with the same phase, although with a substantially decreased amplitude. This is confirmed by a group working at Stanford[4]. The Birmingham group have, however, failed to confirm this result and find many long period oscillations which vary in period, phase and amplitude from one day to the next[5].

All these observations necessarily suffer from the fact that the sun is only visible for part of the day and, as a consequence, the data sets are modulated by a 24 hour period. Any periods found which are harmonics of a day thus need to be considered most critically. 160 minutes is exactly 1/9 of a day — could this oscillation appear simply as the result of the method of analysis? The Crimean and Stanford groups, aware of this possibility, point out that the period is now found to be 160.01 minutes.

At the other end of the time scale are the five minute oscillations first discovered by Leighton in 1960. A detailed study of this region over some three years by the Birmingham group[6], showed that these five-minute ($\sim$3mHz) oscillations had a well defined structure and consisted of >20 well defined discrete frequencies with a mean spacing of alternate lines of 135.6μHz. Interpreting these data in terms of the then current solar models Iben and Mahaffy[7] and Christensen-Dalsgaard *et al.*[8] suggested a heavy element abundance $z \simeq 0.004$ in contrast to the standard model value of $z = 0.02$.

The solution to the 24 hour modulation problem may be found in three ways: (a) by placing many observation stations around the globe, (b) by observing at one of the earth's poles, (c) by operating from a suitable space satellite. Each of these solutions have both advantages and disadvantages: (a) would require redundancy at any given longitude to overcome weather problems, (b) is subject to atmospheric effects as the sun is always close to the horizon, (c) includes all the technical problems associated with a space program. Also the costs involved increase rapidly as one proceeds from (a) to (c).

The polar solution has been taken by Grec *et al.* and is described in this issue of *Nature* (see p.541). The stresses of an austral summer were amply rewarded by the results of an excellent experiment which resulted in 120 hours of uninterrupted observations. The preliminary analysis confirms the detailed structure and spacing found in the five-minute oscillation. However, those data relating to the longer periods do not show convincing evidence for the existence of a 160 minute oscillation. It is only when a superposed epoch analysis similar to that used by the Crimean and Stanford groups is used that the 160 minute period emerges. Admittedly the 24 hour modulation associated with daytime observation is no longer present in these data, but the earth does still rotate about its axis once every 24 hours, even at the pole. Hence any instrumental or atmospheric effects would have to be clearly eliminated.

Interpretation of the five-minute structure depends on the assignment of the modes observed. All the Doppler shift measurements are strongly biased to low order modes since the integral disk is observed. Hence it is customary to assume l_0, l_1 . . . modes, where l_0 is the simple radial oscillation l_1 alternate radial and axial expansions and contractions and higher l values correspond to more complex shape deformations. Once l has been assumed then for a given frequency ν, the number of radial overtones, n, may be estimated and the results compared with theory.

In a revival of the standard solar model Christensen-Dalsgaard and Gough present a paper in the present issue of *Nature* (see p.544), in which the standard value for the heavy element abundance is retained, $z = 0.02$, and the observational structure of the five-minute oscillations is fitted by taking into account the effect of the solar atmosphere. However it is clear from the models listed that these are very insensitive to the observed frequency separation. Indeed it appears that the only significant change in $\Delta\nu$, the frequency separation, occurs when low z values are considered. At the recent Eslab symposium[9] a mean spacing of 135.2 $\pm$ 0.2μHz was reported which would still appear to favour the $z = 0.004$ value. A direct comparison of the predicted frequencies with the 25 which have now been measured to an accuracy of $1:10^3$ may yield a more conclusive test as to which model to use.

All interpretation of the data depends critically on the correct identification of the mode concerned. This may be experimentally determined by considering two dimensional observations of the solar disk. Such work is at present in progress[10] and will hopefully resolve any mode identification problems. The experimental observations of independent groups have firmly established the discrete structure of the five-minute oscillations although the mode identification and reconciliation with theory is still unsatisfactory.

Clearly if we do not understand our own closest star, the implications on the whole field of cosmology are enormous, and continued efforts by both theorists and experimentalists are urgently required.

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Coronavirus come of age

from B.W.J. Mahy

ALMOST thirty years after the pioneering work of A.W. Gledhill and C.H. Andrewes at the Mill Hill laboratories established the essential features of murine hepatitis virus (MHV) infection (*Brit. J. exp. Pathol.* **32**, 559) the first international conference on the coronavirus group, of which MHV is the best studied member, has been held in Germany*. The meeting consolidated much new and interesting data on a group of viruses responsible for a wide range of acute and chronic diseases. These presently include respiratory and enteric disease in humans, bronchitis in birds, transmissible gastroenteritis and encephalitis in pigs, diarrhoea in calves and dogs, peritonitis in cats, and both demyelinating encephalitis and hepatitis in rodents. A recent report of the isolation of coronaviruses from the brains of multiple sclerosis patients (Burks *et al. Science* **209**, 933; 1980) has intensified interest in the group.

