependent advantages for the element due to its effect on the host.
Selfish elements are likely to have profound effects on the evolution of genetic systems (Hurst, 1992). Non-Mendelian elements are known to affect host biology in intricate ways, including tampering with the sex determination of their hosts, and can cause parthenogenesis or cytoplasmic incompatibility. They are known, in some cases, to influence the degree of sexuality of their hosts: bacterial conjugation uses plasmid-encoded genes (Hickey, 1992), and a mitochondrial plasmid in the slime mould *Physarum polycephalum* forces fusion of otherwise asexual mitochondria (Kawano et al., 1991).

It appears that selfish elements that stimulate sexuality in their hosts can spread to high frequencies even if very deleterious, and could affect the frequency of sex in a population in which they arose. Such conflicts between selfish elements and their hosts over levels of sexuality could contribute to the instability of facultative sex.

Where populations of a facultative sexual species differ in their level of sexuality, selfish elements should be considered a potential cause and could be detected by their non-Mendelian inheritance.

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**References**


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