have been strongly selected for because of its importance for maintaining fertility.

It is clear that expression of tissue-specific self antigens in the thymus is sufficient to prevent autoimmunity (*12, 13*). The straightforward mechanism that would explain why aire-deficient mice develop disease is that pathogenic self-reactive T cells were not eliminated by clonal deletion. However, further studies are needed to understand how tissue-specific T cells escaped tolerance induction in the periphery, and to identify the events that trigger autoimmunity in the aire-deficient mice. Another explanation concerns immune regulatory cells that may be generated by self proteins in the thymus (*14*). The absence of these regulatory cells in aire-deficient mice or humans would provide an environment that encourages the development of autoimmunity (*15*). Although further studies are needed, current evidence suggests that the aire-deficient mice develop an autoimmune profile similar to that of mice depleted of regulatory cells [reviewed in (*11*)]. Further exploration of mice that lack aire will provide exciting insights into the mechanisms and initiating events of human autoimmune disease.

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PERSPECTIVES: COSMOLOGY

A New Window to the Early Universe

Eric Hivon and Marc Kamionkowski

The big news at the recent Cosmo '02 workshop in Chicago (*1*) was the announcement of the first detection of polarization in the cosmic microwave background (CMB), the 2.726 K radiation left over from the big bang (*2*).

In 1968, Rees predicted that the CMB must be polarized if it is a relic from the early universe (*3*). Ever since, astronomers have sought observational evidence. The race for detection heated up after precise measurements of temperature fluctuations (*4–8*) provided increasing confidence in our ability to understand the CMB. The new discovery, reported by the Degree Angular Scale Interferometer (DASI) collaboration, not only confirms our theoretical grasp of the CMB, but also opens a whole new window to the early universe.

Early-universe cosmology merges the search for new laws of fundamental physics, beyond the standard model of particle physics and Einstein's gravity, with the search to understand the origin and evolution of the universe. The mean thermal energies of the particles that filled the universe microseconds after the big bang greatly exceed those accessible with the most powerful terrestrial particle accelerators. The early universe thus provides a test bed for new ideas in ultrahigh-energy physics—if it has left a trace in today's universe, the big bang's cosmic debris. Fortunately, a truly pristine cosmological relic exists: the CMB.

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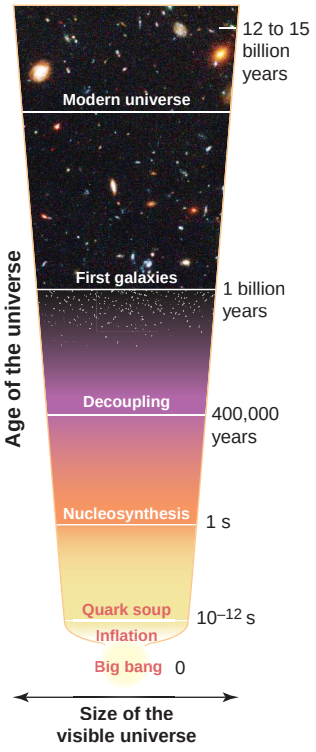
To a good approximation, the temperature of the CMB radiation is the same in all directions in the sky. However, at the level of 1 part in 10^5, there are small variations. The CMB radiation was emitted ~14 billion years ago when electrons and nuclei first combined to form atoms, at a time when the universe was ~400,000 years old. Thus, the angular temperature variations reflect variations in the properties (such as density, pressure, temperature, and velocity) of the primordial universe.

The temperature patterns at the CMB surface of last scatter were probably inscribed even earlier, just fractions of a microsecond after the big bang. Particle theories suggest that in the extreme temperatures that existed then, gravity may have briefly become a repulsive, rather than attractive, force. The enormously accelerated expansion during the ensuing period of "inflation" can explain the remarkable smoothness of the CMB and produce the primordial mass inhomogeneities imprinted in the CMB temperature.

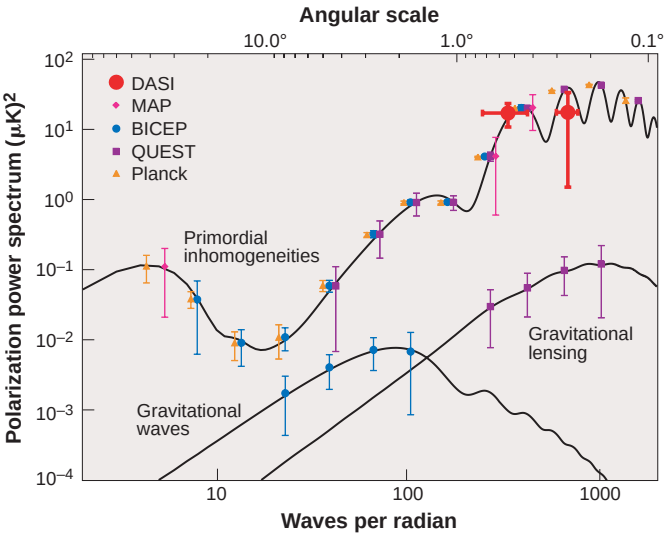
Existing CMB temperature maps allow the temperature power spectrum, which quantifies the size distribution of hot and cold spots, to be determined. Comparison with predictions of inflation models for primordial inhomogeneities then provides constraints for several cosmological parameters (such as the mass density, the geometry of the universe, and its expansion rate). Moreover, the oscillatory pattern seen in the CMB power spectrum (*9*, *10*) confirms that the primordial inhomogeneities are consistent with inflation.

