plants with low levels of RIN4. Reductions in RIN4 levels also cause reductions in RPM1 levels and (for as yet unknown reasons) resistance to both *P. syringae* and, intriguingly, the unrelated fungus-like *Peronospora parasitica*.

All of which suggests that RIN4 sits at a crossroads between susceptibility and disease resistance, and that RPM1 guards *A. thaliana* against pathogens that use AvrRpm1 and AvrB to manipulate RIN4 activity[3] (Fig. 1). So, when susceptible plants are infected by *P. syringae*, the Avr proteins interact with RIN4, induce its phosphorylation, and increase its concentration, thereby inhibiting basal defences and leading to susceptibility. But in plants that are resistant to *P. syringae*, these manipulations are somehow sensed by RPM1, which launches a local cell-death programme that leads to resistance.

So Mackey *et al.*[3] have shown how one R protein and two Avr proteins work at the molecular and cellular levels, causing either disease or the hypersensitive response according to the balance of power between the proteins. In so doing, the authors have answered the questions (at least for this set of proteins) of how an R protein can sense the presence of its cognate Avr proteins — through their manipulation of RIN4 — and what the Avr proteins do. It is known that some fungal and bacterial Avr proteins function in susceptible plants as 'virulence factors', thought to be required for maximum virulence of the pathogen[11]. Mackey *et al.*[3] have revealed that Avr proteins can do this by increasing the activity of a plant defence inhibitor.

This study should give a boost to those studying the molecular interactions between plants and microbes. It is likely that the direct interaction shown for the rice and rice-blast fungus proteins[6] is the exception, not the rule; mechanisms like that described by Mackey *et al.*[3] may be more common. Many labs are now hunting for virulence-related targets of Avr proteins, akin to RIN4, in other model gene-for-gene systems. It will be interesting to see whether different pathogens use the same targets. For instance, if the *P. parasitica* Avr proteins (which have not yet been identified) also interact with RIN4, that might explain why plants that are susceptible to *P. syringae* are also susceptible to *P. parasitica*. Another question is whether different Avr proteins from the same pathogen are recognized by the same plant protein, as are AvrB and AvrRpm1. I anticipate that most pathogens have a set of Avr proteins that work together to afford full virulence.

Finally, as mentioned above, some Avr proteins — such as those from the tomato pathogen *Cladosporium fulvum*[8] — are detected by LRR motifs on the outside of plant cells, rather than inside. Might a similar guard mechanism protect against pathogens like these, too? Support for this idea comes from the finding that the hypersensitive response of tomato to one *C. fulvum* Avr protein (Avr2)[12] requires not only the cognate R protein (Cf-2) but also a further tomato protein (Rcr3), found outside cells, which might be a virulence-related target[13]. Perhaps the R protein protects this target from the pathogen protein. Molecular guards may be widely used to prevent plant proteins from being subverted for pathogenic purposes[4]. ■

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Relativity

Testing times in space

Steve K. Lamoreaux

We take for granted that physical 'constants', such as the speed of light, are fixed values. But they might not be, and experiments in space may allow us to investigate this possibility.

A basic assumption of Einstein's theory of relativity is that the fundamental physical laws and parameters do not depend on the position, orientation or uniform velocity of the laboratory in which they are measured — a property generally known as Lorentz invariance. Relativity has been tested, implicitly and explicitly, in countless experiments; as yet, no failure of the theory has been observed. But most explicit tests have been confined to laboratories on Earth. In *Physical Review Letters*, a theoretical analysis by Bluhm *et al.*[1] shows that experiments in space — some already planned for the International Space Station — could offer better sensitivity, as well as extending the range of tests that could be performed.

Some of the most exacting tests of relativity have involved atomic clocks. These 'tick' by electrons moving between energy levels emitting a photon with a certain frequency. The tests compare the tick rates of two different atomic clocks as a function of their orientation and velocity through space. The idea is that, if the two clocks are based on different types of energy-level transitions, any failure of Lorentz invariance would show up as a relative shift in the two frequencies of the clocks, because the physical 'constants' governing the ticks of the clocks would not actually be constant, but would change with the clocks' orientation and velocity.