During the first half of the meeting, on structure and replication, it became clear that, in addition to the characteristic morphological features of the group, coronaviruses from whatever species are unified by the possession of a large infectious single-stranded genome of 6 to 7 $\times$ 10^6 molecular weight. Both the mechanism of expression of this genome, and the protein products, have unique features. M.C. Lai (Los Angeles) for a murine coronavirus and S.I.T. Kennedy (La Jolla) working with avian infectious bronchitis, each presented evidence that the genome is positive-stranded, with a capped (m^7G) 5′-terminus and a stretch of poly(A) at the 3′-terminus. In infected cells six virus-specific RNA species are consistently found, ranging in molecular weight from 0.6 $\times$ 10^6 up to genome size. T_1 ribonuclease mapping studies (S.I.T. Kennedy and J.L. Leibowitz, La Jolla) show that these RNAs form a 'nested set', the sequence of each RNA being contained

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within the sequences of all larger RNAs; the 3′-termini of all the RNAs are common, and they all extend inward from the 3′ end of the genome. *In vitro* translation experiments by S. Siddell (Würzburg) and B. van der Zeijst (Utrecht) showed that each subgenomic RNA is a messenger species which specifies a single primary protein product translated from its unique 5′-terminal sequence. Nothing is known at present as to the mechanism by which these subgenomic RNAs are synthesised, although UV target size measurements suggest that each is independently initiated on a negative strand template, and not derived by processing from a larger species (van der Zeijst). A membrane-bound RNA-dependent RNA polymerase activity present in cells infected with a porcine coronavirus was described by D. Brian (Knoxville), but as yet no evidence as to the nature of replicative intermediate molecules has been obtained.

Of the three well-defined virion proteins, one is a 60K nucleocapsid protein phosphorylated by a virion-bound protein kinase, and the others are envelope glycoproteins. The largest (90K) forms the petal-like structures (peplomers) of the 'crown' (from which the group derives its names), and apparently has a conventional mode of synthesis similar to the glycoproteins of other enveloped viruses. The smaller glycoprotein (23K) is embedded in the envelope lipid bilayer, and is largely unaltered by treatment of the virus particle with bromelain, which removes the peplomers; this protein thus fulfils a similar role to that of the membrane protein of other enveloped viruses such as influenza. Glycosylation of this coronavirus membrane protein has unique features. R. Rott (Giessen) showed for a bovine coronavirus that the 23K protein contains no fucose or mannose. H. Niemann and H. Klenk (Giessen), P. Rottier (Utrecht) and K. Holmes (Bethesda) all reported that synthesis of the 23K glycoprotein is not inhibited by tunicamycin; this indicates that, in contrast to all other virus glycoproteins studied so far (including the 90K corona-virus protein) dolichol-linked N-acetylglucosamine plays no part in biosynthesis. L. Sturman (Albany) showed that in the presence of tunicamycin virus particles still matured, but were released from the cells as 'spikeless' virions lacking the 90K protein.

Comparisons between the genomic and subgenomic RNAs of coronaviruses differing in pathogenic potential or species of origin were reported by several workers. T_1 ribonuclease mapping studies by B. Lomniczi (Budapest) gave rise to at least 11 different genome RNA fingerprints within 13 isolates of avian coronavirus orginally classified as infectious bronchitis by pathological criteria. However it is likely that this technique provides too fine an analysis of genome structure for useful strain comparisons. S. Weiss (Philadelphia) described the *in vitro* synthesis of a representative DNA copy of the genome of MHV strain A59. Using this cDNA probe, she found considerable sequence homology with other murine coronaviruses and a low level of homology with 229E virus, a human coronavirus. Extension of such studies to the virus isolates from multiple sclerosis brain tissue, which were obtained by passage of the tissue in mice, should help to identify the origin of these agents.

The second half of the meeting was devoted to persistency and pathogenesis. Although little is known of the molecular mechanisms underlying organotropism and pathogenesis following coronavirus infection, some advances were reported. Coronavirus-induced disease is very dependent upon the age at infection, genetic background, and route of inoculation of the host. K. Pickel (Würzburg) showed that mice were fully susceptible to fatal JHM virus infection up to the age of 21 days, but thereafter became fully resistant. Resistance could be induced by transfer of immune spleen cells from adult mice to baby mice, or by priming of adult non-immune spleen cells in baby mice with UV-inactivated JHM virus, but not by non-immune spleen cells alone. R. Knobler (La Jolla) confirmed that fatal encephalomyelitis induced by JHM virus is an autosomal dominant trait; the ability of the virus to induce demyelinating lesions depended upon the cell tropism of selected mutants to replicate in oligodendroglial cells. H. Wege (Würzburg) reported that injection of JHM *ts* mutants into preimmunised rats by the intracerebral route causes a high rate of subacute to chronic demyelinating disease with similarities to virus-induced demyelination in man. Rats survive normally after intraperitoneal injection of similar virus doses.

