Structural Virology

Lecture 9

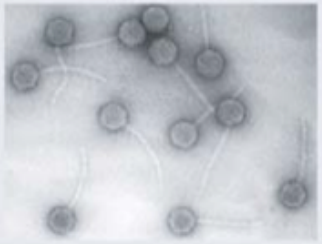
Pavel Plevka

Bacteriophages

DNA

dsDNA

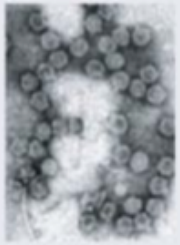
Myoviridae **e.g. T4** ***Lytic***
Prolate head
Contractile tail



Siphoviridae **e.g. λ**
Lytic : Lysogenic
Isometric head
Long, non-contractile tail

Podoviridae **e.g. T7** ***Lytic***
Isometric head
Short, non-contractile tail

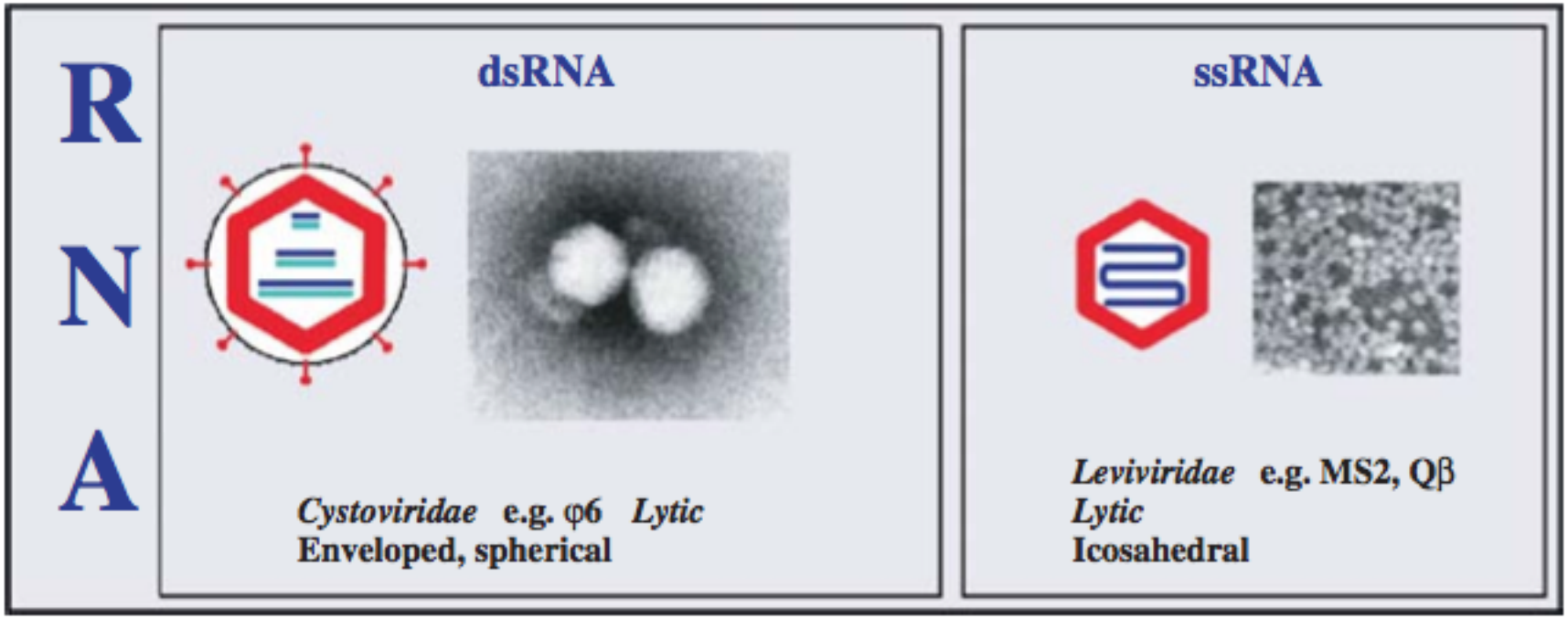
ssDNA



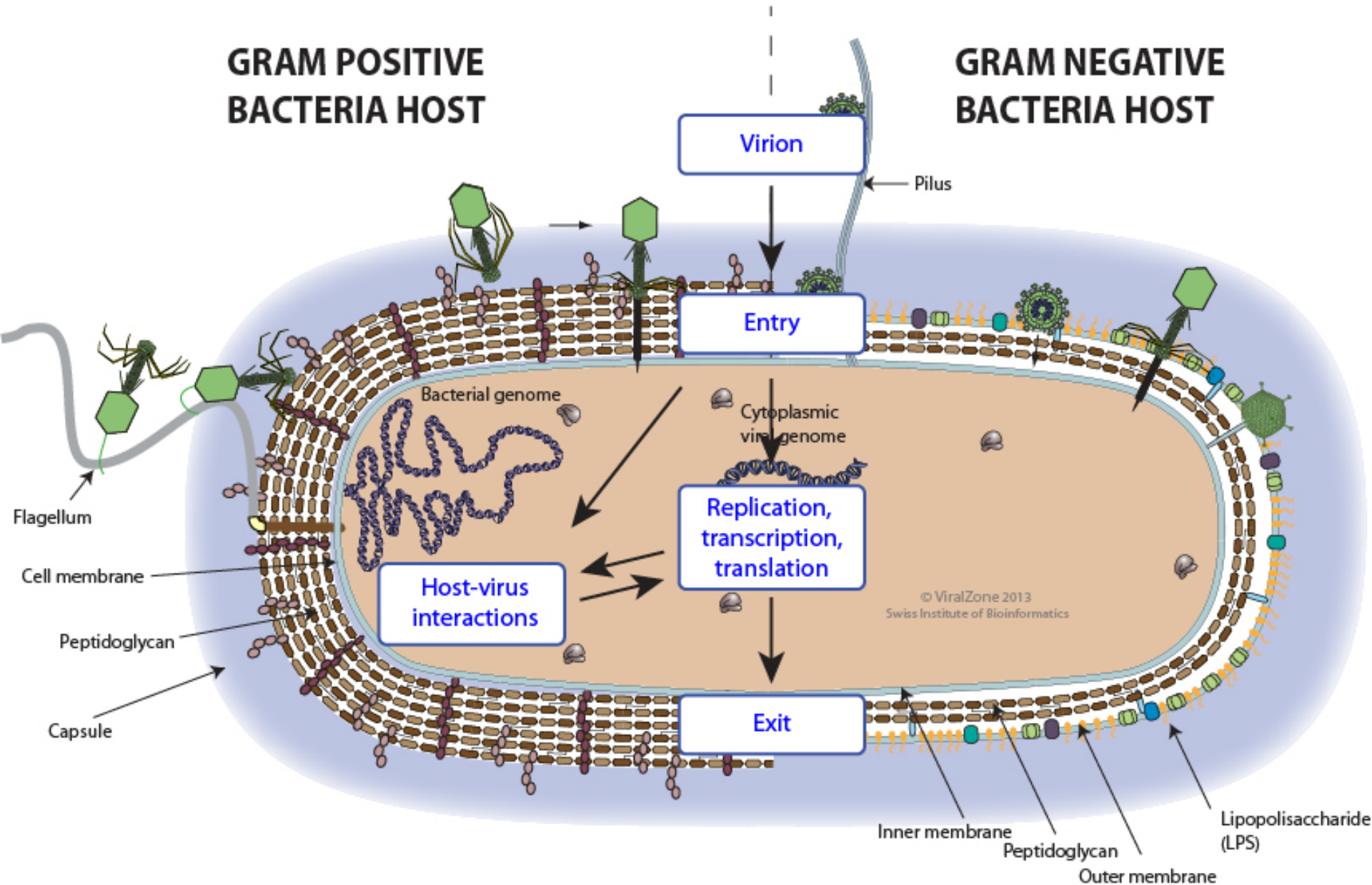
Microviridae **e.g. φX174** ***Lytic***
Small, icosahedral

Inoviridae **e.g. M13, fd, f1**
Non-lytic
'Chronically infecting'
Flexible, thin filament

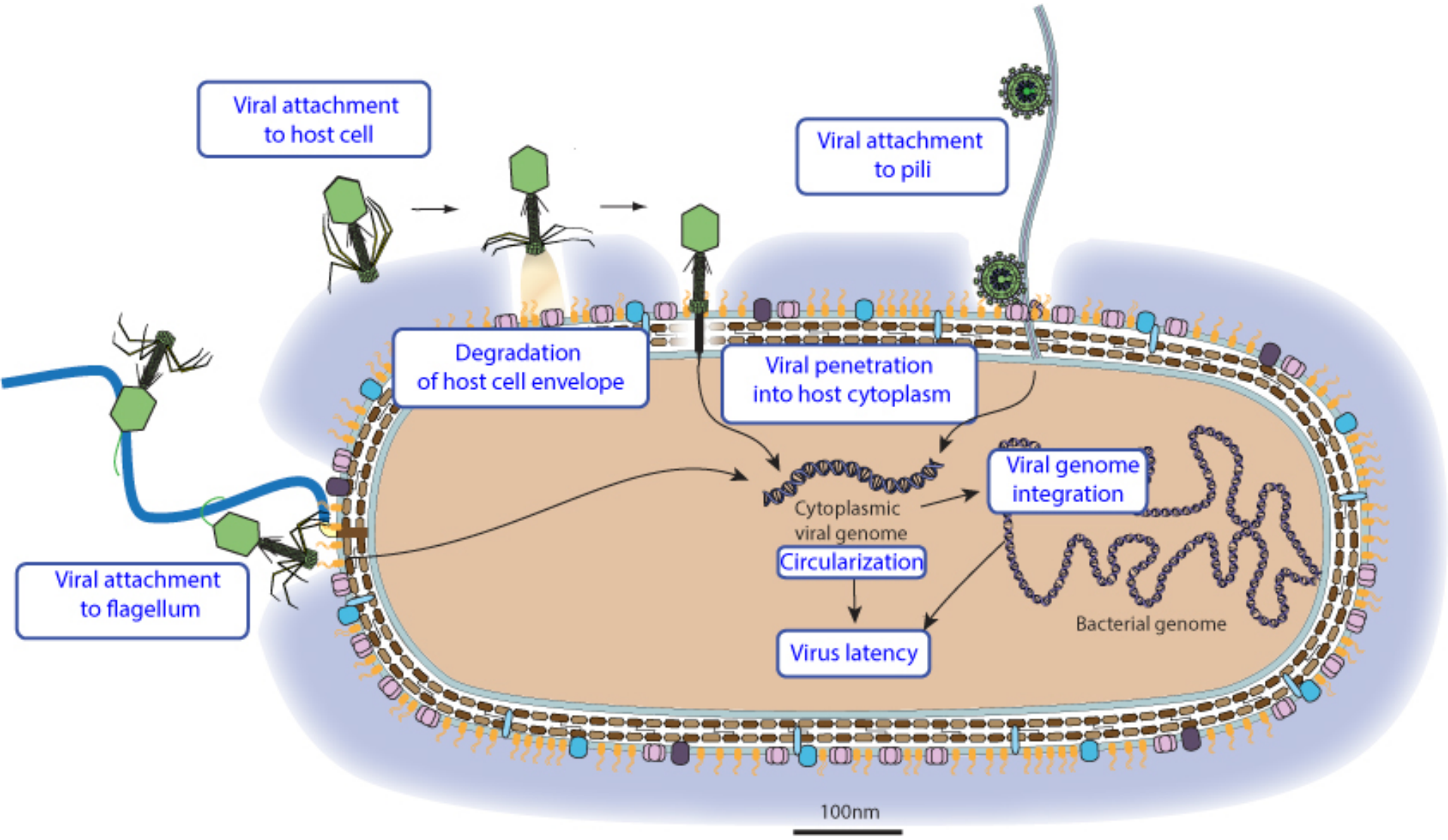
Bacteriophages



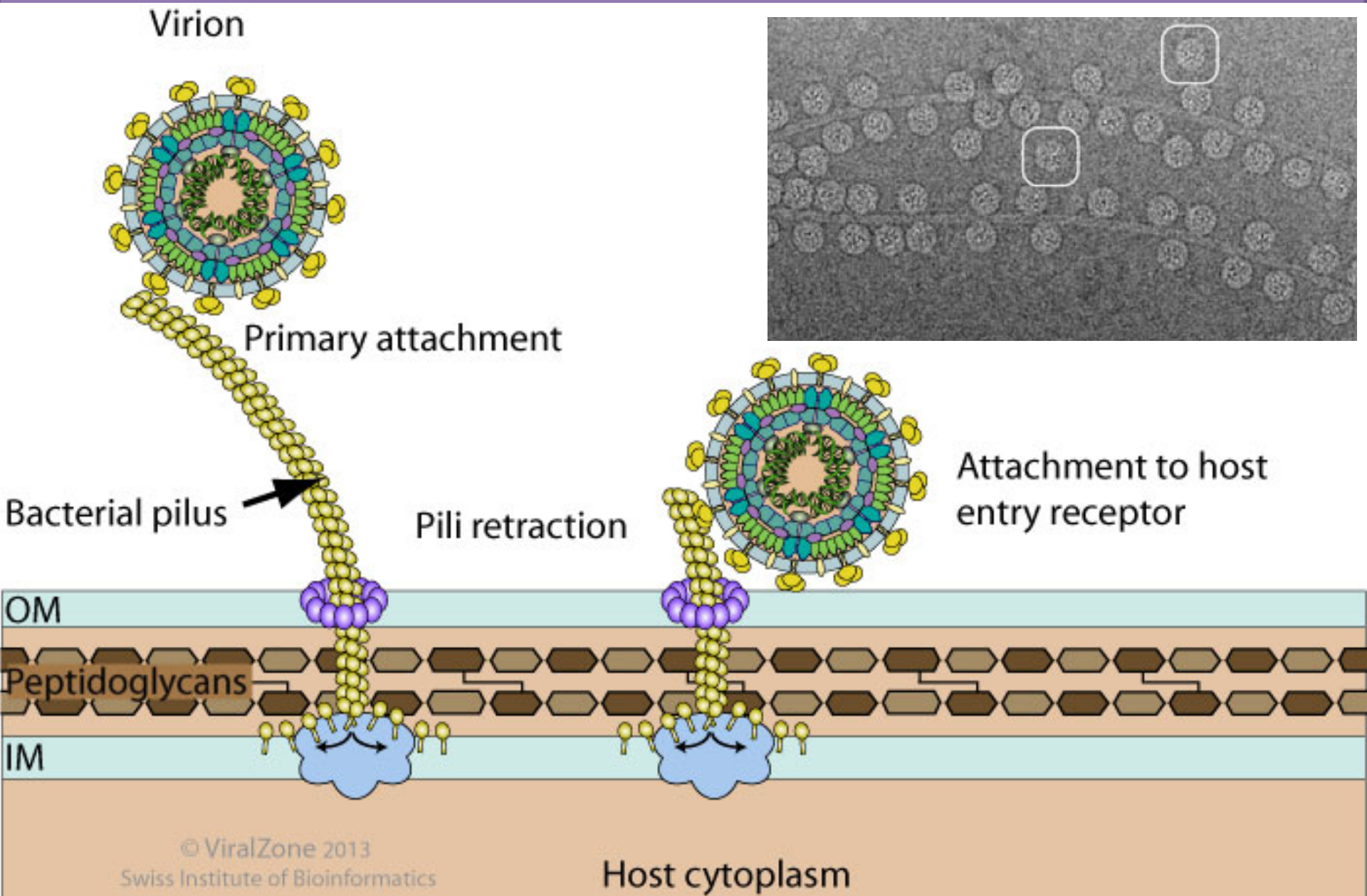
Phages of gram positive and gram negative bacteria



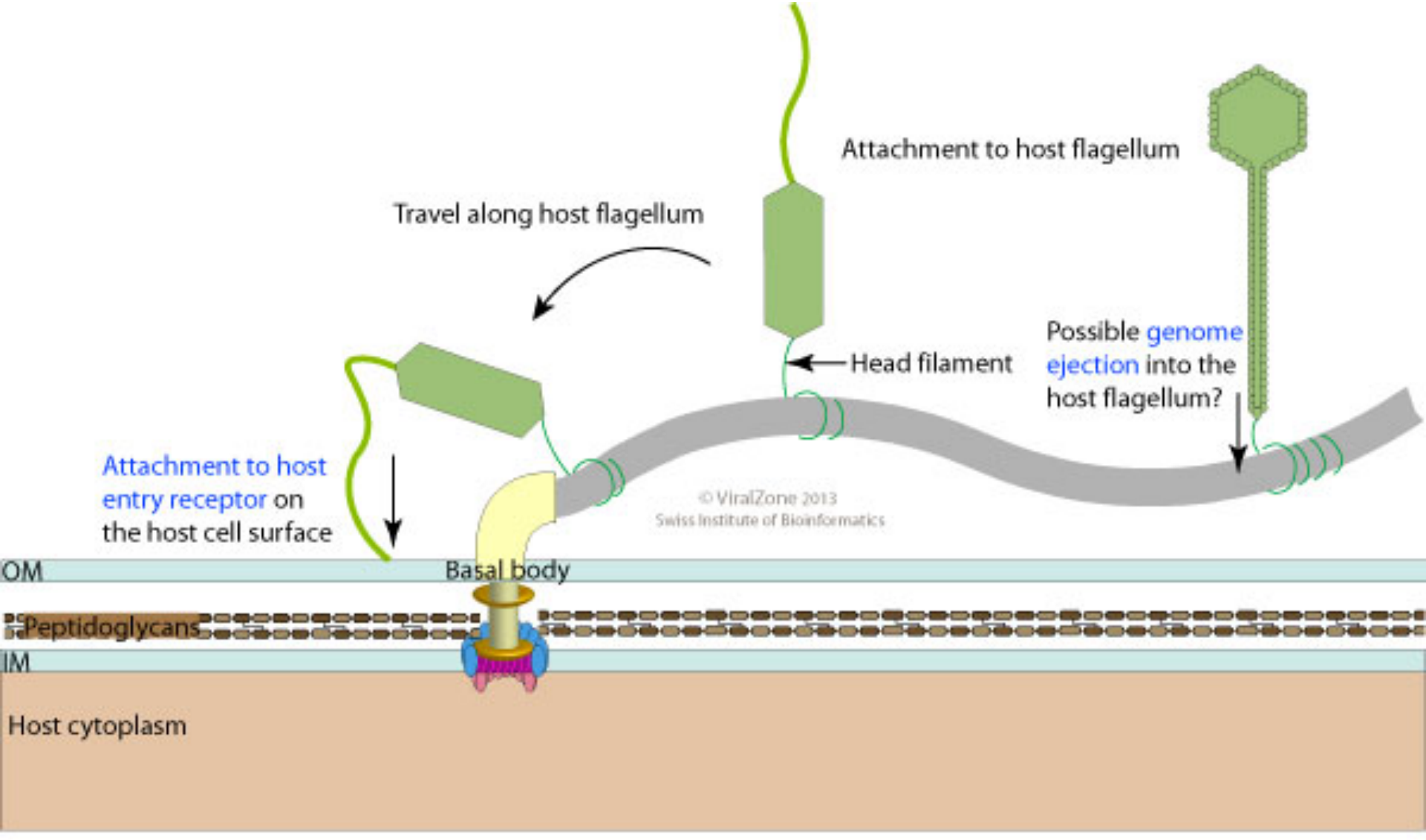
Phage entry


Viral attachment to host cell
Viral attachment to pili
Degradation of host cell envelope
Viral penetration into host cytoplasm
Viral attachment to flagellum
Cytoplasmic viral genome
Viral genome integration
Circularization
Virus latency
Bacterial genome
100nm

