TERMINATION OF DNA REPLICATION

Termination Event is different at:

- Circular Replicons
- Linear Replicons

TERMINATION OF REPLICATION
(OF CIRCULAR DNA)

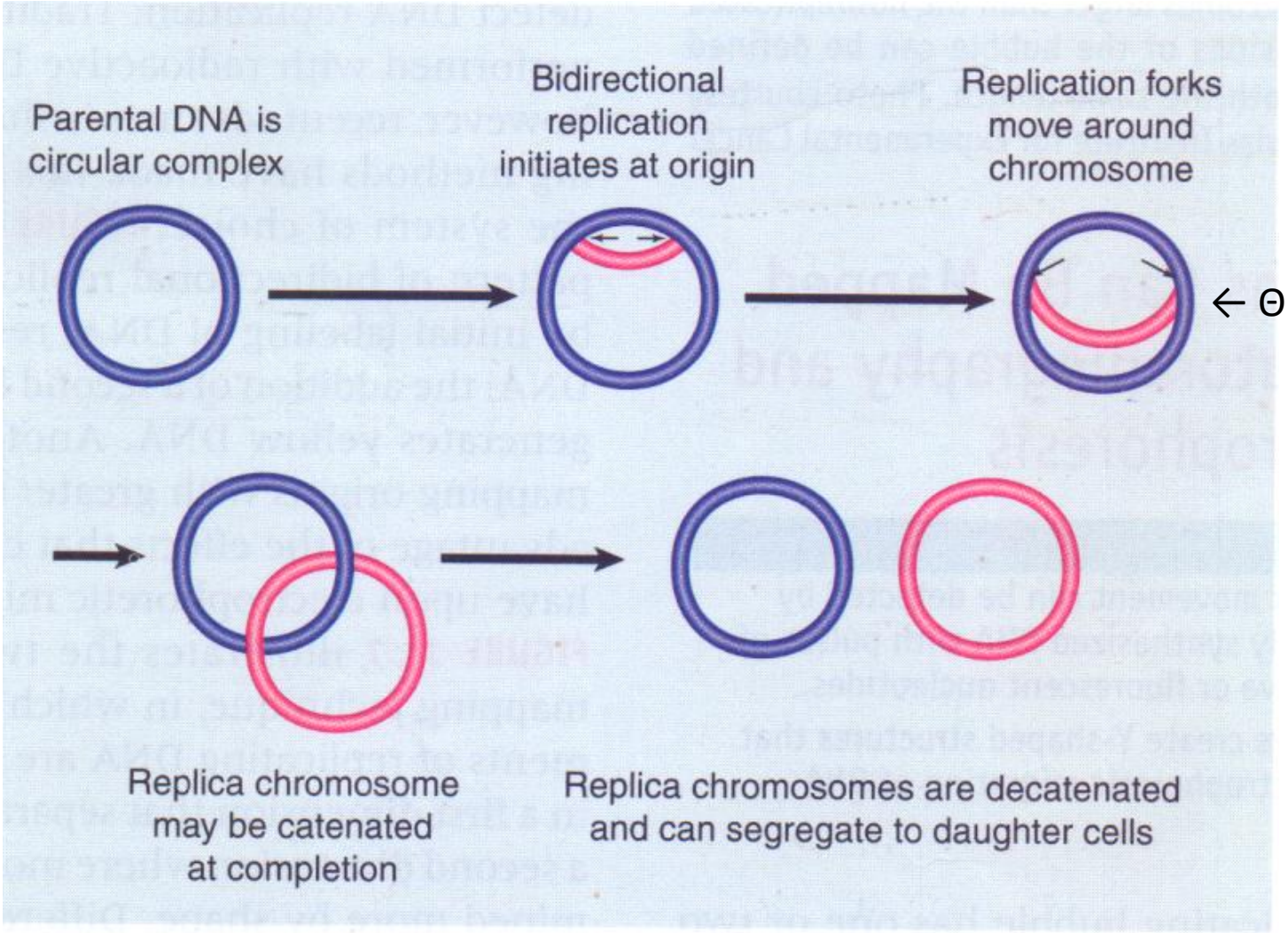
Circular Replicons:

