tunately, is probably not. If eIF1 and 1A were added after a short delay, complex I disappeared to be replaced by complex II in similar yield. But delayed addition of excess competitor mRNA together with eIF1 and 1A showed that this was not a case of direct conversion of complex I into complex II on the original mRNA. Rather, the pre-formed complex I must have first dissociated and the appearance of complex II must have resulted from a fresh attempt by the primed 40S subunit to scan the mRNA.

Taken together, these observations provide clues as to the functions — not necessarily mutually exclusive — of eIF1 and 1A. They may be necessary for successful scanning to the initiation codon (but for this they must presumably be present before the pre-initiation complex has interacted with the mRNA); they may prevent the formation of the abortive complex I; or they may accelerate the rate of dissociation of complex I. In the first of these possibilities, it could be that the two factors form an essential part of the 'motor' that drives scanning. An alternative explanation is that they prevent the scanning process pausing at non-AUG triplets, or dissociate any subunits that have stalled at these sites.

Other evidence supports the idea of such a surveillance function, at least for eIF1. First, mutations in the gene encoding yeast eIF1 (originally named *SUI-1*) allowed initiation to occur at a UUG codon. The implication is that wild-type eIF1 normally dissociates the initiation complex, or does not allow it to form, when a mismatched codon/anticodon interaction occurs, and that the mutant form was somehow defective in surveillance[4,6]. Second, in initiation of translation of encephalomyocarditis virus RNA (which, unusually, is by direct internal ribosome entry at the eleventh AUG from the 5′ end, and probably involves no scanning[7]), addition of eIF1 dissociates any complexes formed with the 40S subunit bound at AUG-10; AUG-10 is not used significantly as an initiation site even though it is only eight nucleotides upstream of AUG-11 (refs 2, 7). Finally, and most surprisingly, mutations in yeast eIF1 increase the frequency of misreading of the genetic code within the body of the mRNA (ref. 8), suggesting that wild-type eIF1 may monitor the accuracy of codon/anticodon interaction not only during 40S subunit scanning, but also during the actual decoding of the mRNA sequence.

After the major surprise delivered by Pestova *et al.*, the way forward is not immediately obvious. Undoubtedly, yeast genetics has a contribution to make, and structural studies of eIF1 and 1A might be instructive. What we would really like to know is which of the other eIFs or ribosomal components eIF1 and 1A interact with during initiation. One thing is certain, however — these two factors will never again be marginalized. □

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Statistical mechanics

Brownian motion and microscopic chaos

Detlef Dürr and Herbert Spohn

Einstein's 1905 paper[1] on Brownian motion is his most cited article, and one of the most cited physics papers ever. But nearly a century later, we are still learning from this phenomenon. On page 865 of this issue, Gaspard *et al.*[2] report a high-precision measurement of the position of a colloidal particle suspended in water at thermal equilibrium, providing direct experimental evidence for chaotic dynamics of the fluid on the microscopic scale. Counter-intuitively, perhaps, this strengthens our conviction that chaos underlies the smooth behaviour of matter on macroscopic scales.

At the turn of the last century the atomistic structure of matter, although theoretically well established through the kinetic theory of gases, lacked acceptance because there was little direct experimental evidence for molecular motion. Einstein argued that the erratic path of a small particle suspended in a fluid resulted from the random collisions with the molecules of the fluid. This motion was first systematically described by the botanist Robert Brown in 1828, whence the name Brownian motion. Einstein predicted that its behaviour should be regular, on the average, with the mean square displacement of the Brownian particle growing linearly in time (a hallmark of diffusive behaviour). He related the proportionality factor to Avogadro's number — in other words, to the number of molecules that, according to the atomistic theory, should be around to strike the particle.

Experiments by Perrin in 1909 confirmed this diffusive motion of the Brownian particle, which at the time was regarded as the most direct evidence for the atomistic picture of the world. Kappler repeated the experiments in 1931. He suspended a small mirror in a dilute gas and observed a reflected light signal that looks very similar to Fig. 2 of Gaspard *et al.* on page 866. This experiment led to a determination[3] of Avogadro's constant to within 1%.

Immunology

Fetal fascination

A mother readily rejects organ transplants from her offspring. Owing to the contribution of paternal genes, her child's tissues express different antigens to her own — and that's what gets her immune system going. Yet she carries these genetically disparate fetuses to term. What protects a fetus from attack by its mother's immune system? Reporting in *Science* (281, 1191–1193; 1998), Andrew Mellor and colleagues propose that, in mice, rapid consumption of the amino acid tryptophan at the maternal–fetal interface paralyses the mother's aggressive T cells.

Early in pregnancy, placental cells seem to synthesize indoleamine 2,3-dioxygenase (IDO), an enzyme that degrades tryptophan and can suppress T-cell activity in vitro. Pregnant mice exposed to an IDO inhibitor rapidly aborted their fetuses, unless the embryos were a result of inbreeding and, thus, had a similar genetic make-up to their mothers.


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The inhibitor had no effect in mice lacking B and T cells, but when the females were supplemented with T cells their sensitivity to the inhibitor was restored and their pregnancies terminated. So, maternal T cells, directly or indirectly, mediate fetal rejection if they are not kept in check by IDO. Although it is not clear whether exhaustion of the tryptophan supply, or an obscure property of IDO, numbs the maternal T cells, it looks as though mothers do not reject their young because they're IDOlized from the start.