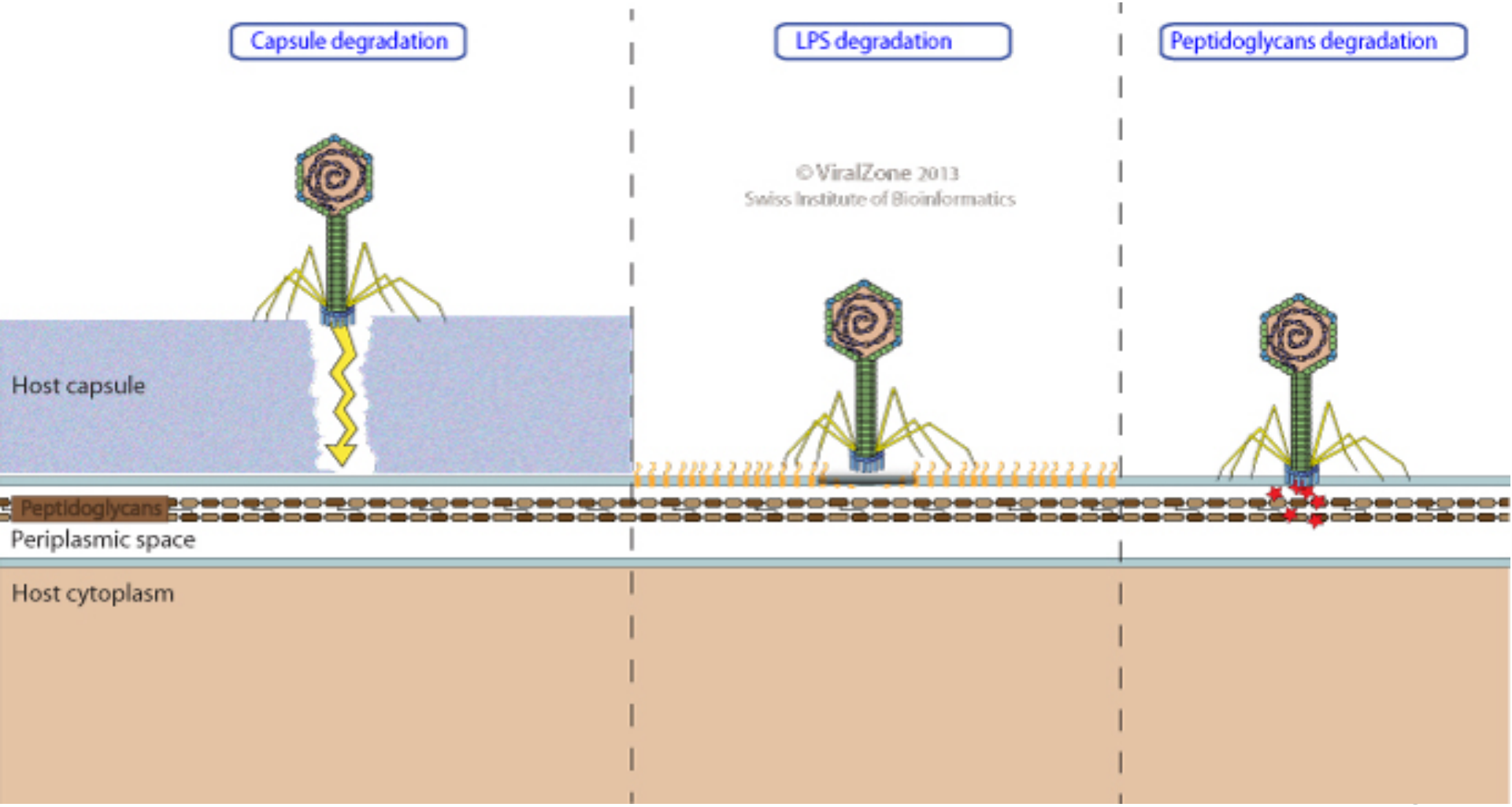
Viral attachment to host cell pilus



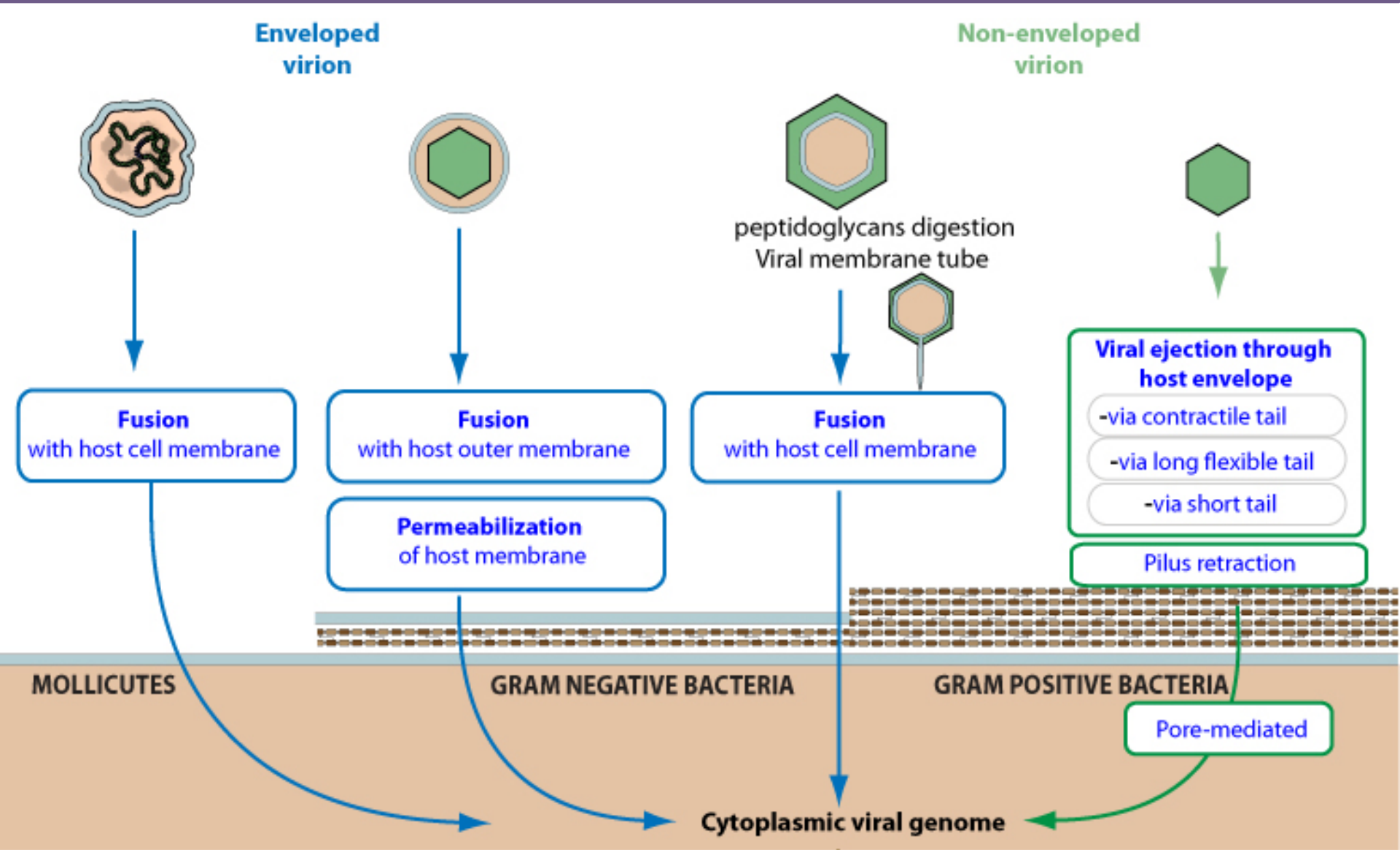
Viral attachment to host cell flagellum



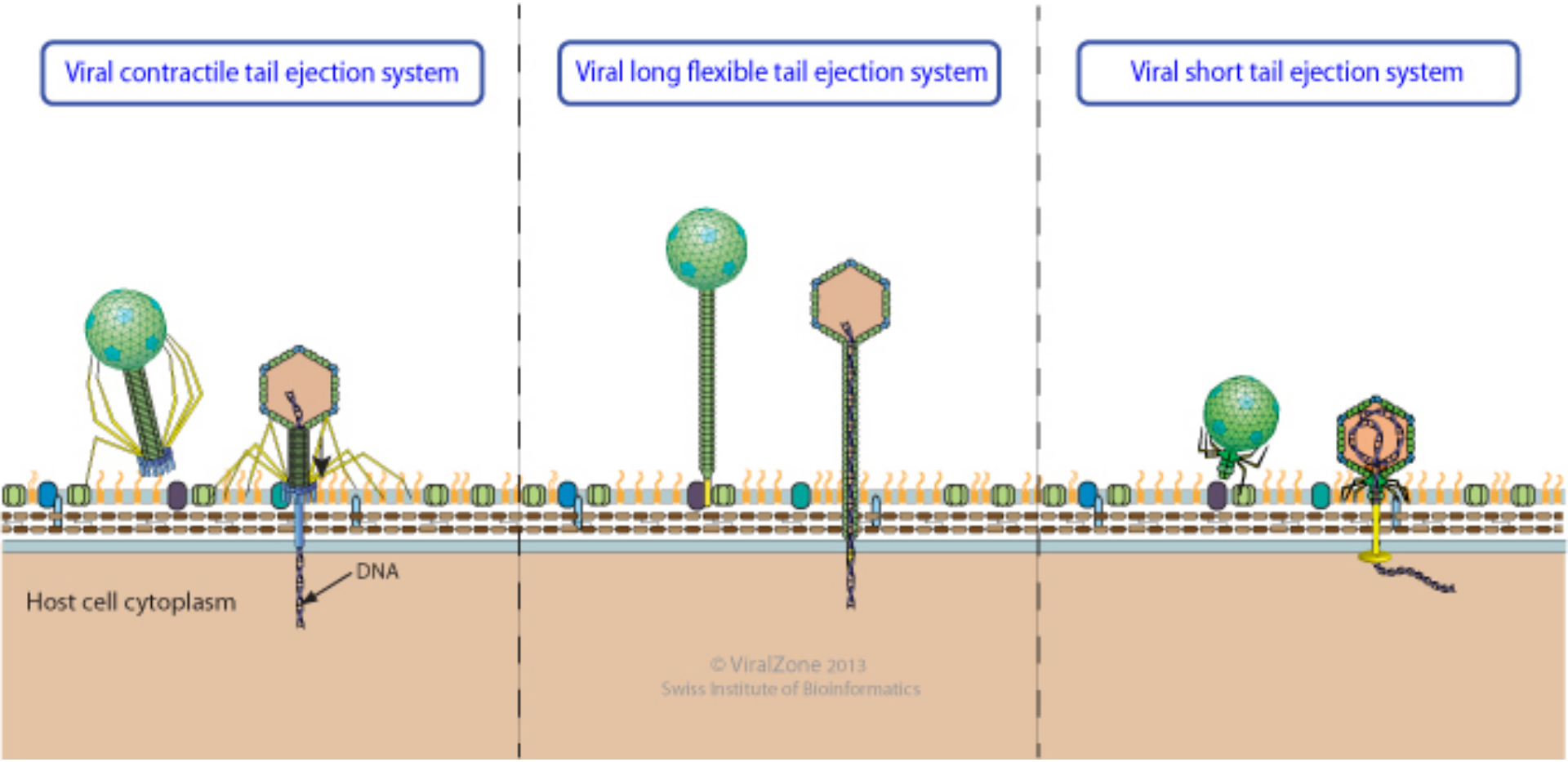
Degradation of host cell envelope components during virus entry



Phage penetration into host cytoplasm

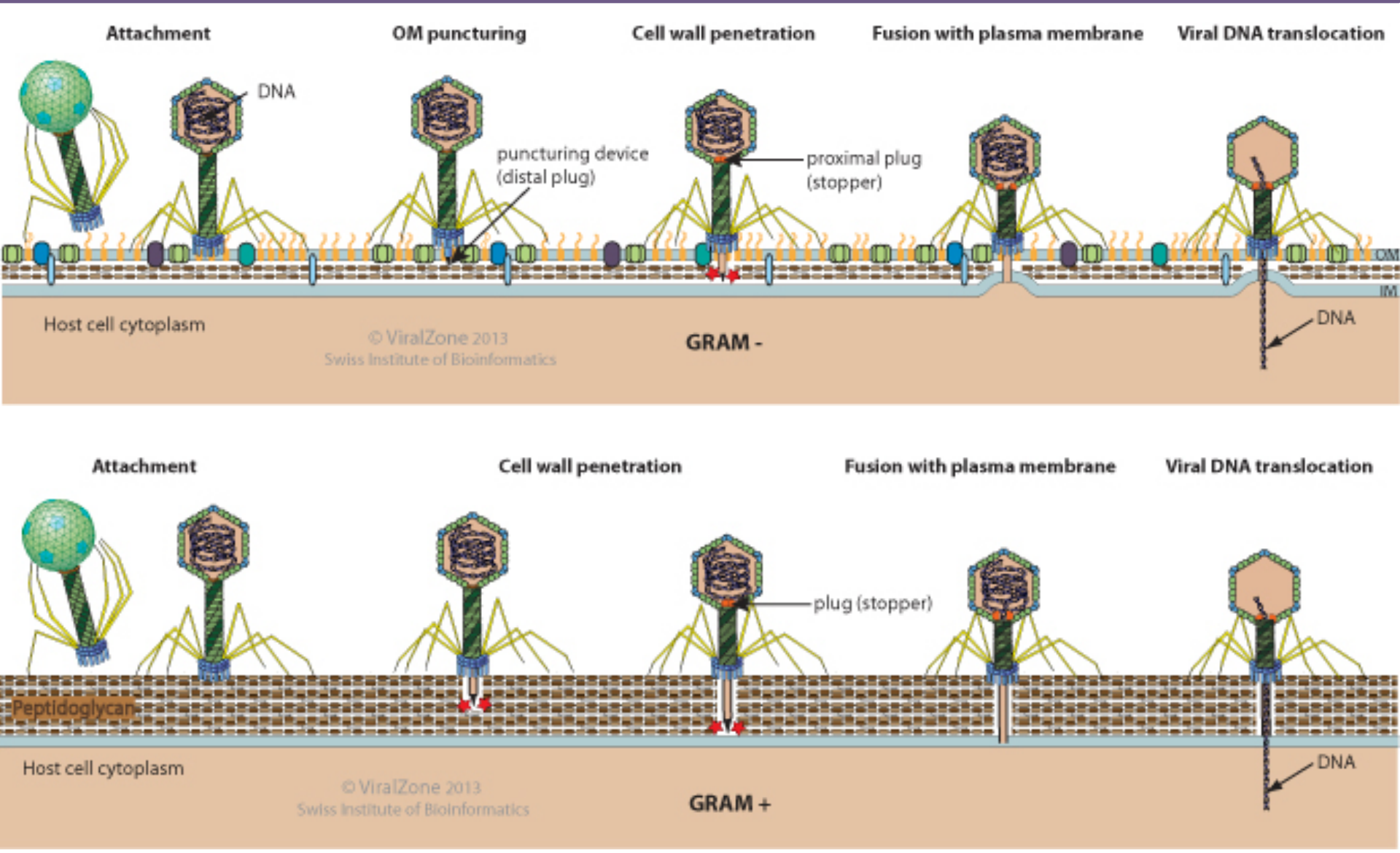


Genome ejection through host cell envelope

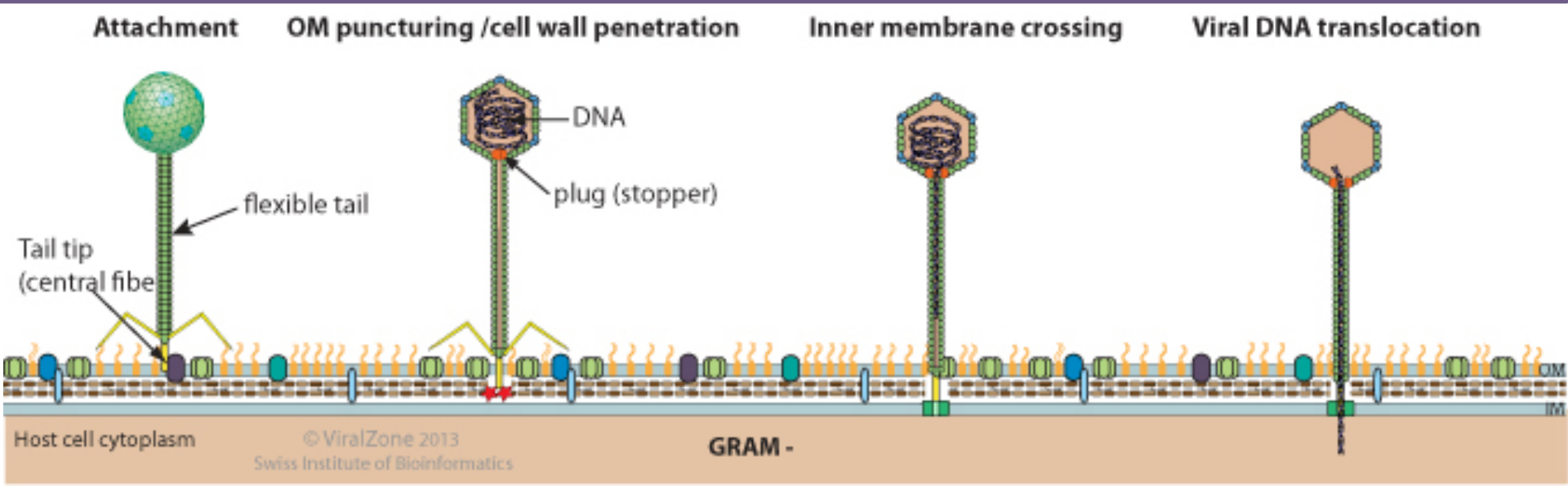


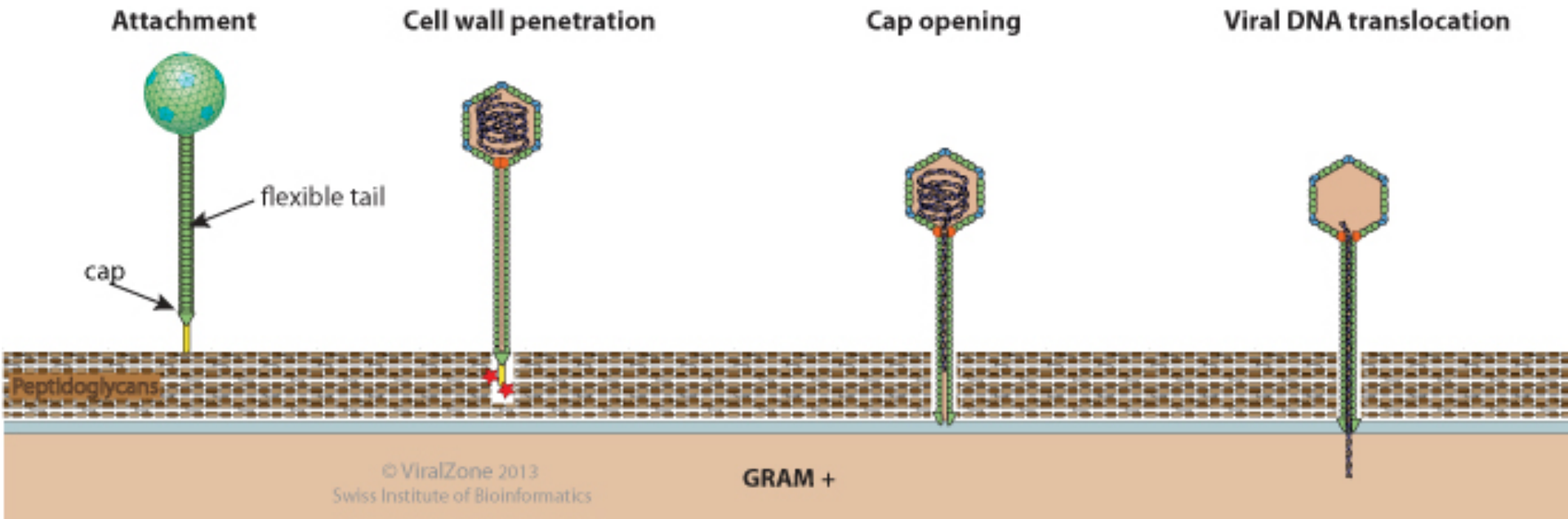
Myoviridae Siphoviridae Podoviridae

Viral contractile tail ejection system

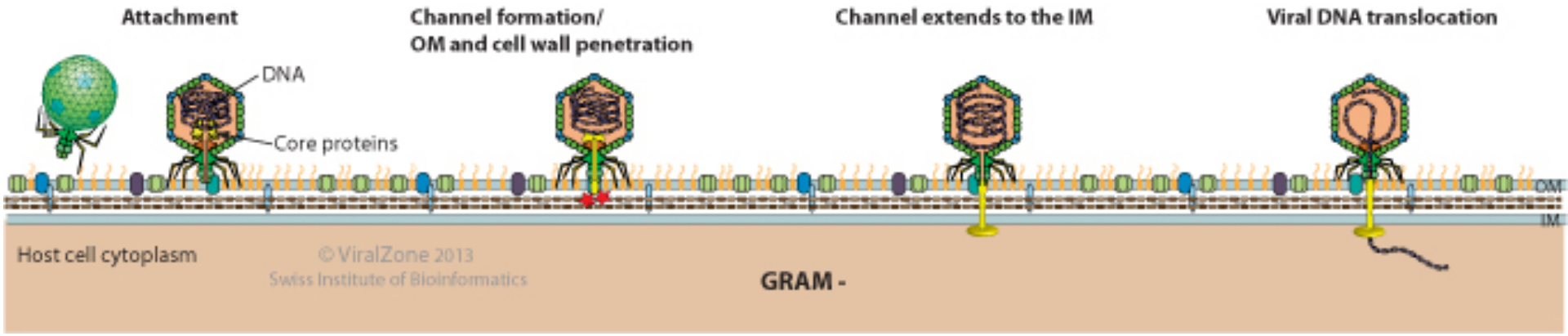


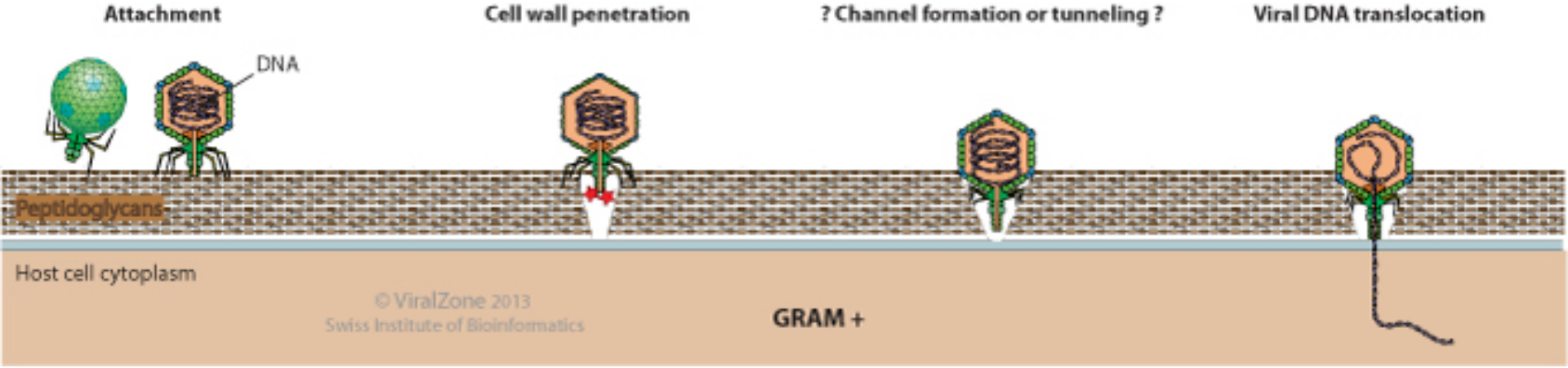
Viral long flexible tail ejection system