Bacterial Chromosome

Plasmids

Many Bacteriophages

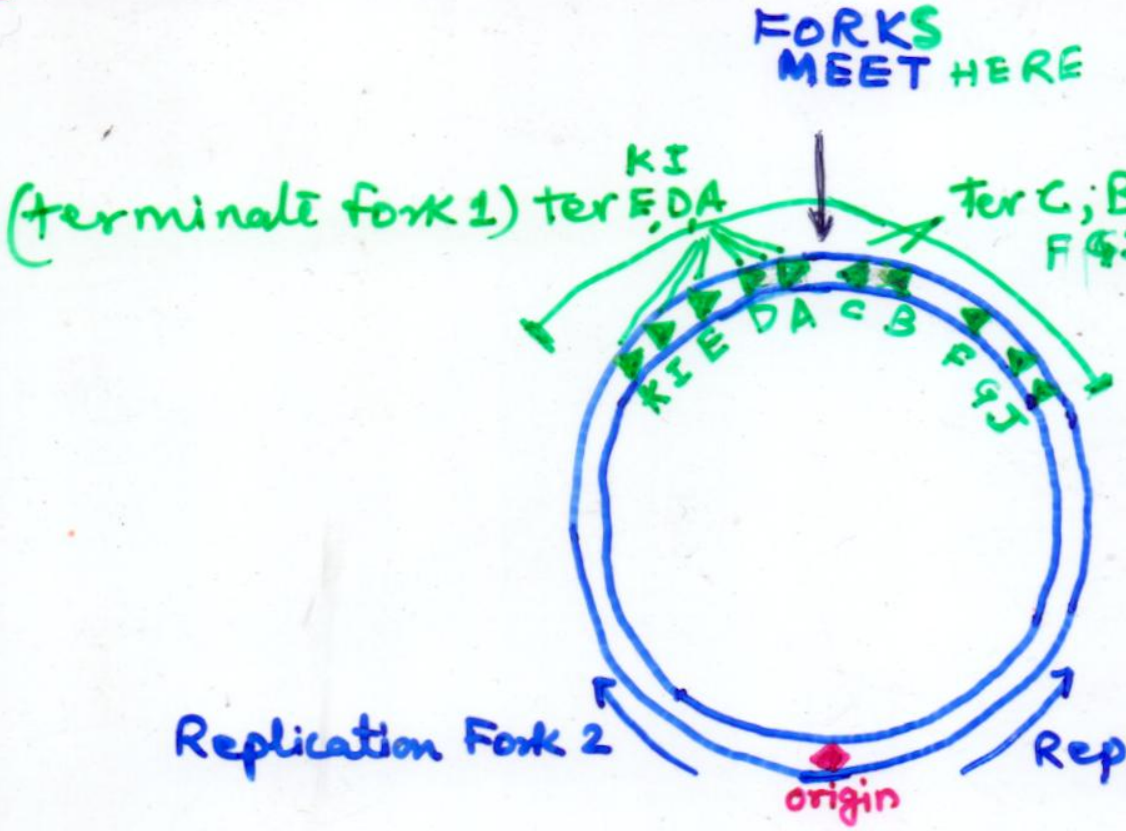
Cp & Mt DNA



← Θ (theta Structure)

FIGURE 11.8 Bidirectional replication of a circular bacterial chromosome is initiated at a single origin. The replication forks move around the chromosome. If the replicated chromosomes are catenated, they must be disentangled before they can segregate to daughter cells.

Replication termini in *E. coli* are located beyond the point at which the replication forks actually meet



- **Termination Sequences are unidirectional i.e., they function in only one orientation.**
- ***ter* site is recognized by a unidirectional contrahelicase protein Tus in *E. coli* and RTP in *B. subtilis*.**

Common Features of Ter Sequence :- (23 bp consensus seq.)

```
1                   10                  20
- AATTAGTATGTTGTAACT AAAGT-
- TTAATCATACAACATTGA TTTCA-
```

tus gene product : • 36 KD protein (necessary for termination)

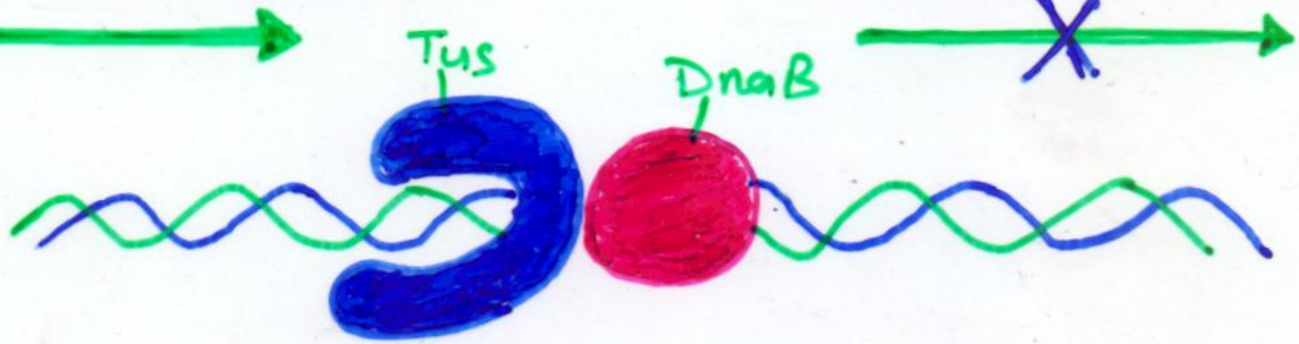
Tus - Termination utilization substance (E. coli)