Several investigators have studied the mechanism of resistance at the cellular level. F. Bang (Baltimore), who had shown as early as 1960 that peritoneal macrophages taken from MHV resistant mice were also resistant to infection *in vitro*, now reported that macrophage resistance is also dependent upon associated lymphocyte action and may also involve interferon. Extension of these studies from macrophages to primary mouse hepatocyte monolayer cultures by H. Arnheiter (Zürich) confirmed that the hepatocytes were genetically resistant to virus infection as were the mice themselves. Although interferon treatment reduced virus titres in susceptible cell cultures, addition of anti-interferon antiserum did not augment the susceptibility of resistant hepatocyte cultures. Thus it can be concluded that such cells are intrinsically resistant to virus infection, though by what mechanism remains to be determined.

Molecular lines in the red

from a correspondent

THE FIRST OBSERVATIONS of molecular emission in the far infra-red (IR) from an interstellar cloud have been made by a team at the University of California (D.W. Watson, J.W.V. Storey, C.H. Townes, E.E. Haller and W.L. Hansen *Astrophys. J.* **239**, L129; 1980). These observations were made from the NASA Kuiper Airborn Observatory in January 1980 at an altitude of 12.5 km, using a liquid helium-cooled Ge:Sb photodetector in a metal-mesh, scanning Fabry–Pérot interferometer. The two $J = 21 \rightarrow 20$ and $J = 22 \rightarrow 21$ rotational lines of CO were observed in emission at 124 and 119 μm from the Kleinmann–Low region of the Orion molecular cloud. The CO molecule in interstellar clouds has previously been observed in the millimetre and submillimetre regions of the spectrum, where it has been shown to be one of the principal molecular species containing carbon in dense molecular clouds such as Orion. The significance of the new 124- and 119-μm observations is that for these rotational transitions to be observable at all, the CO must be much hotter (500–1,000K) than the temperature of the CO molecules observed in the microwave ($\sim$100K). These high temperatures indicate that the CO observed in the far IR is present in a post-shock gas, corroborating earlier evidence obtained from H_2 observations that a shock wave is propagating into the Orion cloud.

This observational technology opens up an entire new spectral range for observations of molecular species in the interstellar medium. Until now observations of interstellar clouds have been limited mainly to the microwave and radio regions at the long-wavelength end of the spectrum, and to the visible and near ultra-violet regions at the short end of the spectrum. The IR region of the spectrum is a rich arena for remote-sensing applications, but it has been essentially closed to interstellar observations by a combination of detector problems and atmospheric absorption. The development of far-IR techniques for observation of the interstellar medium increases the potential for new discoveries concerning the structure, dynamics, chemistry and evolution of interstellar clouds. □

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In contrast to other positive strand RNA viruses, the corona-viruses readily establish persistent infections in the host. For example, chronic hepatitis or chronic demyelination of the central nervous system occur with certain virus-host combinations. Not surprisingly, persistent infections are relatively easy to establish in cell culture *in vitro*, and such model systems have some unusual features. K. Holmes (Bethesda), N. Hirano (Morioka) and S. Stohlman (Los Angeles) each reported that in cloned cell cultures persisently infected with MHV only 10–20 percent of the cells express coronavirus antigens detectable by immuno-fluorescence, but 100 percent are resistant to superinfection with homologous virus. G. Chaloner-Larsson (Ottawa) has obtained very similar results with a human coronavirus (229E) persistent infection of L 132 cells. Further characterisation of such *in vitro* systems is sure to provide much-needed insight into the way these viruses establish such an intimate relationship with the host. Summing up the meeting, D. Tyrrell (Harrow) emphasised the very wide range of diseases now known to be caused by these viruses, and the value of their study as models of virus pathogenesis. As the meeting convener, V. ter Meulen (Würzburg) pointed out, virtually every laboratory currently working with coronaviruses was represented amongst the seventy participants, and the collective presentation of their data undoubtedly served to strengthen and unify their purpose in unraveling the molecular biology of this unique group of viruses.

Drosophila at Kolymbari

from M. Ashburner

FOR the second time the Greek Orthodox Academy at Kolymbari, on the northern shores of Crete, was host to a meeting of *Drosophila* biologists*. Not surprisingly, the scientific sessions were dominated by discussions of the molecular structure of the *Drosophila* genome. Restriction maps and nucleotide sequences were so common that I am sure more than one participant considered that his colleagues, but naturally not himself, had fallen into the trap so carefully avoided by Dr Watson, of confusing hard work with hard thinking. Nevertheless some very interesting facts were brought to our attention: interesting if only for the reason that they were quite unexpected.

