time? Also, because Eaton and colleagues studied only *Drosophila* larvae, and examined only a few target genes, it is not known whether this mechanism also operates in *Drosophila* and vertebrate embryos. Suggestively, however, insect egg yolk contains abundant lipoprotein, and lipoprotein synthesis occurs in the yolk-sac visceral endoderm of early mouse embryos[17,18].

We also wonder which of the several varieties of mammalian lipoproteins could be involved in morphogen diffusion, and if they provide additional specificity. And, finally, could the diffusion of morphogens not associated with lipids, such as members of the transforming growth factor-β/activin/Dpp family, also be mediated by lipoproteins? Thus, from this marriage, we expect many interesting progeny. ■

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Planetary science

Saturn's retrograde renegade

J. Brad Dalton

Data from the Cassini–Huygens mission provide convincing evidence that the saturnian moon Phoebe formed elsewhere in the Solar System, and was only later captured by Saturn's gravitational pull.

In the next few years, the Cassini–Huygens spacecraft will return a wealth of data from its orbital tour of Saturn's rings and moons. Although many images are released to the public almost immediately, it takes time to conduct detailed scientific analyses of the observations. Stunning results from early encounters with the moons are now beginning to trickle in.

On 11 June 2004, shortly before it permanently entered Saturn's orbit, Cassini–Huygens made its closest approach to the planet's outermost moon, Phoebe (Fig. 1; see also Box 1, overleaf). Phoebe is a small (around 220-km-diameter), irregular satellite in an eccentric, inclined, retrograde orbit — moving counter to the direction of the planet's rotation, in contrast to the more common, prograde, movement. Scientists have long suspected[1,2] that Phoebe did not form alongside Saturn and its regular satellites, which occupy roughly circular, low-inclination, prograde orbits. Two papers in this issue[3,4] provide additional evidence for this hypothesis.

Johnson and Lunine[3] (page 69) use density and volume calculations, determined from navigation and imaging systems on board Cassini, to suggest that Phoebe is more similar to objects found in the Kuiper belt, a collection of small, icy bodies beyond Neptune, than it is to its siblings in orbit about Saturn. Clark *et al.*[4] (page 66) interpret spectral observations from Cassini's Visual and Infrared Mapping Spectrometer to reveal a complex array of surface materials ranging from minerals to volatile organic compounds.

A number of these compounds have not yet been observed on the regular saturnian satellites, but are typically found in primitive bodies of the outer Solar System, such as comets, certain types of asteroid and, again, objects in the Kuiper belt. As the Kuiper belt is thought to contain material left over from the formation of Saturn, Uranus and Neptune, such an origin for Phoebe still keeps it in the family, albeit as a more distant, 'prodigal' child of Saturn. But converging lines of evidence now suggest that Phoebe formed even farther from the Sun and only later ventured inwards. Its progress was then arrested by gravitational interactions with the Saturn system.

The compositional diversity of Phoebe, in fact, seems unlike that of any single object studied to date within the Solar System. Clark *et al.*[4] have identified the presence of iron-bearing minerals, and possible phyllosilicates (the family of sheet silicates that includes clays and micas). The latter, if present, would indicate some degree of aqueous processing, possibly in a parent body or even before the formation of the protoplanetary nebula — the cloud of gas and dust from which planets are formed around a newborn star, such as the Sun. Spectral evidence for two crystalline silicate families, the olivines and pyroxenes, is also consistent with the presence of primitive materials left over from the formation of the Solar System.

The spectral observations also point to a wealth of volatile compounds — among them water-ice, carbon dioxide and several organic compounds, including alkanes, aromatic compounds, nitriles and other cyanide compounds — indicating an origin somewhere in the frozen outer reaches of the solar nebula, rather than in the hotter, drier inner Solar System where the terrestrial planets and the asteroid belt formed. An origin beyond Saturn's orbit also makes more sense when considering the orbital dynamics required for outward migration from the asteroid belt, against the gravitational pull of the Sun.