RTP - Replication termination protein (B. subtilis)

- Tus binds to the consensus seq., where it provides a contra-helicase activity and stops DnaB from unwinding DNA.
- The leading strand continues to be synthesized right up to the ter element, whereas the nearest lagging strand is initiated 50 to 100 bp before reaching ter.
- Tus protein bind to DNA assymmetrically. (α-helixes of the protein protrude around the double helix at the end that blocks the replication fork).

DNA accessible
(Replication proceeds)

DNA blocked
(Replication terminates)



Tus binds to ter asymmetrically and blocks replication in only one direction.

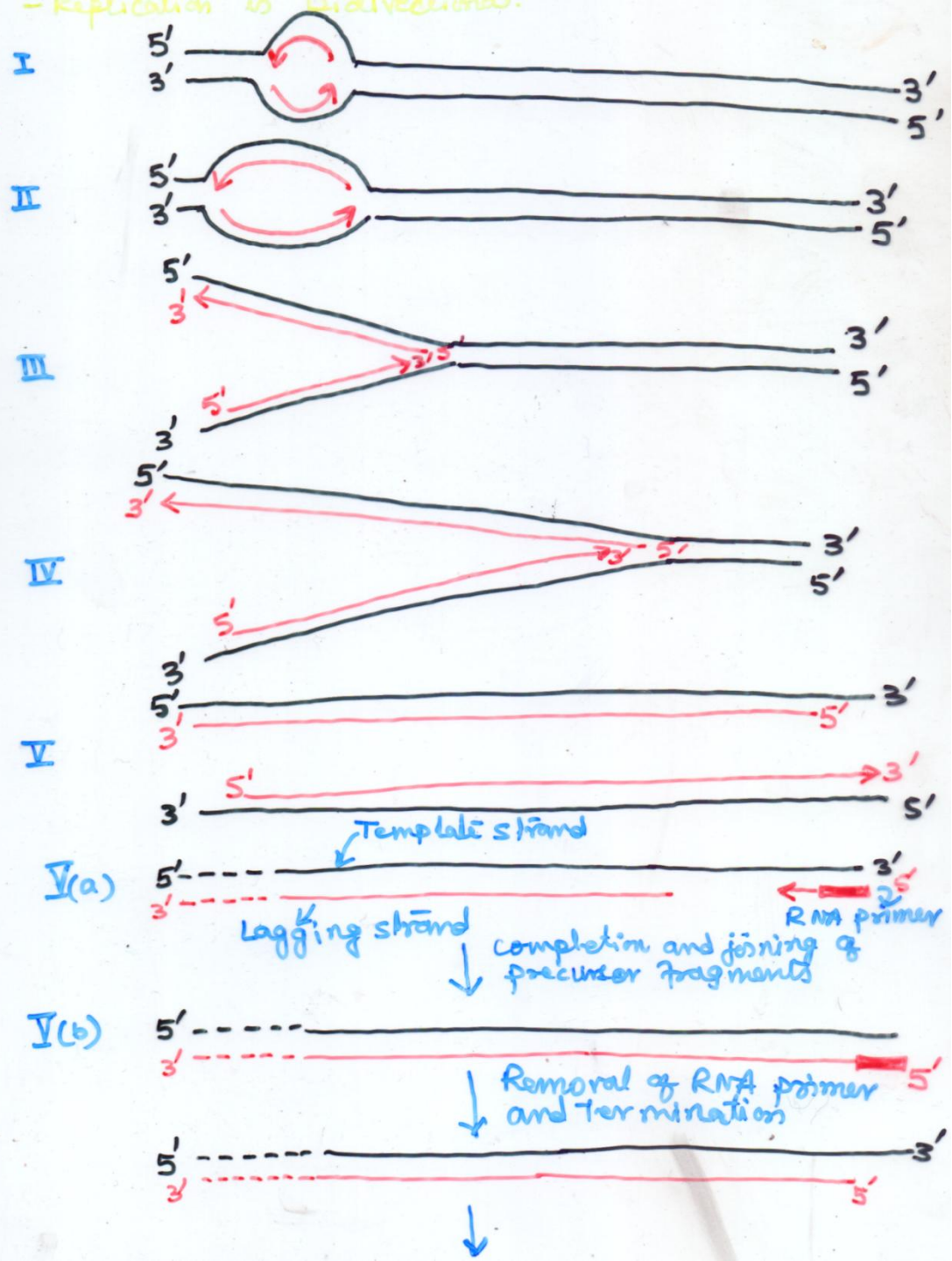
Functions of *ter*-Tus System

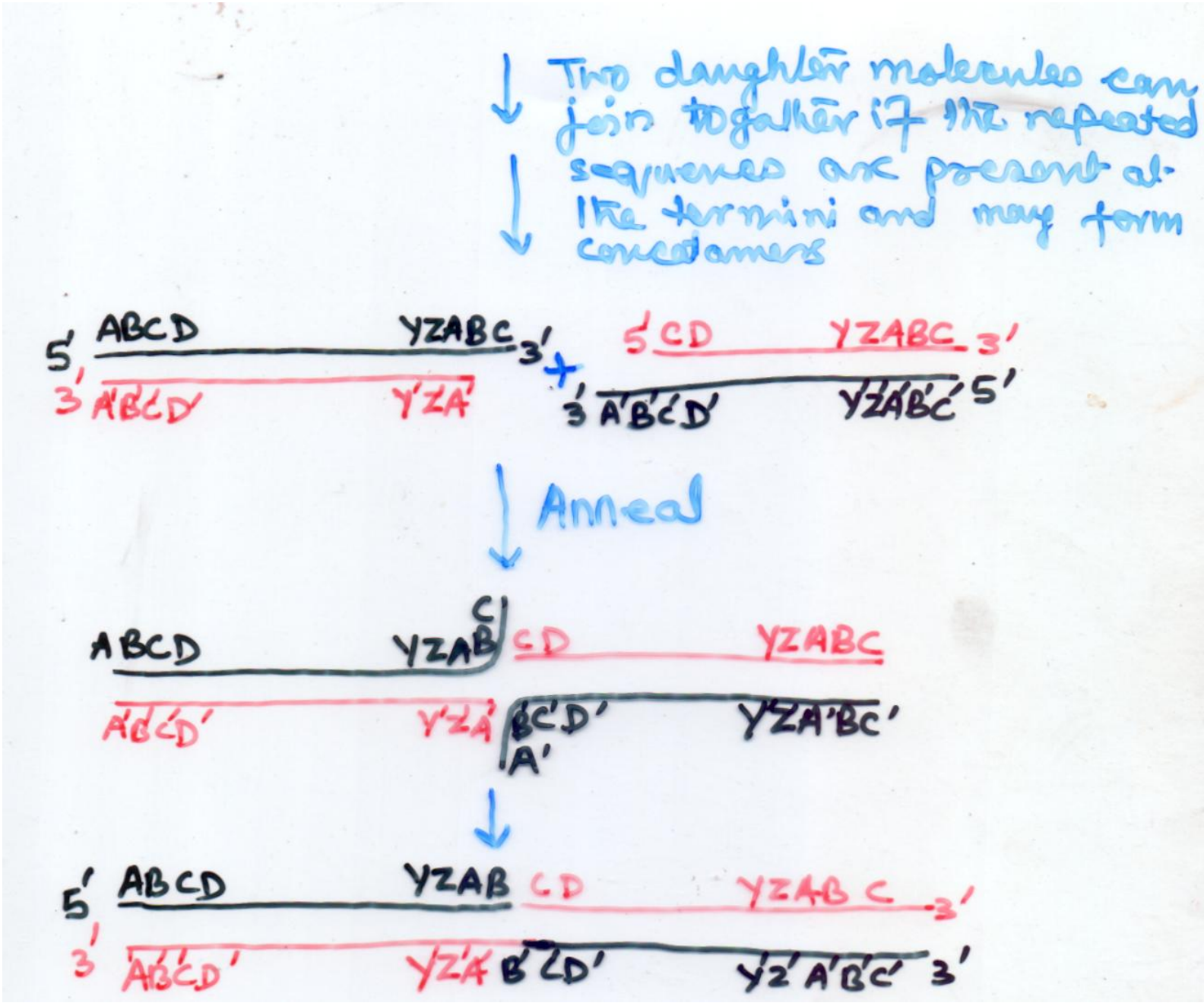
- The function of ter-Tus system in vivo is not clear.
- Because deletion of ter site and tus gen in E. coli has no effect.
- The advantage of a specific termination strategy in E. coli may provide an opportunity for regulating the decatenatio of interlocked rings.

