Gm(a) negative immunoglobulin contains a peptide which Dr Wang and his colleagues showed to differ by just one amino-acid from the characteristic peptide of Gm(a) globulin. The amino-acid shift was from glutamate (non-Gm(a)) to aspartate (Gm(a)), which can be effected by a single base change on the gene.

BIOLOGICAL CLOCKS

Behaviour and Metabolism

from a Correspondent

PLANTS and animals seem to be able to estimate time with uncanny accuracy, which is demonstrated by daily metabolic rhythms, and the migration of birds and the flowering of plants at specific times of the year. Living things must have a reference for such accurate timing. The biological clock is thought to be a form of oscillator, perhaps analogous to a pendulum. In constant conditions, the oscillator will have a period characteristic only of itself, but in nature, light or some such stimulus would force the oscillator to have a period of about twenty-four hours. Most biological clockwatchers reason that living organisms have their own internal time standard. Professor F. A. Brown of Northwestern University, Illinois, is almost alone in believing that the living organism can sense subtle stimuli from the environment, which act as pacemakers for the internal clock. In a recent article (*Canad. J. Botany*, **47**, 287; 1969) he has marshalled the evidence from some twenty years of research into a most plausible argument.

Two facts underpin his principal contention. From the pattern of their daily rhythms it is clear that some organisms, held in apparently constant conditions, can measure periods of twenty-four hours very exactly. Furthermore, these rhythms are directly related to the daily fluctuations in primary cosmic radiation. This might seem a meaningless correlation, because primary cosmic rays do not reach the Earth's surface, but these fluctuations exactly mirror image fluctuations in the Earth's geomagnetic field. Brown wondered, therefore, whether living organisms could sense these weak magnetic fields. The test was to "run" mud snails or planarian worms in a particular compass direction in constant conditions of light and temperature. The extent to which they veered from this original direction was found to be closely correlated with the time of the month and of the year. A change in the geomagnetic environment, caused by turning the apparatus or holding a magnet underneath, resulted in a predictable change in the direction the animals would take. Experiments of this sort have convinced Brown that living organisms can detect subtle variations in the Earth's geomagnetic field. He suggests that plants and animals use these fluctuations as a time "grid" on which they can encode the information necessary for timing their physiological rhythms. Few biologists would agree that Brown has a cast-iron case for his theories, but nobody can doubt that he has an impressive array of experimental results to back them up.

If biological rhythms are controlled by an internal timer, it would be reasonable to suppose that this might be an oscillating biochemical reaction. Such a reaction has been sought for some time, and now E. Kendall Pye at the University of Pennsylvania has provided what seems to be the first evidence that pro-

longed oscillations in a biochemical reaction can exist *in vivo* and *in vitro* (*Canad. J. Botany*, **47**, 271; 1969). In some anaerobic conditions, glycolysis in yeast cells pulses in a rhythmic manner, which can be observed as a rise and fall in the concentration of reduced diphosphopyridine nucleotide. The mechanism which Pye has experimentally elucidated for this reaction fits Higgins's general theory of oscillating reactions. This requires that the substrate be fed into the system at a steady rate, and that the product of one of the reactions in the sequence activates the enzyme which catalyses that reaction. The product of this reaction must then be removed by a further enzyme step. Pye has found that glucose is supplied to the glycolytic system at a steady rate. As is well known, it is phosphorylated enzymatically to glucose-6-phosphate, and then converted to its isomer fructose-6-phosphate (F6P). Phosphofructokinase (PFK) catalyses the phosphorylation of F6P to fructose-1,6-diphosphate (FDP) with the concomitant production of ADP. If this reaction is initially slower than the rate of supply of glucose, F6P and ADP will gradually increase. Now Pye can demonstrate that ADP is the activator for PFK, so the rate of phosphorylation will increase until it is proceeding faster than the supply of glucose. The concentration of ADP will decrease and with it the rate of phosphorylation. The cycle recommences when the rate of phosphorylation has fallen below the rate of supply of glucose. Overall control of the rhythm is probably maintained by changes in ADP concentration affecting the reaction catalysed by 3-phosphoglycerate kinase later in the glycolysis sequence.

Pye makes it quite clear that no known rhythm in yeast can be correlated with this metabolic oscillation, but the system does possess many characteristics which make it suitable as a model for the type of timing reaction thought to underlie biological rhythms.

PHAGE GENETICS

Another Repressor

from our Cell Biology Correspondent

ON page 541 of this issue, Pirrotta and Ptashne report the isolation of a second coliphage repressor, this time of the phage 434, using the techniques which Ptashne developed to isolate the λ phage repressor. Not surprisingly, because phage 434 is very closely related to phage λ , the 434 repressor closely resembles the λ repressor and differs from the *lac* operon repressor of *E. coli* isolated by Gilbert and Muller-Hill. The two phage repressors are not, however, identical in function or physical properties. The 434 repressor will bind only to operator sites known collectively as the immunity region of 434 phage DNA. Conversely, if, by genetic recombination, the immunity region of λ phage is replaced by the corresponding region of phage 434, the hybrid phage (λ imm434) is sensitive to the 434 repressor, not the λ repressor.

Pirrotta and Ptashne identified one of the protein fractions, produced by chromatographing extracts of 434 infected *E. coli* on phosphocellulose, by two now classic sorts of experiments. First, they showed that mutants of phage 434, containing mutations in the repressor gene, produce repressor protein with changed chromatographic properties. One of the mutants they used yields a repressor which elutes at lower salt