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A Physiological Barrier for the Maintenance of Anisogamous Sex

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There are at least four conceivable factors which could be responsible for the maintenance of anisogamous sex: (1) long-term group selection, (2) short-term ecological, natural selection, (3) trade-offs between female sexual fertility and parthenogenetic fertility and (4) female dependence on a male gametic contribution. There is evidence for the action of each of the first three factors, while the fourth seems to be evolutionarily impossible, at first sight. But selection on male and female gamete production physiology could, in principle, produce female germ lines which depend on male gametes for their perpetuation. There is circumstantial evidence that this has in fact occurred in the Mammalia, and critical experiments to test this hypothesis are proposed.

1. Introduction

Anisogamous sex is subject to a nominal two-fold selective disadvantage relative to apomictic, or vegetative, parthenogenesis, because apomictic females can produce twice as many daughters as fertilized females, all of which carry two alleles from the mother, rather than one, at each locus, other things being equal (Maynard-Smith, 1971). Nevertheless, males are extremely prevalent, and there is as yet no simple evolutionary explanation of this which is widely accepted (Maynard-Smith, 1978). (Charlesworth, 1980, has shown that this disadvantage is not two-fold with alternation between sexual and asexual reproduction, and there are a variety of cases in which it does not arise at all, but the basic evolutionary problem remains (Maynard-Smith, 1978, pp. 38–42).)

The older orthodoxy was that sex enables species to "respond so much more rapidly to whatever selection is in action, that if placed in competition *on equal terms* with an asexual organism similar in all other respects, the latter would certainly be replaced by the former" (Fisher, 1930, p. 144). However, the short-term evolutionary problem posed by parthenogenesis is *not* one in which the organisms compete "*on equal terms*", because of the nominal advantage of parthenogenesis. Nonetheless, Fisher's idea is

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perfectly valid in the context of group selection, when there is differential survival and fissioning of populations or species. Indeed, the taxonomic distribution of parthenogenetic varieties strongly suggests that they are doomed to early extinction (Maynard-Smith, 1978, pp. 51–54; Suomalinen, 1950), which is precisely in accord with Fisher's (1930) view.

Secondly, there are good arguments to be made for the view that short-term ecological selection mechanisms act to maintain anisogamous sex in at least a minority of cases. The best of these is Williams' (1975) "balance" argument. When parthenogenetic and sexual reproduction alternate in a species life cycle, facultatively or in a fixed cyclical pattern, mutations resulting in more frequent parthenogenesis must arise commonly, and would eventually eliminate sexual reproduction because of its nominal disadvantage, were it not for some short-term *counterbalancing* selection favoring sex. In particular, Williams argues that temporal and/or spatial environmental variation should throw the advantage to sex because of the greater variability of sexually produced offspring. In favor of this hypothesis, Williams (1975, pp. 4–7) cites the evident association between sexual reproduction and offspring subject to an unpredictable environment, relative to that of the parent. Levin (1975) gives one class of circumstances where such ecological selection pressures are likely to be of the required intensity, the coevolutionary struggle between plants and their pests.

Thirdly, in taxa where there are no known parthenogenetic lines, such as Aves or Mammalia, there does not seem to be any compelling argument against the view that the range of potential "evolutionary tinkering" (Jacob, 1977) does not include viable parthenogenesis. If anisogamous sex was maintained only by natural selection, between sexual and asexual alternatives on a group or other basis, then most dioecious species should give rise to parthenogenetic varieties on occasion, even if they are only short-lived. This is true of many plant species, and perhaps more animal taxa than are known to do so at present, but the evidence is that parthenogenesis in animals rarely gives rise to offspring of sufficient viability (Maynard-Smith, 1978, p. 49). Thus it has been suggested that selection in, or perhaps between, obligate sexual metazoan species gives rise to reproductive physiologies which cannot readily mutate to apomictic female reproduction (Maynard-Smith, 1971; Williams, 1975, pp. 103–105).

There are two ways by which the reproductive physiology could maintain this barrier to successful animal parthenogenesis. Firstly, the female reproductive system could be so canalized to maximize sexual fertility that any mutation which significantly "switches" reproduction to parthenogenesis must have side-effects such that females carrying it cannot reproduce themselves. Thus a barrier to parthenogenesis will have arisen as a result

of the side-effects of alleles which improved sexual fertility. This is a self-evidently reasonable hypothesis for animal groups with a high degree of physiological complexity. Heterogametic chromosomal determination of female sex and a degenerate heterochromosome, as in Aves, is an obvious example of a sexual adaptation which disrupts the route to parthenogenetic reproduction via self-fertilization (Maynard-Smith, 1978, p. 45).

