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Part 1 Biological perspectives

1 The evolution of the sexual arena

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Introduction: the *Scala Naturae* of reproduction

In the early 1950s, a *Scala Naturae* view of the evolution of sex was fashionable and alas it still survives in some quarters 40 years on. The *Scala Naturae* embodied a ladder of 'improvements' in our evolution, exemplified by a succession of modern species. Its peak of reproductive sophistication was seen as being a man and a woman. Primitive asexual creatures such as bacteria, plants and coelenterates, which simply bud or divide into two, provided the first steps of the ladder. An excess of cell division leads to their multiplication, thereby providing safety in numbers.

The next steps on the *Scala* constituted protection of the reproductive products, spores and seeds. Dormancy is the reproductive tactic, especially among primitive bacteria, fungi and even plants such as angiosperms. Viviparity was seen as showing the 'highest' form of care and protection and its peak was achieved in mammals, although a few other species also show this form of reproduction.

However, diversity was seen to be a 'Good Thing', partly because it dealt with variable or patchy environmental conditions, partly because nature was varied in time and space and needed to be kept track of. So mutations suddenly became useful on the evolutionary scene. Before this point they could simply be considered as 'useless' mistakes in genome replication, which primitive creatures could not avoid. However, they landed simple asexual creatures into Muller's ratchet trouble if you were a clone (Morell, 1997). We find meiosis and fertilization on the next step of the ladder, their purpose being to recombine 'good' mutations (and also to maintain ploidy).

Eventually, it was claimed, anisogamy was followed by isogamy and, in turn, the next step up showed the beauties of oogamy and the evolutionary advent of spermatozoa and eggs, which was considered to be the ultimate in reproductive sophistication. Some individuals at the next level specialized in very small gametes and became males, whilst others went in for yolky eggs and became females. Dalcq (1957) described this level in a fashion typical of his time: 'The puzzle for embryology is to determine how the fussy mobility of the sperm and the deep and perilous inertia of the egg contrive between them to animate a new individual.'

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Some of these creatures, which were basically sexual, nevertheless reverted to parthenogenesis. Perhaps they did better without sex and, for example, produced well-camouflaged stick insects. Some either lost part of their sexuality by having haploid males (hymenopterans) or alternated sex with parthenogenesis, e.g. *Daphnia* and aphids) (Cohen, 1977).

The top steps were occupied by mammals, which acquired internal fertilization and viviparity and this was the 'best' way to reproduce. But large numbers of spermatozoa and oocytes (even though many oocytes became atretic) were difficult to understand in this context. 'There seems no reason for this prodigality under the conditions of mammalian reproduction', wrote Asdell in 1966.

It is now recognized that, as a result of the oddities of modern organisms being chosen to represent steps on the evolutionary ladder, practically all of these assumptions were wrong.

A better history of reproduction

Graham Bell's scholarly book *Masterpiece of nature* (not to mention my own textbook *Reproduction*) took these older ideas apart. Some criticisms of the old ideas are set out below.

'Primitive' organisms

In 1911, Dobell pointed out that to refer to the 'man-like ancestor of apes' is as correct as the more usual 'ape-like ancestor of man' and he even suggested a re-evaluation of the status of the 'primitive' protista in the evolutionary argument (protista being the group containing the amoeba, with some human-like aspects of its biochemistry). Also, Margulis (1981) emphasized the 'sexual' nature of *all* bacteria and reminded us that even the archaea swap DNA strands. The first two-thirds of organisms in the evolutionary story (all prokaryotes) apparently had rampant sex and recombination, including variants which looked, and still look like some of today's prokaryotes, very similar to male/female differentiation and spore production (Catcheside, 1977). Thus, today, there are no modern representatives of the lowest steps of the reproductive *Scala* and those for the higher levels are, at least, misleading.

Spermatozoa may well have evolved from early infective prokaryote symbionts that had acquired a genome-carrying role. Today's protozoans, especially ciliophorans such as suctoria, have a most advanced reproductive system, which includes viviparity and meiotic processes that are much more complex than our own (Roeder, 1997). So we cannot use contemporary protista (which were among the earliest eukaryotes) to illumine or exemplify steps in our own evolution. They have their own ways of doing things.

