100 YEARS AGO

As nest-building fishes are comparatively few, naturalists will read with interest an account given in the August issue of the *American Naturalist*, by Messrs. Young and Cole, of the manner in which the brook-lamprey (*Lampetra wilderi*) makes a structure of this nature. It is believed that the males precede the females at spawning time and commence nest-building before the arrival of the latter. The nest is made among pebbles, but it does not seem that the lampreys follow any definite plan in its construction. They affix themselves to such pebbles as require removing from the nest, and then endeavour to swim straight away with them. In the case of a heavy stone two lampreys may join forces. The number of fish in a nest may vary from one to thirty or forty; but there are generally between three and twenty-five.

From *Nature* 20 September 1900.

50 YEARS AGO

A sample of blood sent to us because of the presence of most unusual antibodies has proved, on investigation, to have even more extraordinary Rh antigens. The blood is unique in our experience, and in the literature, in that it has the antigen D, but lacks any detectable representative of the C and E allelomorphic series of antigens. The donor of the blood is homozygous for this deficiency, owing without a doubt to her parents being second half cousins. Her mother is heterozygous for the condition; her father and two brothers are dead. The genotype of the donor may be written —*D*—/—*D*—, the dashes representing the absence of *C*, *c*, C^w, c^v, C^u and the absence of *E*, *e*, E^u. The absence of these antigens was demonstrated in negative results of agglutination tests in saline and in albumin, of indirect anti-globulin tests, of trypsin tests and of absorption tests. … In the serum of the donor we have so far been able to identify anti-*e*, anti-*C* and anti-*c*. The finding of both anti-*C* and anti-*c* in one serum is extraordinary but not altogether unexpected. … Whatever the exact genetic mechanism, the fact that *C* and *E* are involved supports from an unexpected angle Fisher's tentative suggestion that the order of the genes on the chromosome would be found to be *D C E*. It also seems that the very controversial question of whether the genes are separable or not is settled in the most convincing way of all — by their separation.

From *Nature* 23 September 1950.

cells. However, the early results of trials being conducted at the Defence Evaluation and Research Agency, at Farnborough in Hampshire, offer hope that the process can be developed on a commercial scale and contribute to the cost reduction required to allow titanium to become a mainstream engineering material. Chen and colleagues also point out that the principle of oxygen ionization and removal by electrolysis can be applied to several other metal oxides. Here we have the intriguing possibility of producing pre-alloyed metals from mixed-oxide precursors.

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Molecular biology

Small subunit, big science

James R. Williamson

Ribosomes are the cell's protein factories, and consist of two subunits, the large and the small. The structure of the small subunit of a bacterial ribosome has now been solved at atomic resolution, and is described in papers by Ramakrishnan and colleagues on pages 327 and 340 of this issue[1,2]. These reports come shortly after the appearance of an independent, slightly lower-resolution structure of the small subunit[3]. Because this is the subunit where the genetic code is read, the new structural information shows in molecular detail how messenger RNAs (mRNAs) are faithfully translated into proteins.

The ribosome is a fundamental cellular component, found in both prokaryotes (loosely, eubacteria, which lack a nuclear membrane) and eukaryotes (which have such a membrane). It synthesizes all of the proteins in the cell, using mRNA as the template. The ribosome acts in concert with a variety of smaller factors which help to orchestrate the process, but the two main functions are entrusted to the ribosome itself: decoding the genetic code in the mRNA, and catalysing the formation of chemical bonds between amino acids, resulting in the polypeptide chains of proteins.

The large and small subunits of the eubacterial ribosome are known as 50S and 30S, respectively, from their rates of sedimentation in a centrifuge (the entire ribosome is 70S). A ribosome's catalytic site, the peptidyl transferase centre, is in the 50S subunit, and the structure of this subunit from the bacterium *Haloarcula marismortui* was described last month at a resolution of 2.4 Å (refs 4,5). Decoding of the mRNA occurs on the 30S subunit, and it is structural determination of 30S, to 3 Å from *Thermus thermophilus*, that is now described by Ramakrishnan and colleagues[1,2]. Together, these papers complement the earlier 7.8 Å structure of the entire 70S ribosome[6].

