The hard X-ray Sun in stereo

from John C. Brown

VIRTUALLY on the eve of launch (14 February, 1980) of the first ever solar hard X-ray imaging telescope, aboard NASAs Solar Maximum Mission (SMM), a group of US researchers has scooped some of its expected results without the use of imaging instruments. Kane and Anderson of Berkeley and Evans, Klebesadel and Laros of Los Alamos (*Astrophys. J. Lett.* **233**, L151; 1979) have obtained quantitative information on the spatial structure of a solar hard X-ray source by simultaneous observations from two separate spacecraft. Their results provide invaluable insight into the process of electron acceleration which is central to the solar flare problem.

At the time of observation (5 October, 1978 around 0632 UT) an International Sun Earth Explorer (ISEE-3) was located near the Earth while Pioneer Venus Orbiter (PVO) was 12.5 degrees eastward as seen from the Sun (see Figure). Fortuitously, a flare occurred in an active region A some 15 degrees behind the solar limb which consequently occulted different parts of the flaring solar atmosphere from the two spacecraft. As a result (see Figure) ISEE-3 observed only X rays emanating from altitude (C–D) in the source greater than 25,000 km above the photosphere (A) while PVO observed all emissions (B–D) from above 700 km altitude. At burst peak the PVO flux above 50 keV photon energy exceeded the ISEE flux, extrapolated to the same energy range, by a factor of 600 and had a spectrum harder by about +2 in the power-law exponent. We can thus conclude that the hard X-ray source is concentrated at altitudes below 25,000 km, particularly at higher photon energies, with a factor of 600 above 50 keV. This result is a great advance on previous behind-the-limb results from single spacecraft which established the existence of a high altitude source component but gave no information on the differential height structure.

The importance of hard X-ray bursts lies not in the bremsstrahlung X rays themselves but in the energy of the electrons emitting them. These electrons represent a significant, and perhaps a large, fraction of the total energy released by magnetic field dissipation in a solar flare. How severe are the demands that this places on the electron acceleration process depends strongly on the hard X-ray source model assumed. In particular the acceleration efficiency involved is modest if the bulk of the source electrons are in a relaxed quasi-thermal state. On the other hand, if the source electrons are non-thermal they lose most of their energy by collisions to the cooler thermal plasma rather than to bremsstrahlung and a far greater total electron energy is required.

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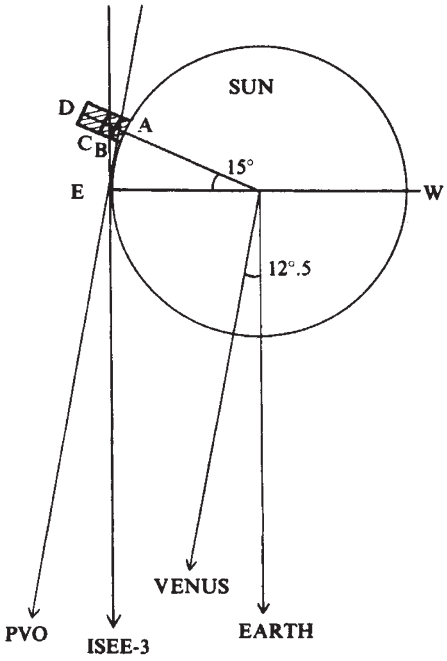

Schematic showing directions of the two spacecraft as seen from the Sun and the different heights in the X-ray source (hatched area) seen from each spacecraft.

Two possible cases of the latter situation are the descending electron beam (thick target) model (with acceleration near D in the Figure) and the trap model where fast electrons are confined in a magnetic arch after acceleration. Although these latter models pose problems for acceleration mechanisms, they provide a plausible interpretation of impulsive chromospheric emissions in flares in terms of electron bombardment. The greatest single source of ambiguity in modelling hard X-ray bursts to date has been the lack of spatial resolution.

There seems to be no ready interpretation of Kane *et al.*'s results in terms of the trap model since this predicts comparable X-ray fluxes from the trapped (coronal) electrons and those precipitating down the limbs to the chromosphere (unless by chance ISEE just glimpsed part of the arch summit at C). A thermal model just might fit the facts if quasi-thermal emission emanated from CD at energies up to around 50 keV while the high energy electron tail escaped downward. The most convincing interpretation at present, however, is the thick target model which predicts a difference of +2 in spectral index between coronal and chromospheric components, and much greater total flux at low altitudes (Brown & McClymont *Solar Phys.* **41**, 135; 1975). The PVO/ISEE flux ratio would then require an acceleration site D located at a plasma column depth of 2.5×10^{18} protons cm^{-2} above the 25,000 km level C. For quiet Sun conditions the plasma density n here is around 10^8 cm^{-3}, but such a low density could not sustain a stable reverse current to neutralise the descending beam. Reverse current stability demands $n \gtrsim 5 \times 10^9$ cm^{-3} which is consistent with the density enhancements typical of active regions. It will be of great interest to see whether a similar source distribution with height occurs in other bursts or if these are more consistent with one of the other source models.

