Commentary

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What life is for: a commentary on Fromhage and Jennions

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Perhaps Darwin's most important contribution to science was to give us a natural theory for seemingly super-natural organismal design. Random variants that happen to have higher fitness leave more offspring, so high-fitness variants eventually take over the population. This is why whales became such proficient swimmers and divers, why Batesian mimics look so much like other species, and why cheetahs are adapted to catch gazelles while gazelles are adapted to get away from cheetahs. R. A. Fisher's fundamental theorem of natural selection [1] (really a fundamental theorem of adaptation [2]) formalized the notion that individual fitness increases in the course of selection (though its meaning is subtle [3]). It gives us a sort of meaning of life, perhaps not the kind that gives us peace on our deathbeds, but at least the kind that lets us understand how organisms behave on the path to theirs.

This meaning of life received an important update with W. D. Hamilton's work on social behaviour and inclusive fitness [4,5], and now Hamilton's views appear to have received another surprising update in a recent paper by Lutz Fromhage & Michael Jennions [6]. They argue we have been using the wrong inclusive fitness and that the right one is an intuitive 'folk inclusive fitness' that was discarded by theorists years ago. I have read many challenges to inclusive fitness over the years and most are misguided or outright wrong. The logic of this new paper is challenging, as witnessed by its supplemental list of 40 questions and answers that attempt to address confusions that arose during the writing and review process. I struggled hard with the paper and this comment is an attempt to help others through the process.

I note at the outset though that this is not a dethroning of inclusive fitness. Instead, it is really a clarification of how inclusive fitness should be defined and a deepening of its justification. Hamilton's update on the meaning of life was necessary because the old one failed for certain social behaviours, most obviously for altruism. Why might a social insect worker evolve to give up its own fitness to help rear siblings? Hamilton [4,5] found the answer in kinship and the gene-sharing that it generates. What matters in genetic evolution is the number of gene copies surviving, and one can enhance this not only by producing offspring but by helping other relatives. So, altruists giving up one offspring ($r = 1/2$) could gain if their actions produce more than one full-sibling ($r = 1/2$) or more than two half-siblings ($r = 1/4$). This led George Williams [7] and Richard Dawkins [8] to consider that the best way to view evolution and adaptation might be from the point of view of a gene; replicators are what drive adaptation and individuals can be viewed almost as epiphenomena. But Hamilton preferred an individual-level work-around that he called inclusive fitness [4,5]. Individuals can be viewed as if they are acting to maximize not traditional fitness in terms of offspring, but an inclusive fitness that includes its effects on relatives, weighted by relatedness.

Hamilton defined inclusive fitness as an individual's fitness, augmented by its effects on the fitness of others, each multiplied by relatedness, and then stripped of components due to the individual's social environment [4,5]. Fromhage & Jennions [6] argue that the last part—the stripping away of social effects—should be deleted, leaving us with a simpler 'folk' definition that has been widely used but thought theoretically incorrect. To explain this move, I need to first backtrack a little.

Hamilton's inclusive fitness perspective has led to tremendous advances in understanding social adaptations and the role of relatedness [9]. However, it was not theoretically watertight. Hamilton's math strictly justified inclusive fitness only for additive fitness effects, for example, when getting a cost c and a benefit b gives you a total of $-c + b$. For this additive case, inclusive fitness ties in neatly with optimization theory [10] and leads to an important improvement in Fisher's fundamental theorem [11].

A cost plus a benefit giving a total of $-c + b$ seems logical but in biology one plus one often does not equal two. In many cases, fitness will be either more or less than the sum of its parts. For example, some cooperative behaviours have threshold effects requiring multiple cooperators to get any useful result. And the cooperative division of labour may work only with the right fractions of each type of labourer.

One of the many beauties of Hamilton's inclusive fitness is that it was independent of allele frequency and genetic details like dominance. But this particular beauty is due to the additivity assumption; when we remove that, allele frequency and genetics start to matter. Their effects may be modest enough to allow other advantages of inclusive fitness to stand [12]. But a disconcerting theoretical upshot is that this seems to mean there is no single inclusive fitness but multiple inclusive fitness effects that depend on the particulars of the gene in question. If the differences are sufficiently small this might not be a problem for most empirical work [12].

But from the theoretical and philosophical perspectives, the lack of agreement is troubling. If inclusive fitness is the meaning of life, then do we now have multiple contradictory meanings? How do we choose among them? What is actually maximized by natural selection? Here is where Fromhage & Jennions [6] step in. According to their analysis, the inclusive fitness that matters most for long-term evolution is that of a low-penetrance gene for the behaviour in question, that is, a gene that is only rarely expressed. They call such a gene a reference gene. They support this conclusion with models that show that, when there is a difference in inclusive fitness effects of different kinds of genes, a population state is stable only if it is stable against a low-penetrance mutant. In a rough sense, when there are differences, a low-penetrance allele wins out.

The reasons are a bit complicated. In a population-genetic model such as Hamilton's, every genetic effect on fitness must be, and is, counted exactly once. When Hamilton switched from the standard fitness perspective of his formal model to the inclusive fitness perspective, that condition had to be maintained. He was now re-assigning the benefits of altruism from the standard fitness of beneficiaries to the inclusive fitness of actors, and he needed not to double count. So, his inclusive fitness is the actor's fitness, *not including the social effects of others*, plus the actor's effects on the fitness of relatives times relatedness. The 'not including' clause is necessary to avoid double counting fitness effects of the behaviour, attributing them to both actor and beneficiaries [13].

