from waste water, and the anammox bacteria perform this job quite admirably. Although they have not yet been isolated in pure culture, the microbes concerned[2] and the catalytic pathway[3–6] of the anammox process have been identified, largely through the efforts of Keunen, Jetten and colleagues at the University of Nijmegen. The specifics of the anammox pathway are quite remarkable, and especially startling (Fig. 1) are the highly toxic and reactive intermediates that are formed — hydroxylamine and hydrazine, the second of which finds a very different use as rocket fuel.

The location, structure and biophysical properties of the ladderanes suggest that they have a specific function in anammox bacteria. The enzymes that drive the process are localized in a special intracellular compartment, the anammoxosome (Fig. 1)[6,9]. This is the same place in which Damsté *et al.* find the ladderanes. Presumably, the rigid structure and dense packing of the ladderane membranes help to contain the noxious anammox intermediates. This would be analogous to the way that eukaryotic organelles called lysosomes compartmentalize digestive enzymes, protecting the rest of the cell from damage.

To test this hypothesis, Damsté *et al.*[1] examined the permeability of the ladderane membrane. Unlike other membrane compartments in the cell, the anammoxosomes were completely impervious to a variety of agents. So the unique structure of the ladderanes does seem to play a role in compartmentalizing the anammox intermediates. In evolutionary terms, one might ponder which came first: the ladderanes, or the anammox pathway? Now that we know what to look for, a search for wider distribution of these lipids may shed light on the question.

"The cell consists of numerous half-living chemical molecules suspended in water and enclosed in an oily film. When the whole sea was a vast chemical laboratory the conditions for the formation of such films must have been relatively favourable." Thus J. B. S. Haldane[10] imagined the early evolution of one of the most defining structures of life, the cell membrane. Given current theories about those promiscuous times, when lateral genetic transfer is thought to have exceeded vertical transmission[11], the invention of a defined cell barrier and the emergence of the cell as 'self' was certainly a turning point in the evolution of cellular life. The variety of membrane lipid structures existing in those early times could well have been quite diverse. But innovations in membrane lipid structure as dramatic as that described by Damsté *et al.* appear to be generated rarely today.

These new observations[1] will certainly help in understanding the physiological processes that occur in anammox bacteria, and the mechanisms of subcellular compartmentalization in prokaryotes. They may well also provide insight into evolution and innovation in membrane lipid structures in general. ■

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Evolution

The good, the bad and the lonely

Franziska Michor and Martin A. Nowak

In game theory, 'loners' who choose not to participate in fact promote cooperation between players. The dynamics of the game show phase transitions and complex phenomena reminiscent of statistical physics.

Hungarian-born genius John von Neumann, in a rare moment of humility, confessed that he considered himself a failure: according to his own ranking, he was only the third-best mathematician of the time. Yet von Neumann not only built one of the first computers and achieved breakthroughs in fields as diverse as operator theory, mathematical logic and hydrodynamics, he also created several fields of mathematics from scratch. Two of these fields, game theory[1] and cellular automata[2], are merging in the study of evolutionary dynamics[3]. Earlier this year, Hauert *et al.*[4] pushed this development further by investigating the effects of voluntary participation in 'public-goods games' — players can choose whether or not to join in a game (or interaction) that may benefit them. That work is now extended by Szabó and Hauert[5], writing in *Physical Review Letters*, to a large interacting community of players on spatial grids.

The quest for cooperation is as old as evolution itself. In the *Origin of Species*, Darwin noted that natural selection cannot directly promote altruistic acts where individuals reduce their own competitive ability but increase that of others. Yet cooperation is abundant in nature. The standard explanations that have been developed for this include kin selection, group selection and reciprocity[6–11].

The essence of cooperation is captured by the public-goods game. Each individual of a group can decide whether or not to invest some money in a common pool. The common pool is increased by some amount and then equally distributed among all group members regardless of whether or not they made a contribution. The optimum outcome

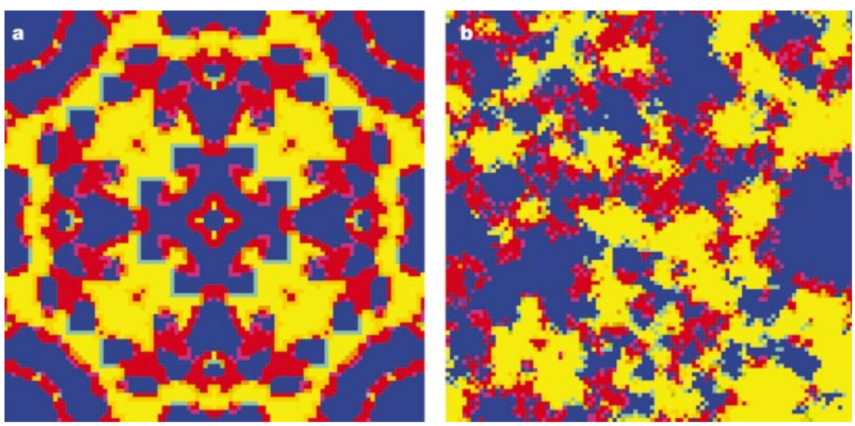

Figure 1 **Evolutionary kaleidoscope.** a, **Players in a public-goods game are represented as cells distributed spatially on a grid. Cooperators are shown in blue, defectors in red and loners in yellow. Players may change their strategy in each round of the game. For this simulation, all strategy updates are synchronous. Intermediate colours indicate players who have updated their strategies in the last round of the game.** b, **Another simulation shows the effects of asynchronous strategy updating and small amounts of noise in the system. In both cases, there is coexistence between cooperators, defectors and loners. Szabó and Hauert[5] show that the dynamics of such systems have much in common with models in statistical physics.**

for the group occurs if everybody cooperates. But the temptation is to 'free ride': those who don't contribute (defectors) always get a higher pay-off than cooperators who do contribute. If everyone defects, however, no one will enjoy the public goods. Self-interest is self-defeating! This social dilemma threatens the success of public enterprises such as social security, the conservation of environmental resources or group defence against external threats. Notice that the well-known 'prisoner's dilemma' is a public-goods game for groups of two people.