TERMINATION OF REPLICATION
(OF LINEAR DNA)

PROKARYOTE GENOME

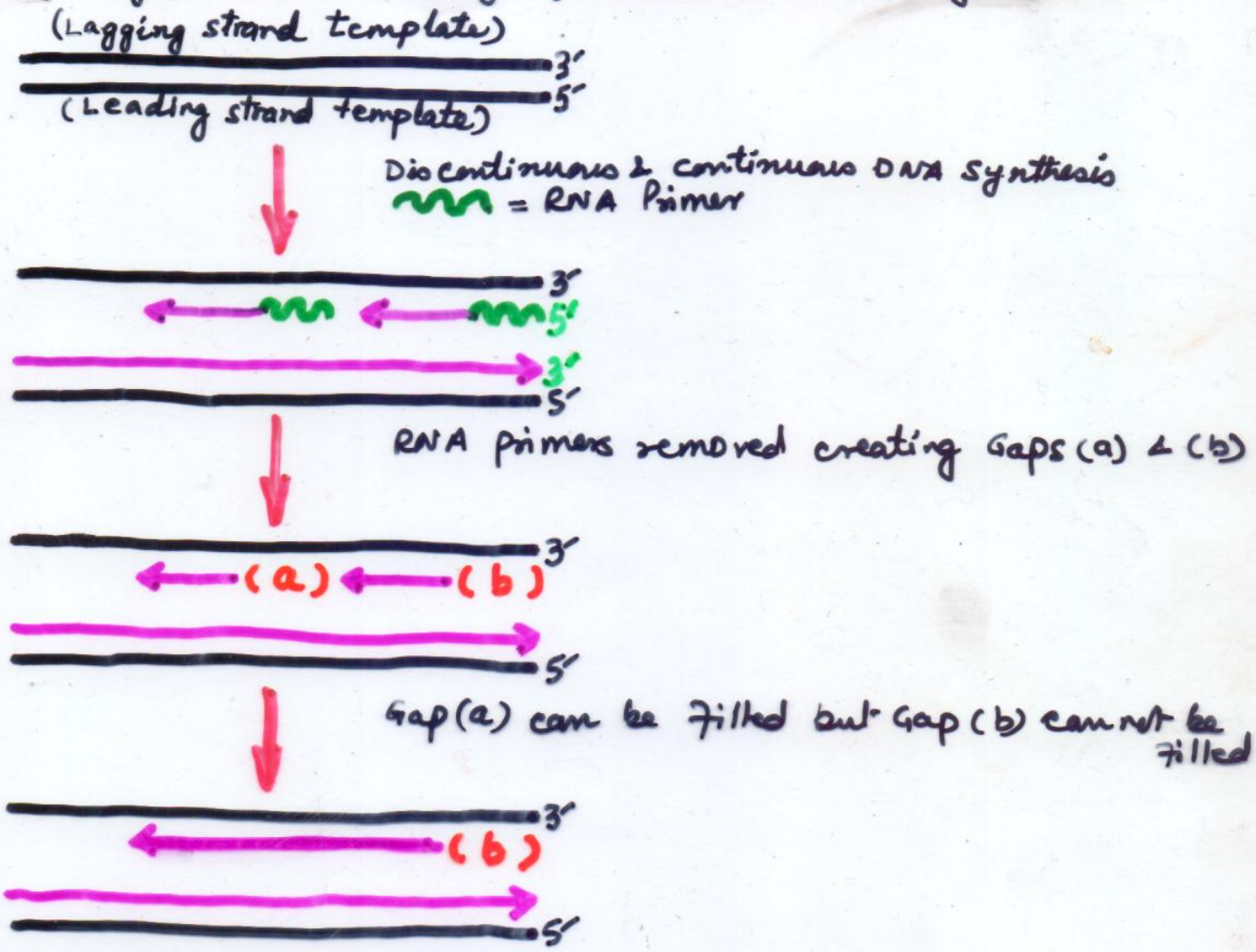
(Phage T_7)