Secondly, the fertilizing male gamete could provide some physiological resource or repair some deficiency, either being required for normal zygote development. This hypothesis is clearly *not* reasonable at first sight, since most sperm cells appear to provide little more than chromosomes to complete the chromosomal complement of the diploid zygote. Moreover, even if sperm cells were to contribute additional "resources" of some type to zygotes, at an initial stage in their evolution, selection acting on males, or male organ systems in hermaphrodites, presumably should redirect these resources to increase the likelihood of successful fertilization. However, such contribution to zygote fitness *could* be selectively favored if it was a concomitant of adaptations which increase fertilization success. This in turn may seem inconceivable, but such a selection mechanism can in fact be formulated, as is shown below.

2. A Male Gametic Contribution Hypothesis

The proposed hypothesis is based on the consequences of large-scale gamete production for gamete quality. In effect, it is suggested that natural selection first acts on male gamete production to force a male gametic contribution and then acts on female gamete production to make female germ cells irretrievably dependent on this contribution.

Consider the purely mitotic phase of gamete production. Under conditions of rapid division, it is possible that one of the daughter cells of a particular mitosis could have some fundamental nuclear defect, but the cytoplasmic machinery provided by the parent cell might nevertheless allow continued division of this deficient cell. (Such a deficiency could be pathological *or* adaptive; see below.) Eventually all such cell lineages must be irreversibly destined to extinction. All the descendant cells are living, but "committed" to cell line termination. Kirkwood & Holliday (1975*a*) have developed a model which shows that this process of commitment leads to far-reaching consequences for clonal survival. While this model certainly isn't completely general (Lerner, 1979), it illustrates many of the important features of clonal reproduction when it is subject to commitment. Most importantly, it is assumed that each new mitotically produced daughter cell has a specific probability of initiating a committed cell line, all descen-

dants of which will ultimately cease dividing. In the model, clonal populations are allowed to grow in size up to a certain maximum, half the population then being discarded, and the remainder left to grow again. This process is repeated until the clone goes extinct or achieves a stable, immortal distribution of committed and uncommitted cell types.

The important feature of the model is that newly committed cells reproduce at the same rate as uncommittted cells during the doubling period. Halving can then result in a dilution of potentially immortal cell lines, and their eventual total loss, which would *not* occur if (a) the clonal population grew without frequent and heavy loss of cells, (b) a relatively low proportion of committed cells were produced at each division of an uncommitted cell, (c) committed cell lines ceased reproduction within very few cells divisions of irretrievable commitment, or (d) some combination of (a), (b), and (c). Effectively, the clones go extinct because of sampling dilution effects.

If too many committed cell lines arise and proliferate in gonadal clones which must produce many gametes over a long period, then sampling dilution like that of Kirkwood & Holliday (1975*a*) can result in gonadal clone extinction, and thus sterility. The higher this frequency of commitment, the more divisions of committed cell lines, and the higher the level of gamete production, the sooner sterility occurs.

Thus, male gonads must retain a very high percentage of uncommitted germ cell lines, if the male produces extremely large numbers of sperm cells over a long period, as in animal groups like the Mammalia. By contrast, mammalian and other females are not as subject to this constraint, because they never produce such large numbers of gametes. The key factor for the evolution of sex is that males producing sufficiently many sperm cells can be relied upon to make an investment which forestalls the commitment of their germ cell lines. (Apomict species and varieties clearly must make such an investment to preserve their germ lines, and it follows from the above that males or females producing many gametes also must do so. It is *not* being suggested that parthenogenetic lines cannot be viable because such an investment has prohibitive physiological costs.)

However, females in some sexual species need not necessarily forestall the commitment of their germ line cells. Some of the requirements for potential lineage immortality may be provided by the sperm in surplus. When this is the case, females can forego some of the investment in potential immortality for *their* gonadal germ line cells. Natural selection would favor those females which relied on the sperm's provisioning of this requirement and reallocated the cellular resources to other functions. Though this reallocation would no doubt be small, it could nevertheless have radical effects on the subsequent evolutionary alternatives. When natural selection

has brought about this reallocation, eggs will require male fertilization to rescue the germ line from eventual extinction due to the proliferation of the germ cell line (and its descendants) to the limit of its commitment. As a result, successful parthenogenetic varieties generally will not arise from such species, and the nominal advantage of parthenogenesis over anisogamous sex will be of no importance.

