Pax Argentinica

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Colonizing species often lose genetic variation. Usually this has harmful effects, but in Argentine ants it has led to loss of clan warfare and formation of supercolonies that overwhelm native species.

In the first and second centuries, most of the Mediterranean region flourished under the Pax Romana. Wars with foreign enemies continued at the frontiers, but the peaceful core of the empire gave border provinces the advantage of friendly forces at their flanks and rear. A paper by Tsutsui and colleagues, just published in *Proceedings of the National Academy of Sciences*[1], shows how a biological version of this system has been reinvented by the Argentine ant, *Linepithema humile*. The study yields some fascinating insights into the causes of both ecological and evolutionary success.

The Argentine ant is a superb invader of non-native habitats, particularly, as it happens, around the Mediterranean and areas with similar climates such as California. It achieves high population densities, often controlling huge areas to the near exclusion of other ants[2]. We rarely understand why invading species succeed, although a common advantage is that they leave their predators, parasites and pathogens behind. Although this explanation could apply to Argentine ants, it seems that the most serious enemies left behind were the warring clans of its own species.

In their native Argentina, ants from different colonies fight (Fig. 1), as most ants do, and the species is not ecologically dominant[3]. Its dominance in non-native areas seems to be associated with a very unusual trait. There, the nests are not distinct colonies. Instead, they form a vast supercolony within which there is little aggression and extensive interchange of both workers and queens. Such ants are called unicolonial because a whole population effectively becomes one colony[4].

The advantages of peace are shown by lab experiments pairing Argentine ant colonies that were either mutually tolerant or mutually aggressive. Tolerant pairs had lower mortality, and higher feeding and growth rates[5]. Earlier field studies in California[2,6] showed that the high population densities associated with tolerance help Argentine ants to outcompete native ants, towards which they are anything but tolerant. The Argentine ants win, not because of the individual prowess of the fighter-workers, which are 2–3 mm in length, but because of their ability to rapidly recruit legions of troops from their network of nests. So peace with flanking nests generates advantages in competition with other species.

How was this Pax Argentinica attained? The Romans achieved their peace in part by extending citizenship to their former foes. Tsutsui *et al.*[1] have now shown that the Argentine ants introduced into California and elsewhere took a similar step, albeit inadvertently. Colony membership in social insects — their citizenship — is based on kinship. Usually colony boundaries are fiercely guarded because the only way that non-reproductive workers can pass on their genes is to ensure that their work benefits a closely related reproductive queen. So how a species evolves to ignore colony boundaries is a real puzzle.

Tsutsui *et al.* show that colonies in native Argentina behave as expected, in that aggression depends on the degree of genetic difference, as assessed by seven microsatellite loci in nuclear DNA (these are useful markers because of their high variation and because they are probably neutral in terms of natural selection). Closely related colonies are tolerated; others are not. The population introduced into California has, not surprisingly, passed through a genetic bottleneck — that is, a temporarily small population in which genes are lost through chance effects known as genetic drift. In this case the ants lost two-thirds of the variability (heterozygosity) at the microsatellite loci. So all of the ants are genetically alike, and those applying the old similarity-tolerance rule could be fooled into accepting everyone as kin.

Support for this view came when Tsutsui *et al.* found a small number of mutually aggressive nest pairs in the Californian population: the relationship between genetic similarity and degree of aggression was the same as in Argentina. So, paradoxically, the ecological success of the introduced populations stems not from adaptation but from the loss of an adaptation — colony recognition — due to genetic drift.

This is not the first time that life has crafted new cooperative units out of formerly independent ones. Many of the major transitions of evolution take this form[7]. Independent molecular replicators became compartmentalized into cells and linked into chromosomes; free-living bacteria became organelles in more complex eukaryotic cells; and cells united in multicellular organisms. A few of these organisms, notably the social insects, evolved colonies that are so cooperative that they are sometimes called superorganisms. In merging colonies to build a super-superorganism, the Argentine ant is one of a few social insects that adds another Russian doll to the series.

Is this the next major evolutionary transition? Do we face a future dominated by unicolonial ants? Some homeowners may feel that this future is already here, but the long-term success of unicolonial species seems doubtful. Although unicoloniality has evolved several times in ants, it does not seem to give rise to large and successful branches of the ant tree[4]. There is a good reason for this, one that echoes a reason cited by some scholars

Figure 1 **In combat — Argentine ants fighting. Fighting is common between colonies in the species' native Argentina, but rare in populations introduced elsewhere. As Tsutsui *et al.*[1] show in studies in California, such peaceful behaviour seems to stem from errors of kin recognition. Paradoxically, these errors, which result in peaceful cooperation between nests, give the species a powerful advantage in battles with competing species.**

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for the fall of the Roman Empire — a decay of civic virtue.

Without kin discrimination, relatedness in supercolonies becomes indistinguishable from zero[8], which has two consequences. First, workers that can no longer aid close relatives may evolve more selfish strategies. It may not be coincidental that the best example of ultraselfish 'greenbeard genes' comes from another ant with unicolonial characteristics[9]. Here, workers possessing one allele at a genetic locus selectively murder queens lacking that allele.