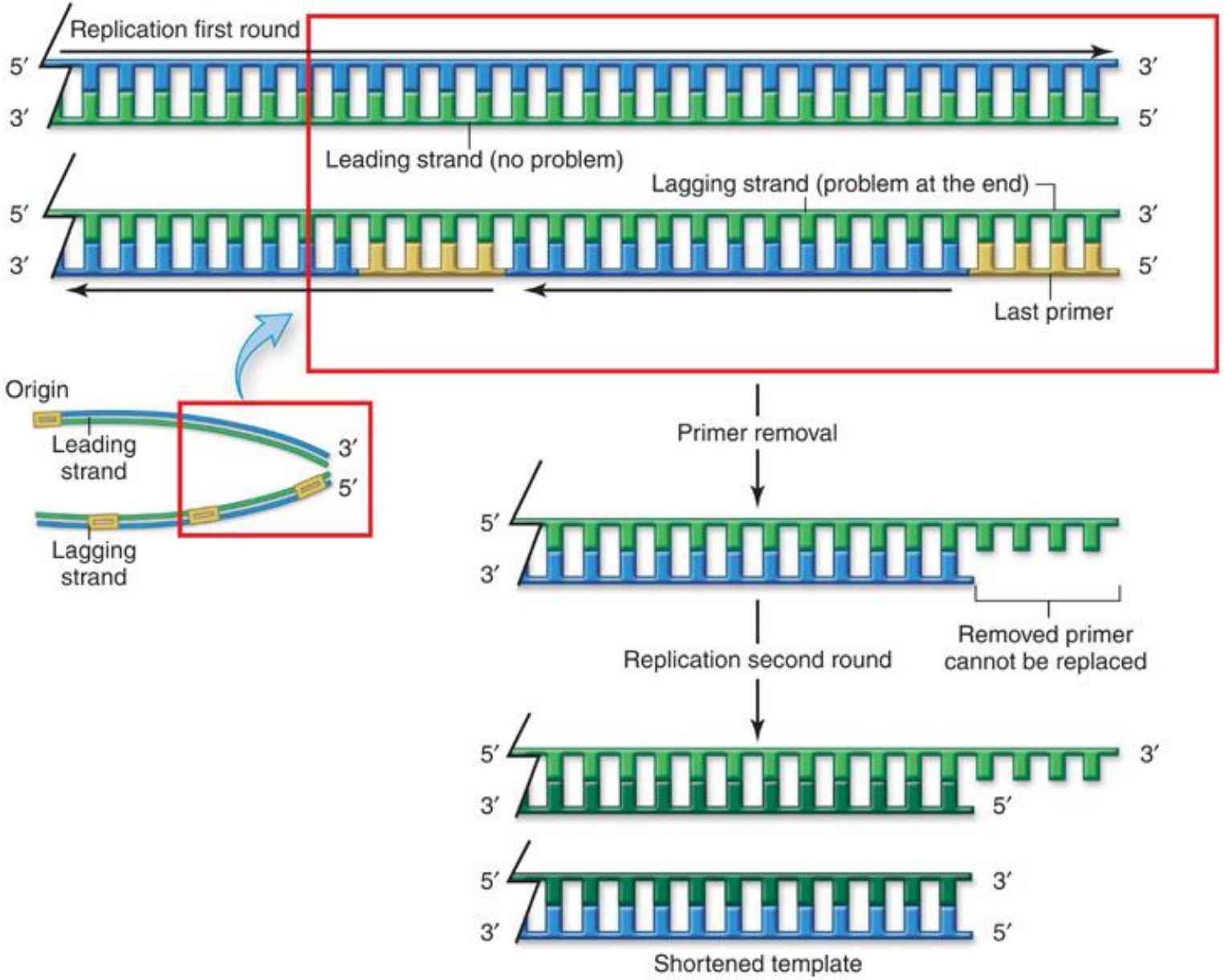

I
II
III
IV
V
V(a)
Template strand
Lagging strand
RNA primer
completion and joining of precursor fragments
V(b)
Removal of RNA primer and termination


Two daughter molecules can join together if the repeated sequences are present at the termini and may form concatamers
5' ABCD YZABC 3'
3' A'B'C'D' Y'Z'A'
5' CD YZABC 3'
3' A'B'C'D' Y'Z'A'B'C' 5'
Anneal
ABCD YZAB C CD YZABC
A'B'C'D' Y'Z'A' B'C'D' Y'Z'A'B'C'
A'
5' ABCD YZAB CD YZABC 3'
3' A'B'C'D' Y'Z'A' B'C'D' Y'Z'A'B'C' 3'

EUKARYOTIC GENOME

A hypothetical difficulty encountered during the replication of the ends of linear chromosomes. A gap is left following synthesis on the lagging strand





Eukaryotic DNA Replication

- **Telomeres – repeated DNA sequence on the ends of eukaryotic chromosomes**
  - ✓ **produced by telomerase**
- **Telomerase contains an RNA region that is used as a template so a DNA primer can be produced**