However, while it seems extremely unlikely that parthenogenesis could evolve in one step in a species with male gametic contribution, it is conceivable that it could evolve by means of more circuitous routes. For example, it could do so via an intermediate stage in which the sperm chromosomes are retained at first in order to preserve germ line perpetuation and somatic cell function, but then discarded before the production of gametes. Gynogenesis, in which the parthenogenetic female requires copulation with males of a closely related species, is circumstantial evidence for such an evolutionary route, and it occurs sporadically throughout the animal kingdom (Maynard-Smith, 1978, p. 47).

3. Physiological Background for the Hypothesis

The proposed hypothesis depends on three background assumptions: (1) the existence of the described commitment and clone extinction process in the dividing cells of some animal species, (2) a cost to the avoidance of commitment in such cases, and (3) the possibility of commitment rescue by sperm chromosomes. The cogency of these assumptions will now be considered.

Firstly, with regard to evidence for commitment, it is now well-established that laboratory cultures of diploid fibroblasts, when cultured so that they reproduce quickly, exhibit progressively slower reproductive rates, and finally cease dividing altogether (Hayflick, 1974), although individual cells may continue to survive for some time (Bell *et al.*, 1978). This is surprising in view of the expectation that in a growing clonal population there would be natural selection for those cell lines which divide more rapidly. Slowly reproducing cells should be eliminated. Yet all such cultures have been found to reach a point at which it is impossible to select subclones which are capable of continued division. The conclusion offered by Kirkwood & Holliday (1975*a*) is that *in vitro* somatic cells must be committed some time before any reduction in reproductive rate occurs, and the fit of commitment models to *in vitro* data can be quite good (Holliday *et al.*, 1977). It is noteworthy that, while the conditions provided for *in vitro* mammalian cell cultures are essentially unlike those of *in vivo* tissues which do not undergo sustained division and heavy cell losses, gonadal clones

which produce very high numbers of gametes over a long period *are* subject to conditions like those *in vitro*. Cells lost from the diploid clone due to meiosis formally correspond to the cells removed from *in vitro* cultures. Thus gamete production is potentially subject to the same extinction dynamics as *in vitro* clonal population growth.

However, it must be said that the fundamental causes of these *in vitro* phenomena remain controversial (cf. Bell *et al.*, 1978; Hayflick, 1974; Orgel, 1973). The evidence shows no more than the plausibility of assuming that commitment processes are of importance in the evolution of gamete production. It does not prove that they are.

Secondly, there is some evidence for a cost to the avoidance of commitment, but it is much less direct. This evidence centers on the factors responsible for the *in vitro* commitment of somatic cell cultures, again assuming that there is some correspondence between *in vitro* and *in vivo* cellular proliferation. In particular, Kirkwood (1977) has argued that the physiology of somatic cells allows *in vitro* commitment because any *in vivo* effects of the commitment process would occur only at late ages, with little impact on fitness. (This is but a special case of the Williams, 1957, early-benefit/late-cost pleiotropy theory of senescence.) Kirkwoood's (1977) argument rests on the hypothesis that the maintenance of potentially immortal cell lines requires physiological resources which are not required by cell lines which allow commitment. Kirkwood's (1977) argument receives empirical support from the apparent rough correspondence between species maximum lifespan and the number of cell culture doublings before commitment (Lamb, 1977, p. 133). This evidence indicating that his argument is basically sound in turn suggests that Kirkwood's assumption that the avoidance of commitment has a cost is correct as well. Again, however, this is not an absolute demonstration of the validity of the required assumption.

Thirdly, given that (1) commitment is accepted as a fundamental possibility in at least some *in vivo* cellular populations and (2) Kirkwood's (1977) potential immortality cost argument is valid, then the hypothesis proposed here only requires that (3) the uncommitted property of male gonadal tissue be transmissable to the zygote by the sperm. This in turn depends on the molecular biology of commitment, which unfortunately still remains unknown. In particular, some hypothesized commitment mechanisms in the literature are not compatible with this requirement, while others are. These commitment mechanism hypotheses therefore merit discussion here.

