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# Why are equally sized gametes so rare? The instability of isogamy and the cost of anisogamy

Hiroyuki Matsuda[1]* and Peter A. Abrams[2]

[1]*Ocean Research Institute, University of Tokyo, Minamidai 1-15-1, Nakano-ku, Tokyo 164-8639, Japan and* [2]*Department of Zoology, University of Maryland, College Park, MD 20742, USA*

## ABSTRACT

The aim of this study was to determine the circumstances in which equally sized gametes (isogamy) can be maintained in a population that has already evolved mating types. We analysed the evolutionary dynamics of gamete sizes when there are two mating types. The models and conclusions differ depending on: (1) whether size-determining loci are linked to loci-determining mating types; (2) whether gamete size does or does not affect gamete success; and (3) whether viable mutations with large effects on size are possible or not. In all cases, the reproductive success of a zygote depends on the sum of the sizes of the two uniting gametes, and the number of gametes produced is inversely proportional to gamete size. When size is not closely linked to mating type, it is possible for isogamy to be stable under a wide range of conditions, particularly when mutations of large effect are deleterious. However, when size is linked to mating type, isogamy can only be stable when there are significant direct effects of size on gamete survival and mating success; even then, it may only be locally stable. When isogamy is stable, it results in a lower rate of increase than in asexual forms and, in some cases, can be associated with a lower rate of increase than anisogamous forms of the same species. Thus, the cost of anisogamy is generally less than two-fold. Different explanations for the rarity of isogamy are compared.

*Keywords*: anisogamy, convergence stability, cost of sex, dimorphism, evolutionary stability, isogamy, mathematical model.

## INTRODUCTION

Most multicellular organisms have anisogamy, or different mean sizes of gametes of different sexes or mating types. It is generally believed that isogamy, or equal gamete sizes of different mating types, occurred in the first sexual organisms. Although there are many examples of isogamy among algae, fungi and protozoans (reviewed in Bell, 1982; Hoekstra, 1987), anisogamy has a much wider taxonomic distribution. Attempts to use evolutionary theory to understand this restricted distribution have met with limited success, as have attempts to understand the distribution of isogamy within groups with both isogamous and anisogamous species. Bell (1978, p. 269) concluded that 'exceptions are so numerous as to constitute a serious obstacle to full acceptance of the synthetic theory, despite the general

* Author to whom all correspondence should be addressed. e-mail: matsuda@ori.u-tokyo.ac.jp

trend of the data', and Hoekstra (1987, p. 91) summed up the comparative evidence as being 'a bit disappointing'. We use a series of mathematical models to help understand what might account for the comparative scarcity of isogamy. The models also produce some new hypotheses that may help explain some of the anomalies in the comparative data.

Most researchers believe that the evolution of mating types preceded the evolution of gamete size dimorphism (Hoekstra, 1987; Maynard Smith and Szathmáry, 1995). Hoekstra (1982, 1987) has proposed several possible mechanisms for the evolution of mating types in a randomly mating population. The simplest assumes that gamete adhesion was initially brought about by two complementary molecules. Each mating type is formed by the loss of one of the two types of molecule. A genotype with both adhesion molecules can eventually be excluded if it has difficulty adhering to an individual with only one type of molecule, or if it pays a high cost for producing both molecules. This will result in two mating types if selection eventually reduces recombination between the two adhesion loci to zero. Maynard Smith and Szathmáry (1995) interpreted these conditions as being relatively easy to satisfy, although Hoekstra (1987) expressed some reservations. Here, we will simply assume that gamete types evolved before size dimorphism. This is supported by the fact that most isogamous species (as well as all anisogamous ones) have well-defined mating types (Hoekstra, 1987).

Explaining the comparative scarcity of isogamy is equivalent to explaining the comparative prevalence of anisogamy. Anisogamy is thought to be the origin of all other forms of sexual dimorphism and asymmetry in gender. Anisogamy is also widely believed to be the basis of the two-fold cost of sexual reproduction (Maynard Smith, 1978; Bulmer, 1994). The evolution of anisogamy has been explained primarily by two types of theories (Bulmer, 1994). The first are based on the co-evolution of the sizes of gametes of two sexes or mating types, given that more small gametes can be produced, but the fitness of a zygote is either an increasing or unimodal function of its size. Parker *et al.* (1972) developed a simple evolutionary game theory model of this scenario, which has been extended by Bell (1978), Charlesworth (1978), Maynard Smith (1978, 1982), Hoekstra (1980, 1987), Parker (1982), Cox and Sethian (1985) and Bulmer (1994). The second type have been adapted to prevent competition between cytoplasmic symbionts (Cosmides and Tooby, 1981; Hurst and Hamilton, 1992) or parasites (Hoekstra, 1990; Hurst, 1990). Uniparental cytoplasmic inheritance prevents destructive competition between unrelated symbionts transmitted in the gametes of the two parents. The small size of one gamete type may be a side-effect of excluding cytoplasmic elements from that gamete type. At present, the relative importance of these two mechanisms for the evolution of anisogamy is unknown. However, it is important to note that uniparental inheritance of organelles has been achieved without gamete size dimorphism in some protists (Whatley, 1982; Maynard Smith and Szathmáry, 1995). It is therefore unlikely that ensuring uniparental cytoplasmic inheritance can be the universal explanation for anisogamy.

In this article, we focus on the first potential mechanism for the evolution of anisogamy – the co-evolution of gamete sizes. Thus, all of our models are modifications of the basic framework introduced by Parker *et al.* (1972) and further developed by Maynard Smith (1978). This model assumes that the population initially lacks mating types. It is based upon two effects of larger gamete size on fitness: a negative effect due to decreased gamete number and a positive effect due to increased zygote size. The model that we analyse in most detail includes the same effects on fitness, but assumes that two mating types exist and that size-determining loci may be closely linked to the loci that determine mating type. Although

Charlesworth (1978) analysed models with two mating types, he assumed a zygote fitness function that precluded isogamy. Our work also differs from that of Parker *et al.* (1972) and Maynard Smith (1978) in considering contexts in which mutations with large effects on gamete size either do not occur, or, if they do occur, result in a dramatic decrease in gamete survival or mating ability. We also consider the possibility that gamete size has a direct effect on gamete survival or mating success. In addition to examining the requirements for isogamy to persist, we compare the costs of isogamy and anisogamy relative to asexual forms. Our results suggest that there is a cost of isogamous sex, and that this may occasionally be greater than the cost of anisogamous sex.

