perhaps more likely, whether a rearrangement or modification of the first active site takes place after the first step).

This two-site model for the spliceosome fits well with earlier genetic and biochemical data indicating that independent recognition of the splice-site sequences takes place at each step[1,7]. For example, a specific block of the second splicing step (resulting in the accumulation of splicing intermediates) occurs with certain point mutations in either the branch point or splice sites of the intron, or in U2 or U6 snRNAs.

A similar phenotype can also be observed in yeast strains that have mutations in genes encoding splicing factors, or in mammalian splicing extracts treated with the protein phosphatase inhibitor okadaic acid. It is possible that in at least some of these cases the phenotype may arise because of a failure to switch the RNA intermediates in the spliceosome to the active site required for catalysis of the second step.

It will be of great interest now to probe the stereochemistry of the mechanism used by group II self-splicing introns. Unlike pre-mRNA introns, group II introns self-excise and do not require *trans*-acting factors. But they do use a two-step transesterification mechanism that generates identical RNA intermediates and products to those formed in the spliceosome, and it is tempting to speculate that there is an evolutionary relationship between pre-mRNA introns and contemporary group II self-splicing introns — that is, both may be descended from a common ancestral intron, but have diverged such that the intramolecular RNA base-pairing interactions that structure self-splicing introns are provided in *trans* for pre-mRNA introns by the spliceosomal snRNAs[8,9]. Evidence pointing to striking similarities between interaction domains in self-splicing introns and base-pairing interactions detected in the spliceosome is consistent with, but does not prove, this model — as discussed by Weiner[10], these similarities may reflect a process of chemical determinism rather than reflecting an evolutionary relationship.

If future analyses show that pre-mRNA and group II self-splicing introns have identical stereochemistry, the issue remains open. But if group II introns accept the R_P phosphorothioate diastereomer, at either splice site, we will know that they are not in fact related to pre-mRNA introns after all. Given the recent history of surprises in the RNA field, I am eagerly awaiting the answer and making no predictions. □

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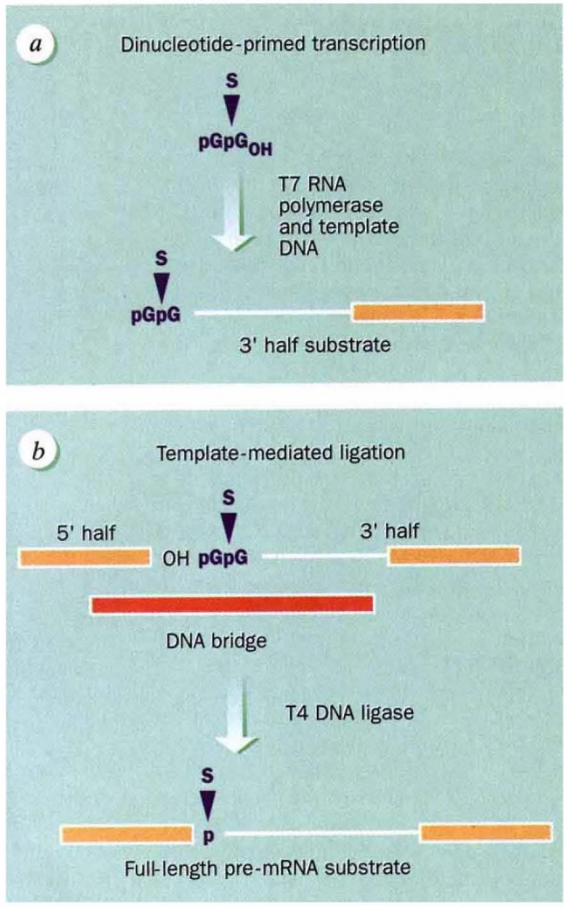

The template-mediated ligation method[2], for introducing modifications at preselected sites in RNA, is illustrated here for insertion of a single phosphorothioate at the 5′ splice site in a pre-mRNA[1]. *a*, The 3′ half-molecule is made by dinucleotide-primed, *in vitro* transcription of a DNA template containing the desired sequence adjacent to a phage polymerase promoter. The dinucleotide containing a single internucleotide phosphorothioate was made by chemical methods and the 5′ phosphate was added enzymatically. The R_P and S_P phosphorothioate diastereomers can be separated by chromatography of the dinucleotides and hence used to prepare separate 3′ half-molecules with either configuration. *b*, The corresponding 5′ half-molecule (also prepared by *in vitro* transcription) is joined to the 3′ half-molecule using T4 DNA ligase, with the two RNAs precisely aligned for ligation on a single-stranded DNA bridge spanning both sequences. The product is a full-length pre-mRNA substrate containing a single S_P or R_P phosphorothioate linkage at the 5′ intron–exon junction.

RÉSUMÉ

Beaver boom

THE spectre of population bottlenecks looms large for conservationists; the worry is that after a population crash, loss of genetic variation and inbreeding depression may compromise the species' recovery. H. Ellegren *et al.* have come up with heartening news on that score (*Proc. natn. Acad. Sci. U.S.A.* **90**, 8150–8153; 1993). By the mid-nineteenth century the beaver had disappeared from Sweden and its numbers stood at maybe a few tens of individuals in Norway. But introduction of animals from Norway into Sweden in the 1920s and 1930s paid off, for Swedish beavers now number around 100,000. Ellegren and colleagues find that this population explosion occurred despite unusually low genetic variability, including that in the major histocompatibility complex. The results show that limited MHC polymorphism does not necessarily compromise recovery of an endangered species (at least over short ecological timescales).

Greater crater

OF the suggested causes of the mass extinctions at the end of the Cretaceous and start of the Tertiary era 65 million years ago, a giant meteorite impact is probably the front runner. The buried geological structure at Chicxulub, Mexico, is thought to be the remnant of the impact crater.

V. L. Sharpton and collaborators, writing in last week's *Science* (**261**, 1564–1566; 1993), now say that the diameter of the structure may be far greater than the earlier estimate of 200 km. Beyond the three concentric circles detected in earlier gravity maps, they find broken arcs of a fourth. If these mark the outer rim of the original crater, it was huge: about 300 km across, making it the site of one of the largest known impacts on any planet in the inner Solar System in the past four billion years.

Turning yellow

NOT least among the trials of advancing decrepitude is the increasing opacity of the lens. In severe cataracts this results from loss of the short-range structural order, to which the lens owes its transparency. Now G. Suàrez *et al.* (*J. biol. Chem.* **268**, 17716–17721; 1993) have examined normal lenses from people between 6 and 82 years old by X-ray scattering: it turns out that scattered intensity increases rather abruptly from the age of about 55. This parallels, and by implication is caused by, accretion of a fluorescent, urea-insoluble fraction in the lens protein. Such cross-linked aggregates are secondary products of nonenzymic glycation by the Maillard reaction (formation of Schiff bases from reducing sugars and protein amino groups), which generates characteristic fluorophores and yellowing. The melancholy message may be to lay off the chocolates (as well as everything else).