(a) The most widely discussed hypothesis for the commitment mechanism is the protein error catastrophe of Orgel (1963, 1973). This theory hypothesizes that errors in the synthesis of the proteins which act as components of the DNA-RNA-protein translating apparatus could feed back on them-

selves, leading to very low translational fidelity and the ultimate breakdown of protein synthesis. This theory has been subjected to protracted theoretical (e.g. Goel & Islam, 1977; Kirkwood & Holliday, 1975*b*) and experimental (e.g. Bozcuk, 1976; Dingley & Maynard-Smith, 1969; Fulder & Tarrant, 1976; Harrison & Holliday, 1967) scrutiny. Perhaps it is fairest to say that it remains extremely controversial. The error catastrophe theory is consistent with conjectures (1) and (2) (Kirkwood, 1977), but not (3). Sperm cells generally contribute very little translating "machinery" (ribosomes, tRNAs, amino acyl synthetases) to the zygote, having negligible cytoplasm. The vast majority of such material is provided by the egg. If the unfertilized egg were already committed because of a mounting error catastrophe, then the sperm would make little or no difference.

(b) It has also been suggested that commitment is due to disproportionate replication of cytoplasmic constituents which replicate independently of the nucleus (Kirkwood & Holliday, 1975*a*). Mitochondria are evidently the best candidates for such a role. However, this mechanism poses all the problems that the error catastrophe theory does, because sperm cells make little cytoplasmic contribution, and moreover in vertebrates sperm mitochondria are destroyed by the egg (Cohen, 1977, p. 139), so that conjecture (3) could not possibly hold. Centrioles are another possibility, but the sperm centrioles are routinely discarded in some mammalian species (Austin, 1968, p. 86).

(c) An alternative theory is that uncommitted somatic cells can be interpreted as immortal stem cells from which committed cells are produced, and then proliferate, according to an irreversible program or "clock" (Bell *et al.*, 1978; Holliday & Pugh, 1975; Kirkwood & Holliday, 1975*a*). From the discussion of the first two commitment mechanism hypotheses, it is evident that a commitment mechanism which could lead to selection for a necessary male contribution to germ line maintenance must involve changes to the chromosomal complement itself. If commitment were due to cytoplasmic developmental events, sperm could not forestall the commitment of ova. On the other hand, if major physiological changes occur in female germ line nuclei which adapt them to the production of better ova but render them utterly dependent on sperm nuclei for the creation of zygote nuclei which can perpetuate the germ lines, then such an adaptive developmental program could underly an indispensable male gametic contribution.

(d) A fourth possibility is that commitment could be due to pathological disruption of the nucleus. This in turn could arise in several ways, two of which are erosion of DNA fidelity (cf. Linn *et al.*, 1976) and massive proliferation of selfish DNA (cf. Doolittle & Sapienza, 1980; Orgel & Crick 1980) impeding the replication of translated DNA. Either of these

two mechanisms of progressively "poisoning" the nucleus could produce commitment because the cytoplasm of those cells which are dividing rapidly will be provided with many constituents produced by instructions from the DNA of earlier cell generations. Therefore a rapid somatic mutational process with lag effects could arise, with consequences for cell proliferation like those observed *in vitro*. Furthermore, different mechanisms of nuclear disruption could act together, reinforcing the effects of one another.

Whether the phenomenon is adaptive or pathological, it is clear that commitment must be dependent on the properties of nuclei for the male gametic contribution hypothesis to work. Thus reproductive success must in turn depend on special properties of sperm nuclei. Perhaps one of the strongest criticisms to be made of this hypothesis is the past lack of evidence indicating an important role for sperm nucleus structure. But recent experiments now show that the structure of mammalian sperm chromatin is an important determinant of male fertility (Evenson *et al.*, 1980). There is also evidence that commitment is *not* cytoplasm-controlled (Wright & Hayflick, 1975).

Either of (c) or (d) could be responsible for commitment in normal cell cultures, and thereby allow the operation of the selective mechanism outlined in the previous section. However, the discovery of the mechanism of commitment in cell cultures is a task of as yet insurmountable difficulty. On the other hand, a direct empirical attack on the hypothesis of male gametic contribution should be relatively feasible, even with the issue of molecular mechanism left in abeyance. (In this respect, the problem of male gametic contribution is like that of mendelism. Both theories can be tested using aggregate effects, both are plausible but require experimental test, and both must depend on molecular mechanisms of considerable complexity and obscurity.) Accordingly, the next section is devoted to the physiology of sexual reproduction itself with regard to empirical evidence for male gametic contribution of some kind and possible hypothesis-testing experiments.

