50 YEARS AGO

The July issue of *Man* contains several articles of general interest … A. D. Lacaille illustrates a number of very large British Acheulean coups de poing, and a puzzling rock-carving from the Val Camonica is discussed by Dr. Anati of Paris. The site is near where the great glacial valley debouches on to the north Italian plain, and many rock-carvings there have been known for a long time. They include animals and humans treated in a conventional manner somewhat recalling the Copper Age paintings of Las Figuras in south-west Spain. The little group in question seems to indicate either a phallic or a ritual scene. The author suggests a date for this art group somewhere towards the start of the first millennium B.C. Is not this somewhat too early?
From *Nature* 10 December 1960.

100 YEARS AGO

The Anatomy of the Honey Bee. By R. E. Snodgrass. — In this modest pamphlet the author has given to entomologists an original, trustworthy, and excellently illustrated account of the structure of the honey bee … Many volumes have been written on the honey bee, yet no surprise can be felt that Mr. Snodgrass has been able to add new points to our knowledge and to correct errors in the work of his predecessors … He expresses scepticism as to certain positive statements that have been made on controverted details of physiology and reproduction; for example, "concerning the origin of the royal jelly or of any of the larval food paste … we do not know anything about it." There is a present-day tendency unduly to disparage the results obtained by former workers, and such a statement will strike many readers as extreme.
From *Nature* 8 December 1910.

COSMOLOGY

Hydrogen was not ionized abruptly

When and how the first stars and galaxies ionized the primordial hydrogen atoms that filled the early Universe is not known. Observations with a single radio antenna are opening a new window on the process. SEE LETTER P.796

JONATHAN PRITCHARD & ABRAHAM LOEB

Four hundred thousand years after the Big Bang, the Universe had cooled sufficiently for hydrogen atoms to form. Hundreds of millions of years later, the first stars and galaxies had produced ionizing ultraviolet radiation that broke the hydrogen atoms into their constituent electrons and protons. This process, termed reionization, marks a major cosmological phase transition. When and how rapid this transition was are important open questions[1]. On page 796 of this issue, Bowman and Rogers[2] implement a new technique that allows them to rule out models in which reionization occurs abruptly.

Their approach uses a simple radio antenna operating at low frequencies to measure the absolute radio intensity of the sky. Cosmic hydrogen atoms can emit or absorb light with a wavelength of 21 centimetres, a signal that is stretched (redshifted) on its way to Earth through the expansion of the Universe[3]. The redshifted 21-cm hydrogen signal, which falls within the radio regime, is expected to cut off at short, observed wavelengths that correspond to later times when the Universe was ionized. The authors' experiment to detect the global reionization step (EDGES) searches for the associated spectral step in the sky's intensity[4].

Our knowledge of the epoch of reionization is surprisingly limited. The lack of ultraviolet (UV) absorption by diffuse neutral hydrogen along the line of sight to the most distant quasars[5] (accreting black holes) indicates that the Universe is largely ionized at a redshift of less than about 6 — a billion years after the Big Bang. Yet observations of the cosmic microwave background[6] — radiation left over from the Big Bang — indicate that the Universe was filled with neutral hydrogen at much earlier times. Clearly, a transition must have occurred from a neutral to an ionized Universe, but even recent observations of high-redshift galaxies with the Hubble Space Telescope tell us little

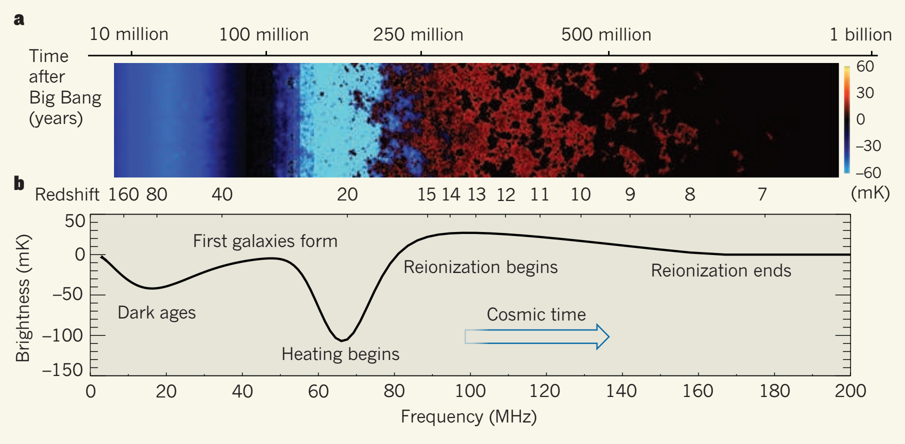

Figure 1 | The 21-centimetre cosmic hydrogen signal. a, Time evolution of fluctuations in the 21-cm brightness from just before the first stars formed through to the end of the reionization epoch. This evolution is pieced together from redshift slices through a simulated cosmic volume[9]. Coloration indicates the strength of the 21-cm brightness as it evolves through two absorption phases (purple and blue), separated by a period (black) where the excitation temperature of the 21-cm hydrogen transition decouples from the temperature of the hydrogen gas, before it transitions to emission (red) and finally disappears (black) owing to the ionization of the hydrogen gas. **b**, Expected evolution of the sky-averaged 21-cm brightness[8] from the 'dark ages' at redshift 200 to the end of reionization, sometime before redshift 6. The frequency structure within this redshift range is driven by several physical processes, including the formation of the first galaxies and the heating and ionization of the hydrogen gas. There is considerable uncertainty in the exact form of this signal, arising from the poorly understood properties of the first galaxies. Bowman and Rogers[2] study the final phase, in which the progressive ionization of the gas cuts off the signal.

about the galaxies that must have driven reionization[7].