## A MODEL OF THE EVOLUTION OF GAMETE SIZES WHEN SIZE IS DETERMINED INDEPENDENTLY IN EACH MATING TYPE; NO EFFECT OF GAMETE SIZE ON GAMETE SUCCESS

We begin by developing fitness functions for the case in which there are two mating types, denoted 1 and 2. These functions are then used to develop a model for the dynamics of gamete sizes. The size of type-1 gametes is denoted $x_1$, and the size of type-2 gametes is denoted $x_2$. The size of the zygote is the sum of gamete sizes from the two parents. The reproductive success of a zygote increases with its size, $x_1 + x_2$, according to the function $f$. The mating success of each gamete is assumed to be independent of its size in this first model, but may be a function of the population sex ratio. Based on these assumptions, the fitnesses of a type-1 individual with gamete size $x_1$ and a type-2 individual with gamete size $x_2$ that mate with each other (in a population with average gamete sizes $x_1^*$, $x_2^*$) are:

$$F_1(x_1, x_1^*, x_2^*) = M_1(x_1, x_1^*, x_2^*)(R_1/x_1) f(x_1 + x_2) \tag{1a}$$

$$F_2(x_2, x_1^*, x_2^*) = M_2(x_2, x_1^*, x_2^*)(R_2/x_2) f(x_1 + x_2) \tag{1b}$$

where $R_i$ is the total reproductive investment of an individual of mating type $i$. The function $M_i$ is the mating success of gamete type $i$ of size $x_i$.

Mating success $M$ depends on the ratio of gamete numbers in the population. If the phenotypic variance in gamete size within each mating type in the population is sufficiently small, the ratio of type-2 to type-1 gametes can be appoximated by $R_2 x_1^*/sR_1 x_2^*$, where $s$ is the sex ratio of individuals: (number of type 1)/(number of type 2). In addition, a small variance in size implies that we may assume that an individual of each mating type mates with an approximately average-sized individual of the other type. In this case, we may refer to $x_1^*$ and $x_2^*$ as the sizes of the 'wild-type' gamete, and equations (1a,b) may be rewritten as:

$$F_1(x_1, x_1^*, x_2^*) = M_1(x_1^*, x_2^*)(R_1/x_1) f(x_1 + x_2^*) \tag{1c}$$

$$F_2(x_2, x_1^*, x_2^*) = M_2(x_1^*, x_2^*)(R_2/x_2) f(x_1^* + x_2) \tag{1d}$$

By associating a size with a mating type, we implicitly assume that the elements determining size in mating type $i$ are either expressed only in type $i$ or are tightly linked to the allele at the sex-determining locus that specifies mating type $i$. Except for the presence of two mating types and the mating success function, $M$, these fitness expressions are identical to those proposed by Maynard Smith (1978), and follow the basic assumptions of Parker *et al.* (1972). If there is a significant variance in gamete sizes of either type within the population, the mean sex ratio (number of type 2)/(number of type 1) generally cannot be

approximated by the inverse ratio of mean sizes, $x_1^*/x_2^*$. In addition, if there is a large variance in gamete sizes within either mating type, and if reproductive success is a non-linear function of zygote size, the mean reproductive success of a zygote with an $x_i$ gamete may not be well-approximated by $f(x_i + x_j^*)$. Formulae (1c) and (1d) may then be inaccurate, and the following analysis may not be valid. We relax the 'small variance' assumption below by exploring an individual-based simulation model.

Given that the variance in trait values is sufficiently small to use equations (1c,d), we also assume that the size of gametes of each mating type evolves independently. This is appropriate when size-determining factors for one mating type are genetically uncorrelated with size-determining factors for the other mating type. Given these assumptions, the rates of change of the mean gamete sizes are:

$$\mathrm{d}x_1^*/\mathrm{d}t = g_{x1}\partial F_1(x_1, x_1^*, x_2^*)/\partial x_1|_{x1 = x1^*} = g_{x1}R_1M_1(x_1^*, x_2^*)[-f(x_1^* + x_2^*)/x_1^{*2} + f'(x_1^* + x_2^*)/x_1^*] \quad (2a)$$

$$\mathrm{d}x_2^*/\mathrm{d}t = g_{x2}\partial F_2(x_2, x_1^*, x_2^*)/\partial x_2|_{x2 = x2^*} = g_{x2}R_2M_2(x_1^*, x_2^*)[-f(x_1^* + x_2^*)/x_2^{*2} + f'(x_1^* + x_2^*)/x_2^*] \quad (2b)$$

where $g_{x1}$ and $g_{x2}$ are additive genetic variances (Iwasa *et al.*, 1991), partial derivatives are evaluated at $x_1 = x_1^*$ and $x_2 = x_2^*$, and primes denote derivatives. The genetic variance parameters are often assumed to be constant in polygenic models, but may vary with time or with mean trait values (Abrams *et al.*, 1993). If the partial derivative of fitness with respect to individual trait value is positive, mutants with slightly larger gamete sizes than the wild type are favoured, and size will evolve towards larger sizes; if the partial derivative is negative, size will decrease. There is a biological minimum size, denoted by $x_{\min}$, which is assumed to be identical for both mating types. A size threshold is required as it is necessary for a gamete to at least include a complete genome, but the minimum size may be considerably larger than the size of a naked set of chromosomes.

