Hamilton Symposium

Introduction to William D. Hamilton Symposium

On 7 March 2000, William Donald Hamilton died in Oxford, England, from malaria contracted during a field expedition to the Congo. With his death, the field of evolutionary biology arguably lost its greatest practitioner since Charles Darwin. W. D. Hamilton made major contributions to many areas of evolutionary biology, but perhaps his greatest impact was on the discipline of behavioral ecology. The topics that he focused his energies upon include kin selection, reciprocity, sex-ratio selection, the evolution of senescence, alternative reproductive strategies, selfish gains of group living, haplodiploidy and the evolution of eusociality, parasite–host arms races, and the role of parasites in both mate choice and the evolution of sex. His contributions formed a foundation for the new field of sociobiology, and his theories provide the bases for a good deal of the theoretical and empirical work currently being done in behavioral ecology.

Given the intellectual contributions of the man and the magnitude of the void caused by his loss, the International Society for Behavioral Ecology decided to honor the life of William Hamilton in two tangible ways. The first was to hold a symposium in his honor at the Eighth International Behavioral Ecology Congress in Zurich, Switzerland, on 10 August 2000. The proceedings of the symposium are published in the pages that follow. The second is to sponsor a William D. Hamilton Lectureship to be presented at each future ISBE Congress. The society's executive council will biennially select a distinguished evolutionary behaviorist to present this lecture.

William Hamilton was, first and foremost, a passionate natural historian. He traveled throughout the world, but especially loved its tropical regions. He repeatedly stated that he obtained many of his research ideas from simple observations made in nature. Yet Hamilton was no ordinary natural historian. He had the knack of selecting research topics that had broad evolutionary implications. He sought out unanswered questions—evolutionary paradoxes—that were not readily explicable by current natural selection theory. As Richard D. Alexander so aptly expressed it, "Bill's originality of mind often turned the barely articulated ideas of distinguished predecessors—ideas overlooked or neglected by all the rest of us—into magnificent theoretical edifices affecting our view of all life" (*Natural History,* vol. 6, 2000, pp. 44–46).

Hamilton may have taken his ideas from nature, but he developed his hypotheses in the form of rigorous mathematical models. In an interview with Frans Roes, he said: "Often I use mathematics because I need to straighten out my own ideas. I have a somewhat illogical brain, and unless I put it through the mill of mathematics, I can continue to believe in the impossible for a long time" (*International Society of Human Ethology Newsletter,* vol. 12, 1997, pp. 3–7). The math helped to make his assumptions clear and his predictions more precise. This, in turn, enabled others not only to understand his innovative ideas but also to design better empirical tests of his theories.

For our symposium, we selected three of the theoretical edifices that owe much to William Hamilton: kin selection and social evolution, sexual selection and parasites, and parasites and the evolution of sex. We asked David Queller, Manfred Milinski, and Paul Schmid-Hempel to summarize and comment on Hamilton's contributions to each area. We trust that readers will find the symposium papers to be valuable personalized synopses, not only of Hamilton's contributions, but also of current unresolved issues in each area.

It is too soon to measure the full magnitude of William Hamilton's impact on evolutionary biology, but it is safe to say that it will be immense. We can state with certainty that his ideas on inclusive fitness and reciprocity have revolutionized the ways in which we view social conflict and cooperation. The jury currently is more mixed on the relative importance of his thoughts concerning parasite–host arms races as a primary cause for the evolution of sexual reproduction. But there can be little doubt that succeeding generations of evolutionary biologists in general, and behavioral ecologists in particular, will continue to find fertile ground in the innovative ideas first suggested or formalized by Hamilton. He will be sorely missed. We hope that the symposium papers that follow will help readers to put some of Hamilton's contributions into perspective.

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W. D. Hamilton and the evolution of sociality

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Bill Hamilton was always at his best in small groups, and I would like to open and close my reflections with some thoughts generated by two small scientific meetings that Bill Hamilton attended. I was not present at the first meeting, in Tvarminne, Finland, but a photograph from the meeting made an impression on me. In the foreground stood Pekka Pamilo, the organizer of the meeting, with a rather worried expression on his face. In the background was Bill Hamilton, skating across the ice. Bill had brought his ice skates, intent on taking every advantage of this visit to the north. It turned out, however, that the ice was quite thin, so the organizers attempted to dissuade Bill. They made a general request that speakers at the meeting should please not attempt any ice skating, at least until after they had delivered their talks. Bill followed the letter of this request, but did not follow its spirit. After giving his talk, he donned his skates and set off.

This picture brought to mind all sorts of associations. How can one not remember J. B. S. Haldane's musings about being willing to rescue two drowning brothers, or eight cousins. I hope Pekka will forgive me if I try to imagine his thoughts about the possibility of Bill falling though the ice. "Well, I do not think I am related to him . . . On the other hand, everyone in Finland is more or less related! But then, he is not from Finland, is he? Still, we may not share many genes, but we do share a great many memes."