Provision for propagules

Bacterial organization increases simply so that the cells can multiply; that is, the bacterium continues its vegetative, trophic physiology and this results in two individuals arising from one. Cell wall, cell contents and genome are added continually until splitting or budding occurs. This is true vegetative (trophic) reproduction, as in the grasses. We should note that such bacterial daughters (and, indeed, viral particles) are the products of two genomic generations. The daughter bacterium has its own genome, of course, but most of its cell contents and wall are inherited directly from the mother and are thus not specified by its own genome; viral particles also have their infective mechanism and protein coat specified by earlier DNA and not by their own integral genome. This is true of most propagules (Cohen, 1977). They have at least two generations of genomes contributing to their fitness. Parents not only donate genome (usually recombined), but, of greatest importance to the early life of the offspring, they also provide mitochondria, a complete working cellular machinery, a DNA readout and replication kit, yolk or starch. According to Mendel, peas had ‘factors’ carried on the chromosomes and a ‘packed lunch’ from mother in their cotyledons. This is the ‘privilege’ story emphasized elsewhere in connection with the maternal contribution to reproduction (Cohen, 1979). It represents the *other* secret of successful reproduction.

Sex is not simply a recombination of mutations

The best criticism of naïve *Scala* thinking is Bell’s (1982) the *Masterpiece of nature*, which is what Erasmus Darwin called sexuality. To put it briefly, it had been thought that sexual creatures went out and conquered the variable and unpredictable world by their own versatility, providing a few progeny with matching adaptations. But Bell cited a host of examples in the literature, demonstrating that it is the *asexual* forms (parthenogenetic, amazonogenetic, and many other forms that had lost the ability to reproduce sexually) which actually go out and conquer. Sexual creatures related to these forms are found only in glacial relicts and equally stable ecologies. Bell found about a hundred cases of sexual forms going out to conquer diverse habitats (and he deals adequately with the probability of asymmetry in the reporting), compared with thousands of asexual forms. So the real world told us that the story of stick insects giving up sex in favour of better camouflage had to be re-evaluated; at this point the whole concept of sex being maintained in order to give versatility in a hostile world had to be rethought. A good overview of the classical position is provided by Smith (1972), but it is well worth reading Bell (1982) to put sex and spermatozoa into a more modern context.

Spermatozoa and eggs are not the ‘ultimate development’

Many reproductively successful creatures, however, have avoided simple sexual reproduction. Non-cellular protistans had different sexual problems, which have been explored elsewhere by Bell (1989). Further, the persistence of sexual dimorphism cannot be attributed merely to history (‘we’ve got it right, so we might as well get on with it’), because the diversity of spermatozoa and egg-like forms among animals and plants suggests that loss or gain of sexual function has occurred many times during their evolution. Red algae and some ascomycete fungi, for example, have complex sexual systems with no motile stages, and ciliate protozoa have developed a vegetative macronucleus for multiplication between episodes of sexual reproduction. Eggs have different systems also, with those of nematodes, spiralia and frogs differing as much as angiosperm embryo sacs from fern archegonia. There seemed to be no alternative to the view that sex was useful, but was often lost and sometimes reacquired as a new adaptation. We could not, however, explain why. Certainly, the idea that our sperm/egg system was the goal to be achieved explains nothing.

Mammals have not got the best method of reproduction

The suggestion derived from nineteenth century natural history books that mammals have the best and most sophisticated mode of reproduction does not hold up in the face of knowledge of the variety of reproductive strategies and tactics elsewhere in the animal kingdom (Cohen, 1977). Giraffes and gnus, for instance, are impressive in that they produce big, well-programmed young that are able to recognize their mothers and are afraid of wild dogs and hyaenas (frequently the subject of television natural history programmes). But the parasitic flatworm *Gyrodactylus* is much *more* viviparous. Its uterus has two generations of progeny at the same time and sometimes even three. In this respect, even the tsetse fly *Glossina* may be regarded as being more viviparous than a mammal, because its larva is fully developed when it is laid and it burrows, pupates and emerges as a full-sized fly without feeding after it leaves the oviduct.

Revolutions in reproductive theory

There have been further revolutions in our thinking that are even less easy to relate to naïve nineteenth century views, because there are a number of questions that had not occurred to us until DNA-based genetics developed in the 1950s. At least three of these questions are relevant in the context of this book and need to be considered alongside the evolution of sex and spermatozoa. The prevalence of heterozygosity (that is, too many mutant alleles occurring at too many loci) is one. Canalization (the standardization of phenotypes in spite of heterozygosity) and 'gene conversion' (the non-reciprocal nature of genetic recombination) are others. These new ways of thinking, based in part on molecular biology, are very relevant to sperm function. Thus, we find, that many earlier views are no longer valid in today's world.