Given the above assumptions, the evolutionary equilibrium occurs where equations (2a) and (2b) are both equal to zero. The necessary and sufficient conditions for local stability of this equilibrium point differ from the conditions for each gamete size to maximize fitness, conditional on the size of the other gamete type. The latter conditions represent a Nash equilibrium, and are equivalent to each gamete size being uninvadible by any mutant types. We will begin by reconsidering the conditions for a Nash equilibrium, because these help to understand the full stability conditions for equations (2a,b). The equilibrium point specified by setting equations (2a,b) to zero represents a local Nash equilibrium if $x_1$ maximizes fitness in mating type 1, conditional on $x_2$, and $x_2$ maximizes fitness of type 2, conditional on $x_1$. In both cases, the fitness maximization criterion is simply:

$$\partial^2 F_i/\partial x_i^2|_{xi = xi^*} < 0 \qquad \text{for } i = 1,2 \quad (3)$$

In the case of isogamy, $x_1^* = x_2^* = x^*$, and the Nash solution is implicitly given by:

$$x^* = f(2x^*)/f'(2x^*) \quad (4)$$

This is the same solution that Maynard Smith (1978) obtained for a similar model without mating types. We use $x^{**}$ to denote the gamete size that satisfies equation (4); thus, $2x^{**}$ is the Nash equilibrium zygote size. Expanding inequality (3), using equation (4) shows that

the Nash equilibrium condition is $f''(2x^{**}) < 0$. Thus there is an isogamous equilibrium that is uninvadible by mutants of small effect, provided that equation (4) has a solution for a size where zygote fitness is a decelerating function of size. The Nash solution specified by equation (4) implies that a line passing through the solution $x^*$ must be tangent to the zygote fitness curve, $f$, at $2x^*$; this graphical technique was introduced by Maynard Smith (1978) and is shown in Fig. 1. The figure also shows the zygote size that would maximize fitness in the absence of sex (denoted $z^{**}$). Nash solutions exist for two of the three fitness curves that are illustrated; these are discussed in more detail below.

Condition (3) is a local condition for a Nash equilibrium. As pointed out by Maynard Smith (1978, 1982), a mutant with a much smaller size may be able to invade such an equilibrium. Suppose that a mutant with the minimum gamete size is possible and occurs in mating type 2. If

$$F_2(x_{\min}, x^{**}, x^{**}) = (M_2R_2/x_{\min})f(x_{\min} + x^{**}) > F_2(x^{**}, x^{**}, x^{**}) = (M_2R_2/x^{**})f(2x^{**}) \quad (5)$$

this mutant can invade an isogamous population where each gamete type has the size specified by conditions setting equations (2a,b) to zero (Parker *et al.*, 1972). Inequality (5) is satisfied if the ratio $x^{**}/x_{\min}$ is greater than the ratio $f(2x^{**})/f(x_{\min} + x^{**})$. This requirement is satisfied by the fitness functions, $f$, used in several previous models (Parker *et al.*, 1972; Maynard Smith, 1978; Bulmer, 1994). However, there are two reasons why this is not a satisfactory explanation for the predominance of anisogamy. The first is that there is no guarantee that viable mutant gametes that are much smaller than the mean size can occur, be viable and breed true. Since Fisher (1930), evolutionary theory has assumed that mutants of large effect are likely to suffer greatly reduced fitness. If only mutants of small effect are viable, then the condition for local stability of isogamy is simply that the zygote fitness function should have a negative second derivative at the equilibrium. Even if macro-mutations occur and produce viable gametes, it is not clear that the zygote fitness function and minimum zygote size are always such that condition (5) is satisfied. Maynard Smith (1978, p. 153) argued against functions that do not satisfy inequality (5) as follows: '[these conditions] are very severe, since they imply that if $2m^*$ [$2x^{**}$ in our notation] is the optimal mass for a zygote, then a zygote of half that mass has almost zero probability of survival. I doubt whether [this situation] . . . has ever existed . . .'. Condition (5) may be difficult to satisfy if the minimum gamete size is not very small or if zygote fitness declines very rapidly with size. Furthermore, it is quite conceivable that zygotes below a certain size have almost no probability of survival. In the absence of comparative data on the shapes of the zygote fitness versus size function, there is little basis for arguing against zygote fitness functions that produce uninvadible isogamous Nash equilibria, such as that in Fig. 1A. Charlesworth (1978) investigated a genetic version of a model that is equivalent to ours and found no conditions with an isogamous equilibrium at intermediate sizes. This was because he restricted his attention to a zygote fitness function with a positive second derivative ($f(x) = x^k$, where $k > 1$), which eliminates the possibility of a Nash equilibrium. There is no basis for assuming that fitness can continue to increase indefinitely at an accelerating rate with size, as implied by the function used by Charlesworth. Thus, the previous models of the evolution of gamete sizes based on zygote fitness versus gamete number (Parker *et al.*, 1972; Bell, 1978; Maynard Smith, 1978; Hoekstra, 1980) provide little basis for believing that isogamy should be rare or taxonomically restricted.

We now turn to the conditions for the local stability of the dynamic system specified by equations (2a,b). The isogamous equilibrium point of equations (2a,b) is again given implicitly by equation (4). The zygote size at this equilibrium is $2x^{**}$. The necessary and sufficient conditions for the equilibrium to be locally stable are that the trace of the Jacobian matrix of equations (2a,b) is negative and that the determinant of that matrix is positive. When evaluated at the equilibrium point, these two conditions become:

$$f''(2x^{**}) < 0 \tag{6a}$$

and

$$(2f - f'x^{**})(2f - 3f'x^{**} + 2f''x^{**2}) > 0 \tag{6b}$$

Condition (6a) is identical to the condition for the equilibrium to be uninvadible (Nash). However, condition (6b) must also be satisfied for local dynamic stability; this condition corresponds to the game theory concept of convergence stability (Eshel and Akin, 1983; Christiansen, 1991; see Discussion). Replacing $f'x^{**}$ by $f$ (i.e. using condition 4), condition (6b) reduces to:

$$(f)(-f + 2f''x^{**2}) > 0 \tag{7}$$

Because $f$ is a positive function, it is clear that condition (7) cannot be satisfied if $f''$ is negative. If $f''$ is positive, then condition (6a) cannot be satisfied. Therefore, the isogamous equilibrium of the dynamic system is always convergently (or dynamically) unstable. A small deviation in the mean size of one gamete type leads to further selection for that direction of change in size, and selection for the opposite direction of change in the other gamete type.

This result is independent of the form of the zygote fitness function and, therefore, constitutes a very general explanation for the rarity of isogamy, provided that gamete size is determined independently in each sex. Gamete sizes appear to be genetically uncorrelated in anisogamous species, and it is known that the isogamous alga, *Chlamydomonas reinhardii*, has a mating type locus consisting of a cluster of very tightly linked genes with diverse functions (Galloway and Goodenough, 1985). Once there is some difference in the mean size of the two gametes, there will be selection for factors that limit the expression of size-influencing loci to one mating type. This is expected to lead to evolution away from an isogamous equilibrium.

