

Bounded brainpower? from Paul Davies

Is there a limit, due to fundamental physics, on the rate at which information can be processed in a computer? "Yes" claims Jacob Bekenstein, the co-inventor of the quantum black hole. In a provocative paper published in *Physical Review* a year ago, he claimed that the bread and butter of information transfer — energy and entropy — cannot be varied at will, but are constrained by the bound

$$\frac{\text{entropy}}{\text{energy}} < \frac{k \times \text{size}}{\hbar c} \quad (1)$$

where $\hbar = h/2\pi$, the size of the system is defined in some suitable all-embracing sense, and k , h and c are respectively Boltzmann's constant, Planck's constant and the velocity of light.

Bekenstein went on to assert (*Nature* 292, 112; 1981) that this bounded ratio of entropy to energy also constrains the rate of information processing to be less than

$$\frac{\pi k \times \text{energy}}{\hbar} \quad (2)$$

Taking into account the need to flush out the heat produced in a hypothetical computer by the information's energy, Bekenstein estimated the upper limit to be about 10^{15} bits per second (still pretty fast).

Now all this has been called into question by David Deutsch of Oxford University's Department of Astrophysics. In *Physical Review Letters* (48, 287; 1982), Deutsch challenges the fundamental basis of Bekenstein's analysis — the existence of an entropy to energy bound [equation (1)]. Energy, he points out, is not itself a measurable quantity in non-gravitational physics. Only energy differences are relevant to devices such as computers. Bekenstein's formula (1) might work for systems such as black holes, where gravity plays a part, but it has no business to interfere where

gravity is unimportant. (Energy, having mass, is a source of gravity, so its absolute value can be measured gravitationally.)

Deutsch reworks Bekenstein's calculation for energy differences and finds that there is no upper bound on the entropy to energy *difference* ratio. He then argues that it is this ratio that is relevant to information processing. The essential point is that not all the energy carried by the information generates heat in the computer, only the energy change due to the encoding procedure. The rest is invisible to everything except the gravitational field. He also throws in, for good measure, the retort that, in any case, it is in principle possible, even in quantum physics, to retrieve information by measurements that leave the information undisturbed, and hence do not produce heat.

So the current state of play is that Bekenstein's bound (1), while not incorporating the newtonian gravitational constant G explicitly, is nevertheless a gravity formula in disguise, to be used only when the system concerned runs on gravity power. In that case, if a computer is too big, its thinking time is limited by the speed of light; too small and it implodes into its own black hole. In this sense, bound (1) may provide a genuine limit, which Deutsch estimates at around 10^{42} bits per second!

Alas, even the gravitational applications of equation (1) have recently been called into question by William Unruh, Robert Wald, Don Page and Stephen Unwin in some lively exchanges (*Physical Review D*, in the press). Evidently the embattled Bekenstein has caught the attention of more than the computer industry.

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discrete (though the two haptens did compete for the binding site).

In light of these considerations, there are two distinct explanations of the physical basis of monoclonal cross-reactions. One interpretation is illustrated in Fig. 1a, where protein antigens A and B share a small and precise detail of their surface topology. Such a determinant might not normally be detected using conventional antisera in which most of the antibodies will be directed against other A-specific or B-specific structures; only dissection of the antibody response using the monoclonal technique reveals the shared structure. The question then becomes one of just how significant such small homologies are.

In the second explanation (Fig. 1b), the two protein antigens have dissimilar structures but interact with the same antibody molecule. It is notable that the

two different antigens could still compete for binding to the antibody because of steric constraints, even though their reactive epitopes, by analogy with the myeloma 460 example, occupy discrete sites on the molecule. However, the affinity of the antibody for antigens A and B would then be expected to be much lower than in the alternative model illustrated in Fig. 1a. In the second model (Fig. 1b) there is no reason to assume any biological relationship between the cross-reacting antigens; the only factor of interest in the system is the existence of the cross-reactive antibody itself. The production of such antibodies, for instance, could contribute to an autoimmune response induced by a structurally completely unrelated antigen. These two models represent the extreme alternatives and of course it must also be possible for the epitope on antigen A to be

only partly homologous to the epitope on antigen B, so that the antibody binds antigen A with higher affinity. Detection of such cross-reactions, whatever their molecular basis, means that reaction with a monoclonal antibody cannot itself be interpreted as proving molecular identity. For example, the reaction of a monoclonal antibody with two different cell types still requires biochemical verification that an identical molecule is being recognized in each cell. Similarly, such reactions might constrain the use of monoclonal antibodies in radioimmunoassay. Clearly, both of the extreme models have some validity, and examples of both types of cross-reaction will be discovered. Our bias is that the physical basis of the majority of cross-reactions detected so far is nearer to that illustrated in Fig. 1a, because they seem so highly specific. For example, the Pillemer and Weissman antibody shows no detectable binding to Thy-1-negative mutant lymphoma cells or to any IgG except that of the T-15 idiotype, and one of the SV40 T monoclonals has a very high affinity for T yet uniquely recognizes a single low-abundance 68,000 host protein on Western blots of total proliferating cell homogenates. (It does not recognize any protein at all when the extracts are made from the same cells in a quiescent state.)

The question then becomes one of just how functionally significant these small homologies between proteins are. That some are significant is nicely illustrated by the sweet-tasting proteins thaumatin and monellin. Hough and Edwardson¹⁴ have shown that polyclonal antibodies against thaumatin mimic the sweetness receptor, in that other sweet-tasting substances displace ¹²⁵I-labelled thaumatin from the antibody with an efficiency that correlates well with their relative sweetness. Of particular interest is the very effective competition between thaumatin and another very sweet-tasting plant protein, monellin, because the primary sequences of these two proteins show surprisingly little homology. Thaumatin has a single chain of 207 amino acids, and monellin has two chains totalling 94 amino acids; the homology is limited to five identical tripeptides¹⁵. We can infer that the antibody response has been selective for the biologically active region of the molecule, and by concentrating itself in a biologically relevant structure has mimicked a receptor.

A similar example of receptor mimicry by antibodies can be seen in the studies of Sege and Peterson¹⁶ where anti-idiotypic antibodies, raised against antibodies to insulin, were found to possess insulin-like activity themselves in biological tests. Cross-reactive monoclonal antibodies may therefore lead us to discover biologically important relationships between proteins and other macromolecules that could not have been detected by other means. After all, biological macromolecular interactions are all about three-dimensional shape