The other thought that comes to my mind is one that has been noted frequently since Bill's recent death from malaria. Bill Hamilton was a risk taker, not just in his life, but also in his science. In his work, too, he sometimes skated on thin ice, traveling where others would not. E. O. Wilson once used exactly this metaphor to describe a certain kind of scientist who is always drawn to the dangerous or to the forbidden: "They are the taboo breakers who enjoy the whiff of grape-shot and the crackle of thin ice" (Wilson, 1978: 283). When Bill skated on thin ice in Finland, the results were satisfactory: the ice may have crackled but it did not give way. When he skated on thin scientific ice, the results were usually not just satisfactory, but glorious.

Bill Hamilton's most glorious ideas were kin selection and inclusive fitness. Talking about Hamilton's contributions to inclusive fitness is a bit like talking about Isaac Newton's contributions to dynamics or Charles Darwin's contributions to natural selection. He invented the idea, and he developed most of its important implications. There were some forerunners, as there always are in science. I think of Hamilton's contribution as a fusing of two traditions. First, there was population genetics. Hamilton didn't completely invent the idea of kin selection. The idea was foreshadowed by Haldane (1955), Fisher (1958), and Williams (Williams and Williams, 1957). However, none of them developed it in any detail, perhaps because they did not appreciate its general importance in nature. For that we can thank animal behaviorists, particularly those like Wynne-Edwards (1962) and Emerson (1960), who believed that cooperation was very common in nature. Bill neatly hybridized the two traditions. If cooperation and altruism were important in nature, then we needed an explanation that was consistent with population genetics, and so inclusive fitness was born.

Hamilton was well suited to make this match. Those acquainted with Hamilton only through his best-known papers may think of him as a theoretician and might conclude that he had the theoretician's superficial knowledge of the natural world. But in fact it was his mathematical skills that were hard won, while as a natural historian he was, well, a natural. You can see evidence of this in many of his papers, but it comes out particularly in his lesser known papers on insects under bark (Hamilton, 1978) and on fig wasps (Hamilton, 1979).

So was Hamilton's contribution a simple merging of the insights of an ethologist and a population geneticist? No, it wasn't that simple, for several reasons. First, there was a lot of thin ice between these areas, and skating from one to the other was not encouraged in the early 1960s. Geneticists were leery of anything that smacked of eugenics. That included any application of population genetics to behavior. It included most of all applications to understanding social behavior, something we have always been a little touchy about. If nature was nasty, rude, or bawdy, better not to know about it, let alone let the public know. Let me illustrate the idea in an unconventional way, with a bit of verse that I call "Family Values":

> Would I jump in a lake
>   To save my drowning cousin?
> It's not a risk I'd take
>   For him plus half a dozen.
> But if you raise the stake
>   And make the prize my brother?
> Now that's a deal I'll make. . .
>   If you'll just toss in another.

If this poem, and the Haldane quip it is based upon, elicit chuckles, it is in large part because they treat a topic that is uncomfortable for us. Most humor is built on discomfort of one form or another. In this case, we recognize that we make unconscious judgments akin to these, with awkward balances of self-interest and family interest, but we don't like to see ourselves as calculating self-servers. Now throw in a good dash of genetics, and the mixture becomes truly taboo. Perhaps that's why Haldane and others did not pursue the topic.

Bill's recollections of his graduate career (Hamilton, 1996) describe the price that he paid for his desire to be where the ice is thin. He had difficulty finding advisors. He had no desk. He had no invitations to talk about his work. It was not even clear that his thesis work, which would produce some of the most heavily cited papers in evolutionary biology (Hamilton, 1964a,b), would be acceptable for a Ph.D. For someone who was not socially outgoing in the first place, the effect of this isolation was severe. He feared that he might be a crank; why else would all these manifestly smart people fail to see the interest in what he was doing? He took to working in train stations and public parks simply to have some minimal level of human interaction.

Mary Jane West Eberhard made a telling point in her talk about Bill at a recent meeting (West-Eberhard, 2000). She noted that Bill's life serves as a counter-example to those critics who said that sociobiological knowledge was dangerous. He was proof that one can see all that is grim in the depths of our nature and still live a life of decency and kindness. Bill would have been uncomfortable with hagiography. His writings allude to a knowledge of the dark side of human nature, obvious to him through introspection, so clearly his thoughts were not always saintly. But whatever dark thoughts swirled in his mind, on the surface—and this is where it counts—he was basically a gentle man. Despite his highly critical mind, I never heard him criticize anyone in anything but the kindest, most self-effacing manner. He did not judge people by credentials and had time for people that others might consider to be amateurs or even crackpots, George Price being a notable example. And while he no doubt appreciated the recognition he eventually received, particularly given his lonely days as a graduate student, he did not seem to crave recognition excessively. Dawkins reported one example where Bill gave credit to someone else for an idea that was really his own and had to be confronted with the evidence from his own paper (Dawkins, 2000). Then, as Dawkins described it with an adverbial tour de force, Bill "eeyorishly" admitted that, yes, he'd had the idea, but the other fellow had put it much better.

