pain to decrease when a putative sensor molecule (the $P2X_3$ receptor) is absent. Surprisingly, animals lacking $P2X_3$ receptors became more, not less, hypersensitive after inflammation. Perhaps this result is an artefact of the gene-knockout approach used, and might not occur with short-term use of drugs that block $P2X_3$ receptors. But this might be wishful thinking, and we should take seriously the possibility that the suppression of these receptors would aggravate inflammatory pain.

Possibly the most unexpected finding from these analyses[2] is that the $P2X_3$-receptor-deficient mice no longer showed any neuronal activity in the spinal cord in response to mild skin warming. It is a mystery how we sense pleasant warmth, when the skin temperature rises from 20 °C to 40 °C; no role for $P2X_3$ receptors has ever been proposed. By contrast, we are fairly certain that the mechanism for sensing harmful heat (45 °C and above) involves the vanilloid receptors[10,11]. Perhaps $P2X_3$ receptors are expressed on heat-sensing neurons as well as on pain-sensing ones, and become more active when skin is warmed. However, it would be premature to come to such a provocative conclusion, given that Souslova *et al.* made recordings of neuronal activity in spinal neurons. Spinal neurons receive their input from sensory neurons that extend from the skin to the spine. Sensing the temperature at the skin is just the first in a series of molecular events that carry the signal from skin to spinal cord. A disruption at any point could cause the defects seen in the $P2X_3$-deficient mice.

These results clearly show the importance of ATP and the $P2X_3$ receptors in sensing certain types of pain. But many pieces of the puzzle are still missing. Little is known about how ATP is released, for example, or how long it survives after a harmful event. ATP might contribute only temporarily to the pain caused by tissue damage: it is quickly degraded outside cells[12], and channels made of only $P2X_3$ receptors desensitize in less than a second[4,5].

Also, behavioural models for measuring pain are much more sensitive to persistent than to transient signals, so they are better suited to getting to the bottom of the roles of slower molecular messengers, such as bradykinin, rather than ATP. The formalin-induced model of pain used by Cockayne *et al.* and Souslova *et al.* undoubtedly causes tissue damage, yet it is hard to know how it relates to the pain caused by a more natural injury, such as falling off a bicycle. But, despite these limitations, the train of discovery from injecting cytosol into blisters to knocking out $P2X_3$ receptors from mice has provided unexpected insights into pain transduction, and an unequivocal direction to clinical research. ■

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Astronomy

The red ragged edge

Brian G. Marsden

It is not particularly surprising that the properties of asteroids should change between the inner and outer parts of the main asteroid belt between Mars and Jupiter. After all, this belt marks the transition between the rocky planets of the inner Solar System and the gas giants of the outer Solar System. What is perhaps more unexpected is that a similar transition should occur in the Kuiper belt — an even greater ring of icy bodies orbiting beyond Neptune. Three years ago, Tegler and Romanishin[1] reported the results of a photometric survey of these distant bodies, showing that they fall into two distinct groups based on their colour, but the reason for the two colours was a mystery. On page 979 of this issue[2], Tegler and Romanishin present a follow-up survey that demonstrates