This seems to follow from Hamilton's math but it does so only up to a point. I noted this previously [14] in connection with a paradox proposed by Scott Creel [15]. Creel's mongooses live in obligatory social groups, with one pair dominating reproduction, while the others help. This is clearly one of these troubling cases of non-additive effects; a dominant alone gets zero offspring, a subordinate alone also gets zero, but together they get something positive. Obviously, a dominant will pass on more genes than a helper, but Creel noted

that Hamilton's rule seemed to say otherwise. Subordinates get positive inclusive fitness through their help, but if you strip away these effects from the dominant's inclusive fitness it becomes zero because all of its reproduction depends on the social effects of the subordinates.

My half-solution was to re-assess Hamilton's reason for stripping social effects: the need to avoid double counting [14]. In Hamilton's one-locus model, this makes sense, but there are almost certainly at least two categories of mongoose sociality genes that are conditionally expressed. There are some genes that affect the decisions of dominants and other genes that affect the decisions of subordinates. If these are distinct genes, nothing in Hamilton's single-gene derivation, let's say for the inclusive fitness for a dominant's gene, justifies stripping the effects of subordinate genes. For conditional genes like this, there is no double counting of the gene's effects when we include benefits due to a relative expressing other genes, so we should not strip.

This solves the problem for genes expressed conditionally based on roles like dominant and subordinate. But what about cases where there is a gene acting in both parties with non-additive effects? I punted on this question, simply noting Hamilton's inclusive fitness in these cases depends on the genetics [14]. But Fromhage & Jennions [6] argue that a parallel solution applies and that we should therefore use IF_{folk} , which does not strip away the social effects. More accurately, Hamilton's inclusive fitness effect would give the correct gene dynamics for any particular gene, but this would be gene-specific, but IF_{folk} would do a better job for long-term evolution.

The basis for this is their result that, when inclusive fitness effects depend on the genetic details, it is the low-penetrance reference genes that are the key to stability. When a low-penetrance gene is expressed in the actor, it will normally not be expressed simultaneously in the partner, even though they are related. There is therefore no risk of double counting and no cause to strip social effects from the actor's fitness. And since an effect from a partner is not double counting, it needs to be included as part of the single counts.

Fromhage & Jennions frame their result as an example of Leigh's parliament of the genes [16]. Just as a meiotic-drive 'outlaw' gene gets tamed by the majority of genes in the genome, a low-penetrance reference gene prevails because it represents the genome's majority interest and therefore wins out over other types of genes. There is a sense in which that is true. When an organism behaves so as to better propagate a reference gene, the rest of the genome does benefit in the sense that all of the individual's genes pass on more copies, even those genes whose genetic details would have led the population to a different place. But the analogy is confusing in another sense. Unlike the case of meiotic drive, there is no real conflict here. This can be seen in the fact that, once the reference-gene equilibrium is reached, other genes are not selected to fight back. A better explanation, it seems to me, is that different genes are differently constrained by their genetics and low-penetrance genes are best able to reach the solution that they all would agree upon if they only had the right variation. It is not unlike the case where a beneficial mutant, let's say for tail length, takes the population either partway to the optimum or somewhat past the optimum. Mutations at other loci will jump in to get still closer to the optimum but that is not really conflict. It is just that variation at the first locus was too constrained to reach the optimum it shares with other genes.

Both of these are examples of Hammerstein's 'streetcar' model [17]. He noted that the details of population-genetic models can sometimes mislead because those details—such as dominance, penetrance, and pleiotropy—can be altered by the entry of new mutants with different details. Each successful mutant jumps on the streetcar and causes it to move to the next stop but then a new mutant can jump on. The streetcar does not come to a final stop until no more mutants, of any kind, can invade.

What are the implications of this work for past work on inclusive fitness and social evolution? It should be welcome news to naturalists, who would like to have a phenotypic maximand that is independent of the genetic details, because they rarely know those details [13]. But, if it is correct, the new result also raises a troubling question. If we have been calculating inclusive fitness incorrectly all these years, do we need to throw out all past work on the topic? I think the answer is, for the most part, no. The reason is that we do not usually test kin selection ideas by actually estimating inclusive fitness. Fitness is hard to measure and inclusive fitness is that much harder. Instead, we have tended to test inclusive fitness predictions in other ways. We use phylogenetic comparative tests [18,19], tests of how individuals choose among inclusive fitness alternatives [20,21], experimental evolution tests [22,23], or molecular evolution tests [24,25]. Often these focus on the

role of relatedness in enhancing cooperation, since that is the most novel part of kin selection theory, but they can also probe the roles of cost or benefit differences [26].

The Fromhage & Jennions [6] paper does have potentially important implications for the tangle of non-additive kin selection models in the literature. For each model, we should ask whether it allows a sufficient diversity of mutants to reach the end of the streetcar line. Specifically, what would happen if we introduced low-penetrance mutants into the model? A recent example seems instructive. A model seemed to refute the inclusive fitness prediction that monogamy promotes altruistic sterility [27] but the inclusive fitness conclusion was restored when low and intermediate penetrance alleles were allowed [28]. Perhaps, much of the weeping and wailing over inclusive fitness being messed up by non-additive effects [29] has been misplaced. If so, Fromhage & Jennions [6] might mark the end of the wars over inclusive fitness. Alternatively, it may signal the start of the next battle.

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