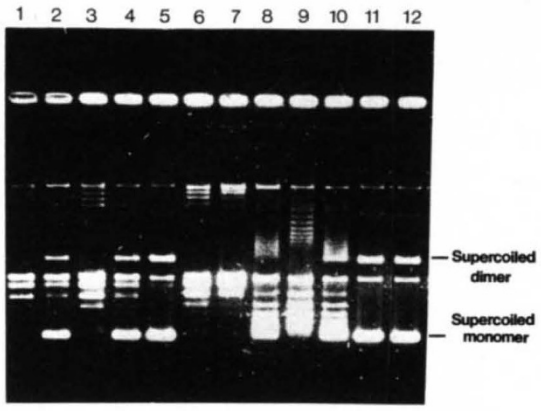

Fig. 2 Agarose gel electrophoresis of plasmid DNA, showing the effect of tyrosine protein kinases on the activity of type I DNA topoisomerases. The following were added to samples of supercoiled DNA: lane 1, 20 ng and lane 2, 2 ng of *E. coli* DNA topoisomerase I incubated without $pp60^{src}$; lanes 3–5, 200, 20 and 2 ng respectively of *E. coli* DNA topoisomerase I incubated with $pp60^{src}$; lanes 6–8, 1, 0.1 and 0.01 units respectively of calf thymus DNA topoisomerase I incubated without TPK75; lanes 9–11, 1, 0.1 and 0.01 unit respectively of calf thymus DNA topoisomerase I incubated with TPK75; lane 12, no topoisomerase.
Methods: Topoisomerase and protein kinase were incubated for 60 min in conditions described in Fig. 1 legend, except that 1 mM ATP was used instead of [γ-^{32}P]ATP. The topoisomerase was then diluted and assayed. The reaction mixture for *E. coli* DNA topoisomerase I contained 50 mM NaCl, 10 mM Tris-HCl *p*H 7.5, 100 μg ml^{-1} gelatin, 6 mM $MgCl_2$ and 0.5 μg of supercoiled pUC8 plasmid DNA. The reaction mixture for calf thymus DNA topoisomerase I contained 150 mM NaCl, 20 mM Tris-HCl *p*H 8, 100 μg ml^{-1} gelatin, 1 mM EDTA and 0.5 μg of supercoiled plasmid DNA. After incubation at 37 °C for 30 min, the reaction was stopped by adding 1% SDS, and the mixture analysed by electrophoresis on a 0.8% agarose gel.

and chromatin assembly are probably coupled *in vivo*[15]. The degree of DNA supercoiling in transcriptionally active chromatin is probably controlled by balancing the relaxing activity of DNA topoisomerase I and the supercoiling activity of a 'gyrase' consisting of DNA topoisomerase II coupled with ATP and unknown factor(s). A correlation between the proliferation state of eukaryotic cells and DNA superhelicity has been observed by several investigators[16–18]. When the rate of cell growth is high, DNA is more negatively supercoiled, and vice versa[16–18]; there is no clear explanation for this alteration of supercoiling. Postsynthetic modification of topoisomerases may represent one possible mechanism of regulating cellular proliferation. The products of retroviral oncogenes, including several membrane-associated tyrosine protein kinases[19], and membrane-associated growth factor receptor tyrosine protein kinases (such as that for epidermal growth factor) share the ability to stimulate growth, possibly through common mechanisms. Such stimulation of growth must involve activation of replicative processes and increased levels of transcription and translation. It will be of interest to determine whether retroviral- or cellular-encoded protein kinases affect topoisomerases either by direct interaction or through another tyrosine protein kinase that shuttles from the plasma membrane to the nucleus, transmitting a growth signal. For example, it is known that the binding of epidermal growth factor to the plasma membrane results in the internalization of a portion of the receptor molecule[20,21].

We propose that the receptor kinase might affect growth processes by either migrating to the nucleus and directly phosphorylating a topoisomerase, or by phosphorylating another kinase which in turn passes to the nucleus and phosphorylates a topoisomerase. The same possibilities exist for growth signal transmission by plasma membrane-associated viral tyrosine kinases. However, the activity of such kinases should be independent of an external growth signal. Although there exist no data indicating that viral tyrosine kinases are internalized, experiments from our laboratory and elsewhere have shown that proteolytic fragments of $pp60^{src}$ contain kinase activity[19]. In addition to phosphorylation by tyrosine protein kinases, it has been shown previously that DNA topoisomerases from various sources can be modified *in vitro* by phosphorylation of a serine residue[22], or by poly(ADP) ribosylation[23]. It remains to be determined which, if any, of these reactions is important *in vivo*.

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Errata

Unusual abundance of glyceraldehyde 3-phosphate dehydrogenase pseudogenes in vertebrate genomes

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Nature **312**, 469–471 (1984)
IN the issue of 29 November the above letter appeared with an incorrect title.

Modelling the global climate response to orbital forcing and atmospheric carbon dioxide changes

N. G. Pisias & N. J. Shackleton
Nature **310**, 757–759 (1984)
THE legend to Fig. 1 was incorrect and should read:

Fig. 1 Linear variance spectra for *a*, solar insolation at 65° N in June; *b*, the benthic oxygen isotope record from core V19-30; *c*, the simulated ice volume from the simple ice sheet model of Imbrie and Imbrie[8]; and *d*, for the time derivative of the benthic oxygen isotope record from core V19-30. All spectral calculations are from 326 data points spanning the last 340 kyr. Bandwidth shown is for spectral calculations from 120 points of the sample auto-covariance functions. Important periods associated with orbital parameters are labelled.