Standardisation in human cytogenetics

At the Fourth International Conference on Standardisation in Human Genetics, held in Paris in 1971, a Standing Committee was appointed to examine problems relating to standardisation in human cytogenetics and to make recommendations thereon between international standardisation conferences.

During the past four years the Standing Committee has been responsible for publication of the Report of the Paris Conference and a supplement to that report. In addition, the Standing Committee sponsored a workshop on human cytogenetic registries, held in Edinburgh in April 1975 (*Nature*, **256**, 456; 1975) and on the recommendation of this workshop, appointed an international advisory committee on cytogenetic registries.

The terms of reference of the Standing Committee call for elections to a new committee no later than the International Congress of Human Genetics in October, 1976 and the possibility of holding the next standardisation conference at that time. For these reasons the committee has recently circulated recommendations to the participants of the Paris Conference, which have been approved as follows: (1) That a standardisation conference on the lines of the Paris and Chicago Conferences could not be justified in 1976 and, therefore, that no such conference should be held in conjunction with the Fifth International Congress of Human Genetics in Mexico City in October, 1976; (2) That a Standing Committee charged with the task of monitoring developments relating to standardisation and nomenclature in human cytogenetics should be maintained; (3) That an open meeting of all interested human cytogeneticists should be held at the Fifth International Congress of Human Genetics in Mexico City in October, 1976. At this meeting a report of the Standing Committee would be received and a new Standing Committee elected. The existing Standing Committee will be acting as a nominating committee and will be preparing a slate of nominations for consideration by the meeting in Mexico City. These nominations will take into account regional and sectional interests to ensure, so far as possible, a fully representative Standing Committee.

Suggestions for nominations should be sent to the Standing Committee. The time and place of the Mexico City meeting will be announced later and circulated to those requesting this information. Nominations and requests for further information should be addressed to: Dr John L. Hamerton, Department of Genetics, Health Sciences Children's Centre, 685 Bannatyne Avenue, Winnipeg, Manitoba, R3E OW1 Canada.

effect is still prevalent, since roughly 999 out of 1,000 dopant atoms still seem to be suppressed. It remains to be seen whether this apparent inefficiency in doping can be improved on. The important discovery, however, is the fact that even a few dopant atoms are not suppressed. Junction action is thereby produced and a new device technology may even be in the making. The extent to which this technology could compete with single-crystal semiconductor technology depends less on the inefficiency of doping mentioned above, which can be countered, than on the achievement of low minority-carrier recombination-generation rates in the junction regions. High rates lead to high reverse currents in rectifiers and loss of efficiency in photovoltaic applications. It will be a much more challenging task to make these recombination rates suitably low but success in doing so could have a greater impact than the much-researched 'amorphous threshold switch' technology, which now seems to have lost any commercial momentum it ever had. An amorphous p–n junction technology would have much in common with the increasingly popular silicon-on-sapphire technology except that the serious restrictions in area imposed by the dimensions of sapphire crystals would have been removed and the way thus opened for integrated circuits as large as the page on which this column is written. □

Superfluid within superfluid

from P. V. E. McClintock

At last, somebody has gone out on a limb and named an encouraging number for the temperature of the anticipated superfluid transition among the ^{3}He atoms of a liquid ^{3}He–^{4}He solution. According to Patton and Zaringhalam of the Massachusetts Institute of Technology, writing in a recent issue of *Physics Letters* (**55A**, 95; 1975), the transition is likely to take place under conditions which can be achieved experimentally.

They are brave men. The first estimates of the superfluid transition temperature T_c of pure liquid ^{3}He were wrong (too high) by a factor of more than fifty. Experimenters eagerly sought the phenomenon, but failed to find it at the predicted temperature: the theorists then increased the sophistry of their calculations and revised their estimates of T_c downwards, a cycle which was repeated several times. This procedure was so utterly demoralising for those doing the experiments (being the classical brainwashing technique of repeatedly raising the victim's hopes and then dashing them again) that, when the superfluid transition finally did manifest itself in Osheroff's cryostat at Cornell, it took several weeks for him and his co-workers to realise the significance of what they had discovered. Hence the notable reluctance, so far, of most theorists to predict a T_c for ^{3}He–^{4}He solutions.

