reside in regions that have been highly preserved during evolution, and are reminiscent of those that generate altered physical characteristics in yeast⁶. In fact, the RNA is thought to be essential in yeast⁷. Ridanpää *et al.* discovered no patients in whom the relevant gene was absent, or in whom both copies of the gene were not expressed at all, implying that the RNA is equally important in humans.

Are there any clues in all of this to how mutations in the MRP RNA component might produce the varied physical characteristics seen in CHH? Given that MRP is involved in copying mitochondrial DNA, might some dysfunction in mitochondria be responsible for CHH? This seems unlikely, for at least two reasons. First, although some of the physical features of people with CHH overlap with those of people with mitochondrial disorders, most do not. Second, the vast majority of MRP is found in the nucleolus. The reduced levels of the MRP RNA in patients with CHH are still greatly in excess of those needed for mitochondria to function properly.

But it is less clear whether processing of the 5.8S ribosomal RNA in the nucleolus would be problematic. The ribosome is needed to translate messenger RNAs into proteins, so the correct processing of the 5.8S RNA is crucial for translation. It seems reasonable, then, that the mutations seen in CHH might hamper the accurate processing of the 5.8S ribosomal RNA at times in development when key proteins need to be synthesized.

Another possibility is that we need to look to other pathways, and other organisms, for hints as to how these mutations in the MRP RNA gene produce functional defects. There is no clear precedent for a nuclear, RNA-encoding gene causing a major disease, but this could be because — unlike the MRP RNA gene — there are generally multiple copies of such genes in the human genome. Even so, mutations in multi-copy human mitochondrial DNAs encoding transfer and ribosomal RNAs are involved in mitochondrial diseases⁸, with mouse models now emerging for studying the nature and progression of a given disorder⁹.

An intriguing possibility comes from a recent study of yeast (cited by Ridanpää *et al.*), in which a mutation in a protein component of MRP leads to a prolonged and abnormal arrest in cell division¹⁰. Similar defects in people with CHH would be consistent with their failure to develop a normal number of immune cells, for example. Moreover, mutations in the RNA component of MRP in the fission yeast *Schizosaccharomyces pombe* result in atypical cellular morphology¹¹. We should not be surprised if this RNA has even more functions. But, given that the mutations within the coding part of the gene are found in both CHH patients and

yeast, and that these mutations are likely to affect the function of the MRP enzyme, it would be surprising indeed if RNA processing were not part of the final picture of cartilage–hair hypoplasia.

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Animal husbandry

Assessing the welfare state

Michael Mendl

Animals kept for human use should surely have conditions that are as conducive to their welfare as possible. A study of captive mink illustrates how animal welfare can be assessed.

Do mink in fur farms suffer if they are denied access to resources such as water for swimming? This seemingly esoteric question encapsulates much of the debate about animal welfare and the conditions in which animals are kept on farms, in laboratories and in zoos. It is also deceptively complicated, as is evident from the item by Mason and colleagues on page 35 of this issue¹. The take-home message of their paper, however, is that science can inform argument about animal welfare by providing objective evidence about how animals respond to captivity.

There are two main scientific approaches to the issues². One is based on the proposal that animal welfare is compromised when normal biological function is impaired^{3,4} — as seen, for instance, in low growth rates, behavioural abnormalities and immunosuppression. The aim of this approach is to measure a variety of 'welfare indicators' to obtain a comprehensive view of the animal's biological state⁴. But interpreting and integrating the measures to provide an overall welfare assessment is by no means straightforward^{2,4}. For instance, is an animal that exhibits high levels of abnormal behaviour

Materials science

All chopped up

In the constant push for higher-capacity hard drives, K. Koike *et al.* have found a way of doubling the density of data storage in magnetic media (*Applied Physics Letters* 78, 784–786; 2001).

Conventional high-density magnetic recording media consist of films composed of magnetic grains. Bits of data are stored on these grains, the size of which limits the amount of stored data. More data can be encoded if the grains are smaller and more tightly packed. But if the grains are too small, they become unstable and can 'forget' their information because the domains (magnetized regions) produced by the grains can affect each other through thermal instability. In other words, a '1' can be changed

into a '0' by a small temperature fluctuation. The highest density of reliable data storage on so-called continuous magnetic media reported so far is 65 billion dots per square inch. An image of continuous media showing the domains is seen above on the left.

Koike *et al.* chopped up a magnetic block to double the density of storage, with potential to increase this even further. They reduce the problem of thermal instability by physically separating clusters of grains

using focused ion beam lithography (an atomic knife) to cut grooves into the block. The image on the right shows domains from these discontinuous media: this denser pattern can store more data.

So can we expect colossal hard drives soon? Not just yet. The fabrication process has not been perfected, and data recording and retrieval are very slow. But if these problems are resolved, we may have even more games, movies and music at our fingertips. **Josette Chen**

but low physiological stress responses better or worse off than one displaying the reverse?

