sufficient to turn off transcription of their own genes. The repressor proteins have a limited lifespan so they eventually decay, and a new wave of repressor gene transcription commences. The properties of the system have evolved to generate oscillations with a period of about 24 hours[6,7]. All known components of animal circadian clocks have homologues in both *Drosophila* and mouse[1]. These include the transcriptional activator Clock, the putative transcriptional repressors Timeless and Period (three isoforms in the mouse: mPer1, mPer2 and mPer3), and blue-light receptors called cryptochromes (two isoforms in mouse: Cry1 and Cry2)[8–11].

The function of cryptochromes in animal circadian clocks is enigmatic. In plants and *Drosophila*, cryptochromes clearly participate in the light entrainment of circadian clocks, but in the mouse their function as light receptors is still controversial[8,10,12]. Nonetheless, mouse cryptochromes are uncontested components of the mammalian pacemaker, as mutant mice with defects in both cryptochrome genes, *cry1* and *cry2*, lack circadian rhythms when kept in constant darkness and display constitutive expression of the genes *mper1* and *mper2* (refs 8,10,13). The photoreceptors used to entrain peripheral zebrafish clocks are unknown, but Whitmore *et al.* may be able to use their *in vitro* system to test whether cryptochromes are valid candidates. The recording of action spectra may be the first step towards this goal.

In mammals, peripheral clocks are synchronized by different mechanisms from those in *Drosophila* and zebrafish (Fig. 1). *Drosophila* and zebrafish are both small and semitransparent, and their peripheral oscillators can be directly light-entrained by light receptors[2,5,9,11] (such as cryptochromes in *Drosophila*). In mammals, which are opaque, this mechanism is obviously not feasible for setting the time in peripheral oscillators. In these organisms, light adjusts the circadian pacemaker in part of the brain called the suprachiasmatic nucleus through signals from the eyes, and this master pacemaker then synchronizes peripheral clocks using chemical signals[14]. Curiously, neither retinal rods nor cones are required for the light entrainment of mammalian clocks, so the light-capturing cells and their photoreceptors remain to be identified[15,16]. ■

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Physics

Brane new worlds

Jerome Gauntlett

It is common sense that at everyday scales we live in a world with three large spatial dimensions. Lisa Randall and Raman Sundrum have recently made the bold suggestion in *Physical Review Letters*[1] that an extra dimension of infinite extent may supplement the three spatial dimensions we observe. Not only do they claim that this can be entirely consistent with current observations, they also argue in a second paper that closely related scenarios could hold the key to some fundamental issues in attempts to unify particle physics with gravity[2].

The idea that the four space–time dimensions that we observe (three space and one time) could be supplemented by extra dimensions was first put forward by Theodor Kaluza and subsequently developed by Oskar Klein in the 1920s. The motivation then was to achieve a unification of Maxwell's theory of electromagnetism and general relativity, which is Einstein's theory of gravity. They considered an extra fifth dimension curled up in a small circle that would be undetected at much longer length scales. Although Kaluza and Klein's model turns out to give wrong predictions and so cannot be a correct description of the real world, the beautiful idea of extra dimensions with finite extent ('compact dimensions') has become a central component of string theory — the leading candidate to unify all of the known forces of nature.

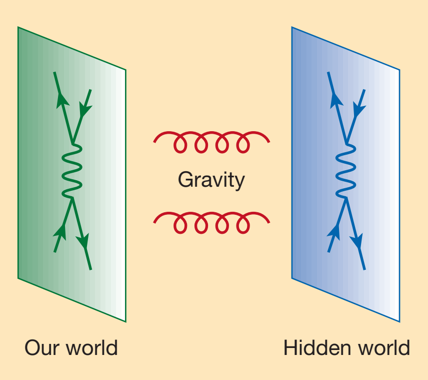

Figure 1 **In 'brane-world' scenarios it is proposed that our world is a three-brane propagating within an ambient space–time of higher dimension. Particle physics is confined to the brane and interacts with the extra dimensions and other 'hidden' three-branes through gravitational interactions. Randall and Sundrum[1,2] argue that it is possible to have an extra dimension of infinite extent if the ambient space–time is curved in a particular way.**

Some of the ingredients in the Randall–Sundrum papers were in fact suggested by developments in string theory. String theory was originally conceived of as a theory of oscillating objects with one spatial dimension, or strings. It is now known that in order for string theory to be mathematically consistent it must also include a rich spectrum of extended objects of higher dimension: 'membranes' with two spatial dimensions, 'three-branes' with three, and so on. Understanding the properties of these branes is very much an active area of research.

One of the key ideas in the papers by Randall and Sundrum is that the four-dimensional space–time we observe at everyday scales is actually the evolution in time of a three-brane moving through an ambient space–time of higher dimension (Fig. 1). In such 'brane-world' scenarios, particle physics is confined to the brane but the particles can interact with the ambient space–time through gravitational interactions. When all the extra spatial dimensions of the ambient space–time are compact, these interactions can be so weak as to have escaped detection by experiments thus far.

Before the paper by Randall and Sundrum[1] it seemed almost obvious that the ambient space–time in which the three-brane lives should not be of infinite extent. In the simplest example with a single, flat, infinite extra dimension, Newton's law of gravity would be modified: the force between two masses on the three-brane would be inversely proportional to the cube, not the square, of the distance between them. The surprising observation made by Randall and Sundrum is that if the extra dimension were infinite, and if the embedding space–time has a very particular curvature, then it is possible for the predicted corrections to Newton's law to be consistent with experimental results.

This remarkable insight has stimulated a flurry of subsequent papers developing the ideas and determining the implications for cosmology and particle physics. Directions being pursued include verifying in more detail how four-dimensional general relativity emerges on the three-brane, and studying ways in which the framework can be embedded in string theory.