## THE EVOLUTION OF GAMETE SIZES WHEN SIZE IS NOT ASSOCIATED WITH MATING TYPE

It is important to compare the results of the preceding section with a model based on the assumption that size-determining loci are not linked to mating type loci and are expressed in both mating type loci. Mean sizes of both mating types are the same, and a rare mutant with a different size will occur in both mating types. Consequently, the fitness of a particular size can be expressed without writing separate fitness expressions for each mating type. In this case, there is no distinction between the sizes of the two gamete types, and the fitness of an allele of size $x$ in a population with size $x^*$ is proportional to $F(x, x^*) = (R/x)(f(x + x^*))$. Again $dx^*/dt$ is proportional to $dF(x, x^*)/dx$, evaluated at $x = x^*$. The fitness function $F$ is identical to that in Maynard Smith's (1978) model. It is easy to verify that, if there is an equilibrium with $f'' < 0$, it is locally stable – that is, stability conditions are the same as for a

Nash equilibrium in the sex-linked model. Stability of such an isogamous equilibrium to invasion by microgametes is described by inequality (5). If microgametes can occur and invade, the result is dimorphism of both mating types. As Charlesworth (1978) has argued, such a situation will favour reduction in recombination, and each size will eventually become associated with a particular mating type. If there are no mating types, the above fitness function, $F(x, x^*) = (R/x)(f(x + x^*))$, applies to all individuals and the predicted evolutionary outcome is the same. If there are three or more mating types, the analysis becomes difficult, but this situation appears to be very rare (Hoekstra, 1987).

Returning to equations (2a,b), there are generally two asymmetric (anisogamous) stable equilibria at which one of the gametes has the minimum possible size. We can assume that $x_1^* > x_2^*$ at that equilibrium without loss of generality. Because of this size relationship, we will refer to $x_1$ and $x_2$ as the egg and sperm size, respectively. At the stable equilibrium, sperm size is

$$x_2^* = x_{\min} \tag{8a}$$

and egg size is implicitly given by

$$x_1^* f'(x_1^* + x_{\min}) = f(x_1^* + x_{\min}) \tag{8b}$$

The resulting stable zygote size is the value of $x_1^* + x_{\min}$ that satisfies equation (8b). Note that if $x_{\min}$ is close to zero, egg size will be very close to the size of an optimally sized asexual offspring. The latter maximizes $(R/x)f(x)$, so it is specified by $xf'(x) = f(x)$.

We present three examples of the evolution of gamete sizes using three different functional forms of the zygote fitness function, $f$: (A) $f(z) = \max(0, s \log(z))$, where $s$ is a positive constant; (B) $f(z) = 1 - \exp(-z^2)$ (used by Bulmer, 1994); and (C) $f(z) = z^6/(1 + z^6)$. All three of these are roughly similar in form, with zygote fitness being extremely low at small size, accelerating at larger sizes, and then decelerating and levelling-off. We assume that $x_{\min} = 0.001$ in Figs 1 and 2. In case A, the Nash solution is $x^{**} = 0.824$. Because $f(z) = 0$ for $z < 1$, a mutant with any gamete size less than 0.176 will clearly not be able to increase, and we can show that the Nash solution is uninvadible by any mutant smaller than the Nash value. Thus, this is an example in which microgametes cannot invade the isogamous equilibrium (see Fig. 1A). However, if size evolves independently in each sex, isogamy is convergently unstable and the gamete sizes approach $x_1 = 2.718$ and $x_2 = x_{\min} = 0.001$, as shown in Fig. 2A. In case B (Figs 1B and 2B), there is no positive Nash solution, since $(\partial F/\partial x)$ evaluated at $x = x_1^* = x_2^*$ is always negative. The anisogamous equilibrium (1.12, $x_{\min}$) is convergently stable, as shown in Fig. 2B. In case C, there is a Nash solution (0.561, 0.561). This differs from case A in that a mutant with gamete size $x_{\min}$ can invade the Nash equilibrium in this case. However, even if such small mutants cannot occur, the Nash solution is convergently unstable when gamete size is determined independently in each sex. In this case, the gamete sizes approach 1.307 and $x_{\min}$, as shown in Fig. 2C. If size is determined by loci that affect both sexes and are not closely linked to the sex-determining locus, then the isogamous equilibrium in case C is locally stable, but is globally unstable if micromutants are possible.

The current distribution of isogamy and anisogamy may have been influenced by interclade competition between lineages that are similar except for mating type. It is therefore instructive to compare the rate of increase of a population whose gamete sizes are described by the various potential equilibria in each of these examples. In each case, the rate of increase at the anisogamous equilibrium is half the rate of increase of the asexual

