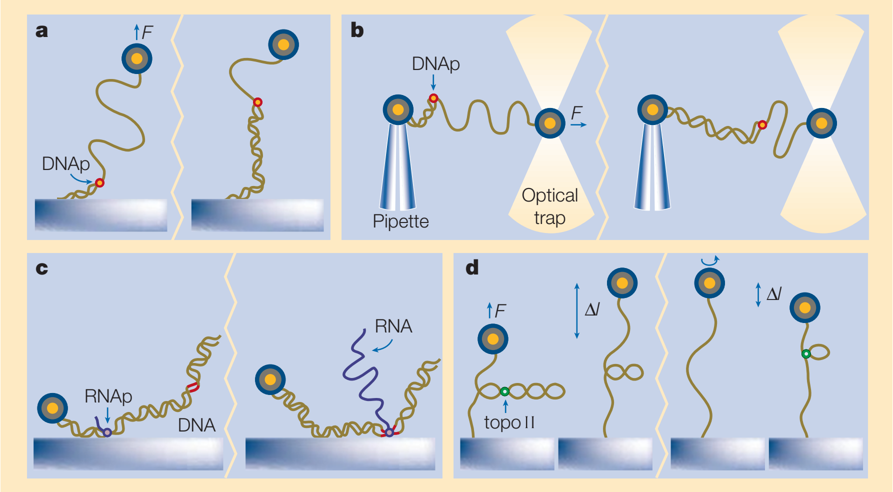

Figure 1 **Single-molecule experiments.** a, **The ends of single-stranded DNA (ssDNA) are attached to a glass surface and a magnetic bead. Fluctuations in the bead's Brownian motion give a measure of the applied force *F*. Addition of nucleotides initiates DNA replication by DNA polymerase (DNAp)** (a, right panel)**. As the elastic properties of ssDNA differ from those of double-stranded DNA, the extent of replication can be monitored by measuring changes in the extension of the DNA molecule as a function of force.** b, **Single-stranded DNA is attached to two beads held in a pipette and optical trap. DNAp synthesis of a second DNA strand is initiated by nucleotide addition** (b, right panel) **and monitored by following changes in the system's extension at a fixed applied force or its tension if the two beads are held at a fixed distance.** c, **An RNAp attached to a glass surface is 'fed' with template DNA, whose downstream end carries a polystyrene bead. The length of the DNA tether is inferred from the bead's fluctuations. The complete template is transcribed unless a terminator DNA sequence (red) induces the enzyme to pause** (c, right panel) **and stop. A lack of increase in tether length over time indicates pausing, whereas termination results in the release of the DNA template and RNA transcript.** d, **The activity of individual topoisomerase II (topoII) molecules as a function of ATP concentration can be monitored by following the discrete jumps (Δ*l*) in the length of an ssDNA molecule** (d, left panel)**. Rotation of the magnetic bead induces the formation of thermally activated DNA cross-overs, which are 'clamped' by topo II, even in the absence of ATP, thus reducing the effective length of the DNA strand by Δ*l*** (d, right panel)**.**

the interaction forces and conformational changes associated with fundamental biological events. Even protein folding is being brought within the reach of single-molecule observations (X. Zhang, Stanford Univ.), through the combined use of micro-mechanical manipulation and optical probes.

No doubt new challenges will emerge to add to the existing questions. As H. Berg (Harvard Univ.) and H. Buc (Inst. Pasteur) pointed out, there are two prerequisites for tackling them successfully. First, physicists must get to grips with biology to identify the most relevant biological questions. Second, they will have to develop new physical concepts that allow for a meaningful interpretation of molecular 'individuality', the inevitable structural and functional fluctuations captured in single-molecule experiments. The trick — to paraphrase K. Kinosita (Keio Univ.) — will be to distinguish between the fluctuations that are telling us something profound about the translation of molecular events into macroscopic behaviour, and those that should be ignored. ■

Magdalena Helmer is a Senior Editor at Nature.

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erratum In Daniel Weihs' News and Views article "No hibernation for basking sharks" (*Nature* **400,** 717–718; 1999), which discussed a paper by David Sims (*Proc. R. Soc. Lond. B* **266,** 1437–1443; 1999), it was stated that the energy content of copepods was previously assumed to be three orders of magnitude larger than currently accepted. This should have read three orders of magnitude smaller. Likewise, previous estimates of the energy cost of swimming should have been between one and two orders of magnitude too small — not, as stated in the article, too big. These errors make no difference to the overall conclusions discussed in the News and Views article.

