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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circular spot that generally appears to have radiating dark, jet-like streaks. In many ways, the vents mapped from the Voyager imaging data appear to resemble closely terrestrial calderas or pit craters (Masursky *et al. Nature* **280**, 725; 1979). The floors of these features range from externally shallow to about 4 km in depth. However at least 300 caldera-like features have been detected randomly distributed over Io's surface and not therefore controlled by strongly patterned convection cells.

The south polar region is certainly important in these discussions. McCauley *et al.* (*Nature* **280**, 736; 1979) have observed white or bluish patches along scarps and faults, particularly in this region. Such features are diffuse, sometimes variable and obscuring the surface, suggesting that they may be cloud produced by gas leaking out of the interior of the satellite and condensing into some form of snow. Certainly, Pearl *et al.* (*Nature* **280**, 755; 1979) have detected a tenuous atmosphere of sulphur dioxide, while several observers (Fanale *et al. Nature* **280**, 761; 1979; Nash & Nelson *Nature* **280**, 763; 1979; and Smythe *et al. Nature* **280**, 766; 1979) indicate the presence of this material on the surface of Io. The surface is then probably a mixture of sulphur and sulphur dioxide. So there may be reservoirs of liquid sulphur dioxide on Io analogous to the lakes and oceans of the Earth. How therefore can we account for the plume features?

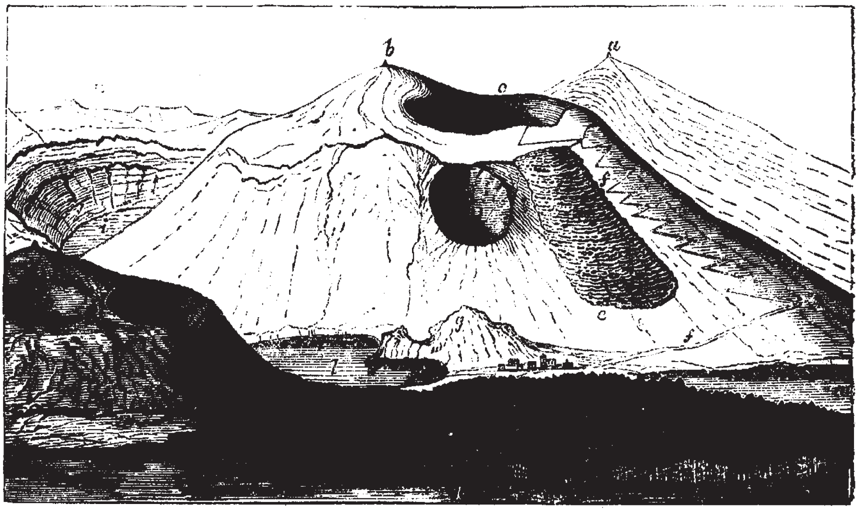
In certain locations, the observations suggest that ice clouds are issuing from fractures in Io's crust, and there is no doubt that liquid sulphur dioxide would escape to the surface along a fault or at the base of a scarp. Certainly, as it reaches the surface the sudden reduction in pressure to below the critical point would cause the liquid to explode into an ice fog that would spread out and then ultimately fall back to the surface again. The process may also erode material along the scarps as well, as McCauley *et al.* (*op. cit.*) suggest. Could this procedure account for the larger plumes that have been observed?

Smith *et al.* (*op. cit.*) suggest that this is the case, with the liquid sulphur dioxide causing violent reactions. This model requires large segregated pools of sulphur below the satellite's surface, and there are certainly some volcanic-like flows that may be of pure sulphur as Sagan (*Nature* **280**, 750; 1979) suggests.

However, an alternative view is taken by Carr *et al.* (*Nature* **280**, 729; 1979) who suggest that the volcanism is not primarily driven by the tidal forces, but by a mechanism in which the sulphur-enriched silicate magma erupts through a silicate crust enriched in sulphur. The variations in the physics and chemistry of the magma chambers may then account for the different types of eruption and therefore the different features on Io. Certainly it is difficult to imagine that volcanism on Io has continued at the same rate throughout the history which is implied by the tidal heating model. The other volcanic bodies, Mars, Venus, Moon and Earth, have certainly had variable periods of volcanism. So why should Io be different?