I can give another small illustration from my own experience. In 1985 I published a paper using Price's rule to obtain a new expression for inclusive fitness (Queller, 1985). Alan Grafen then chided me (Grafen, 1985), quite rightly, for having neglected to cite Hamilton's paper using Price's rule (Hamilton, 1970). My only excuse is that Bill had read my paper in manuscript without ever pointing out the omission, which he must have noticed. For that matter, I had learned about Price's rule directly from Bill in seminars at the University of Michigan. If I remembered Price's rule well and forgot Bill's uses of it, it is partly because of the selfless way that Bill taught the subject.

There is a another reason that Hamilton's contribution cannot be viewed as a simple merging of naturalist and theoretical traditions. He did not just come up with any old theoretical model. For example, one could model the evolution of altruism for some particular limited set of conditions (George and Doris Williams had already done this; Williams and Williams, 1957), but then one has to wonder how general the conclusions are. And it is also possible, as other modelers later showed, to add so many mathematical bells and whistles that we lose track of the general theme. In contrast, what Hamilton came up with was a theory that was not only basically true, but also beautiful and elegant. I'm not speaking of the mathematical derivation in his 1964 paper, which was actually rather gruesome. I'm speaking of the result, what has come to be

known as Hamilton's rule. It is so simple that even a non-mathematical mind can easily understand it and wield it, and so general that it can often be applied to new social evolution problems without any fresh mathematical modeling.

How was this simple elegance achieved? I think there are two main reasons. First, Hamilton was willing to make assumptions that allowed the result to be simple without seriously compromising the biology. For example, he assumed that selection would be weak. Stronger selection has the effect of distorting the relatednesses away from their familiar values, and it makes them dependent on genetic details such as dominance. Hamilton's assumption was justified because weak selection is presumably common. For that matter, it's probably not so bad an approximation for stronger selection. A little distortion of correlation coefficients doesn't matter too much to someone interested in the real world, where estimates of parameters are typically only good to about one significant digit anyway.

The second reason inclusive fitness is so useful is its inversion of fitness calculation methods. Instead of grouping together all effects of others on x's fitness, it calculated all the inclusive effects of x on others' fitnesses. This actor-centered approach is what makes the method so easy to apply. In Hamilton's own words: "The social behaviour of a species evolves in such a way that in each distinct behaviour-evoking situation the individual will seem to value his neighbors' fitness against his own according to the coefficients of relationship appropriate to the situation" (Hamilton, 1964b: 19).

It has become clear in recent years that the same behaviors can also often be understood as a form of group selection—not the old group selection of Wynne-Edwards, but nevertheless a method that involves partitioning of selection into within-group and between-group components (see Sober and Wilson, 1998). But the fact remains that almost no one uses these methods much to think about and solve interesting problems. Each of the two methods can dissect social evolution into component parts, but where inclusive fitness divides nature neatly at the joints, other methods seem to hack clumsily through the long bones.

Inclusive fitness and kin selection were important on several levels. First, of course, they provided an explanation for the evolution of altruism. We still don't know whether Hamilton's famous haplodiploid hypothesis, based on three-quarters relatedness (Hamilton, 1964b, 1972), explains the origin of eusociality. But it seems certain that the answer does lie within his more general framework of relatedness, costs, and benefits. For the study of social insects, another result of inclusive thinking was perhaps even more interesting. The theory did not simply explain the altruism that we already knew about. It also predicted something we did not know much about: conflicts within colonies. Because inclusive fitness interests often differ even among close relatives (Hamilton, 1972), there can be conflicts over who should be queen, conflicts over who should lay the male-destined eggs, and conflicts over sex ratios (reviewed in Queller and Strassmann, 1998). Studies in these areas have amply satisfied the requirement that a good theory should not just explain what is known, but also make novel and successful predictions.

I think a parallel phenomenon occurs in the world beyond social insects. Perhaps even more important than the explanation of altruism itself was the general validation given to selfish gene models. If selfish genes are to be of any value in explaining the evolution of social behavior, they simply must be able to explain the cases where the behavior is not phenotypically selfish. Otherwise the method must be counted as a failure. So kin-selected explanations of altruistic behavior gave life to selfish gene explanation in areas where kinship was not paramount. Hamilton's own work clearly shows this. He didn't stop with altruism. He made pioneering contributions in many other areas. The accompanying pieces in this issue describe his contributions to the study of sexual selection and parasites, but

his work also included important contributions to senescence theory (Hamilton, 1966), sex ratios (Hamilton, 1967), selfish herds (Hamilton, 1971), dispersal (Hamilton and May, 1977), tit-for-tat cooperation (Axelrod and Hamilton, 1981), and within-individual conflict (Hamilton, 1967). This truly formidable list of accomplishments, and the whole selfish gene tradition of which it is a part, emerged from a confidence based on Hamilton's success in solving the potentially fatal problem of altruism.