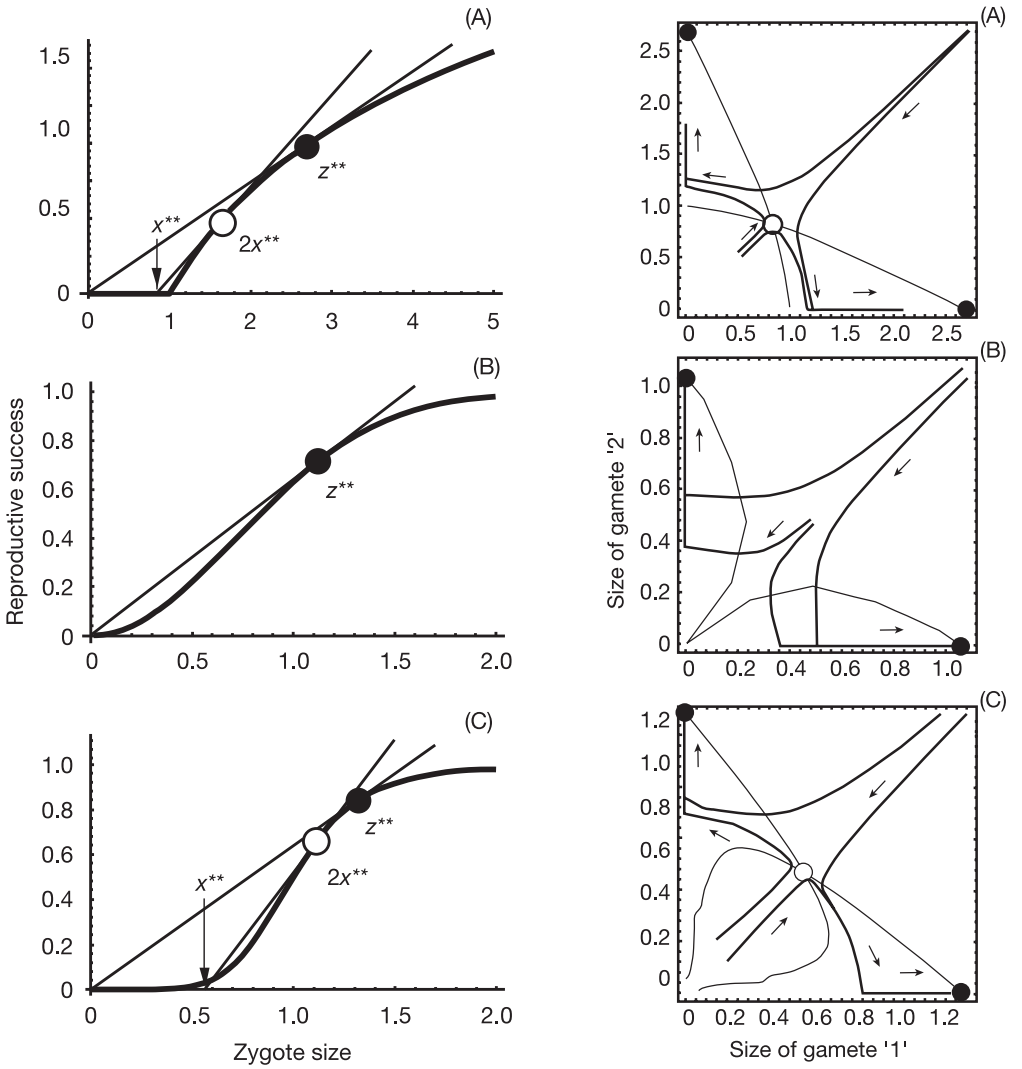


**Fig. 1.** (Left) The relationship between reproductive success of a zygote $f(z)$ and its size $z$ for (A) $f(x) = \max(0, \log z)$, (B) $f(x) = 1 - \exp(-z^2)$ and (C) $f(x) = z^6/(1 + z^6)$. Solid circles ($z^{**}$) show the optimum zygote size that maximizes the parent fitness in asexual reproduction. This is approximately the zygote size at the anisogamous equilibrium when $x_{\min}$ is close to zero. Open circles ($2x^{**}$) show the symmetric Nash solution of zygote size, in which each gamete size is $x^{**}$ and $x^{**}$ is given by equation (4). Tangents from the origin and from point ($x^{**}$, 0) give these solutions. See text for details.

**Fig. 2.** (Right) Evolutionary dynamics of egg size (the larger gamete) and sperm size (the smaller gamete) for the three zygote fitness functions used in Fig. 1. The narrow lines show the isoclines for equations (2a,b) with each fitness function. The bold lines are two pairs of evolutionary trajectories obtained using equations (2a,b); two of these begin near the isogamous equilibrium, and two begin with both gametes having close to the asexual optimal size. The solid circles show the anisogamous equilibria given by equations (8a,b). The open circles show the symmetric Nash solution given by equation (4).

equilibrium; zygote size is identical in asexual and anisogamous populations, but only half of the individuals in the anisogamous sexual population contribute significant biomass to the zygotes. The rate of increase at the isogamous equilibrium is reduced by having smaller-than-optimal zygote sizes, even though all individuals contribute significantly to zygote biomass. The ratio of fitness at the isogamous equilibrium to that at the asexual equilibrium is approximately 0.93 in example C and 0.82 in example A. Thus, in each of these cases, the transition from isogamy to anisogamy would result in less than a two-fold cost in terms of population growth rate. It is possible for the transition from isogamy to anisogamy to result in an increase in fitness. This is shown in Fig. 3A, which generalizes example C so that the zygote fitness function is $f(z) = z^n/(1 + z^n)$. There is an isogamous equilibrium for $n > 2$, and this equilibrium is locally stable provided that sex- and size-determining loci are not closely linked. There is also an anisogamous equilibrium for all finite values of $n$, provided that the minimum gamete size is sufficiently small. The fitness at the isogamous equilibrium, relative to asexual fitness, is show in Fig. 3A. It can be seen that the fitness of isogamous sexuals is less than half the fitness (rate of increase) of asexual forms for $2 < n < 2.183$. Thus, for a limited range of parameter values in this model, evolving anisogamy increases population growth rate. The population growth rate of the anisogamous form is always approximately half that of the asexual when the smaller gamete is very small. Although a lower growth rate of isogamy relative to anisogamy occurs for a limited range of parameters in this model, the cost of anisogamy is always less than two-fold and often substantially less.

Another example is the zygote fitness function, $f(x) = \max[0,\ b(x - x_0)/(1 + a(x - x_0))]$. This is a Monod function that is zero until $x = x_0$, where $x_0$ is the minimum size for survival. In this case, the ratio of the fitness of an isogamous species to an asexual species is a function of the product $ax_0$, which is shown in Fig. 3B. Either a large half-saturation constant, $1/a$, or a small minimum zygote size for survival, $x_0$, results in a substantial disadvantage of isogamy relative to asexuality, although this is never as large as the two-fold cost of anisogamy. Given that we know almost nothing about the form of the zygote fitness versus size function, it is difficult to draw firm conclusions about the relative rates of increase of isogamous and anisogamous lineages of the same species.

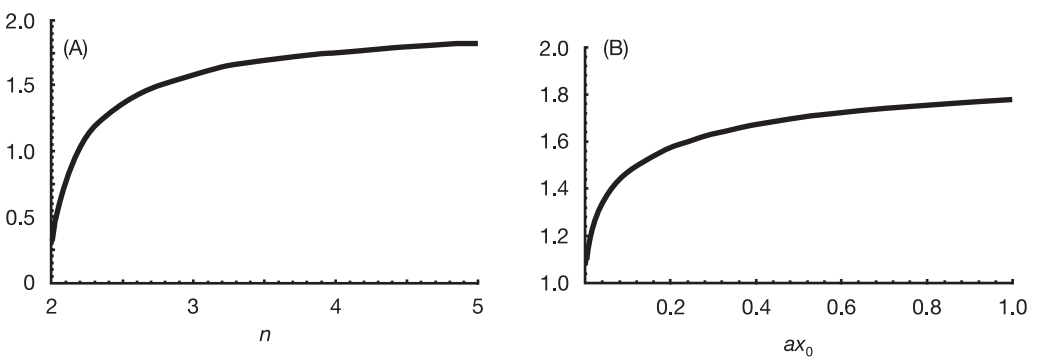


**Fig. 3.** The fitness of an isogamous form relative to an asexual form of the same species. (A) The zygote fitness function is $f(x) = x^n/(1 + x^n)$, and the relative fitnesses are plotted for different exponents, $n$. (B) The fitness function is $f(x) = \max[0,\ b(x - x_0)/(1 + a(x - x_0))]$. Here, the ratio of isogamous to asexual fitness only depends on the product, $ax_0$.

