



Figure 2 | Three priming mechanisms. Interaction of the primase with the helicase is necessary for primer synthesis at a lagging-strand priming site. The primase makes primers in the opposite direction to helicase movement, leaving three ways by which the replisome might resolve this directional problem. **a**, The whole replisome can pause for primer synthesis; **b**, it can promptly release the primase; or **c**, as described for the first time by Pandey *et al.*¹ and Manosas *et al.*², the replisome can continue to move forward while the primase–helicase interaction persists. This produces a priming loop that eventually collapses into the lagging-strand trombone loop, probably on transfer of the primer to the lagging-strand polymerase.

resonance energy transfer (FRET), which uses the interaction between fluorescent dyes as a readout of the proximity of molecules to each other. The dyes were arranged on the lagging-strand template so that they would come close enough together for FRET to occur if a priming loop were formed. FRET was observed only under conditions where, and about as often as, primers were made. The FRET data¹ can be explained only by the formation of a priming loop on the lagging-strand template while leading-strand synthesis continues (Fig. 2c).

In another single-molecule study, Manosas *et al.*² studied the T4 replisome, in which the primase and helicase are separate proteins that interact during primer synthesis. They used an ingenious experimental design consisting of a double-stranded DNA hairpin structure that contains priming sites when in a single-stranded form. The DNA is attached to a magnetic bead that is stretched at a constant low force by a magnetic field. Videomicroscopy of the bead movement allows measurement of the length of the DNA. As the helicase converts the hairpin to single-stranded DNA, the DNA lengthens and then subsequently contracts as the hairpin reanneals behind it. The changes in DNA length allow measurement of the rate of helicase action in real time. Using this system, the authors² showed that helicase–primase interaction and subsequent primer synthesis did not result in helicase pausing. Most of the time, reannealing of the hairpin was blocked by the persistence of a primase-bound primer, indicating that the primase had been released promptly by the helicase at the priming site (Fig. 2b). Less frequently, the rate of DNA lengthening decreased for about half a second, and then there was an immediate jump in length. This observation can be explained only by the formation and subsequent release of a priming loop (Fig. 2c). When the helicase and

primase were artificially fused together as in the T7 replisome, priming-loop formation was markedly increased, and blocks to reannealing (by released primase-bound primer) were not observed.

An unusual aspect of Pandey and colleagues' work¹ is the high efficiency of priming achieved by the T7 primase on their short templates. Priming sites are trinucleotides that occur frequently in single-stranded DNA templates. They are generally used inefficiently by the primase for primer synthesis, and it is thought that only a fraction of primers are functionally extended by the lagging-strand polymerase. These factors account for the relatively long (1–2 kilobases) Okazaki fragments. When studying lagging-strand priming during leading-strand synthesis by the T7 replisome on long templates, the van Oijen group³ clearly observed pauses coincident with primer synthesis. These occurred at relatively low frequency, consistent with the size of Okazaki fragments — but the authors' single-molecule experimental set-up could not detect priming loops. Reconciliation of these observations³ with those of Pandey *et al.*¹ is not straightforward, and may indicate that replisome pausing occurs during or soon after functional primer synthesis, while mechanisms involving primase dissociation and priming-loop formation ensure that the replisome is not unnecessarily slowed during more frequent, non-productive priming events. ■

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3. Lee, J.-B. *et al.* *Nature* **439**, 621–624 (2006).
4. Yuzhakov, A., Kelman, Z. & O'Donnell, M. *Cell* **96**, 153–163 (1999).



50 YEARS AGO

A Survey of Soils in the Kongwa and Nachingwea Districts of Tanganyika. By B. Anderson — Everyone knows the dismal sequel to the ambitious scheme for the mechanized production of ground-nuts in East Africa, which was characterized by the failure to employ pedological methods on pedological problems. After the horse had departed, some effort was made to shut the stable door and a very competent soil surveyor was set to work to make a proper study of the soils of the Kongwa and Nachingwea districts. The publication under review presents his results and shows what can be achieved by one trained pedologist working 'on the cheap' with limited facilities, but with specialized technical assistance from various institutions. The moral for would-be planners of land-use is obvious.

From *Nature* 19 December 1959.

100 YEARS AGO

It may be of interest to record a fact which has come under my notice while engaged in the development of a uranium mine in Turkestan. The ore is oxidised and calcareous, and contains uranium, vanadium, and copper, radium being present in accordance with Prof. Rutherford's formula, which gives the quantity of it in relation to the uranium. The uranium is on the average 3.8 per cent., but in some places reaches the ratio of 30 per cent. and more ... As I know from the literature of the subject that vanadium and uranium are toxic substances, I instruct the workmen to wash their hands well before going to their dinner and after their work. "We do this," they say, "but at the same time we know that in actual practice a cut on a hand, which lasts for a long time in a coal mine, here, when powdered by the ore, gets well very quickly."

From *Nature* 16 December 1909.

50 & 100 YEARS AGO