HISTORY OF SCIENCE

Hoyle's Equation

Donald D. Clayton

The paper that first explained how the elements form in stars did not receive the acclaim it deserved because it did not display its key equation.

One of the grand theories of science holds that the chemical elements and all of their isotopes were synthesized from hydrogen and helium by nucleosynthesis—nuclear reactions within young massive stars (*1*). The abundances of elements today are thus the product of natural history and evolution. Although this theory is now accepted, the scientific paper that forms its foundation (*1*) has been strangely underappreciated in comparison with later works (*2, 3*). Recently, researchers gathered at an international conference at the California Institute of Technology (*4*) to celebrate the anniversary of two groundbreaking 1957 publications (*2, 3*) that according to its Web site "opened the whole field of nuclear astrophysics into a diverse and thriving scientific and intellectual enterprise." However, I would like to look back at the issue of how this early work of Fred Hoyle (shown in photo) came to be both poorly understood and incongruously undercited.

Stellar pioneer. Fred Hoyle on the Caltech campus in February 1967.

In attending and speaking at the conference (*5*), it became clear to me that even experts are unaware of the contents of Hoyle's 1954 paper. Its undercitation probably resulted from the omission of a written equation that is central to the theory and from which the essence of the origin of the elements can be derived. Subsequent nucleosynthesis theory tended to focus on the specific nuclear processes responsible for specific sets of natural isotopes. Limited controversy did erupt in 1983 after W. A. Fowler, a Caltech coauthor of the paper known as B^{2}FH (for the initials of its authors) (*2*), was awarded the Nobel Prize in physics for his experimental role in clarifying nucleosynthesis rates in stars whereas Hoyle as creator of the theory of nucleosynthesis was omitted.

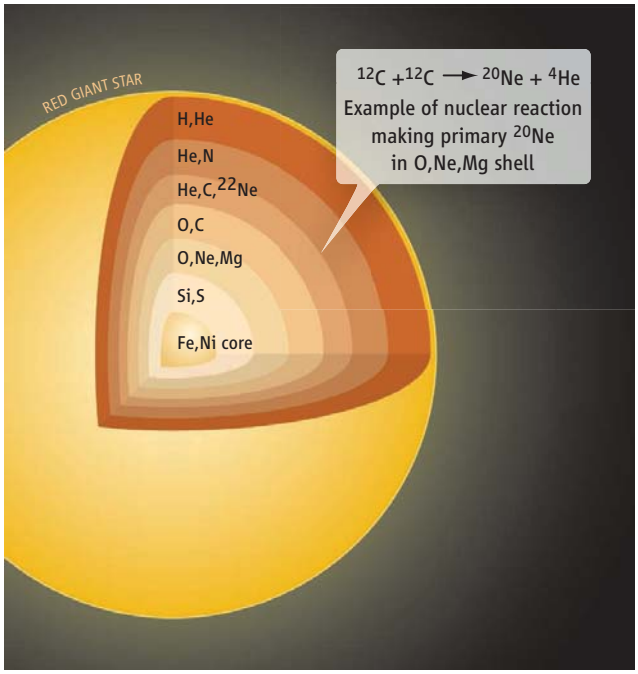
In what follows, I will offer my own "Hoyle's equation" as determined from my reading of his 1954 paper (*1*). Hoyle's equation addresses the origin from initial hydrogen and helium of the set of very abundant isotopes in stars more than 10 times as massive as the sun—what is now called "primary nucleosynthesis." By contrast, B^{2}FH (*2*) contributed creatively to the "secondary processes" of nucleosynthesis, those that change one preexisting heavy nucleus into another but do not increase the metallicity (that is, the abundance of elements heavier than helium) of the galaxy as it ages. Hoyle's words and quantitative arguments (*1*) are more sweeping than the detail-oriented sequels. Hoyle's discussion is phrased in terms of the mass Δm_{new} of new primary isotopes that are ejected from massive stars, which he saw as their source. His approach to stellar nucleosynthesis takes their galaxy-wide rate of production dm_{new}/dt to be the product of the death rate of stars and the mass Δm_k of isotope k ejected at time t from each star.