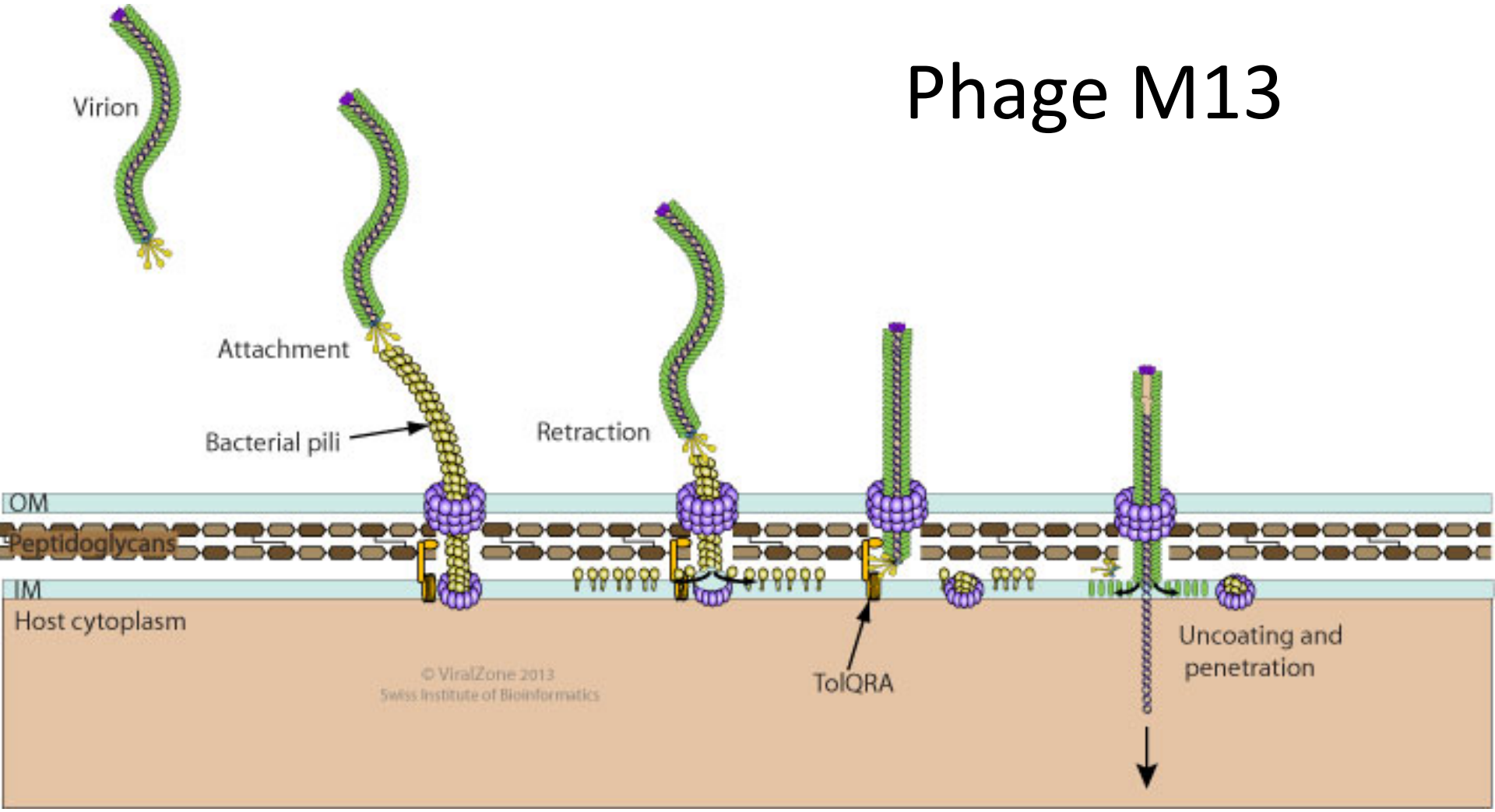


Viral short tail ejection system

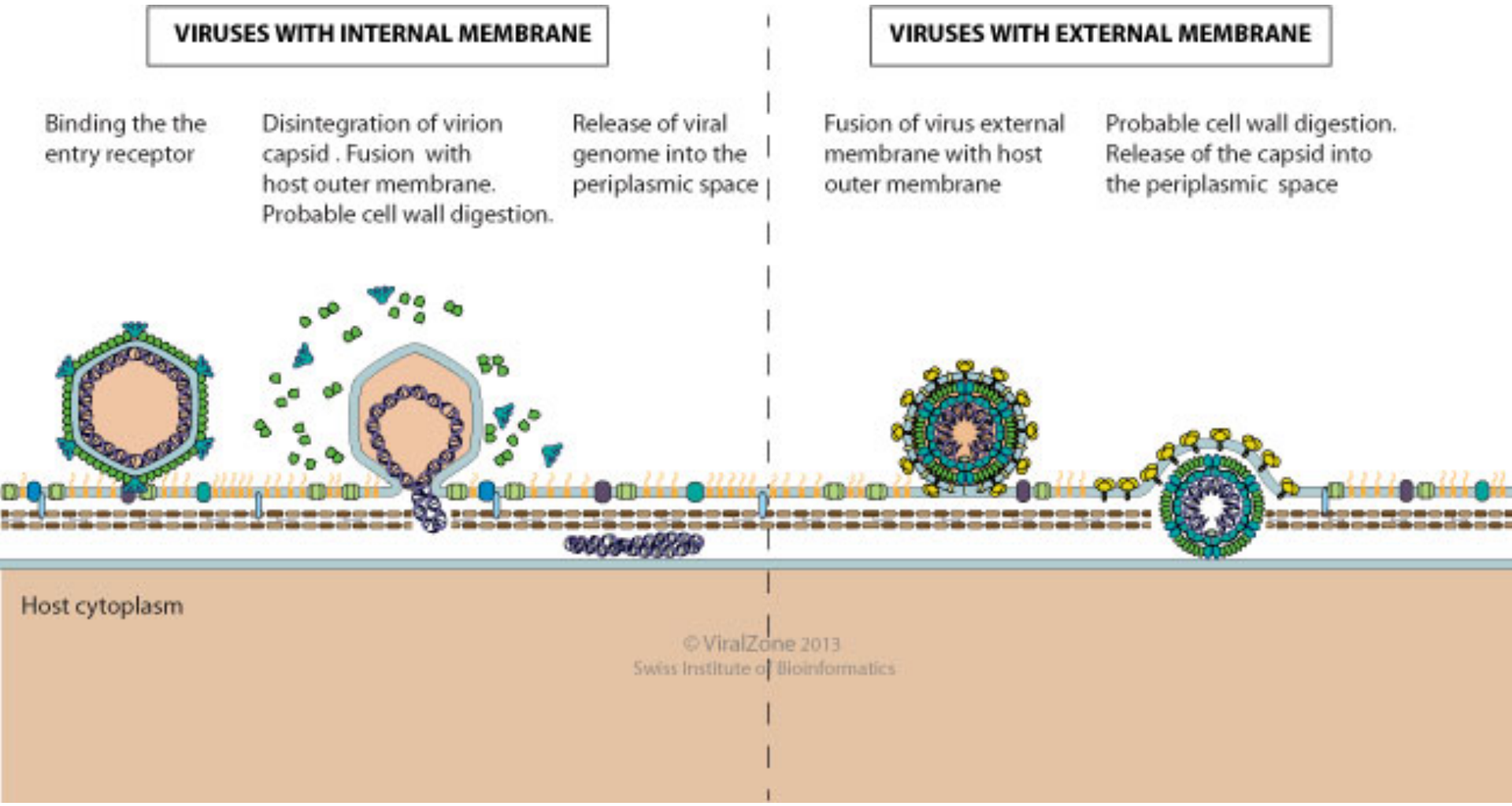




Viral penetration into host cytoplasm via pilus retraction



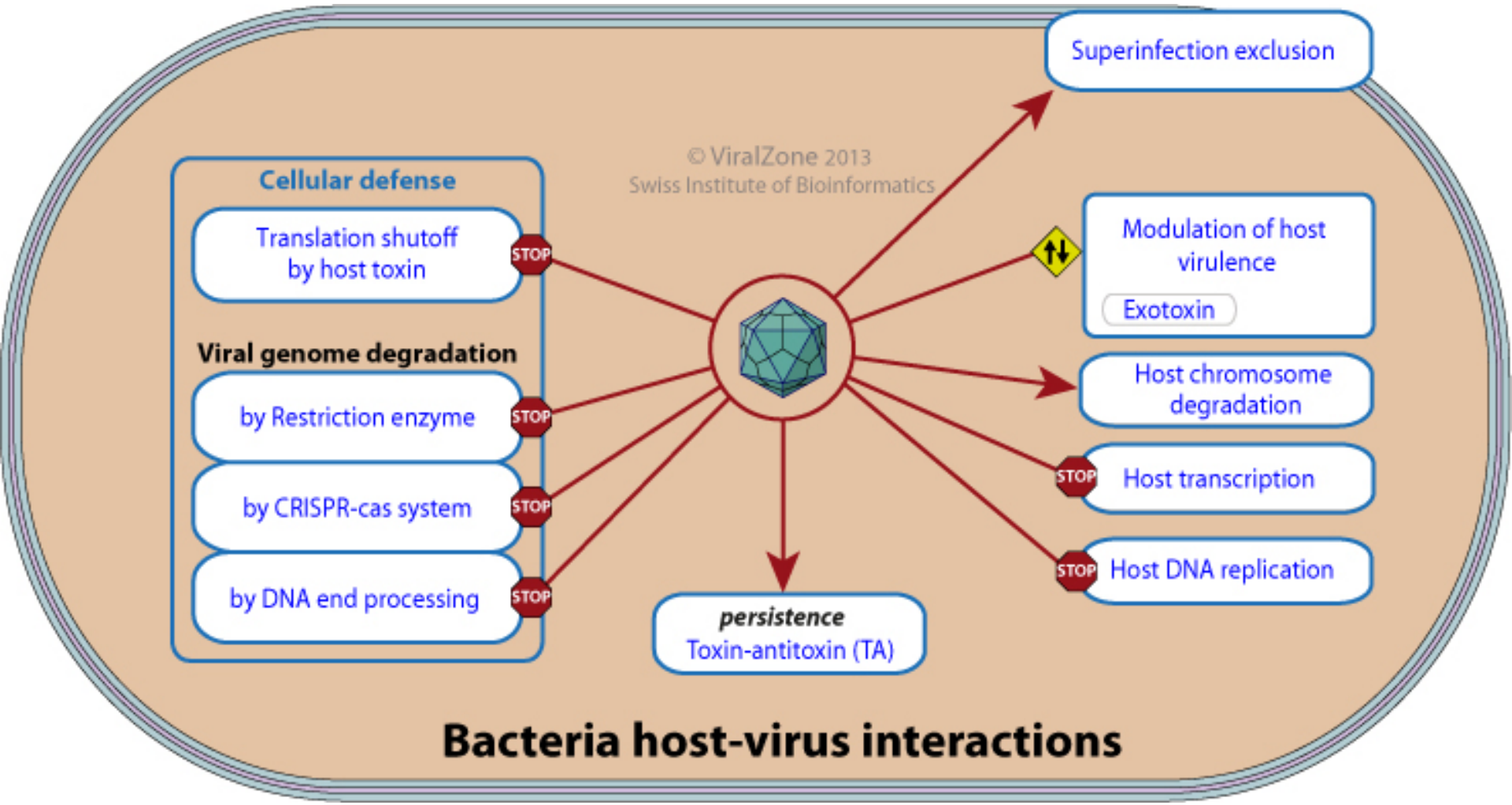
Fusion of virus membrane with host outer membrane



