PERSPECTIVES: COSMOLOGY

The Saga of ^{3}He

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The realization (*1*) that clues about the early universe could be gleaned from the abundance ratio of deuterium (D or ^{2}H) to ordinary hydrogen (H or ^{1}H) in a glass of one's favorite wine was an important step in cosmology. The D/H ratio in terrestrial samples showed that the Big Bang produced relatively large quantities of D, indicating that the universe has a much lower density than was popular at the time. Along with H and D, the Big Bang produced the stable isotopes ^{3}He, ^{4}He, and ^{7}Li (*2*). Could one also gain cosmological insights by measuring the ^{3}He/^{4}He ratio in a helium-filled balloon?

In the balloon, one would find that ^{3}He/^{4}He ~ 10^{-6} by number; extending the survey to continental rocks would yield ~10^{-8} (*3*). The small abundance ratios and large differences among terrestrial samples might surprise aspiring cosmologists expecting 10^{-4} on the basis of Big Bang calculations. The reason for this discrepancy has long been appreciated: Unlike D, terrestrial He is not a fair "cosmic sample" because Earth formed essentially without helium or other chemically inert elements. Most terrestrial helium is ^{4}He and is the product of radioactive decay of elements such as uranium and thorium.

No natural radioactive decay produces ^{3}He, and hence there should be no terrestrial ^{3}He. Excess ^{3}He on Earth is therefore normally taken as an indication for unusual processes such as the testing of nuclear weapons or the infusion of extraterrestrial material. For example, recent studies, based in part on the ^{3}He/^{4}He ratio in gas trapped in fullerenes, indicate that the massive Permian-Triassic extinction was caused by an asteroid impact (*4*).

To measure the cosmic helium signature, we must look beyond Earth. It quickly becomes clear, however, that departures from the primordial abundances are the norm rather than the exception as elements are transformed through stellar nucleosynthesis and cosmic ray collisions.

In the solar system, ^{3}He can be measured by analyzing ^{3}He/^{4}He in physical samples, such as the solar wind and meteorites (*5*). The most accurate value to date was measured in Jupiter's atmosphere by the Galileo Probe (*6*). These observations show that as predicted by computer models, the D initially present in the outer parts of the Sun has been converted to ^{3}He via nuclear reactions. One can infer that in the protosolar nebula from which the Sun formed, $^3\text{He}/^4\text{He} = (1.66 \pm 0.05) \times 10^{-4}$.

Physical samples provide one more ^{3}He abundance: that of the local interstellar medium (*7*). Neutral helium atoms from the local interstellar medium occasionally wander across the termination shock region that separates the solar system from interstellar space. These atoms can be caught up and ionized in the solar wind and have a distinct velocity distribution. By counting the helium ions in this component of the solar wind, the Ulysses spacecraft measured a ^{3}He/^{4}He ratio of $2.48\ (+0.68/-0.62) \times 10^{-4}$. Compared with the protosolar value, the Ulysses value is not inconsistent with the notion that the ^{3}He abundance at the Sun's location in our galaxy has grown in the 4.6 billion years since the birth of the Sun.

Hot on the trail. The Rosette Nebula is one of the many low-density HII regions in which ^{3}He has been detected in the expanded sample.

To look yet further afield, we require remote observations. But remote measurements of ^{3}He are so difficult that it is challenging even to detect ^{3}He in the solar spectrum (*8*). This is because for most spectral transitions, the difference between ^{3}He and ^{4}He is so small that the ^{3}He feature blends into the wings of the much stronger ^{4}He spectral line. Beyond the local interstellar medium, only one spectral transition allows detection of ^{3}He: the 3.5-cm spin-flip transition, the analog of the widely used 21-cm line of ^{1}H. There is no corresponding transition in $^4\text{He}^+$. Detecting this very weak line is a challenge even for the world's largest radio telescopes.

The $^3\text{He}^+$ line can potentially be observed in the ionized gas of star-forming regions (HII regions) like the Orion nebula or of planetary nebulae blown out of stars like the Sun at the end of their lives. But to determine its abundance requires accurate line parameters; furthermore, the corresponding amount of hydrogen must be measured to obtain the abundance ratio ^{3}He/H. The second step is often as difficult as the first because the strength of the $^3\text{He}^+$ line depends on the nebular density, n, whereas all measures of H depend on n^2. The density and ionization structure of the nebula must be modeled to derive accurate values for ^{3}He/H (*9*).