In the coming months SMM will disgorge vastly more hard X-ray source spatial data than are contained in Kane *et al.*'s results. Specifically it will yield detailed information on horizontal source structure and so test whether electrons really do bombard the chromosphere. On the other hand the SMM telescope is limited to photon energies below 30 keV and, furthermore, has no spatial resolution along the line of sight. Thus the 'stereo' data of Kane *et al.* will remain unique until we are again fortunate enough to have two spacecraft and a flare in the right places at the right time. □

Tailoring liposome structure

from Gregory Gregoriadis

THE idea that drugs entrapped in lipid envelopes (liposomes) may provide a better means of delivery to specific sites within the body has aroused wide interest. Much of the interest in the liposomal carriers has no doubt stemmed from the almost unlimited number of potential versions in terms of composition, size and other characteristics. Indeed, correct choice of these parameters has, in some instances, led to liposomal preparations best suited for optimal drug action (for reviews of various aspects of liposomes see *Liposomes and their uses in Biology and Medicine* (D. Papahadjopoulos ed.) *Ann. N.Y. Acad. Sci.* **308**, 1978; *Liposomes in Biological Systems* (eds G. Gregoriadis & A.C. Allison) John Wiley and Sons Ltd, 1980). Recently, attempts have been made to rationalise liposome development by tailoring their structure to the particular biological milieu in which they are intended to act.

The ability to control the extent to which liposomes in the blood retain their entrapped drugs is obviously important to those interested in applying them systemically. Although in many cases drugs must be transported intact to where they are needed, in others their gradual release in the circulation may be preferable, especially when membrane barriers will prevent liposomes from reaching target sites.

In the blood, drugs are released from liposomes much more rapidly than expected from normal solute diffusion

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through the bilayers (see reviews). This is attributed to the massive transfer of the liposomal component lecithin to the plasma high density lipoproteins (HDL) in turn leading to the loss of the carrier's integrity and ability to retain solutes (Krupp *et al. Biochem. biophys. Res. Commun.* **72**, 1251; 1976; Scherphof *et al. Biochim. biophys. Acta* **542**, 296; 1978; Chobanian *et al. Biochemistry* **18**, 180; 1979). It now seems that the plasma-induced structural damage to liposomes can be exploited to 'instruct' them either to retain entrapped drugs or release them at predetermined rates. Unilamellar or multilamellar liposomes can be made more stable in the circulation by incorporating cholesterol. Through modulation of phospholipid loss to plasma HDL (Kirby *et al., FEBS Lett.* **111**, 324; 1980), cholesterol controls bilayer permeability to solutes in the blood of injected animals in inverse proportion to its concentration (Gregoriadis & Davis *Biochem. biophys. Res. Commun.* **89**, 1287; 1979; Kirby *et al. Biochem. J.* **185**, 591; 1980). Sphingomyelin also has a similar effect *in vitro* (Finkelstein & Weissmann *Biochim. biophys. Acta* **587**, 202; 1979) although not necessarily by the same mechanism. Liposomes designed to retain their full drug load are expected to minimise the systemic toxicity of such drugs as the antimonials and metal chelators being tested in the intravenous treatment of experimental visceral leishmaniasis (Black *et al. Trans. Roy. Soc. Trop. Med. Hyg.* **71**, 550; 1977; New *et al. Nature* **272**, 55; 1978; Alving *et al. Proc. natn. Acad. Sci. U.S.A.* **75**, 2959; 1978) and iron loading (Guilmette *et al. Life Sci.* **22**, 313; 1978; Young *et al. Br. J. Haematol,* **41**, 357; 1979) respectively.

On the other hand, controlled release of drugs should promote their access to cells (tumours, for example) with which liposomes may not be able to interact directly (Rustum *et al. Cancer Res.* **39**, 1390; 1979). However, toxicity to normal tissues equally accessible to slowly diffusing drugs cannot be excluded. Therefore, for tissues which are amenable to hyperthermia, an alternative approach based on the property of liposomes to become leaky at the melting temperature of their phospholipid component (Yatvin *et al. Science* **202**, 1290; 1978; Scherphof *et al. Biochim. biophys. Acta* **556**, 196; 1979) may prove more useful. In this way, liposomal drugs delivered systemically can be released near and concentrate selectively in, appropriately preheated target areas such as tumours, infected or inflamed tissues (Weinstein *et al. Science* **204**, 188; 1979).