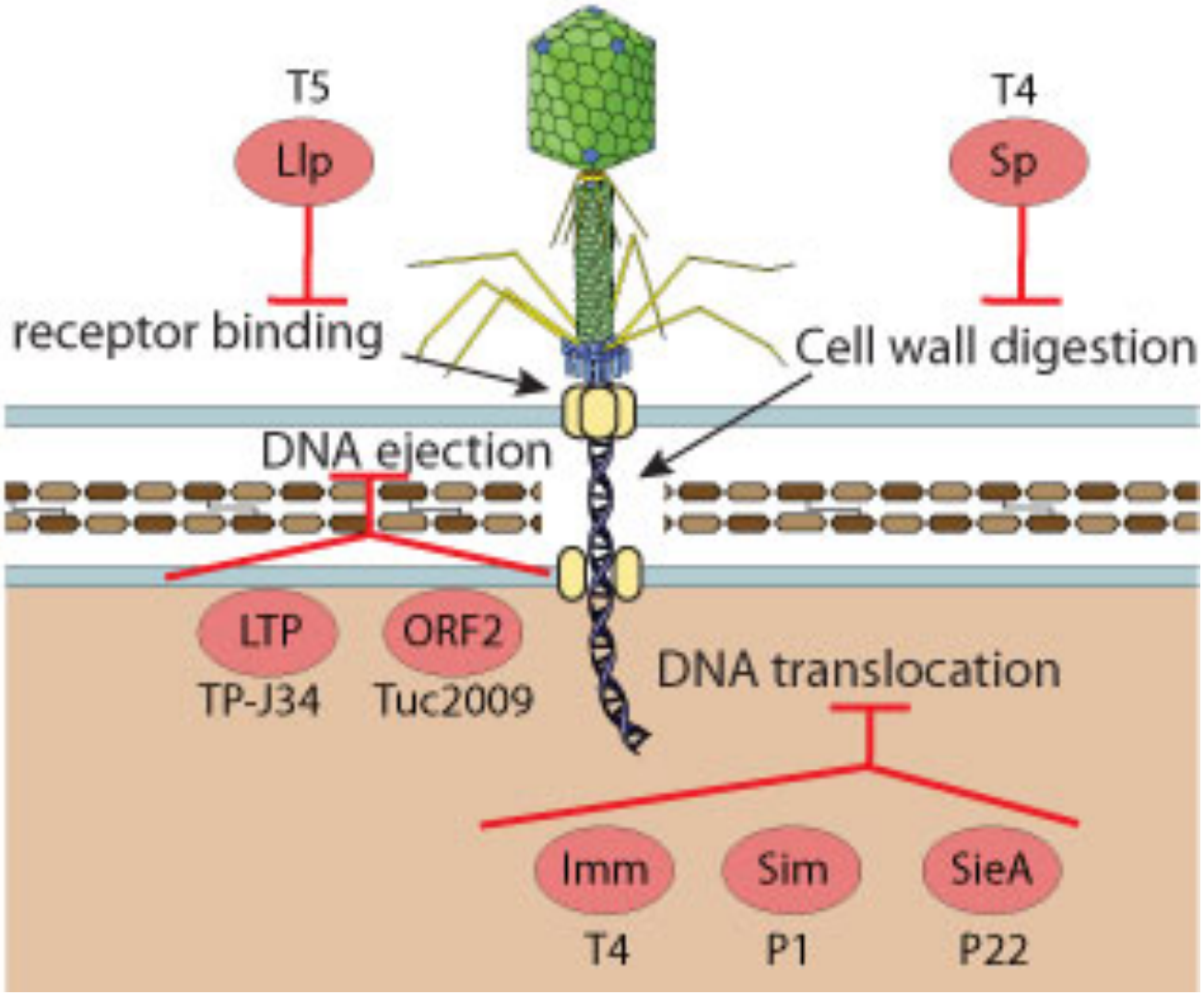
Cystoviridae

Corticoviridae

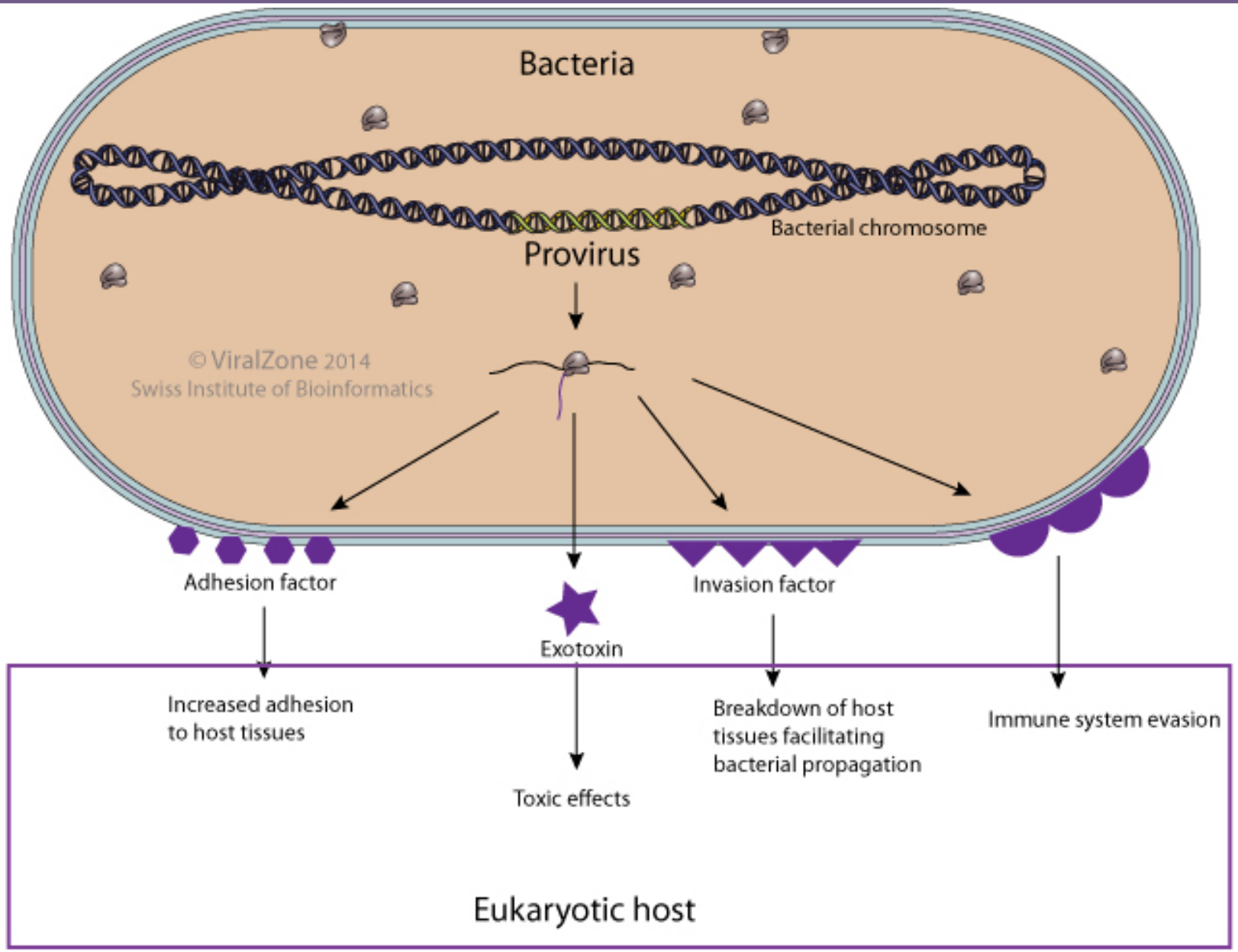
Phage-bacteria interactions



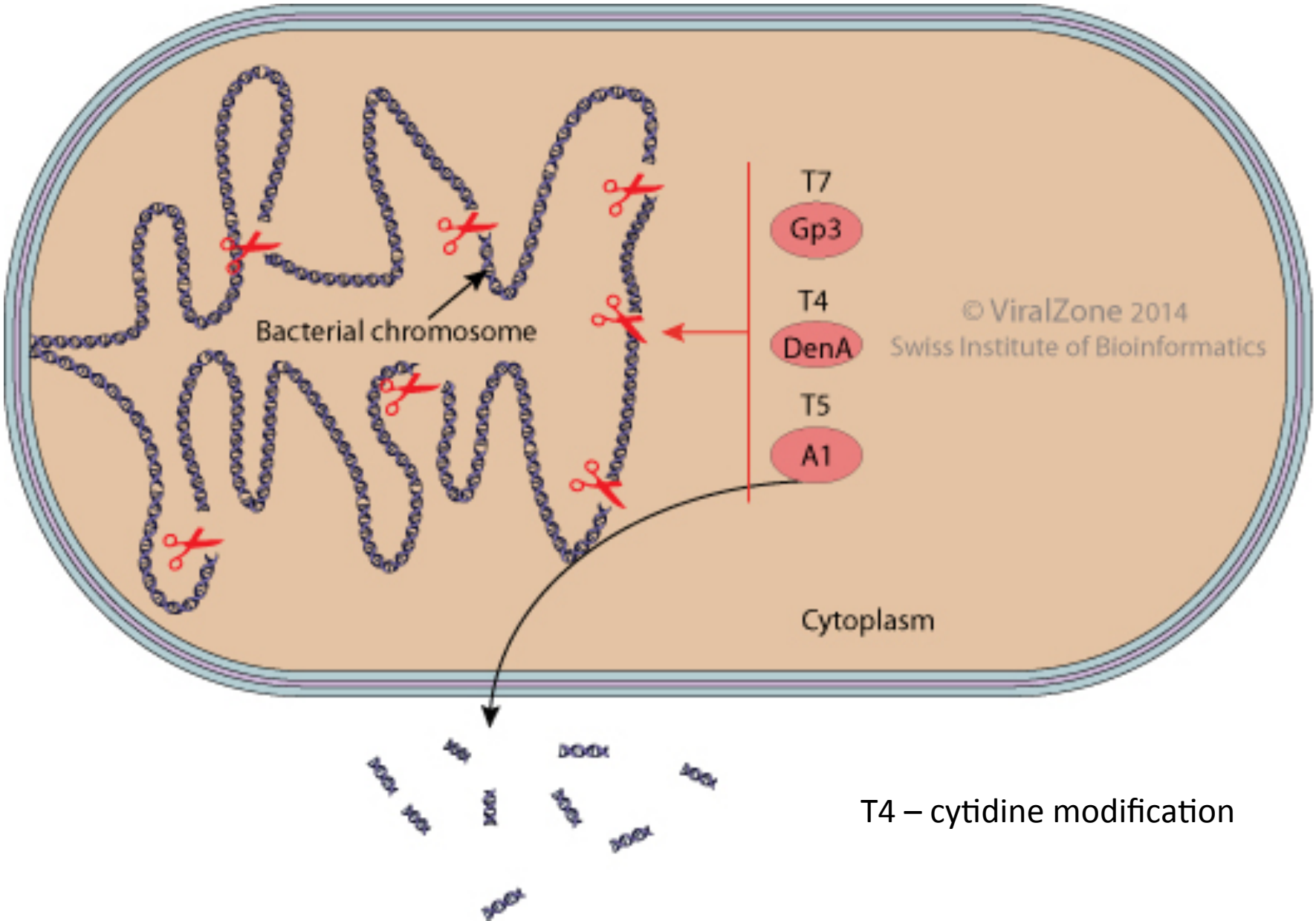
Superinfection exclusion



Modulation of host host virulence by virus

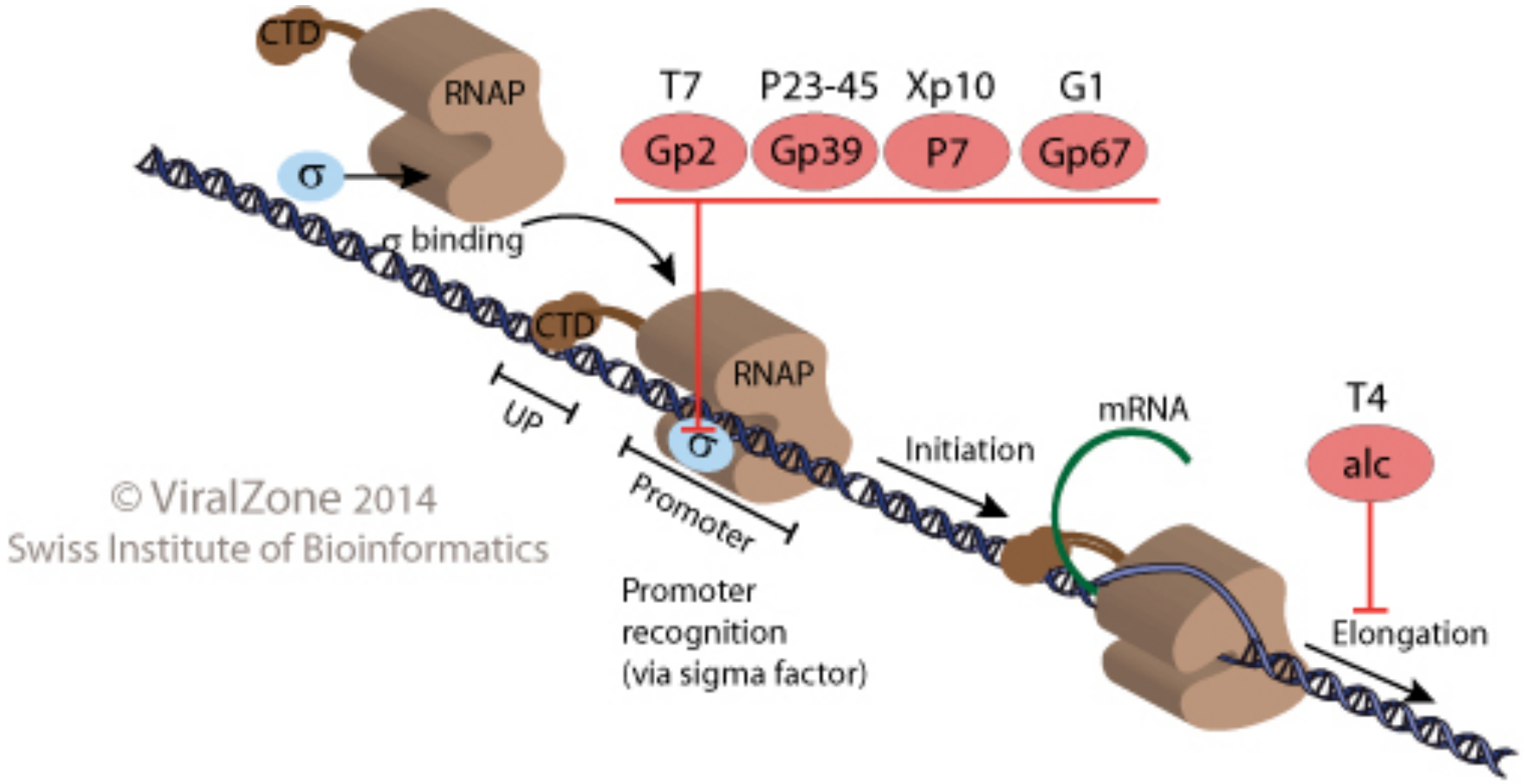


Degradation of host chromosome by phage

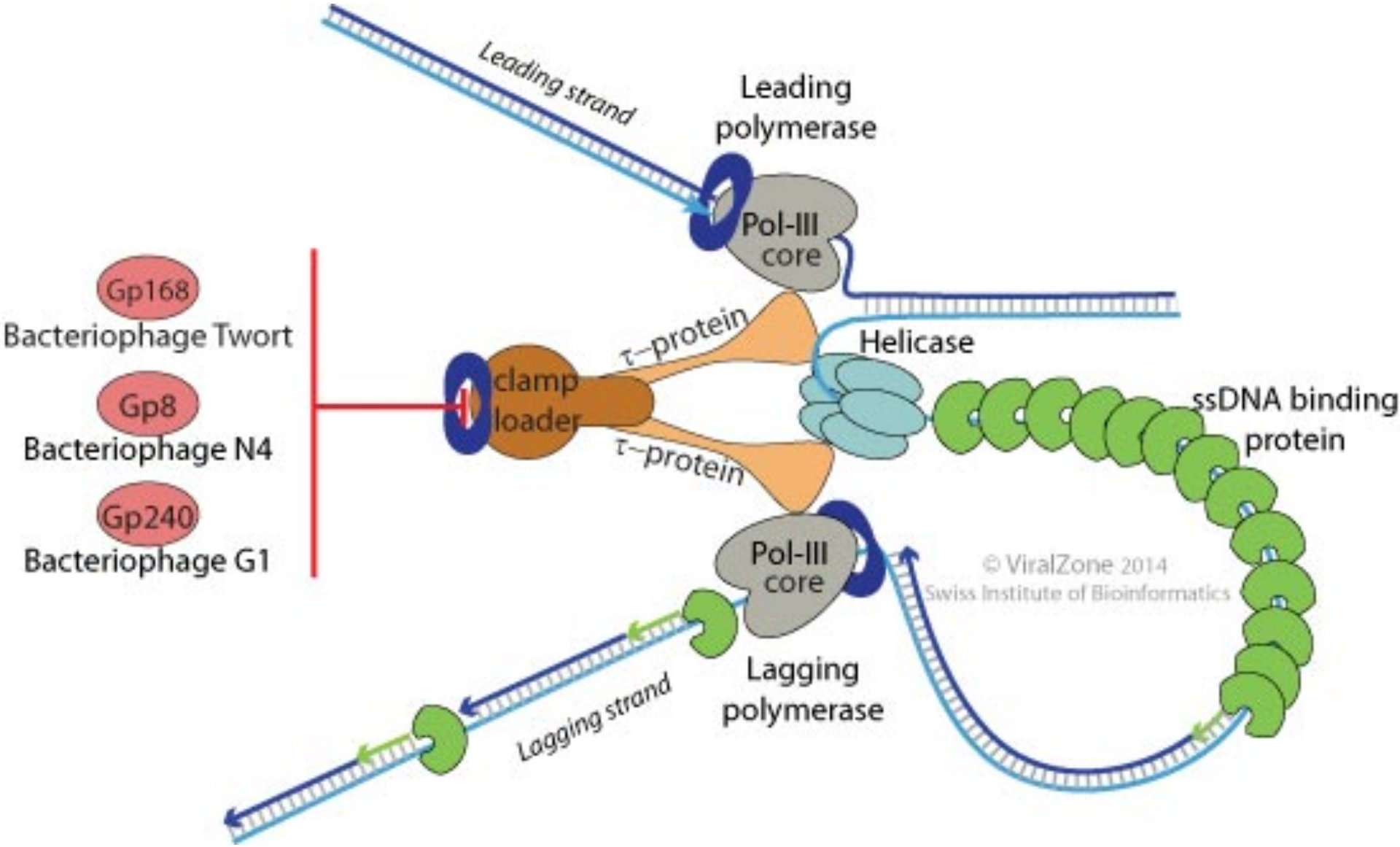


T4 – cytidine modification

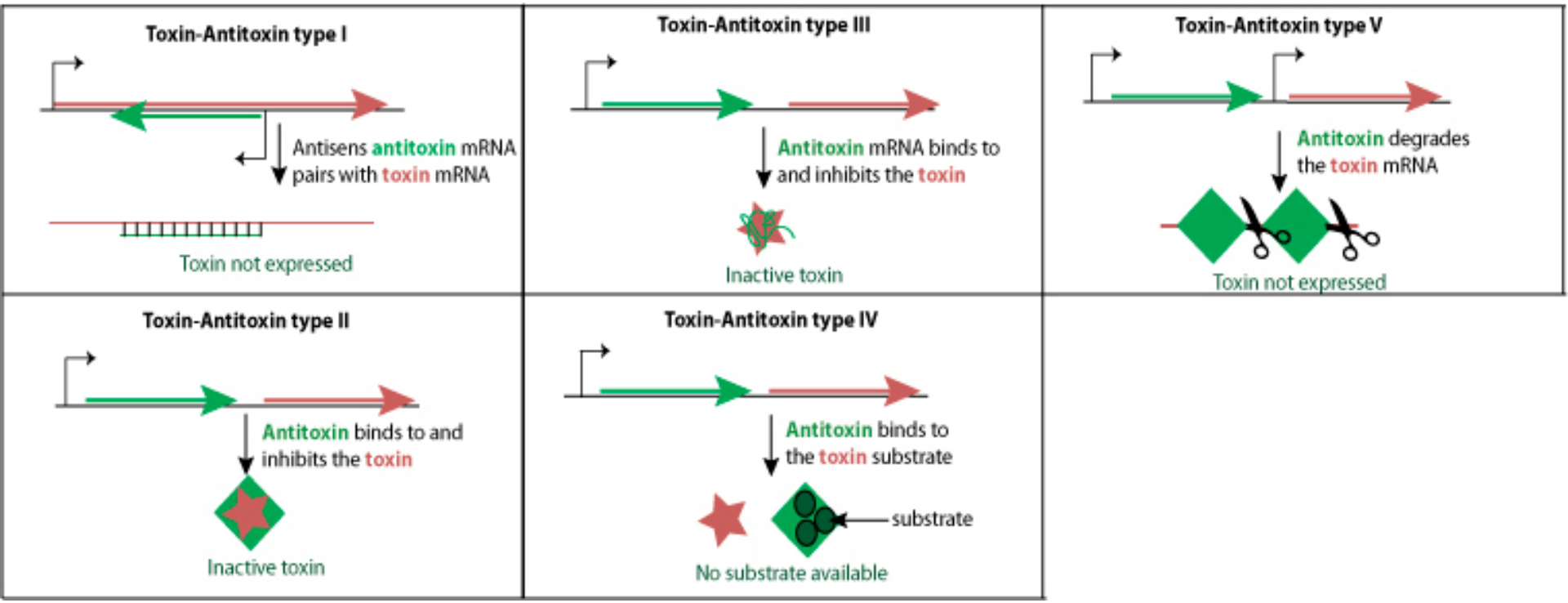
Phage host transcription shutoff

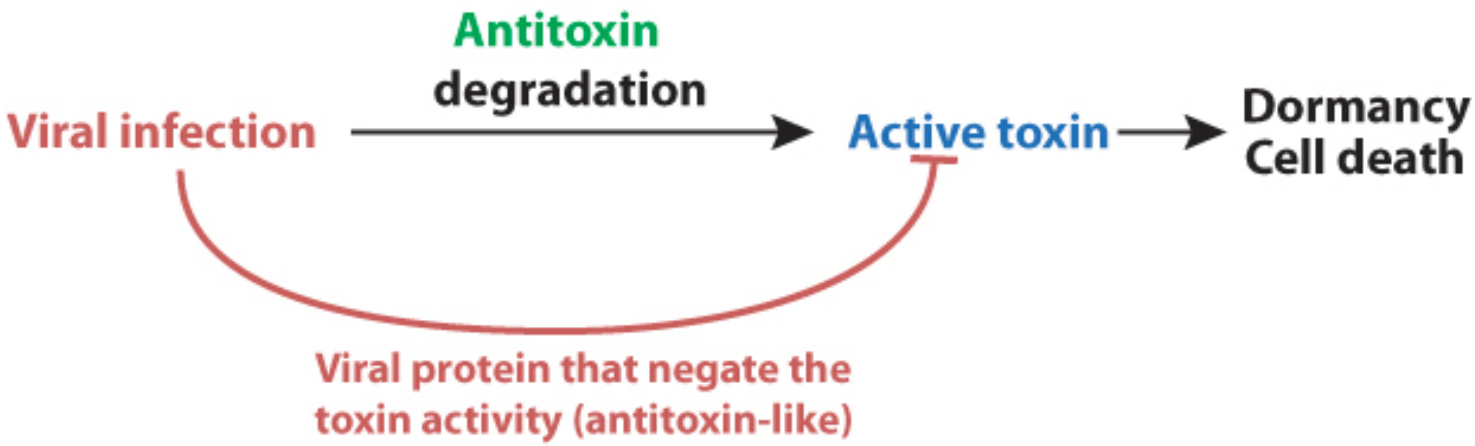


Inhibition of host DNA replication by virus

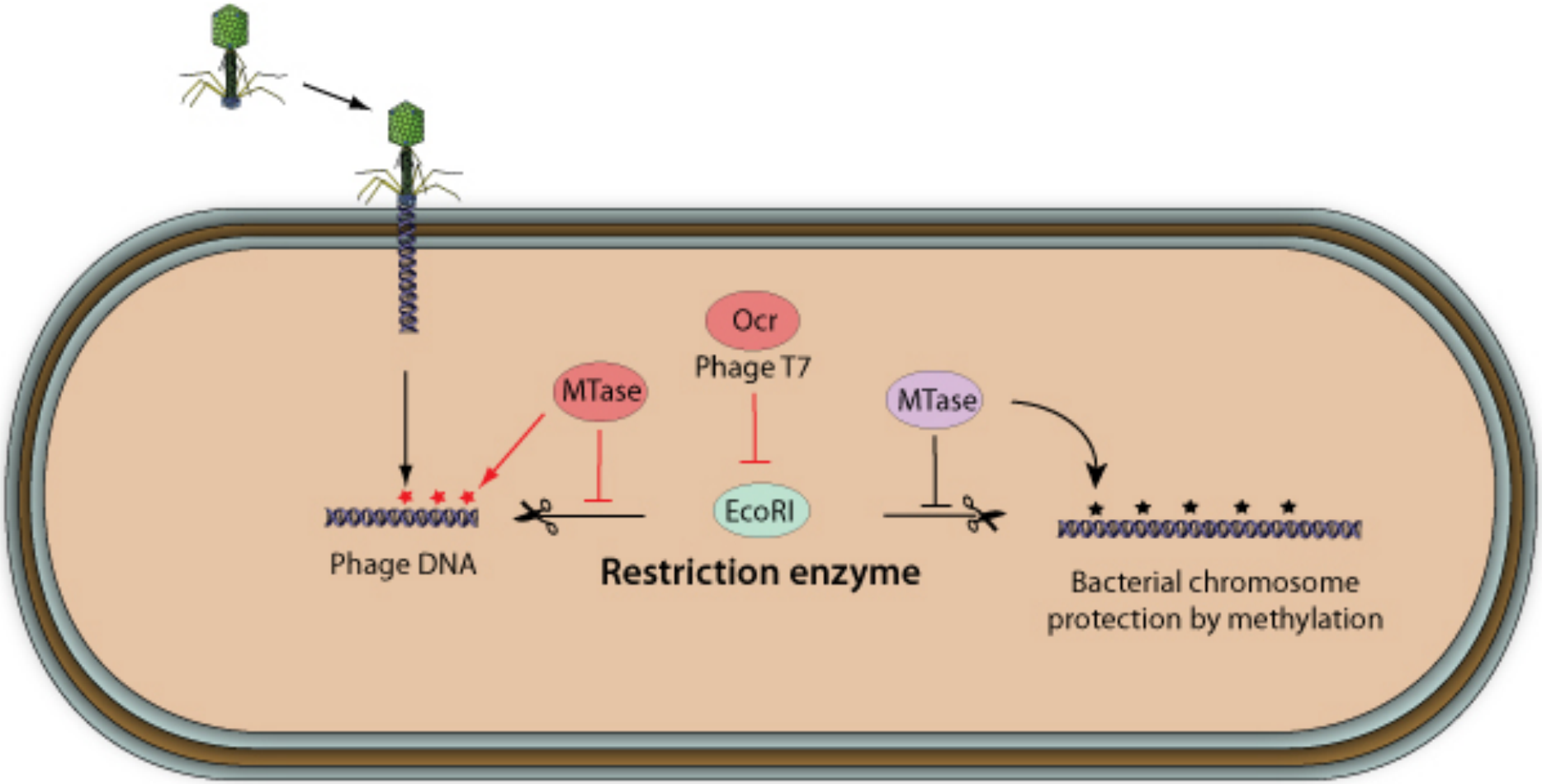


Toxin-antitoxin systems as antiviral defense

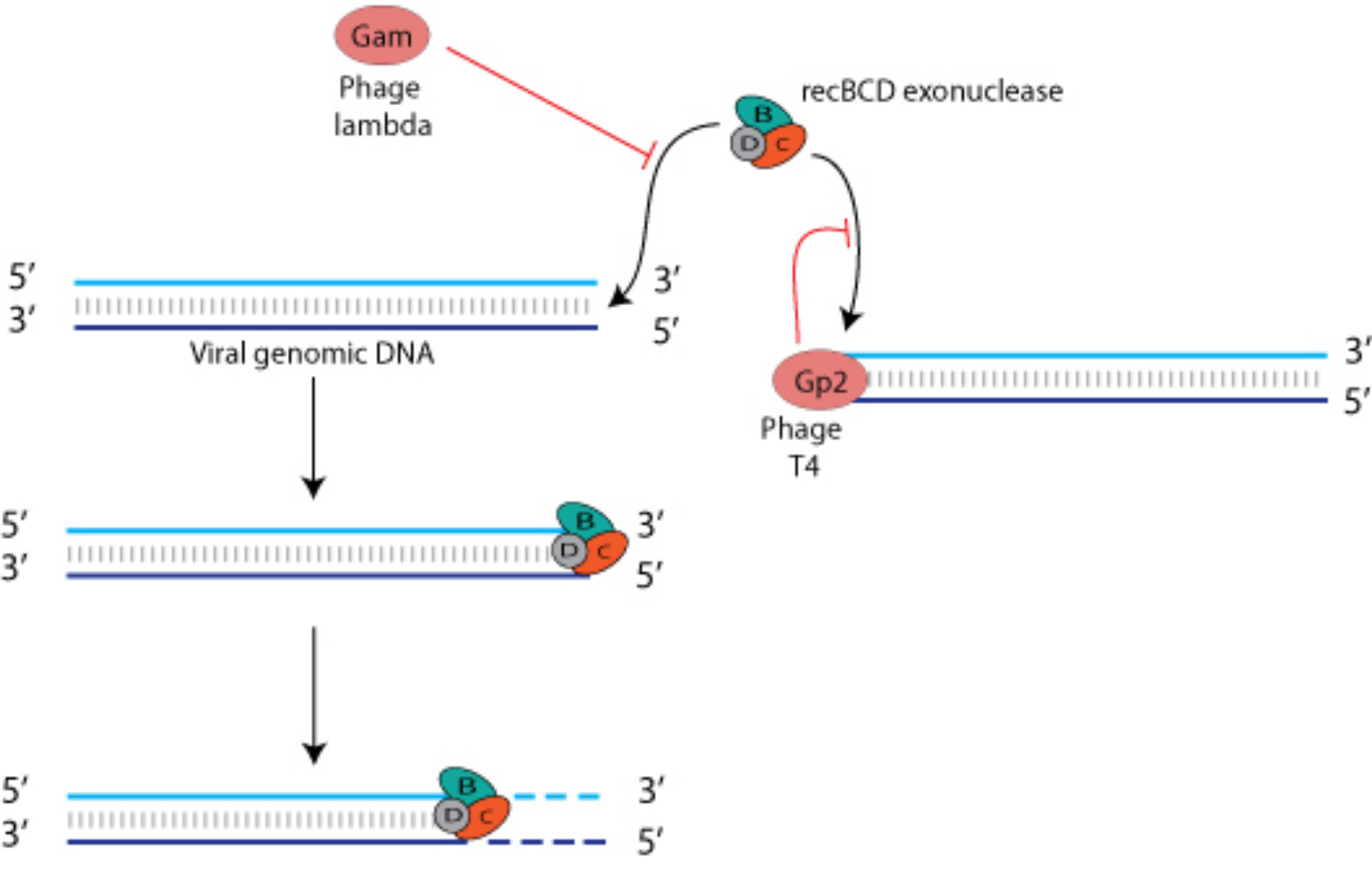




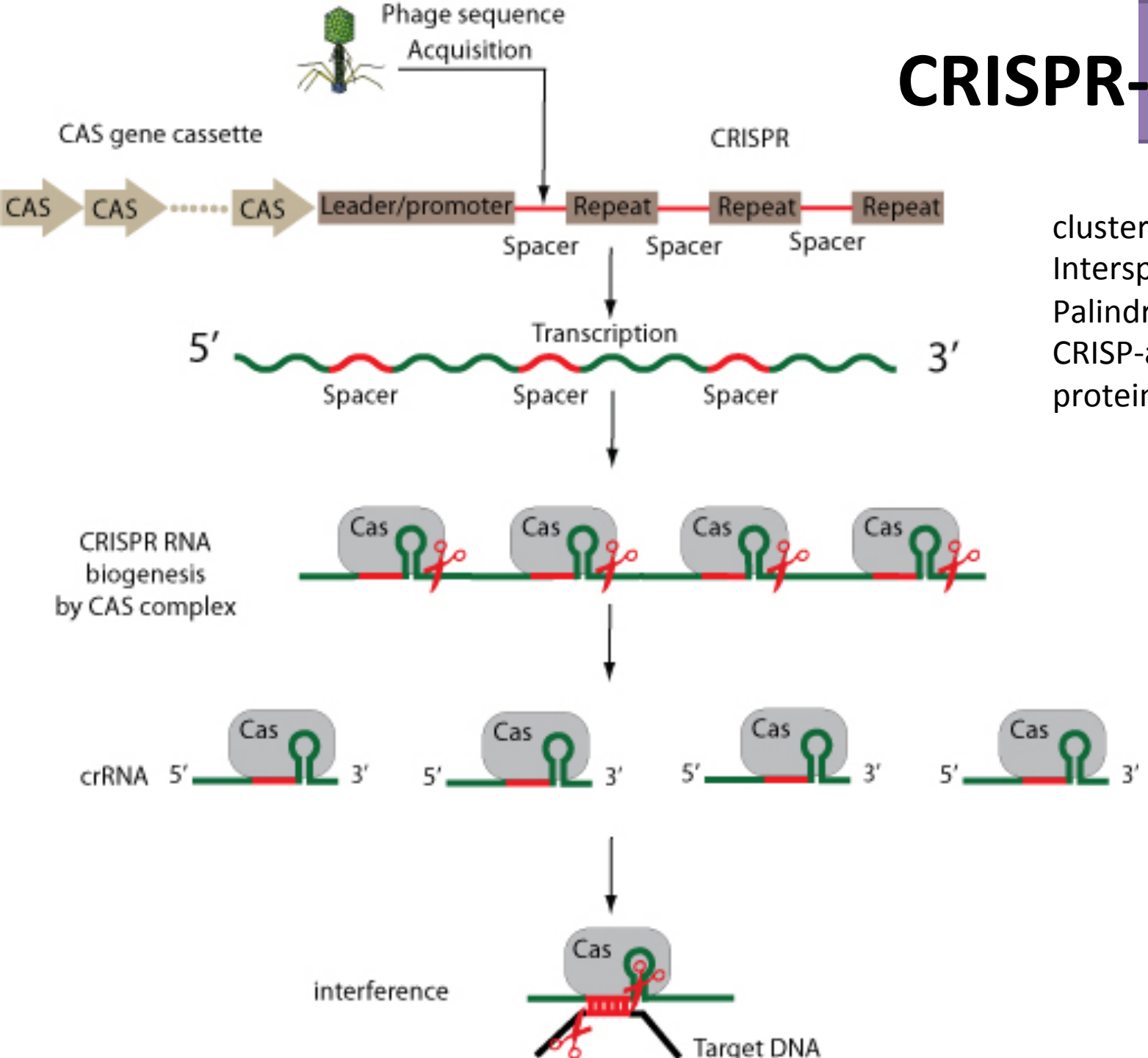
Restriction-modification system evasion by virus



