matters arising

Simplification of palindromic telomere theory

CAVALIER-SMITH's motive in devising his palindromic model for telomeres[1] was to surmount the obstacle of the replication of the 3′ end of a linear molecule of DNA (Fig. 1). His palindromic end with related hairpin bend, however, makes the 3′ end unnecessary and therefore, by the usual rules of natural selection, improbable.

This can be achieved by a slight modification of his original model (Fig. 1). This has the attraction of not only being simpler, five steps replacing seven, but also of explaining the special property of telomeres which distinguishes them from any other end of a linear DNA molecule, namely a chromosome break: their stability.

The essence of my model is that the self-paired telomeric palindrome is the normal condition, in G1, G2 and M. Then the phosphate backbone of the double helix is continuous through the telomere. Similarly, DNA replication will proceed continuously through the telomere thus making the terminal RNA primer redundant.

This self-paired state is temporarily lost as the result of S and restored via denaturation. The endonuclease that nicks the end of the palindrome and allows the unfolding and refolding in the new configuration must be telomere specific, making it probable that all telomeres of one genome carry the same palindrome. Without this manoeuvre sister chromatids would remain attached end-to-end leading to non-disjunction at anaphase.

A philosophical attraction of my modification of the model is that the sister molecules (sister chromatids) participate equally in the process, in contrast with the original model in which one complete molecule is produced at once and the sister molecule is incomplete and has to go through a complex manoeuvre to correct itself. My model also requires one S phase, at the start. The original model starts and ends with DNA synthesis.

Finally, my model may be open to experimental confirmation. If the telomeric palindrome is long enough, the asymmetry between sister telomeres, one being old and one wholly new, might be detectable in autoradiographs of the first metaphase after labelling in S with ^{3}H-thymidine. Wilson and Thomas report palindromes up to 12,000 nucleotides long[2]. As there are only two telomeres per chromosome the possibility of recognising telomeric palindromes in DNA extracts would be like searching for the proverbial needle (or should we say hairpin?) in a haystack.

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[1] Cavalier-Smith, T., *Nature*, **250**, 467–470 (1974).
[2] Wilson, D. A., and Thomas, C. A., *J. molec. Biol.*, **84**, 115–144 (1974).

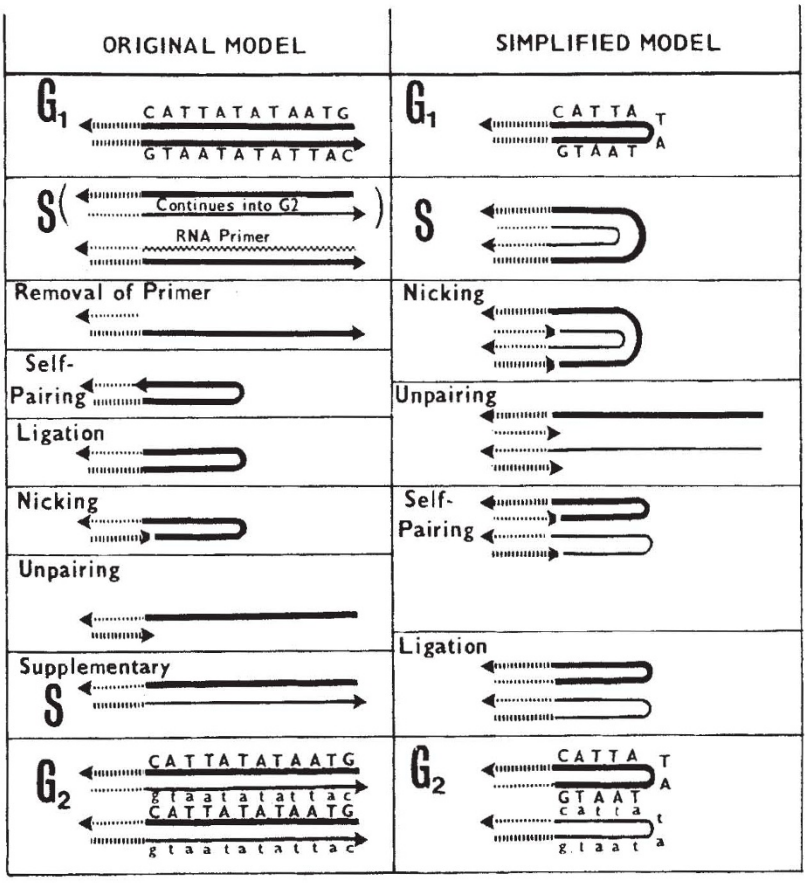

Fig. 1 Two models for the replication of telomeres. ——, Old DNA; ——, new DNA; ~~~~, RNA. The arrowheads indicate the 3′ ends of the phosphate backbone. Capital letters nucleotides of old DNA. Small letters, new DNA. Entire line, the palindrome. Dotted line, the rest of the DNA molecule (of indefinite length).