Hauert *et al.*[4] proposed a new and surprisingly simple mechanism to promote cooperation. Rather than allowing cooperation or defection as the only strategic alternatives, they added a third option — 'loners', who do not participate in the game but instead receive a small, independent pay-off corresponding to a modest income from some self-sufficient occupation. Those who choose to participate in the public-goods game must forgo the loner's pay-off. Equivalently, one could regard the pay-off as the avoidance of a fixed cost for participating in the public-goods game.

In this game, defectors dominate cooperators, as they do in a game without loners; but loners dominate defectors, because in a world of defectors, the public-goods game yields nothing, and loners avoid the cost of participating. Cooperators, on the other hand, dominate loners, because the public-goods game pays in the absence of defectors. The circle is closed. The outcome depends on the details of the underlying evolutionary dynamics, but there are oscillations in the frequencies of the three strategies. For example, if players always adopt the strategy providing a higher pay-off, then the oscillations of the frequencies of all three strategies are stable and robust. The updating mechanism of best-reply dynamics — switching to the best strategy, given the composition of the population at a certain point in time — leads, through damped oscillations, to a stable equilibrium among all three strategies. Hence, the social dilemma is relaxed: instead of defectors winning the world, there is coexistence among cooperators, defectors and loners.

Voluntary participation, though, is only a 'Red Queen' mechanism for cooperation. The Red Queen in Lewis Carroll's *Alice's Adventures in Wonderland* always has to run to stay on the same spot. Similarly, the oscillations among cooperators, defectors and loners lead to average pay-offs that are no larger than having no public-goods game at all. Volunteering does not lead to the fixation of cooperators, but it prevents the fixation of defectors in the population. It needs other mechanisms, such as punishment[12,13], to achieve a stable regime of all-out cooperation. Interestingly, however, optional participation does not require individual recognition.

In spatially extended games, as investigated by Szabó and Hauert[5], voluntary participation is even more successful in promoting cooperation than in well-mixed populations. In the computer simulation, players are represented by cells on a spatial grid. The size of the neighbourhood determines the number of players that interact in the public-goods game. Players with a higher pay-off have an increased probability of being imitated by their neighbours. Hence, successful strategies spread locally. Clusters of cooperators do better than clusters of defectors, but isolated defectors flourish if surrounded by cooperators. In spatial versions without volunteering, there is coexistence between cooperators and defectors for a restricted range of parameters. Adding loners greatly increases the range of parameters allowing coexistence. Hence, optional participation enables the survival of cooperation under circumstances that would normally favour the dominance of defectors.

The intriguing spatiotemporal patterns show cyclic, complex behaviour and coexistence of all three strategies (Fig. 1). Some of the cellular games are closely related to models in statistical mechanics, such as the Ising model for magnetic spins. Spatial games exhibit phase transitions and the full range of complex phenomena observed in the world of cellular automata[14]. Hauert has designed a beautiful web page (www.univie.ac.at/virtuallabs) where visitors can run simulations for their own choice of parameters and initial conditions. Sometimes, extreme parameter values or small system sizes lead to the extinction of strategies; for example, extinction of defectors in small societies leads to homogeneous populations of cooperators.

At the dawn of life on Earth (or elsewhere), replicating molecules had to cooperate to take the first step towards increasing complexity and stability of molecular and later cellular ecosystems. Multicellularity requires cooperation among cells. Cooperation is common in animal societies, but it is often confined to interactions among related individuals. Large-scale cooperation among unrelated individuals seems to be a particularly human trait. Of course, cooperation is always threatened by defection; oscillations between 'war and peace' have been a recurring theme in the cooperation literature. The new work shows that it is optional, rather than compulsory, interactions that promote cooperation. ■

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Immunology

Catch us if you can

Wayne M. Yokoyama

Tumours have ways of evading the body's immune system. A surprising example involves a mechanism that at first sight would seem to have the opposite effect and improve immune responsiveness.

How can tumours develop when the immune system should instead attack and destroy them? Especially difficult to understand is the situation in which tumour cells display surface molecules that should identify them as abnormal, and so should specifically activate immune cells. This makes little sense from the tumour's point of view. These molecules should flag the tumour cells for destruction, unless they somehow give the tumour an advantage — a situation that should remind those of a certain age of the Dave Clark Five, and the immortal lines of one of this 1960s band's songs: "Here they come again, Catch us if you can." On page 734 of this issue, Groh *et al.*[1] offer insight into this puzzle. They describe a mechanism of tumour evasion that may also apply to the impairment of other immune defence systems, and which may well have clinical potential.

Immune 'effector' cells express surface receptors that are involved in activating the cell by transmitting signals to the cell interior[2]. In the case of specialized immune cells termed cytotoxic T lymphocytes, or CTLs,