Review

Adaptation and the genetics of social behaviour

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In recent years much progress has been made towards understanding the selective forces involved in the evolution of social behaviour including conflicts over reproduction among group members. Here, I argue that an important additional step necessary for advancing our understanding of the resolution of potential conflicts within insect societies is to consider the genetics of the behaviours involved. First, I discuss how epigenetic modifications of behaviour may affect conflict resolution within groups. Second, I review known natural polymorphisms of social organization to demonstrate that a lack of consideration of the genetic mechanisms involved may lead to erroneous explanations of the adaptive significance of behaviour. Third, I suggest that, on the basis of recent genetic studies of sexual conflict in *Drosophila*, it is necessary to reconsider the possibility of within-group manipulation by means of chemical substances (i.e. pheromones). Fourth, I address the issue of direct versus indirect genetic effects, which is of particular importance for the study of behaviour in social groups. Fifth, I discuss the issue of how a genetic influence on dominance hierarchies and reproductive division of labour can have secondary effects, for example in the evolution of promiscuity. Finally, because the same sets of genes (e.g. those implicated in chemical signalling and the responses that are triggered) may be used even in species as divergent as ants, cooperative breeding birds and primates, an integration of genetic mechanisms into the field of social evolution may also provide unifying ideas.

Keywords: genetics of behaviour; adaptation; conflict; altruism; indirect genetic effects; pleiotropy

1. INTRODUCTION

The success and increased complexity of organisms in the course of evolution is thought to have depended on a small number of major transitions in how information is transmitted from one generation to the next (Maynard Smith & Szathmáry 1995). One such transition was the shift from solitary organisms to societies with a marked reproductive division of labour (eusociality). This transition has led to the tremendous ecological success of social insects, which are now dominant in many terrestrial ecosystems. This success stems from the benefits conferred by sociality, which allows individuals in a group to more efficiently modify their environment and conduct tasks that could not be performed by single individuals (Hölldobler & Wilson 1990).

Over recent years much progress has been made in understanding the selective forces involved in the evolution of social behaviour. There is currently no doubt that kin selection has been the *all important* selective force for the evolution of reproductive altruism (Bourke & Franks 1995; Queller & Strassmann 1998; Foster *et al.* 2006; Lehmann & Keller 2006). Numerous genetic studies in insects, other

invertebrates and vertebrates have shown that eusociality with reproductive division of labour evolved in groups of highly related individuals, such as those formed by a mother and her offspring (Reeve & Keller 1996; Hughes *et al.* 2008). However, kin selection theory also predicts that groups of cooperating individuals should be the scene of potential conflicts, because, in contrast to cells of an organism, group mates are not genetically identical. Over the last decade much attention has focussed on within-group conflicts, in particular in social Hymenoptera. While these studies have revealed striking cases of conflicts being modulated by variation in kin structure (e.g. Trivers & Hare 1976; Bourke & Franks 1995; Sundström *et al.* 1996; Ratnieks & Helanterä *in press*), there are also many situations where variation in relatedness does not, or only to a very small extent, influence the dynamics of conflicts (Hammond & Keller 2004; Langer *et al.* 2004; Ratnieks *et al.* 2006). This has led to the realization that the proximate mechanisms affecting the relative power of parties need to be considered if one is to understand the resolution of potential conflicts (e.g. Beekman & Ratnieks 2003; Helms *et al.* 2005). In this essay, I argue that an important need for further progress is the inclusion of genetic mechanisms, in particular those underlying intraspecific variation in behaviour and social organization. I also suggest that a lack of understanding of the genetic basis of traits under

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investigation may lead to erroneous conclusions about their adaptive significance.

2. THE GENETIC PATHWAYS TO SOCIAL EVOLUTION

The first basic question, which is starting to attract attention, is to what extent changes in social behaviour are due to changes in gene regulation rather than to sequence differences at genes influencing behaviour (Robinson & Ben-Shahar 2002). That differences in gene expression can lead to major behavioural differences and even marked morphological differences is well illustrated by the differences between queens and workers. In many social insects, queens and workers have extremely divergent morphologies and behaviour. However, usually these differences do not stem from genetic differences but rather from environmental factors triggering differential gene expression during development. At the adult stage, queens and workers typically have thousands of differently expressed genes (Miura *et al.* 1999; Evans & Wheeler 2001; Whitfield *et al.* 2002; Gräff *et al.* 2007; Goodisman *et al.* 2008) just as different tissues or cell types in a multicellular organism.

