tive cooling method that is used to create the superfluid droplet affects only the most energetic atoms in the gas. A more likely model, therefore, is that at the birth of a superfluid droplet, its energetically lowest-lying collective vibrations are excited by quantum 'noise' in the surrounding atomic gas. The result is a 'fuzzy' quantum object, whose strongly oscillating nature initially hinders growth. After these vibrations have largely damped down, the droplet can grow further by the classical, collisional process already mentioned.

So how can we observe the quantum nature of the nascent superfluid droplet? This requires a measurement that is sensitive to non-local properties spread over a large part of the Bose–Einstein condensate. A particularly dexterous possibility is to perform an interference experiment in which the atomic cloud falls through a double slit (Fig. 1). Ritter *et al.*[2] in essence perform this experiment, with a double slit created by microwave fields that preferentially extract atoms from the condensate in two different places, and an interference pattern analysed by looking at the number of detected atoms as a function of time.

Hugbart *et al.*[1] implement another possibility, using an ingenious spectroscopic method to measure the number of atoms in the Bose–Einstein condensate that have a certain velocity. Notwithstanding the quite different methods, both experiments clearly show the fuzzy, vibrating quantum nature of the superfluid droplet at birth. The main difference between the findings of the two experiments lies in the precise nature of the vibrations that are excited. Hugbart *et al.* observe quadrupole-shaped oscillations of the droplet, whereas Ritter *et al.* observe subtle fluctuations in superfluid flow that hardly affect the shape of the droplet. This difference is possibly related to the much more elongated shape of the superfluid droplet in Hugbart and colleagues' experiment, although more work is required to clarify the reasons for this qualitative difference.

These experiments[1,2] allow us a first glimpse of the birth and initial growth of a Bose–Einstein condensate. That is already leading to new qualitative insights into this fundamental process, but the experimental results cry out for the detailed, quantitative comparison with theory that will allow a precise understanding of the process. A further attractive option is to study the birth of the superfluid droplet in the presence of an optical lattice — a web of laser beams that creates a regular array of sites to which the atoms of the ultracold gas are attracted. For a sufficiently attractive optical lattice, the Bose–Einstein condensate would have to form not from a normal gas, but from yet another phase of matter, a Mott insulator, in which every site of the optical lattices is filled with exactly one atom. Ritter and colleagues also have experience with creating these states, so such an experiment might not be too difficult for them to carry out. ■

Henk T. C. Stoof is at the Institute for Theoretical Physics, Utrecht University, Leuvenlaan 4, 3584 CE Utrecht, the Netherlands.
e-mail: h.t.c.stoof@phys.uu.nl

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MOLECULAR BIOLOGY

RNA in control

Benjamin J. Blencowe and May Khanna

In bacteria, some messenger RNAs can sense the need for their protein product and accordingly regulate expression of their own genes. A similar type of RNA regulation has now been revealed in higher organisms.

The functional capacity of RNA, beyond its role in protein synthesis, frequently amazes, as examples of RNA-mediated gene regulation are continuously emerging. One type of such regulation found in bacteria involves RNA structures called riboswitches. These are sequences of nucleotide bases in messenger RNAs that contain structural domains called aptamers. Aptamers act as sensors by binding to a specific small-molecule building-block, or metabolite. The protein product of the riboswitch mRNA is often involved in the biosynthesis or transport of the same metabolite[1]. On binding to a metabolite, aptamers undergo a conformational change that alters the mRNA's access to the machinery required for either its transcription from a gene or its translation into a protein. Thus, riboswitches regulate the intracellular levels of bacterial metabolites. However, it was not known whether they have similar functions in eukaryotes (fungi, plants and animals). On page 497 of this issue, Cheah and colleagues[2] reveal a mechanism by which riboswitches regulate the expression of genes involved in vitamin B_1 biosynthesis in the fungal species *Neurospora crassa*.

50 YEARS AGO

Completion of construction on the Dounreay fast reactor is expected towards the end of the year... One of the main objects for the Dounreay reactor will be to develop fuel elements capable of burning fissile atoms rapidly, and able to withstand high heat ratings with high outlet temperatures for the coolant. The use of plutonium as a fuel will be investigated, to illustrate the economics of a system based on the breeding of plutonium from natural or depleted uranium. The economics of the chemical processes required to handle highly active irradiated fuel will form part of this study, since there is no requirement for separation of 'poisons' in the shape of fission products with high capture cross-section for neutrons, but rather a means of re-forming fuel which may have suffered extensive mechanical damage from the fission process.
From *Nature* 25 May 1957.