Marie-Thérèse Heemels

All this glosses over a crucial assumption. In his derivation, Einstein simply assumed that successive collisions with the fluid molecules would be statistically independent in approximation. So in essence the position of the Brownian particle is a sum of independent random variables, and as in the theory of random errors that yields diffusive behaviour. But a truly microscopic analysis would have to treat the Brownian particle plus fluid as a dynamical system with very many degrees of freedom, governed by Newton's equations of motion, so deterministic dynamics must somehow account for the assumed statistical independence.

As early as 1918 Smoluchowski[4] had already identified the instabilities of mechanical motion as the main ingredient for the statistical independence of collisions. Today, an intricate mathematical theory has been developed in which such notions have a precise meaning. It turns out that Brownian statistics, such as the power spectrum found by Gaspard *et al.*, are a generic property[5] of dynamical systems with so-called hard chaos, in which the motion depends sensitively on initial conditions and there are no traces of quasiperiodic motion.

But, although microscopic chaos is sufficient to produce Brownian motion, it may not be necessary. The analysis of simplified models[6], such as a hard sphere immersed in an ideal gas and an impurity in a harmonic crystal, has shown that the motion may be Brownian even when the full dynamical system, particle plus fluid, is not chaotic. In these models it is largely the randomness of the initial conditions of the fluid molecules that leads to the erratic motion of the suspended particle.

Gaspard *et al.* show that the fluid in their experiment has chaotic dynamics after all. This points at an apparently general property of systems with many particles. From experience we know that fluids effectively maintain a well-defined local temperature and pressure. Of course, there can be turbulent motion, but even then a small fluid element is approximately in thermal equilibrium, and that is the basis of all of hydrodynamics. Also, external perturbations hardly change such a state of local equilibrium. If the motion of the fluid particles were quasiperiodic (governed by a finite number of frequencies) this stable macroscopic behaviour would be hard to explain.

Only chaotic mechanical motion generates enough intrinsic noise to ensure a robust average behaviour. Chaos is usually defined mathematically in terms of positive Lyapunov exponents, which characterize the exponential divergence of nearby trajectories in phase space (this exponential divergence is what makes these systems sensitive to initial conditions). For many-particle systems, the evidence points to a spectrum of Lyapunov exponents that scales with system size and has a positive part. Nevertheless, there can be pockets in phase space with quasiperiodic motion, where all Lyapunov exponents are zero, especially when forces are attractive. Presumably, such a mixed phase space will have little effect on the observed macroscopic features of fluids, because observable properties such as local temperature, velocity, and pressure are not sensitive to such fine dynamical details — but a great deal of effort is still required to understand, on the microscopic level, what degree of chaos in a mechanical many-particle system is needed in order to ensure the regular macroscopic behaviour we see around us. ☐

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Mimicry

Sheep in wolves' clothing

Graeme D. Ruxton

Avoiding being eaten is a vital activity for many animals. They can in part do so by looking like other, unpalatable species, and the study of this strategy (known as mimicry) has a long and distinguished pedigree — so long, in fact, that from the textbooks one might think that the topic was pretty much sewn up. In a paper in *Animal Behaviour*[1], however, MacDougall and Stamp Dawkins come up with a new angle. They argue that the ability of a predator to discriminate between types of prey has to be taken into account. The complications that introduces may well require revision of thinking on mimetic systems.

Aposematic coloration, where unpalatable, poisonous or dangerous animals adopt conspicuous markings, is a well-known phenomenon. The usual explanation is that predators learn to associate these markings with unpleasant experiences, and so are less likely to attack similarly marked individuals in future. This mechanism leads to selection pressure for similarity of markings between species, and hence mimicry; this can be seen in the many insects, some of them completely harmless, which have the yellow and black stripes characteristic of wasps. Traditionally mimicry is divided into two types: Müllerian, where two unpalatable species both benefit from sharing the mortality costs of predator learning; and Batesian, where a palatable species benefits from its resemblance to an unpalatable species, which in turn pays a cost because the palatable mimic degrades the quality of its aposematic signal.

There are two major objections to this story. First, it has been argued that true Müllerian mimicry can exist only in highly specialized and unrealistic circumstances[2], because there will always be a difference in palatability between two species and so the less palatable one will always be disadvantaged by the mimetic relationship.

Second, theory predicts that Müllerian mimics should be monomorphic, because the more similar-looking unpalatable individuals there are, the more there are to share the costs of attacks by naive predators. In contrast, the palatable Batesian mimics should be polymorphic; the reason is that the protection individuals of a given morph get from mimicking an unpalatable species decreases with the frequency of palatable mimics. It is strange, then, that several unpalatable (and so, by the definition

Figure 1 **Morphs and mimicry. The viceroy butterfly, *Limentis archippus,* occurs as two morphs and was once thought to be a polymorphic Batesian mimic. It turns out, however, that it is less palatable to its natural predators than the species that were assumed to be its models — the monarch (*Danaus plexippus,* left) for one morph and the queen (*Danaus gilippus*) for the other. In conventional theory, it is hard to explain cases of polymorphic Müllerian mimicry such as this. But the new ideas of MacDougall and Stamp Dawkins[1] may account for its occurrence.**