The following two sections extend the basic model considered here in two ways. The first looks at a much more detailed and realistic model to determine whether the assumptions of little variance in size within a gamete type and infinite population sizes, which underlie equations (2a,b), are likely to have significantly biased the results. The second returns to the simple analytical model, but includes the possibility that a gamete's size can have a direct effect on either its survival or its probability of achieving fertilization.

## SIMULATION OF INDIVIDUAL-BASED MODELS

To investigate cases in which the variance in gamete sizes within a mating type is large, we consider a simple 'individual-based model' (DeAngelis and Gross, 1992; Kawata and Toquenaga, 1994). The individual-based model changes the population composition in two steps – selection and mutation. First we describe the selection process. We assume that the population consists of $N$ hermaphrodite individuals, each of which invests an amount $R$ for 'female' gametes and an amount $r$ for 'male' gametes. Each individual, $i$, is haploid and is characterized by two quantitative traits, egg size ($x_i$) and sperm size ($y_i$), for individual $i$ ($i = 1, 2, \ldots, N$). (We depart from our earlier notation of $x_1$ and $x_2$ to avoid double subscripts.) Individual $i$ produces $R/x_i$ female gametes with size $x_i$ and $r/y_i$ male gametes with size $y_i$. The mating success per gamete is 1 for the sex with a smaller total number of gametes, and the ratio of the abundances of the two gamete types for the sex with the larger number of gametes is:

$$M = \min(1, \Sigma_i(r/y_i)/\Sigma_i(R/x_i)) \qquad \text{and} \qquad m = \min(1, \Sigma_i(R/x_i)/\Sigma_i(r/y_i)) \tag{9}$$

If the number of gametes in the population is sufficiently large, the mean reproductive success of gamete $i$ is $\Sigma_j f(x_i + y_j)/N$ for a female gamete and $\Sigma_j f(x_j + y_i)/N$ for a male gamete. Because of non-linearity of $f$, the mean fitness of zygotes involving eggs of individual $i$, $\Sigma_j f(x_i + y_j)/N$, differs from the fitness ($f(x_i + y^*)$) of an egg that combines with a sperm having the mean sperm size in the population ($y^* = \Sigma_j y_j/N$). Therefore, the expected fitness of individual $i$ (denoted by $H_i$) is given by:

$$H_i = F_1 + F_2 = (RM/x_i)\,\Sigma_j f(x_i + y_j)/N + (rm/y_i)\,\Sigma_j f(x_j + y_i)/N \tag{10}$$

To generate a phenotypic distribution for the next generation, we pick $N$ numbers independently from 1, 2, . . ., $N$ with probability $H_i/\Sigma_j H_j$. Thus, individuals with higher expected fitness have a greater chance of being chosen, and may be chosen more than once. After making $N$ selections, we renumber individuals to 1, 2, . . ., $N$ ($N = 256$ in the simulations reported here).

In the second step of the simulations, each phenotype may change its trait value because of mutation. We assume that individual $i$ has a female gamete size $x_i(1 + \exp(a))$, where $a$ is a uniformly random variable between –0.005 and 0.005. Mutations affecting male gamete size occur in the same way, and are independent of mutations in female gamete size.

The evolution of gamete sizes proceeds by iteration of these two steps. We assume that the initial phenotypic distributions are given by $x_i = x^{**}(1 + \exp(a))$ and $y_i = x^{**}(1 + \exp(a'))$, where $x^{**}$ is implicitly given by equation (8b) and both $a$ and $a'$ are again independent random variables that are uniformly distributed between –0.005 and 0.005. We used the zygote fitness function from cases A and C of Figs 1 and 2: $f(z) = \max(0, s\log(z))$ and $f(z) = z^6/(1 + z^6)$. Figure 4 shows typical examples of the evolution of the phenotypic distributions of gamete sizes under these assumptions. Isogamy was again convergently

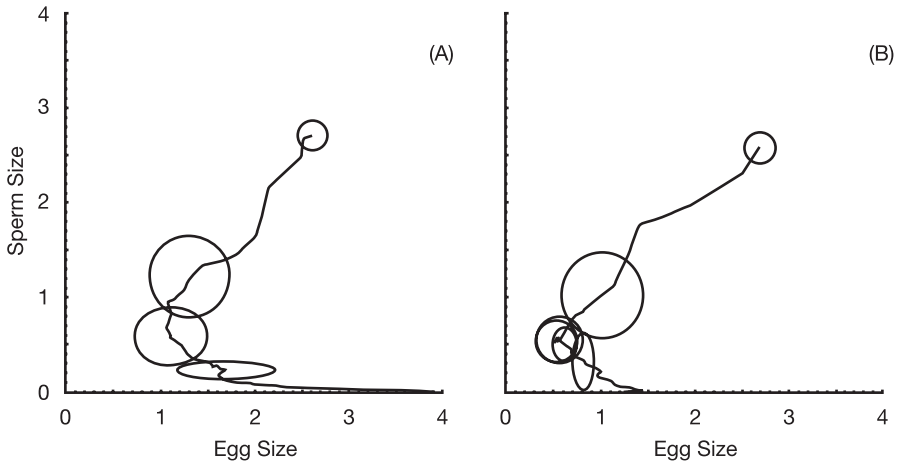


**Fig. 4.** Change in phenotype distributions based on the individual-based simulation described in the text. The solid line shows the change of the mean gamete sizes determined every 10 generations. Each ellipse represents the standard deviation of phenotypes for the initial generation, and the 100th, 200th, 300th and 400th generations.

unstable. In spite of a significant effect of genetic drift in the population mean trait values and a large variance in the sizes of eggs, mean sperm size decreased and approached the minimum size in all simulations.

