

is absent from the spinal cord, but P2X₃ located presynaptically on the central terminals of C-fibres may be. In contrast, mRNA for both P2X₁ and P2X₂ occurs in the spinal cord^{8,9}.

This model can explain the induction of pain by exogenous ATP in a human blister-base model¹⁴, and is consistent with reports that P2X antagonists are analgesic in animals^{15,16}. Clearly, if ATP, and more specifically P2X₃ purinoceptors, are involved in nociception, then the development of an antagonist selective for P2X₃ could prove useful in pain relief. Lack of P2X₃ in other tissues could confer a degree of specificity, leading to fewer side-effects.

The pharmacological detection and delineation of P2 purinoceptor subtypes has been severely hampered by the inadequacies of the available ligands, such as the susceptibility of many agonists to

metabolism by extracellular nucleotidases⁷, and the almost complete absence of selective antagonists. So their definition by recombinant biology^{1,2,8,9} constitutes something of a breakthrough. Other subtypes of P2X are also likely to be identified, as ATP activates ligand-gated cation channels in the heart, skeletal muscle and epithelial cells, yet mRNA for the three known subunits is absent from these tissues. The unequivocal structural subtyping of these receptors and their differential distribution means that the discovery of selective therapeutic agents for pain relief is a realistic goal. □

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GRAVITATIONAL DYNAMICS

Universal twists

Stacy McGaugh

THE dynamics of self-gravitating stellar systems and the large variety of complicated and beautiful manifestations thereof observed in galaxies has long fascinated and befuddled astronomers. Progress in understanding the origin and endurance of such features as spiral arms, galactic warps and related phenomena was discussed at the conference* which marked the sixtieth birthday of Professor Donald Lynden-Bell of the University of Cambridge. Although general enough, the conference title does not do justice to the breadth and depth of the topics discussed, or indeed to the contributions Lynden-Bell has made to astronomy.

A favourite subtopic of his which still exercises astronomers is the dynamics of disks and the Local Group of galaxies. Gravitational instabilities in disks could be the cause of features like spiral arms, warps and lopsidedness. These features are observed to be very common in galaxies, but as discussed by many speakers, most mechanisms for exciting them are effective only for relatively short periods. Such disturbances should quickly damp out (on orbital timescales of a few $\times 10^8$ years), so why are these features so common in galaxies $\sim 10^{10}$ years old? Some source of continuing excitation is required (S. Tremaine, Canadian Inst. Theoretical Astrophysics, Toronto), and it is not yet obvious which of the various suggested mechanisms is responsible, although some have been ruled out. Possibilities that remain viable include a Coriolis force

from a twisting halo of dark matter or the rattling induced by a halo composed of massive ($\sim 10^6$ solar mass) objects (J. Ostriker, Princeton Univ.) or tidal interactions between galaxies (A. Toomre, Massachusetts Inst. Technol.).

The disk of our own Galaxy has a quite substantial warp indicated by a flaring of gas which sets in around the edge of the stellar disk. Our own Galaxy resides in a group and is closely interacting with two much smaller satellite galaxies, the Magellanic Clouds. But it seems that this particular interaction is not strong enough to cause the observed warp. A more massive or nearer neighbour might suffice, and just last year a new dwarf galaxy, Sagittarius, was discovered very near to the far edge of the disk of the Milky Way. This led to the bold suggestion (D. N. C. Lin, Univ. California, Santa Cruz) that perhaps this recently discovered galaxy is responsible for the observed warp. Although a warp could be generated in principle by the close passage of an object on an orbit consistent with that of Sagittarius, initial reaction to this idea was sceptical. The sticking point is that to induce the observed warp, a greater mass (by at least a factor of three) is required than is obviously provided by Sagittarius. Although there are substantial uncertainties in the estimates of the mass of Sagittarius, most relevant systematic effects are likely to lead to an overestimate rather than an underestimate. Nonetheless, dwarf galaxies are generally believed to be associated with relatively more dark matter than brighter giants, and after all, something must be doing the damage.

An interesting result pertaining to the Local Group as a whole questioned the venerable timing argument. Given the mass of the main players (our own Galaxy and the Andromeda nebula), it is possible to use orbital dynamics to constrain the age of the Universe. But the usual calculation makes the assumption that this occurs in isolation. Although asymptotically true, this is not really the case from the beginning of a homogeneous universe. Accounting for this with a clever analytical approach, Lynden-Bell's student A. Whiting (Univ. Cambridge) argued that the age might be overestimated by a factor of up to $\sqrt{2\pi/3}$. Although the real effect may be smaller, this could help to reconcile current estimates of the Hubble constant, and the relatively low age of the Universe inferred therefrom, with one of the traditional arguments for a higher age.

The conference concluded with a vigorous discussion (Lynden-Bell) of the cosmological implications of Mach's principle. This essentially states that local inertia is determined by the distribution of mass-energy throughout the Universe. The apparent causality problems of this statement (so simply put) kept Einstein confused for some time. In his own words, "These were errors of thought which cost me two years of excessively hard work".

In essence, Mach's principle notes that it makes no sense to measure acceleration in some mystical absolute space, but only with respect to a remote frame of reference such as that defined by the distant stars. In this way Mach devastatingly criticized Newton's absolute space without providing a usable alternative. This has cosmological implications because it means we can never know the appropriate boundary condition to apply to Einstein's equations for the entire Universe. How can we presume space to be asymptotically flat, or to have any other arbitrary geometry in the absence of matter?

Like Einstein and Wheeler, Lynden-Bell feels that imposing the flat-space boundary condition at infinity is unsatisfactory, so that the only solution which makes sense is no boundary and so no boundary condition at all. The only symmetrical Universe for which this is the case is a closed one ultimately fated to recollapse. Lynden-Bell argues that space-time without mass-energy does not obey the no-boundary condition and therefore does not exist. In his world space-time is caused to exist by energy. Whether the Universe is bound to follow this powerful theoretical argument is another matter, but Donald has been right more than once and we would do well to heed him now. □

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