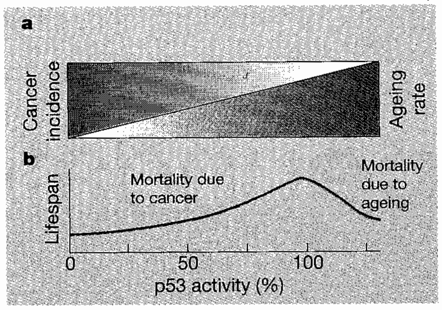

Figure 2 **Balancing cancer and ageing.** a, **Increases in p53 activity reduce the incidence of cancer but increase the ageing rate. Conversely, decreases in p53 activity increase cancer incidence but may decrease the rate of ageing.** b, **As a consequence, the influence of p53 on lifespan may result from a delicate balance between its antitumour and pro-ageing effects, such that too little p53 increases mortality from cancer whereas too much p53 increases mortality from ageing.**

mutations and promotes premature ageing in mice[8]. Tyner *et al.*'s results add an interesting twist to this hypothesis — they suggest that ageing may be due in part to cellular responses to damage, and not damage per se (Fig. 1b). These responses protect most people from cancer during their reproductive years, but they may come at a price.

All of these models can be loosely linked to p53. The SIR2 protein can suppress p53 activity in mammalian cells[9,10]. Cellular responses to telomere malfunction involve p53 (ref. 11), and a lack of p53 can counteract some of the effects of a lack of telomerase (an enzyme that regenerates telomeres) in mice[12]. Finally, doses of radiation that promote premature ageing in mice activate p53 efficiently[13]. Despite these connections, p53 has been on the periphery of ageing research — until now.

The new work[3] also has other implications. The ageing of whole organisms has been linked to cellular senescence *in vitro*, a process that also involves p53 and was initially linked to the finite lifespan of cultured human fibroblast cells[14]. Senescent cells remain metabolically active but cannot proliferate; they also show changes in gene expression that could produce alterations at the tissue level[15]. 'Replicative' senescence is triggered by telomere erosion and can be prevented by telomerase. But the same events can also be produced in response to, for example, DNA damage, oxidative stress and suboptimal cell-culture conditions[14]; telomerase has no effect here. Confusion over the exact process has led to a semantic debate, but it is clear that senescence parallels apoptosis as a cellular response to stress. These facts, coupled with the new results[3], suggest that tissue ageing *in vivo* results from many factors, not just telomere attrition as has been suggested.

It might seem paradoxical that overactive p53 suppresses cancer but promotes ageing, given that the incidence of cancer usually increases with age. But the problem can be resolved by the fact that cancer results from the malfunctioning of p53 in single cells, whereas ageing involves a tissue-wide process. So, cells with inactive p53 ultimately shorten lifespan because cancer develops. Conversely, cells with abnormally high p53 activity do not contribute to cancer, but instead undergo cell death or senescence. With time, these changes may compromise tissue physiology, shortening lifespan through ageing. So p53 activity must be tightly controlled to balance a predisposition to cancer (too little p53) and premature ageing (too much p53; Fig. 2).

Finally, Tyner *et al.*'s work[3] could have ramifications for understanding and treating human diseases. For example, p53 might contribute to premature ageing syndromes or age-related disorders in humans. And although longevity is complex and involves many p53-independent factors, it is conceivable that variation in lifespan is influenced by variation in p53's response to cellular damage. The results also raise the disturbing possibility that the DNA-damaging drugs used to treat cancer in young people might prompt p53 into action and accelerate age-related disorders later on. This is a testable hypothesis, and the prospect alone underscores the need for less toxic anticancer drugs. But perhaps the most provocative implication is that, if p53 is involved in ageing, then drug-related approaches to interfere with this process may come at a price — the disruption of our natural mechanisms for keeping cancer at bay. ■

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Cosmology

A baryometer is back

Corinne Charbonnel

The usefulness of helium-3 as a probe of the early Universe has been in doubt. A rethink of stellar theory and new observational data put those doubts to rest.