## CAN DIRECT EFFECTS OF SIZE ON GAMETE FITNESS STABILIZE ISOGAMY?

It is likely that gamete size will have some direct effect on either gamete survival or rate of encountering – or success in combining with – members of the opposite gamete type. The possible consequences of such effects are best investigated by returning to our analytical model. Thus, we modify the fitness formulae in equations (1a,b) by multiplying each by a survival rate function, denoted $l(x_i - x_0)$, where $x_0$ is the size that maximizes gamete survival. The function $l$ reaches a maximum value (<1) when its argument is zero. Because we are interested in the stability of an initially isogamous system, we assume that each gamete type has an identical survival function. (After anisogamy has become established, it is likely that the survival functions for the two mating types will come to differ from each other.) Equations (2a,b) then become:

$$\mathrm{d}x_1^*/\mathrm{d}t = g_{x1}\, R_1 M_1(x_1^*, x_2^*)$$
$$[-l(x_1^*)f(x_1^* + x_2^*)/x_1^{*2} + l(x_1^*)f'(x_1^* + x_2^*)/x_1^* + l'(x_1^*)f(x_1^* + x_2^*)/x_1^*] \quad (11a)$$

$$\mathrm{d}x_2^*/\mathrm{d}t = g_{x2}\, R_2 M_2(x_1^*, x_2^*)$$
$$[-l(x_2^*)f(x_1^* + x_2^*)/x_2^{*2} + l(x_2^*)f'(x_1^* + x_2^*)/x_2^* + l'(x_2^*)f(x_1^* + x_2^*)/x_2^*] \quad (11b)$$

The stability conditions for the isogamous equilibrium are rather complex. However, the important features can be seen without writing out the full conditions. The first local stability condition, analogous to equation (6a), is that the trace of the Jacobian matrix of

system (11) is negative; this must again be satisfied at a Nash equilibrium, as noted above. The second stability requirement, that the determinant of the Jacobian is positive, is given by:

$$[R_1R_2M_1M_2(2fl - xlf' - 2xfl' + x^2f'l' + x^2fl'')$$
$$(2fl - 3xlf' - 2xfl' + 3x^2f'l' + 2x^2lf'' + x^2fl'')]/x^6 =$$
$$[R_1R_2M_1M_2(xlf' + x^2f'l' + x^2fl'')(-xlf' + 3x^2f'l' + 2x^2lf'' + x^2fl'')]/x^6 > 0 \quad (12)$$

Because the left-hand side of this inequality is an increasing function of the absolute value of $l''$, a large magnitude of $l''$ will always result in convergence stability. In reaching the final expression in equation (12), we used the equilibrium condition $xlf' + xfl' = fl$, which is analogous to equation (4). Because the gamete fitness function, $l$, has a maximum at $x_i = x_0$, its second derivative is expected to be negative unless the isogamous equilibrium is far from the size that maximizes gamete survival. The magnitude of $l''$ is a measure of the strength of stabilizing selection due to the direct effects of size on gamete survival and mating ability. As one would expect, sufficiently strong direct selection can stabilize an isogamous equilibrium.

This result may be illustrated by considering $l(x) = l_{\max} - (x - 0.5)^2$ and $f(z) = \max(0, s\log(z))$. In this case, the symmetric Nash solution, $x^{**} = 0.725$, is convergently stable, as shown in Fig. 5. However, this Nash solution is not globally stable; the basin of attraction of this equilibrium depends on parameter values and is affected by the functional forms of $l(x)$ and $f(z)$. Figure 5 shows the two alternative anisogamous equilibria in this system. It is important to note that the system can be shifted to one of the anisogamous equilibria without the immediate invasion of microgamete producers. Cox and Sethian (1985) also found alternative stable equilibria in a model of gamete size evolution where there was direct selection on gamete size due to effects on motility. However, they did not include separate mating types.

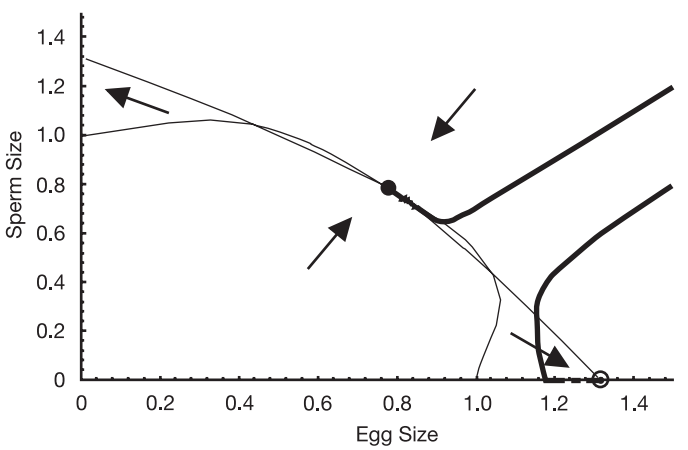


**Fig. 5.** Evolutionary dynamics of egg size (the larger gamete) and sperm size (the smaller gamete) when there is a direct effect of gamete size on gamete fitness. We assumed $f(z) = \max(0, s\log(z))$ and $l(x) = 1 - q(x - 0.7)^2$. The thin and bold curves show zero isoclines and trajectories obtained using equations (11a,b). The solid circle is a locally stable state that implies isogamy. The two initial states shown have egg and sperm sizes of (1.5, 1.2) and (1.5, 0.8), respectively.

## DISCUSSION

The title of this paper begins, 'Why are equally sized gametes so rare?' A related question is, why is isogamy apparently taxonomically restricted? The theory presented here adds to the number of potential theories. We will begin by explaining how our models account for the rarity of anisogamy, and then discuss explanations based on previous theory.

The models investigated suggest that there are two central conditions, either of which could result in the persistence of isogamy. The first is that size-determining factors do not become linked to sex-determining factors in the genome. The second is that there is strong, direct stabilizing selection on gamete size, as the result of size-associated differences in gamete survival or mating success. Of the factors that influence gamete size, it is likely that some will be tightly linked to the sex-determining locus. This provides a mechanism for the beginning of evolution towards anisogamy. Once the mean sizes of gametes of different mating types are unequal, there is further selection to reduce recombination between size and sex loci (Charlesworth, 1978). Nevertheless, it is clear that, currently, anisogamous species have achieved tight linkage or sex-limitation of expression of size-determining loci. This means that the path from anisogamy back to isogamy is effectively blocked. Even if there is a change in the environment that leads to a fitness function with a globally uninvadible isogamous equilibrium (a Nash equilibrium), the linkage of size- and sex-determining factors will prevent the return to that equilibrium. On the other hand, isogamous equilibria are always susceptible to destabilization by a change in the shape of the zygote fitness function that allows an increase of types producing small gametes, or the linkage of size- and sex-determining factors in the genome. At least many locally stable isogamous equilibria are invadible by gametes that are sufficiently small. All of this suggests that there should be a long-term evolutionary trend away from isogamy.