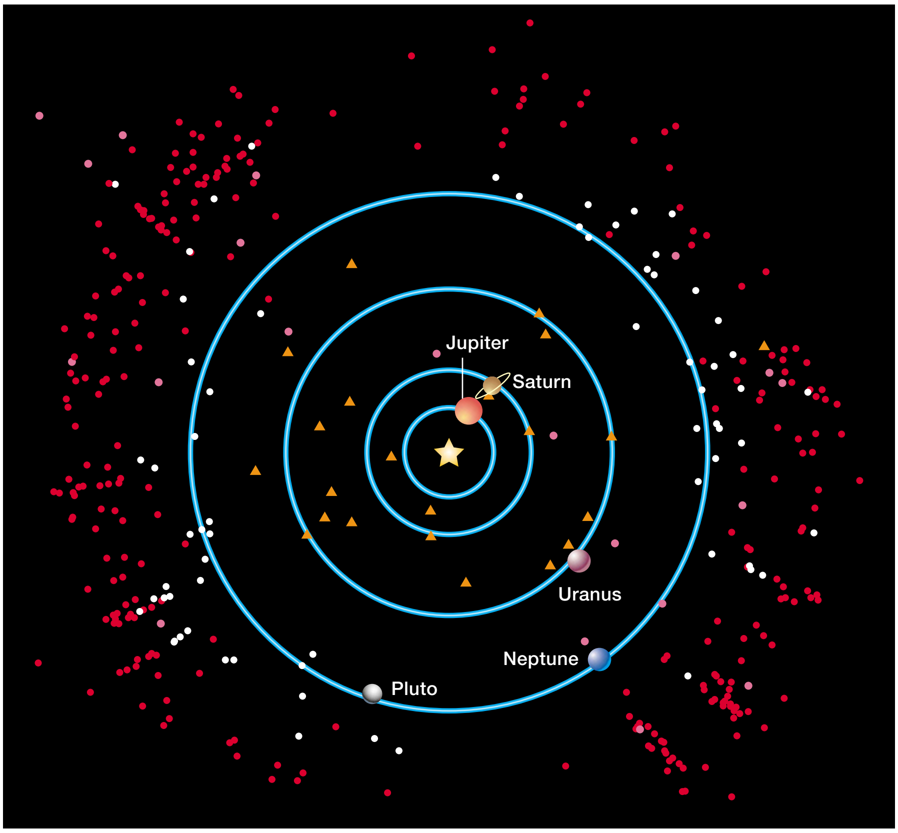


Figure 1 **Snapshot of the outer Solar System, as it was on 16 October 2000. The outer Solar System contains the giant planets Jupiter, Saturn, Uranus and Neptune, along with Pluto and other smaller objects. (The inner Solar System, containing the four rocky planets, is too small to be shown.) Pluto's non-circular orbit takes it from its present position at 30 AU from the Sun through the Kuiper belt of icy bodies beyond Neptune to a distance of 50 AU from the Sun. The Kuiper-belt objects (KBOs) include the 'classical' KBOs (red circles), 'Plutinos' (bodies with orbits similar to Pluto; white circles) and 'scattered-disk objects' (magenta circles). Icy comets known as Centaurs (orange triangles) are thought to have escaped from the Kuiper belt, and can be found throughout the outer Solar System. Tegler and Romanishin's photometric surveys[1,2] of KBOs and Centaurs suggest that the classical KBOs found beyond 40 AU may be 'redder' than the other KBOs.**

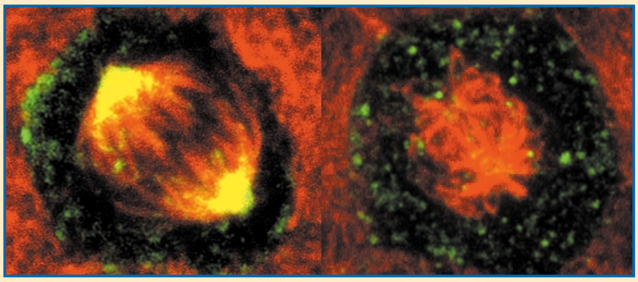
Neurobiology

Convoluted communications

Normal brains are convoluted in appearance. But those of children suffering from lissencephaly, or 'smooth brain', are not — with tragic consequences (mental retardation, epilepsy and an early death). The cause is mutation of one of the two copies of a gene known as *LIS1*, which means that neurons fail to migrate to the cerebral cortex during development. But what provides the link between *LIS1* mutations and the defects in migration? Three papers in *Nature Cell Biology* tackle the question.

One way of studying the function of a gene is to delete both copies in the embryos of an experimental organism and see what happens. But this can't be done with *LIS1*, because the embryos die. So Zhao Liu *et al.* (*Nature Cell Biol.* **2,** 776–782; 2000) took another approach. Using the fruitfly *Drosophila melanogaster*, the authors knocked out both *LIS1* genes in developing neurons only in the 'mushroom body', a structure analogous to the human cortex. This resulted in severe abnormalities in the appearance and numbers of neurons (normal adult flies have about 500 neurons, but the mutants had only about 50). Liu *et al.* suggest that the low cell numbers resulted from a defect in cell proliferation.

This interpretation ties in with the results of Nicole Faulkner *et al.* (**2,** 784–791), who found that the division of mammalian cells in culture was dramatically inhibited when *LIS1* was overexpressed or suppressed. Chromosomes did not attach properly to the microtubule-based 'spindle'



that separates duplicated chromosomes, and the orientation of the spindle became random (compare the right-hand spindle in the picture with the normal one on the left). Faulkner *et al.*, and Deanna Smith *et al.* (**2,** 767–775), also showed that LIS1 protein and components of cytoplasmic dynein — a molecular motor involved in cellular processes that require microtubules — occur in the same regions of cells.

The authors' studies went beyond those described here. But it seems that LIS1 and dynein (and dynactin, its companion complex) ensure that developing nerve cells divide at the right time, and in the right orientation. Mutations in *LIS1* apparently disrupt these processes, perhaps leading to a failure of neurons to migrate properly to the cortex. **Amanda Tromans**

a possible link between the colours of these objects and their distances from the Sun.