In Earth-based experiments, the orientation and velocity of the clocks are determined by the Earth's rotation and revolution about the Sun, and by the motion of the Solar System relative to the Universe as a whole. Typically, the differential clock frequencies are measured as a function of time. Given the Earth coordinates of the clocks, together with the time and date, the time-dependent orientation of the clock can be determined. Then, any violation of relativity can be correlated with some aspect of orientation or velocity.

An example of a clock comparison experiment is to test whether the speed of light, c, is a universal constant — is there a limiting speed for matter, c_m, that is different from the speed of light? For instance, my colleagues and I have sought[2] a difference in the values of these numbers by comparing the behaviour of two atomic nuclei, ^{199}Hg and ^{201}Hg. In an applied magnetic field, the magnetic-moment vector of a nucleus precesses about the field direction at a particular frequency (this process is also the basis of magnetic resonance imaging). The ^{199}Hg nucleus is spherical and so its orientation in space (usually defined relative to distant, 'fixed' stars) does not affect the precession frequency. But the ^{201}Hg nucleus is egg-shaped — its lack of spherical symmetry means that the angle between its velocity vector and its magnetic moment becomes important; and if c_m is not identically equal to c, a shift in the precession frequency of ^{201}Hg compared to that of ^{199}Hg appears. In this Earth-bound experiment, no difference between c_m and c was detected, implying that if such a difference exists, then $1 - c_m/c < 10^{22}$ — a rather astoundingly accurate limit.

This experiment is prototypical of many of the experiments described by Bluhm *et al.*[1], and we can question whether there would be an advantage to performing it in space. Among the advantages that Bluhm *et al.* specifically address is the ability to change the orientation and velocity of space-borne clocks to arbitrary directions; orientation changes could also be made more rapidly than the once-per-day change for an Earth-based experiment (which would avoid problems due to slow drift in the clock frequencies). In fact, in the specific case of the Hg-nuclei experiment, there would only be about a factor of two to be gained if it were performed in space. But for other experiments there could be greater advantage; moreover, some tests that are impossible on Earth could be done in space.

A parameter that could be significantly varied in a space-borne experiment is the gravitational potential that the clocks are subjected to. On the basis of astronomical observations it has been claimed[3] that the fine-structure constant α (which characterizes the strength of the electromagnetic interaction between photons and charged particles such as electrons) is time-dependent; and a possible dependence of α on the gravitational force has been suggested[4] in the context of string theory — an abstract mathematical theory in which elementary particles are modelled as standing waves in a closed string loop, and which is generally beyond the reach of laboratory experiments. Whether α is dependent on gravity could be one of the few testable predictions of string theory.

A NASA team has proposed[5] a measurement of the effect of the gravitational force on α. The project, called the SpaceTime mission, would send a spacecraft carrying three atomic clocks (Hg^+, Cd^+ and Y^+ ions stored in three separate radiofrequency traps) to within four solar radii of the Sun. The third clock can be thought of as an on-board observer that allows the principal data analysis to be done in real-time on the spacecraft. As the craft approaches the Sun, it will experience an enormous gravitational potential for a few hours. The expected sensitivity to any change in α is around one part in 10^{16} — more than sufficient to test the string-theory prediction of one part in 10^{10}.

Could Earth-based laboratory experiments ever match this precision? String theory also predicts an annual modulation $\Delta\alpha/\alpha \approx 2\times10^{-14}\ \mathrm{yr}^{-1}$ because the Earth's orbit around the Sun is not circular. The most accurate laboratory tests[6,7] have achieved $\Delta\alpha/\alpha < 4\times10^{-14}\ \mathrm{yr}^{-1}$, so the predicted effect is still unobservable. But there is a proposal[8] to measure $\Delta\alpha/\alpha$ with sensitivity better than $10^{-15}\ \mathrm{yr}^{-1}$, which is at the level of the astronomically observed variation. This level of sensitivity would provide an Earth-based laboratory test of string theory — but still with 10,000 times less sensitivity than SpaceTime.