Do we live in an open Universe that will expand forever, or in a closed Universe whose expansion will eventually reverse? Part of the answer can be found by accurately estimating the amount of ordinary — baryonic — matter in the Universe. One way of reaching such an estimate stems from one of the predictions of Big Bang theory: that production of light nuclei (deuterium, helium-3, helium-4 and lithium-7) occurred within the first seconds of the Universe, in a process known as Big Bang nucleosynthesis. A precise measurement of cosmological baryon density requires determination of the primordial abundances of light nuclei, and for those estimates to be consistent with each other[1].

On page 54 of this issue[2], Bania, Rood and Balser report the first reliable assessment of the primordial abundance of ^{3}He. Their result is based on two decades of radio observations of star-forming H II regions and planetary nebulae in our Galaxy, the Milky Way, and on theoretical developments in the field of stellar evolution. Beyond the observational challenges, which in themselves are considerable, the main difficulty in using Big Bang nucleosynthesis as a cosmological probe lies in departures from the primordial abundances. Almost everywhere, the chemical composition of the Universe has been modified by processes such as stellar nucleosynthesis and cosmic-ray collisions. To infer the primordial abundances of the light elements from those measured, this chemical evolution has to be understood and quantified.

According to the classical theory of stellar evolution, formulated in the early 1970s, low-mass stars such as our Sun should be producing large amounts of ^{3}He. One dying star, the planetary nebula NGC3242, does indeed do this. NGC3242, which is slightly more massive than the Sun, previously synthesized fresh elements in its interior, and is ejecting them into the interstellar medium. Among those elements is ^{3}He, and it is being produced in the amounts predicted. In consequence, the expectation has been that the amount of ^{3}He in the Galaxy would increase over time[3].

Helium-3 can be observed only in relatively young objects in the Milky Way, such as the Sun, the local interstellar cloud[4], a

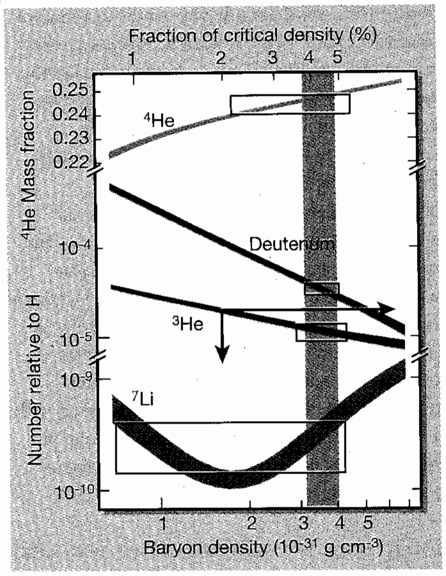

Figure 1 **Big Bang nucleosynthesis predictions for the primordial nuclei. The boxes indicate the observational estimates for the primordial abundances of ^{4}He (observed in galactic H II regions), deuterium (inferred from the absorption spectra of high-redshift quasars) and ^{7}Li (deduced from the surface of the oldest stars in our Galaxy). For ^{3}He, the horizontal arrow points to the upper limit of the abundance, relative to hydrogen. The vertical arrow points down to the lower limit of the baryon density inferred from the ^{3}He upper limit, assuming a Hubble constant of 65 km s^{-1} Mpc^{-1}. The horizontal lines of the black box over the dark-blue ^{3}He theoretical band indicates the range of abundances derived from the H II region S209; the vertical lines show the allowed range of baryon densities, which agree with the range of densities determined from deuterium abundances as shown by the vertical blue band. Modified from ref. 9.**

few planetary nebulae, and H II regions. The H II regions, which have just formed out of matter that has undergone 12 billion years of chemical evolution, should be particularly rich in ^{3}He. But when Bania and collaborators started to look at them in 1984, 'the ^{3}He problem' emerged: there was no evidence of ^{3}He enrichment having occurred. In consequence, the usefulness of ^{3}He as an indicator of baryon density — as a 'cosmological baryometer' — was thrown into doubt.