Whether or not workers evolve selfish strategies, the second, larger problem is that they cannot improve or even sustain their cooperative behaviour[10]. Without relatedness, adaptive modifications of cooperative worker behaviour cannot be favoured and maladaptive ones cannot be disfavoured. Random drift will become important again, this time because of the absence of any opposing force rather than a small population size. The ants are like a casino gambler who is lucky once but cannot quit: chance got them their stake, but over the long run it can only lead to ruin.

Either way, Argentine ants may evolve to control themselves, with their Pax Argentinica falling under an assault of unbridled nepotism, or with their society suffering the lingering death of decay by drift. Of course, either process could take a very long time. As to the question of controlling the ants in California, Tsutsui *et al.*[1] suggest a counterintuitive strategy that might give the ants a push down the nepotistic path. If the main enemies the ants left behind are themselves, perhaps we should introduce more of them. The resulting increase in genetic variation could re-establish the lost kin discrimination. If so, the ants can return to battling among themselves, giving native species a fighting chance. ■

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Gene regulation

Neutralizing noise in gene networks

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The thousands of chemical reactions that sustain living cells involve interactions between individual molecules. Such interactions are stochastic, happening discretely and randomly. This so-called noise is inherent in every molecular event that takes place in a cell. In particular, it can cause sizeable, random fluctuations in the concentrations of expressed proteins and RNA. But often the events in an individual cell, or even a whole organism, are not at all unpredictable. The gestation of multicellular organisms, for instance, follows a pattern and time course so predictable it could be used to set a watch. And all too familiar to the frequent traveller is the circadian rhythm, which is driven by a molecular clock with a precise period of oscillation. For years, researchers have wondered how biology achieves such predictability despite its inherent noisiness.

On page 590 of this issue[1], Becskei and Serrano provide insight into a possible mechanism by which cells may accomplish this impressive task. They show, using a synthetic gene circuit, that negative feedback can dramatically reduce variability in gene expression.

Earlier modelling studies[2] showed that noise in gene expression could lead to qualitative differences in a cell's phenotype if the expressed genes act as inputs to downstream regulatory thresholds. Recent experiments — including our own[3] — have also shown that internal noise can lead to premature switching between stable states[3] and irregular oscillations[4,5] in synthetic gene-regulatory networks. It has been suggested that the inclusion of feedback in gene-regulatory circuits could improve their robustness to internal noise[3–6]. Until now, that suggestion has remained unverified by direct experimentation.

The steady state of a noisy system can be characterized as a competition between stabilizing system dynamics and destabilizing random fluctuations. The addition of negative feedback counteracts the internal noise by enhancing the stabilizing action of the system dynamics. This effect can be visualized using a simple physical analogy. A ball (representing the level of gene expression) rolling in a salad bowl (representing the gene network) will ultimately come to rest at the bottom of the bowl. Shaking the bowl (the internal noise) will push the ball away from the bottom, while the shape of the bowl will push the ball back towards the bottom. Adding negative feedback to a gene network is equivalent to making the sides of the salad bowl steeper.

Becskei and Serrano[1] use linear stability analysis of a mathematical model to show that negative feedback can double the stability of gene expression in a simple gene network. They confirm this effect with simulations that show a reduction in the variability of gene expression. To test their predictions experimentally, Becskei and Serrano construct a synthetic gene network in the bacterium *Escherichia coli*. The network includes a TetR (tetracycline repressor)-regulated promoter region[7] placed upstream of the gene encoding the tetracycline repressor itself (Fig. 1). This system constitutes a negative feedback loop, because the promoter is inhibited by the repressor whose expression it drives. To measure the output of the system, Becskei and Serrano fuse the

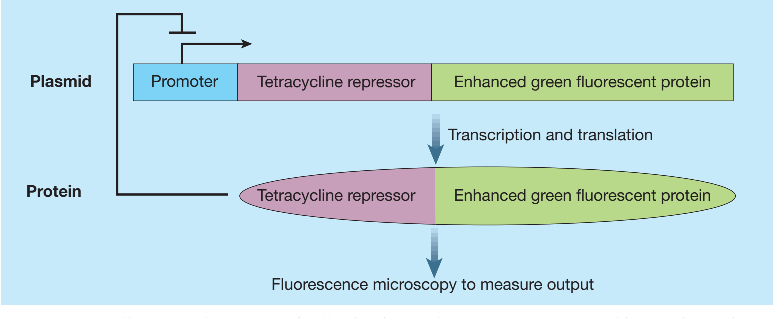

Figure 1 **Controlling noise by negative feedback. The synthetic gene network used by Becskei and Serrano[1] includes a tetracycline-repressor-regulated gene promoter to direct transcription of the repressor gene itself. The repressor protein then inhibits transcription from the promoter. The resulting negative feedback stabilizes expression of the repressor around a particular steady-state level. If the repressor exceeds this level, it will strongly inhibit its own synthesis, and repressor levels will decline. Conversely, when the repressor falls below the steady-state level, it will reduce the inhibition and repressor synthesis will increase. The gene encoding enhanced green fluorescent protein is also fused to the gene construct, allowing quantification of the output of the network.**