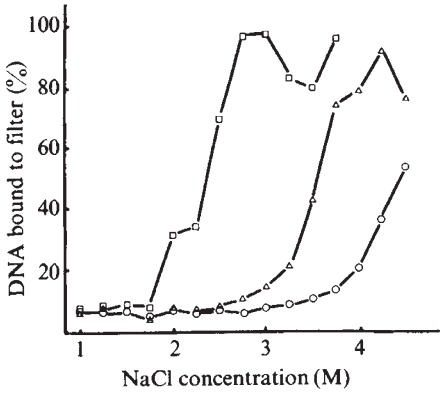

Fig. 3 Dependence of DNA binding on temperature. Aliquots (5 ml) of PM2 DNA at concentrations of 0.25 μM nucleotide in 10 mM Tris-HCl (*p*H 8.0) and various amounts of salt were incubated at 50 °C (□), 23 °C (△) and 0 °C (○). They were then filtered through nitrocellulose filters which had been prewashed with 5 ml salt solutions at the same temperatures. The filter speed was 9 s per 5 ml.

itself, or single-strand regions formed in junctions between B and Z segments, bind the DNA to the nitrocellulose filter.

A double logarithmic plot of the apparent equilibrium constant (DNA bound to the filter divided by DNA passing through the filter), according to the equation $\log K = r \times \log(I) + \text{constant}$, where I = molar NaCl, gives approximately straight lines with slopes between 13 and 10 (Fig. 2). The high value of r indicates that the transition is cooperative. The average value of 11 is the same as that reported by Pohl and Jovin[1] for the salt-induced cooperative transition of poly(dG–dC)·poly(dG–dC) with an average length of 34 base pairs.

CD studies indicate that Z DNA segments can also be induced by high salt in naturally occurring DNA[5,6]. Changes of the CD spectrum similar to those induced by high salt have also been observed in DNA or in poly(dG–dC)·poly(dG–dC) alkylated with mitomycin C[7]. This observation and our observation with AAAF- and UV-treated DNA suggest that DNA damages facilitate the transition of the DNA helix from a B form to a Z form.

The Z form in damaged DNA might be favoured for steric reasons. Thus, in oligonucleotides *N*-(deoxyguanosin-8-yl)-acetylaminofluorene, the major adduct in AAAF-treated DNA, assumes the *syn* configuration found in the Z DNA rather than the *trans* configuration found in B DNA[8]. Alternatively, a DNA

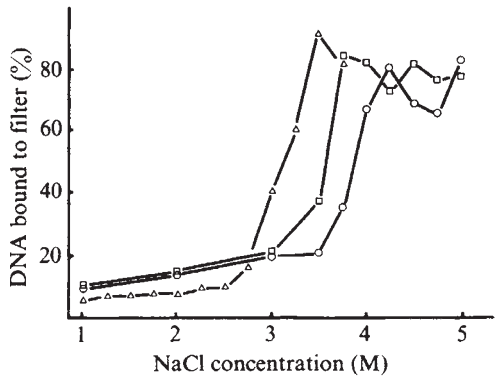

Fig. 4 Retention of native and linear PM2 DNA at 37 °C in dependence of the NaCl concentration. △, Native PM2 DNA; ○, linear PM2 DNA; □, linear PM2 DNA exposed to 600 J m^{-2} of UV light. Linear DNA was prepared by incubating 0.2 mM PM2 DNA nucleotide for 3.5 h with 25 units ml^{-1} of restriction endonuclease *Msp*I (New England Biolabs) in 10 mM Tris-HCl (*p*H 7.5), 10 mM $MgCl_2$, 6 mM KCl and 100 μg ml^{-1} acetylated bovine serum albumin. After incubation, the DNA was extracted with an equal volume of chloroform-octanol (9:1) and dialysed against 10 mM Tris-HCl (*p*H 7.5). Filtrations were carried out as described in Fig. 3 legend.

structure containing B and Z segments might require that the hydrogen bonding between some base pairs is disrupted. DNA damages might therefore favour the Z structure because of interference with hydrogen bonding. Indeed, AAAF treatment and UV treatment lower the melting point of DNA[9,10]. Furthermore, an increase in temperature leads to a transition at a lower salt concentration (Fig. 3). The influence of temperature on the transition is not at the level of the formation of Z form itself (at least in regions with an alternating G–C sequence), as the transition in poly(dG–dC)·poly(dG–dC) is not temperature-dependent[1].

The transition of segments of the DNA from a B form to a Z form requires unwinding of the DNA helix. In a negatively supercoiled DNA molecule, unwinding of the DNA will remove the supercoils and, depending on the degree of transition, introduce positive supercoils. Since removal of negative supercoils is associated with a considerable decrease in free energy[11,12], one would expect that the B–Z transition is favoured in DNA containing negative supercoils. As shown in Fig. 4, when the negatively supercoiled PM2 DNA is converted to a linear form by treatment with the restriction endonuclease *Msp*I (*Msp*I is an isoschizomer of *Hpa*II which cleaves PM2 DNA at a unique site[13,14]), the transition is induced at a much higher salt concentration.

It will be of interest to demonstrate that Z DNA-like structures also occur at physiological salt concentrations. Indeed, this is the case for DNA damaged extensively with AAAF or with mitomycin C, and, with the appropriate DNA binding proteins present, the transition might also occur with DNA containing fewer lesions. Such Z DNA-like structures might be the trigger for the initiation of DNA repair processes. One would predict from such a mechanism that the presence of negative supercoils is important for DNA repair—it has been demonstrated in *Escherichia coli* that gyrase antagonists which prevent negative supercoiling inhibit the restoration of infectivity of UV-irradiated phage λ DNA[15]. Transitions of DNA segments from a B form to a Z form and vice versa might also be involved in other aspects of regulation of DNA metabolism, a mechanism which would be compatible with the key role of DNA gyrase in *E. coli*[16].

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Corrigendum

In the letter 'β-Endorphin alters luteinizing hormone secretion via the amygdala but not the hypothalamus' by N. Parvizi and F. Ellendorf, *Nature* **286,** 812–813 in paragraph 2, lines 2/3, the reference to 'Basolateral hypothalamus' is incorrect and it should read 'mediobasal hypothalamus'.