DNA end degradation evasion by virus

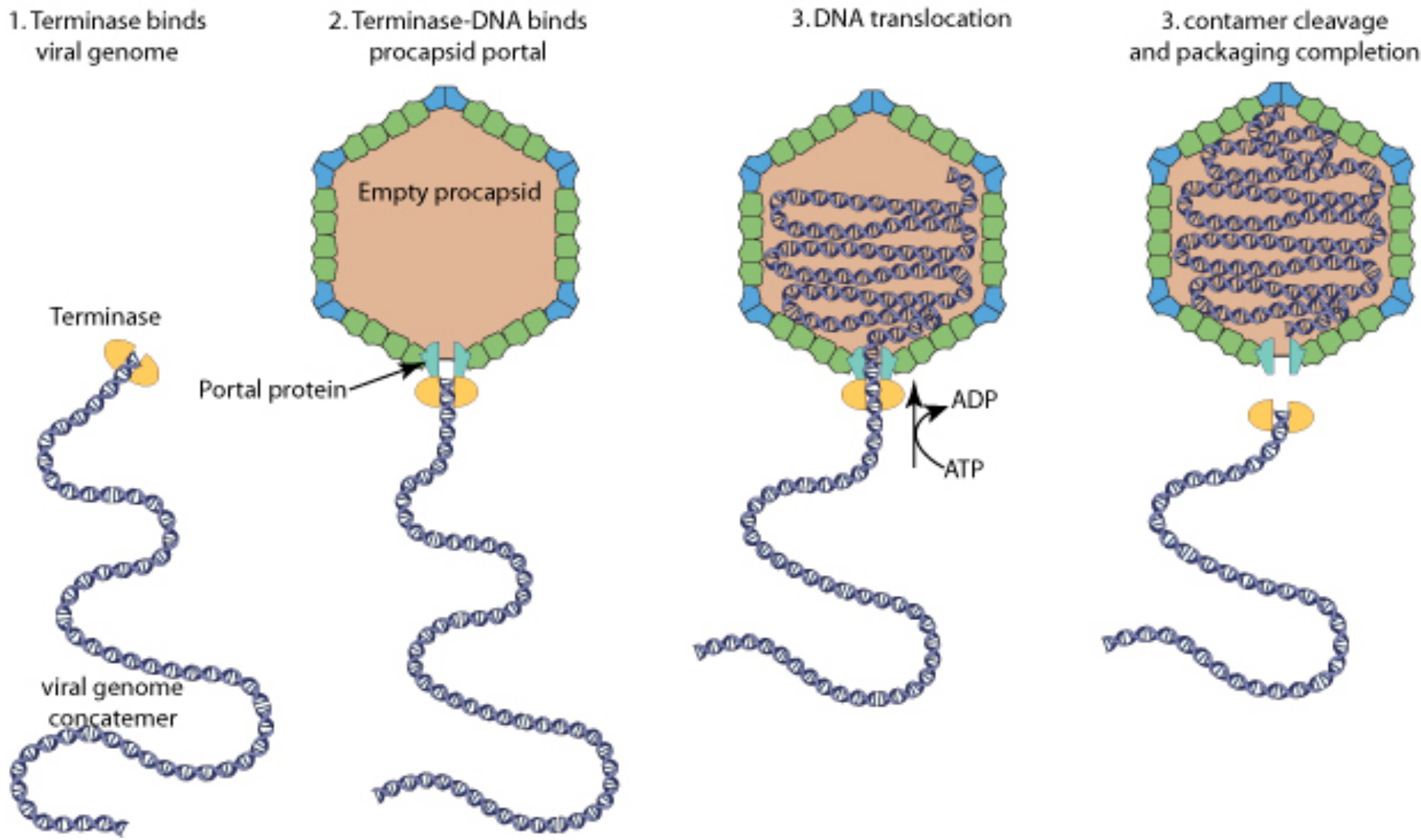


CRISPR-cas

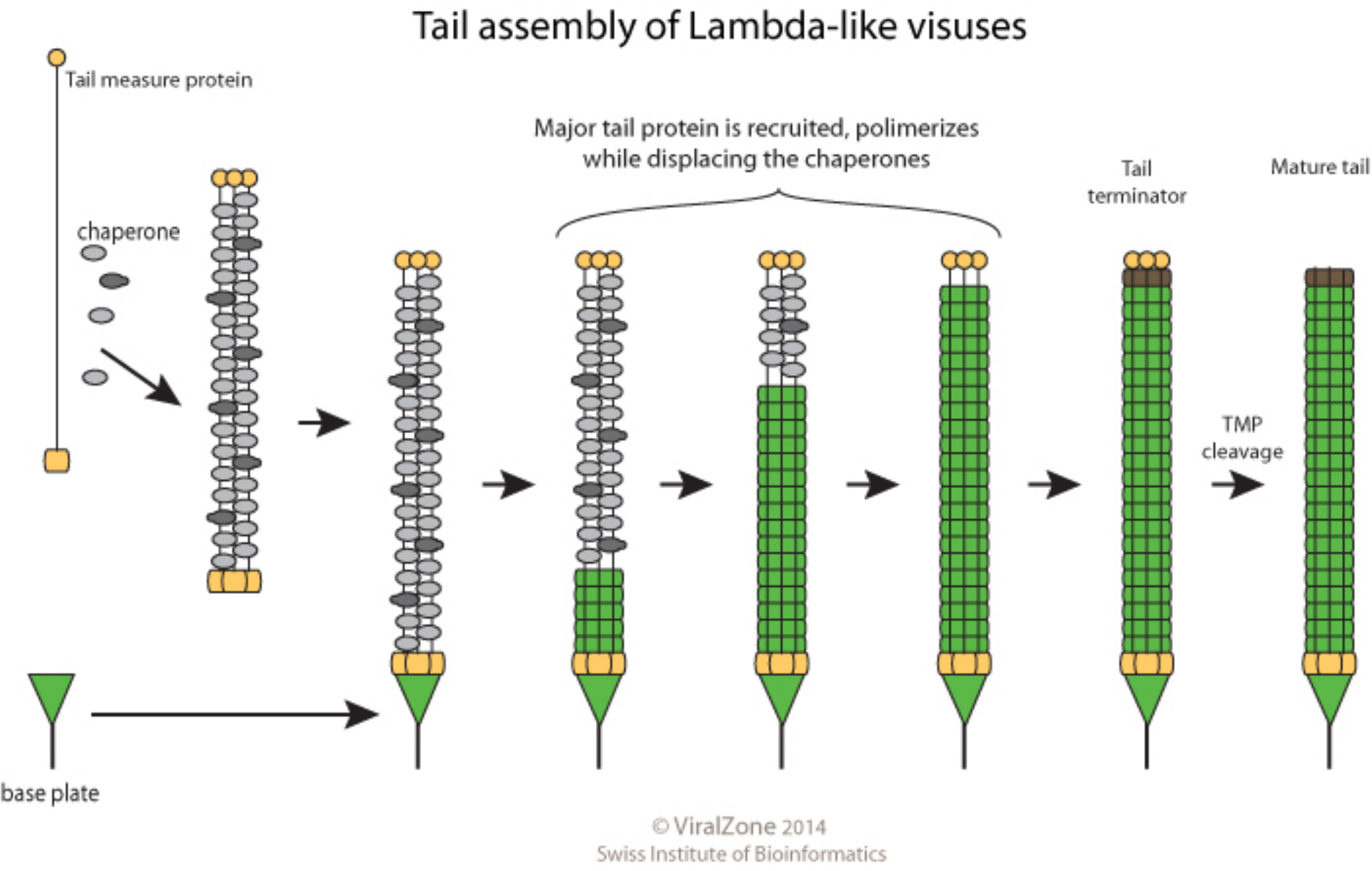


clustered Regularly Interspaced Short Palindromic Repeats / CRISP-associated proteins

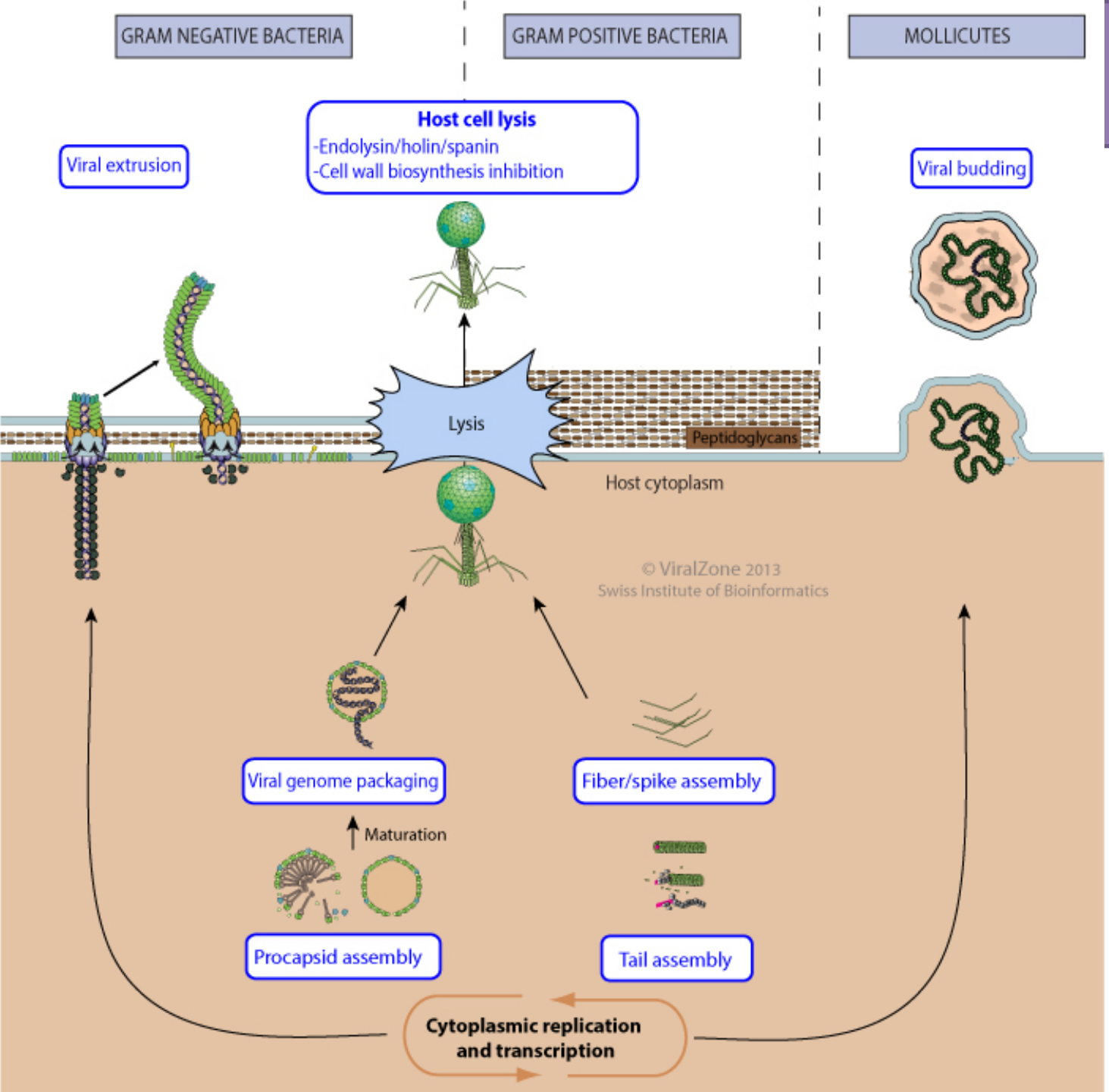
Phage genome packaging



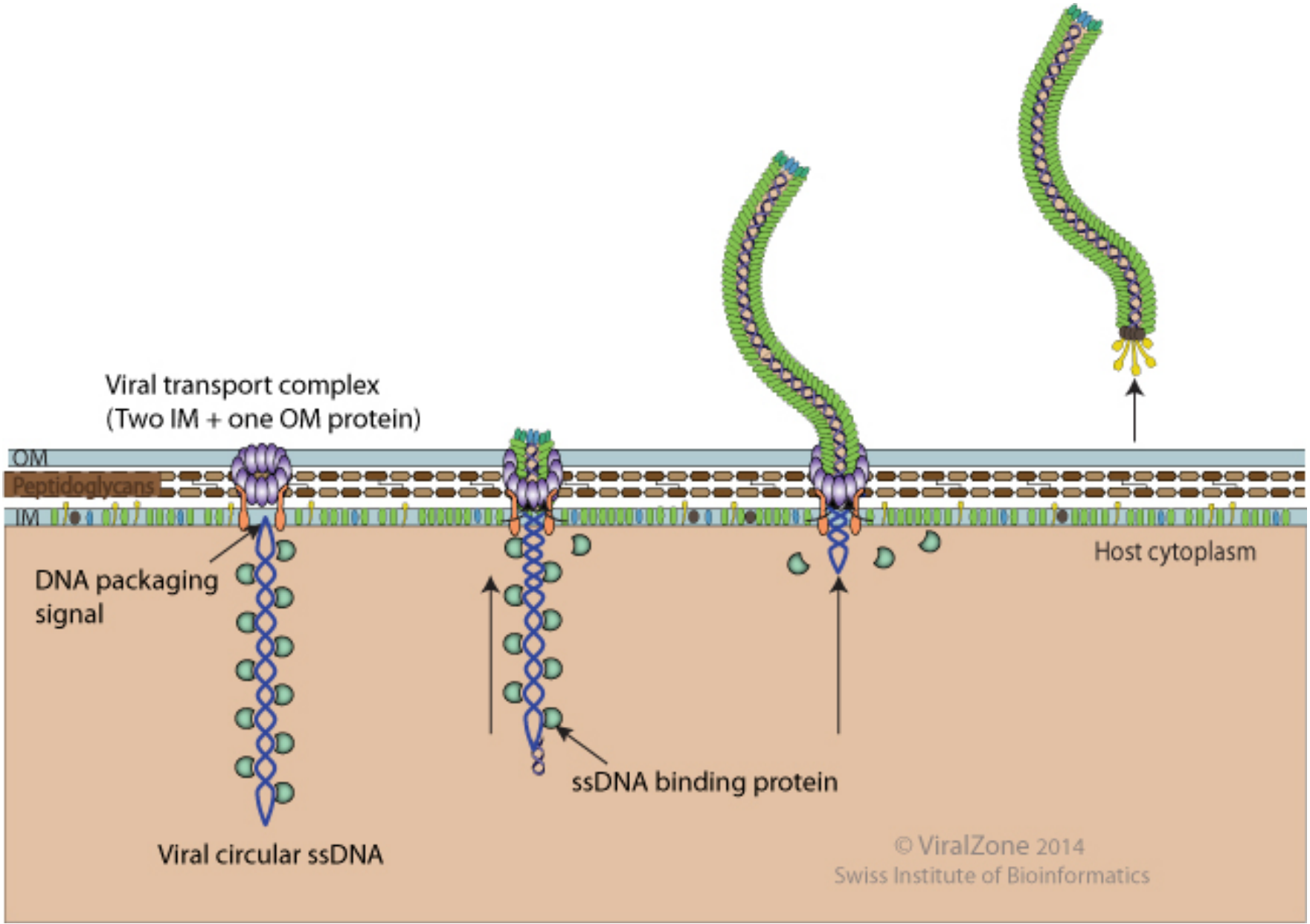
Tail assembly

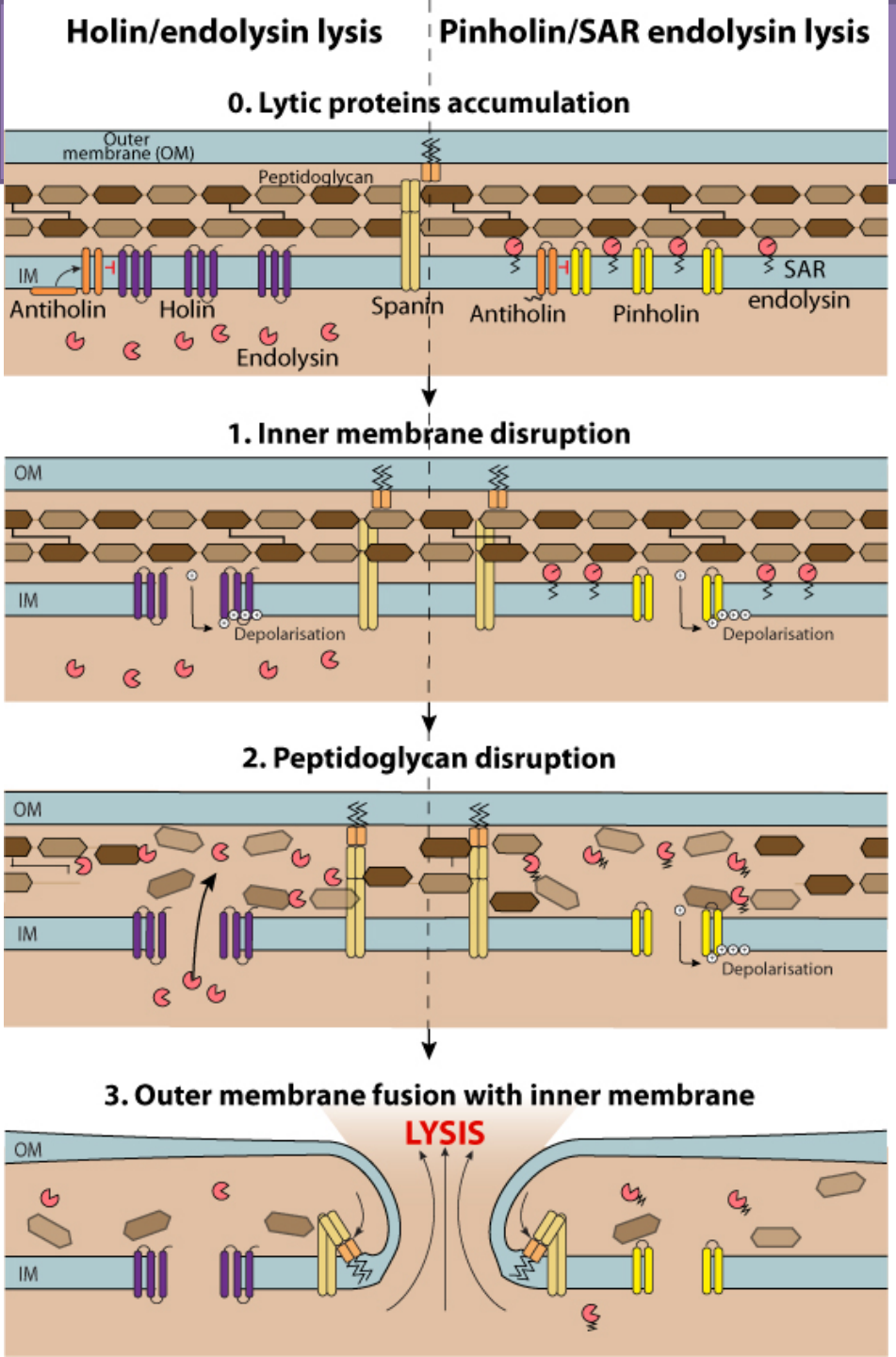


Phage exit


GRAM NEGATIVE BACTERIA
GRAM POSITIVE BACTERIA
MOLLICUTES
Host cell lysis
-Endolysin/holin/spanin
-Cell wall biosynthesis inhibition
Viral extrusion
Viral budding
Lysis
Peptidoglycans
Host cytoplasm
© ViralZone 2013
Swiss Institute of Bioinformatics
Viral genome packaging
Fiber/spike assembly
Maturation
Procapsid assembly
Tail assembly
Cytoplasmic replication
and transcription

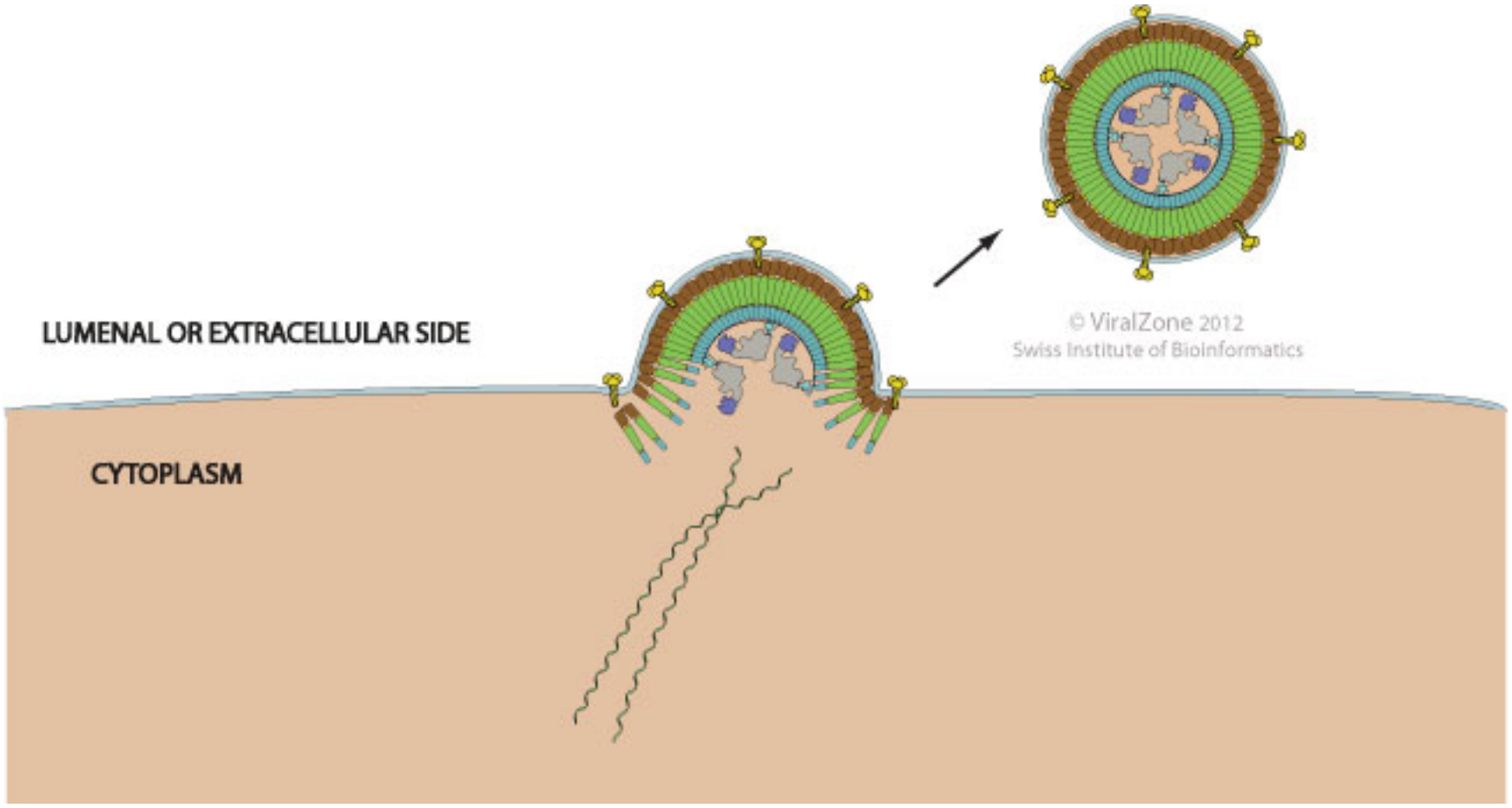
Phage extrusion





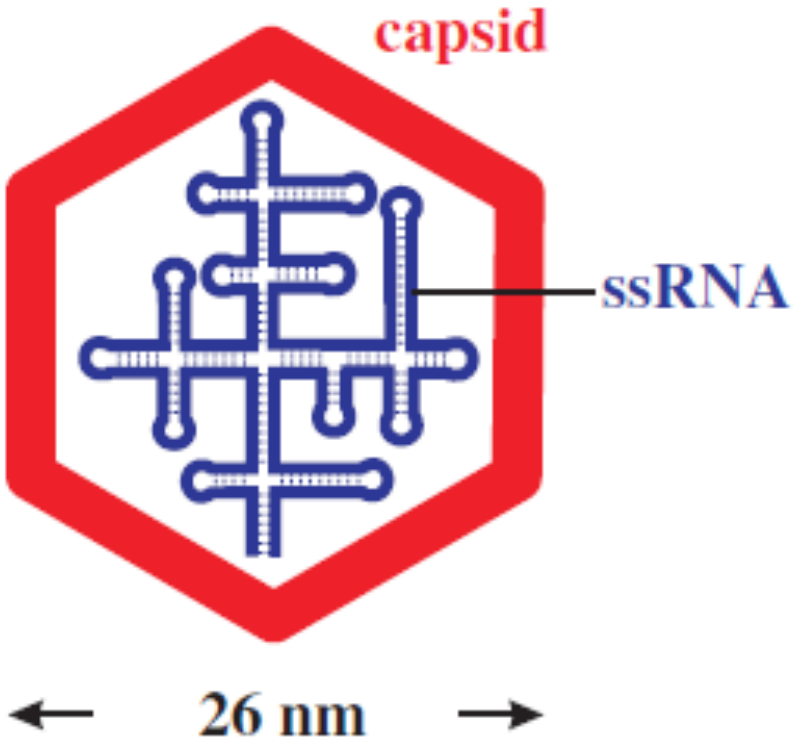
Holin/endolysin/spanin cell lysis by phage