The explanation favoured in previous discussions of this topic are that the isogamous equilibria determined by most zygote fitness functions permit the invasion of microgametes, with the concomitant establishment of anisogamy. This argument depends on: (1) high rates of recombination between sex-determining and size-determining loci; (2) a possibility of viable microgametes arising *de novo* in a species with much larger gametes; and (3) zygote fitness functions and minimum gamete sizes that satisfy the invasion criteria given by inequality (5). It is possible that all of these prerequisites are frequently satisfied. We know very little about the genetic architecture determining gamete traits, the shape of zygote size versus fitness relationships, or the possibility of successful macromutants. At most, however, this seems likely to provide one of a number of possible explanations for the comparative lack of isogamy.

The model considered in most detail here is based on approximations that are valid if the phenotypic variance is sufficiently low, if the selection is sufficiently weak, and if fitness of each individual depends only on its own trait value and the population mean trait value (Iwasa *et al.*, 1991; Abrams *et al.*, 1993). We relaxed these assumptions using an individual-based simulation model that allowed a large phenotypic variance and strong selection. The simulation makes some assumptions, such as a uniform distribution of mutational effects on gamete sizes, haploidy and a fixed relatively small population size. However, it is unlikely that these assumptions would affect the basic result; in the presence of linkage between size- and sex-determining factors and in the absence of direct effects of size on gamete success, isogamy is convergently unstable. Although we cannot rule out the occurrence of stable isogamy under other circumstances, the agreement of the analytical results (based on small

variances, infinite population sizes and weak selection) and the simulations suggests that it is unlikely. The analytical results are valid for any form of the zygote fitness function. Thus, it is probable that the instability of isogamous equilibria is a very common feature in natural systems.

As was noted in the Introduction, the comparative patterns of isogamy have proven difficult to explain. Knowlton (1974), Maynard Smith (1978) and Bell (1978) argued that larger and/or more complex organisms should have a steeper relationship between zygote size and zygote fitness. They argued that steeper relationships were more likely to favour anisogamy, and reasoned that this should lead to a correlation between adult size and anisogamy. This trend appears to be true in the algae (Bell, 1978; Madsen and Waller, 1983), but there are many exceptions. The argument is weakened by the lack of concrete knowledge of the form of the zygote fitness functions. The correlation can also be viewed as a consequence of the smaller zygote size that arises from gamete size evolution under isogamy. If smaller zygotes tended to produce smaller adults, this would translate into a association between isogamy and smaller adult size.

The one factor in our models that can produce long-term stability of isogamy is direct stabilizing selection on gamete size. There are many potential reasons for such selection. Gametes in organisms with external fertilization are likely to experience selection on size because size affects mobility, maximum longevity and probability of being consumed by predators. It is somewhat surprising that this factor has been neglected in most previous models. Our results show that isogamy (at a size larger than the minimum possible gamete size) is more likely to be explained by direct effects of size on gamete fitness, rather than by particular forms of the zygote fitness function. An empirical prediction from these results is that isogamy should be more common is species whose gametic phase is a larger fraction of the entire life-history. Because smaller forms often have shorter adult phases, this could also account for the association of isogamy with small adult body size (Bell, 1978; Madsen and Waller, 1983).

It is common to associate the two-fold cost of sex with the presence of anisogamy (e.g. Maynard Smith, 1978; Bell, 1982; Michod, 1995). However, the results presented here suggest that populations with stable isogamy also experience a cost relative to asexual forms, because isogamy results in zygotes that are smaller than the fitness-maximizing size. It is theoretically possible, although perhaps unlikely, that the cost of sexual isogamy exceeds the two-fold cost of anisogamy. Nevertheless, the disadvantage of anisogamous lineages relative to similar isogamous lineages is likely to be considerably less than two-fold.

The isogamous equilibria in our basic models are cases where the size of each gamete type has a higher fitness than all other alternative sizes. Nevertheless, when size-determining loci are sex-linked or sex-limited in their effects, such equally sized gametes cannot persist. Previous work on evolutionary dynamics has provided other examples where uninvadible equilibria (Nash equilibria or evolutionarily stable strategies (ESS's)) can be dynamically unstable or genetically unattainable (Eshel and Motro, 1981; Lande, 1981; Eshel and Akin, 1983; Thomas, 1985; Cressman *et al.*, 1986; Taylor, 1989; Charlesworth, 1990; Hastings and Hom, 1990; Lessard, 1990; Christiansen, 1991; Abrams *et al.*, 1993; Geritz *et al.*, 1997, 1998). The isogamous equilibria that arise here are local ESS's but are not 'convergence stable' (using the terminology of Christiansen, 1991; Geritz *et al.*, 1997, 1998). At such an equilibrium, no mutant with a slightly different size can increase when rare. However, if mean size deviates from its equilibrium value, mutants that are still further from the equilibrium will be favoured, so the equilibrium will be unstable. Eshel and Akin (1983)

were the first to point out the possibility of convergence instability of Nash equilibria, in systems of two or more evolving entities. If the evolution of anisogamy in multicellular organisms arose from isogamy, convergence instability is likely to have played a major role in the origin of anisogamy and of other asymmetries of gender.

Recent work on some insects, particularly *Drosophila* species, has revealed the presence of giant sperm (Pitnick and Markow, 1994; Pitnick *et al.*, 1995; Karr and Pitnick, 1996), with lengths greater than adult body length. Thus, it is clear that the smaller of two gamete types need not always evolve to the smallest possible size. Moreover, it is known that, in many species, only part of these giant sperm enter the egg (Karr and Pitnick, 1996). These phenomena are beyond the scope of the theory proposed here. The functional significance of giant sperm is still very unclear, but, at least in some cases, it is unlikely that they contribute significantly to zygote nutrition (Pitnick *et al.*, 1995).

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