More than 150 years elapsed between the first calculations of the orbits of asteroids and the first observations that provided a real physical understanding of these bodies. The colour of sunlight reflected off asteroids can be measured through different-coloured filters. Such photometric measurements of several asteroids in the 1950s revealed that their colours fell into two main groups, which were interpreted as differing in surface composition. One group is only slightly redder than the Sun in colour, meaning that their surfaces reflect all wavelengths more or less equally, whereas the other group is significantly redder than the Sun because they absorb more of the blue sunlight. The first group tends to dominate the outer part of the asteroid belt, whereas the redder ones prevail in the inner belt.

During the past decade more than 300 faint objects have been found in the belt beyond Neptune (Fig. 1), which is located at 30 astronomical units from the Sun (1 AU is essentially the Earth–Sun distance). For these objects, only a few years elapsed before knowledge of their orbits was supplemented by physical studies. The idea of a population of small bodies beyond Neptune is variously attributed to Kuiper[3] and Edgeworth[4], although Leonard[5] wrote of a possible 'ultra-neptunian zone' of bodies within months of the discovery of Pluto. In 1964 Whipple[6] predicted that Pluto's companions would be dormant comets up to 100 km in radius and between 30 and 50 AU from the Sun. This is how we see the population of 'Kuiper-belt objects' (KBOs) today.

Pluto is now generally considered to be a member of the Kuiper belt, although its non-circular orbit brings it closer to the Sun than Neptune at its closest approach (its perihelion) and out to 50 AU at its farthest (its aphelion). Fortunately, the 165-year orbital period of Neptune is precisely two-thirds that of Pluto. This '2:3 resonance' restricts the relative configurations of the pair and prevents them from passing within 18 AU of each other[7]. Three of the first six KBO candidates found during 1992–93 have orbits similar to that of Pluto. Known as 'Plutinos', they share the 2:3 resonance that prevents them from getting too close to Neptune[8]. Two others have orbits that are much more nearly circular, with distances ranging between 41 AU at perihelion to 47 AU at aphelion. These objects — sometimes known as 'classical' KBOs — are also safe from encounters with Neptune.

Most of the KBOs found since 1993 follow the same general pattern (Fig. 1). Classical KBOs make up the bulk of the Kuiper belt, being five times more numerous than Plutinos of comparable size. They have mean distances of 41–47 AU, but can reach 38 AU at perihelion and 53 AU at aphelion. There are also objects that avoid Neptune by means of other resonances, and there is a population of 'scattered-disk objects'[9], which have highly non-circular orbits. These scattered-disk objects bear some relation to the 'Centaurs', which are broadly dispersed throughout the outer Solar System (Fig. 1). The first known Centaur, Chiron, has been seen to emit gas and dust like a comet. So it is reasonable to conclude that Centaurs are once-dormant comets that have escaped from the Kuiper belt over many millions of years. In some cases they eventually turn into the short-period comets found inside Jupiter's orbit.

Tegler and Romanishin's combined surveys[1,2] include 36 objects, of which 13 are Plutinos, 13 are classical KBOs and 8 are Centaurs. Like the main-belt asteroids, these KBOs and Centaurs appear to come in two colours. One group has surfaces that are best described as 'grey', whereas the other group is noticeably redder. With this larger sample it is possible to look for correlations between colour and distance. The authors find that the Centaurs and Plutinos with perihelion distances of up to 40 AU are evenly split between the two colour groups, but the nine classical KBOs with perihelion distances greater than 40 AU are exclusively 'red'. Four of the classical KBOs have perihelion distances of less than 40 AU, and three of these are grey. But there is a big difference between the angles at which the orbits of these red and grey classical KBOs are inclined to those of the giant planets. Whereas the reds have relatively low orbital inclinations of up to 13°, the three grey ones all have inclinations in excess of 24°, so perhaps they are not so classical after all.

If the high-inclination classical KBOs are a different subpopulation, the fact that all ten 'genuine' classical KBOs are red is a remarkable result, seemingly more exclusive than the colour groupings in the asteroid belt, which later turned out to be more complex. It suggests that the truly classical KBOs are a pristine population that is so safe from encounters with Neptune that it is not subject to significant long-term orbital variations. After all, if these bodies could evolve into Plutinos or Centaurs, some 'reverse' evolution back to classical orbits would be inevitable, in which case it would be hard not to pollute the population with grey members. In contrast, the grey high-inclination objects, with perihelion distances merging with those of the scattered-disk objects, may have participated in dynamical evolution with the Plutinos and Centaurs.

An alternative theory would allow some dynamical exchange between populations of KBOs, but argue that some physical process ensures that surfaces become redder whenever objects are confined to the ragged edge of the Solar System beyond 40 AU. What this process could be is unclear. An object in the Kuiper belt is so far from the Sun that being at 38 AU rather than 42 AU would appear to make little difference to how much sunlight it receives. Clearly, photometric and orbital investigations of more KBOs are needed. Nonetheless, in this first attempt at combining the two, KBO studies have come of age. ■

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Behavioural ecology

Why are some males dull?

