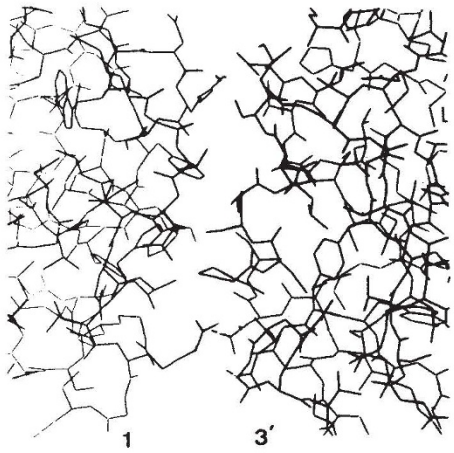

Fig. 4 Contacts between molecules 1 and 3′. The two molecular envelopes are complementary over an area of ~0.28 nm^2. About 12 intermolecular contacts <0.4 nm (involving residues Asn 113, Arg 114, Asp 119, Arg 125 of molecule 1 and Asn 65′, Asp 66′, Gly 67′, Ser 81′, Thr 89′ of molecule 3′) ensure a coupling between the molecules. The 15–20 well-localized water molecules in the intermolecular zone reinforce this coupling.

and Asn 103 of molecule 1 and Thr 47 and Asp 48 of molecule 2, which is characterized by distances between the mean atomic positions which are smaller than the van der Waals' distances.

We have shown that X-ray diffuse scattering can provide information not accessible by classical crystallography. In the case of hen egg-white lysozyme in the orthorhombic form, correlated rigid-body displacements of several molecules have been detected. It must be emphasized that, for this study, the diffuse scattering provides direct information only about rigid-body displacements of the molecules, that is intermolecular motions and intermolecular contacts. It is very likely that other protein crystals display diffuse scattering features due to intramolecular motions (such as domain motion). Their analysis can be performed in a similar way as the one reported here; our study must be considered as an initial study to develop a new approach to protein dynamics.

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Erratum

The *Tetrahymena* ribozyme acts like an RNA restriction endonuclease

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In this article corrections for the last four paragraphs were not incorporated on page. The corrected version is printed here.

Sequence-specific endoribonucleases might have many of the same applications for the study of RNA, that DNA restriction endonucleases have for the study of DNA[6]. The pattern of restriction fragments could be used to establish sequence relationships between two related RNAs, and large RNAs could be cleaved to fragments of a size more useful for study. The 4-nucleotide specificity of the ribozyme is ideal for cleavage of RNAs of unknown sequence; an RNA of random sequence would have an average of 1 cleavage site every 256 bases. The automatic end-labelling of one fragment during ribozyme cleavage is a practical advantage.

Development of the ribozyme as a useful tool for molecular biology has just begun. The cleavage efficiency of large RNA substrates needs to be improved, so that digestion is complete. The effects of denaturants such as urea and formamide must be further explored; they appear to increase the specificity of cleavage, and at the same time they should melt the secondary structure of the substrate to maximize the availability of target sequences. Finally, mutagenesis of the active site of the ribozyme must be continued to ascertain how many of the 256 possible tetranucleotide cleavage enzymes (of which we have investigated only four) work with acceptable efficiency and specificity.

Some protein ribonucleases cleave RNA substrates with high specificity by recognizing a combination of RNA structure and sequence; the structure is more important (for instance RNase III (ref. 28) and RNase M5 (ref. 29). On the other hand known proteins that cleave single-stranded RNA substrates are only specific for mononucleotides or dinucleotides (for instance, RNase T_1 cleaves after guanosines[30]). Thus, the L-19 IVS RNA is considerably more sequence-specific for single-stranded RNA cleavage than any known protein ribonuclease.

RNA sequence recognition often involves recognition of RNA by RNA. Triplet codons in messenger RNA are recognized by anticodons in transfer RNA, and ribosome binding sites in prokaryotic mRNA are recognized using the Shine–Dalgarno interaction with 16S rRNA. It is easy to imagine uses for sequence-specific protein ribonucleases in pre-mRNA splicing and 3′-end generation, but there is no evidence for such enzymes. Instead, 5′ splice sites in pre-mRNA are recognized using the U1 small nuclear RNA[13,31] and the 3′ end cleavage site of histone H3 pre-mRNA by U7 snRNA[32]; much of the sequence discrimination is provided by complementary base-pairing. Perhaps it is difficult to construct an active site in a polypeptide to bind an unstructured stretch of nucleotides specifically. It may be possible that in certain reactions involving RNA substrates, RNA catalysis has not been superseded by protein catalysis for the simple reason that RNA does the job better.