Finally, in recent years it has become increasingly clear that a theory of altruism and cooperation is important for a much grander reason than solving the annoying puzzle of the social insects. It is also needed to explain a much more pervasive kind of cooperation; the evolution of the organism itself (Maynard Smith and Szathmáry, 1995) Why do cells cooperate in a body? Why do formerly independent bacteria evolve into organelles? How did replicators get together in the first place? Organisms, though they compete selfishly with each other, are themselves cooperative entities. Cooperation is therefore fundamental to all of life.

I began with a small scientific meeting in Finland. Let me close with another one, in Castiglioncello, Italy. The highest scientific compliment I have ever received was one that Bill delivered there, actually to my wife and collaborator Joan Strassmann. Bill had, many years previously, done field work in Brazil on the troubling question of how sociality could be maintained in wasps with many queens. We had recently helped show, with molecular tools that had not been available to Bill, how relatedness was kept at levels consistent with kin selection (Queller et al., 1988, 1993; West Eberhard, 1978). What he said to Joan was "Now I will have to think up a different question to ask St. Peter when I meet him." Of course, this was ridiculously inflated praise, a reflection of Bill's generosity rather than his acumen. He was no doubt signaling this exaggeration by his use of the religious reference, since Bill did not seem to be a conventionally religious man. Instead, he is some one who saw his afterlife more in terms of burying beetles (Hamilton, 2000) than in terms of meeting St. Peter.

Still, I'd like to run with idea for just a moment. In the sad days after Bill died, the thought of him interrogating St. Peter gave me a certain amount of solace, and perhaps even pleasure. It's not that I can imagine what Bill's question was. Nor was it the thought of him receiving a satisfactory answer. Instead, what appeals to me is the impact on old St. Peter. I imagine him at first flummoxed because he couldn't answer the question, then annoyed because he had never thought of it himself, and finally intrigued by the implications. I imagine him spending his free moments over the next few centuries thinking about it, making new observations on the teeming life below, scribbling some population genetic equations in the margins of his heavenly register, and perhaps running some simulations on God's fastest supercomputer. Perhaps I overestimate St. Peter's curiosity, but Bill's questions have always had that kind of effect. That they will long continue to do so is his legacy to us.

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Bill Hamilton, sexual selection, and parasites

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Darwin (1871) first introduced the idea that males with elaborate ornaments have a net benefit because they are preferred as mates. Evidence for such preferences is now abundant (e.g.,

Andersson, 1994). A more troublesome problem has been to understand the evolution of female preferences for handicapped males. Until the early 1980s, there were mainly two theories: (1) Fisher's (1930) runaway process, which predicts that the male character and the female preference could, through genetic correlation in the offspring, advance together with ever-increasing speed. This was ''easy to see,'' as Fisher wrote, and therefore he did not provide a formal proof. (2) Zahavi's (1975) handicap principle: a female prefers a male with a handicapping trait because this male must have high viability (i.e. good genes), to be able to survive with the handicap. Both hypotheses appeared to resist any theoretical proof that was based on conventional population genetics. For example, the problem with all good genes models is that if females prefer to mate with the males that have the good genes for high viability, then these genes become quickly fixed in the population and nothing will be revealed by the handicap except the handicap itself. So females should stop preferring handicapped males.

In the early 1980s both hypotheses suddenly received support. Lande (1981) and Kirkpatrick (1982) showed with elaborate genetic models that Fisher's runaway process can work [actually O'Donald (1980) had paved the way]. But it was Bill Hamilton and Marlene Zuk (1982; see also Hamilton, 1982) who proposed a new good genes hypothesis that predicted substantial additive heritability for viability genes ad infinitum. Hamilton and Zuk (1982) suggested that genes for resistance might have important effects on fitness and always remain heritable. The interaction between host and parasite is unusual because it produces cycles of coadaptation. These cycles can ensure a continual source of fitness variation in genotypes.

Imagine a host and a parasite population in which individual hosts differ in their resistance to different genotypes of the parasite. Some hosts are resistant to parasite A, some to parasite B. If a female chooses a male that is resistant to parasite A, when this is the more common parasite genotype, she is obviously getting a selective advantage because her offspring will be more likely to be resistant to the common disease. So the next host generation may be more resistant to parasite A. Now parasite B can successfully infect the host population, and females should prefer males that are resistant to B. The process will be cyclical because new resistant genotypes that arise in the host species will provoke the evolution of new parasite genotypes; these in turn will provoke the evolution of new host genotypes; and so on ad infinitum. This provides a plausible reason that a population may have substantial additive heritability for disease resistance. Then a male who is unmistakably outstanding in health and vigor offers females that mate with him an inherited healthiness in their offspring that is well above average (Hamilton and Zuk, 1982).

How do females detect the males that are resistant to the currently predominating parasite? Hamilton and Zuk's (1982) clever insight was that the method a female uses should have much in common with those of a physician checking eligibility for life insurance. The choosing animal should unclothe the subject, weigh, listen, observe vital capacity, and take blood, urine, and fecal samples. Instead, if a male can present an elaborate bright plumage, produce a song that is energetically costly, and display with an exhausting athletic behavior, it likely has the currently needed genes for resistance because it so demonstrates that it is healthy.

