closer together, letting electrons hop more easily. The variation with magnetic field arises from a neat piece of atomic physics. An electron has an intrinsic angular momentum, or spin, whose axis may point in any direction in space. Each manganese atom in $La_{1-x}Ca_xMnO_3$ has its own 'core spin', formed of three localized electrons with parallel spins, and may also carry 'itinerant electrons', which can hop from manganese to manganese. On a given site, an itinerant electronis constrained by the 'Hund's coupling' of atomic physics to have its spin axis parallel to that of the core spin. The consequence is that the amplitude for an electron to hop from one site to another depends on the relative orientation of the core spins at the two sites, being greatest when the core spins are parallel and least when they are antiparallel. Because an applied magnetic field tends to align the core spins, it increases the hybridization.

At low temperature, and in the composition range $x \geqslant 0.5$, $La_{1-x}Ca_xMnO_3$ is a charge-ordered insulator. Mori *et al.* have discovered that this charge-ordering takes the form of stripes, and that the fundamental unit is surprisingly complex: it is a sort of sandwich, comprising a pair of stripes with one itinerant electron per manganese, bracketing a stripe of manganese sites with none (Fig. 1). Lattice distortions also occur, most notably a 'Jahn–Teller' displacement in which some Mn–O bonds become shorter than average and others longer. This basic three-row sandwich unit is repeated throughout the crystal, with the mean spacing between units set by the average charge density.

The discovery is important for several reasons. The structure of the stripes was not anticipated, so theorists will have to re-examine their models. Also, the charge density variation across the stripe is large, so properties of stripes may be more easily studied than in other compounds. Moreover, the manganite materials exist in a wide variety of crystal forms, so a detailed study of the effect of lattice structure and dimensionality on stripe formation should be possible.

But most importantly, the sensitivity of the hybridization to pressure and magnetic field should allow experimentalists to study its effects in detail. For example, we already know that the low-temperature insulating stripe phase may be converted into an electrically conducting phase by applying pressure or a magnetic field[4]. Presumably this metal–insulator transition is caused by increased quantum fluctuations coming from the increase of hybridization with pressure or field, and it will be interesting to see whether the resulting metal is a realization of the 'fluctuating stripe phase' postulated for high-temperature superconductivity. □

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S. MORI *ET AL.*

Biomathematics

Merging lines and emerging levels

Karl Sigmund and Eörs Szathmáry

Talk of the 'higher principles of life' has a ring of vitalism to it. So it must have taken Michael Polanyi considerable pluck to argue in 1968, at the onset of the spectacular advances of biochemistry and molecular genetics, that life has an 'irreducible structure'.

He wrote: 'We can recognize a strictly defined progression, rising from the inanimate level to ever higher additional principles of life. ... Evolution may be seen, then, as a progressive intensification of the higher principles of life'[1]. This 'progress', nowadays described as a series of major transitions in evolution[2], is often due to the emergence of new units. We are used to seeing individuals as the units of selection, but they are groups of cells, which include, in turn, groups of organelles descended from some proto-cells, and whose nuclei are groups of genes.

Why should we then have qualms about viewing groups of individuals (societies, colonies or species) as units on their own? The emergence of new levels of organization was the subject of a workshop at the École Normale Supérieure in Paris in January*.

The fact that this workshop was attended by evolutionary biologists and mathematicians in almost equal numbers reflects a significant trend. Biologists' favourite adopted science is chemistry, but chemistry does not tackle many basic problems, such as the co-evolution of hosts and parasites, the merger of lineages, or the tuning of mutation rates. It is *populations* of virus particles, or immune cells, or hosts, that regulate one another's frequencies. The feedback loops of these ecosystems are too complex to be understood by verbal arguments alone, and can only be analysed by mathematical means.

Both mathematicians and biologists have become more aware of the advantages of talking to each other[3,4], but this association does not come naturally. R. A. Fisher, a founding father of population genetics, attributed the difficulties of understanding between mathematicians and biologists to their vastly different training[5].