Whether systemic drug release or transport intact to target cells is required, the need for liposomes to persist in the blood for some time seems to rule out the use of the rapidly removed large liposomes (which may nonetheless be preferable for drug transport to the fixed macrophages or for capture in lung capillaries) and to favour the small unilamellar version. This, when uniformly sized, exhibits a linear rate of clearance and a half life which can be reduced as appropriate by the incroporation of negative charge.

Liposomes may also be introduced into the body other than through the circulation, and here the characteristics of the route of entry also influence the fate and efficiency of action of the liposomal drugs.

For instance, in arthritic rabbits injected intra-articularly with cortisol palmitate anchored on the lipid framework of liposomes, the degree and duration of the anti-inflammatory activity of the steroid is greatest in the initial acute phase of inflammation and is probably related to the phagocytic activity of the synovium (at later phases there are marked changes in its content of cell types) (Shaw *et al. Br. J. exp. Path.* **60**, 142; 1979). Interestingly, a similar beneficial effect of the liposomal steroid has been demonstrated in a few patients with rheumatoid arthritis (de Silva *et al. Lancet* **i**, 1320; 1979).

In another topical use potentially applicable to the chemotherapy of pulmonary metastases, an anti-tumour agent entrapped in positively charged liposomes and administered through the intratracheal route acted in the lung without adverse side effects in other tissues (McCullough & Juliano *J. natn. Cancer Inst.* **63**, 727; 1979).

After injection into tissue (which is of a wider therapeutic scope), liposomes can either disintegrate locally or migrate into the lymph nodes draining the injected tissue (Segal *et al. Clin. Sci. molec. Med.* **49**, 99; 1975). It has now been shown (Osborne *et al. Int. J. Nucl. Med. Biol.* **6**, 75; 1979) that localisation in the primary and secondary regional lymph nodes is enhanced dramatically when small uncharged liposomes are used. In addition to its obvious usefulness in the detection and treatment of tumours of the lymphatic system lymph node localisation of liposomes may also be the cause of their immunopotentiating property (Allison & Gregoriadis *Nature* **252**, 252; 1974; Morein *et al. Nature* **276**, 715; 1978; van Rooijen & van Nieuwmegen *Immun. Commun.* **8**, 381; 1979). This immunopotentiating effect has already shown promise in vaccine development (for example in conjunction with hepatitis B virus surface antigen for a vaccine against hepatitis, Manesis *et al. FEBS Lett.* **102**, 107; 1979).

It has become apparent that ways of controlling the fate of locally applied liposomes can extend beyond simple manipulation of their size and charge. A related development is the finding (Mauk *et al. Science* **207**, 309; 1980) that the rate of disintegration of liposomes in injected tissues can be varied widely by the incorporation of various sugars and amino sugar derivatives of cholesterol into the lipid structure. These derivatives seem to mediate binding of the associated carrier to the intercellular or cell surface components which, in turn, controls its endocytosis. Such modifications could prove useful in cases where interaction of liposomes with and uptake by cells (for example, gut cells after oral administration) is at present poor or non-existent. □

Io: the electrified satellite

from Garry E. Hunt

OF the 14 Jovian satellites, Io, one of the four planet-sized Galilean moons, presents the greatest anomaly, not only of the Galilean satellites but also among all the other bodies in the Solar System. During the recent Voyager encounters spectacular eruptions were seen on Io which have been initially interpreted as evidence for extensive volcanic activity (Smith *et al. Science* **204**, 951; 1979; Smith *et al. Science* **206**, 927; 1979). But is this the only possible interpretation? Gold (*Science* **206**, 1071; 1979) suggests an alternative explanation of these dramatic observations. He suggests that the passage of Io through the powerful magnetic field of Jupiter induces electric currents in Io's crust which heat up areas of the surface and cause the ejection of volcanic-like plumes of gaseous and solid material. Is this hypothesis possible?

There is no doubt that the eruptions on Io were probably the least expected, and most exciting, results of the Voyager mission. Certainly before the mission, the generally accepted view was that the surface of Io would be heavily cratered rather like the Moon. However Peale *et al.* (*Science* **203**, 892; 1979) had pointed out that since Io is subjected to resonant gravitational forces exerted by its sister moon Europa, its orbit would be distorted from its approximately circular path. Consequently, Io would be affected also by Jupiter's powerful gravitational field so that this repeated tidal flexing would create an enormous amount of frictional heat in the satellite's interior. This heat would ultimately have to be dissipated through the surface of Io. Would this necessarily result in widespread volcanism?

Smith *et al.* (*op. cit.*) observed eight active plumes on the first Voyager encounter, of which six were still active at the time of the second flyby three months later. In both cases, material was seen to reach altitudes of 70-280 km at ballistic speeds of up to 1 km s^{-1} (Cook *et al. Nature* **280**, 743; 1979). Interestingly, all except one of these plumes lie within ±30° of the equator (Strom *et al. Nature* **280**, 733; 1979). The eruption sites appear as regions with a central dark or black irregular to

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