

revealed that phagosomes fused with the ER during, or shortly after, pathogen engulfment at the cell surface¹¹. This was an important finding because a protein-translocation channel called the Sec61 complex is embedded in the ER membrane. Sec61 both imports newly synthesized proteins into the ER and exports proteins from it, targeting the proteins for degradation by the proteasome^{12,13}. So it was predicted that the Sec61 complex might be delivered to the phagosome after fusion with the ER. If true, it could be the missing link in the cross-presentation pathway — the transporter responsible for exporting exogenous proteins from the phagosome into the cytosol.

The two groups^{1,2} now provide evidence to support this hypothesis. Looking at phagosomes from dendritic cells¹ and macrophages², respectively, they showed that Sec61 is indeed present on the phagosome membrane. And both groups found that a fluorescently tagged version of the protein ovalbumin could be exported from the phagosome into the cytosol. But did protein export involve Sec61? To find out, Desjardins and colleagues looked at the export of the cholera toxin A1 subunit (CTA1). This protein moves from outside the cells to the ER and is then exported from the ER into the cytoplasm through the Sec61 channel^{14,15}. The authors observed that CTA1 could also be exported from the phagosome into the cytoplasm, which strongly suggests that, after Sec61 is delivered to the phagosome, it can still export proteins.

What happens to proteins once they have been exported from the phagosome? First, they must be turned into peptide antigens by the proteasome. Desjardins and colleagues showed that proteasomes are associated with the cytosolic side of the phagosome membrane. And both groups showed that TAP and the MHC class I molecules are delivered to the phagosomes and remain active. Their further analyses revealed that the peptide antigens are loaded onto MHC class I molecules inside the phagosome.

So it seems that after the exogenous proteins are exported from the phagosome through the Sec61 channel, they are degraded by the proteasome and the resulting peptide antigens are shuttled back into the phagosome by TAP. There, they are loaded onto MHC class I molecules on the inside of the phagosome membrane. The results confirm observations¹⁶ that the phagosome is a fully competent antigen-processing compartment for the MHC class I pathway.

The new studies provide strong support for a model of cross-presentation in which ER-phagosome fusion occurs. But they do not show that such fusion is necessary. Arguments have also been made that cross-presentation occurs only in cultured cells and might not be relevant in animals¹⁷. Now that a molecular mechanism governing cross-presentation has been proposed,

experiments to test the importance of this immunological process are certain to follow. But the debate on cross-presentation continues — to resolve it, the professionals will have to reveal all of their secrets. ■

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Plasma physics

Cosmic waves in the lab

Rod Boswell

An Alfvén-wave maser, a feature of atmospheric and astrophysical science, has been created in a laboratory, and opens the way for further Earth-bound investigations of cosmic phenomena.

In general, to be an observational astronomer is to be a spectroscopist, unravelling the workings of the cosmos through the varying wavelengths of radiation detected. Observations that began at optical wavelengths now extend to wavelengths ranging from hundreds of kilometres down to tens of nanometres, and satellites have also proved immensely useful in refining our image of the Universe. But, despite the assiduous measurements, the radiation is often produced, particularly at radio and X-ray wavelengths, by very complex processes that we struggle to understand. Nevertheless, a positive step has now been taken: in *Physical Review Letters*, J. E. Maggs and G. J. Morales report the resonant amplification of a typical astrophysical wave in their laboratory — an Alfvén-wave maser

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For some years, the aim of these authors has been a laboratory study of magneto-hydrodynamic turbulence — that is, turbulence in the interactions between a plasma and a magnetic field. The first step on the way is to create the basic element of the phenomenon, an Alfvén wave. Postulated in 1942 by Hannes Alfvén (*Nature* **150**, 405–406; 1942), an Alfvén wave is a low-frequency electromagnetic wave that can be generated in magnetized plasmas throughout the Universe. These waves are thought to be intimately involved in diverse phenomena, such as the precipitation of electrons through the atmosphere in the auroral regions that are connected with the dazzling northern and southern lights — and that can take out power distribution systems. Alfvén waves are also implicated in the heating



Figure 1 Unique facility — the Large Plasma Device at the University of California, Los Angeles. In a helium plasma inside this 19-metre-long column of magnets, Maggs and Morales have created an Alfvén-wave maser.

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of electrons in the solar corona and in the dynamics of solar flares.

In many situations, an Alfvén wave might not propagate freely but instead be trapped between reflective surfaces, for example between the Sun's photosphere and corona, in the intervening layer known as the chromosphere. This is analogous to light waves trapped between the mirrors of a resonant cavity of a laser. Laser action at microwave frequencies — a 'maser' — is a known astrophysical phenomenon. So Maggs and Morales set out to demonstrate a laboratory-based maser for Alfvén waves.

In general, laboratory experiments attempting to mimic the behaviour of the aurora, the solar chromosphere or more exotic cosmic objects have met with scepticism, if not outright hostility, in the astrophysical community. Ever since William Gilbert, in about 1600, used a magnetized sphere — a terrella — to explain the magnetic compass to Queen Elizabeth I, many brave attempts have been made in terrestrial laboratories to pin down exotic cosmic phenomena. Designing a terrestrial experiment to study Alfvén waves is certainly not a simple exercise — several conflicting scalings need to be satisfied if the sceptics are to be convinced. For example, it is extremely difficult to make a laboratory experiment long enough and wide enough to allow the wave to propagate in a natural way and not have it cramped up and its motion constricted. Also, the laboratory plasma needs to be created from a background gas, which will collide with the plasma and damp out waves. This really does not exist in the vacuum of space.