4. The Mammalia as a Test Case

The theory of indispensable male gametic contribution offered here depends on the action of commitment mechanisms (c) or (d) of the preceding section, which in turn requires that both somatic and male germ line cells proliferate rapidly and extensively in the course of growth and reproduction. Without such proliferation, there would not be the lag effect between the development of some crucial deficiency in the nucleus and the termination of cell division. Such a rapid onset of cellular deficiencies relative to the rate of division would prevent commitment because of clonal natural

selection. In addition, taxa such as Planta and Coelenterata, in which there is generally no early and complete separation of the germ line, cannot be subject to the proposed selection mechanism, as the prevalence of asexual varieties throughout the Planta suggests. Finally, species with prolonged and high levels of female gamete production cannot become subject to the proposed mechanism. Whatever the distribution of male gametic contribution, it certainly cannot be universal if it arises only on the basis of the proposed mechanism.

There are, in fact, relatively few large taxa in which the gonadal commitment mechanism could operate: only large-bodied, muticellular, and anisogamous sexual taxa with high male gamete output, low female gamete output and germ line separation. (On the other hand it is such taxa which are most problematic in their mode of reproduction, Williams, 1975, p. 103.) Perhaps the most prominent taxon in which indispensable male contribution could be of uniform importance in the maintenance of anisogamous sex is the Mammalia. Indeed, there is no record of a viable parthenogenetic mammalian variety being established in nature *or* in the laboratory. There is such a wealth of circumstantial evidence for indispensable male-contribution selection among mammals that, if such selection was found lacking in these species, it would seem relatively fruitless to look for it elsewhere. (Though it could, nevertheless, have sporadic importance.) Some of this circumstantial evidence follows.

Both the relative number of cell divisions between the development of mature gonadal germ line cells and the total production of gametes are vastly different in mammalian males and females. Oogania divide mitotically a limited, finite number of times to produce only a few million cells which then enter the prophase stage of meiosis. This occurs early in female development. From that point until fertilization, there is no further cellular division in the female germ line. By contrast, spermatogonia divide indefinitely many times over a long period to produce hundreds of billions of spermatozoa (Setchell, 1978, pp. 210–218), an essential requirement for the male-contribution hypothesis.

The production of sperm involves a great deal of cellular degeneration after both mitotic and meiotic division, for reasons which have remained obscure (Hogarth, 1978, p. 10). The level of wastage appears to be extremely high, on any conventional physiological hypothesis. However, such cellular wastage can be explained as a testis adaption which acts to discard germ line cells with disrupted chromosomes, thereby forestalling germ line commitment.

The utilization of sperm by mammalian females is inexplicably wasteful, compared with sperm-utilization by organisms like hymenopterans, and

the female tract's machinery for sperm transport to the egg has been considered "curiously crude" (Austin, 1972), if not actively resistant to fertilization (Cohen, 1977, pp. 107–113). This may be explained as a *female* adaptation to ensure that the male has a germ line with sufficient chromosomal integrity to produce large sperm numbers per ejaculate. If ova need sperm chromosomes for germ line rescue, then sperm quantity could be used by the female's reproductive tract as a test of sperm quality. Thus potential male-contribution due to commitment-rescue is a recognizable gamete feature which affects zygote viability, and one which can be detected before fertilization.

Mammalian testicles must descend to ensure fertility, yet the risks of mechanical castration are thereby enormously enhanced, with obviously drastic effects on Darwinian fitness. By contrast, females exhibit no such adaptation. Evidently, there is some crucial feature of sperm production which depends on temperature and can result in a substantial fitness penalty, outweighing the castration risk. Germ line commitment necessarily results in sterility, as discussed. On the present hypothesis, a reduction in germ line commitment probability due to the decrease in testicular temperature could provide fitness benefits sufficient to override a substantial increase in castration risk.

Though all of these puzzling circumstances can be readily explained in terms of the male gametic contribution hypothesis, they do not constitute any sort of proof of its validity. Indeed, it should be possible to develop alternative hypotheses which can explain each one of these phenomena separately. Looking for more detailed corroborative evidence of this kind would help underpin the male-contribution hypothesis. But a more efficient attack on the question of the validity of this hypothesis would be to try to refute it experimentally, irrespective of its subsidiary commitment mechanism hypotheses, by directly demonstrating the superfluity of the spermatozoon's chromosomes.