It can be taxing to listen to the other side, especially if you are '*fort en math*' and accustomed to rank at the top of France's intellectual scale. On several occasions, eminent mathematicians have developed ambitious biological speculations without the help of biologists, and altogether failed to convince them. And, indeed, someone accustomed to seeing mathematics as the queen of science, rather than its servant, will find it difficult to work with biologists.

The new emphasis of biomathematics is on explaining large evolutionary transitions in terms of nonlinear, local interactions between replicating units. Such interactions often lead to coherent structures whose existence is strikingly obvious in computer simulations, but which cries out for a mathematical underpinning; and this needs expertise on bifurcations of dynamical systems, hydrodynamical limits of interacting particles, and nonlinear partial differential equations — areas in which France is currently leading.

One spectacular challenge for such experts is the hydrodynamical slime-mould model of F. Siegert (Univ. Munich), in which two-dimensional arrays of isolated single cells use chemical gradients to form a three-dimensional, multicellular aggregate with a twisted scroll wave running along its axis, which makes it move, comically, like a real slug[6].

Other self-generated spatial correlations overturn conclusions derived under the assumption of completely mixed populations of hosts and parasites. In the completely mixed case, parasites tend to kill all the hosts and then die; but with spatial variation, self-replicating clusters of parasites and hosts can form (D. Rand, Univ. Warwick; M. van Baalen, Univ. Paris VI).

Spatial considerations also modify the concept of fitness, usually defined as individual reproductive success. In the case of the Prisoner's Dilemma, for instance, which is frequently used (possibly overused) as a toy model for the evolution of cooperation, fitness translates as the speed of travelling waves of defectors and tit-for-tat players, as these waves can overwhelm populations of the opposite type (R. Ferrière, ENS, Paris).

M. Boerlijst (Univ. Amsterdam) and P. Hogeweg (Univ. Utrecht) argued that the blobs and spirals seen in their computer simulations are emerging 'units of selection' protecting otherwise unstable feedback loops of self-replicating molecules, or of parasites and hosts. The blobs play the part of a protective membrane, as in a primitive multicellular organism. ▶

* *Units of Selection and the Major Transitions of Life*, Paris, 30–31 January 1998.

Beyond the semantics raised by these hotly debated proposals lurks the problem of how to compare fitness differences across levels of selection, a problem that is unavoidable if one wants to understand the organization of a genome able to modify its own mutation rate (B. Godelle, Univ. Paris XI)[7] or the transition from unicellular to multicellular eukaryotes — a transition that must cause smouldering conflicts within the developmental system of the emerging entity (R. Michod, Univ. Arizona).

A careful analysis of symbiosis and mutualism stresses that analysis at different levels — physiological, ecological and evolutionary — may lead to different conclusions (U. Dieckmann, Intl Inst. Appl. Syst. Anal.; R. Law, Univ. York). Even in the face of persistent physiological exploitation of one partner by the other, evolution can select for stable symbiotic structures: such adaptations lead to a kind of dependence that is more like addiction than mutual benefit.

This may shed light upon the origin of mitochondria in eukaryotic cells. Suggestions favouring a very early acquisition of mitochondria suffer from two unsolved problems: the method of acquisition (no sensible alternative to phagocytosis has ever been suggested), and the initial advantage of such an association. Perhaps proto-mitochondria were once parasitic, and only later evolved into ATP-generating slaves. As one of us (E.S.) pointed out, isogametic sex may have been crucial, as it allows the spread of moderately harmful intracellular symbionts.

Scenarios of this type vastly expand the range of conditions under which separate lineages can be expected to merge into symbiotic units. This leads one to hope, on yet another level, that mathematicians and biologists will find their emerging association of mutual benefit. They may eventually become addicted to each other's company. □