Maggs and Morales' experiment was performed using the Large Plasma Device (at the Basic Plasma Science Facility at the University of California, Los Angeles), a unique facility with 90 magnetic-field coils surrounding a column of helium plasma 19 m long (Fig. 1). At one end of the column, a pulsed voltage draws electrons out of a thermionic cathode towards an anode made of copper mesh, located 55 cm away. The accelerated electrons drift into the 19-m vacuum chamber and strike neutral, low-pressure helium gas, generating a plasma that is more than 50% ionized.

The resonant cavity is formed by the space between the cathode and the semi-transparent anode: inside, Alfvén waves are spontaneously amplified, but they seep through the anode into the main plasma region, in which they can be detected. The magnetic field, the plasma density and the degree of ionization need to be manipulated so that the ion cyclotron frequency (the frequency with which the positively charged ions rotate around the magnetic field) is much greater than the ion neutral collision frequency (the rate at which plasma collides with the background gas). This means that the Alfvén waves are not damped in the

plasma column. The Large Plasma Device is one of the very few experimental devices in the world in which such a happy combination of operational parameters can be achieved.

Using small magnetic loop antennae inserted into the plasma column, Maggs and Morales measured a broadband noise spectrum with a peak at 60% of the ion cyclotron frequency, and an upper limit of 70% of that frequency defined by the length of their resonant cavity. This noise was identified as a type of Alfvén wave called a shear wave. The *pièce de résistance* of the experiment was their observation of spontaneous amplification of the resonant mode (at 60% of the ion cyclotron frequency) for selected values of the confining magnetic field and plasma current. Maggs and Morales describe the phenomenon as "spectacular flares of

extremely coherent signals [that] develop at low magnetic fields and extremely high plasma currents" — a little reminiscent of sci-fi writer E. E. 'Doc' Smith perhaps, but nevertheless explosively descriptive of the growth and subsequent decay of their Alfvén maser.

Maggs and Morales' experiment demonstrates the great potential for carrying out experiments of cosmic importance in the laboratory. It will no doubt be a boon for the many theoreticians wishing to test their theories of magnetohydrodynamic turbulence and of Alfvén-wave-induced heating of stellar atmospheres. ■

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Stem cells

To be and not to be

Haifan Lin

It has long been proposed that stem cells function by dividing to generate an identical daughter cell and a cell that becomes more specialized. New work illustrates such asymmetric division and its molecular basis.

Stem cells have the unique ability to perpetuate themselves while continually replenishing tissues throughout the life of an organism. This ability has long been attributed to a distinctive asymmetry in their division, such that when a stem cell divides, it gives rise to both an exact copy of itself and a new type of cell that will differentiate into mature cells of the tissue. This asymmetry hypothesis — reflecting a 'to be and not to be' fate decision — can be traced back to the embryologist E. B. Wilson and his contemporaries more than a century ago. But direct evidence for asymmetric division has so far been reported in only a few well-defined stem-cell systems. In these cases, the molecular mechanisms that regulate asymmetric division have also been explored. Work by Yamashita and colleagues¹, reported in *Science*, now showcases an elegant example of asymmetric division, and identifies key new molecules involved in the process.

A hefty roadblock to the study of how stem cells divide has been their elusive nature. Stem cells are rare, and physically resemble their differentiating daughter cells, so they are difficult to recognize in a tissue. It is fair to say that even today — and despite rapid progress in stem-cell research — the identity of stem cells in most tissues remains a matter of debate. (Embryonic stem cells, which are well characterized, exist before tissues form.) This 'identity crisis' has been overcome in only a few cases, such as neuroblasts and germline stem cells in the fruitfly *Drosophila*,

and ventricular-zone progenitor cells in the brains of mammalian embryos^{2,3}.

In flies, a neuroblast divides asymmetrically (Fig. 1a, overleaf) to renew itself and to produce a smaller ganglion mother cell², which goes on to generate specific nerve cells. In fly ovaries, germline stem cells are always in contact with a subset of signalling cells called cap cells⁵. These stem cells also divide asymmetrically, producing a stem-cell daughter that retains contact with the cap cells, and a differentiating daughter that is displaced one cell away⁴ (Fig. 1b). Such oriented asymmetric division has also been demonstrated by electron microscopy for germline stem cells in the fly testis⁵, where the signalling cells are called hub cells (Fig. 1c). Yamashita *et al.*¹ have used immunofluorescence microscopy to observe a large number of stem-cell divisions (more than 500) in fly testes, nicely confirming the orientation and asymmetry of division.

The key question here is: what tells one daughter cell to be a stem cell and the other not to be? For fly neuroblasts, the solution seems to depend solely on the cell itself². The neuroblasts are derived from embryonic epithelial-type cells, and inherit their polarity, with one end being 'apical' and the other 'basal'. This allows molecules that determine cell fate to be segregated along the apical-basal axis. The mitotic spindle (the structure that separates chromosomes during division) is also oriented along this axis, such that the plane of division is perpendicular to the