Gold (*op. cit.*) however, suggests that all these geologically-based interpretations are unsatisfactory. While there is no disputing the altitude and speed of the material in these plumes, he suggests that such behaviour is unlikely for sulphur compounds under volcanic conditions. He indicates that for such material to reach the observed speed of up to 1 km s^{-1}, it would have to be heated to about 6,000 K. Certainly the temperatures that can be expected in any volcanic region are likely to be below 1,500 K for nearly all rock-forming minerals. Furthermore, volcanic activity is supposedly more extensive on Io than on the Earth, so that the internal heating of Io would therefore be greater. But Gold calculates an Ionian heat flow of only 46 erg cm^{-2} s^{-1} from the data of Peale *et al* (*op. cit.*) compared with 65 erg cm^{-2} s^{-1} for the Earth.

With these inconsistencies, further examination of the Io eruptions is required. Gold points out that the satellite resides in the intense Jovian magnetosphere so that it will be electrically heated. Certainly Io, with a density of 3.5 g cm^{-3}, is composed of materials that conduct electricity and currents will flow through it as the satellite moves through the Jovian magnetic field. If this electric arc interpretation is correct, then the outbursts would repeat in a systematic way, controlled by the repetition cycle of the external field configuration. Local hot spots would be created, which is consistent with the observations by Hanel *et al.* (*Science* **204**, 972; 1979). The strong concentration of the majority of the plumes around the equatorial region indicates that this mechanism is appropriate in that region. However, in other locations, such as those of the poles, sulphur dioxide venting may be more appropriate. The eruption characteristics of Io may therefore be a complex mixture of volcanism and the results of the special electrical environment in which the satellite resides. Whatever the explanation there is little doubt that Io is in a hyperactive state, with the youngest surface currently known in the Solar System. ☐



100 years ago

Lipari is about ten and a half square miles in area. The highest point is 1,978 feet above the sea. Everywhere the island betrays its volcanic origin. Tuff, pumice, liparite (quartz-trachyte), and obsidian, are constantly met with; at San Calogero a hot spring (198°F.) pours forth water charged with carbonic acid and sulphuretted hydrogen, while the Bagno Secco discharges steam, sulphurous acid, and (it is said, but I think the statement requires confirmation) hydrochloric acid.

Vulcano is undoubtedly the most interesting member of the group from a volcanic point of view. It lies between four and five miles to the south of Lipari, and contains a semi-active crater, which, as regards its usual dynamic activity, occupies a mean position between Vesuvius in its present state of action, and an actual solfatara like that of Puzzuoli. Sulphur, alum, and boracic acid are the substances procured from the crater. We noticed also sublimates of sulphide of arsenic, and salts of copper were found in association with some of the aluminous incrustation; also chloride of ammonium. I have been assured by two eye-witnesses that blue and green flames sometimes issue from clefts in the bottom of the crater.

Prof. A. Cossa (*Gazetta Chimica Italiana*, 1878, p. 235-246) has pointed out that Vulcano furnishes the richest supply known of caesium and rubidium. The Faraglioni, also called *rocca dell' alume*, is a trachytic mass much decomposed by sulphurous and sulphuric acids; potassium-alum is found in its cavities, associated with the sulphates of aluminium and calcium, with chloride of ammonium, and with the alums of thallium, caesium, and rubidium. The most complex mixture of volcanic products hitherto found was discovered by Cossa on the edges of a small fumerole at the bottom of the crater of Vulcano. It was found to consist of the sulphides of arsenic and selenium, chloride of ammonium, boracic acid, sulphate of lithium, together with caesium- and thallium-alums, and traces of the alums of potassium and rubidium. From *Nature* **21**, 26 Feb., 401; 1880.