In later generations, other resistance genes against other parasites need to be detected. Again, females can use the same preference for elaborate adornment to detect those males that are resistant to the new parasite. Hamilton and Zuk (1982) predicted for comparisons among species that species that show strongly developed epigamic characters should be subject to a wider variety of parasites. In species where disease
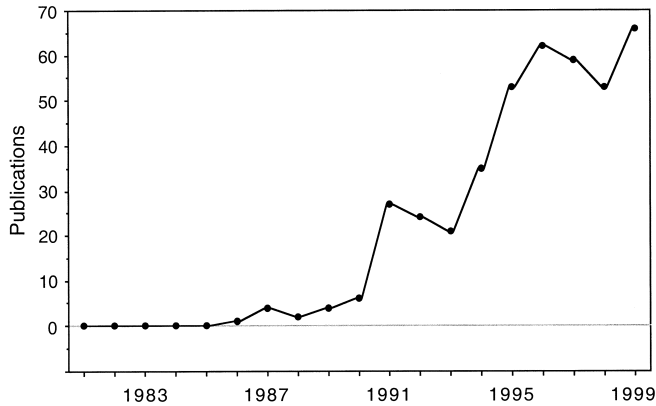
Figure 1
Publications per year on sexual selection and parasites; source ISI WoS using key words "parasite" or "parasites" or "parasitized" and "mate" or "mates" or "sexual selection."

is relatively unimportant, animals should be less showy. Within a species, preferred mates should have the smallest parasite burden; parasites should reduce the showy character, and females need to see this character when they prefer parasite-free mates.

Hamilton and Zuk (1982) provided a comparative test of blood parasites and showiness of many species of North American birds. As predicted, they found a highly significant association over species between incidence of chronic blood infections and striking display characters. Several years later new comparative results from other authors (e.g., Read, 1987; Ward, 1988) supported the Hamilton-Zuk hypothesis. However, the following generation of comparative tests did not (e.g., Read and Harvey, 1989). Actually, there seemed to be cycles of supporting and nonsupporting comparative studies. Taken together, it appears now that the comparative evidence is equivocal.

It is certainly true that the Hamilton-Zuk hypothesis provoked a whole generation of behavioral ecologists to regard sexual selection and the potential role of parasites as the major topic for at least two decades of research. The five previous behavioral ecology conferences each had several sessions on mate choice. Sexual selection had been a minority topic during the time before the Hamilton-Zuk hypothesis.

In 1986, there was a Dahlem Workshop on "Sexual Selection: Testing the Alternatives," which appeared to set the stage for research on sexual selection for the years to come. All participants signed the cover of the book (Bradbury and Andersson, 1987). However, Bill Hamilton's signature is difficult to detect: modest as he always was, he is hiding in the bottom-right corner of the back cover.

I found the Dahlem conference extremely stimulating, especially because I had been lucky to be in Bill's discussion group. Thereafter I worked next door to Bill at Oxford for half a year and found him always to be enthusiastic about the natural history of animals—and he was completely addicted to thinking of parasites!

In 1990, the first experimental intraspecific tests of the Hamilton-Zuk hypothesis were published (Milinski and Bakker, 1990; Møller, 1990; Zuk et al., 1990). This was only the beginning of a movement that almost took over many journals (Figure 1). According to my subjective statistics (see Andersson, 1994, for a balanced view), most intraspecific tests supported the Hamilton-Zuk hypothesis. At the present International Society for Behavioral Ecology Conference at Zürich, there is at least 1 plenary talk, 77 short talks, and numerous posters on sexual selection. Immunology and immunogenetics

seem to be more important now than these fields were in previous conferences. Suppose for a moment that Bill Hamilton had not existed. Could one think of a behavioral ecology conference that presents a keynote talk on "the origin and evolution of the vertebrate immune system"?

What did Bill Hamilton tell us about his more recent thoughts on sexual selection? The most recent paper, as far as I know, that he devoted entirely to mate choice was published in 1990 and was entitled "Mate Choice Near or Far." This paper was from a talk that he had given at a symposium on parasites and sexual selection. It is full of neat ideas; for example, he argues that in many monogamous species courtship is such a lengthy affair that "it has come to seem to me unlikely that a bird needs to rely on looking for bright, tidy plumage or listening to momentary expressions of energy and co-ordination made in complex melodic song" (341). And later he says, "but if all this casts doubt on showiness for monogamous choice it leaves us with a dilemma: if not for monogamy, and yet still used for sexual display, what else is showiness for?" (341). And then he argues in a very entertaining way that he thinks that all the showiness is just for attracting extrapair copulations:

It now seems to me that it may be much more in regard to these events than in regard to seasonal pair bonding that bright coloration of males plays its part. The female who is dissatisfied with the seeming genetic quality of her mate probably has had no chance to perform any detailed assessment of other males in her vicinity; but she may well be able to appreciate the relative qualities of advertisements that are being broadcast through brilliant plumage and song from males at their territory posts on nearby trees. . . . It will be those supposed monogamists, where brightest males are contrasted to dull females, that reveal most "infidelity" by females and variable negligence of maternal care by males. (342)