A major challenge will be to identify the mechanisms involved in the developmental switch, in particular the causal environmental and social factors and how they mediate changes in gene regulation. A first step in this direction has come from a pioneering study in the honeybee *Apis mellifera* where the experimental decrease in the methylation level of worker-destined larvae has been shown to result in the production of many larvae with queen-like phenotypic characteristics (Kucharski *et al.* 2008). This suggests that the specific food (i.e. the addition of royal jelly, pollen and worker glandular secretions in addition to honey) provided to queen-destined larvae may affect the level of methylation and thereby alter the processes of gene expression and caste determination. Interestingly, a recent study in humans also suggested a role of nutrition on patterns of methylation. Individuals who were prenatally exposed to famine during the Dutch Hunger Winter in 1944–1945 had, six decades later, less DNA methylation of the imprinted *IGF2* gene than their unexposed siblings (Heijmans *et al.* 2008).

The suggestion that early-life environmental conditions can cause epigenetic changes that persist throughout life has important implications for our understanding of the dynamics of within-group conflicts. It has been proposed that, in addition to kin selection, parental manipulation could be another mechanism favouring altruism in social insects (Alexander 1974; Michener & Brothers 1974). For example, the reproduction of workers may be prevented if they are physically dominated by the queen or if they are underfed (making them poor potential reproductive individuals). However, it was pointed out that the parental manipulation hypothesis contained a flaw because a gene causing an adult to act against the interests of an offspring will be counter-selected when it is present in juveniles, through these juveniles having a parent bearing the gene (Dawkins 1976; Parker & Macnair 1978; Bourke & Franks

1995; see also Smiseth *et al.* 2008 for a review of models of parent–offspring conflict). Importantly, however, these arguments are based on simple genetic or game-theoretical models and the conclusion might be altered if the expression of the trait is conditional and/or if imprinting mechanisms are involved in parental manipulation. While some theoretical work has been conducted on the potential role of differential expression of genes inherited from the mother and father (Haig 2000; Queller 2003; Kronauer 2008), it remains to be investigated how imprinting and epigenetic *trans*-generational effects on behaviour may affect conflict resolution.

3. GENETIC ARCHITECTURE, HETEROZYGOTE ADVANTAGE, PLEIOTROPY AND ADAPTATION

Adaptation, including in social life, can never be perfect because of constraints in the genetic system, including mutation, drift, inbreeding, selection, pleiotropy, linkage disequilibrium, heterozygote advantage and gene flow (Crespi 2000). The fire ant *Solenopsis invicta* provides a good example to illustrate how these effects can lead to surprising and unexpected behaviours. This species exhibits a fundamental social polymorphism with a monogyne form in which colonies have a single queen and a polygyne form where colonies contain several queens. As in many other ants, this difference in queen number is associated with differences in a wide range of reproductive and social traits, including queen phenotype and breeding strategy and the mode of colony reproduction (Ross & Keller 1995). In the polygyne form, the probability that a queen will be accepted in an established colony is strongly associated with their genotypes at the locus *Gp-9* (General protein-9). All homozygous *Gp-9^{BB}* queens are killed by workers when they initiate reproduction (Keller & Ross 1993, 1998). Intriguingly, *Gp-9^{BB}* queens are heavier and more fecund than queens with alternate genotypes (*Gp-9^{Bb}* and *Gp-9^{bb}*), raising the question of why workers selectively eliminate queens with apparently the ‘best’ phenotype. To resolve this paradox, it was suggested (Keller & Ross 1998) that the execution of reproductively superior queens may represent a mechanism selected to maintain multiple queens within a colony if, as has been demonstrated in some ants, polygyny is advantageous under some ecological conditions. However, further genetic and behavioural studies revealed unexpected twists to the story and a completely different explanation for the workers’ behaviour. This is because the *Gp-9^b* allele was found to be a kind of green beard gene inducing workers carrying one copy of that allele to selectively kill queens lacking the same allele (Keller & Ross 1998).