Daedalus

Unchained energy

In an atomic explosion, an initial neutron collides with a nucleus in the charge. It fissions, releasing more neutrons, which fission more nuclei, and the resulting fast chain reaction runs away. But a practical bomb cannot wait for a random neutron to set it off. It fires a quick blast of neutrons into the charge at the moment of initiation. Enormously amplified by successive generations of fission, they get the chain-reaction off to a flying start.

Daedalus is now adapting the idea to the explosions in an internal-combustion engine. They too are chain reactions, the links in the chain being the free radicals liberated by combustion. Sadly, these chains are usually terminated prematurely. Unburnt and partly burnt fuel emerge in the exhaust, polluting the atmosphere.

So Daedalus's new 'radical engine' has a powerful xenon ultraviolet flash-lamp directed into each cylinder. A brief instant after the charge is ignited, the flash-lamp fires, suddenly photolysing the mixture and flooding it with radicals ripe for chain-amplification. Combustion roars away. With radical creation outpacing quenching, it goes to completion at last. Only carbon dioxide and steam emerge from the exhaust.

The radical engine will need careful optimizing. Fired too soon, a flash may detonate the whole charge very suddenly, causing engine 'knock'. Fired too late, it may shine uselessly on a few dying radical chains. Possibly several spaced flashes of different intensity will do the best job. But when properly understood, radiant radical-amplification will give internal combustion a splendid new lease of life. Not only will a radical engine be cleaner, and able to burn all sorts of fuels now too smoky or sluggish for the job. By varying the timing and intensity of its flashes under electronic control, it will be more efficient, too. It will be able to burn the charge faster or slower, optimizing the pressure-profile of each power-stroke for the current speed and load.

The technique might also work with solid high explosives. In mines, tunnels and similar confined spaces, truly clean and fumeless blasting would be very welcome. And fast-acting flash electronics might produce what is now only a figure of speech — a true controlled explosion. With its pressure adjustable in space and time, it could be a splendid tool for forming and shaping hard, intractable alloys and ceramics. Indeed, it could even lead to new and neater designs of atomic bomb.

David Jones

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new metallic behaviour at $B=0$ and the quantum Hall metal, and raises the possibility that both share a common physical origin.

The notion that 2D metals cannot exist in the absence of a magnetic field dates back 20 years, when powerful 'scaling' theories indicated that any amount of disorder would trap electrons, so preventing conduction and the existence of a metallic state[3]. These arguments are based on the quantum-wave nature of the electrons, whereby a travelling electron wave can be scattered from impurities back to its starting point. If these returning waves interfere constructively, the electrons become localized in one place and are less able to diffuse through the solid. At high temperatures this effect is weak and the sample *appears* metallic. As the temperature is reduced quantum interference becomes more important, so that at absolute zero all the electrons are localized and completely unable to move. Low-temperature experiments with both thin-metal films[4] and 2D sheets of electrons in field-effect transistors[5,6] confirmed these theoretical predictions, and for nearly two decades it was generally accepted that there can be no 2D metal at $B=0$.

It is a historical coincidence that at about the same time as a consensus was being reached that no metallic states could exist in 2D systems, the quantum Hall effect was discovered. The classical Hall effect occurs when a current-carrying conductor is placed in a perpendicular magnetic field. This produces a Hall voltage across the conductor, which rises linearly as the magnetic field is increased. In contrast, the Hall voltage measured in 2D semiconductors at extremely low temperatures rises in steps with a series of abrupt transitions between well-defined plateaux at which the Hall voltage is precisely quantized. It is only possible to explain this quantization of the Hall voltage by the existence of both localized (insulating) and extended (metallic) electron states that persist to $T=0$. So, increasing the magnetic field reveals a series of insulator–metal transitions as the current-carrying electrons alternately find themselves in localized and extended states. Despite many years of intense study, it is still not clear what happens to these extended states as the magnetic field goes to zero. Some argue that, below some non-universal magnetic field, the extended states simply disappear; others suggest that, at low magnetic fields, they 'float' up to higher energies, becoming inaccessible to electrons at low temperatures[7].