In the late 1950s (see Haldane, 1957; Fisher, 1958) and even as recently as the mid 1990s (Korol *et al.*, 1994), it was assumed that all members of each species had much the same genome, except for those with mutations (either 'good' ones coming into the population or 'bad' ones being lost by death or reduced breeding of the organisms carrying them). Whether alleles were 'good' or 'bad' was measured by one-dimensional 'fitness'. However Lewontin & Hubby (1966) turned this view over. They showed, and it has been amply confirmed since then, that about a third of protein-specifying loci (genes) have variants somewhere in the population, even in parthenogenetic species, and that about 10% of loci are heterozygous in individual wild animals. This means that organisms in that population, represented by parents of the 10% heterozygotes, have different alleles at approximately 10% of their loci (Lewontin, 1974). Unlike Mendel's pea plants, laboratory mice or *Drosophila*, nearly all wild animals and angiosperms produce gametes which differ across many axes, with multiple alleles occurring at many of them. Some lengths of chromosome are inhibited from crossing over and have sets of alleles that are haplotypes (as in the histocompatibility loci of mammals). In addition, some animals, such as the cheetah, are surprisingly homozygous even in the wild. But the reproductive message is that, contrary to the Haldane, Fisher and laboratory models, genotypes within a species are amazingly varied (Rollo, 1995).

What needs to be explained, therefore, is the *phenotypic* similarity of organisms in a population, despite their different genetic blueprints (Rollo, 1995). Waddington (1956) had laid the foundations of this in his concept of 'canalization'. Wild species had 'balanced genomes', so that a frog developing at 8 °C ended up looking like the same animal that it would have been had it developed at 28 °C, by using a different developmental route and by using different variants of temperature-sensitive enzymes. Equally, the same frog would be produced even if there were several 'less useful' alleles present and, indeed, there usually are (Rollo, 1995).

In Birmingham, we had three populations of zebra fishes. First, there were wild (pet shop!) *Danio (Brachydanio) rerio*, whose developmental stability resistant was 500 rad of X-rays. Fifty per cent of these failed to develop, but few of the rest had overt abnormalities. In a long-finned domestic variant, whose canalization was compromised by inbreeding, 50–100 rad resulted in 50% abnormal developments, including enlargement of the pericardium, as well as eye and blood vessel abnormalities. The third population comprised 'zebra crossings', whose five-generation-back ancestors had been crossed with *Danio nigropunctatus*, then consistently back to *Danio rerio*. These crossings destroyed the balance of their genomes, so that without irradiation, they produced about 50% abnormal developments. What had happened is that they had lost their canalization of development and showed noticeable asymmetry of fin ray number and other abnormalities.

The general lessons to be learned from these observations are that genetics in natural populations is much more variable than we had thought and that phenotypic stability is hard won. So, for gamete biologists, minds should be kept open to the possibility that, at least in K-strategist species (those producing relatively few zygotes), gametes are selected to construct or maintain balanced genomes.

The third revolution is still proceeding. The Mendelian recombination model for meiotic processes has been an accepted textbook diagram for almost 80 years. It claims that homologous chromosomes associate into bivalents, each forming two chromatids. Non-sister chromatids then break and rejoin, without any interpolations or deletions, forming a new chromosomal array for assortment into spermatids, ootids or polar bodies. These meiotic products can easily be examined in mycelial ascomycetes. In these organisms there is a postmeiotic mitosis, which allows any mispairing in postmeiotic products to be discriminated, so that each makes two ascopores. It can be observed that non-reciprocal exchange, called 'gene conversion', appears in up to a third of asci (each containing 8 ascospores). This is best explained by the resolution of heteroduplex DNA segments (whose bases do not pair properly) into neighbouring ascospores by postmeiotic mitosis. This non-reciprocal exchange can be seen in ascomycete fungi, but there is good evidence that such non-Mendelian repairs or reconstructions occur *wherever* there are meiotic processes (Smith *et al.*, 1995; Roeder, 1997). The relevance here is that if ascomycetes do indeed show us the general meiotic picture in detail, then most spermatozoa and ootids have unresolved heteroduplexes, because unlike ascomycetes they do not have postmeiotic mitosis, which could resolve them into two different DNA duplexes in the daughter cells. Hanneman *et al.* (1997) have recently published an analysis of this in mouse spermatids. Cohen (1967) showed that this could explain sperm numbers if those spermatozoa with heteroduplexes were not used for fertilization. Cross-species comparisons showed that, as the number of recombination events rises linearly, the number of spermatozoa offered for each fertilization rises logarithmically. If a large proportion of spermatozoa are not to fertilize, the reciprocal of this, at least, would have to be offered at copulation. For example, if only 6 per 1000 spermatozoa were permitted to reach the site of fertilization, at least a thousand would have to be offered for six fertilizations to be accomplished. (It would be expected that *all* spermatozoa *could* fertilize, if they reached the right place at the right time; a 'confession mechanism' for heteroduplexes – if that is what caused the problems – would prevent most spermatozoa from getting the chance.)