There is another piece of his prose that is as entertaining as it is enlightening:

Searching for an island in the morass of possibilities that opens, one might at first seize on the top pair as inevitably stable: surely the female of that pair must have the male that she wants. But if "good genes" have begun to rule, even this is not so. While we easily imagine that the top male is distracted from guarding his nest by invitations from other females, what is it we expect his mate, the top female, to be doing? Is she likely to be working hard on her own to support her mate's brood? Surely not: the top female may be having plenty of invitations too. These come from the lowly males. They are sending hints to her that she is welcome to play cuckoo at their nests—with the proviso, of course, that she allows a copulation first. Their signals may be imagined to convey something like this. "Look how dull I am. How can you possibly doubt—I am your true working father. I and my mate (but quiet about her) will look after your eggs better than you can." In the light of this thought it becomes not even clear that a top male will want the absolutely top female to be his mate, or vice versa. (Hamilton, 1990: 344)

Bill Hamilton's view of mate choice had become rather sophisticated even 10 years ago.

Bill Hamilton has been a member of the advisory committee of our Max Planck Institute at Ploen. For this task he spent 4 days at our institute in December 1999. He was full of plans and ideas and so enthusiastic that he appeared to be able to go on forever. Many of us would not have done the kind of research which we did without Bill Hamilton's ideas. His memes will continue to keep us working at least for the next decades.

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Wondering about sex: W. D. Hamilton's contribution to explaining nature's masterpiece

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Sexual reproduction, or sex for short, is an extremely successful breeding strategy. With some exceptions, metazoan organisms use sex, and even among protozoans or bacteria, some forms of sex exist, defined by its consequence of gene exchange (Bell, 1982). Yet, theory has so far failed to provide a universal and satisfactory explanation for the adaptive advantages of sex in Darwinian terms. This question captured William D. Hamilton's imagination for some 20 years, starting in the mid-1970s. His answer traces back to Haldane (1949) and was critically stimulated by George C. Williams (1975). In Hamilton's view, short-term advantages resulting from antagonistic coevolution by parasites favors sex, despite its inherent cost as compared to the asexual (parthenogenetic) alternative.

An annoying consequence of sex is visible in a well-known myth. When Noah loaded his ark, he took two individuals of each species—one male and one female—on board. Given the limited carrying capacity of his ark, Noah clearly had to accept a twofold cost of sex. Indeed, sexual species are forced to produce males in addition to females. If males were equally costly to produce, this requires that half of the resources available for breeding have to be invested in males whose only function is to fertilize the daughters. In most species, males provide little parental effort. To make matters worse, and as a consequence of having males, any one offspring that a female produces receives only half of her genes, the other half being from her mate. Although the precise definition often varies between students of the problem, there is such a thing as a "twofold cost" of sex compared to the asexual alternative (Maynard Smith, 1978). Bell (1982) defined sex by its aspects of mixis and syngamy, that is, the merging of genetic information, generally from different sources, into a single offspring. Sex is therefore conceptually different from reproduction because it changes the genetic state of the cell rather than the number of cells as happens with reproduction (Bell, 1982). We nevertheless speak of "sexual reproduction" because in higher organisms these two processes have become inextricably linked. This is not the end of the dilemma, however. Recombination of genes is a major defining feature of mixis and syngamy in higher organisms. Recombination universally breaks up gene combinations and therefore destroys a successful genotype that has, in fact, managed to survive and is now able to reproduce. The combination of these adversities makes the adaptive value of sex hard to explain.

Fisher (1930) realized that sexual reproduction, in particular the process of genetic recombination, leads to an increase in the genetic variance among offspring. According to his fundamental principle of natural selection, the rate of evolution is directly proportional to the extant amount of (additive) genetic variance present in a population. Therefore, sexual populations can respond to selection faster than asexual populations. Another way to put it is that sex and recombination allows allocating independently arising favorable mutants to one offspring much more efficiently. Asexuals have to wait for these independent mutations to occur one after another in the same lineage in order to find them combined in a single offspring (the "Fisher-Muller model"). This long-term advantage for a sexual population, so Fisher (1930) argued, favors sex and makes it spread and be maintained against the asexual alternative over long periods of time. This paradigm, which in essence was also shared by August Weismann and Hermann Muller, remained very much unchallenged for nearly 30 years. However, in the rebellious climate of the 1960s, evolutionary biologists started to doubt the validity of arguments based on long-term benefits for entire sets of individuals. Indeed, Crow and Kimura (1965, 1969) realized that Weismann, Muller, and Fisher all relied on group selection to explain sexual reproduction.

Group selection arguments of the kind postulated by Fisher (1930) were diametrically opposed to Hamilton's (1964) concept of kin selection and the implied process of direct, short-term benefits for alternative genetic information. From his own work on extreme sex ratios in a variety of insect species [e.g., fig wasps (Hamilton, 1967)], Hamilton could see that in small, localized and therefore inbred populations, the consequences of sex for recombination are more or less eliminated. At the same time, females in such populations can easily reduce their production of males and thus avoid some of the costs of sex without compromising efficient reproduction.

