now coming from a group at the Max Planck Institute at Seewiesen and Erling-Andechs. Wever proposes that in man opportunities for social interaction are more important synchronizing agents (*zeitgebers*) than any purely physical stimuli.

In his experiments, human subjects, either alone or in pairs, lived for several weeks in an underground isolation chamber, and were subjected to a 12 h light : 12 h dark cycle of artificial illumination. This was the only source of external timing, and all subjects failed to become entrained by it. Their rhythm of sleep and wakefulness and their rectal temperature cycle lagged behind the lighting cycle, drifting away from it with a phase difference of about an hour a day. In contrast, subjects who in addition were summoned by the sound of a gong at regular intervals to give urine samples and to perform a series of tests, all became entrained, and indeed changed phase appropriately in response to 6 h phase shifts in the imposed 24 h rhythm.

Non-linear oscillators are believed to be responsible for circadian rhythms. The theory of such mechanisms makes it clear that even very weak coupling of an oscillator to a periodic source allows entrainment. Even so, light as such is evidently too weak to act as a *zeitgeber* in man. Though Wever's results do not indicate what the most effective periodic stimuli might be, it seems very likely that alarm clocks, going to work, lunch time, and the like, by virtue of their social and psychological significance have become the periodic events by which the biological clocks of man are set.

MULTIPLE SCLEROSIS

Myelin Milestones

from our Molecular Biology Correspondent

THE study of demyelinating diseases is an area in which protein chemistry is now skating very close to the surface of medicine. In the experimentally induced condition, allergic encephalitis, an animal after injection with a myelin constituent becomes sensitized against its own central nervous tissue. The fraction with this cataclysmic activity is the basic protein A1, which is one of the two major protein components of the membrane, of which it comprises some 30 per cent. It is also known that a nonapeptide fragment of this protein suffices for activity, and according to Westall *et al.* (*Nature*, **229**, 22; 1971) A1 from animals in which the crucial residues, tryptophan, glutamine and lysine or arginine, are absent from this part of the chain also possesses no encephalitis-inducing activity. Westall *et al.* have further demonstrated the absolute requirement for tryptophan, followed after four residues by glu.lys or glu.arg, by testing a series of twelve synthetic peptides.

The sequences of complete A1 chains have now been reported by Eylar (*Proc. US Nat. Acad. Sci.*, **67**, 1425; 1970), and by Carnegie (*Nature*, **229**, 25; 1971). Eylar has determined both the bovine and the human sequences, which have 170 and 172 residues, and differ from one another at twelve points, including a dipeptide insertion in the human protein. The vital tryptophan residue is at position 116 (referred to the bovine sequence). Carnegie's sequence of human A1 is not quite complete, and, moreover, differs from that of Eylar at several points, and grossly in one tryptic peptide. Both authors agree that a previously reported electrophoretic heterogeneity may arise in part from unusual modifications in one arginine residue.

It has also now emerged that the tryptophan-containing sequence may not be the only lethal site. In guinea-pigs, specific modification of the single tryptophan leads to inactivation. In rabbits, however, the remote peptic peptide, 43–91, causes encephalitis. This is confirmed by Chao and Einstein (*J. Biol. Chem.*, **245**, 6397; 1970), who find that all of several chemical modifications of the tryptophan lead to inactivation towards guinea-pigs, whereas activity towards rabbits is retained. They refer in passing, moreover, to a striking finding, whereby guinea-pigs, injected with the modified, inactive material, become resistant to the effects of the native A1 protein.

One must suppose that A1 must play some essential structural part in the membrane. It differs from most proteins found in membranes, which tend to be predominantly acidic, and is apparently a random coil in the extracted state. Eylar notes that the basic amino-acids are spread out along the chain, and that there are five clusters of non-polar and negatively charged residues in the sequence, one of which contains the tryptophan site. So far there seem to be few ideas about the mechanism of the auto-immune process, though Carnegie offers a speculation, based, however, on unconvincing structural arguments, whereby 5-hydroxytryptamine interacts with the vital tryptophan and a nearby phenylalanine—though the latter, as Westall *et al.* show, is unnecessary for activity. The suggestion then is that this binding site is blocked by an immune interaction. The assumption in all this work is that the experimental condition is related in its causes, no less than in its manifestations, to the real human disease.

More about Mycoplasmas

OUTSIDE the world of veterinary medicine mycoplasmas are a comparatively ignored group of organisms. They have a certain curiosity value as the smallest free living organisms known, intermediate in size between viruses and bacteria, and they are often a cause of concern in laboratories working with cultivated eukaryotic cells, cultures of which mycoplasmas often contaminate, but beyond that they are generally forgotten. Attitudes may change, however, because at least one form of arthritis in swine results from mycoplasmal infection and the suggestion that arthritis in man may have a similar cause cannot be airily dismissed. Investigations of the basic biology of mycoplasmas such as those reported in next Wednesday's *Nature New Biology* by Slater and Folsome and Gourlay and his colleagues may therefore prove to be of more than just academic interest.

Slater and Folsome, working with *Mycoplasma laidlawii* A, have adopted the approach used to demonstrate inducible enzymes in bacteria to show that maltose induces an enzyme involved in its metabolism, α-glucosidase, in *M. laidlawii*. When mycoplasmas grown on a medium containing glucose are transferred to a medium in which maltose is the principal energy source, there is a lag before the cells begin to multiply in the new medium and to synthesize proteins including the α-glucosidase. Once the lag is over, however, the amount of this enzyme in the cells induced by maltose is some ten-fold greater than in control cultures maintained throughout in a glucose-containing medium. And by comparing the specific activities of the α-glucosidase and other enzymes in cells growing in either of the two media Slater and Folsome have ruled out any suggestion that the apparent induction results from some trivial artefact. Furthermore, they have shown that glucose does not suppress the induction of this enzyme by maltose and that it is possible to isolate partially constitutive mutants.

Clearly, the expression of the genome of mycoplasmas is regulated and there may well be close parallels between the molecular mechanisms which effect such regulation and those acting in bacteria. Mycoplasmas also share another important characteristic with bacteria and other cells; they are susceptible to infection by viruses. Last year Gourlay reported (*Nature*, **225**, 1165; 1970) the first discovery of a virus which infects mycoplasma. He and his colleagues have now further characterized this agent. The virus particles appear as short rigid rods, about 150Å by 900Å, with rounded ends, and because they are labelled when they are grown in a medium containing tritiated thymidine but not when they are grown in a medium containing tritiated uridine, Gourlay and his colleagues believe they must have a DNA rather than an RNA genome.