derived (O. Uhlenbeck, University of Colorado, Boulder). Remarkably, only seven specific nucleotides of the ribozyme and six of the RNA substrate are absolutely required for activity. The simplicity of the active site of these ribozymes makes them extremely attractive candidates for detailed structural analysis.

Hepatitis delta virus (HDV), a circular satellite RNA of hepatitis B virus, increases the severity of viral hepatitis. HDV RNA can undergo autocatalytic cleavage and ligation *in vitro* in a manner similar to plant viroid and satellite RNAs (D. Gottleib, Drexel University). However, the structure at the cleavage site does not resemble the hammerhead[5], suggesting that there are undiscovered types of catalytic RNA structures waiting to be defined.

Splicing reactions

Whereas the processing reactions mentioned above involve only cleavage of the RNA substrates, splicing entails both cleavage and ligation. The essential similarities between three types of splicing reactions — group I intron self-splicing; group II intron self-splicing; and nuclear-pre-messenger RNA splicing (*c*, *d* in the figure; see ref. 6) — were enumerated by T. Cech (University of Colorado, Boulder). First, all are two-step reactions, in which the 5′ splice site is cleaved in the first step and the 3′ splice site cleaved in the second. Second, all the cleavage-ligation reactions seem to occur by transesterification mechanisms. Third, there are similarities in the conserved bases at the splice junctions, which when mutated can lead to comparable effects. For example, 5′ splice-site mutations can result in activation of cryptic 5′ splice sites in group I introns and nuclear pre-mRNAs. Conversely, mutation of the conserved guanosine at the 3′ splice site abolishes 3′ splice-site cleavage but not the first step of splicing for both group I introns and nuclear pre-mRNAs.

The various systems differ, however, with respect to the elements that determine selection of the 5′ splice site. For nuclear pre-mRNAs, the intron sequences near the 5′ splice junction are required for determining the 5′ splice site, whereas in group I and group II introns, flanking exon sequences have the principal role. Single-base substitutions in intron sequences flanking a nuclear pre-mRNA 5′ splice site, for example, can decrease or abolish cleavage at that site (see refs 7,8), whereas the first six nucleotides of a group II intron can be altered without affecting the accuracy of 5′ splice-site cleavage (P. Perlman, Ohio State University).

The most obvious difference between self-splicing and nuclear pre-mRNA splicing is that in the latter the catalyst must be assembled from several parts. The pieces (splicing factors) include multiple proteins as well as four small nuclear ribonucleoprotein particles (snRNPs), termed U1, U2, U5 and U4/U6. These pieces are assembled with the pre-mRNA into a structure called the 'spliceosome' in which the cleavage-ligation reactions occur.

The order of snRNP binding during assembly of the yeast spliceosome, reported by J. Abelson (California Institute of Technology), turns out to be identical to the mammalian pathway, although the prerequisites may be subtly different. In yeast, for example, U1 snRNP binding requires both the 5′ splice site and branch point, whereas in the mammalian system only the 5′ splice site is required. In both the mammalian and yeast systems, 5′ splice-site cleavage requires prior binding of U1 snRNP to the 5′ splice site. But aberrant splicing of 5′ splice-site mutants is not completely corrected by compensatory mutations in U1 snRNA (M. Rosbash, Brandeis University; C. Guthrie, University of California, San Francisco). These results implicate at least one other *cis*- or *trans*-acting component in addition to yeast U1 snRNP in specifying the precise position of 5′ splice-site cleavage. Selection of the 3′ splice site is potentially quite complex, as at least two *cis*-acting elements (the branch point and 3′ splice site) can play a role in the appropriate experimental conditions (A. Weiner, Yale University). The ability to reconstitute snRNPs from their snRNA moieties and protein components (our own work) should facilitate future studies on spliceosome assembly.

The reaction pathways of group II intron self-splicing and nuclear pre-mRNA splicing are identical (*d* in the figure), strongly suggesting that the collective RNA moieties of the snRNPs provide at least some (perhaps all) of the catalytic function. Individual domains of self-splicing group II introns, when

George Eugene Uhlenbeck (1900–1988)

GEORGE UHLENBECK, who died on 31 October, was primarily known as one of the originators of the notion of electron spin. This idea was the result of an intensive collaboration with S.A. Goudsmit, a collaboration encouraged and stimulated by Paul Ehrenfest, their professor at Leiden University. The idea of Uhlenbeck and Goudsmit was one of the two final touches that were added during 1925 to the so-called vector model of atomic structure, the other being Pauli's exclusion principle. It gave a clear-cut explanation of mysterious quantum numbers that arose in the analysis of complex spectra. Two years later Pauli showed how the spin of the electron could be dealt with in non-relativistic quantum mechanics; in the relativistic theory of Dirac, the spin appears as a necessary consequence of the formalism. And the notion of spin is not confined to the electron but is a universal feature of particle physics.

Rockefeller University

Why was this important work never rewarded with a Nobel prize? Pauli received his for the exclusion principle in 1945; would it not have been logical to let a Nobel prize to Uhlenbeck and Goudsmit follow? Was the Nobel committee disturbed by the fact that, completely unknown to Uhlenbeck and Goudsmit, Ralph Kronig had had the same idea before and had discussed it with Pauli, who discouraged him? Or did it consider that the subsequent work of these two candidates, although valuable, was not quite of Nobel class? Neither argument sounds convincing.

Uhlenbeck's later work deals with various topics. Together with Konopinsky, he developed a somewhat different version of Fermi's theory of nuclear β-decay, which revealed interesting insights, but was later abandoned. The main emphasis of his work, however, is on statistical mechanics. With E. Beth, Uhlenbeck formulated the quantum mechanics of the second virial coefficient (the second term in a power expansion of the equation of state for a non-ideal gas). And with B. Kahn — who later, during the occupation of The Netherlands, fell victim to Nazi antisemitism — he made considerable progress in the theory of condensation. Uhlenbeck moved to the United States before the outbreak of World War II and during the war he headed the theoretical division of the Massachusetts Institute of Technology radiation laboratory, where he mainly studied problems of noise.

After the war he devoted more time to teaching. A project to write a comprehensive treatise on the foundations of statistical mechanics was frustrated by the untimely death of his collaborator T.H. Berlin, but he did publish two smaller volumes based on lecture notes. He also wrote valuable papers on the equation of state, brownian motion and the kinetic theory of transport phenomena. Uhlenbeck was an outstanding lecturer and his students, at Ann Arbor, Utrecht and Rockefeller University will remember him as a wise and benevolent counsellor. H.B.G. Casimir

H. B. G. Casimir, formerly Research Director of the Philips Company at Eindhoven, lives at De Zegge 7, 5591 TT Heeze, The Netherlands.