The 30S subunit serves as the assembly guide for all of the factors needed in protein synthesis. The mRNA is a copy of the genomic 'repository' DNA sequence that encodes a gene product, and is bound to the 50S subunit in complex with transfer RNAs (tRNAs) via codon–anticodon interaction. The tRNAs are 'charged' with an amino acid, and deliver the appropriate amino acid specified by the codon. There are three tRNA binding sites on the ribosome, the A (acceptor), P (peptidyl) and E (exit) sites, each of which is occupied in succession by a particular tRNA

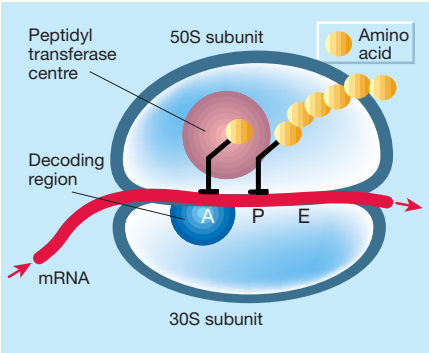

Figure 1 **The two essential functions of the ribosome. The 30S (small) subunit contains the messenger RNA decoding site, and the 50S (large) subunit the peptidyl transferase centre. The mRNA threads through the subunit interface, and is decoded. The three transfer RNA binding sites, A (acceptor), P (peptidyl) and E (exit) then handle amino-acid selection, addition and completion of polypeptide synthesis. Here a charged tRNA is shown in the A site, and a nascent peptidyl-tRNA in the P site; the E site is vacant. Increasingly sophisticated structural characterization[1–5] of the subunits and the ribosome as a whole will allow these events to be investigated in molecular detail.**

during the protein synthesis cycle. The tRNAs bridge the large and small subunits, with the anticodon arm of the tRNA pointing towards the 30S subunit for decoding, and the acceptor arm of the tRNA pointing into the 50S subunit for peptidyl transferase (Fig. 1).

After protein synthesis begins, the growing peptide chain is covalently attached to the tRNA bound in the P site. The terminal amino group of the growing polypeptide is aimed into the A site, ready to link to the next amino acid to be delivered. The critical decoding event occurs as charged tRNAs bind to the A site and — in some unknown fashion — the cognate codon–anticodon interaction is sensed by the 30S subunit, triggering peptide-bond formation on the 50S subunit. The entire complex must then shift down the line to prepare for the next round of peptide-bond formation in the process known as translocation.

The new information on ribosome structure[1–5] finally provides a molecular face to players that have long been known by their functions. The 30S subunit in particular is among the most intensively studied of cellular components, and a vast amount of genetic and biochemical information has accumulated about it over the past 40 years. Confronted with just the crystallographic coordinates, it would have been impossible to ascribe function to structural features. But this is not the case, and we can readily recognize the familiar functional sites. The locations of the A-, P- and E-site interactions with tRNA are clearly recognizable, and are in agreement with the biochemical and genetic data.

Furthermore, one of the papers[2] presents analysis of the 30S subunit in complex with several antibiotics. The significance of this is that antibiotics often work by inhibiting ribosome function, so blocking protein synthesis. Together with existing information about the effect of antibiotics on translation, the 30S antibiotic data provide insights into the mechanism of decoding and translocation.

The 30S subunit has a very different architecture to that of its 50S partner. In the 30S, clear domain boundaries are evident, and potentially flexible regions can be seen in cryo-electron microsopic reconstructions[7,8]: large movements, on the scale of tens of angstroms, must occur on the 30S subunit during translocation of the mRNA from one codon to the next. In contrast, the 50S subunit is monolithic[7,8], its components being intricately folded and packed into a rigid structure. These unlikely colleagues — the squat and stolid 50S subunit and the lithe and flamboyant 30S subunit — work together to carry out one of the most intricate functions of all cells.