Computer models of stars like the Sun suggest that they produce ^{3}He, perhaps in large quantities; late in their evolution, the ^{3}He is mixed to the surface and much of it reaches the interstellar medium in stellar winds and planetary nebulae (*10*). Disentangling the stellar and primordial components of interstellar ^{3}He in galactic HII regions thus requires knowledge of the chemical evolution of our galaxy and multiple, difficult measurements of ^{3}He/H throughout our galaxy.

In the late 1970s, the ^{3}He abundance in the interstellar medium was expected to be larger than that in the protosolar system and ^{3}He/H to be higher in places with enhanced stellar processing, that is, in the inner galaxy. But abundances derived from the 3.5-cm line did not match these expectations. Very little ^{3}He was found, and it was most abundant where it was least expected (*11*, *12*). Abundances for star-forming HII regions were consistent with those in the protosolar and local interstellar medium but did not show the expected gradient with position in the galaxy, suggesting no stellar production of ^{3}He (*13*). In contrast, at least some low-mass stars have produced substantial amounts of $^3\text{He}^+$, as shown by the high abundances observed in planetary nebulae (*14*).

The elements of a solution began to emerge just as the "^{3}He problem" (*15*) appeared most bleak. By the mid-1990s, it

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became clear that the HII regions targeted in many of the earlier observations were not ideal either for detecting $^3He^+$ or for the modeling required to derive $^3He/H$ (*16*). One of the main difficulties arises from the radiation from bright HII regions, which reflects off the radio telescope superstructure. There are many low-density HII regions (*9*) that are better targets. Reliable abundances determined for a greatly increased sample of HII regions (see the first figure) confirmed that there was no substantial variation with position in our galaxy. The most accurately determined $^3He/H$ abundances were all roughly $(1.9 \pm 0.6) \times 10^{-5}$ (*13, 17*).

Out with the old. The National Radio Astronomy Observatory 140 Foot Radio Telescope during its last scientific observing run, July 1999. The Robert C. Byrd Green Bank Telescope is seen during construction in the background.

At the same time, improvements in stellar models showed how ^3He production could be almost completely suppressed (*18, 19*). Rotationally driven mixing could destroy the ^3He produced earlier in the life of a star by mixing ^3He into the deeper, hotter regions of these stars, where it would be fused to ^4He. Mixing would not occur in stars with very low rotation rates, explaining the $^3He/H$ found in some planetary nebulae. Mixing would also produce changes in other abundances, particularly the carbon isotope ratio, $^{12}C/^{13}C$. This ratio can be measured in stars, enabling statistics to be collected on what fraction of stars do not mix and thus enrich the interstellar medium in ^3He. Taking these factors into account in models for the chemical evolution of the Milky Way yielded abundances that began to resemble observations (*20*).

^3He is now well enough understood to be used as a cosmological probe (*17*). D, ^3He, ^4He, and the fluctuations in the cosmic microwave background all suggest that the amount of ordinary baryonic matter (made of protons, neutrons, and electrons) in the universe is only about 4% the amount that would be required to reverse the expansion of the universe.

We are only beginning to understand the evolution of ^3He within the Milky Way. In the next few years, observations of ^3He should be greatly facilitated by the Robert C. Byrd Radio Telescope now undergoing commissioning in Green Bank, WV (see the second figure). Its design should eliminate the superstructure reflections that limited earlier observations. The currently observed sample of planetary nebulae is highly biased. Increasing the sample size with the new telescope should allow the consequences of this bias to be evaluated. The HII region survey can be extended to a larger fraction of our galaxy than for any other isotope. ^3He could well become the most widely used constraint to models of the chemical evolution of our galaxy.