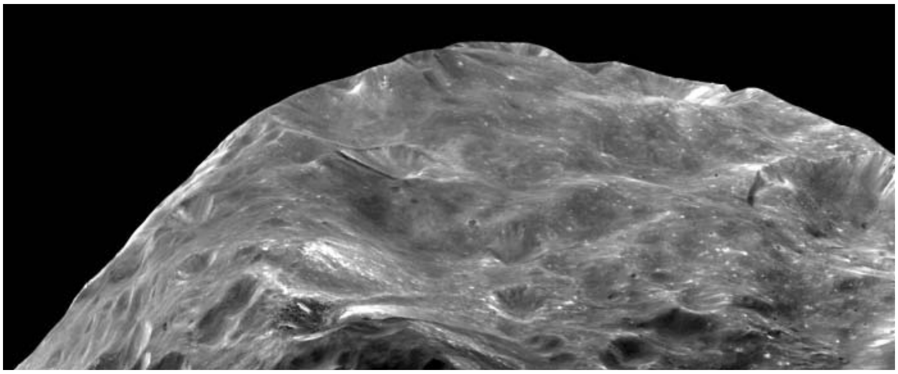

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Figure 1 **One battered rock. This stunning image of Phoebe's pitted surface, as seen by the Cassini Imaging Science Subsystem, reveals its long and complex history. The region shown is near the satellite's south pole and is around 120 km across; the largest craters are up to 4 km deep. Bright patches of water and other ices, as well as dark regions hosting complex organic compounds and minerals, indicate an origin far from its current orbit around Saturn. Results from Cassini[3,4] suggest that Phoebe may have formed as far out as the Kuiper belt, beyond Neptune's orbit, and may even contain cometary material pre-dating the formation of the Solar System.**

Box 1 The Cassini–Huygens mission to Saturn

The Cassini–Huygens spacecraft is a joint endeavour of NASA, the European Space Agency and the Italian Space Agency, ASI. With a dry weight of 5.6 tonnes, it is the largest interplanetary spacecraft ever built, and consists of two parts — the orbiter Cassini and the Titan probe Huygens. The components are named after Jean-Dominique Cassini (1625–1711), discoverer of the saturnian moons Dione, Iapetus, Rhea and Tethys, and Christiaan Huygens (1629–95), who first observed Saturn's rings and Titan, its largest moon.

- 15 October 1997: Launch from Cape Canaveral. Helped on its way by 'stealing' rotational energy in three fly-pasts of Venus (April 1998, June 1999) and Earth (August 1999).
- 30 December 2000: Sends back high-resolution images as it passes Jupiter at a distance of 9.7 million kilometres.
- 11 June 2004: First detailed images of Phoebe, on the edge of the Saturn system, from a range of 2,000 kilometres.
- 1 July 2004: Permanently enters orbit around Saturn, sending back spectacular images of the planet's rings.
- 26 October 2004: First close pass of Titan, which, with a diameter of 2,700 km, is the largest of Saturn's 34 known moons.
- 25 December 2004: The Cassini orbiter releases the Huygens probe to coast down to Titan's surface.
- 14 January 2005: Huygens enters Titan's cloudy atmosphere, touching down two-and-a-half hours later. The probe continues sending data for well over an hour from the surface, allowing a detailed picture of its composition to be made. (More will appear on this topic in a later issue.)

In the next three years, Cassini will make numerous further passes of Titan, as well as other moons — including Iapetus, Enceladus, Tethys and Rhea — in the course of 75 orbits of Saturn before its fuel supply is exhausted. **J.B.D.**

The findings of Clark *et al.*[4] dovetail nicely with Johnson and Lunine's analysis[3], which finds Phoebe's mass, volume and density to be more consistent with those of Pluto and Neptune's giant satellite Triton than those of the regular saturnian satellites (with the exception of Hyperion and Titan, which were excluded from the analysis). Because the composition of Phoebe should reflect that of the region in which it formed, this new knowledge could place constraints on the composition and evolution of the early solar nebula, as well as the various worlds spawned within it.