As Bluhm *et al.*[1] point out, space-based experiments have greater potential to discover new types of gravitational effects. For example, the SpaceTime clock-comparison experiment will be able to probe new gravitational physics far beyond what can be done in a terrestrial laboratory. ■

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Developmental biology

An arresting activity

Nicholas S. Duesbery and George F. Vande Woude

Vertebrate eggs pause at a crucial stage in their development, starting again only after being fertilized by sperm. Another component of the activity that ensures this arrest has been identified.

The process of vertebrate egg development consists of oocyte growth coupled with specific pauses at various stages of maturation. The final pause is known as the metaphase II arrest, from which eggs are released only after being fertilized by sperm. The cellular activity that ensures this arrest has been known for 30 years by the alias 'cytostatic factor' (CSF), ever since Masui and Markert[1] showed that egg development is arrested by CSF before fertilization. Subsequently it has been established that a signalling pathway involving the Mos protein is a key component of CSF activity. However, inactivation of CSF and the Mos pathway occurs after fertilization triggers the resumption of development, suggesting that as-yet-uncharacterized elements of CSF are required to maintain the developmental arrest. On page 850 of this issue, Reimann and Jackson[2] define a new, Mos-independent component of CSF, which regulates the degradation of proteins required for developmental arrest in eggs. Their work provides new insight into the regulation of CSF, and raises questions about the contribution of the Mos pathway to CSF activity.

There are two processes by which cells normally divide: mitosis and meiosis. During mitosis, cells replicate their chromosomes (producing a '4*n*' DNA content) and segregate them equally to each of two daughter cells (which are therefore '2*n*'). By contrast, during meiosis of female germ cells (oocytes), the replicated (4*n*) chromosomes undergo two successive 'reductive' divisions — separating first a set of chromosomes (2*n*) in the first polar body and second a set of replicated chromosomes after fertilization — to generate a haploid set (1*n*) in the egg. By contrast, male meiosis (spermatogenesis) proceeds through the first and second meiotic divisions to produce four (1*n*) germ cells (sperm). Progression through female meiosis (oogenesis) to produce one unfertilized egg occurs in a stepwise fashion in response to defined extracellular cues. In vertebrates, female germ cells pause just before the first meiotic division and undergo an extended period of growth, which is necessary to accumulate resources for early embryonic stages of development. Having accomplished this, oocytes become competent to respond to hormonal signals and resume meiosis.

Resumption of meiosis is accompanied by the activation of maturation-promoting factor (MPF; Fig.1) — a complex consisting of a regulatory protein, cyclin B2, and a catalytic protein, Cdc2. The activity of MPF is controlled by the association of these proteins with each other, and by two competing enzymes, the Myt1 kinase and Cdc25, that either add or remove phosphate groups from Cdc2. Active MPF is required for dissolution of the envelope surrounding the nucleus and formation of the 'spindle' apparatus that will segregate homologous chromosomes.

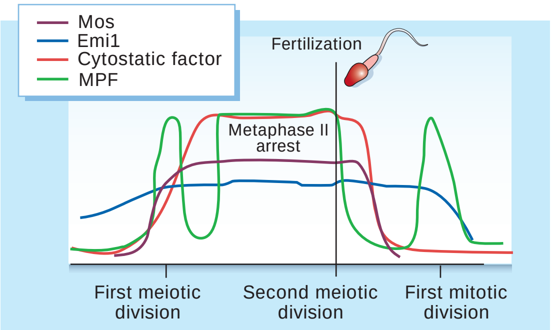

Figure 1 **The ups and downs of protein activity during meiosis in vertebrate eggs. The activity of maturation-promoting factor (MPF) is carefully controlled to ensure that oocytes carry out the first division of meiosis (as MPF levels first peak), and then arrest before fertilization triggers the second division (when MPF levels are again high). Cytostatic factor (CSF) is an activity that maintains high levels of MPF in arrested oocytes. The molecules that make up CSF have been a mystery, although a role has been proposed for the Mos protein[3]. Reimann and Jackson[2] show that the Emi1 protein can block the destruction of a component of MPF (cyclin B2) and so keep MPF levels high during the arrest. Emi1 may work with Mos to induce and maintain this arrest.**