Hoyle explained that gravitational contraction causes temperature increases after each central nuclear fuel is consumed, and he described the nuclear burning and associated nucleosynthesis of Δm_k during each sequential advanced core evolution. Because those massive stars all evolve almost instantaneously in comparison with galactic time scale, Hoyle takes $B_{M>}(t)$ to be the birth rate of massive stars at time t. It must on average equal their death rate if the numbers of stars are to change only slowly. The subscript $M>$ characterizes stars too massive to become white dwarfs; for these stars, Hoyle (*1*) predicted that collapse of the final central evolved core is inevitable. So, for the massive stars that his paper focused on, "Hoyle's equation" expresses the rate of ejection of new primary isotopes from carbon to nickel as

$$dm(\text{C-Ni})/dt = B_{M>}(t)\ \mathbf{Ev}^{\text{nucl}}\ \Sigma_k \Delta m_k$$

where $\mathbf{Ev}^{\text{nucl}}$ expresses the nuclear and stellar evolution of a massive star, and $\Sigma_k \Delta m_k$ is the sum over k isotope masses.

Hoyle identified the new primary isotopes created within each successive core burning phase. Each burning core is smaller than the one before, so that the star takes on an onionskin structure containing the residual Δm_k of each burning phase (see the figure). Hoyle also correctly stated that neutrino emission governs the collapse time scale when core temperature exceeds 3×10^9 K. Hoyle's equation expresses a modern view of the nucleosynthesis that increased metallicity during galactic history. Hoyle missed only the full set of reactions involved during silicon burning and the relative numbers of protons and neutrons involved in the nuclear statistical equilibrium. Curiously, B^{2}FH, published 3 years later, with Hoyle as one of its coauthors, did not focus on Hoyle's massive-star picture or on his equation, an oversight that I attribute to his lack of careful proofreading



New elements in stars. A massive star develops an onionlike structure with zones in which different elements have been synthesized by nuclear reactions.

The author is in the Department of Physics and Astronomy, Clemson University, Clemson, SC 29634, USA. E-mail: cdonald@ clemson.edu

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of a manuscript drafted by E. M. and G. R. Burbidge (*6*).

It is unfortunate that he did not put to paper the equation he envisioned and described verbally. Had he done so, unambiguous scientific visibility of his achievement would have followed more easily. In that spirit, I submit Hoyle's equation as implicit in the arguments of his pioneering 1954 paper and suggest that it is one of the landmark papers in the history of science.

References and Notes

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MOLECULAR BIOLOGY

The Two Faces of miRNA

MicroRNAs can enhance or repress messenger RNA translation, depending on whether cells are proliferating or arrested in the cell cycle.

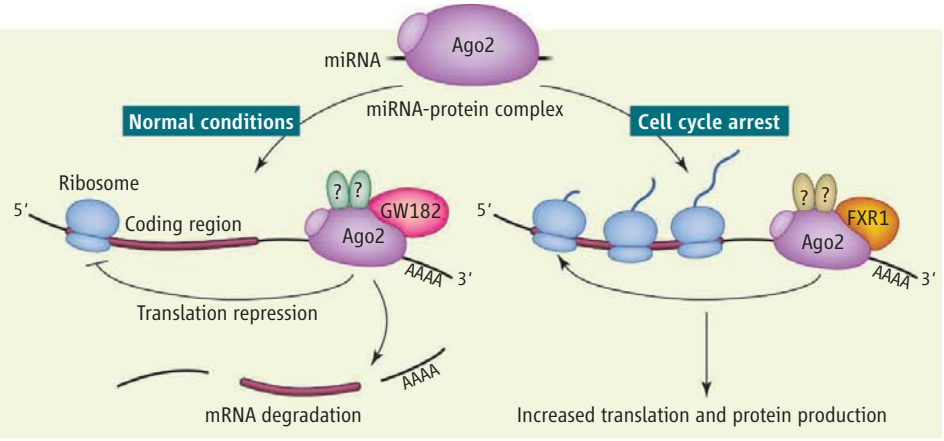
J. Ross Buchan and Roy Parker

MicroRNAs (miRNAs) are 20- to 22-nucleotide RNAs that regulate the function of eukaryotic messenger RNAs (mRNAs) and play important roles in development, cancer, stress responses, and viral infections. miRNAs are well known to inhibit the translation of mRNAs into protein and to promote mRNA degradation. On page 1931 of this issue, Vasudevan *et al*. (*1*) show that miRNAs can also increase translation, broadening the effect of these small RNAs on protein expression.