But ways have been found out of this quandary, both through theory and now observations. The lack of increase in ^{3}He abundance can be accounted for if most low-mass stars consume most of their ^{3}He before it can be emitted into the interstellar medium. This requires physical processes which the classical theory of stellar evolution did not take into account, but which have been revealed by anomalous carbon isotopic ratios observed at the surface of old stars. These anomalies could be explained by stellar rotation: by inducing internal mixing, rotation simultaneously leads to the destruction of ^{3}He inside stars, so it is not emitted into the interstellar medium. About 10% of stars would be unaffected, however, NGC3242 being one of them. This alternative view[5] results in a much reduced ^{3}He contribution from low-mass stars compared with that in the classical scheme of events.

Bania and collaborators[2] now report progress on the observational side of things. They have tenaciously continued to sample H II regions, increasing the number covered and so probing a large part of the Galactic disk. Obtaining these data is quite a feat, as it has involved accumulating measurements of extremely weak spectral lines of ^{3}He at centimetre wavelength with the National Radio Astronomy Observatory's 140-foot telescope. Deriving an estimate of ^{3}He abundance from the resulting spectra is also no easy job, as it requires technically demanding modelling of the complex structure of the sources. One of the authors' refinements was to select for their sample H II regions with relatively simple structure, for which it was easier to achieve accurate determinations of ^{3}He abundance.

Bania and colleagues find that, wherever H II regions are in the Galaxy, they all have a similarly low ^{3}He content. Taken together with the theory that rotating stars will emit negligible ^{3}He into the interstellar medium, this implies that the value of ^{3}He in H II regions provides an upper limit to its primordial abundance, and a lower limit to the baryon density.

The upshot of Bania *et al.*'s 20 years of hard labour, then, is that they have rehabilitated ^{3}He as a reliable cosmological baryometer. Their estimate of primordial baryon density is in excellent agreement with that derived from the low abundance of deuterium measured in the absorption spectra of high-redshift quasars[6], and from the high content of ^{4}He in H II regions in metal-poor dwarf galaxies[7] (Fig. 1). It implies that ^{7}Li has been depleted by about a factor of two in the oldest stars in our Galaxy. The estimate also agrees with an independent determination based on measurements of temperature anisotropy in the cosmic microwave background radiation by the MAXIMA and Boomerang experiments[8].

That estimate, however, is low — only about 4% of the amount required to close the Universe, assuming a value for the Hubble constant of 65 km s^{-1} Mpc^{-1}. So the answer to the question we started with is that the Universe cannot be closed with baryonic matter only. But other evidence implies the existence of 'dark matter', or 'missing mass', the search for which now constitutes one of the most exciting areas of research at the interface between particle physics and cosmology. ■

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Neuroscience

Sounds, signals and space maps

Catherine Carr

The auditory system transforms information from one frame of reference into another to create a map of space in the brain. The source of a visual signal that guides this transformation in barn owls has now been found.

When a barn owl hears a noise, it can pinpoint where the sound came from because its brain has a mental map of how the noises it hears fit into the space around it. Various auditory cues are used to construct this 'auditory space map', but it must also be guided by visual inputs, because — assuming reasonable eyesight — vision provides more reliable, topographically organized information. But what part of the brain transmits this information to the auditory map, and what form does the information take? On page 73 of this issue Hyde and Knudsen[1] provide an answer. They suggest that a signal from the optic tectum region of the barn owl's brain provides topographic, point-to-point instructions about the correct representation of auditory spatial cues.

For a hungry barn owl, it is vital to be able to use sounds to locate potential prey — hence the importance of the mental map of those sounds in space. This map is found in the midbrain, specifically the optic tectum. But it is initially produced nearby, in the inferior colliculus[2], using auditory localization cues to tune individual neurons. Such cues include differences in the time it takes for sounds to reach each of the ears, and differences in the level of sounds that arrive at each ear. The map is then relayed to the overlying optic tectum, where it is aligned