A solution of a few percent ^{3}He in ^{4}He is stable down to the lowest temperatures and is, even without the expected transition, of considerable intrinsic interest. The ^{3}He atoms exist and move in a background aether—the liquid ^{4}He—which is itself a superfluid whose transition temperature lies at the relatively high value of 2 K. At low temperatures, where the ^{4}He entropy is essentially zero, the ^{3}He atoms dominate the behaviour of the liquid. In fact, if one completely ignores the presence of the ^{4}He (except insofar as it results in each ^{3}He atom having an effective mass which is larger than the bare atomic mass), and simply treats the ^{3}He atoms as though they were an ideal gas, one gets the right answers for most of the liquid's properties.

Now, it is known that an attractive interaction occurs between the ^{3}He atoms of a solution and, at a sufficiently low temperature, this is expected to give rise to the formation of Cooper pairs, and hence to superfluidity. It is not yet clear whether the relative angular momentum of the atoms in a pair will be zero, as for the Cooper pairs of electrons in a superconductor, or unity as is apparently the case in superfluid pure ^{3}He. The situation would certainly be very peculiar in either case, however, since the superfluid ^{3}He which was formed would exist in another, completely separate but interpenetrating superfluid, the ^{4}He, which is fundamentally different in nature in that it does not acquire its superfluidity through the formation of Cooper pairs. The bizarre physical properties to be expected of such a system were discussed in considerable detail by Khalatnikov in his invited address (Khalatnikov, Mineev and Volovick:

Proc. 14th. Inf. Conf. on Low Temp. Phys., North Holland Pub. Co., Amsterdam, **5**, 102; 1975) to the recent LT14 conference in Helsinki—but he was careful to avoid alluding to any numbers. In particular, he did not make any mention of a value for T_c

Patton and Zaringhalam have now described a theory which, with one adjustable parameter, gives a reasonable description of the pressure dependence of T_c for pure ^{3}He. They fix this parameter by fitting their theory to the experimental results already obtained and then, together with a variety of other experimental information, use it to derive a value of T_c for a ^{3}He–^{4}He solution. They conclude that, for a saturated solution of 8.85% ^{3}He in ^{4}He under a pressure of 20 bar, $T_c = 0.9$ mK. This result is some 10,000 times larger than an earlier prediction by Østgaard (*Phys. Lett.*, **94A**, 433; 1974) of $\sim 10^{-4}$ mK.

These calculated values of T_c may be compared with 0.7 mK, the lowest temperature to which pure ^{3}He has so far been cooled. Making thermal contact to a ^{3}He–^{4}He solution is rather more difficult then to pure ^{3}He at these temperatures, however, so that cooling a solution below 0.9 mK may not necessarily be quite within present experimental capabilities; but it certainly cannot be far removed.

Remembering the bitter experience of the theoretical T_c values for pure ^{3}He, a certain level of scepticism is inevitable in relation to Patton and Zaringhalam's 0.9 mK. It is nonetheless encouraging, and we should not have to wait very long for their prediction to be put to the test in an actual experiment. □

No need for glycophorin?

from a Correspondent

IT is a truism that any breakthrough in science, as in art, fashion or sport, quickly becomes a commonplace. Nowhere is this more obvious than in protein sequencing. However, although the complete sequencing of a protein no longer has, perhaps quite the same impact as previously, the sequencing of a membrane protein is still a relatively rare occurrence. This has been achieved recently for glycophorin, a major protein of the human erythrocyte membrane (Tomita and Marchesi, *Proc. natn. Acad. Sci. U.S.A.*, **72**, 2964–2968; 1975; see *News and Views*, **258**, 478; 1975). Some of the sequence is familiar from earlier publications by Marchesi and his colleagues. In particular the now famous sequence of 23 amino acids lacking charged residues and enriched in hydrophobic residues such as leucine, isoleucine and valine, is placed firmly towards the carboxyl terminal of the polypeptide chain. This sequence is thought to be responsible for integrating the protein into the hydrophobic environment of the membrane. A segment of the polypeptide chain at the carboxyl end is believed to protrude internally whereas the amino terminal sequence, bearing a large amount of carbohydrate, is on the outer side of the membrane.