Two major challenges for detecting the 21-cm signal involve foregrounds and calibration. The cosmic signal is dwarfed by radio emission from the Milky Way, as well as by terrestrial radio emission. Despite the favourable location of the EDGES experiment in the Australian outback, transmission from local radio and TV stations causes the loss of isolated regions of the spectrum. In addition, Galactic radio emission from energetic electrons spiralling in magnetic fields forms a spectrally smooth foreground that is one-thousand times brighter than the 21-cm signal. This smooth Galactic foreground can be fitted with a simple polynomial, and so removed, leaving the cosmic signal in the residuals. Unfortunately, this procedure removes much of the signal, potentially throwing the baby out with the bath water.

Another important limitation of the current experimental set-up is the absence of a method for calibrating the frequency response of the radio antenna. This necessitates fitting a combination of the foregrounds and the antenna's response. Given these limitations, it is impressive that the authors[2] are able to achieve residuals at the level of tens of millikelvin, comparable to the expected signal, and to place weak constraints on the duration of reionization.

Bowman and Rogers' technique allows them to rule out only models in which reionization occurs most abruptly — corresponding to a redshift interval of less than 0.1. As yet, the technique has had little effect on most models of the reionization epoch and the first galaxies. Figure 1 shows the expected evolution of the Universe as traced by emission or absorption of the 21-cm spectral line[8]. There is an initial absorption regime where the hydrogen gas is cooling through its cosmic expansion, and the excitation temperature of the 21-cm transition, which characterizes the relative populations of its two energy levels, is held equal to the gas temperature by collisions between hydrogen atoms. This absorption dies away as the gas gets diluted. Then the first stars form and emit UV photons that again set the excitation temperature of the 21-cm transition equal to the gas temperature, reinvigorating a second absorption trough. As these stars die, some of them produce black holes whose X-ray emission is expected to heat the gas to above the temperature of the cosmic microwave background, pushing the 21-cm signal into emission.

The authors[2] focus their efforts on this final phase, in which the signal is seen in emission and the progressive ionization of the diffuse hydrogen gas cuts off the signal, indicating the end of reionization. The same technique could ultimately be applied to detecting earlier periods for which our picture of the astrophysics is highly uncertain.

In the meantime, considerable time and money is being dedicated to the construction of low-frequency radio interferometers such as MWA, LOFAR and PAPER, which will target spatial fluctuations in the 21-cm signal (Fig. 1a). The EDGES experiment represents a cheaper method for measuring only the sky-averaged, broad-brush features in the evolution of the signal. Despite its limitations, it opens the possibility of an alternative experimental avenue that should be pursued in parallel to the more ambitious interferometers. Bowman and Rogers[2] have taken the first step on this journey, which will hopefully lead to new insights about the first stars and galaxies and the reionization epoch. ■

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VIROLOGY

One protein, many functions

The Lassa virus nucleoprotein coats the viral genome to make a template for RNA synthesis. A study shows that it also binds the 'cap' structure of cellular messenger RNAs and directs immune evasion using a novel mechanism. SEE ARTICLE P.779

FÉLIX A. REY

Lassa fever is a dreadful human haemorrhagic disease caused by the Lassa virus, a member of the Arenaviridae family[1]. The disease is prevalent in West Africa, causing 5,000 deaths each year and infecting hundreds of thousands more[2]. Arenaviruses are distributed worldwide and cause persistent infection in rodents, in which they generally don't cause disease. Humans become infected by exposure to material contaminated by infected mice, for example when the animals infiltrate food stores. The Lassa virus genome is a negative-sense, single-stranded RNA (nsRNA) molecule, and is coated by a nucleoprotein to form a nucleocapsid — a complex in which multiple copies of the nucleoprotein wrap around the genomic RNA, each one contacting a fixed number of nucleotides. In this issue (page 779), Qi *et al.*[3] report the crystal structure of the Lassa virus nucleoprotein, and reveal that it has a striking array of activities.

The nucleocapsids of nsRNA viruses serve as templates for the virus's polymerase enzyme (also known as the large or L protein), which replicates the genome to make new infectious particles. Qi and colleagues' crystal structure[3] shows that the Lassa virus nucleoprotein is made of two domains — an amino-terminal domain and a carboxy-terminal domain — with a positively charged groove in between, where the genomic RNA is expected to bind. This organization has been observed in all nsRNA viruses for which the nucleoprotein structure is known.

Before replication, the polymerase transcribes the genome into messenger RNA molecules to be translated into the viral proteins. Efficient translation of mRNAs by cellular ribosomes occurs if the mRNAs have a 'cap' structure at the 5′ end of the molecule. But arenaviruses, along with a subset of nsRNA viruses (those that have segmented genomes; Fig. 1, overleaf), cannot themselves cap mRNAs. They therefore steal caps from cellular mRNAs and transfer them to nascent viral transcripts, in a process known as cap snatching. Arenaviruses do this by cleaving off the 5′ end of cellular mRNAs using an 'endonuclease' activity that resides in the amino-terminal domain of the L protein[4,5], and then transferring the mRNA fragment to nascent transcripts.

Qi and colleagues' structure of the Lassa virus nucleoprotein shows that its amino-terminal domain has a cap-binding site, which holds the 5′ end of cellular mRNAs in place while the L protein cleaves off the rest. This additional function of the arenavirus nucleoprotein has not been observed in counterparts of the protein from any other virus family. The authors[3] show that when key residues in the cap-binding site are mutated, transcription is impaired.