The second approach equates an animal's welfare with its subjective experiences^{5,6}. Animals may grow, reproduce and appear to be healthy, yet still have poor welfare if they experience subjective suffering such as prolonged frustration from having little space in which to move. Here, largely, is the cause of public concern about animal welfare — if non-human animals were shown to lack conscious subjective experiences, that concern would almost certainly wane. For the scientist, the problem is that subjective states such as those that we call frustration, anxiety or pain are difficult to measure or cannot be measured at all.

Advocates of this approach have therefore developed methods based on the assumption that animals suffer if denied resources that they are strongly motivated to obtain, or exposed to stimuli that they will work hard to avoid⁵. Theories that emotions are important in motivating animal behaviour lend support to this assumption^{7,8}. The methods involve finding out how much animals value resources by testing their preferences or, using techniques borrowed from human consumer economics, by measuring how high a price, in terms of time and energy, they will pay to access or avoid them^{5,9}. These 'motivation'-based methods have limitations⁵ — for example, sweet foods may be preferred in the short term but do not enhance health and welfare in the long term — but they circumvent the problem of integrating many different welfare indicators.

Most people in this field acknowledge that the 'welfare indicators' and 'motivation' methods complement each other^{2,4,5}. Even so, the two approaches have largely been used in isolation — Mason and colleagues¹ achievement is to have brought them together. The authors investigated whether the small wire-mesh cages used to house farmed mink cause frustration by preventing natural activities such as swimming or using several nest sites. Sixteen individually housed mink were each given access to seven cages containing resources such as an alternative nest site or a water pool. When made to work for access to the resources by pushing through weighted doors, mink worked hardest for the water pool. This conclusion was reached using four different calculations of how the mink valued each resource — a comprehensive analysis that sets new standards in animal welfare studies.

Following the assumption of the 'motivation' approach, these findings suggest that depriving mink of a water pool may result in suffering and poor welfare. Mason *et al.* tested this assumption by measuring changes in welfare indicators when the mink were prevented from visiting the pool for 24 hours. They observed a rise in urinary cortisol, an endocrine indicator of stress, that was not

accompanied by an increase in activity and was indistinguishable from that seen when an essential resource, food, was removed for the same duration.

By using the 'motivation' and 'welfare' methodologies together, Mason *et al.* provide powerful evidence that the mink value the water pool highly and exhibit stress responses in its absence. So lack of a water pool may compromise the welfare of mink even if their growth and health are good. Answers to a number of remaining questions could strengthen this conclusion. The roles of expectation and experience of a resource in determining response to deprivation remain to be tackled. So too does the problem that resource valuation depends on what else is available (for instance, chewable objects might have been valued more highly if they were the only resource offered). Furthermore, deprivation of a valued resource may be stressful only in the short term, or if no adequate substitutes are available. For example, removing the highly valued alternative nest site did not induce a cortisol rise, perhaps because the animal's own nest was still accessible.

What of the wider implications? Captive animals are often denied resources or opportunities to behave in ways that, intuitively, would seem to be important to them. Confinement prevents domestic sows from building nests before they give birth; there

is usually no dust-bathing substrate in cages for laying hens; and most laboratory rodents have limited opportunity to construct burrows or enclosed nests. Techniques such as those used by Mason *et al.* should allow us to go a good deal further than intuition in deciding whether these resources and opportunities are indeed highly valued by the animals, and whether their absence causes frustration and stress. If so, scientific argument for their provision will be strong and should form the basis for decisions to alter housing conditions, even though such decisions will inevitably be coloured by political, economic and practical considerations. ■

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Condensed matter

Memories of paste

David A. Weitz

Pastes are not the simple materials they appear to be. It seems they have a 'memory': after a force has been applied, they recover and move back in the opposite direction.

Pastes are familiar materials we use every day, for example, when we brush our teeth. They are prototypic 'soft' materials: they behave as a solid until a sufficiently large load or stress is applied, at which point they flow like a fluid. So a squeeze is all that is required to put toothpaste on a brush. But the way pastes and similar soft solids behave remains poorly understood, partly because it is difficult to perform reproducible experiments on these materials — their properties seem to change with time and depend strongly on their history. As they discuss in *Physical Review Letters*, however, Cloitre, Borrega and Leibler² have developed new experimental techniques and show that the way a paste recovers from an applied stress is remarkably like the behaviour of glasses and gels^{3,4}.

Pastes typically consist of a suspension of small particles in a background fluid. These particles are crowded, or jammed together

like grains of sand on a beach, forming a disordered, glassy or amorphous structure, and giving pastes their solid-like character. This jamming together gives pastes some of their most unusual properties. The particles exert large forces on their neighbours, but in solid pastes the material, and hence each individual particle, is stationary, so the net sum of the forces on each particle must be zero. Because of the high degree of disorder inherent in any paste, some of these local force balances will be precarious. A very small change, perhaps induced by a fluctuation in temperature, can disrupt the balance, causing a relaxation in the structure that can ripple through a large volume because of the close proximity of the particles and the requirement that all local forces have to be balanced.

After relaxation from such a small disturbance, the new state is likely to be more stable and disruptions will be less probable.