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Conservation biology

Inbreeding leads to extinction

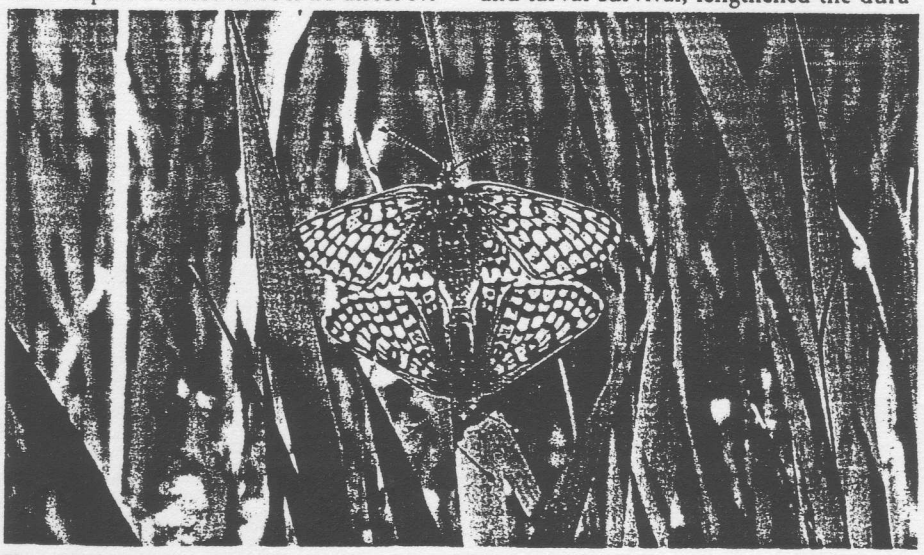
Richard Frankham and Katherine Ralls

Do genetic problems contribute to the endangerment and extinction of wild populations? Conservation biologists initially thought[1] that they would — and seriously so. But it is extremely difficult to demonstrate that inbreeding contributes to the extinction of wild populations. On page 491 of this issue, however, Saccheri and colleagues[2] provide the first direct evidence that it does, with their elegant work on a wild butterfly metapopulation in Finland.

Theoretical work in the 1980s indicated that small populations in the wild suffer from increased extinction because of an unavoidable increase in matings between close relatives. Inbreeding reduces reproductive success in populations of naturally outbreeding species, both in captivity[3,4] and in the wild[4], and it also increases extinction rates in laboratory populations of fruitflies and mice[5]. However, in an influential paper[6], Lande argued that random demographic and environmental events will drive small wild populations to extinction before genetic factors come into play. Environmental events, ranging from annual variation in climatic variables (such as rainfall) to catastrophes (such as disease epidemics), do increase the probability of extinction. Furthermore, inbreeding typically interacts with demography by reducing fecundity, juvenile survival and lifespan. Because there is no direct evidence that inbreeding contributes to extinction of wild populations, some researchers have continued to question the relevance of genetic factors[7,8].

The Glanville fritillary butterfly (*Melitaea cinxia*; Fig. 1) studied by Saccheri *et al.*[2] has a predictable yearly life cycle. Adults emerge, mate, and lay eggs in June. Caterpillars feed in conspicuous family groups of 50 to 250 individuals, then diapause (suspend development) from August until March of the following year, and resume feeding and pupate in May. The butterfly metapopulation consists of numerous small populations that breed in about 1,600 suitable dry meadows of different size and varying distance from one another. Some populations are very small, often consisting of the offspring of a single pair of butterflies. Consequently, populations in individual meadows often disappear, but many meadows are eventually recolonized, with an average of 200 extinctions and 114 colonizations per year.

Because small population size results in both inbreeding and loss of genetic variation, the degree of genetic variation in a population serves as a measure of the extent to which it is inbred. Saccheri *et al.* determined the genotypes of female butterflies from 42 populations at eight variable genetic loci (polymorphic loci). They sampled relatively large, non-isolated populations, as well as smaller, relatively isolated populations. The authors found that populations with less genetic variation were more likely to become extinct. Furthermore, multiple logistic regression showed that genetic diversity predicted extinction risk after accounting for all known demographic, ecological and environmental causes of extinction in this well-studied butterfly metapopulation. Inbreeding reduced the egg hatching rate and larval survival, lengthened the dura-



I. SACCHERI

Figure 1 **Doomed liaison — a mating pair of Glanville fritillary butterflies (*Melitaea cinxia*). From their studies of a metapopulation of this species, Saccheri *et al.*[2] found that inbreeding contributes to the extinction of wild populations.**