In addition to these effects, the locus *Gp-9* is also strongly associated with queen behaviour. After their mating flight, *Gp-9^{BB}* queens typically attempt to start a new colony independently by feeding their progeny from their body reserves. By contrast, queens of the two other genotypes do not fly far and try to enter established colonies rather than starting a new one on their own. Interestingly, these behavioural differences are tightly correlated with an important

physiological difference as only *Gp-9^{BB}* queens accumulate sufficient fat reserves before their mating flight to raise a first cohort of workers alone (Ross & Keller 1995; DeHeer *et al.* 1999; Keller & Ross 1999).

The strong association between the genotype at *Gp-9* and all these behavioural, morphological and physiological differences most likely results from the combined effect of several linked genes in the genomic region marked by *Gp-9*. This region is expected to have many of the unusual properties of regions containing the sex-determining genes in species with sex chromosomes because the *b* haplotype is found only in the polygyne social form, just as the Y chromosome is found only in males in species with male heterogamety. As a result, the *Gp-9^b* region is predicted to (i) accumulate genes beneficial in the polygyne social environment (as the Y chromosome accumulates genes beneficial to male function; Rice 1987); (ii) evolve reduced recombination to preserve associations of genes advantageous for polygyny (as occurs for genes advantageous to males on the Y chromosome; Charlesworth *et al.* 2005); and (iii) accumulate deleterious alleles and transposable elements (because of reduced recombination; Charlesworth *et al.* 2005). Consistent with these expectations, the *Gp-9* genomic region is characterized by low recombination (Ross 1997; Krieger & Ross 2005; Wang *et al.* 2008), the *b* allele behaves as a homozygous lethal allele (Ross 1997; Keller & Ross 1999; Hallar *et al.* 2007), and two transposons are preferentially expressed on the *b* haplotype (evidence suggests that at least one of them likely reflects a single insertion in the *b* haplotype; Wang *et al.* 2008).

This example illustrates the danger of searching for adaptive explanations without a clear understanding of the genetic basis of the behaviour. The consideration of selection at the individual or colony levels only would have led to an erroneous explanation of why workers eliminate the heavier and more fecund queens in polygyne colonies. This is an important point, in particular because of the current confusion by many scientists in how selection works at the different levels of biological organization.

Similarly, it is likely that the interpretation of the social behaviours of many other organisms would change if one had information on their genetic bases. In this respect, it should be mentioned that pleiotropy is probably the rule rather than the exception for many traits, particularly for behaviours which are the product of many sensory, integrative, motivational and motor processes. For example, a recent study (Ducrest *et al.* 2008) predicted that, and provided evidence for, the widespread association between the degree of melanin-based coloration and many physiological and behavioural traits in vertebrates stems from the melanocortins binding to the melanocortin-1-receptor (regulating the eumelanin synthesis), also binding to five other melanocortin receptors with very different functions. Similarly, it has been suggested that the pleiotropic linkage of a gene in stalk and spore formation might be an important component stabilizing cooperation in the social amoeba *Dicystostelium discoideum* (Foster *et al.* 2004). A big challenge will be to determine how commonly suites of behavioural

differences in social organisms are similar due to pleiotropic effects and also determine to what extent pleiotropy affects the adaptive values of traits.

4. GENES, COOPERATION AND MANIPULATION

In insect societies with strong queen–worker dimorphism, it was thought that queens could manipulate workers into pursuing actions that are contrary to their inclusive fitness through ‘pheromonal queen control’, whereby chemicals exuded by the queen(s) replace physical intimidation in forcing workers to behave in ways that increase queen fitness (e.g. Wilson 1971; Fletcher & Ross 1985; Hölldobler & Wilson 1990). However, this view was challenged on the basis that pheromonal queen control had never conclusively been demonstrated and was evolutionarily difficult to justify (Keller & Nonacs 1993). The main arguments proposed against the pheromonal queen control hypothesis was that, if workers have their fitness significantly reduced, there would be strong selection to escape control by building up tolerance or immunity to the queen pheromone. To retain strong control, queens would therefore be required to continually produce new compounds to stay one step ahead of the workers, and/or to invest more and more resources in producing larger quantities of the pheromone as effective dosage levels increase. As both of these solutions would eventually lose cost-effectiveness, queens would probably gain more overall fitness by allowing workers to win in some respects rather than indulge in an escalating arms race that would eventually decrease overall colony productivity. Later experimental studies have indeed concluded that queen pheromones are more likely to be honest signals to which workers respond in a way that generally increases their own inclusive fitness (e.g. Cuvillier-Hot *et al.* 2004; Endler *et al.* 2006; Bhadra & Gadagkar 2008; Smith *et al.* 2009).