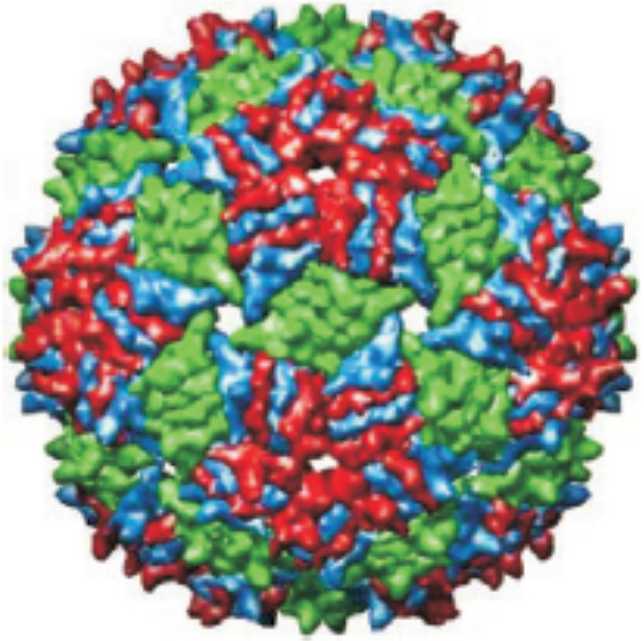
Phage budding



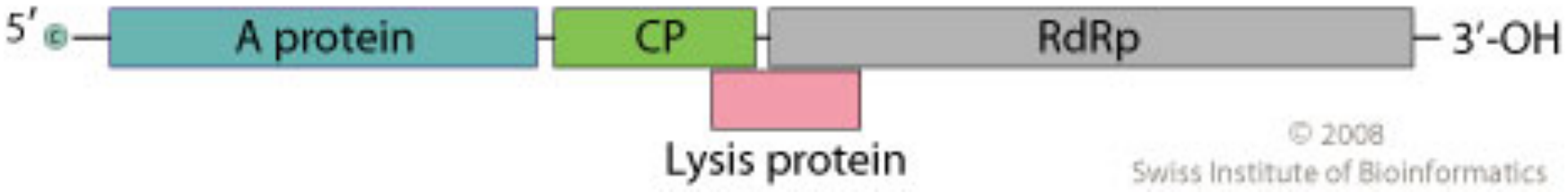
Plasmaviridae

Bacteriophage MS2

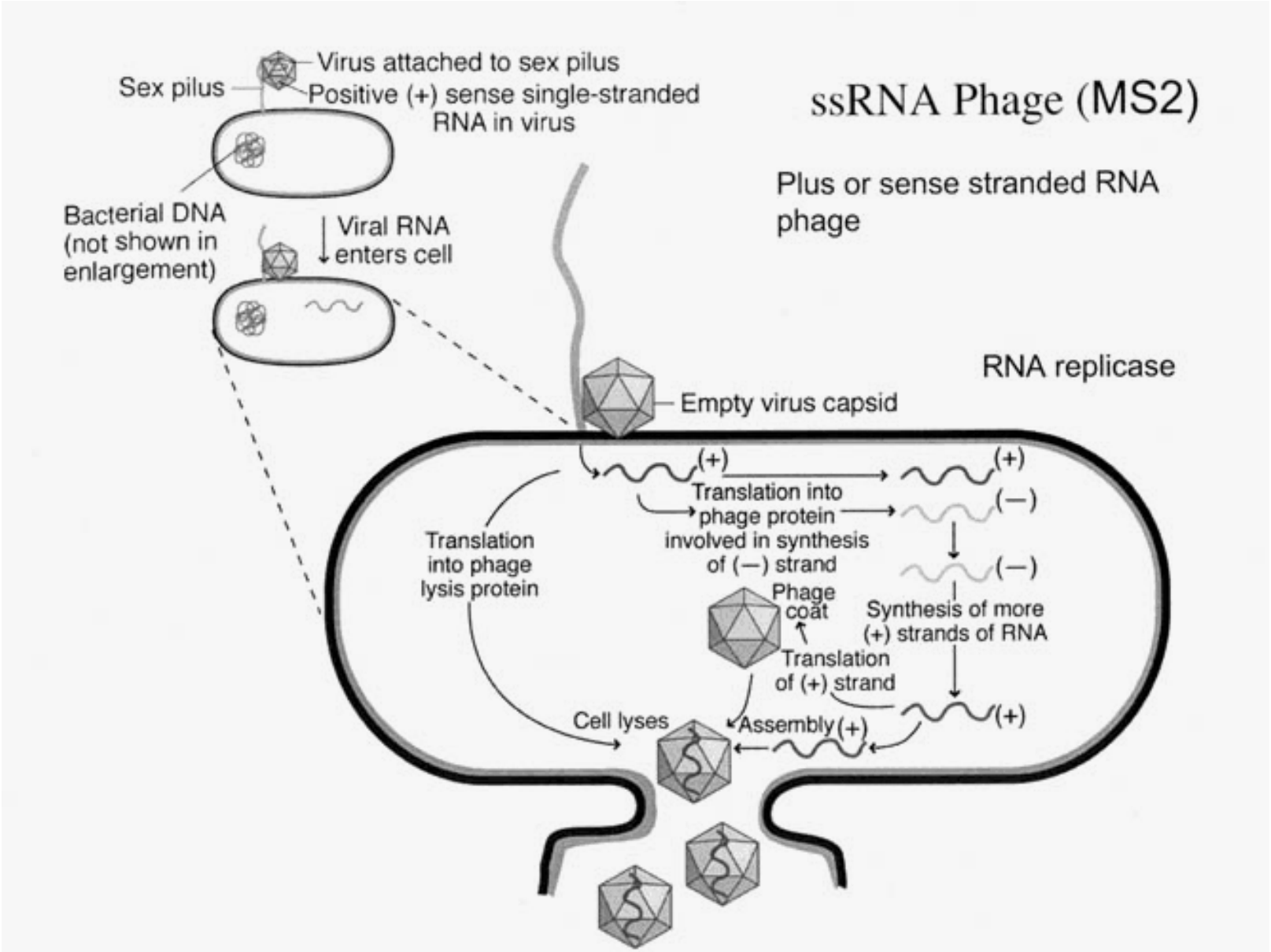




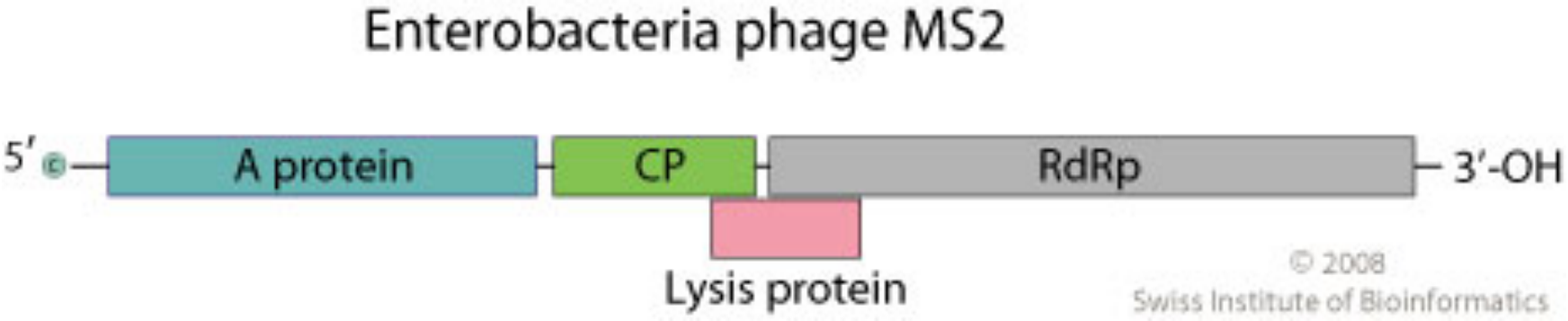
Enterobacteria phage MS2



MS2 life-cycle



Leviviridae gene expression regulation



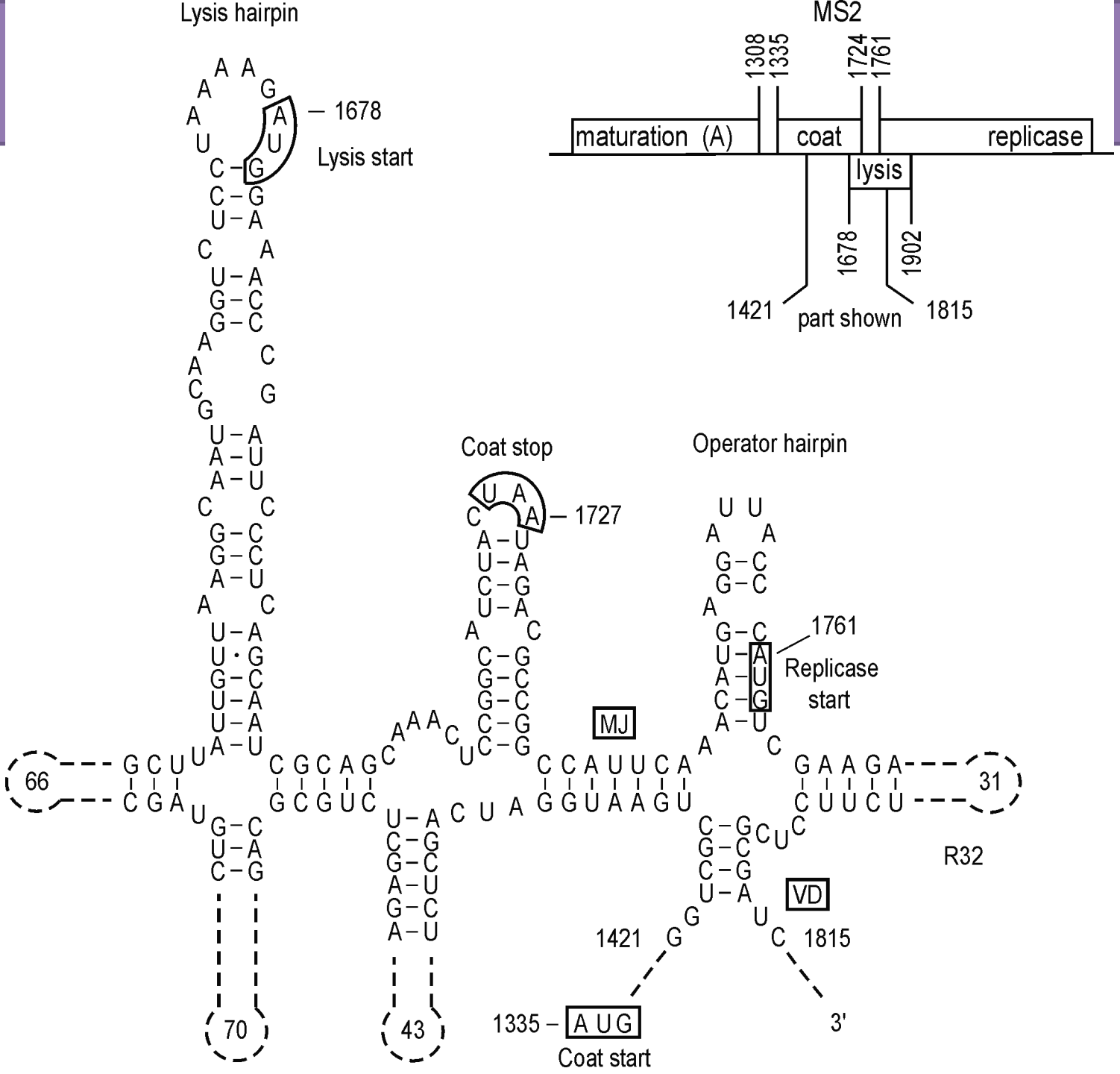
The gene for the most abundant protein, the coat protein, can be immediately translated.

The translation start of the replicase gene is normally hidden within RNA secondary structure, but can be transiently opened as ribosomes pass through the coat protein gene.

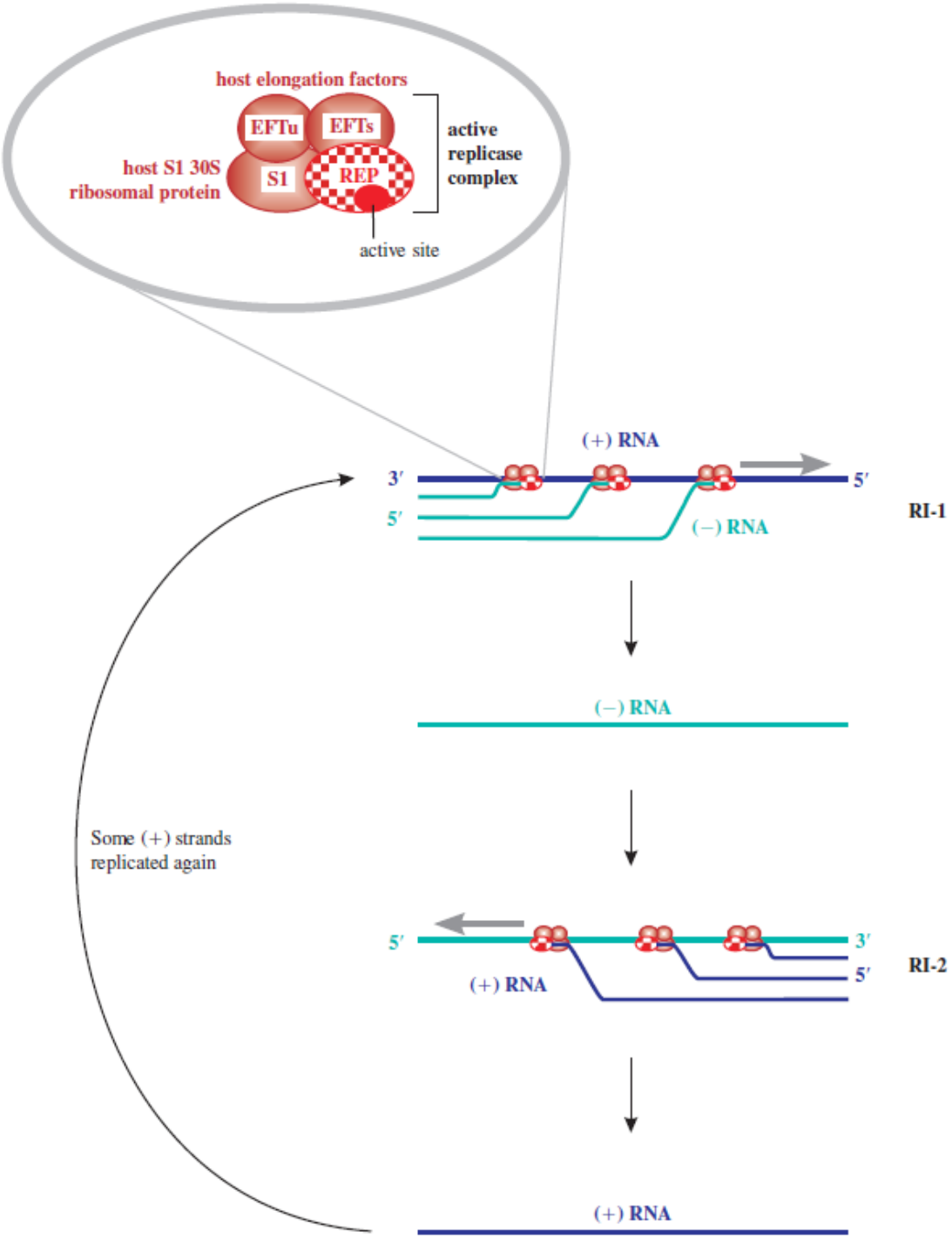
Replicase translation is also shut down once large amounts of coat protein have been made; coat protein dimers bind and stabilize the RNA "operator hairpin", blocking the replicase start.

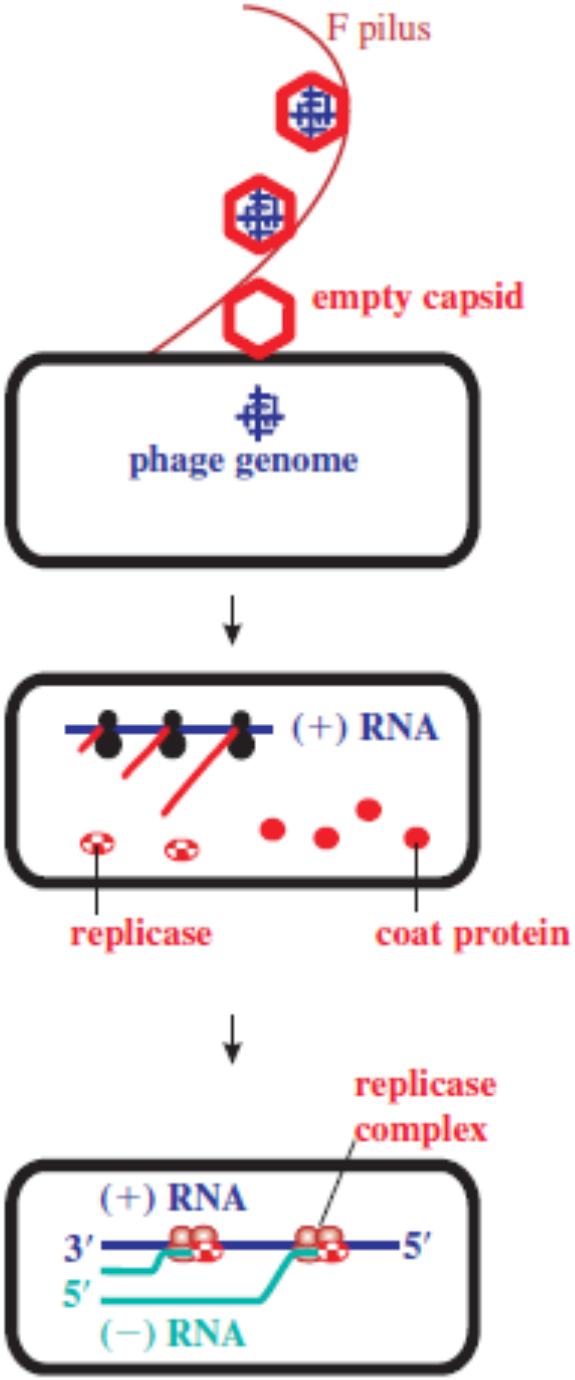
The start of the maturation protein gene is accessible in RNA being replicated but hidden within RNA secondary structure in the completed MS2 RNA; this ensures translation of only a very few copies of maturation protein per RNA.

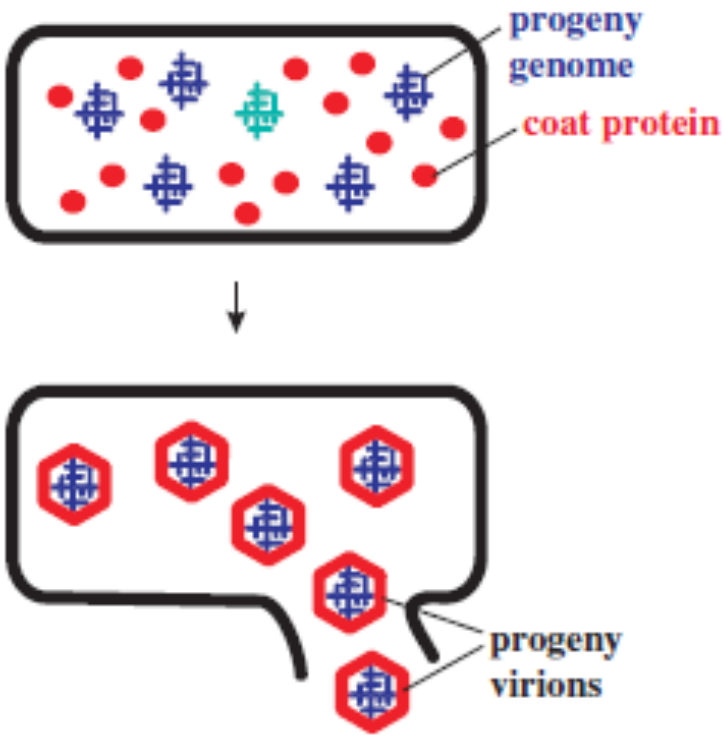
The lysis protein gene can only be initiated by ribosomes that have completed translation of the coat protein gene and "slip back" to the start of the lysis protein gene, at about a 5% frequency.


Lysis hairpin
1678
Lysis start
MS2
1308
1335
1724
1761
maturation (A)
coat
replicase
lysis
1678
1902
1421
part shown
1815
Coat stop
1727
Operator hairpin
1761
Replicase
start
MJ
66
70
43
31
R32
VD
1421
1815
1335
AUG
Coat start
3'

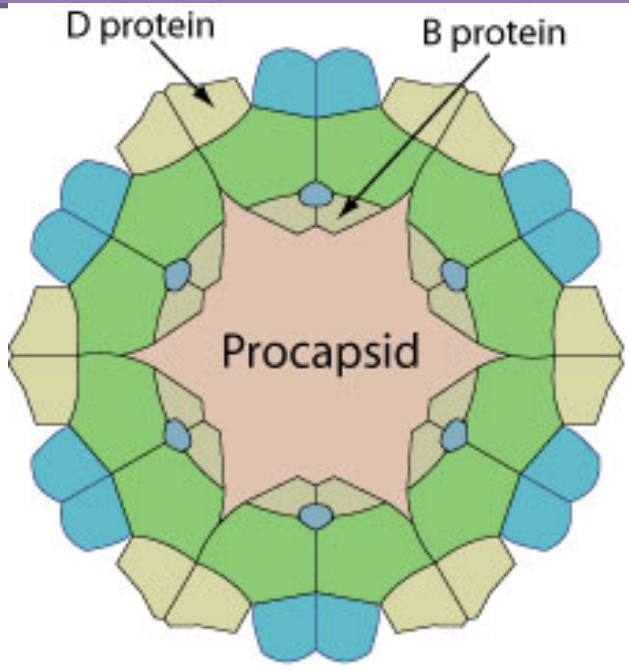
Leviviridae replication

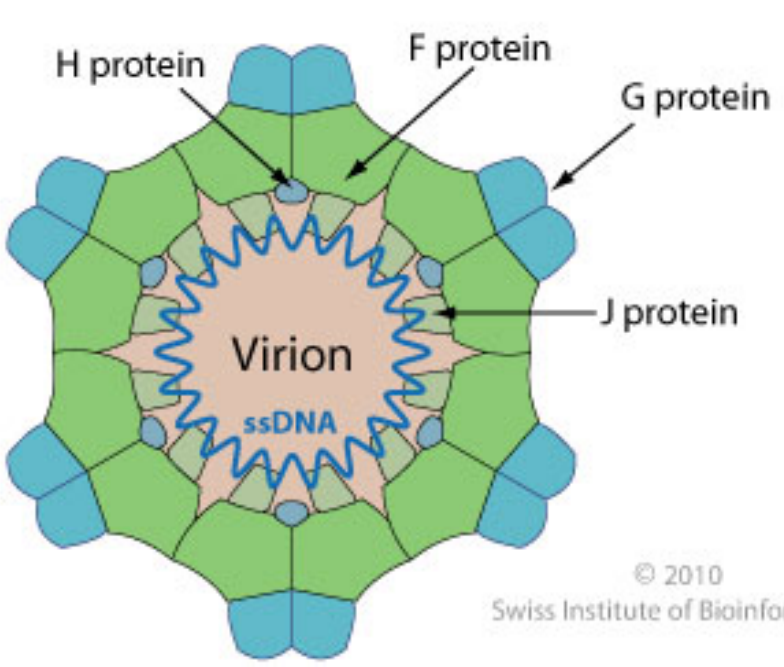


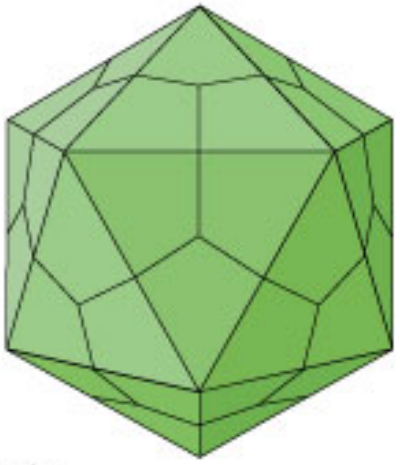

F pilus
empty capsid
phage genome
(+) RNA
replicase
coat protein
replicase
complex
(+) RNA
3′
5′
5′
(−) RNA