The function of this quantitatively important constituent of the erythrocyte membrane is unknown. Some recent results suggest that it may be dispensed with altogether without undue effect on the survival either of the erythrocyte or of the person carrying these cells.

The starting point for this work was the identification of a rare genetic variant in humans which affects erythrocyte surface antigens. The En^a antigen is present on the surface of almost all human erythrocytes except in some very rare individuals. Three families are known with this trait: two in Finland and one in England (Dainborough *et al.*, *Vox Sang.*, **17**, 241–255; 1969; Furuhjelm, *et al.*, *Vox Sang.*, **24**, 545–549; 1973). These individuals, who are clinically normal, also show unusually weak activity of another common erythrocyte antigenic system called MN. It has been known for many years that MN antigenicity is associated with glycophorin and this prompted Tanner and Anstee (*Biochem. J.*, **153**, 271–277; 1976) to look for this component in En(a–) erythrocytes. It turns out that the erythrocytes apparently lack glycophorin completely. Erythrocyte En(a–) membranes analysed by SDS polyacrylamide gel electrophoresis have normal peptide composition except for the loss of glycophorin and a minor glycoprotein species of slightly smaller molecular weight.

Tanner and Anstee then tried to label glycophorin in En(a–) erythrocytes with lactoperoxides. In normal erythrocytes, glycophorin and another membrane protein are readily iodinated by this means. In En(a–) erythrocytes however, only one membrane component was labelled and this was not glycophorin.

What these results imply, therefore, is that glycophorin itself is not absolutely required for the function of the erythrocyte. This is surprising on two counts; first, glycophorin is one of the two most abundant proteins of the erythrocyte membrane. Together with a component called protein 3 it accounts for almost half of the membrane proteins. Second, there is considerable evidence that glycophorin and protein 3 form a non-covalent complex in the membrane. It has been suggested (see Rothstein *et al.*, *Fedn Proc.*, **35**, 3–10; 1976) that the complex plays a coordinated role in anion transport. Although protein 3 appears to be the more directly involved in anion transport, it will be interesting to see if the quite drastic changes in the composition of membrane protein of En(a–) erythrocytes result in any physiological effects on ion transport. □

Aspects of tumour biology

from M. J. Bevan and I. S. Trowbridge

The Armand Hammer Symposium in Tumour Biology was held at The Salk Institute, San Diego in January 1976.

THE origin of the cancer cell and its interaction with the immune system were the main themes of the Symposium.

In the opening session, David Baltimore (Massachusetts Institute of Technology) and Charles Heidelberger (McArdle Laboratory, Madison) discussed viral and chemical oncogenesis respectively. Baltimore showed that the resistance to infection by N-tropic or B-tropic murine leukaemia viruses conferred by the FV-1 locus is probably at the level of transcription implying that FV-1 is a regulatory gene coding for a repressor. Viral DNA could be made and integrated into the genome of resistant host cells but unlike the case of sensitive host cells virtually no viral RNA was produced. He also described the *in vitro* transformation of murine bone marrow and foetal liver cells by Abelson Leukaemia virus and its quantitation by a focal assay. Whether the target cell for transformation is a pre-B cell or a more primitive stem cell and how many such cells are present in the various haemopoietic organs is uncertain. It seemed unlikely that a B-cell itself is the target as no immunoglobulin-bearing cells were transformed.

Heidelberger established that chemical carcinogens actually transform normal cells rather than select pre-existing malignant cells from within the population of "normal" cells in his *in vitro* fibroblast cultures, by showing that frequencies of transformation greater than 50% are possible. He also described evidence that chemical carcinogens do not cause transformation