derivative exists in which the *bgl*F gene (encoding a protein necessary both to transport and phosphorylate salicin) contains an insertion sequence called IS103 (the IS are a class of transposons about 1 kilobase long which on insertion inhibit the expression of structural genes). In this derivative, activation of R^0 and excision of IS103 must occur before the strain can grow on salicin. MacConkey–salicin plates are used to identify Sal^+ revertants in Sal^- colonies. This medium contains enough peptides to allow colonies to grow to about 10^9 cells in 3 days, and a dye which responds to sugar fermentation. On these plates, Sal^- cells form white colonies and if any Sal^+ variants arise then, after a delay, red papillae appear on the surface.

Hall's investigation started with the observation that after a 2-week incubation more than 60 per cent of colonies of the Sal^- double mutant showed papillae on MacConkey–salicin plates. As the combined mutation rate of the two individual mutations in growing cells was about 10^{-20}, this high frequency was unexpected. What goes on in old colonies that is different from logarithmic growth? The key result of the paper is that most colonies of the double mutant, when sampled after 12 to 13 days (just when the first papillae are beginning to appear), contain between 10 and 50 per cent of Sal^- mutants from which IS103 has excised. This result argues strongly that excision of IS103 precedes the regulatory mutation in Sal^+ revertants. The surprisingly high proportion of excision mutants in the colonies (reminiscent of Shapiro's results[4] on analogous transposon systems) indicates that a burst of excision activity occurs during late stages of colony growth. Does the high proportion of excision mutants reflect a specific or a general effect? And is it influenced by selection? Clear-cut results are reported, showing there is no increase in mutations to valine resistance within old colonies, and that no excision mutants can be detected in colonies on MacConkey plates without salicin. Also reported is an experiment, persuasive rather than convincing because of technical problems, indicating that Sal^- excision mutants have no selective advantage over double mutants during colony development.

Hall interprets his results as showing that in the period between 8 and 12 days up to 50 per cent of cells within colonies experience excision of IS103. The resulting mutants provide a population of cells sufficiently large that a replication-independent $R^0 \rightarrow R^+$ mutation occurs in one and generates a Sal^+ cell that grows by using salicin to form a papilla. The excisions occur only in medium containing salicin, despite the fact that the excision confers no selective advantage and serves only to create the potential for a secondary selectively advantageous mutation.

This interpretation is certainly thought-provoking, but I think there are grounds for deferring acceptance of it at present. First, there is the difficulty of understanding how salicin, which supposedly cannot enter mutant cells, nonetheless influences excision. Second, there is a lack of controls on whether any other transposon activity is correlated with IS103 excision. And third is the feeling, arising from published studies on the *bgl* operon, that excision of IS103 should confer some selective advantage to cells in the presence of salicin. This is because changes in supercoiling, both positive and negative, are known[5] to induce the cryptic *bgl* operon. Some alteration in DNA topology would seem to be a likely occurrence in cells comprising old colonies.

As an alternative to Hall's interpretation, an explanation based on orthodoxy is that physiological conditions in old colonies induce a burst of random transposition activity in a fraction of the cells. Some of these events lead to excision of IS103, and if salicin is present these cells have a selective advantage, eventually comprising a large proportion of the viable cells in the colony, and subsequently sporting the second mutation that leads to a Sal^+ revertant. In the absence of salicin, growth of all the cells remains restricted and the mutagenic effects of transposition eventually lead to cell death.

Hall's paper is undoubtedly a provocative contribution to the debate on the origin of mutants, and highlights two general points which have been alluded to by other contributors to the debate, but are worth stressing. First, some of the mutagenic systems which have been discussed refer to events promoted by transposons, whereas others refer to effects related to point mutations. These two classes of event are basically distinct, they have different molecular explanations and occur at different frequencies. It would seem prudent not to extrapolate from one system to the other. Second, the question of what goes on in old colonies under deprived conditions on agar plates, which is the essence of the present problem, will lead to an interesting liaison between the old and the new microbiology. It will mean a return to studies of impurities in media, cannibalization of dead cells, and even what constitutes cell death. Together with these considerations, it is necessary to find molecular answers to questions relating to local topology inside such cells, their osmotic properties and, crucially, the structure of mutants generated in these (to us) novel conditions. □

1. Cairns, J., Overbaugh, J. & Miller, S. *Nature* **335**, 142–145 (1988).
2. Stahl, F.W. *Nature* **335**, 112–113 (1988).
3. Hall, B.G. *Genetics* **120**, 887–897 (1988).
4. Shapiro, J.A. *Molec. gen. Genet.* **194**, 79–90 (1984).
5. Higgins, C.F. *et al. Cell* **52**, 569–584 (1988).

Neville Symonds is Professor of Microbial Genetics at the University of Sussex, Falmer, Brighton BN1 9QG, UK.

Daedalus

Corporate strategy

Last week Daedalus decided that the fat cells of the body are digital information-storage elements. A full cell is stable; so is an empty one. But a partially full one, even in perfect reaction equilibrium, is not. If its fat droplet begins to grow, it will become thermodynamically more stable, and will grow by further synthesis; let it shrink, and its increasing thermodynamic instability will shrink it ever faster until it is completely hydrolysed. Judging by the high metabolic turnover of our adipose tissues, this gain and loss of fat droplets is going on all the time. This makes no sense if fat is merely an inert fuel store, but is just what you would expect of an active data-processing system. The filling and emptying cells, says Daedalus, must be moving digits around in the manner of a 'bucket-brigade' delay line or magnetic-bubble memory.

Now a fat cell takes hours or days to switch between its full and empty digital states. Our fat cannot go in for quick-fire decision making; it must be entrusted with the basic, slowly evolving, instinctive aspects of our nature, like our body image and sense of identity. This agrees with popular stereotypes and the claimed formal distinction between 'fat' and 'thin' personalities, and the changes of character and emotional style often reported by those who have lost or gained significant amounts of fat. People who claim to feel their emotional certainties in their bones are slightly misplacing the source of the sensation!

To verify these bold speculations, DREADCO's biochemists are launching sharply focused, high-intensity ultrasonic beams into small areas of the fatty tissue of DREADCO volunteers. The idea is to set into resonant vibration those fat droplets which happen to be tuned exactly to the chosen frequency. Each droplet will soon fission, like an over-excited atomic nucleus, giving two smaller droplets. The thermodynamic doom which awaits small droplets will soon react them away completely. Thus the tiny area targeted by the ultrasonic beam will be sprayed with copious bit-errors. Adipose tissue, like the brain, probably uses a robust summation logic rather than a vulnerable binary code; even so, the local data should be well scrambled. The resulting psychological changes in the volunteers will take a day or so to emerge. By matching the site of each ultrasonic scrambling to its emotional effect, the DREADCO team should soon work out the exact distribution and nature of our fatty data. The way will then be open for a new psychoadipotherapy, healing and refreshing those stubborn personal obsessions and distorted self-images that conventional therapies cannot reach. David Jones