Reproduction and redundancy

Charles Darwin, Wallace and the early twentieth century embryologists were all impressed by the 'profligacy of Nature'. They were impressed, also, by the beauty of biological adaptation: Nature, it was believed, was profligate with well-adapted organisms, rather than most organisms being mistakes of the evolutionary process. The number of spermatozoa, for example, was seen as another indication of Nature's overprovision, not as a profligacy error. Only in the period of material shortage after the Second World War were biologists to begin to question this philosophy. Typical of the reversal of thought is Saunders' (1970) statement that 'The egg has solved its problem'. Almost without fail, each egg produced in the right environment forms a new individual, which in turn makes sperm or eggs that begin another generation. In this new paradigm, the overwhelming numbers of spermatozoa were seen as a puzzle to be explained, because biological efficiency, not profligacy, was the expectation. Two classes of explanation were offered, paralleling the ecological explanations of prodigality of, for example, fish eggs (the female cod fish lays about 40 million eggs in her life, of which only two, on average, survive to breed). It was considered that gametes were either being offered up to a dangerous world (Antonie van Leeuwenhoek in 1658 had said that 'There must be many adventurers, when the task is so difficult . . .') or the process of their production (like that of some early computer chips) was such that a vast excess of failure was an inevitable outcome (Cohen, 1967, 1971, 1973, 1975*a*). Bishop (1964), for example, suggested that most spermatozoa had defects inherited from the male that produced them, but in the female tract were winnowed down to useful ones. This could be explained, however, as being due to heteroduplexes in DNA.

[An interesting error was that large numbers of spermatozoa were necessary to expose the range of Mendelian possibilities. But if, for instance, only 10 spermatozoa are used, it makes no difference to the assortment of genes in each spermatozoon, whether 10, 20 or 30 million spermatozoa are offered in the first place. In other words, you do not have to deal all the cards to guarantee that each hand is random.]

Nature's overproduction is now seen in a new light by ecologists, and we should perhaps take this new way of thinking on board for spermatozoa too. The energetic 'costs' of reproduction, which in the 1960s and 1970s were seen as the major currency of ecology (Philippson, 1964) are now, with the demise of 'balance' ecological models, regarded as impossible to calculate. Here is an example other than that of spermatozoa. Nauplius larvae of barnacles contribute greatly to the spring zooplankton of the North Sea and they include those of *Sacculina* (aberrant barnacles, which are parasitic on crabs), as well as the larvae of the acorn barnacle *Chthamalus.* Who pays energetically for these larvae? Is it perhaps the crabs, because parental barnacles provide yolk more in the parasite than in the free-living organisms? Alternatively, could it be the bounty of the sun via phytoplankton? How do we calculate the energetic cost of a human ejaculate with 200 million spermatozoa in it, relative to that individual's physiological arithmetic? It is about 5% of skin cell loss, 3% of gut cell loss, or less than 1% of erythrocyte turnover (but these are anuclear and cost less). In such an economic biological model, spermatozoa have been supposed to contribute to female nutrition. But, except for a few cases such as leaf-eating monkeys (which are deficient in nucleic acids), and some queen termites (which receive only sugar solutions from the workers and need spermatozoa from the kings to make eggs), arithmetic of this kind is clearly inappropriate. Surely the cost of ejaculates to a man, or to a bull, is incalculable (but see Dewsbury, 1983, for a good comparative attempt). So how can profligacy or efficiency be measured against loss, sperm heterogeneity or sperm effectiveness as a reproductive strategy?

