

study [19], *earlybird* (*Ebd*) was identified as a short-period mutant in a direct screen for clock-defective animals; *Ebd* was shown to be identical to the *Rab3a* locus. Interestingly, here, as with *LIP1*, the *Ebd* mutant was found to have normal expression levels of core-clock genes. *LIP1* and *Rab3a* are both GTPases suggested to be working post-translationally on as yet unknown targets.

PRA2 from pea was isolated as a gene encoding a small GTPase that mediates photomorphogenesis [20]. The *lip1* mutant is also perturbed in light perception [8], but there are two key differences between *LIP1* and *PRA2*. For one thing, *PRA2*, and not *LIP1*, is a typical Rab/Rho, in that it is membrane-localized [20]. Furthermore, *LIP1* function in the clock can be uncoupled from photomorphogenesis. Collectively, it looks as if divergent systems have incorporated GTPases as biochemical mediators. But for *LIP1*, this is probably the extent of analogy, as it is degenerative within the Rab/Rho clade, and it is not obviously membrane sequestered. Understanding how *LIP1* functions within the *Arabidopsis* oscillator holds great promise towards opening our eyes to the biochemical and cell-biological events of the plant circadian oscillator.

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Social Evolution: The Decline and Fall of Genetic Kin Recognition

Animals should benefit from the ability to recognise their kin, yet curiously this faculty is often absent. New theory confirms that genetic kin recognition is inherently unstable, explaining its rarity.

Andy Gardner and Stuart A. West

Cooperation abounds in the natural world, and biologists are faced with the difficulty of reconciling this fact with the principle of the 'survival of the fittest'. A fundamental step in our understanding of cooperation

was provided by W.D. Hamilton's theory of inclusive fitness [1]. This reveals that altruistic behaviour, where an individual pays a direct fitness cost in order to enhance the fitness of others, can be favoured by selection if individuals tend to promote the reproductive success

of their genetic relatives. This raises the question of how altruists ensure that their selfless behaviour is directed primarily towards their kin. One possibility is genetic kin recognition, where individuals identify close kin on the basis of physical similarity because relatives look more similar than unrelated individuals [1,2]. Despite the apparent incentive for such kin recognition, however, there is relatively poor empirical support for this mechanism in nature. A new theoretical study of genetic kin recognition by François Rousset and Denis Roze [3] reveals that, left



Figure 1. Despite the possible benefits, kin recognition is surprisingly absent in many animals, in situations where it might be expected.

(A) The parasitoid wasp, *Nasonia vitripennis* [15] (Photo by D. Shuker and S. West); (B) swarm-founding wasps, *Parachartergus colobopterus* [16] (Photo by J. Strassmann); and (C) the ant, *Formica exsecta* [17] (Photo by R. Kümmerli).

to its own evolutionary devices, this mechanism will drive itself to ruin (Figure 1).

Though genetic kin recognition seems straightforward, the theoretical issues have remained murky for decades. Hamilton [1] perhaps foresaw some of the difficulties when he wrote that evolutionary changes driven by individual advantage are liable to disrupt mechanisms of kin discrimination. This initial caution seemed to have been justified when Crozier [4] provided the first mathematical model of genetic kin recognition and found that the mechanism could not be sustained. The model, developed for understanding social behaviour of colonial marine invertebrates, assumes that each individual bears an inherited genetic 'marker', and that upon encountering a neighbour bearing the same marker the two individuals engage in a reciprocal, cooperative interaction. Crozier pointed out that those individuals bearing a common marker more readily enter into social interactions, and hence enjoy a higher reproductive success than those individuals bearing rare markers. Thus, already common markers become more common still, and eventually all individuals carry the same marker. At this point, it fails to be diagnostic of kinship, and there has been a breakdown of kin recognition. Crozier suggested that, if genetic kin recognition is to be stabilised, then marker diversity must be maintained by some extrinsic process, such as balancing selection imposed by host-parasite interactions.

Grafen [5], however, argued that Crozier's model fails to capture relevant biology. In particular, because Crozier assumed that social interaction always increases the fitness of both parties, there is no reason for individuals to limit interaction to kin only. Grafen suggested that Crozier's form of kin recognition was unstable because it was not useful to the individual, but that it could be made advantageous if cheating were possible in social interactions. He outlined a verbal model in which separate genetic loci encode the marker and altruism traits. In a structured population, neighbouring individuals with matching marker genes are likely to be close kin, and hence have higher than average genetic similarity (relatedness) across the whole genome, including at the loci for altruism. Thus, genetic kin recognition provides a way for altruists to ensure that they interact preferentially with other altruists, which makes the mechanism advantageous.