The CMB polarization contains yet more cosmological data than that provided by the temperature maps alone. Most light is unpolarized (the orientation of the oscillating electric field that makes up the electromagnetic wave is random). But light can also be linearly polarized (the field is more likely to oscillate in a given direction). In the CMB, the polarization indicates a direction at the surface of last scatter. However, the polarization amplitude is very small—just ~7% of the temperature-fluctuation amplitude for the polarization from primordial inhomogeneities.

Inflationary models make many predictions for the statistical properties of the polarization (*11*).



From smooth to structured. The big bang may have been followed by a period of rapid inflation, during which the resulting "soup" of particles coalesced into nucleons and lighter elements. Matter and radiation eventually became decoupled, the former gravitationally clumping into the structure of the modern universe and the latter yielding the microwave background we see today. The seeds from which galaxies grew should be apparent in the variations in the radiation background.



Current and future polarization data. The polarization power spectrum determines the correlation of polarization over patches of sizes indicated on the top axis. (Top curve) Prediction for the polarization from primordial inhomogeneities produced by inflation. The large-angle bump in this curve is the enhancement from early star formation. (Lower curves) Inflationary gravitational-wave and gravitational-lensing signals. These can be distinguished from the larger mass-inhomogeneity signal with geometric properties of the polarization. DASI data points are shown in red. Future experiments will go beyond DASI in sensitivity to detect some of these other signals. We show the data points that experimentalists hope to achieve with some of these new experiments (*17*).

The current DASI results (see the figure) are not nearly precise enough to test these predictions fully, but they are a dramatic first step. They detect the polarization with high confidence (5σ), and the measured amplitude is consistent with that expected.

Far more will be learned with more precise polarization maps. First, the polarization will provide much more precise velocity maps because it is due primarily to the velocity at the surface of last scatter. In contrast, the temperature pattern is due to a combination of the mass inhomogeneity and velocity. Second, the polarization will provide a test for inflation theories, which predict a unique polarization pattern (*12*, *13*). Third, polarization might map the mass distribution in the more recent universe through the effects of weak gravitational lensing (*14*). The galaxies between us and the surface from which the CMB radiation was emitted induce a gravitational bending of light that leads to an identifiable distortion to the CMB polarization pattern. Finally, polarization with large coherence patches is generated by rescattering of CMB radiation from intergalactic debris produced by the onset of star formation.

DASI has ended a 34-year quest to detect the CMB polarization, sounding the starting gun for a new race to peer further back in time, with more precision than ever before. Many more CMB polarization experiments are in progress or planned. NASA's recently launched Microwave Anisotropy Probe (MAP) (*15*) should detect the large-angle polarization induced by early star formation. This should be followed by increasingly precise ground and balloon experiments leading to launch of the European Space Agency's Planck satellite (*16*) in 2007. If the recent past is any indication, studies of the CMB will continue to advance cosmology, even after Planck.

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PERSPECTIVES: NEUROSCIENCE

GABA Becomes Exciting

Rüdiger Köhling

Epilepsy is one of the most common neurological diseases, affecting 1 to 2% of the world's population (*1*). It is caused by a state of neuronal hyperexcitability, or more precisely, by massive hypersynchronous discharges from large numbers of neurons in the brain (*2*). Numerous studies have sought to unravel the mechanisms underlying epileptic seizures. Despite a consensus view that voltage-gated ion channels controlling cell excitability and synaptic processes responsible for communication among neurons are involved (*3*), the specific events leading up to epileptic discharges are largely unknown. On page 1418 of this issue, Cohen *et al.* (*4*) shed light on the underlying causes of epileptic seizures with their in vitro study of brain tissue from 21 patients with temporal lobe epilepsy. Their findings suggest that interneurons producing the inhibitory neurotransmitter GABA together with aberrantly behaving excitatory pyramidal neurons in the hippocampal region can precipitate epileptic seizures.

Pharmacological interventions for the treatment of epilepsy rely principally on drugs that reduce cellular excitability (for example, by blocking voltage-gated channels) or that modulate synaptic communication, usually by enhancing the activity of inhibitory GABA receptors. However, a dampening of intrinsic neuronal activity or a restriction of synaptic communication may impinge upon the normal functioning of the brain, resulting in unacceptable side effects. Thus, it is critical that therapeutic interventions be targeted to specific neuronal subpopulations, such as "pacemaker" neurons that initiate spontaneous discharges, or to a particular subtype of excitatory or inhibitory synapse. In this context, two important questions must be addressed: Are there distinct neuronal populations that initiate epileptic discharges? And if so, what type of synapse coordinates synchronization of these discharges?

Three principal factors are thought to contribute to the initiation of epileptic discharges. The first is a population of excitatory neurons with the ability to generate so-called intrinsic bursts, that is, barrages of action potentials. The second is an increase in glutamatergic (excitatory) synaptic transmission particularly via recurrent connections; the third is a decrease in the efficacy of GABA-mediated (inhibitory) connections (*2*, *3*). It has been proposed that an "imbalance" between excitatory and inhibitory synaptic transmission that

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