Interestingly, a similar type of argument has also been made with regard to male–female conflict between mating partners. However, given that recent studies of sexual conflicts in *Drosophila* are revealing unexpected sophistication in the males’ ability to manipulate females, the theoretical and empirical basis of queen control in social insects needs to be re-evaluated. During mating, *Drosophila* males have been shown to transfer more than 100 proteins (e.g. Findlay *et al.* 2008), causing a wide variety of fitness-related effects in females, including decreased sexual receptivity, increased egg production, altered morphology of the reproductive tract, increased production of immune-related peptides and the liberation of juvenile hormone (JH) (reviewed in Wolfner 2002; Ravi Ram & Wolfner 2007). While some of these changes are beneficial to both sexes, others are costly to females.

Information on the role of seminal proteins in sexual conflict, including whether they mediate physiological and behavioural changes against the females’ interest, can be gained by the analyses of the tissues that are targeted by the protein (McGraw *et al.* 2004; Ravi Ram & Wolfner 2007). For example, proteins binding to receptors in the reproductive tract are

unlikely to permit males to force females to behave contrary to their interest. By contrast, proteins acting through neuroendocrine pathways after having entered the female circulatory system (haemolymph) may allow chemical manipulation. Interestingly, at least 10 of the proteins transferred during mating have been shown to pass from the reproductive tract into the circulation system of *Drosophila* females (Ravi Ram & Wolfner 2005), some probably even reaching the brain where they could directly affect the female's behaviour. Further evidence for seminal proteins being implicated in sexual conflict (Rice 2000) comes from their very rapid evolution, the expected pattern if there is antagonistic coevolution between molecules in males and females (Swanson *et al.* 2001; Begun & Lindfors 2005; Findlay *et al.* 2008).

The apparent ability of males to chemically manipulate females during the process of mating re-opens the question of whether pheromonal queen control really does not occur in social insects. In contrast to the conflict between males and females, an additional issue that needs to be considered in the case of social insects is that chemicals are generally distributed among all colony members. Thus, a queen producing a chemical aimed at preventing workers from reproducing may suffer herself from the effect of the chemical (Keller & Nonacs 1993). Chemical manipulation would thus require the queen to be much less sensitive than workers to pheromone produced. It is necessary, therefore, to precisely identify the pheromones involved and their target in workers. Most current studies consist of searching for an association between the fertility of queens and their chemical signature. Ultimately, it will be important to determine whether queen-produced pheromones exclusively bind to antennal receptors (which would support the view that they are honest signals) or whether they also enter the worker circulatory system and mediate hormonal changes directly affecting reproduction (which would be consistent with pheromonal queen control). If pheromones entering the circulatory system of workers are to be identified, it will also be interesting to determine if they also affect queen physiology or whether queens evolved immunity to their own chemicals.

5. DIRECT AND INDIRECT EFFECTS

All behaviours are modulated by interactions between genes and the environment. In social organisms, social interactions are a key component of the environment. To understand the link between genotypes and phenotypes, therefore, requires determining how an individual's phenotype is influenced by its own genes (direct genetic effects) and those expressed in social partners (indirect effects) (e.g. Moore *et al.* 1997; Linksvayer & Wade 2005). While indirect effects are increasingly being recognized as an important component of the genetic architecture of species (e.g. Moore *et al.* 1997; Linksvayer & Wade 2005), there are still almost no empirical data on such effects. One of the social systems where indirect effects have been studied is the fire ant *Solenopsis invicta*, where the behaviour of *Gp-9^{BB}* workers was shown to depend on the ratio of *Gp-9^{Bb}* workers in their

colony (Ross & Keller 1998, 2002). When this ratio is lower than 5–10 per cent, *Gp-9^{BB}* workers accept only a single queen per colony that must also bear the genotype *Gp-9^{BB}* (i.e. they exhibit a typical monogyne behaviour). However, when there are more than 5–10 per cent of *Gp-9^{Bb}* workers, *Gp-9^{BB}* workers will accept many additional queens (up to hundreds), but only *Gp-9^{Bb}* queens. Thus *Gp-9* exerts indirect genetic effects, in that a threshold ratio of *Gp-9^{Bb}* workers induce changes in the social behaviour of all colony members (even those lacking the *b* allele) and determines a fundamental aspect of social organization (monogyne versus polygyne social organization).