It is perhaps not widely appreciated that about two-thirds of the ribosome's mass is composed of RNA. With atomic knowledge of the 30S and 50S structures, and how they assemble into the overall 70S ribosome, one point stands out — the most essential functions of the ribosome are carried out by RNA[9]. Historically, biologists have concentrated on genes and proteins. The dogma that nucleic acids are the repository of information and that proteins catalyse chemical reactions was overturned only 15 years ago by the demonstration of catalytic RNAs[10,11]. Despite increasing support for the RNA-world hypothesis, which sees RNA-based life-forms as the progenitors of modern cells, most biologists did not seriously consider the possibility that RNA could be playing more than a bit part in reactions such as protein synthesis. Well, wake up and smell the coffee. In the ribosome, it has turned out that most of the intersubunit interface is RNA[6], the peptidyl transferase centre is RNA[4,5,12], and the decoding site and most of the A and P sites are RNA[1–3]. It appears that the modern ribosome is composed of a somewhat geriatric, but functionally vital, RNA scaffold that is propped up and doted upon by its protein grandchildren. The ribosome is one colossal RNA enzyme. ■

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Astronomy

Galactic rotation in real time

John Kormendy

On page 349 of this issue, Andrea Ghez and colleagues[1] present the first measurements of the acceleration of stars orbiting the nucleus of our Galaxy. These stars are part of a dense cluster associated with the compact radio source known as Sagittarius A*, which is thought to be at the actual centre of the Milky Way. Measuring the accelerations of stars in galactic orbits (and not just their velocities) is a technical tour de force. These accelerations are enormous on a Galactic scale; at 3–6 mm s^{-2} they are comparable to those experienced by the Earth as it orbits the Sun. With these measurements, the authors help to identify Sagittarius A* as the supermassive black hole at the centre of the Milky Way. They also test — and provide support for — fundamental assumptions about the dynamics of the Galactic centre and our understanding of violent activity in galactic nuclei.

Ghez *et al.*[1] took a series of infrared images of the nucleus of the Milky Way with the 10-metre Keck telescope on Mauna Kea, Hawaii. The Galactic centre is 8 kiloparsecs away (1 parsec = 3.26 light years) and Ghez *et al.* study an area 0.2 parsecs across. By taking short exposures they freeze the jitter in the image caused by turbulence in the Earth's atmosphere and produce images with 0.05 arcsec (0.002 parsecs) resolution. From such an image, one can accurately determine stellar positions. The stars nearest the centre move significantly in just a few years, so Ghez *et al.* can measure the two components of their velocities that are in the plane of the sky. If the central star cluster is in equilibrium, then its dynamics tell us the total mass enclosed inside it.

Past velocity measurements[2–5] have already established that a dark mass equal to 2.6×10^6 solar masses ($M_\odot$) lies in the vicinity of Sagittarius A*. For the first time, Ghez *et al.* provide acceleration measurements for three stars within 0.005–0.013 parsecs of Sagittarius A* (Fig. 1, overleaf). Acceleration vectors provide important new information about the dark mass by pointing to the location of the gravity source. The acceleration vectors are still fairly uncertain — observations span only 4 years — but they intersect within 0.002 ± 0.0016 parsecs of Sagittarius A*. This strengthens the association of Sagittarius A* with the dynamically detected dark mass — an object with enough mass to bend the orbits of stars moving at speeds of up to 1,350 km s^{-1}.

Sagittarius A* is widely believed by astronomers to be the Galaxy's central black hole. It is appropriately tiny — similar in radius to the orbit of Mars around the Sun[6]. Nevertheless, for a black hole of a few million solar masses, it is surprisingly dark. The strong gravity of a black hole prevents radiation escaping from inside a certain radius (the Schwarzschild radius). But gas that is still falling toward the point of no return is accelerated to almost the speed of light in an