pound this ratio is as high as five visibles to ten lethals, and approaches unity in the youngest germ cells tested (brood VII). This extraordinary efficiency of chloroethyl methanesulphonate in mutating morphogenesis loci is unprecedented among all known mutagens.

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Preparation of Cell Suspensions from Rat Livers

Dulbecco and Vogt[1] have prepared suspensions of rat liver cells by tryptic digestion in order to produce tissue cultures from single cells. We thought that such suspensions might be suitable for studies of cellular respiration, but found that they contained too few intact cells and many mitochondria. The respiration of mitochondria was found to be unaffected even by concentrations of trypsin strong enough to lyse intact cells. An accidental observation suggested that a technique of mild acid digestion without added enzyme might be effective. A solution similar to Dulbecco and Vogt's phosphate buffer saline[1] was used. The phosphates were replaced by the equivalent amount of phosphoric acid and the solution brought to the selected *p*H value with potassium hydroxide. The most acid solution used was at *p*H 2·3. This produced the greatest yield of separated cells; but they barely respired. More alkaline solutions yielded fewer cells, but with increasing alkalinity the respiration-rate rose until with extraction at *p*H 4 a suspension could be obtained with a respiration-rate of the value given by Krebs[2] for liver slices. In practice we thought it best to use a medium of *p*H 5, which when mixed with the chopped tissue gives a *p*H value of nearly 6.

The method finally employed is as follows. The liver from a freshly killed six-week old rat is cut into 1-mm. cubes with a battery of razor blades fixed together, washed with phosphate buffer saline, *p*H 7·3, to remove most of the blood, and incubated with phosphate buffer saline, *p*H 5·0, for 10 min. at 37° C. The medium is then poured off and 25 ml. of fresh medium at the same *p*H value added. The tissue is disrupted by being drawn into and out of an inverted pipette about fifty times. Large particles are removed by filtration through glass wool. The cells are spun down at 1,800*g* for thirty seconds, and resuspended in phosphate buffer saline, *p*H 7·3. The suspension at this stage is contaminated with red cells, but these can be reduced in number by spinning at 50*g* for 2 min. Repetition of this procedure will eventually eliminate the contaminants.

Examination of wet films stained with 1 per cent neutral red shows that most preparations contain individual cells with only a few clumps containing up to four cells. If the pipetting is not sufficiently vigorous, the preparation shows large clumps and is discarded. Permanent stained preparations can be made on gelatine-coated slides and stained with hæmatoxylin and eosin (Fig. 1). In such preparations some of the cells tend to adhere to one another.

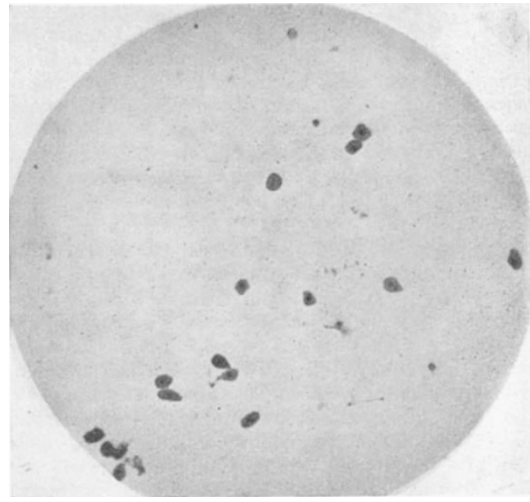

Fig. 1. Rat liver cells prepared as described, stained with hæmatoxylin and eosin. × 60

The Q_{O_2} in the presence of succinate is about −18 and is thus comparable to the values found by Krebs[2].

It is unlikely that such a weakly acid solution hydrolyses the cellular adhesive as does Hornsey's method[3]; it is more probable that some charge effect is involved.

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"The Metaphysics of Science"

In his essay on my Riddell Lectures in *Nature* of February 25, p. 369, Dr. C. K. Grant has quoted fairly and amply from what I have said; but some of his own contributions are, I am afraid, more likely to obscure than to clarify the problem. There are two basic questions.

The first concerns the nature of the laws of physics. Is everything that is logically possible also physically possible, or are the laws like those of statute books such as to exclude certain logical possibilities? To quote Russell's remark that "there is no logical absurdity in the idea that the Universe was created five minutes ago, complete with memories" does not help. The remark is obviously false. Had Russell said "complete with the illusion of memories" he would have avoided one error, but only one. "Logically possible" means, in scientific methodology, logically consistent with the complete body of scientific knowledge. In this sense, to give a striking recent example, Dirac found that a state of negative kinetic energy was logically possible. Answering the question posed above in the affirmative, he concluded that it was