eventually make it possible to obtain mice in which all the genetic information comes from one teratocarcinoma nucleus.

Until now, however, isolation of new teratocarcinoma cell lines has been a lengthy procedure involving transplantation of genital ridges or early embryos into extra-uterine sites such as the kidney or testis. In this environment pluripotent cells in the graft continue to grow and may give rise to tumours containing populations of EC cells which can be maintained during serial transplantation and then tissue culture. These techniques restrict work to inbred strains of mice since, for unknown reasons, tumours containing EC cells fail to develop from grafts into nude or immunosuppressed animals[9].

Over the years, many attempts have been made to circumvent these restrictions by generating EC cell lines from embryos cultured *in vitro*. Now, Martin Evans and Mat Kaufman in Cambridge have at last been succesful (see this issue of *Nature* p.154). Studies in several laboratories suggest that EC cells have more biochemical properties in common with epiblast cells in the inner cell mass of 5½-day blastocysts around the time of implantation, than with pluripotent cells present earlier or later. Normally, the number of epiblast cells is small but this increases when implantation is delayed by treating the mother with hormones. Evans and Kaufman collected batches of delayed-implantation blastocysts, allowed them to attach and spread *in vitro*, harvested the embryonic knobs containing the epiblast cells, dissociated them in trypsin and plated the cells on a feeder layer of non-dividing fibroblasts. After a few days clumps of EC-like cells were located, dissociated and re-seeded, and several cycles of such treatment yielded cultures containing predominantly undifferentiated EC cells.

The trick seems to be to provide conditions in which the pluripotent cells in the embryos are both encouraged to proliferate, either in response to growth factors made by themselves or the feeder fibroblasts, and discouraged from differentiation by disrupting cell–cell interactions. Using this technique Evans and Kaufman have isolated at least 15 new pluripotent teratocarcinoma cell lines, some from outbred mouse stocks. Those which have been analysed have a completely normal karyotype, including two with an XY genotype. It remains to be seen whether these new teratocarcinoma lines are particularly efficient at colonizing normal embryos and, in particular, the male germ line. Meanwhile, the technique opens up many exciting possibilities for exploiting the teratocarcinoma system more fully. For example, EC cells could be isolated from mouse strains carrying electrophoretic variants of X-linked enzymes, or from *T/t* mutants blocked in post-implantation development, and the biochemical properties of these cells followed during the *in vitro* development of mass cultures as embryoid bodies.

One criterion used by Evans and Kaufman to identify their teratocarcinoma stem cells is expression of a specific, cell-surface carbohydrate sequence recognized by one of the monoclonal antibodies made in humans suffering from a rare haemolytic disease known as 'cold agglutinin disease'. These people make antibodies against different, chemically defined, carbohyrate domains of the Ii blood group antigens. The antibodies have been used by Ten Feizi and her colleagues at the Clinical Research Centre in London and Martin Evans in Cambridge as highly specific probes with which to follow the transient expression of carbohydrate sequences on the surface of different cell population during early mouse development[10]. These studies have now been extended by Gooi and the above workers (see this issue of *Nature* p.156) to define the carbohydrate sequence reconized by a monoclonal antibody SSEA-1 raised in mice immunized with teratocarcinoma EC cells[11] and to show that simple glycosylation steps involving addition of branch points or extra fucose or sialic acid groups occur at different stages of development. The significance of these subtle changes in terms of cell interactions, binding of hormones and growth factors, or morphogenesis remains to be seen.

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The ultimate computer

from Paul Davies

BLACK HOLES, it seems, get into everything these days. Jacob Bekenstein who, along with Stephen Hawking, invented quantum black holes, turns his attention to the more practical issue of telegraphy in a recent paper (*Phys. Rev. Lett.* **46**; 623, 1981). In the spirit of Shannon's celebrated analysis of the limits on information transfer through a communication channel, Bekenstein deploys some remarkable arguments gleaned from his experience with more astronomical matters.

The basis of this new departure is an unexpected relation, recently published by Bekenstein himself, connecting the ratio of entropy to energy for any physical system, with its physical size. The ratio is bounded by the dimension of the system, whether it be a black hole (an extreme case) or a box of photons. Using the fact that information is the negative of entropy, Bekenstein turns his new relation inside out to address the problem of energy limitations on information transfer.

The transmission of information is expensive, as every telephone subscriber knows. The pressing question is whether the energy dissipation can, in principle, be arbitrarily reduced by some future technological innovations. Bekenstein says no, even if you try to get the theory of relativity to help. His result is disarmingly simple:

information rate $= (2\pi^2/h \ln 2) \times$ energy

where h is Planck's constant.

Turning to an obvious application, Bekenstein considers the maximum conceivable speed of a digital computer. These days computers are so fast that designers have to worry about the speed of light being a limiting factor. We are already in the era of the relativistic computer. To beat the speed of light one can try to make the device smaller, but then quantum theory threatens. Ultimately an over-compact computer risks imploding under gravity down its own black hole.

In a somewhat rule-of-thumb analysis Bekenstein considers the problem of computer overheating. There is an inevitable entropy generation involved in shunting any information around, and in the end this will melt the system unless it is efficiently cooled. The author considers various cooling mechanisms and their inherent limitations, and eventually comes up with the best performance criterion for the ideal computer: 10^{15} operations per second.

That is pretty fast by contemporary standards, so Bekenstein's limit will not cause too many sleepless nights in the computer industry just yet. Nevertheless, an ultimate bound on any form of technology is intriguing in its own right, and it would be interesting to see whether the idea is followed up.

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