These observations also test a central result of quantum kinetics[5–7] — a theory developed to describe the kinetics of quantum systems on femtosecond timescales. Over such ultrashort time intervals, the behaviour of plasmons and phonons, for example, can no longer be described by semiclassical Boltzmann kinetics, but has to be described by quantum kinetics, which takes the coherent wave nature of the particles into account. This quantum coherence causes memory effects in the scattering integrals that are very different from the simple instantaneous Boltzmann scattering rates. These memory effects are also responsible for the delayed build-up of charge screening observed by Huber *et al.* in their experiment.

It would be of great interest if the charge-screening dynamics in the semiconductor could be measured as the plasma density increases to the point at which the frequencies of the lattice phonon and the collective plasmon oscillations coincide. The resulting state is a mixed phonon–plasmon mode, whose behaviour would be an entirely new topic in ultrafast physics. The same technique could also be used to study the dynamics of the build-up of magnetic polarons in high-temperature superconductors. There are so many systems involving large numbers of particles (from the vibrational dynamics of large biomolecules to nuclei containing lots of protons and neutrons) that many interesting questions remain unexplored. ■

Hartmut Haug is at the Institut für Theoretische Physik, Johann Wolfgang Goethe-Universität, D-60054 Frankfurt, Germany.
e-mail: haug@itp.uni-frankfurt.de

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Evolutionary biology

Counting on immunity

Theo C. M. Bakker and Marc Zbinden

Certain variable immune proteins affect an animal's choice of mate. In some species, females pick males with proteins as dissimilar as possible to their own. Studies of sticklebacks now reveal another mechanism.

In vertebrates, a crucial part of the immune system consists of proteins of the so-called major histocompatibility complex (MHC). There is staggering diversity in the genes that encode these proteins: for example, some MHC genes in human populations come in several hundred different variants (alleles). Yet it is not at all clear how such variability within populations is maintained.

On page 300 of this issue, Reusch and colleagues[1] provide compelling evidence, based on their studies of sticklebacks, for a previously unknown mechanism: females 'count' MHC alleles when looking for a mate. MHC proteins are thought to influence an animal's odour, and, given a choice between the odour of males with many or a few different MHC alleles, female sticklebacks prefer the males with greater numbers. So, by ensuring greater diversity within individual offspring, this 'sexual selection' mechanism also maintains extensive variation within populations.

The MHC genes encode cell-surface proteins — the MHC molecules — that present peptides derived from pathogenic organisms to T cells. This is a crucial step in the immune response to the pathogens. MHC molecules also shape an individual's repertoire of T cells, by displaying peptides from 'self' proteins to immature T cells in the thymus. Any T cells that react to the self-peptides should die, preventing an autoimmune reaction. MHC proteins are divided into two classes: MHC I molecules present peptides from within an individual's cells (such as viral or self peptides), whereas MHC II molecules display peptides from sources taken up from outside the cell (such as bacterial or self peptides). Typically, each class consists of several duplicated genes, so each individual expresses several different MHC molecules that differ with respect to the peptides they can present. For example, Reusch *et al.*[1] could distinguish up to eight different MHC II alleles in individual sticklebacks, and many more within stickleback populations.

So, how is this diversity in MHC alleles in populations maintained? Several potential mechanisms have been proposed, involving natural or sexual selection[2–5]. Pathogens could drive natural selection for MHC variability in two ways. First, an individual with many different MHC alleles can respond to a wider array of pathogens than an individual with less diversity, and so is more likely to survive and pass on its genes to the next generation. Second, because pathogens try to evade the immune system by adapting to common MHC alleles, individuals with new or rare MHC alleles have an advantage.

Sexual selection would maintain MHC variation in a different way. MHC composition somehow influences an individual's odour[6], so females may secure genetic (including MHC) diversity for her offspring by choosing to mate with males with a certain smell. Reusch *et al.*[1] have revealed a new mechanism that influences a female's choice of mate.

The idea that sexual selection underlies MHC diversity is not new. It dates back to a 1976 paper by Yamazaki *et al.*[7], who showed that male mice preferred to mate with females with combinations of MHC alleles that were dissimilar to their own. Since then, such 'disassortative' mating has been repeatedly established for mice, and has also been suggested for humans[5]. Reusch *et al.*[1] explicitly tested whether or not female sticklebacks prefer males with dissimilar MHC combinations, but found that the females did not care whether they had many or few MHC alleles in common with the males. Instead, they simply preferred males with many MHC alleles. The authors investigated the mating choices of female sticklebacks that were ready to spawn by presenting the females with water from two tanks, each of which had contained a different male. Females were most attracted by the odour of males with many MHC alleles.

What makes sticklebacks behave differently from mice and humans? So far, no one has tested the MHC-allele-counting option in these species (for example, in previous mouse studies, strains with limited MHC variation were used). But sexual-selection mechanisms for upholding MHC variation may partly depend on social structure. MHC-dissimilar mating in mice is thought to be a mechanism for avoiding inbreeding, because individuals recognize the odours of former nest-mates[2–6]. This makes sense for populations of house mice, which are structured in family groups. Reproducing sticklebacks are not organized in such groups, and inbreeding is less likely. Moreover, stickleback nests can contain thousands of embryos from different mothers and even fathers. So the familiar odours of former nest-mates are no reliable indication of kinship. The allele-counting mechanism described by Reusch *et al.*[1] is the first known MHC-dependent sexual-selection process that is not confounded by inbreeding avoidance.