The implications for particle physics are particularly exciting because other closely related ideas published by Randall and Sundrum[2] may provide a resolution to the 'hierarchy problem', one of the most important issues in going beyond the Standard Model of particle physics. The Standard Model is a fantastically successful theory of three of the forces of nature: electromagnetism, the weak nuclear force and the strong nuclear force. It unifies electromagnetism and the weak nuclear force into the electroweak force at characteristic length scales of around 10^{-17} cm (roughly the limit of the scales probed by current acceler-ators). There are strong arguments that unifying particle physics with the fourth known force, gravity, into a theory of quantum gravity (string theory, say) will have a characteristic length scale of around 10^{-33} cm. It is very difficult to account for such a vast gap between these two scales without fine tuning the theoretical parameters to an extraordinary extent. This is the hierarchy problem.

The conventional approach for dealing with this problem is to invoke a new symmetry between matter and forces called supersymmetry, which could be detected by the next generation of particle accelerators. An alternative approach (which might also include supersymmetry) is to assume that our world is a three-brane. The first proposals[3,4] along these lines considered a single three-brane embedded in a space–time with at least two extra dimensions that are compact and flat. These dimensions could be as large as 1 mm without violating known experiments. In a string theory setting it is possible that the string length scale could be just below that probed by current accelerators, rather than about 10^{15} times smaller as previously supposed. These schemes are fascinating although they do introduce another hierarchy that needs explaining.

By contrast, Randall and Sundrum suggest that a curved ambient space–time with one extra dimension might provide a better setting. They consider a slab of this space–time bounded at each end by a three-brane. (Slabs of space–time bounded by branes were first introduced in string theory in ref. 5.) One of these branes is our world and the other is a 'hidden' world. Particles on our three-brane interact with the extra dimension and the hidden world through gravitational interactions. By assuming that the distance between the branes is very small, Randall and Sundrum showed that these interactions are weak enough to be consistent with experiment. They also showed how the hierarchy of scales on our three-brane can be accounted for in a fascinating way by the curvature of space–time without introducing any extra hierarchy.

The Randall–Sundrum papers do not provide a detailed model of particle physics beyond the Standard Model. Indeed there are considerable difficulties to be overcome to achieve this goal. But they have provided exciting alternatives to conventional ways in which people thought the unification of particle physics and gravity might occur. Particle physicists, string theorists and cosmologists are currently devoting much effort to developing ideas and deriving predictions that could be tested by the next generation of particle accelerators and gravity experiments. If Randall and Sundrum are on the right track, there could be exciting experimental evidence in the near future. ■

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Cognitive neuroscience

Imaging in the fourth dimension

Thomas Elbert and Andreas Keil

The 1990s, the decade of the brain, saw enormous developments in neuroimaging. Structural details of the brain can now be reconstructed non-invasively as three-dimensional images; and small, task-related changes in cerebral blood flow, even in the deepest recesses of the brain, can be seen. The principles of the functional organization of the brain are being uncovered, and it seems that not only initial processing stages but also complex aspects of perception and cognition can be mapped onto brain structures[1,2]. Nevertheless, cognitive neuroscientists find themselves in an odd, but perhaps not surprising, situation. As the number of studies increases, so does the number of conflicting results. On page 80 of this issue, Patel and Balaban[3] provide an example of what has been missing in neuroimaging — a new approach that adds time as the fourth dimension.

Usually, three-dimensional images of cerebral blood flow, metabolic changes or the activity of populations of neurons are

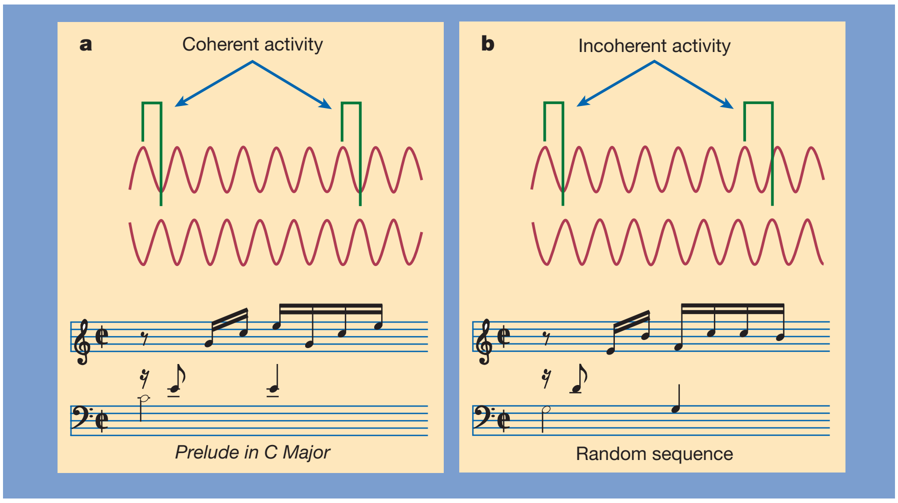

Figure 1 **Music and random notes produce different neural responses. Oscillatory brain activity evoked by repetitive auditory stimulation shows different temporal relationships between widely separated recording sites, depending on stimulus properties.** a, **Patel and Balaban[3] found that predictable, melody-like tone sequences are associated with coherent activity and more constant phase lags of oscillatory responses recorded from distant channels. This synchronization of brain activity in distant areas (the traces shown above the music) may reflect perceptual integration. The example shown here, Bach's *Prelude in C Major*, should produce high coherence.** b, **In contrast, a random sequence of tones showing identical rhythmic structure but no melody should produce incoherent activity of distant channels, with less synchronization between brain regions.**