Against this background of his dissatisfaction with existing explanations, Hamilton was asked to review two books that both appeared in 1975: Michael T. Ghiselin's *The Economy of*

Nature and the Evolution of Sex and George C. Williams's *Sex and Evolution*. While he had some reservations against Ghiselin's treatment, Hamilton found himself in natural agreement with William's stance that "sex must be shown to be advantageous to the individual sexist, not just to population or species as a whole" (Hamilton, 1975: 175). In particular, Hamilton made the remarkable statement that

> it seems to me that [to explain sex] we need environmental fluctuations around a trend line of change. For the source of these we may look to fluctuations and periodicities inherent in our solar system, *and also to the possibility of others generated by life itself.* The latter line of thought tends to carry us back from the egg of sex to the hen of a multi-species system. (Hamilton, 1975: 180 [emphasis added])

Here, the kernel of the idea of antagonistic coevolution becomes visible, although, at the time, Hamilton did probably not think of parasites as the major cause.

This seemed to have changed radically over the following years and took shape in his landmark paper on "Sex vs. Non-sex vs. Parasites" (Hamilton, 1980). There, the idea of negative frequency-dependent selection caused by coevolving parasites is spelled out in mathematical terms and shown to be able to favor sexual over asexual reproduction, at least under some conditions. In this scenario, rare host genotypes have an advantage because they offer only a small target to the generally more rapidly evolving parasites. An implicit requirement is that parasites and their hosts match up to some degree. In other words, a parasite type can only infect one or a few host types, while hosts are susceptible to some but not all parasite types. This matching must reflect some genotypic variation in the host (and parasite, for that matter) because genotypic variation is what is affected by sex. In any case, when rare host genotypes have an advantage, rare host types must increase in numbers. At some point, this inevitably leads to the loss of their advantage due to rarity, and the parasites will now have ample opportunities to catch up on this common host and increase in numbers. Some time later still, the formerly rare host genotypes have become heavily infested by their coevolving parasites and will be at a disadvantage. These hosts will therefore start to decline in numbers, until they have reached their former status of a rare but fit genotype. In the meantime, other host (and parasite) genotypes have also gone through this co-evolutionary cycle. The time lag between the change in the host frequencies and the capacity of parasites to respond by numbers causes host and parasite genotypes to track each other over time. This scenario can create persistent cycles, albeit of irregular shape, with characteristics depending on the exact conditions. More importantly for our discussion, mothers that produce their offspring sexually are more likely to produce, by recombination, rare genotypes for their offspring than asexual mothers that have to wait for mutations to do the same. Therefore, sexual mothers are more likely to have offspring that escape the currently prevailing parasite types—the immediate advantage for the individual sexist that Hamilton was looking for (Hamilton, 1993; Hamilton et al., 1990).

It often happens that, at certain times during the history of a science, new ideas are somehow in the air. This was the case for the problem of sex in the mid-1970s. For example, Levin (1975), considering pest pressures on plants, proposed that recombination, preventing the congealing of the genome into a single linkage group, was selected for by persistent tracking of plant hosts by multiple pathogens and herbivores. A decisive element in the discussion was added by Clarke (1976) and Jaenike (1978) by pointing out that recombination is probably not advantageous simply because it produces new genotypes in offspring but because it generates rare genotypes. This is the essential idea of negative frequency-dependent selection whereby the rare genotypes have a high fitness and the common ones a low fitness. It was Hamilton who fleshed out these ideas in the way we discuss them today.

Van Valen (1973) realized that the geometric distribution of life spans of species, genera, and families over geological time spans, as inferred from palaeontological records, defied any simple notion of how accumulating effects of some kind (i.e., some form of "senescence") could lead to the ultimate death of a species. Rather, such a time-independent risk of extinction could be much more convincingly explained by assuming an ongoing coevolutionary arms race between a species and its competitors and enemies. This is very much like Alice's attempts to follow the Red Queen in *Through the Looking Glass* by running as fast as she can just to discover that both still are at the same place. When Van Valen (1973) used this analogy he did not think so much of parasites in this context. Bell (1982) connected this term to the explanation of sex and especially referred to the temporal dynamics of coevolving hosts and parasites, in contrast to the spatial aspect of among-offspring competition (which he called the "tangled bank"). It is interesting that the implications of the original Red Queen metaphor of Van Valen (1973) and the concept of Bell (1982) are actually quite different. In the coevolutionary race envisaged by Van Valen, species evolve in some direction—for example, toward harder shells in mussels and bigger claws in crabs. The essential feature of host–parasite coevolution, however, is the reuse of genetic information without any apparent evolutionary direction (Hamilton et al., 1990). Therefore, viewed from the outside, species may not appear to evolve at all, while behind this Potemkinian facade there is a violent turnover and recycling of genes as parasites chase their hosts through the genotype space.