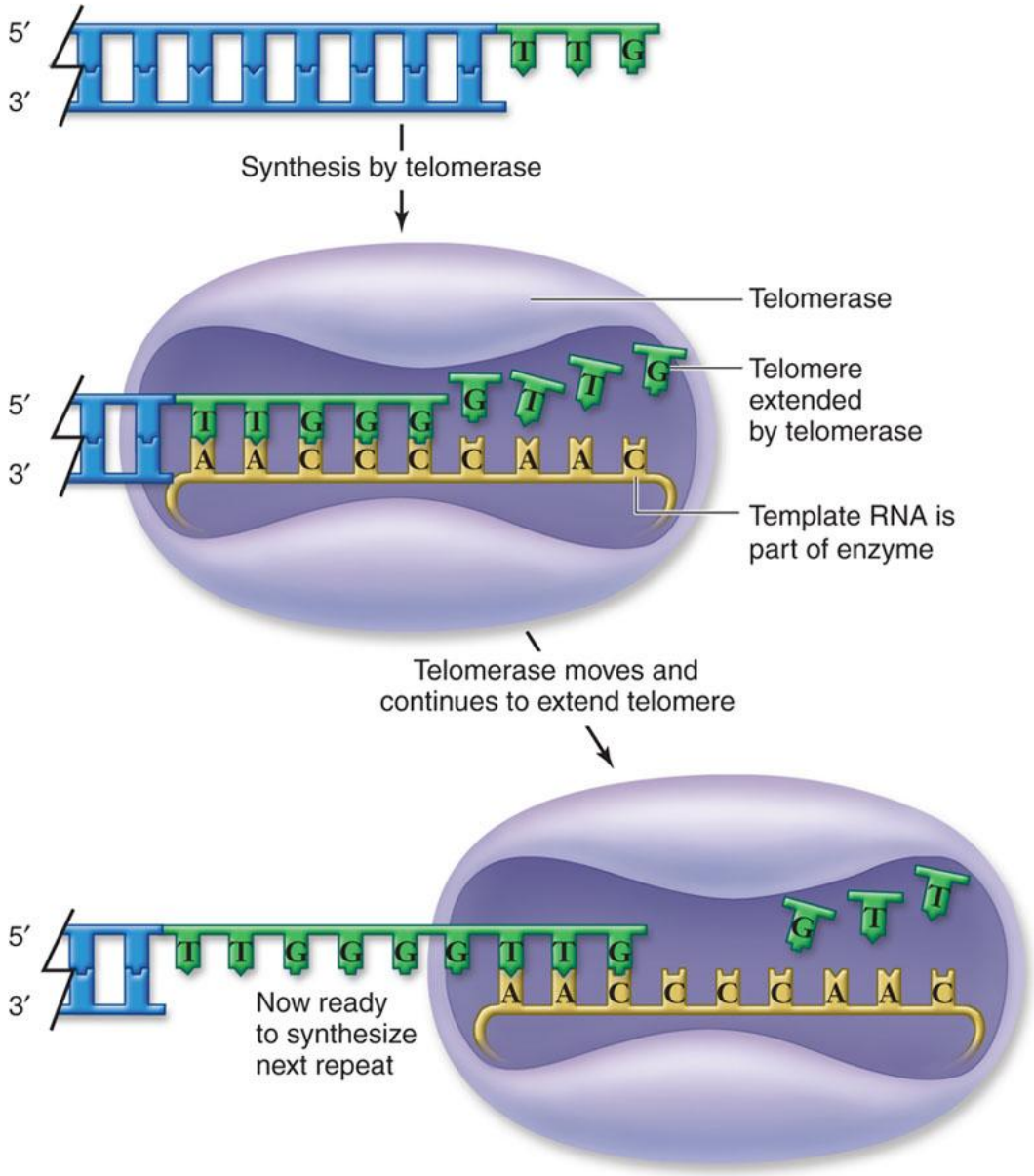
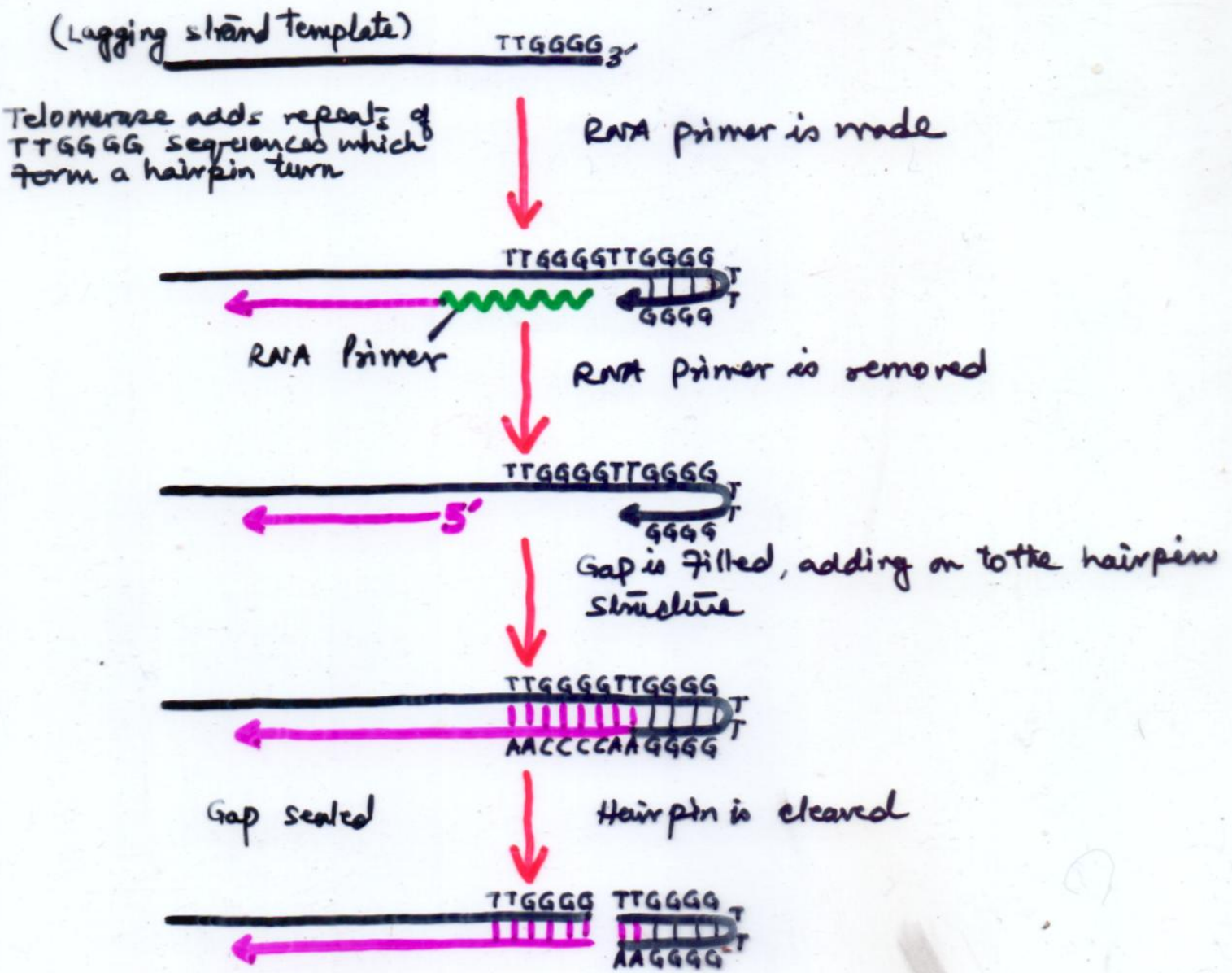


