athan show that their observational interpretation of water-vapour feedback is compatible with results from climate models, and it is worth expanding on this point. Our recent intercomparison[5] of 14 atmospheric general circulation models (GCMs) shows significant disagreements amongst the models' global-mean dF/dT_s values. This, however, is primarily caused by differences in the depiction of cloud feedback. When output from the GCMs is processed in the same way as the data used by Raval and Ramanathan, to average clear-sky regions separately, there is quite good agreement in their clear-sky dF/dT_s values: the average for the 14 GCMs is 2.38 ± 0.16 W m^{-2} K^{-1}, which compares favourably with Raval and Ramanathan's observational value, 2.31 W m^{-2} K^{-1}, derived using the equation above. But if the water-vapour feed-back is suppressed by making $g(T_s)$ fixed in the equation, the observational value would be 3.67 W m^{-2} K^{-1}, significantly exceeding the GCM values.

As Raval and Ramanathan emphasize, their observed water-vapour feedback has a very simple explanation: it is dominated by the saturation vapour pressure of water through the Clausius–Clapeyron equation. The same explanation would seem to apply to the GCMs. With all the uncertainties in our knowledge of climate processes, especially cloud feedback[5], it is gratifying that at least one such process has a simple explanation. □

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DNA STRUCTURE

The turn of the quadruplex?

Maxim Frank-Kamenetskii

WHILE molecular biologists are still wondering how to deal with triplexes, even more unusual DNA structures are surfacing. On page 825 of this issue, Sundquist and Klug[1], demonstrate that artificial DNA molecules, which have one blunt end and an overhanging single-stranded TTGGGGTTGGGG tail at the other end, form remarkably stable dimers in solution. Their observation may have biological implications because these tails are characteristic of the ends of *Tetrahymena* chromosomes, and the ends of chromosomes (telomeres) in other species, including *Homo sapiens*, carry very similar sequences. Chemical probing of the dimers ruled out the possibility of a duplex forming between the tails, and led Sundquist and Klug to the conclusion that the tails are attached to each other by the following unusual mechanism. First the tails fold back, forming hairpins stabilized by Hoogsteen G:G pairs[2]. Then two such hairpins associate forming a stack of four G4 tetrads (See Fig. 4*b* of their paper, page 829). The thymines serve as linking elements in the construction.

For decades, G-rich oligo- and polynucleotides have been notorious because of their ability for inter- and intramolecular aggregation. Gellert *et al.*[3] were the first to suggest that GMP aggregates in the form of G4 tetrads, in which four guanines cohere through Hoogsteen pairing. But comprehensive studies of the G-aggregates were hampered by the lack of adequate experimental tools. Sen and Gilbert[4] applied the chemical-probing technique to this problem, and demonstrated that G-tetrads were formed in aggregates of G-rich strands.

Chemical probing is becoming increasingly popular in studies of unusual DNA structures, such as cruciform, the Z form and the H form. In this method, a DNA carrying an unusual structure is subjected to a chemical reaction with known specificity. The DNA is end-labelled and the reaction sites are converted into chain breaks by treatment with piperidine, just as in the standard Maxam–Gilbert protocol for DNA sequencing, with subsequent separation of the DNA fragments in a denaturing gel. In so doing one localizes the sites of DNA modification by the reagent at sequence resolution. Sen and Gilbert followed the methylation of the guanine N7 position and found that the guanines in G-tracts were not methylated in the aggregates. This provided strong evidence that a structure had been formed in which the guanines were involved in Hoogsteen pairing. The aggregates studied by Sen and Gilbert were tetramers, and in G-tetrads all the N7 positions participate in hydrogen bonding, hence the conclusion that the G-tetrads were responsible for aggregation.

The coherence of telomeres carrying single-stranded tails was first described for *Oxytricha*[5,6]. In these studies DNA molecules were double-tailed, however, so it was difficult to arrive at any definite conclusion about the nature of the aggregates. Sundquist and Klug prepared single-tailed DNA molecules (with *Tetrahymena* telomeric tails TTGGGG-TTGGGG), which enabled them to show beyond any doubt that dimers were formed, not the tetramers postulated by Sen and Gilbert.

At the same time methylation experiments clearly indicated that the N7 positions of all tail guanines from both monomers are completely protected in the dimer, exactly as predicted by Sen and Gilbert. Sundquist and Klug explain their data in terms of the structure shown in Fig. 4*b* of the paper. In contrast with the model of Sen and Gilbert, all adjacent chains in the quadruplex are antiparallel. This implies the formation of not only inter- but also intramolecular quadruplexes. Panyutin *et al.*[7] have recently observed periodic methylation patterns for 27- and 37-long oligo(G), which they interpreted as an indication of the folding of molecules into an intrastrand quadruplex with three loops forming bends. These loops corresponded to the three maxima on their methylation patterns.

The structure proposed by Sundquist and Klug provides a model of recognition and association of two identical, rather than complementary, DNA sequences. It is tempting to speculate that the association of telomeric tails is the first step towards the recognition of homologous DNA molecules by each other in meiosis. This speculation, however, is questionable because we now know the main biological function of telomeric tails: they serve as primers for telomerase, which elongates the ends of chromosomes.

So why do people search for additional functions? The homologous recognition of DNA molecules may be mediated by proteins. This is most probably true for present-day forms of life. But the fact that telomerase carries an RNA molecule, part of which is complementary to the telomeric tail, has led to the assumption that telomeres are molecular fossils of the RNA world[8]. There were no proteins at the time and the ancient RNA had only itself to rely on. More data are accumulating to suggest that the most fundamental processes in eukaryotes conserve ancient principles inherited from the RNA world. Who can guarantee that the principle of homology recognition proposed by Sundquist and Klug is not of this category? □

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■ Editorial note: single-stranded telomeric sequences have been shown to fold back on themselves to form cyclic guanine tetrads (J.R. Williamson, M.K. Raghuraman & T.R. Cech *Cell*; in the press).