



Fig. 4 Absorption (top) and CD (bottom) spectra of two forms of poly[r(G-C)]·poly[r(G-C)]. Absorption spectra were measured with a Gilford model 250 spectrophotometer; CD spectra were measured with a JASCO J500C spectropolarimeter. Both instruments have thermoelectric cell blocks. The absorbance and CD were measured in 10 mM phosphate, pH=7.0, 6 M NaClO₄ at 22 °C (solid line) and 45 °C (dotted line). An extinction coefficient of 6,560 at 260 nm was used for the poly[r(G-C)] at 22 °C (ref. 6). The CD spectrum at 22 °C is similar, but not identical to the spectrum seen in buffer alone. It is identical to that for the polymer in 3 M NaClO₄. At 45 °C, 6 M NaClO₄ the CD spectrum is identical to that seen in conditions of lower perchlorate and higher temperatures, and is similar to that in 20% (v/v) ethanol in 4.8 M NaClO₄.

shoulder at 290 nm; this is very similar to the spectrum of Z-DNA (ref. 5). Two types of CD spectra are seen for poly[r(G-C)]. The first is represented by the spectrum at 6 M NaClO₄, 22 °C. It is identical to the CD spectrum in 3 M NaClO₄ and is similar to a CD spectrum measured in 10 mM sodium phosphate (not shown) which matches the CD spectrum of Gray *et al.*⁶ in 1 mM Na phosphate, 0.1 mM EDTA, pH 7.8. These CD spectra are all presumed to be from an A-type conformation of the poly[r(G-C)] (ref. 7). Because the CD spectrum of the polymer in 6 M NaClO₄, 22 °C and 3 M NaClO₄ are identical, we used the latter solvent at 45 °C for NMR experiments; at 22 °C the NMR linewidths are too broad for analysis. The CD spectra in dilute phosphate differ from those in NaClO₄ by a small change in the band at 285 nm. This band is particularly sensitive to solvent, and diminishes at high ionic strength. This CD band may be correlated with the small differences in phosphorus resonances between the RNA in 10 mM HEPES and in 3 M NaClO₄.

The CD spectrum in 6 M NaClO₄, 45 °C is very different from the others, and is identified as that of Z-RNA. The CD remains positive in the region above 215 nm. The negative bands above 280 nm and below 240 nm in A-RNA change sign in Z-RNA; the positive band near 260 nm remains positive.

The transition temperature for the A- to Z-RNA transition is a function of the solvent conditions. In 6 M NaClO₄, the transition temperature is ~35 °C; in 4.8 M, it is ~45 °C; in 4 M, ~80 °C; in 3 M, it is above 80 °C and not measurable in our

instrument. The addition of ethanol to the perchlorate solution decreases the transition temperature, so that in 4.8 M NaClO₄/20% ethanol, the RNA is in Z-form at room temperature. This temperature dependence of the transition to Z-RNA form is analogous to that of poly[d(G-C)]·poly[d(G-C)]. For that polynucleotide, the Z-form is favoured at higher temperatures in LiCl or ethanol/water solutions^{1,8,9}. However, we have found that solvents which will cause a B to Z transition in poly[d(G-C)], such as 4 M NaCl or 1 M MgCl₂, do not cause an A to Z transition in poly[r(G-C)]. This is consistent with the work of Westerink *et al.*¹⁰ and Uesugi *et al.*⁷ who found no Z transition in these salt solutions for r(G-C) oligonucleotides.

The kinetics of the transition also vary with the solvent and the temperature. In 6 M NaClO₄, a temperature shift from 22 °C to 35 °C results in an A- to Z-RNA transition which takes ~1 h. The reverse transition occurs over 5 h. A temperature shift from 22 °C to 45 °C (or addition of 20% (v/v) ethanol and concomitant dilution to 4.8 M NaClO₄), however, produces the Z-RNA form in ~10 min, although again the reverse transition on lowering the temperature from 45 °C to 22 °C takes several hours.

This is the first major conformational change reported for a double-stranded RNA; it shows that RNA has conformational lability, contrary to current belief. It is consistent with the finding of Uesugi *et al.*¹¹ that r(C-m⁸G-C-m⁸G) exists in a Z-like structure. The transition to Z-form RNA requires more extreme conditions than the transition to Z-form DNA. However, in analogy to Z-DNA, other more physiological environments may be found to favour Z-RNA, and other RNA sequences may also undergo the transition. In any case one should now consider conformations other than A-form when considering double-stranded regions of RNA in ribosomes, viruses and other RNA-protein complexes.

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1. Patel, D. J., Kozlowski, S. A., Nordheim, A. & Rich, A. *Proc. natn. Acad. Sci. U.S.A.* **79**, 1413-1417 (1982).
2. Patel, D. J., Canuel, L. L. & Pohl, F. M. *Proc. natn. Acad. Sci. U.S.A.* **76**, 2508-2511 (1979).
3. Jovin, T. M. *et al. Cold Spring Harb. Symp. quant. Biol.* **47**, 143-154 (1983).
4. Wang, A. H.-J. *et al. Science* **211**, 171-176 (1981).
5. Pohl, F. M. & Jovin, T. M. *J. molec. Biol.* **67**, 375-396 (1972).
6. Gray, D. M., Liu, J.-J., Ratliff, R. L. & Allen, F. S. *Biopolymers* **20**, 1337-1382 (1981).
7. Uesugi, S. *et al. J. biol. Chem.* **259**, 1390-1393 (1984).
8. van de Sande, J. H. & Jovin, T. M. *EMBO J.* **1**, 115-120 (1982).
9. Hall, K. B. & Maestre, M. F. *Biopolymers* (in the press).
10. Westerink, H. P., van der Marck, G. A., van Boom, J. H. & Haasnoot, C. A. G. *Nucleic Acids Res.* **12**, 4323-4338 (1984).
11. Uesugi, S. *et al. J. Am. Chem. Soc.* **106**, 3675-3676 (1984).
12. Hall, K. B., Cruz, P. & Chamberlin, M. F. *Archs Biochem. Biophys.* (in the press).

Erratum

Dynamics of meltwater discharge from Northern Hemisphere ice sheets during the last deglaciation

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IN the above letter, the last four lines of the penultimate paragraph on p. 676 ('anomaly areas... $\delta^{18}\text{O}_{\text{sw}}$ anomaly') are a repetition from a previous paragraph. The correct four lines read:

amount of meltwater discharged into the Canadian Current before 13 kyr BP according to our calculations. This excess may reflect an early marine-drawdown phase of North American deglaciation^{4,23}.