In 1994, strong evidence for a $B=0$ phase transition from an insulator to a metal was found in extremely low-disorder silicon field-effect transistors[8], in apparent contradiction with the prevailing scaling theory. Similar behaviour was subsequently observed in other material systems, independent of the sign of the charge carriers, indicating that the metallic state is a universal property of all low-disorder 2D systems. At present there is no theoretical consensus as to the nature of this unusual metallic phase, but experiments suggest that strong interactions between the charge carriers (not considered in the original scaling theory) and the spin of the electron (or positively charged hole) both play a role[9].

Hanein and co-workers[2] have now carried out an experiment that relates the $B=0$ and quantum Hall metal–insulator transitions. By tuning the carrier density in a high-quality 2D GaAs hole system, they are able to alter the magnetic field at which the quantum Hall metal–insulator transitions occur. Their results are unique because they followed these transitions to much lower magnetic fields than in previous studies[10]. They find that the transition associated with the quantum Hall effect at high magnetic fields evolves continuously into the $B=0$ metal–insulator transition. This implies that the extended states in the quantum Hall regime do not simply disappear as the magnetic field is reduced, nor float up indefinitely in energy, but continue to $B=0$ with some finite energy.

These results are intriguing because they link the quantum Hall effect, which can be understood without considering electron–electron interactions, with $B=0$ metallic behaviour that is only found in strongly interacting systems. A number of questions remain. If the two metals share a common physical origin, it is difficult to reconcile the fact that the $B=0$ metal is destroyed by applying a magnetic field *parallel* to the 2D plane[11,12], whereas the extended states in the quantum Hall regime are not. Furthermore, although some theories attribute the $B=0$ metal to a new, many-body ground state, certain experiments suggest that it may simply be a finite-temperature spin-related scattering effect[13]. If this is the case, then other effects, such as phase-coherent localization, may reappear at even lower temperatures. A great deal of work remains to be done before we can finally answer the simple question: is it possible for a 2D system to be a real metal at $B=0$? □

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Marine biology

No hibernation for basking sharks

Daniel Weihs

The phrase 'gentle giants' and the word sharks do not usually appear in the same sentence — sharks normally evoke the image of a bloody, tooth-filled mouth as in the film *Jaws*. But the biggest species of selachians (sharks) are, in fact, placid, slowly moving grazers that feed by filtering plankton. They swim with a widely opened mouth, engulfing small prey and the water they are in, and using long, bristle-like projections on the gill arches to remove the prey.

The only species of shark that uses this method of feeding — known as ram filter feeding — exclusively is the basking shark (*Cetorhinus maximus*). Because these sharks have to swim with a wide gape (Fig. 1, overleaf) that increases drag and, hence, the energetic cost of feeding, a long-standing theory has been that they may migrate (and even hibernate[1]) during winter, when the concentration of plankton falls below a relatively high threshold[2]. But in *Proceedings of the Royal Society*, David Sims[3] combines behavioural observations and theoretical calculations to show that the threshold for gainful filter feeding is probably much lower for the basking shark, implying that hibernation and migration are not necessary.

Actually, what Sims shows is that we probably do not need complicated explanations such as hibernation. These complex models came about because original investigators assumed the energy content of copepods (the main constituent of the planktonic soup ingested by basking sharks) to be three orders of magnitude larger than currently accepted values. This large overestimation did not result in absurd conclusions (which, presumably, would have alerted previous investigators to the error) because initial estimates of the energy cost of swimming were also between one and two orders of magnitude too big.

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The fact that hibernation is probably not a part of the basking sharks' annual cycle may solve an irksome question — where and how do they hibernate? The meagre literature on basking sharks contains no observations of hibernation. Given that they are large, pelagic fish, some reaching lengths of over 10 m, surely they would have been observed if they hibernated close to the continental shelf. If, on the other hand, they hibernated in midwaters in the open ocean (assuming this is possible at all), the sharks would be exposed to attack by predators or scavengers. At the very least they would have been colonized by symbionts and parasites, which attach themselves to immobile objects. Attacks of either kind, although probably not fatal owing to the size of these sharks, would result in telltale signs on their bodies. No signs of such depredations have been reported.

But if they don't hibernate, where do most full-sized sharks go during the winter? The lower energetic requirements for swimming, calculated by Sims[3] using up-to-date information and theory, help to justify the assumption that basking sharks migrate to deep waters. However, feeding in deep waters is complicated by competition from more agile cephalopods and fish, and the lower feeding threshold may allow the sharks to use feeding grounds not frequented by potential competitors.