100 YEARS AGO

The Khasis are a tribe inhabiting the Khasi and Jaintia Hills in the Indian province of (as it is now called) Eastern Bengal and Assam. They are surrounded on all sides by alien peoples, Tibeto-Burman and Aryan, and are believed to be a survival of a primitive Austro-Asiatic race that once occupied the whole of eastern India until they were conquered and dispossessed in prehistoric times by an invasion of Tibeto-Burmans. The tribal constitution is strongly matriarchal. Inheritance is through the female line, the youngest daughter being the chief heir of her mother; ancestral property can only be owned by women, and the only property which a man can possess is that which is self-acquired. The chief deities are all female. So is the sun, while the moon is represented as a man, and in grammar and vocabulary the feminine element is much more prominent than the masculine.
From *Nature* 23 May 1907.

50 & 100 YEARS AGO

NATURE|Vol 447|24 May 2007

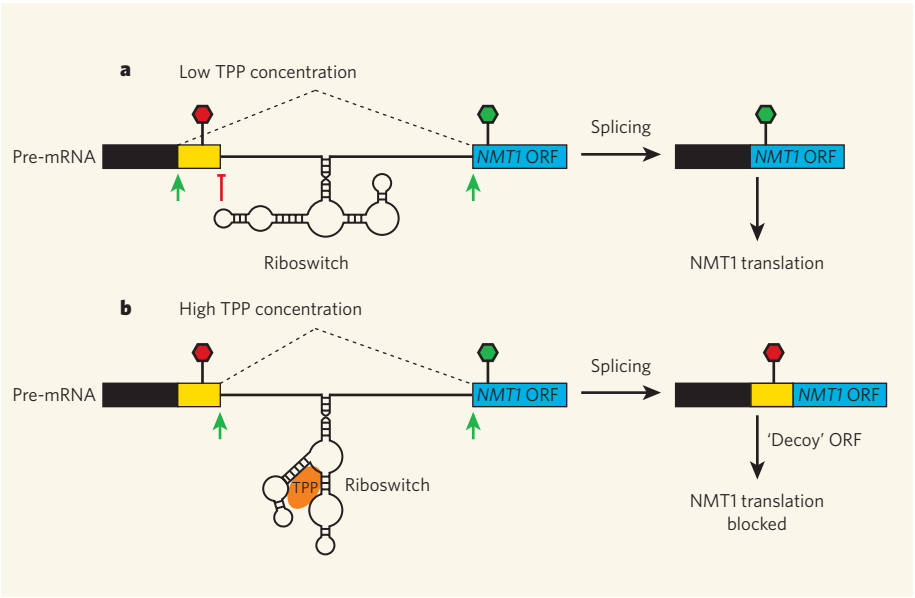

Figure 1 | Regulation of gene expression by riboswitches in *Neurospora crassa*. Cheah *et al.*[2] show that expression of the *NMT1* gene is regulated at the level of pre-mRNA alternative splicing by a riboswitch that binds to thiamine pyrophosphate (TPP). **a**, At low concentrations of TPP, the TPP-binding (aptamer) region of the riboswitch base-pairs with sequences surrounding a splice site (red blocking line) in a nearby non-coding sequence, and prevents its selection by the splicing machinery. A distal splice site (green arrow) is selected, however, resulting in the generation of a shorter *NMT1* mRNA with a coding sequence, or open reading frame (ORF), that translates into a functional *NMT1*-encoded protein (green signal). **b**, At high TPP levels, the aptamer undergoes a conformational rearrangement so that the region that was previously bound to the nearby splice site is now used to bind to TPP. This and other conformational changes (not shown) generate a longer mRNA splice variant that contains short, 'decoy' ORFs (red signal), preventing functional *NMT1* expression.

Unlike coding sequences in bacterial genes, which typically are continuous stretches of DNA, eukaryotic genes contain coding regions (exons) that are separated by non-coding sequences (introns). These genes are initially transcribed into precursor (pre)-mRNAs, which undergo a series of processing steps, including the removal of introns and splicing together of exons, before mature mRNA is generated. A complex macromolecular machinery in the nucleus of eukaryotic cells is responsible for pre-mRNA splicing[3].