In recent years, the community at large has been encouraged to avoid thinking about the real, that is the actual, arithmetic of ecology. Some wildlife films may have encouraged the belief that animals in the wild live long, happy and fulfilling lives compared to those in, for example, agriculture or laboratories (Cohen, 1996). However, the real arithmetic resembles that of spermatozoa, rather than of well-balanced accounts of a corner store. Even K-strategists, such as starlings, lay about 16 eggs in their lives, of which about 2 survive to breed. For some frogs, the figure is 10 000 eggs, of which 2 survive to breed, and for cod 39 999 998 eggs contribute to food chains in order to produce 1 pair of parents. Darwin told us this, but the lesson has been greatly diluted by the great amount of attention devoted to geneticists' experiments with fruit flies or mice. Breeders are selected and are on average different from the rest. This was not what laboratory *Drosophila* tell us, but it is true in Nature. Equally, the possibility that there is sorting among gametes, not merely profligacy, cannot be ignored.

For many years it was believed that Mendelian ratios were proof that the genetic constitution of an egg or a spermatozoon did not affect its chances of fertilization. The 3:1 ratio or 9:3:3:1 proportions showed that, for those particular alleles, there was no discrimination, no bias. They demonstrated further that this was true for many alleles. However, many loci (such as the t-locus in the mouse, SD in *Drosophila* and HLA in humans) did not behave in a Mendelian fashion. Perhaps there could be genetic situations, produced as a result of meiosis, that need not be represented by zygotes. Cohen (1967) came up with the suggestion that the meiotic non-reciprocity in ascomycetes gene conversion could account for sperm redundancy in a new way, if it occurred in all other meioses and prohibited access to fertilization for spermatozoa with problems of this type. C (chiasma number at meiosis) and R (sperm redundancy) data were collected for a wide variety of organisms. Oocyte redundancy in some females was also included. The conclusion drawn from these data (Cohen, 1973) was that spermatozoa were mostly badly made. They needed a test-and-select process to allow some (the few effective ones) to reach the site of fertilization. This initiated a successful research programme, which, unfortunately, has remained a bywater of reproductive theory (Cohen & Adeghe, 1987; Cohen, 1992).

Sperm competition

The concept of sperm competition, which is discussed in more depth in Chapter 2, arose partly because a clever set of observations had led Parker

(1970, 1984) to propose that the major reason for large numbers of spermatozoa being produced by one male was so that they could compete successfully in the female with those from other males. Males who won this battle, like those who won courtship competitions and had successful female-guarding strategies, became ancestors. The others were lost to posterity. The obvious way to compete was to produce more of the cheap-to-produce spermatozoa. More and more evidence in support of this accumulated (see Smith, 1984); for example, in 1979, Short demonstrated that testis size and sperm output in the gorilla, the chimpanzee and man were each related to mating strategies, with the chimpanzee's ten times larger ejaculate having predominated evolutionarily because of the multimale copulations that occur when a female is in oestrus. Gorillas rarely have sperm competition and, accordingly, they have very small testes. Man is intermediate between these two apes with regard to testis size. It has been discovered that there is extra-partner mating in several monogamous species of birds (Birkhead, Chapter 2). Furthermore, DNA paternity assignments in other wild species have shown diversity of paternity and this has indicated that sperm competition (that is, the presence of spermatozoa from two or more males inside a female at the time of ovulation) is much more common than had been thought, perhaps even among mammals (Møller & Birkhead, 1989).

There has been a great deal of recent work documenting sperm competition in insects and birds. Here, the geometry of the female tract determines whether spermatozoa are stacked in a cul-de-sac spermatheca, so that last-male precedence occurs, or whether spermatozoa queue in a tube, so that there is first-male precedence. In their ejaculates some males mimic substances normally used by the female to cause ovulation, and so presumably achieve more ovulations at the expense of subsequent males. A variety of these postcopulatory tactics is seen in animals, ranging from female guarding to copulatory locks and plugs, offensive substances exuded from the mated female to deter further matings, and substances in ejaculates which subvert rejection in the female tract. These have been comprehensively reviewed by Andersson (1994). Darwin (1871) believed that male–male competition for females was a major factor in the evolution of male display, especially in human evolution. But the tactics have turned out to be more detailed and devious than even he would have guessed. Whether they are as devious as Baker & Bellis (1995) supposed is a matter of debate, but, if their data are to be believed, there is a case for sperm competition in man. It is unlikely, however, that it has the baroque theoretical basis which they propose, with 'kamikaze' spermatozoa and other fanciful ideas.

There is one further twist to the story, which pushes Andersson's review into the same historical context as that of Darwin. It is perhaps because we are now beginning to bring context into scientific explanations (Cohen & Stewart, 1994). This has happened later in molecular biology than in some other areas of science (Cohen & Rice, 1996), but the authors of some of the