Diagram of the predicted solution to the hypothetical problem proposed above



Nobelprize.org

The Nobel Prize in Physiology or Medicine 2009

"for the discovery of how chromosomes are protected by telomeres and the enzyme telomerase"

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Elizabeth H. Blackburn

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Carol W. Greider

Photo: Jussi Puikkonen

Jack W. Szostak

Strategies for completing the 5’ end of linear genome

Strategies for completing the 5' ends of linear genomes :

#	Strategy	Mechanism & Example
1.	Concatenation	Linear genome possess redundant termini which allow circularization or concatenation. These structures can be cleaved to generate single genomes with 5' overhanging termini which can be filled by conventional DNA synthesis; eg. bacteriophages T7 and λ
2.	Terminal protein priming	Viruses which initiate strand syntheses with terminal proteins do not need a specific termination mechanism; they initiate at the 5' end of each strand & can complete upto the 3' end eg. adenovirus bacteriophage ϕ29
3.	Hairpin Priming	Another priming strategy which initiates strand synthesis from the extreme 5' end of the strand, eg. parvoviruses
4.	Covalently sealed ends	Some viruses, which are superficially double stranded and linear, have covalently sealed ends so that melting generates a ss circle which can be replicated like circular replicon eg viroids
5.	Telomeres	Enzymes termed telomerases add oligonucleotides to the ends of the linear chromosomes. Although extreme 5' sequences are lost in this method, post replicative telomerase activity can replenish the telomeres so that no actual genes are lost in successive round of replication.