Microarray experiments (Wang *et al.* 2008) revealed that differences at the genomic region marked by *Gp-9* have direct effects on the level of expression of 39 genes in workers (i.e. these genes are differentially expressed between *Gp-9^{Bb}* and *Gp-9^{BB}* workers, irrespective of their social environment) and indirect effects on the level of expression of 91 genes (i.e. the level of expression of these genes in *Gp-9^{BB}* workers depends on the presence or absence of *Gp-9^{Bb}* workers, possibly as a result of changes in the processes of within-colony chemical communication). Remarkably, there is almost no overlap between the genes whose level of expression is influenced by the focal workers' *Gp-9* genotypes and genes whose expression is influenced by the social environment, with only one of the 129 differentially expressed genes appearing in both categories.

There have been very few other studies of indirect genetic effects within social groups. In *Drosophila melanogaster*, the genotypic composition of social groups (single versus mixed genotypes) was shown to affect behaviours and gene expression (i.e. the transcription of the clock gene, pheromonal profile on the cuticle and mating frequency) (Kent *et al.* 2008). Similarly, the mixing within colonies of individuals coming from honeybee strains selected for high and low pollen hoarding revealed that the ovariole number and dry mass of workers produced was influenced by interactions between their genotypes and those of other colony members (Linksvayer *et al.* 2009). In another study with European honey bees, the defensive behaviour of workers was increased when they were in colonies containing Africanized honeybees (Guzmán-Novoa & Page 1994). It will be of great interest to investigate the consequences of such indirect genetic effects on social evolution. For example, it remains to be studied whether variation in within-group genetic diversity may mediate changes in worker behaviour via indirect effects and, if so, whether it might have favoured multiple mating in some species.

6. GENES, DIVISION OF LABOUR AND PHENOTYPIC PLASTICITY

While it used to be thought that the morphological and physiological differences between castes in social insects stem only from environmental effects influencing developmental processes, several exceptional cases of genetic caste determination have recently been discovered (Helms Cahan *et al.* 2002, 2004;

Julian *et al.* 2002; Volny & Gordon 2002; Helms Cahan & Keller 2003; Helms Cahan & Vinson 2003; Fournier *et al.* 2005; Ohkawara *et al.* 2006). In many of these examples, populations contain two distinct genetic lineages and the developmental fate of female brood depends on the genetic origin of the parents; the inter-lineage eggs develop into workers while intra-lineage eggs develop into queens (Helms Cahan & Keller 2003). This system of caste determination has important implications on mating behaviour and social organization. In monogyne species with such a mode of reproduction (e.g. some *Pogonomyrmex* ants), queens have to mate multiply (Gadau *et al.* 2003) to ensure matings with males of both lineages and the production of both worker-destined and queen-destined eggs. In another similar system in the genus *Solenopsis*, some queens mate with males of the same species and others with males of another species (Helms Cahan & Vinson 2003). The presence of many queens in the same nest ensures the production of both queens (conspecific matings) and workers (interspecific matings). Finally, in two other ants (*Wasmannia*, Fournier *et al.* 2005; *Vollenhovia*, Ohkawara *et al.* 2006), the problem of producing both queen- and worker-destined eggs has been resolved by the conditional use of sexual and asexual reproduction. As males and females are from different lineages, queens produce workers by laying fertilized eggs and queens by reproducing clonally.