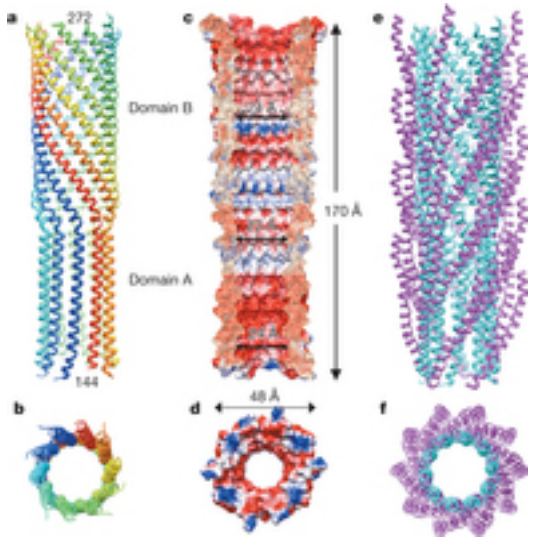

progeny
genome
coat protein
progeny
virions

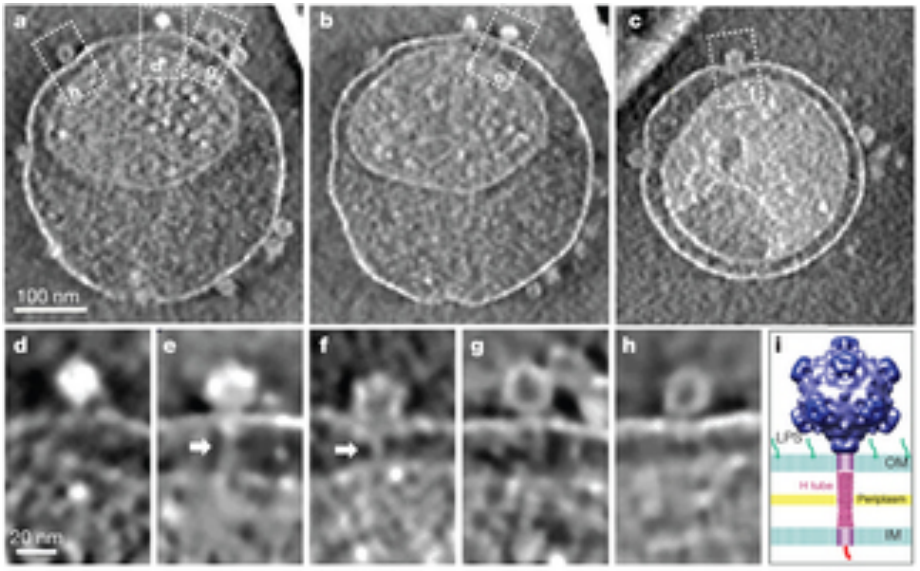
phiX174





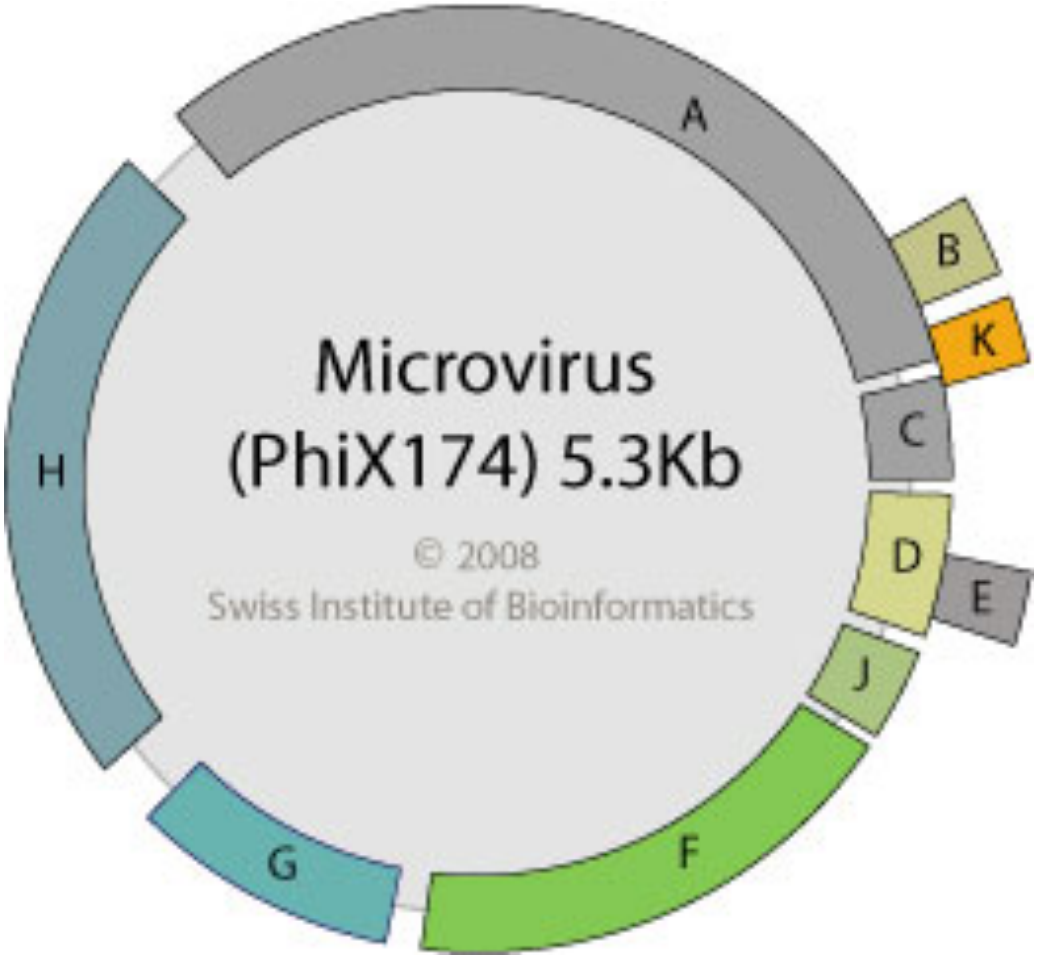




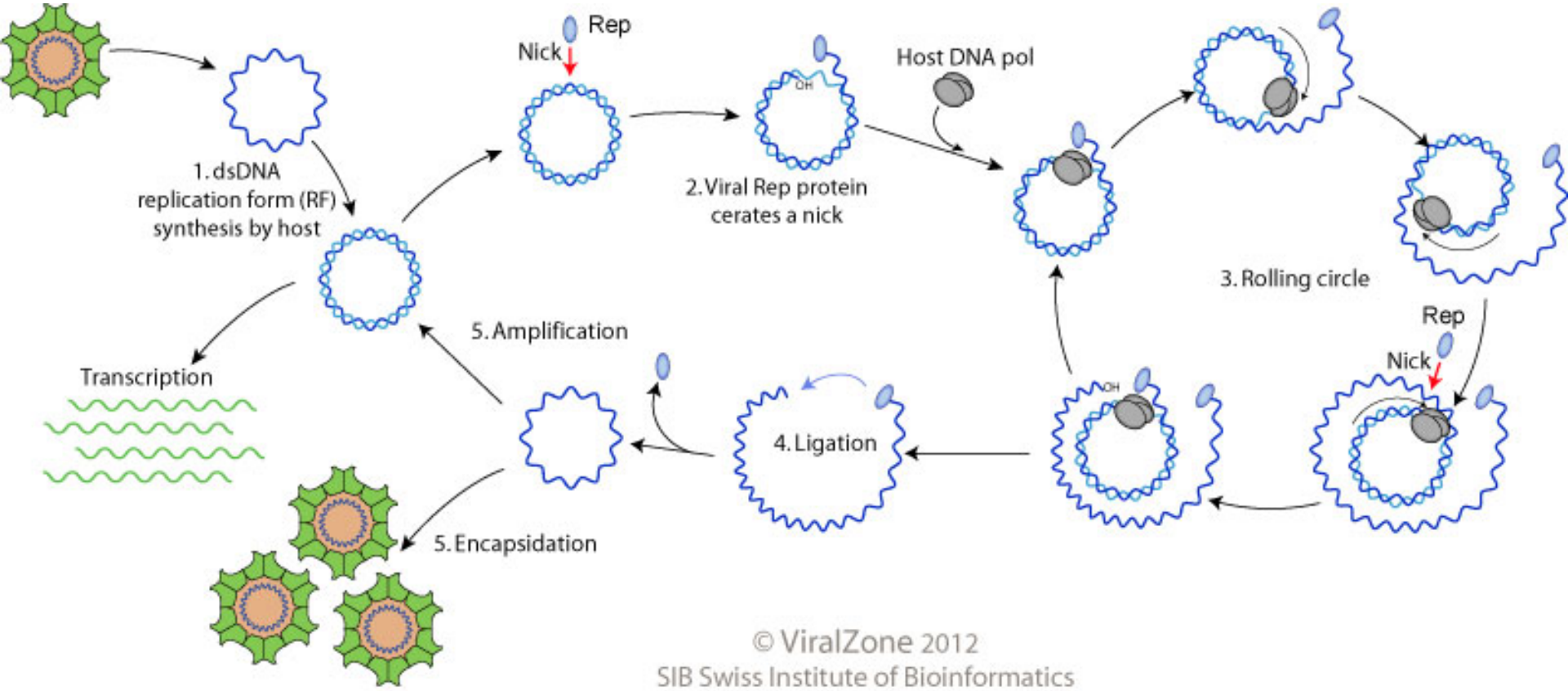


phiX174 genome

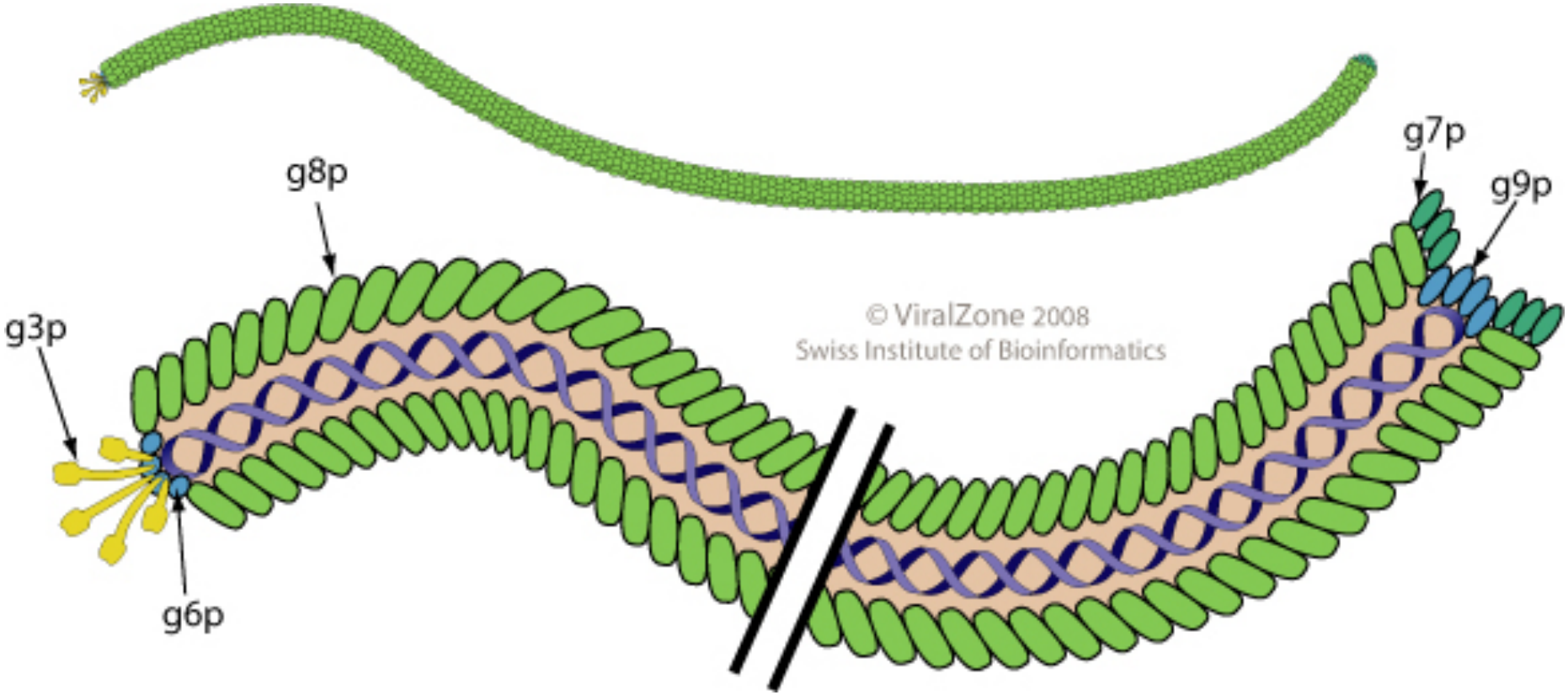
ssDNA(+) genome of 4.4 to 6.1kb



phiX174 rolling circle genome replication

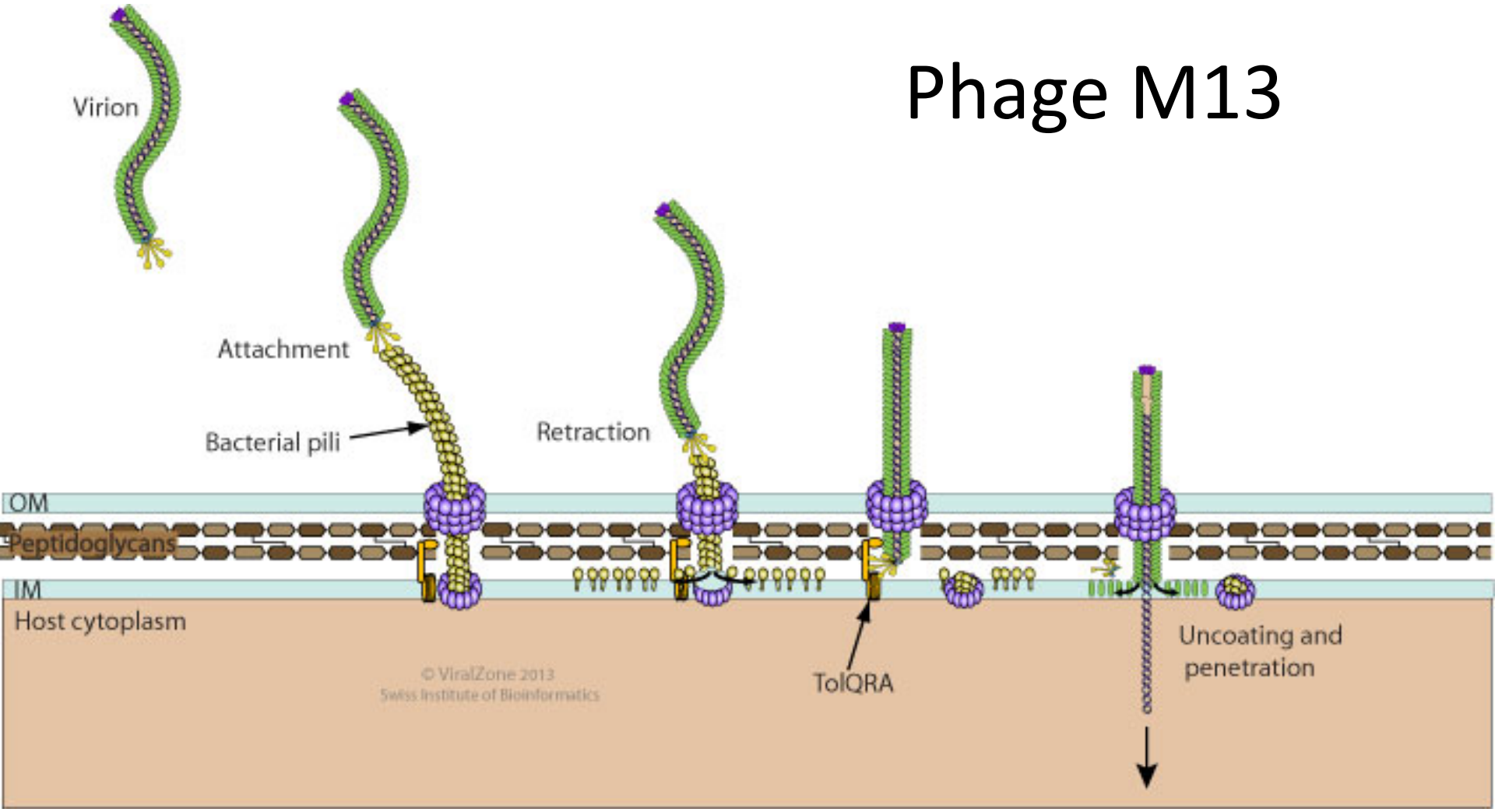


Innoviridae – M13

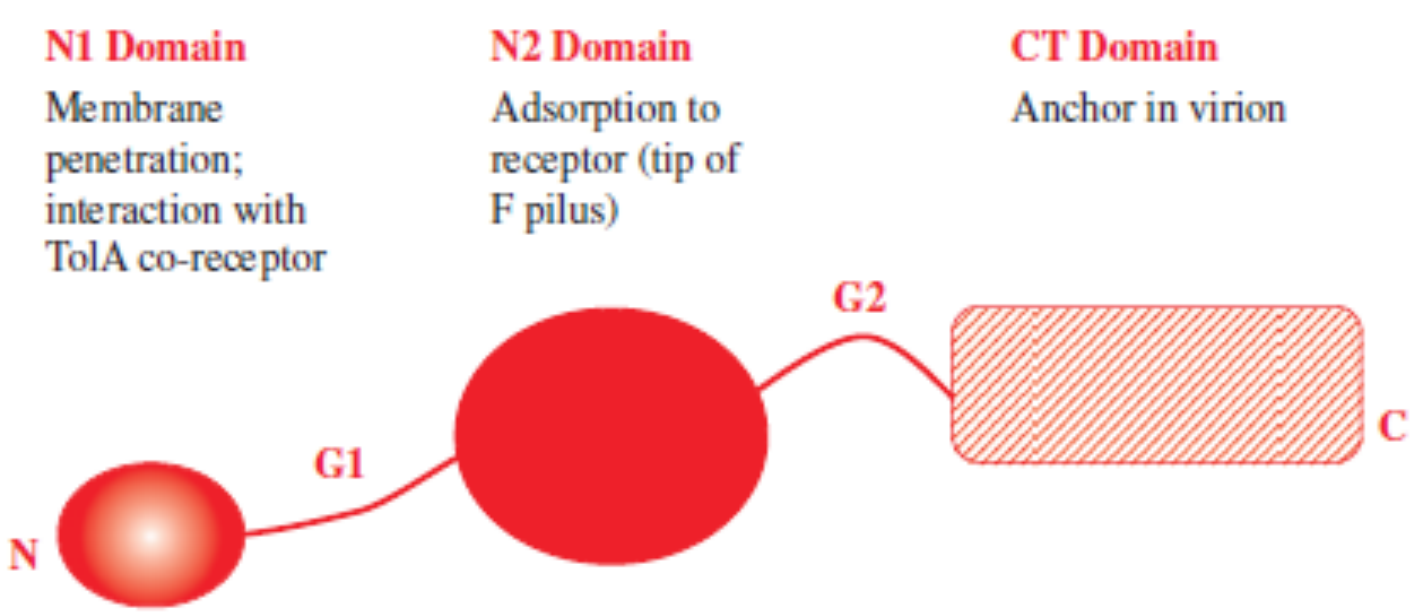


Non-enveloped, rod of filaments of 7nm in diameter and 700 to 2000nm in length. Helical capsid with adsorption proteins on one end.

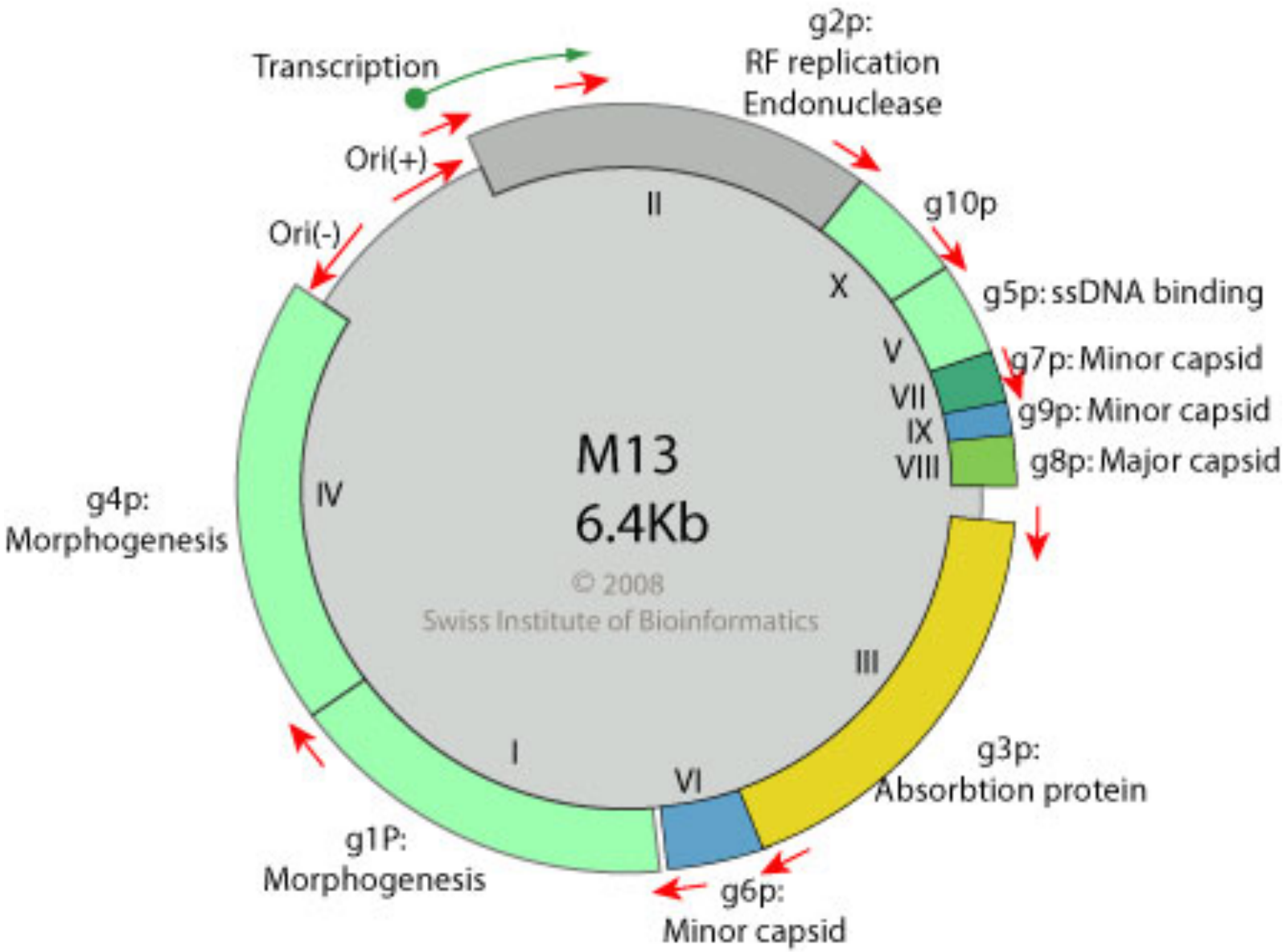
Viral penetration into host cytoplasm via pilus retraction