To function, a miRNA associates with an Argonaute protein, of which there are four in mammalian cells (Ago1 to Ago4). Each miRNA-Ago complex interacts with a specific mRNA, typically through pairing of nucleotide bases between the miRNA sequence and complementary sequences in the mRNA's 3′-untranslated region (3′UTR). Such 3′UTRs are important assembly sites for complexes that affect mRNA localization, translation, and degradation. How Ago-miRNA complexes repress translation and/or promote mRNA degradation is not clear but involves the recruitment of additional protein factors, most notably the GW182 protein (*2*).

Vasudevan *et al*. build on earlier work showing that the 3′UTR of tumor necrosis factor–α (TNF-α) mRNA stimulates translation when mammalian cells are deprived of serum (which contains nutrients and growth factors), arresting the cell division cycle at a particular phase (G_1) (*3*). This stimulation requires Ago2, raising the heretical idea that miRNAs both enhance and repress translation.

Indeed, Vasudevan *et al*. now show that when cultured mammalian cells are serum-starved (G_1 phase arrest), binding of a specific miRNA (miR369-3) to a reporter mRNA (containing the TNF-α 3′UTR) stimulates translation, whereas no stimulation occurs when miR369-3 is absent. In contrast, miR369-3 represses translation during other cell cycle phases. The well-studied "repressive" *let7* miRNA and the artificial miRNA mimic *cxcr* also enhance mRNA translation during starvation-induced G_1 arrest, whereas they repress translation elsewhere in the cell cycle. Thus, multiple miRNAs and associated Ago proteins can enhance or repress translation, depending on the cell cycle state.



Dual functions of miRNAs. MicroRNAs (miRNAs) can boost or block the translation of target mRNAs. Physiological conditions affect the recruitment of regulatory proteins, which can alter a miRNA's effect.

Stimulation of translation involves a change in the proteins recruited to mRNA by the miRNA-Ago complex (see the figure). During cell cycle arrest, the RNA binding protein FXR1 is recruited to mRNA by the miRNA-Ago complex and stimulates translation (*1*, *3*). Whether other activator proteins are recruited, or repressive proteins (such as GW182) are lost, during this condition is unknown.

The diversity of proteins recruited to mRNAs by miRNAs is further broadened by multiple members of the Ago, GW182, and FXR protein families as well as by the expression levels and posttranslational modifications of Ago-interacting proteins. Moreover, the effect of a miRNA-Ago complex can also be modulated by proteins bound to other sites within the 3′UTR. For example, in response to multiple stresses, increased translation of the *CAT-1* mRNA in hepatic cells depends on specific binding sites for miRNA-122 in *CAT-1* mRNA, and binding of the protein HuR to the 3′UTR (*4*).

The roles of miRNAs in multiple stress responses hint that other environmental changes may convert some miRNAs to activating roles (*5*). Moreover, because many of the Ago-interacting proteins (such as FXR1) also bind RNA, some mRNAs might have sequences that constitutively recruit miRNA-Ago complexes that activate translation.

Differential effects of miRNAs at various cell cycle stages or during cellular stress may explain some confusion in the field, including differences in the extent of repression caused by a given miRNA, and the detection of translationally repressed mRNAs with ribosomes. These differences might be explained if cells are distributed differently across the cell cycle in various experiments.

Small RNAs serving as both activators and

The authors are in the Department of Molecular and Cellular Biology, Howard Hughes Medical Institute, University of Arizona, Tucson, AZ 85721, USA. E-mail: rrparker@email.arizona.edu