There is much more for Cassini to do. The nature of the proto-saturnian nebula is still not well known; complementary analyses of encounter data for the regular satellites are likely to shed further light on this problem. The formation of Saturn itself, for example, could have altered the abundances of important species — such as oxygen or water — relative to the protoplanetary nebula[5]. The ring system, as noted by Clark *et al.*, seems to contain similar iron-bearing materials to those seen on Phoebe. It has long been thought that dust from Phoebe could be migrating inwards within the Saturn system, perhaps even providing the bulk of the dark material seen on Saturn's moon Iapetus[6,7]. The similarities between these two satellites, at least as seen from ground-based telescopes and from the Voyager spacecraft, might also be explained by assuming that meteoritic or cometary infall has coated both with similar material.

The many planned encounters with Iapetus and Saturn's other regular satellites are expected to provide definitive answers to these remaining questions. Given the far-reaching implications of this first encounter with tiny Phoebe, we can expect Cassini to provide many more powerful insights during its four-year mission. ■

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Reproductive biology

Fatty link to fertility

S. K. Dey

A short delay in the attachment of embryos to the wall of the womb during early pregnancy adversely affects later developmental processes. New evidence reinforces the need for lipids to regulate this event.

In mammals, the creation of new life depends on the union of a sperm and an egg. The fertilized egg then undergoes several cell divisions to form a differentiated tissue — the blastocyst. Next, an intricate molecular dialogue between blastocyst and uterus initiates the process of implantation, by which the blastocyst attaches to the lining of the uterus[1,2]. Low implantation rates are common in women undergoing assisted reproduction, posing a challenge to both patients and doctors, so researchers are striving towards a deeper understanding of this process. On page 104 of this issue, Ye *et al.*[3] reveal a previously unknown and essential role for a small lipid signalling molecule, lysophosphatidic acid (LPA), in normal implantation.

Normal implantation is initiated only when embryonic development is synchronized with the appropriate preparation of the uterus. More specifically, the embryo must reach the blastocyst stage and gain 'implantation competency'; meanwhile, the uterus — through the coordinated actions of oestrogen and progesterone — must reach what is known as the receptive phase.

This state of uterine receptivity, also termed the window of implantation, lasts for a limited period. It is only during this time that the womb is able to support normal embryonic growth and implantation[1]. Previous studies have shown that when blastocysts implant beyond this window, the delay creates an adverse ripple effect: embryos crowd near the cervix; placentas fail to form correctly; fetuses are resorbed; and the development of remaining fetuses is retarded[4,5]. In other words, the quality of implantation determines the quality of pregnancy and fetal well-being; failure to achieve 'on-time' implantation risks an adverse pregnancy outcome. In humans, implantation beyond the normal window leads to spontaneous pregnancy losses[6].

Tracing the hierarchical landscape of the molecular signalling pathways that govern embryo–uterus interactions during human pregnancy is not easy, because of experimental difficulties and ethical considerations. Experiments in mice, however, have directly shown that lipid molecules known as prostaglandins, generated by the enzyme cyclooxygenase-2 (COX-2), are essential for implantation[5,7]. Their role in reproduction is further illustrated by the poor fertility — caused by deferred implantation — seen in female mice lacking cytoplasmic phospholipase $A_{2\alpha}$ ($cPLA_{2\alpha}$; ref. 4). This enzyme uses the phospholipids that make up cell membranes to generate arachidonic acid, which is in turn used for prostaglandin synthesis by COX-2. These studies establish the importance of lipid signalling through the $cPLA_{2\alpha}$–COX-2 axis in implantation.

When a cell is activated in response to a stimulus, membrane phospholipids can be used to generate numerous lipid signalling molecules, such as eicosanoids and lysophospholipids. Prostaglandins belong to the eicosanoid class. The lipid featuring in Ye *et al.*'s study, LPA, belongs to the lysophospholipid group, and is characterized by a 3-carbon backbone, to which is attached an