MHC diversity is thought to be beneficial, but you can have too much of a good thing. Too much MHC variation in individuals is associated with both an increased risk of autoimmunity and a reduced T-cell repertoire[5]. So you would expect allele-counting mating partners to try to optimize the number of different MHC alleles in their offspring. If so, a female's choice would depend on how many MHC alleles she has herself. In fact, Reusch *et al.*[1] did find that female

FABIAN HERDER/JOACHIM FROMMEN

Figure 1 **Sex and the single stickleback. Male sticklebacks with many different MHC proteins are most likely to be chosen as mates by females.**

sticklebacks with many different MHC alleles tended to be less attracted by males with high MHC diversity.

So, to work out the relative contributions of allele counting and disassortative mating in maintaining MHC diversity in different species, population geneticists need to model both scenarios, taking into account social structure and the costs of autoimmunity. MHC-dissimilar matings can explain the degree of MHC variability in mice[8]. But intuitively, you might think that allele counting is a stronger selective force to favour rare alleles and so maintain MHC diversity.

Female choice may affect many different male characteristics[9]; male sticklebacks, for example, are well known for their visually conspicuous traits (Fig. 1), some of which are associated with parasite resistance[10]. Traits such as degree of redness and body size have an obvious influence on female choice. Such traits may suggest whether or not the male will provide good care to the embryos in the nest, or they may have evolved simply for reasons of attractiveness. But visually conspicuous traits might also reveal a male's MHC make-up or non-MHC genetic background, which could in turn affect the male's MHC-dependent ability to resist pathogens[2]. If so, sexual selection would count even more on MHC. ■

Theo C. M. Bakker and Marc Zbinden are at the Institute for Evolution and Ecology, University of Bonn, An der Immenburg 1, D-53121 Bonn, Germany.
e-mails: tbakker@evolution.uni-bonn.de
mzbinden@evolution.uni-bonn.de

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Statistical mechanics

A departure from equilibrium

David Ruelle

Non-equilibrium processes, such as heat conduction in a bar of metal, remain poorly characterized at the microscopic level. Detailed analysis of simple models can introduce a new degree of understanding.

What do we mean by equilibrium? Take a bar of metal in equilibrium at room temperature and watch it closely. Nothing happens. Now impose an electric potential difference at the ends of the bar: electric current flows, the bar emits some heat, and it is no longer in equilibrium. If we try to describe the physics of our metallic bar at the microscopic level **(**the level of atoms and electrons**)** we find that our fundamental understanding of equilibrium is very good, but our understanding of non-equilibrium states is pretty poor. In one case we can make precise and useful calculations; in the other, hardly any. This situation is unfortunate because the phenomena of life occur far from equilibrium. After 100 years of limited progress in extending the theory of equilibrium to non-equilibrium systems, there are signs that we are finally getting somewhere. In particular, a paper in *Physical Review Letters* by Bernard Derrida, Joel Lebowitz and Eugene Speer[1] provides a simple model of a non-equilibrium system that permits very detailed calculations. They find that the fluctuations around a non-equilibrium steady state are very different from those at equilibrium.

Let us first review the theory of equilibrium founded by Maxwell, Boltzmann and Gibbs more than 100 years ago. When looking at a system at thermal equilibrium we can calculate the probability of a given state having a particular energy by using the Boltzmann formula, which is based on the absolute temperature of the system, T, and the Boltzmann constant, k. When there are many possible states, the probability of a state having energy close to E is known as $d(E)$, a measure of the density of states around energy E. The formula for $d(E)$ tells us that the system is at thermal equilibrium (most states have energies near the equilibrium value, E_0) when $d(E_0)$ is at a maximum, or when the free energy of the system is at a minimum. (The free energy is the amount of energy available for work when the system undergoes a change.) The formula also gives the probability that there are deviations or fluctuations from that value. So at equilibrium there are simple formulas to compute the equilibrium value of the energy, and to study fluctuations around this value. At this level of description the size of the system does not matter, but the energy is a sum of local contributions.

Away from equilibrium we have to start from scratch. In their work, Derrida *et al.*[1] discuss a very simple model: a metallic bar consisting of i lattice sites ($i = 1 \ldots N$). Each site is either empty or occupied by an electron. Each electron jumps randomly (once per second on average) to the next site on the left or right, provided it is empty. The probability that the left or right end of the bar is occupied is ρ_0 and ρ_1, respectively. Assuming that $\rho_0 > \rho_1$ (the non-equilibrium situation) there will be a net flow of electrons from left to right. For large N we can introduce a spatial coordinate $x = i/N$, and calculate the 'density profile' of the system, $\rho(x)$, along the metallic bar. When the system is in a steady state (but not under equilibrium conditions) the optimal density profile turns out to be $\overline{\rho}(x) = \rho_0(1-x) + \rho_1$. This is the macroscopic behaviour that one might expect: a non-equilibrium steady state with an occupation probability that is linearly related to x.

What about the fluctuations? As Derrida *et al.* show, they are totally unlike those at equilibrium. To analyse their model further the authors use a somewhat mysterious matrix method. They find that the optimal density profile $\overline{\rho}(x)$ has fluctuations with probabilities proportional to $\exp\{-NF(\rho)\}$, where F is the non-equilibrium free-energy functional. A functional is a 'function of a function': the free energy is a function of the density profile, which is itself a function of position. This is the point at which the formulae become too complex to reproduce here.

But the expression for $F(\rho)$ is more than a technical *tour de force*. Unlike the free energy in the equilibrium case, $F(\rho)$ is a non-local functional. This means that the free energy cannot simply be calculated by summing the local free energy at each point on the density profile. So the fluctuations around $\overline{\rho}(x)$ are correlated with fluctuations over the whole system. Here we see the kind of long-range order that has been inferred from other studies of non-equilibrium systems. Indeed, the production of entropy according to Boltzmann implies the presence of such long-range correlations. Perhaps the calculation by Derrida *et al.* is a first step to a microscopic understanding of pattern formation in non-equilibrium systems, such as the ordered