There can be little doubt that the major challenge to conventional genetic wisdom revealed by the molecular analysis of the genome of *Drosophila*, and other eukaryotes, has been the discovery of repeated DNA sequences of no fixed abode. The 'type' of these sequences, as far as *Drosophila* is concerned, is that dubbed 'copia', a sequence of some 5 kilobase pairs which is present, in the typical strain of *D. melanogaster*, roughly 30 times. Comparison of the chromosomal locations of this sequence in different strains of *D. melanogster* has shown that these differ between, and even within, strains.

Studies on the sequence organisation of copia, and similar elements, by G. Rubin's laboratory (Harvard Medical School) have revealed striking similarities between copia, a dispersed middle repeat sequence of yeast known as Tyl, and integrated vertebrate retroviruses. Copia is flanked by a direct terminal repeat of 276 base pairs and a comparison of the nucleotide sequence of sites into which copia has inserted reveal that insertion is accompanied by a direct duplication of five base pairs of the 'target' sequence. Other nomadic middle repeat sequences of *Drosophila* appear to have a similar overall organisation to copia but to generate duplications of the insertion site of different sizes (for example four or seven base pairs). The similarities between these elements and bacterial IS sequences are striking; whether these similarities reflect the mechanisms IS sequences and the nomadic eukaryotic elements use for transposition is not yet known.

Copia, and some other nomadic middle repeat sequences of *Drosophila*, were originally cloned by virtue of the fact that their RNA transcripts are particularly abundant, at least in tissue culture cells. Work in both M. Young's laboratory (Rockefeller University) and in Rubin's has now shown that several different transcripts complementary to copia can be found in cells: whether these can all come from any single copia sequence is not known. For many years the function of RNAs complementary to copia has been the subject of some considerable discussion. They are clearly not translated in proportion to their mass yet, as work by both Rubin and J. Lengyel (University of California, Los Angeles) has shown, these RNAs can be translated into polypeptides in a cell free system.

Two genetic approaches to understanding the function of these nomadic sequences were discussed at Kolymbari. Since different stocks of *D. melanogaster* differ in the location of their copia sequences, and since the frequency of copia transposition is reasonably low, it should be possible to build a *Drosophila* strain that lacks copia sequences. Young has made a start to this interesting, but very tedious experiment: at the time of the meeting a strain with only six copia sequences had been made and the flies were apparently no worse for their experience. Only time, and hard work, will tell whether or not copia sequences are necessary for some aspect of *Drosophila's* existence.

The second genetic approach stems from the exciting discovery that at least one well known mutation (white-apricot) is associated with an insertion of copia into the white gene. B. Judd and P. Bingham (Research Triangle) have mapped this copia element within white to the same region as maps the w^{al} allele and W. Gehring's laboratory (Basel) has found that revertants of w^{al} may be accompanied by loss of the copia element from this site.

The role of the insertion of nomadic middle repeat sequences into genes as a cause of spotaneous mutation in *Drosophila* was also highlighted by the molecular study of the bithorax region. W. Bender (Caltech) has now cloned over 145 kilobase pairs of this region and has used these clones to analyse the nature of some of the many mutant bithorax genes. Two (bxd^1 and $bxd^{5\,5}$), both spontaneous in origin, result from large insertions (of about 10 kb) into the gene. Although the insertion sites are not identical they are reasonably close together and each insertion is a repetitive DNA sequence. A spontaneous reversion of *bxd* turns out to have lost most, though not all, of its insertion. It must be most gratifying to E. B. Lewis, who is responsible for the very detailed genetic analysis of this complex locus, to see how well the molecular analysis of these mutations is confirming the genetic data. For example, the dominant mutation *Cbx* was recovered, after X-ray mutagenesis, together with a recessive *pbx* allele: Bender has now shown that *pbx* is a deletion and that the sequence removed from the *pbx* site has been inserted some kilobase pairs away in reverse orientation to give the *Cbx* mutation. Reversion of *Cbx* has been accompanied by an inversion broken within this inserted sequence.

It is to be hoped that the molecular analysis of long regions of the genome will throw some light on the old question of the relationship between genetic organisation and chromosome structure. P. Spierrer (Geneva) recounted his latest travels along the chromosome in the region of the genes coding for xanthine dehydrogenase (rosy) and acetyl cholinesterase. Over 300 kb of DNA (three 'Benders') have been covered and this spans eight polytene chromosome bands and as many characterised genes. As dramatically as any other this experiment demonstrates the variation in location of middle repeat DNA sequences. The DNA cloned for this walk came from two different 'wild type' stocks of *D.*

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