Furthermore, Grafen [5] argued that selection would work to maintain, rather than to erode marker diversity, ensuring evolutionary stability of the mechanism. Rarer markers are a better indicator of relatedness, because it is more likely that two neighbouring individuals who share a rare marker do so due to kinship than due to chance alone. Grafen suggested that this leads to higher levels of altruism among interacting individuals bearing rare markers, because here relatedness is higher and so altruism is more highly favoured. Thus, individuals

with rare markers enjoy more altruistic social partners, and could be fitter than individuals bearing common markers. This indirect benefit to rare markers could protect the marker diversity that is needed for genetic kin recognition to be maintained.

The fate of genetic kin recognition therefore hangs in the balance between Crozier's direct benefit for common markers and Grafen's indirect benefit for rare markers. Rousset and Roze [3], building upon recent extensions of multilocus theory for social evolution [6–9], have developed a two-locus model of genetic kin recognition to determine which of these effects ultimately dominates. They first considered the situation where the rate of recombination between altruism and marker loci and the rate of dispersal are high relative to the fitness consequences of altruism. Here, they confirmed that altruism is favoured given sufficient marker diversity, but also that this diversity becomes exhausted through the process highlighted by Crozier [4]. Thus, while altruism may initially flourish due to the operation of genetic kin recognition, it inevitably falters and ultimately fails as the ability to recognise kin is lost.

Next, Rousset and Roze [3] considered less frequent genetic recombination and dispersal, and found that rare markers become associated with higher levels of altruism, as anticipated by Grafen [5]. This requires relatively large fitness effects of altruism, so that the crucial association is generated more rapidly by selection than it

can be broken down by recombination. If recombination and dispersal rates are very low, there is only weak redistribution of altruism genes between lineages bearing different markers, and the resulting association between rare markers and higher levels of altruism can be strong enough to overpower the direct benefit of common markers. Thus, in rather restrictive conditions, marker diversity is maintained and genetic kin discrimination can be stabilised. More generally, however, the direct benefit for common markers dominates, and the recognition mechanism destabilises, giving only a transient benefit to the marker-mediated altruism. Typically, increasingly violent oscillations in the marker diversity and average level of altruism occur until one marker dominates, after which there is a steady decline and eventual loss of altruism.

Interestingly, Rousset and Roze [3] showed that genetic kin recognition can be stabilised by incorporating mutation into their model, as the reappearance of lost marker genes ensures the maintenance of marker diversity. Tuning the mutation rate from low to high gives violent but stable oscillations, followed by smaller limit cycles, and finally a stable evolutionary end point where genetic kin recognition and altruism are maintained. This explains why some previous simulation studies of genetic kin recognition [10] generated oscillating dynamics whereas others [11] suggested a stable equilibrium. More generally, the authors showed that altruism is only maintained at a reasonable level when mutation rates are very high.

But all is not lost for genetic kin recognition. As Crozier [4] suggested, the mechanism could be stabilised by extrinsic processes that maintain marker diversity. Rousset and Roze [3] have confirmed this by incorporating an *ad hoc* advantage to rare markers into their model and found that, provided this was sufficiently strong relative to the fitness consequences of altruism, genetic kin recognition is

maintained and selflessness prevails. This could explain why, when genetic kin recognition does occur, it often involves genes that are implicated in host-parasite interactions, a potent source of strong balancing selection. The paragon of genetic kin recognition is the detection of major histocompatibility (MHC) genes, involved in immune function, upon which rodents and humans appear to decide their social and sexual relationships [12–14]. If cooperation has been the secret to our evolutionary success, we may have our parasites to thank for that.

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Innexin Function: Minding the Gap Junction

Gap junctions mediate intercellular communication and are critical for development and nervous system function. Initially thought to function solely as stand-alone molecules, it has now been shown that a stomatin-like protein regulates a gap junction channel in *Caenorhabditis elegans*.

Kenneth R. Norman
and Andres Villu Maricq

Adjacent cells can communicate with one another at specialized contacts called gap junctions. At these sites, gap junction proteins make channels which connect the

interior of a cell to that of its neighbor. Each cell provides a hemi-channel which is composed of six membrane-spanning protein subunits and protrudes into the extracellular space; alignment of two hemi-channels from adjacent cells forms the functional channel,