Three experiments could do this. Firstly, any technique allowing the production of viable mammalian parthenogenetic *varieties*, not merely progeny, which make no use of male chromosomes would clearly demolish any application of the theory to Mammalia. Secondly, fertilizing ova with the nucleus of another ovum to produce viable offspring *through several generations* would also constitute a clear falsification. Thirdly, parallel enucleation of large numbers of ova, followed by provision of two unrelated ova nuclei in one treatment and an ovum nucleus plus an unrelated sperm nucleus in the other, would provide a physiological system for directly comparing diploid cell proliferation with and without any male gametic contribution. Given conditions in which such cells could be cultured for a

large number of divisions, the male-contribution hypothesis would require that the cells subject to the second treatment become committed later than those subject to the first. (In these experiments, acrosomes and other nonchromosomal sperm components could be provided without invalidating their utility as tests of the male-contribution hypothesis.)

Naturally, there are other types of experiment which might throw light on the indispensable mammalian sperm contribution hypothesis. Two examples should indicate the possibilities. Goldstein & Lin (1972) found that *in vitro* hybrids of heteroploid hamster cells, from permanent cultures, with diploid human cells, from senescent cultures, were also permanent. (Here "permanent" means capable of indefinite growth in cell numbers.) Norwood *et al.* (1975) obtained similar results with hybrids of two human cell lines. Further experiments along these lines could lead to fairly certain knowledge of the nature of commitment and commitment-rescue. Indeed, experiments using heteroploid, or "transformed," permanent cell cultures might provide means of decisively refuting the hypothesis offered here. However, at present the replicative properties of such cells are open to a number of interpretations. Another promising line of experimental work is that involving the injection of mammalian somatic cell nuclei into amphibian oocytes (e.g. Gurdon *et al.*, 1976). The same sort of experiment using mammalian oocytes could yield valuable information on the *in vitro* perpetuation of mammalian female germ cell lines lacking male gamete contribution. No doubt these types of experiment do not even begin to exhaust the possibilities.

5. Discussion

The male gametic contribution hypothesis for the maintenance of anisogamous sex is only one of the two basic types of physiological barrier to the appearance of viable parthenogenetic lines. And, as mentioned at the outset, the idea that such barriers could be present is not new (cf. Maynard-Smith, 1971; Williams, 1975, pp. 103–105). Nor is the idea of sex as a physiological "rescue". Indeed, the notion that sex allows a form of rejuvenation from senescent deterioration has had a long history (Comfort, 1979, pp. 167–171), and is still current (e.g. Eaves, 1973).

In particular, Cohen (e.g. 1977, pp. 104–113) has developed a theory which abuts quite closely on the present one. He has suggested that the high rate of cellular division during spermatogenesis results in a large number of mistakes of division, producing defective cells, and thereby leading to cellular wastage in the testis. He also suggests that the sperm loss in the female reproductive tract, which he calls an "obstacle race tract", is a female adaptation which ensures that only fit sperm fertilize ova. But

this theory has been criticized on the grounds that it requires a close relationship between individual sperm phenotype and individual sperm genotype, for which evidence is lacking (Hogarth, 1978, pp. 16–17).

The present theory is like Cohen's in that it suggests that the female reproductive tract may be expected to discriminate against deficient sperm. But it is unlike Cohen's in that it is suggested that the physiological discrimination can occur on the basis of the number of sperm cells in the ejaculate, rather than the properties of individual sperm alone. Nonetheless, a discrimination mechanism of Cohen's type is also conceivable in terms of the selection mechanism proposed here, should the female reproductive tract somehow be able to detect the degree to which any sperm carries deficient chromosomes.

Clearly, the present article has raised more questions than it can lay any claim to answering. A great many physiological phenomena have been introduced as relevant to the problem of the maintenance of anisogamous sex, even though their precise molecular biology remains incompletely understood. (As, indeed, remains the case for other evolutionarily important phenomena, such as recombination.) It could be suggested that the male gametic contribution hypothesis requires detailed knowledge of this molecular biology before it can be given serious attention. But it is evident that the elucidation of the molecular biology of commitment, cell wastage in spermatogenesis, and spermatozoon fertilization success will take many years. Meanwhile, long before detailed knowledge of these processes has been achieved, it should be possible to refute the male gametic contribution hypothesis for the Mammalia, if it is false in this case, using experiments like those suggested in the preceding section.

Indeed, it is not argued here that indispensable male gametic contribution has in fact arisen in any species in the course of evolution. Rather, it is argued that it *could* have evolved, in principle, and that if it has evolved in any group of species, it is quite likely to have evolved among mammals.

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