Tore Slagsvold

Birds vary extensively in plumage colour, both between and within species. The males of a species are usually brighter than the females, and older males tend to be brighter than younger birds. But males of the same age within a single population may also show great variety in colour. In such cases, the more brightly coloured males are usually socially dominant and are the mating partners of choice for females[1]. Why, then, hasn't natural selection eliminated the duller varieties?

On page 1000 of this issue, Greene and colleagues[2] suggest one explanation to the puzzle. They studied the lazuli bunting (*Passerina amoena*), a beautiful small finch of North America. Adult lazuli bunting males have turquoise-blue upper parts with a pale cinnamon colour across the breast and sides. Some yearling males are also brightly coloured, but many are dull brown and female in appearance, while still others have intermediate brightness (see the photographs on page 1000). Greene *et al.* show that both the brightly coloured and the dull yearling males sire more chicks than yearlings of intermediate colours. It seems that nature favours the extremes at the expense of those in between. This phenomenon is called disruptive selection, and has been seen only a few times in animals.

Why did the brightly coloured and dull birds succeed where those of intermediate colouring failed? Greene *et al.* found that both bright and dull yearling males occupied territories that included suitable shrub cover, whereas the intermediate yearlings settled on sparsely vegetated areas, where hardly any female would breed. Brightly coloured yearling males succeeded because they possessed the fighting ability necessary to occupy a good territory in the face of competition from adult males. In contrast, dull yearlings obtained a good territory because adult males tolerated their presence. Yearlings of intermediate colouring were too bright to be tolerated by adult males, but were not aggressive enough to fight their way to a good site.

The next question, then, is why adult males tolerated dull yearling males. One possibility is that those adults in possession of good territory had problems in recognizing the true sex of prospecting dull males. But no support for this 'female mimicry' hypothesis[3] has yet been found in the lazuli bunting[4]. Instead, the authors suggest that dull males were accepted because they represented no threat to the mating success of adult males, or to the number of chicks that adult males sired. The dull males might also act as a buffer against even brighter males, which females tend to prefer.

Because of this bias in female preference, adult males may even sire extra young by copulating with the mates of their drab male neighbours. Indeed, DNA 'fingerprinting' showed that the number of chicks sired by adult males was positively correlated with the proportion of immediate neighbours that were dull yearlings. So, both parties seem to benefit from this peculiar system — adult males by 'paternity insurance' and by siring extra young, and dull males by being allowed to occupy a high-quality territory and thereby obtain a mate. In addition, previous occupancy of a good territory helped drably coloured owners to obtain a high-quality territory in the subsequent year. The study provides rare evidence for cooperation between males — a territorial arrangement that

100 YEARS AGO

In the *Atti dei Lincei*, ix. 5… Prof. Grassi describes experiments carried out by a committee with the assistance both of the Italian Government and of the Mediterranean Railway Company, with a view to the prevention and cure of malaria in infected districts. The experiments were carried out in the plains about Paestum, which have long been known as a hotbed of malaria ("malaricissima" is the epithet Grassi applies to the region), and fell into two categories, namely, cure of the disease by the use of quinine, and protection from the bites of *Anopheles claviger* by the use of wire gauze as a covering for windows, doors and even chimneys of houses, the inhabitants of which were required to remain indoors from before sunset till after sunrise, or to go about covered with veils at night. By thus preventing mosquito bites, it was found that the malarial regions could be safely inhabited even at the season when the fever was at its height, and under such conditions the district might be made as healthy as any part of Italy.
From *Nature* 25 October 1900.

50 YEARS AGO

An article in the *South African Archaeological Bulletin* (5, No, 18; June 1950) makes sad reading. At Saulspoort, in the Bethlehem district, rock-shelter paintings occur and an important 'gisement' was identified… The work of excavation was begun; but during a period of the workers' absence intruders arrived who just 'hogged' the site and left a yawning pit where the section should have been. The problem of controls is a difficult one. Too rigid rules defeat their own object. It is, in a subtle way, the general interest in archaeology among all classes that makes the subject live and enables the few professionals to continue the study. Without this general interest the subject would in practice wither. A certain freedom to explore must therefore be given to the amateur; but, of course, stories such as this one are major tragedies. Perhaps the problem could best be tackled through the schools. If the young folk were taught to realize that Stone Age sites are not innumerable and should be respected, that 'hogging' sites is a crime and that excavations should only be attempted either under a competent excavator or after having already had experience in digging, then such grievous happenings as occurred at Saulspoort would no longer occur.
From *Nature* 28 October 1950.