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Parasites and altruism: converging roads

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W.D. Hamilton was most known for his work on two topics: social evolution and parasites. Although at first glance these seem to be disparate interests, they share many attributes and have logical connections within evolutionary biology. Nevertheless, Hamilton's contributions in these areas met with very different receptions, with his place in the field of social evolution assured, but his work on the role of parasites perceived as more specialized. We take an historical approach to examine the reasons for this difference.

1. Introduction

W.D. Hamilton made seminal contributions to evolutionary biology, but he did so from two seemingly disparate approaches: the role of parasites in host biology, and social evolution. These areas may appear quite distinct, and they certainly usually are of interest to non-overlapping groups of specialists. From a broader perspective, however, the two sets of issues are conceptually related, and it is not difficult to understand Hamilton's forging a connection between them. Indeed, other major figures in evolutionary biology and population genetics, from Darwin to Fisher, shared his interest in both topics. Nonetheless, Hamilton's contributions to modern thought about the role of disease in evolution had a very different reception compared with his influence on current thinking about levels of selection and the evolution of cooperation. Whether or not they agree with Hamilton's views on the importance of kin selection, scientists are virtually universal in acknowledging the extraordinary influence those views have had on contemporary discussions of social evolution. By contrast, although one could argue that Hamilton's interest in parasites and disease helped fuel such modern subdisciplines as evolutionary medicine and ecoimmunology, neither of these compares with the juggernaut that was shaped by inclusive fitness theory.

What was responsible for this difference in reception? Below we point out some parallels in Hamilton's two major interests, and then take a historical perspective in an attempt to interpret the ways in which scientists incorporated Hamilton's work. Finally, we speculate on how both inclusive fitness theory and the role of parasites in host evolutionary biology are likely to figure in the future.

2. Parasites and kin: the connection

At the outset, parasites and pathogens seem to be direct opposites of the kind of cooperation that is at the heart of kin selection. And indeed, the kind of coevolution involved in host–pathogen interactions can be described as primarily antagonistic. But Hamilton saw the connection as more of an extended diplomatic interaction than an entrenched conflict. The endless running of the Red Queen means that the terms of battle are continually renegotiated, with greater and lesser harm to each party depending on the stage in the interaction. The basis for the immune system, the major means of defence against pathogens, is recognition of self versus non-self, which leaves plenty of room for variation in the degree to which objects will be treated as harmless or threatening.

Similarly, discussions of altruism centre on who is part of the group and who is not, and one might see inclusive fitness theory as an exploration of self versus non-self in this light as well. Mutualism can veer into antagonism and vice versa, depending on the costs and benefits to the parties involved. From Hamilton's perspective, then, an interest in the effects of pathogens, which so closely track the fluctuations in fitness of the host, followed very naturally upon an interest in levels of selection. As can be seen in the first two volumes of his collected works *Narrow Roads of Gene Land* [1,2], Hamilton moved from a focus on cooperation and group living to one on disease and sex, but tendrils of the former extended into his publications on the latter. But despite Hamilton's appreciation of their similarity, the two topics had had very different receptions from scientific community. Though it took the better part of a decade to gain traction, the work on kin selection and/or inclusive fitness eventually became foundational to evolutionary analysis. His later work on parasites, on the other hand, has remained the province of specialist communities.

Hamilton's work on inclusive fitness and kin selection appeared at a particularly opportune moment in the history of evolutionary theory. The architects of the modern synthesis had just celebrated the 100th anniversary of the publication of Darwin's *Origin*. The bringing together of population genetics and evolutionary theory had established a science that was quantitative, predictive and testable. Hamilton's contributions to the evolution of social behaviour were the culmination of decades of theoretical and empirical work. Indeed, kin selection and inclusive fitness, after a lag, were incorporated into standard practice for evolutionary biology, although heated discussions of their relative importance and implications continue into the present.

