should be clarified in writing with respect to how the reagents will be used, collaborative agreements, and restrictions. Many institutions, including the University of California, have generated formal agreement letters for providing biological reagents to qualified investigators at both nonprofit and for-profit institutions. These letters usually contain statements of ownership by the parent institution and include wording regarding lack of warranty and responsibility for the materials sent. They indicate that the materials are not to be used for commercial purposes nor passed to others without prior written agreement. These written agreements are time consuming but important if painful disagreement or lawsuits, such as occurred with the KG-1 cell line, are to be avoided[4].

The question of biosafety is more important than all of the previous considerations. The history of the Mo cell line is a good example. At the time the Mo cell line was derived, we were unaware that it harboured a human T-leukaemia virus[5]. The patient, Mo, is alive and well; however, the cell line has evolved HTLV-II species that may contribute towards the high degree of malignancy of the cell line[2]. Mo is the only individual thus far reported to harbour this rare virus. Had the cell line been made generally available before the identification of the virus, HTLV-II would have been passed to investigators all over the world with no knowledge of the biohazard involved. Thus, there can be considerable danger in providing cell lines before they are completely characterized.

Lastly, there remains the burden on the originator laboratory of providing DNA, RNA, or proteins derived from these cell lines to laboratories that do not have the facilities to carry human virus-containing cells. For a small laboratory these activities can be incapacitating. The letters, phone calls, preparation of materials for shipment, and actual shipment can severely affect a research laboratory's ability to function. Some materials such as purified lymphokines cannot be made generally available because they are produced in miniscule quantities at great expense.

In summary, all biological reagents developed by investigators associated with my laboratory at UCLA are available to the scientific community at the discretion of the originating investigator and in conformity with the regulations of the University of California.

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Limitations of physical theory

SIR — Your recent view on reducing biology to physics[1] ignores a fundamental problem. If biology is in principle reducible to physics, then so is psychology. Physics is quantum so that the prediction of behaviour would be in the form of a probability distribution of states: which state is observed is found only by observation. Since the observer has been included in the physics, there is no way to determine the outcome unless an observer external to the physics is introduced. This observer is then unexplained by the reduction.

This incompleteness of physics is a consequence of Gödel's theorem. Any comprehensive physical theory must explain structures that can model arithmetic such as human beings and computing machinery. Such a physical theory is then subject to Gödel's theorem and is necessarily incomplete and undecidable. That is, for every algorithm of the theory, there are physical events that cannot be decided by that algorithm. Thus, every comprehensive physical theory, no matter how fully developed, cannot predict the occurrence or non-occurrence of certain events. This incompleteness is a property of the theory; the outside universe may be complete but no theory can prove this fact.

This application of Gödel's theorem to physics is largely metaphysical, but may be related to the existence of the large dimensionless numbers first noted by Dirac[2]. This number D, is of the order of 10^{39} and is roughly equal to the age of the Universe in atomic units, to the square root of the number of protons in the Universe and to the ratio of gravitational to electromagnetic force. In general, D appears in many relations between macrophysical and microphysical quantities. Dirac postulated that D was a constant with resulting gravitational constant variation. Carr and Rees[3], among others, have explained D on the basis of the anthropic principle: observers would not exist to observe this number unless the Universe was such that D had the proper value and relationships. Assuming that Gödelian incompleteness occurs for physical systems with complexity G (measured as the exponential of the entropy or of the negative likelihood), G will be a large number. A human body becomes Gödelian on timescales of the order of a second, so after about 3×10^{13} (infrared) vibrations of the 3×10^{24} molecules in the brain (assuming an average molecular weight of 300) prediction is necessarily incomplete. This crude estimate of 10^{38} for G is relatively near D, but suggests lines of research. For example, the size of the quantum of action may be a result of constructing a theory that applies at universal scales. Application to objects smaller order than $1/D$ times the Universe must bring in incompleteness: for current theories this incompleteness is described by quantum mechanics. Present computing machines process only 100 bits at most 10^9 times per second so that they are far from becoming Gödelian on human timescales.

Any comprehensive physical theory is necessarily incomplete because of Gödel's theorem. This may not reflect incompleteness of reality, only a limitation on the construction of theories using finite sentences, but it is a fundamental limit to reductionism. Attempts to reduce complex systems to physics may succeed formally, but the prediction is a probability distribution of outcomes rather than a definite event. Determining the actual outcome requires another level of observation outside the physics in analogy to the resolution of incompleteness in mathematics by adding new axioms.

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Interstitial fluid

SIR — Bretag asserts[1] that for isolated mammalian tissue synthetic interstitial fluid (SIF)[2] is superior to Krebs' solution. In one respect it is almost certainly inferior, namely the glucose content.

The glucose content of Bretag's solution is 5.55 mM, or about half of that in Krebs'[3]. This is a crucial difference, because although Bretag's is very close to the glucose concentration in normal interstitial fluid, it fails to take into account that in excised tissue the glucose in the bathing fluid often has to diffuse further to its site of utilization than in the body, where the source of glucose is in a neighbouring capillary. In this situation Bretag's solution is effectively hypoglucic.

In a study[4] of the ambient glucose concentration required at 37°C to preserve long-term excitability of myelinated axons in excised vagus nerve of rabbit, 5 mM glucose sufficed in nerve from which the perineurium had been removed but not when the perineurium had been retained, when a concentration in excess of 10 mM was required. The transverse section of these nerves was 0.6×0.4 mm.

Bretag's formula for SIF would be improved by replacing most or all of the 7.6 mM sucrose with glucose.

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