References

1. J. R. Gott, III, D. N. Schramm, B. M. Tinsley, J. E. Gunn, *Astrophys. J.* **194**, 543 (1974).
2. B. D. Fields, *Science* **294**, 529 (2001).
3. D. L. Anderson, *Science* **261**, 170 (1993).
4. L. Becker *et al., Science* **291**, 1530 (2001).
5. G. Gloeckler, J. Geiss, in *The Light Elements and Their Evolution*, L. Da Silva, M. Spite, J. R. Medieros, Eds. (Astronomical Society of the Pacific, San Francisco, CA, 2000), pp. 224–233.
6. P. R. Mahaffy *et al., Space Sci. Rev.* **84**, 251 (1998).
7. G. Gloeckler, J. Geiss, *Space Sci. Rev.* **84**, 275 (1998).
8. D. N. B. Hall, *Astrophys. J.* **197**, 509 (1975).
9. D. S. Balser, T. M. Bania, R. T. Rood, T. L. Wilson, *Astrophys. J.* **510**, 759 (1999).
10. R. T. Rood, G. Steigman, B. M. Tinsley, *Astrophys. J.* **207**, L57 (1976).
11. R. T. Rood, T. M. Bania, T. L. Wilson, *Astrophys. J.* **280**, 629 (1984).
12. T. M. Bania, R. T. Rood, T. L. Wilson, *Astrophys. J.* **323**, 30 (1987).
13. R. T. Rood *et al., Space Sci. Rev.* **84**, 185 (1998).
14. D. S. Balser *et al., Astrophys. J.* **483**, 320 (1997).
15. D. Galli, L. Stanghellini, M. Tosi, F. Palla, *Astrophys. J.* **477**, 218 (1997).
16. R. T. Rood, T. M. Bania, T. L. Wilson, D. S. Balser, in *ESO/EIPC Workshop on the Light Elements*, P. Crane, Ed. (Springer, Heidelberg, Germany, 1995), pp. 201–214.
17. T. M. Bania, R. T. Rood, D. S. Balser, *Nature* **415**, 54 (2002).
18. C. Charbonnel, *Astrophys. J.* **453**, L41 (1995).
19. ______, *Space Sci. Rev.* **84**, 199 (1998).
20. M. Tosi, in *The Light Elements and Their Evolution*, L. da Silva, M. Spite, de J. R. Medeiros, Eds. (Astronomical Society of the Pacific, San Francisco, CA, 2000), pp. 525–534.

PERSPECTIVES: BIOMEDICINE

A Cargo Receptor Mystery *APP*arently Solved?

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Alzheimer's disease (AD), the most common neurodegenerative disease of old age, is characterized by deposits of small amyloid β (Aβ) peptides in the brain. These Aβ peptides are produced by proteolysis of a type I integral membrane protein, the amyloid precursor protein (APP), by the enzymes BACE1 and γ-secretase. BACE1, which generates the amino terminus of Aβ, is a membrane-tethered aspartyl protease (*1*). The identity of γ-secretase, which is responsible for cleaving the transmembrane region of APP and liberating Aβ peptides, is controversial (*2*). However, the presenilins (PSs), a highly conserved family of serpentine membrane proteins, are essential for facilitating this reaction.

Little is known about the subcellular distribution of BACE1 and PS, and it is here that the recent *Nature* report by Goldstein and colleagues offers provocative insights (*3*). These investigators show that BACE1 and PS are found in membrane vesicles transported along the axons of peripheral and central mouse neurons, and that this transport requires APP. These cargo-laden membrane vesicles are bound to a motor protein complex, kinesin-1, which is composed of two components (see the figure). The first is a kinesin heavy chain (KIF5B) containing ATP- and microtubule-binding motifs that is essential for vesicle transport. The second component, called kinesin light chain (KLC), associates with KIF5B and tethers membrane vesicles containing a subset of proteins that are transported along the axon from the neuronal cell body to nerve terminals (*4*) (see the figure). The transported proteins (cargo) include the neurotrophin receptor TrkA, the synaptic vesicle–associated phosphoprotein synapsin 1, and the growth-associated protein GAP-43, which regulates cytoskeletal dynamics in neuronal growth cones. Most surprising is the finding by Goldstein's lab that Aβ peptides can be generated within axons, and within isolated membrane vesicles from sciatic nerves. The authors offer the tantalizing proposal that in disease set-

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