3. Social evolution in the canon

The incorporation of kin selection and inclusive fitness into the standard analyses of the evolution of social behaviour was well established within a decade of publication. This was enhanced by the invocation and application of Hamilton's model from Williams [3] to Dawkins [4] and perhaps most importantly in Wilson [5]. The influence of Wilson's citation was borne out by Seger & Harvey [6], who demonstrated that many authors took their citation of Hamilton [7] directly from the bibliography of *Sociobiology* including the mistaken title 'The Genetical *Theory* of Social Behavior' a la Fisher, rather than 'The Genetical *Evolution* of Social Behavior' a la Hamilton. This error was combined with the general ignorance of the 1970 paper influenced by the work of George Price [8], and the 1975 paper where Hamilton acknowledged that selection might act on groups of unrelated individuals [9]. Though Hamilton by no means abandoned kin selection and inclusive fitness, he broadened his own approach (as did Williams) more than many who cite only the 1964 papers allow.

For many biologists, Hamilton's work also put to rest the kind of mushy 'good of the species' arguments that evolutionary biologists had worked so hard to banish. Wynne-Edwards' 1962 book *Animal Dispersion in Relation to Social Behavior* [10], which presented one long argument for group selection, was a solid target for theorists. Hamilton's theory provided the explanation for the evolution of social behaviour that rendered group selection at least unnecessary and more promisingly, completely wrong. Though Hamilton himself was not motivated in his interests by the publication of Wynne-Edwards' book, the reviewer of his JTB articles, John Maynard Smith, was. In fact, the term *kin selection* was coined by Maynard Smith in his 1964 *Nature* response to Wynne-Edwards. Though he cited Hamilton's 1963 paper in *The American Naturalist*, he also cited JBS Haldane's 1955 *New Biology* paper, and from Hamilton's perspective gave them equal credit for developing the idea of inclusive fitness. Of course, Maynard Smith's term, kin selection, became immediately well known and his 'haystack' model critique of group selection remains influential. This episode strained the relationship between Maynard Smith and Hamilton for many years and though it ultimately might have contributed to the interest in his work, Hamilton never completely forgave Maynard Smith for this slight.

The incorporation of Hamilton's idea of inclusive fitness and his shift in point of view from the organism to the gene became fundamental to the development of the fields of behavioural ecology and the study of behaviour more generally. This incorporation of the idea of inclusive fitness into the developing fields of sociobiology and later behavioural ecology, as well as evolutionary psychology, solidified Hamilton's significance but was also a somewhat restricted view of evolutionary processes. Certainly by the mid-1970s when E.O. Wilson was helping to raise the awareness of the 1964 papers in the *Journal of Theoretical Biology*, Hamilton had already moved on. He had embraced George Price's covariance equation that demonstrated the broader notion of inclusive fitness where statistical association replaced common descent [11]. 'I am pleased to say that, amidst all else that I ought to have done and did not do, some months before he died I was on the phone telling him enthusiastically that through a 'group-level' extension of his formula I now had a far better understanding of group selection and was possessed of a far better tool for all forms of selection acting at one level or at many than I had ever had before' [1, p. 173]. Hamilton was already moving toward his fascination with the evolution of sex and the relationship between parasites and their hosts.

4. A role for parasites?

Hamilton began actively thinking about the role of parasites in host ecology and evolution in the late 1970s and early 1980s, a time when traditional parasitologists were mainly concerned with the effects of wildlife diseases on host demographics and population growth. Much of their work was focused on particular systems, rather than attempting to derive general evolutionary principles. Hamilton followed two threads: the importance of parasites in driving the evolution and maintenance of sexual reproduction [12,13]; and the role of parasites in sexual selection [14,15]. Running through all of his work at this time was an implication that parasites were an overlooked force in evolution. Anderson and May's seminal papers [16,17] helped to bring parasite–host interactions into the forefront of evolutionary biology, in no small part because they pointed out that the difference between what they termed microparasites, such as bacteria and viruses, differ in their effects from macroparasites such as worms and flukes in degree, rather than kind. Peter Price's 1980 book [18] and work by Jaenike and others also helped bring parasites to the awareness of evolutionary biologists and ecologists.