Although these systems of reproduction are highly unusual, I believe that they are much more common than realized. My prediction is that maybe as many as 10 per cent of social insects have such unusual modes of reproduction. This is based on three lines of evidence. First, there is an increasing number of examples of new ant reproductive systems (see Heinze 2008). Second, I know of several unpublished population genetic studies having data inconsistent with conventional modes of reproduction; yet these studies make no reference to the unusual mode of reproduction that must be involved. Finally, controlled mating experiments revealed genetic compatibility effects on caste differentiation in *Pogonomyrmex rugosus*, an ant thought to have an environmental system of caste determination. In this species, the viability of queens and workers depends on genetic interactions between the parental genomes with some parental combinations being mostly compatible with queen development and others with worker development (Schwander & Keller 2008). Because similar controlled mating experiments have never been conducted in other social insects, it is impossible to determine how common such genetic compatibility effects are. Intriguingly, however, many observations are suggestive of incompatibility effects in other social insects. In several social insects where queens mate multiply, patriline are differently represented in queens and workers (Osborne & Oldroyd 1999; Chaline *et al.* 2003; Moritz *et al.* 2005). The explanations proposed so far include nepotism (the preference of closest relatives over less-related individuals) and royalty genes (i.e. alleles increasing the likelihood of their bearers to develop into queens) (Osborne & Oldroyd 1999; Moritz *et al.* 2005; Hughes *et al.* 2008). However,

nepotism between patriline or matriline is rare or absent in social insects (Keller 1997) and royalty genes are unlikely because they would rapidly go to fixation. Thus, it is likely that, as in *Pogonomyrmex rugosus*, the different representation of patriline in queens and workers of many social insects reflects incompatibility effects.

Unequal distribution of patriline has also been reported between morphologically divergent worker castes in the leaf-cutting ants (*Acromyrmex echinator*; Hughes & Boomsma 2008) and three ant species (*Camponotus consobrinus*, Fraser *et al.* 2000; *Pogonomyrmex badius*, Rheindt *et al.* 2005; *Eciton burchellii*, Jaffe *et al.* 2007). Given that discrete worker morphologies also stem from different developmental pathways (Wilson 1971), the unequal distribution of patriline among worker castes and between queens and workers might also be simply due to larval development being affected by genetic compatibility effects. Finally, incompatibility effects may also explain the frequently observed association between patriline and division of labour, whereby particular tasks are preferentially performed by workers of a given patriline (see Smith *et al.* 2008). In the same line, it would be interesting to determine whether incompatibility effects play a role in the establishment of dominance hierarchies in vertebrate societies and small insect colonies.

7. CONCLUSION

In this review I have selected a few examples to illustrate why knowledge of the genetics of behaviour should be of interest not only to those with a proximal or mechanistic interest in behaviour but also to those interested in ultimate questions. In fact, I would go as far as to say that, in many cases, a compelling demonstration of behaviour being adaptive requires one to have a clear understanding of its genetic basis. This is of course a challenging task because the identification of genes involved in social behaviour is still in its early phases (e.g. Robinson *et al.* 2008), and functional analyses are still impossible in most social insects. However, there is no doubt that many new genes will soon be identified setting up the possibility of studies of social behaviour and adaptation from both an evolutionary and mechanistic perspective.

Most of the known genetic polymorphisms influencing social behaviour have been discovered serendipitously during the course of population genetic studies of social insects. In the future it would be helpful to also use a candidate gene approach, for example by investigating genes known to be involved in orchestrating the perception and processing of sensory information or genes known to affect behaviour as for example the vasopressin receptor 1a (*avpr1a*) gene, which is involved in interspecific differences in social and mating behaviour in voles (Young *et al.* 1999; Lim *et al.* 2004) and possibly individual behavioural difference in humans (e.g. Knafo *et al.* 2008; Walum *et al.* 2008). Because these genes are likely to figure prominently in social evolution it would be very interesting to conduct population genetic studies to identify natural polymorphisms affecting behaviour and social organization.

Finally, an integration of genetics may also contribute to bridging of the gap between studies conducted in invertebrate and vertebrate societies. Until recently, studies in these two taxa have typically proceeded independently and, in fact, there has been too little interaction between students of social vertebrates and of social insects. As the same set of genes (e.g. those implicated in chemical signalling and the responses that are triggered) are likely to be implicated in species as divergent as ants, cooperative breeding birds and primates, an integration of genetics in social evolution should provide a general framework helping in bridging the different communities.

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