An important lesson from this story is that classical 'results' need to be checked and rethought in the light of current knowledge. This is especially relevant in studies of marine biology, because the open sea has not been extensively studied — it has been said that mankind knows more about the topography of the Moon than about the bottom of the ocean. However, both the hydrodynamic theory of how fish swim and our understanding of the biochemistry behind the ingestion and use of food have improved over the past three decades. We can be confident in Sims' results because there are now well-established theoretical calculations for swimming thrust and energy requirements[4], and these have been shown to fit a large range of fish sizes[5], including several large species of shark.

JEFF ROTMAN/BBC NATURAL HISTORY UNIT

Figure 1 **Feeding time. The basking shark (*Cetorhinus maximus*) feeds on plankton, which it filters from sea water using bristle-like projections on the arches of its gills. In winter the concentration of plankton is reduced below a threshold level, and sharks were thought to escape starvation by hibernating or migrating. But a study by Sims[3] indicates that the threshold of plankton needed by the sharks is much lower than previously estimated, and that the sharks do not need to hibernate or migrate in winter.**

Much still needs to be done. First, we need to search for the sharks' deep-water winter habitats, and to study their behaviour in these habitats. This can be facilitated using archival tags, which record parameters such as temperature, depth and swimming speed. Although such tags are still under development, some models can detach from the fish at predetermined times and transmit the data to satellites overhead. Second, in arriving at his results, Sims had to make several assumptions that need to be verified. These include catch efficiencies of the gaping mouth, the shape and intake of the ram filter feeding system, assimilation costs and metabolic efficiencies.

Here there is an interesting analogy to what used to be known as Gray's paradox. In the 1930s, Sir James Gray of Cambridge, one of the leading experimental biologists of this century, estimated the efficiency of dolphin muscle. He did this by analogy to human muscle, and concluded that the swimming speeds achieved by dolphins cannot be accounted for by standard hydrodynamics. This resulted in a decades-long search for "the dolphin's secret". Many important discoveries and developments resulted from this search, including advances in hydrodynamic theory, and the study of flexible skin and polymer drag reduction. Finally, in the 1970s, when accurate data were used, the (by then improved) hydrodynamic theory was found[4] to be sufficient to describe cetacean swimming. Studying sharks may yield similar dividends. ☐

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Neurobiology

Cognition by a mini brain

Randolf Menzel and Martin Giurfa

We often expect little from small brains and cognitive miracles from big ones. But all brains were once small, in both evolution and development, reaching their respective levels of cognitive function only gradually. Elementary forms of cognition might, then, be present in small brains, and these could tell us what is really gained when brains become bigger. For example, the fruitfly *Drosophila melanogaster* (the geneticist's delight and the neurophysiologist's torment) has a particularly small brain. Very little is expected of this tiny brain, and, indeed, few impressive behavioural capacities have been found so far — a range of innate response patterns, some artistic sexual foreplay, and rather limited forms of learning[1,2]. But new discoveries bring exciting prospects, using both molecular genetics and behavioural studies to analyse the fruitfly's elementary cognitive functions.

On page 753 of this issue, Liu *et al.*[3] report their results on visual learning by *Drosophila* and its underlying neuronal substrate. They show that individual flies can do quite complex tasks. The authors first conditioned flies to associate visual patterns (the 'conditioned' stimulus) with the presence or absence of heat (the 'unconditioned' stimulus). The idea is that the animals should fly towards the appropriate patterns to avoid dangerous levels of heat. Their behaviour is 'operant', because the flight course that they choose determines delivery of the heat. The experiments were done under particular illumination conditions, which form part of the general 'context' in which the associations are established.

The authors next showed that the flies could 'generalize' this trained response to several other, different environmental contexts. As contexts are ill-defined stimuli, comprising individual features from many modalities, the change in context that the authors introduced was a change in the illumination between training and test: between white and monochromatic broad-band light; between two monochromatic broad-band lights; and between constant white light and white light interspersed with 'dark flashes' (light is switched off for 200 ms). These changes did not affect the performance of the flies. These results show that context generalization — rather than context specificity — guides the insect's learning. But when the authors impaired the fly's normal brain function by eliminating the mushroom bodies (a central brain structure), they found that retention of the trained pattern was strictly bound to the context during learning, and that the flies did not generalize to other contexts.

The study by Liu *et al.*[3] sheds light on two issues: the function of a central brain structure on an elementary form of cognition, and the role of context in learning. Mushroom bodies are prominent paired structures in the insect brain (Fig. 1), and are considered

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