Nonetheless, several obstacles to the widespread acceptance of the importance of parasites remained. Parasites are indeed ubiquitous, but by definition do not kill their hosts. This apparently harmonious coexistence of parasites on and inside their hosts led many biologists to conclude that most parasites must evolve to become ever more benign, so as not to slay the gut that feeds them. According to classical parasitology, then, there was no need for new theory to explain how parasite pressure may have driven the evolution of sexual reproduction or sexual selection. Although the notion that virulence—the degree of harm a pathogen does to its host—itself evolves had been discussed since the time of Koch and Pasteur [19], acceptance of the benign parasite lingered. In more modern analyses, Ewald [20,21], among others, pointed out that not all pathogens are expected to evolve to become more benign, the conventional wisdom about the 'prudent parasite', analogous to the prudent predator, remained, at least among parasitologists themselves. With its emphasis on restraint rather than self-interest, this perspective has a group-selectionist flavour, further linking the ideas of parasites and levels of selection. And of course, while it makes initial intuitive sense that a less-virulent pathogen would survive longer, many circumstances, including the co-infection of multiple pathogen strains or vector-borne transmission, make the evolution of escalated virulence plausible.

Work on evolution of virulence rapidly became complex, with theoretical and empirical efforts to understand the circumstances that lead to benign versus harmful parasites [19,22,23]. This complicated Hamilton's influence on progress in the field, so that unlike the situation with social evolution, no single contribution, by Hamilton or anyone else, became a touchstone for future development of theory about pathogen evolution.

Hamilton's later work with parasites was seen more as a niche concern, with fewer applications to other fields. Parasitologists themselves dismissed the purported relationship between ornamentation and parasite burden proposed in Hamilton and Zuk [14,24], and as Hamilton details in the second volume of *Narrow Roads of Gene Land* [2], the paper was the subject of some controversy and re-analysis [25]. Some of Hamilton's other papers on parasites were published in obscure places [26] or discussed topics that were not viewed as germane to current interests in evolutionary biology.

Many disciplines that looked to evolution as a theoretical guide embraced the ideas put forward in Hamilton [7], including economics, political science and anthropology. Sexual selection had at least some relevance to those fields. By contrast, neither medicine nor parasitology were particularly interested in, or motivated by, evolutionary concerns, despite efforts to bring such ideas to the fore in Darwinian medicine [27]. For Hamilton, his interest in both the effects of parasites on host evolution writ large and the analysis of social evolution were components of a broader issue: how antagonistic coevolution is resolved. Many biologists, however, did not appreciate the connections across these intellectual borders.

5. Historical context

Taking into account the relationship of Hamilton's work on social behaviour in relation to the developments in the field—the post Modern Synthesis development of evolutionary theory was key. In the wake of the architects of the Modern Synthesis—Mayr, Dobzhansky, Simpson, Huxley and Stebbins—Hamilton's work provided the linchpin for the next generation of evolutionary biology. The gene's eye view opened up the social realm to evolutionary analysis and explanation. This approach to evolutionary analysis has generated countless studies and a persistent debate over the relationship between kin selection and group selection; inclusive fitness and multi-level selection and continues to influence contemporary discussions [28]. Hamilton's later work with parasites, on the other hand, occurred during a period of growing criticism of neo-Darwinism and the sociobiology-inspired critiques of adaptationism and optimality. These critiques of adapationism in evolutionary medicine have continued [29,30].

As recent reviews of Hamilton's biography have pointed out, personal memory is often an inaccurate historical guide. Hamilton's recollection of his intellectual isolation during the development of his early theoretical work may have been slightly exaggerated. Perhaps the meetings at tea with Fisher were more influential than his memory permits. If we take this perspective, it becomes clearer that while Hamilton felt particularly intellectually isolated, he was actually working in a vein of theory that had motivated evolutionary thinkers since Darwin.

6. Converging roads in and the future

Inclusive fitness theory holds an assured role in considerations of social evolution. What about parasites? Interest in pathogens, and in the blurring distinction between antagonistic coevolution and mutualism, is expected to continue [31]. Increasingly advanced genomic tools allow scientists to ask detailed questions about the nature of genetic interactions between parasites and hosts, while more sophisticated modelling techniques enable us to examine the outcome of such interactions under different circumstances. Finally, recognition of the importance of the microbiome has highlighted how much internal symbionts, pathogens and other organisms affect the biology of many, if not most, multicellular organisms [32]. All of these are areas that Hamilton would have embraced, given his overarching interests. To him, the evolution of sociality, the way that parasites influenced sex and the importance of microbial symbionts were closely tied. Perhaps seeing them that way would benefit research for the rest of us.

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