Alternative splicing occurs when the boundaries between exons and introns, called the splice sites, are differentially selected by the splicing machinery to generate two or more different mRNAs from the same pre-mRNA. Alternative splicing is a remarkably efficient mechanism for a cell to increase the structural and functional diversity of its proteins, and it plays many roles in gene regulation[4–6]. In almost every known case, the regulation of alternative splicing is achieved through an interplay between protein factors and pre-mRNA sequences at or near the splice sites. The fungal riboswitches identified by Cheah *et al.* break this mechanistic mould, as their action in dictating the choice of splice sites can be explained entirely by a metabolite-induced change in RNA folding, without the direct involvement of proteins.

An initial clue suggesting the possibility of riboswitch-mediated regulation of splicing in eukaryotes came from the observation that, in fungal and plant species[7,8], evolutionarily conserved blocks of sequences, which resemble bacterial aptamers and bind to thiamine pyrophosphate (TPP), are present in the introns of genes involved in thiamine biosynthesis. TPP is a derivative of thiamine, commonly known as vitamin B_1. It was subsequently shown that in the fungus *Aspergillus oryzae*, deletion of a TPP aptamer from the intron of the *thiA* gene (involved in thiamine biosynthesis) prevents this gene from responding when thiamine is added to the growth medium[9].

Cheah and colleagues[2] now show that the addition of thiamine to the growth medium of *N. crassa* results in marked shifts in the alternative splicing patterns of mRNAs for three genes that all contain TPP aptamers. Two of these genes, *NMT1* and *THI4*, are involved in thiamine metabolism, whereas the third gene encodes a protein of unknown function[2]. For *NMT1* and *THI4*, with high concentrations of thiamine, the levels of mRNA splice variants lacking functional protein-coding sequences were increased relative to the levels of splice variants corresponding to functional mRNAs. How do these shifts in alternative splicing patterns occur?

As mentioned earlier, bacterial riboswitches function by undergoing metabolite-induced structural changes, which alter the access of the mRNAs to their transcriptional or translational machineries. A related mechanism involves the TPP aptamer in the *NMT1* mRNA. At low TPP levels, the region surrounding the aptamer is folded such that it favours selection of a distal splice site. The resulting shorter mRNA contains a coding sequence, also called an open reading frame (ORF), for a functional *NMT1*-encoded protein (Fig. 1a). In this conformation, bases in a section of the aptamer pair up with bases overlapping a competing splice site on a nearby non-coding sequence in the pre-mRNA, thereby preventing it from being selected to produce non-functional mRNA.

At high concentrations, TPP binds tightly to the aptamer and causes a conformational rearrangement that prevents it from base-pairing with the nearby splice site. Consequently, this competing splice site is selected by the splicing machinery, and a longer mRNA splice variant is produced, which contains short, 'decoy' ORFs that prevent the expression of the main *NMT1* ORF (Fig. 1b). A feature of this switch is that, although aptamer sequences can bind to both TPP and the competing splice site, the two events are mutually exclusive.

In addition to its unique mechanism of action, the splicing-regulatory TPP riboswitch in *N. crassa* has another intriguing feature: its function resembles more complex strategies that use alternative splicing to coordinate gene activities in higher eukaryotes. For example, the finding that a single metabolite can alter the splicing patterns of at least two genes that operate in the same biochemical pathway is reminiscent of other observations indicating that alternative splicing can be regulated in a coordinated manner to control functionally related genes[6]. It seems plausible that splicing-regulatory riboswitches represent a system that has evolved to coordinately regulate multiple genes in the same biochemical pathway using feedback and, in some cases, feed-forward mechanisms. Presumably, the rapid kinetics and energy-saving advantages afforded by bypassing protein-mediated regulation explain why riboswitch aptamers have persisted during evolution and function at many levels of regulation of gene expression.

This raises a question: to what extent do riboswitches regulate alternative splicing, or other steps in gene expression, in eukaryotes? The answer might be, quite often. In the fungus *Aspergillus nidulans*[10], a splicing-regulatory riboswitch that binds to the amino acid L-arginine was recently discovered in the non-coding region of a gene that encodes arginase — an enzyme required for using arginine as a source of energy. However, a natural role for small-molecule aptamers in regulating splicing has not been found in animal cells, although an artificial riboswitch has been engineered to control splicing in cultured mammalian cells[11].