Hamilton developed his ideas further in the early 1980s. He used a combination of analytical treatment and computer evaluations to consider explicit models for the evolution of sex (Hamilton, 1980). Essentially similar conclusions were also derived in a later study (Hamilton et al., 1981). In these studies, a major problem had to be discussed, too. At the time, models showed that the best conditions for the spread of sex were found when parasites exert strong, truncating selection and hosts have high fecundity. However, these are not the most obvious correlates of sex in nature. Indeed, sexual species typically have low fecundities; that is, they are species of large body size and extensive parental care (such as humans), and most parasites do not kill but rather just debilitate the host. However, the analysis in Hamilton et al. (1981), and especially later in Hamilton et al. (1990) showed that such conditions are not prohibitive for sex to prevail.

Hamilton was deeply interested in a special property of the Red Queen scenario that can explain the maintenance of large amounts of genetic variation in natural populations by selection rather than neutrality. In fact, compared to rivaling hypotheses, such as the mutation-accumulation hypothesis (Kondrashov, 1982), the Red Queen-type coevolutionary scenario suggests that sexual populations stow away temporarily unfit genetic information for a while because such alleles are not eliminated but protected by negative frequency-dependent selection. These alleles necessarily become rare with time but can provide protection during the next, though occasional episode where the selective environment reverses its state (i.e., new types of parasites become common). Hence, whether sex spreads is affected more often by which genotypes occupy the lower end of the fitness scale rather than who occupies the higher end. This is a consequence of the fact that the long-term geometric mean fitness determines the fate of a sexual or asexual variant and not the arithmetic mean fitness. And here, sex fares better than asex, because, after a while, individuals in sexual populations can still generate a rare offspring genotype when the overall parasite pressure on

common types has become strong, whereas the asexual parents carrying the now needed alleles were eliminated (and can only be regenerated by the vastly slower process of mutation). Hence, despite a higher fitness that asexual variants can exploit by carrying the best alleles most of time, they are unlikely to persist through occasional crunch periods when severe parasite pressure against these successful types has built up. During these episodes, recombination furnishes the now advantageous combinations much more quickly than mutation does. As a side effect, Hamilton realized, genetic variation is maintained in the population.

Empirical support for the concept of a parasite-driven Red Queen process is difficult to gather, especially in field systems. The most convincing evidence so far comes from the New Zealand freshwater snail *Potamopyrgus antipodarium,* where a long-term study has provided evidence for a cost of sex (Jokela et al., 1997a), but also for the connection of sex with parasites (especially trematodes; Lively, 1989) and rare-genotype advantage (Lively and Dybdahl, 2000). At the same time, plausible alternative hypotheses could be eliminated (Jokela et al., 1997b; Lively et al., 1998). Nevertheless, Hamilton's theory for the evolution and maintenance of sex is not universally accepted and, in fact, is a matter of heavy dispute (e.g., Barton and Charlesworth, 1998). On the other hand, his vision assembles a number of disparate phenomena under one umbrella—for example, the combinatorial lock-and-key aspects of host defenses against parasites and the advantage of sex through recombination. The field is thus wide open to imaginative research.

Hamilton's vision extended beyond the simple consideration of the conditions for the evolution of sex. In fact, Hamilton formulated one of the most challenging statements during the Dahlem conference in Berlin in 1982, when he stated that "if the idea about parasites is right, species may be seen in essence as guilds of genotypes committed to free fair exchange of biochemical technology for parasite exclusion" (Hamilton, 1982: 271). How coevolution with parasites may promote speciation and how this process could maintain species boundaries remains a major challenge for the future (e.g., Breeuwer and Werren, 1995). Similarly, and perhaps more disturbingly, for behavioral ecologists, Hamilton et al. (1981: 363) found that "if sex is so important then our reliance on coefficients of relatedness in genetical kinship theory is placed in doubt: the coefficients of relatedness currently used fail to asses special advantages possessed by sexual progeny." Indeed, the special combinatorial (epistatic) properties generated by recombination may not be adequately captured by the average genetic relatedness between parents and offspring. If such epistatic effects are strong, as they might be during occasional periods of intensive selection by parasites, the nonlinearity in the selection profile generated by coevolving parasites can counteract kinship benefits. To cooperate with close kin is therefore both a boon and a bane (Baer and Schmid-Hempel, 1999).

There is little doubt that Hamilton's interest in the evolution of sex was a straightforward extension of his thinking on kin selection and on a range of other phenomena, such as skewed sex ratios, group formation, and migration. His unifying principle was that selection operates primarily on genes and over short time scales. While he always stressed that selection operates at any level and all the time, this principle gives selection for the benefit of groups, populations, or species much less weight most of the time. The application of this principle has made behavioral ecology a very successful branch of research. However, we should remind ourselves that Hamilton's legacy is much broader than a series of single concepts that address, for example, the evolution of sociality or sexual selection. Rather, thinking in populations, with their ecology and dynamics of genes, based on sound natural history, is at the heart of the matter to explain the adaptive value of behaviors, or, more generally, the adaptive value of decisions made by organisms in their environment. Whatever direction the field of behavioral ecology takes in the future, this essential distillate of Bill Hamilton's ideas will be with us for a long time to come.

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