Given the discovery of riboswitch aptamers that regulate alternative splicing in fungi[2], and the possible existence of equivalent mechanisms in plants[12], it is reasonable to expect that animals might utilize related strategies

for regulating gene expression. With advances in computational strategies for locating conserved RNA folds in sequence databases, high-throughput methods for monitoring alternative splicing and other steps in gene expression, and prior knowledge of the function of genes involved in small-molecule metabolism, finding other examples of such regulatory modules in eukaryotes seems possible. In any case, we can be almost certain that new forms of RNA-based regulation will continue to emerge and amaze. ■

Benjamin J. Blencowe and May Khanna are in the Banting and Best Department of Medical Research, the Department of Molecular and Medical Genetics and the Centre for Cellular and Biomolecular Research, Donnelly CCBR Building, University of Toronto, 160 College Street, Toronto, Ontario M5S 3E1, Canada.
e-mail: b.blencowe@utoronto.ca

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SUPERNOVAE

Answers and questions

David Branch and Ken'ichi Nomoto

Do we understand the violent and cosmologically significant stellar explosions known as type-Ia supernovae? Yes and no, as astronomers participating in a conference in California agreed.

In mid-March, more than 100 astronomers converged on the Kavli Institute for Theoretical Physics in Santa Barbara, California, for an international conference* on so-called type-Ia supernovae (SNe Ia). Understanding these stellar explosions has a high priority: measurements of their brightness in the late 1990s revealed the existence of a mysterious 'dark energy' permeating space and accelerating the Universe's expansion. This conference was not primarily about exploiting SNe Ia for cosmology, but about assessing our current state of knowledge of where they come from, what exactly their stellar progenitors are, how they work, and how they explode.

A good idea lasts

In 1960, Fred Hoyle and William Fowler[1] concluded that SNe Ia are the result of thermonuclear instability following the ignition of nuclear fuel in 'electron-degenerate' matter. Such matter is formed when a star contracts and the electrons of its matter are compressed to fill every energy level available to them by the quantum-mechanical Pauli exclusion principle. Since then, astronomers have fleshed out the idea. Unlike other supernovae — types Ib, Ic and II, collectively known as core-collapse supernovae and produced only by short-lived, massive stars — SNe Ia are seen in both young and old stellar populations. They are even found in elliptical galaxies, meaning that some of them are produced by long-lived, low-mass stars found in these galaxies.

Most low-mass stars end their lives as electron-degenerate carbon–oxygen white dwarfs, without exploding. A more dramatic fate comes if the white dwarf accretes non-degenerate matter from a companion in a binary system (the single-degenerate scenario) or merges with

**Paths to Exploding Stars: Accretion and Explosion*, Santa Barbara, California, 19–23 March 2007; http://online.kitp.ucsb.edu/online/snovae_c07

HYDROLOGY

Flood of data

P. BATES

If you need more precise measurements of natural events on Earth's surface, get into space. Researchers studying glaciers and earthquakes have for some time followed this principle, exploiting the power of satellite interferometric imaging to map surface displacements down to the centimetre scale. Doug Alsdorf and his colleagues have taken the same approach in their investigations of the periodic floods that occur in the Amazon basin (D. Alsdorf *et al. Geophys. Res. Lett.* **34,** doi:10.1029/2007GL029447; 2007).

The Amazon river has an intimate relationship with its vast floodplain, with an estimated 25% of its average annual discharge flowing and ebbing across it. But very little is known about the behaviour of these floods: not least, gauges of water level are placed only along the main channels, and then only sparsely. There are technical difficulties in taking interferometric measurements of water surfaces with satellite-borne synthetic-aperture radar. But flooded vegetation (pictured) does reflect an adequate signal.

Using data provided by instruments aboard the Japanese Earth Resources Satellite, Alsdorf *et al.* have been able to map the spatial and temporal complexity of floodplain inundation. Their study of floods from three different years takes in an area of the central Amazon basin that includes flows from the Purus river, as well as the Amazon itself.

Water levels in the floods, it turns out, do not take on the pattern that might be expected from a simple correspondence with the levels in the main channel of the river. Rather, there is a complicated interplay in which flow paths and water levels are influenced not only by the main channel and floodplain topography, but also by local and far-reaching hydraulic factors created by the flood itself.

These are proof-of-principle findings, with a practical edge. Modelling of floods is bedevilled by a lack of relevant measurements to test them. Satellite data can help redress that lack, with the ultimate aim of guiding engineering or other solutions to the inundation of areas inhabited by human populations. Furthermore, periodic flooding, and the associated delivery of sediments and nutrients, is a natural feature of wetland ecosystems not only in the Amazon but throughout the world. Some wetlands are under threat and, in some, restoration projects are in hand. Clarification of the relevant networks of water flow in different circumstances would offer another approach to ensuring the long-term success of such projects.

Tim Lincoln