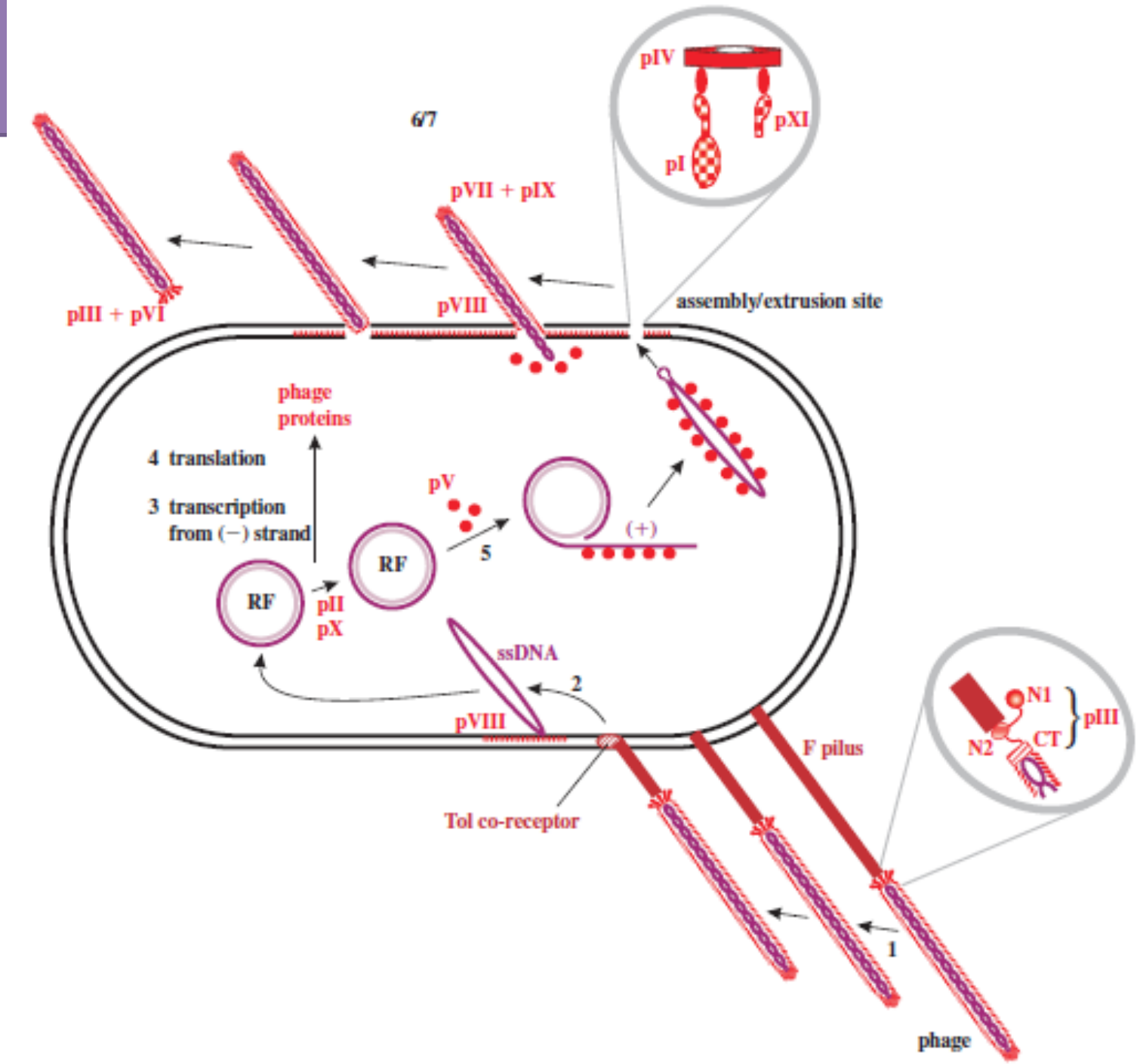


Innoviridae – gene product III

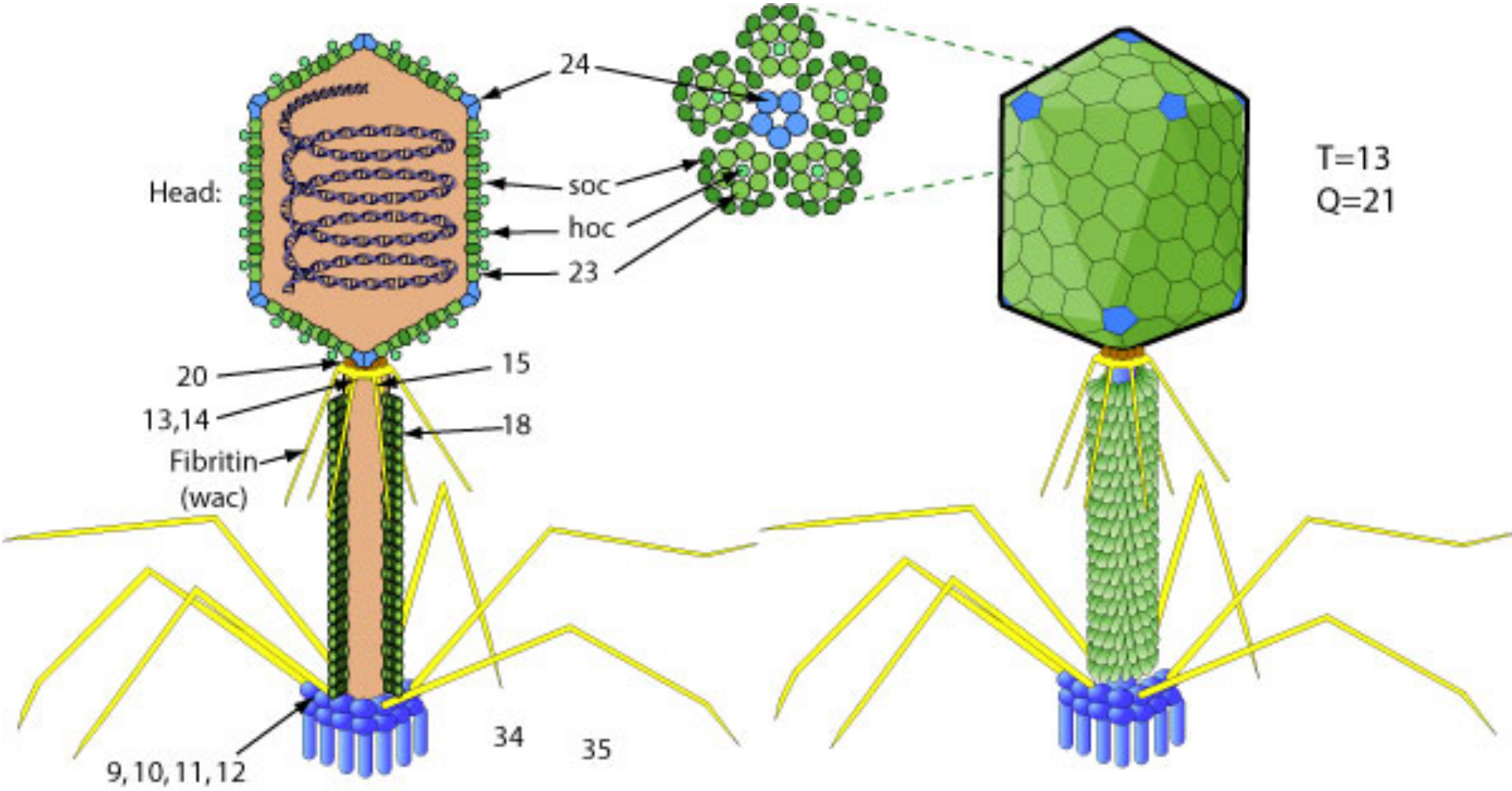


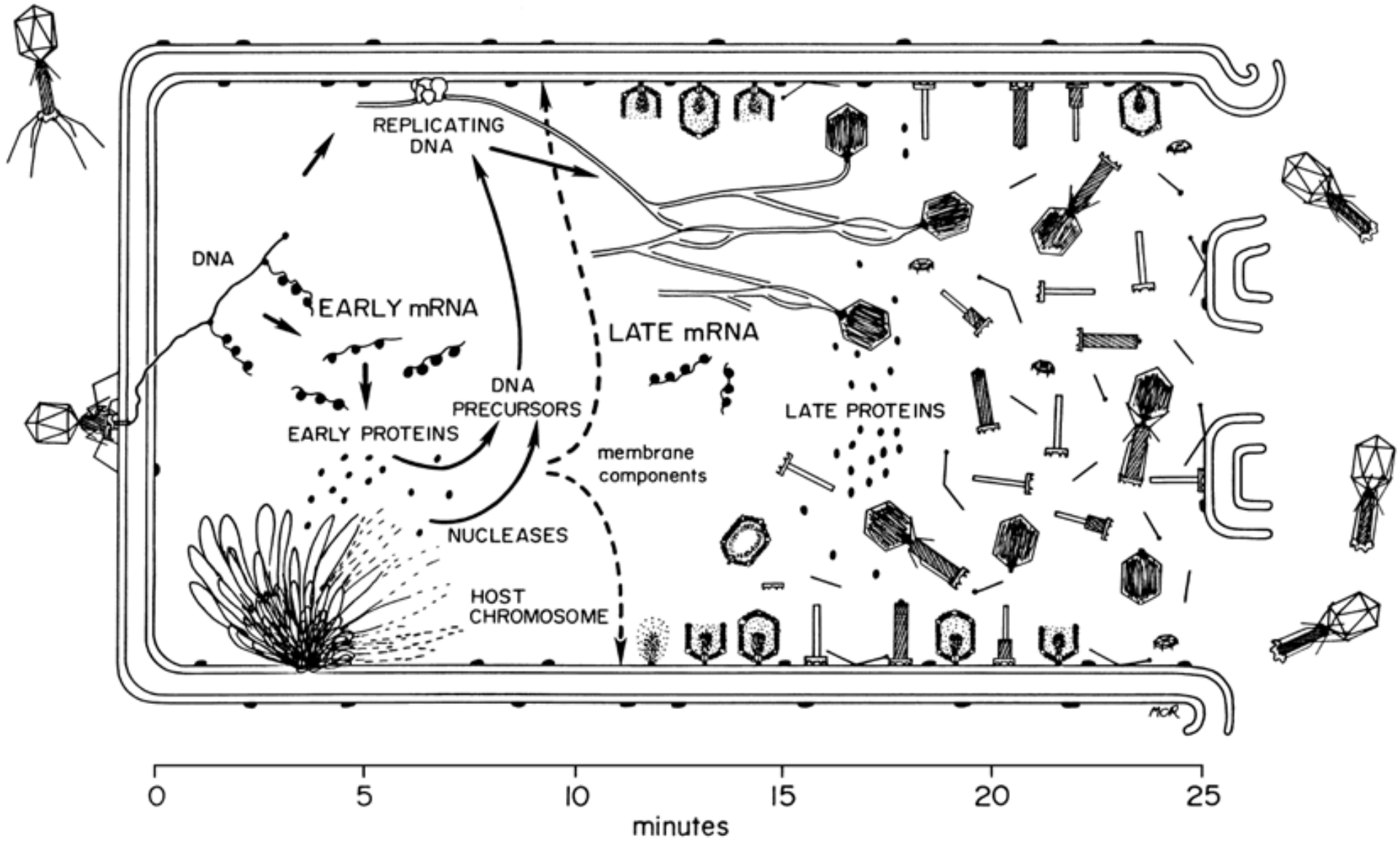
M13 genome (rolling circle replication)



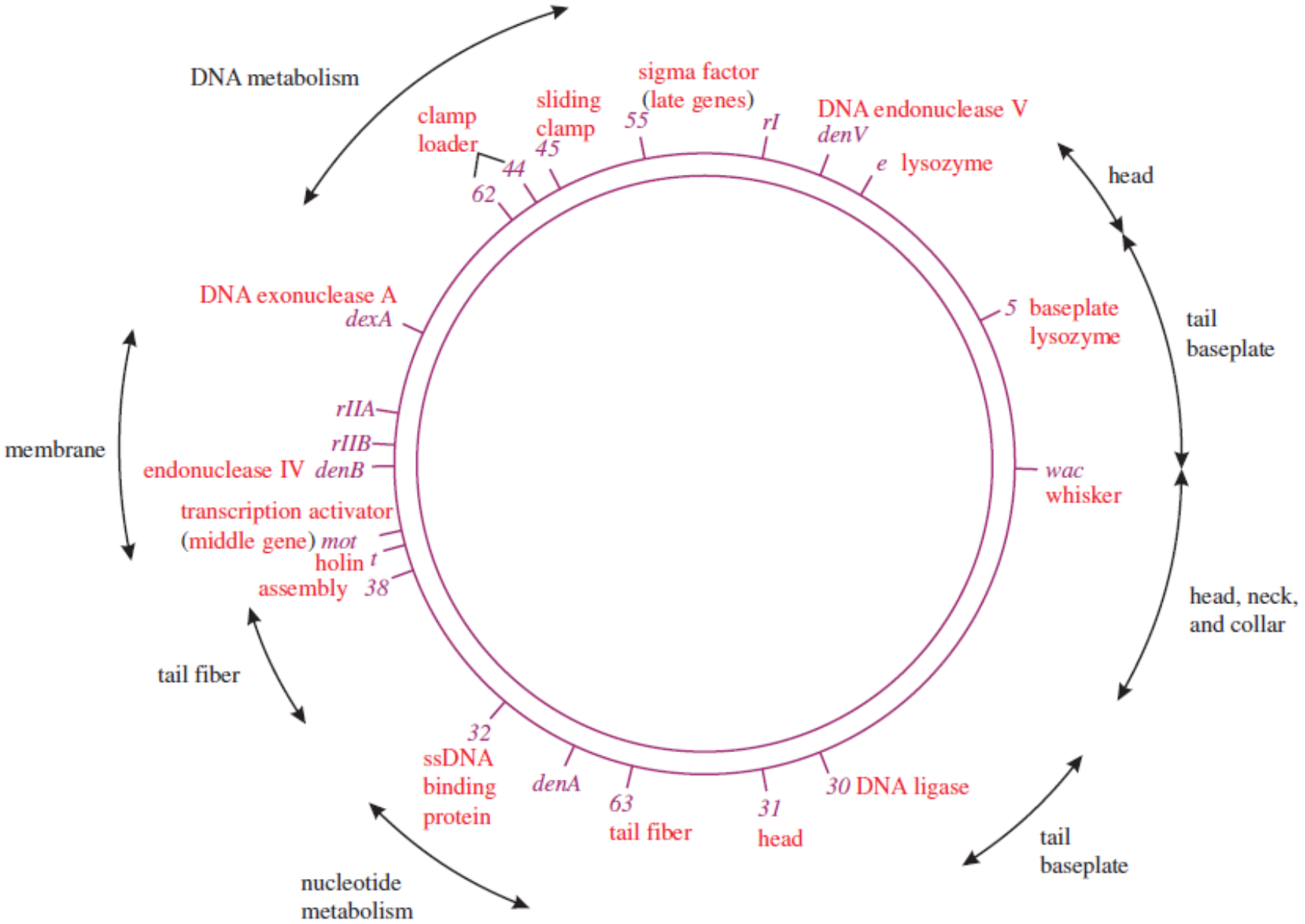

67
pIV
pXI
pI
pVII + pIX
pIII + pVI
pVIII
assembly/extrusion site
phage
proteins
4 translation
3 transcription
from (−) strand
pV
5
(+)
RF
RF
pII
pX
ssDNA
2
pVIII
F pilus
N1
N2
CT
pIII
Tol co-receptor
1
phage

Myoviridae – T4

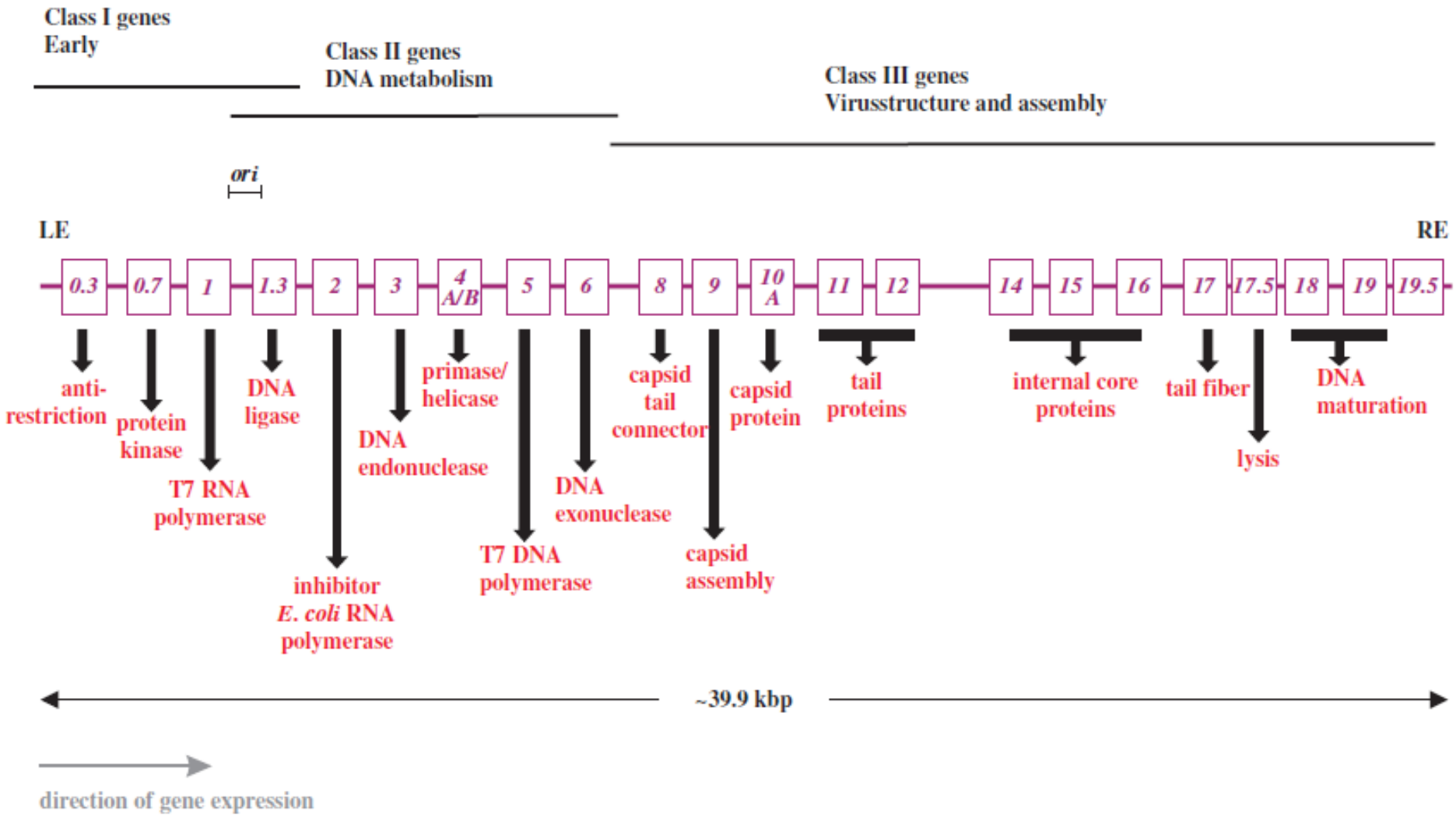



REPLICATING DNA
DNA
EARLY mRNA
LATE mRNA
DNA PRECURSORS
EARLY PROTEINS
LATE PROTEINS
membrane components
NUCLEASES
HOST CHROMOSOME
MGR
0
5
10
15
20
25
minutes

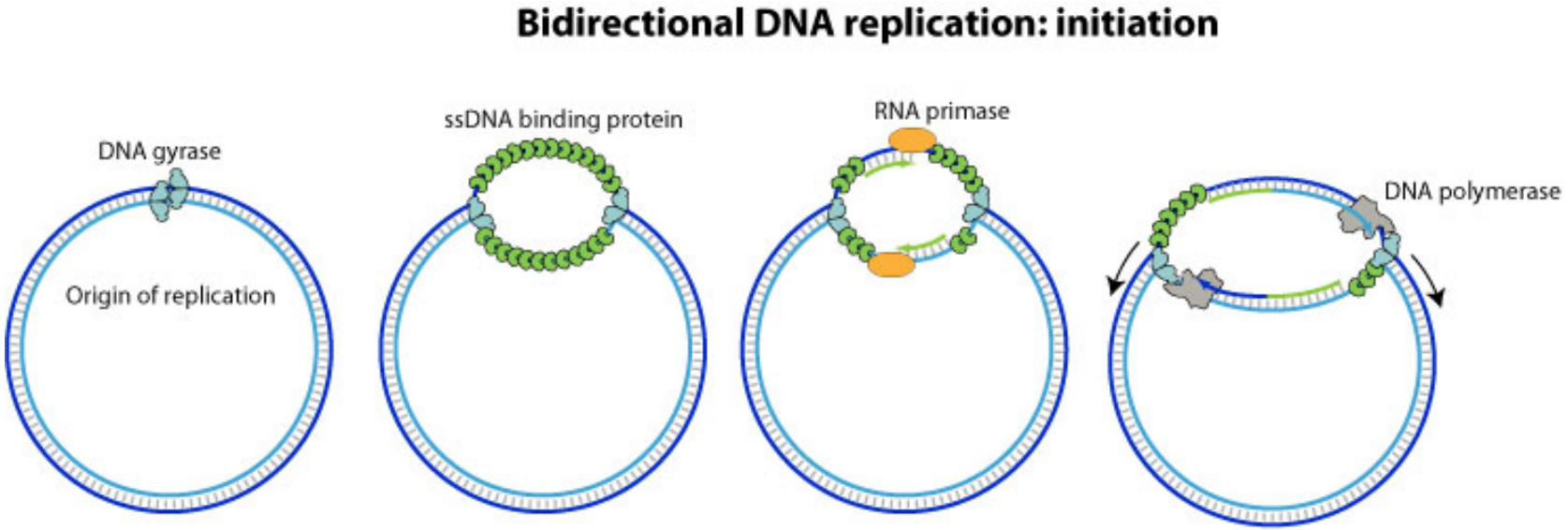
T4 – genome

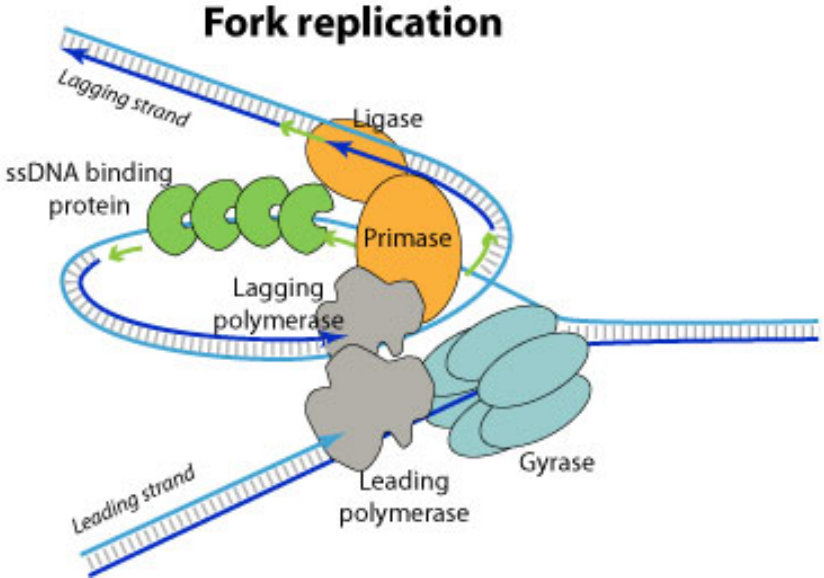

DNA metabolism
clamp loader
sliding clamp
sigma factor (late genes)
DNA endonuclease V denV
lysozyme e
head
tail baseplate
baseplate lysozyme 5
wac whisker
head, neck, and collar
tail baseplate
30 DNA ligase
31 head
63 tail fiber
denA
32 ssDNA binding protein
nucleotide metabolism
tail fiber
assembly 38
holin t
transcription activator (middle gene) mot
endonuclease IV denB
rIIB
rIIA
membrane
DNA exonuclease A dexA
62
44
45
55
rI

Podoviridae – phage T7

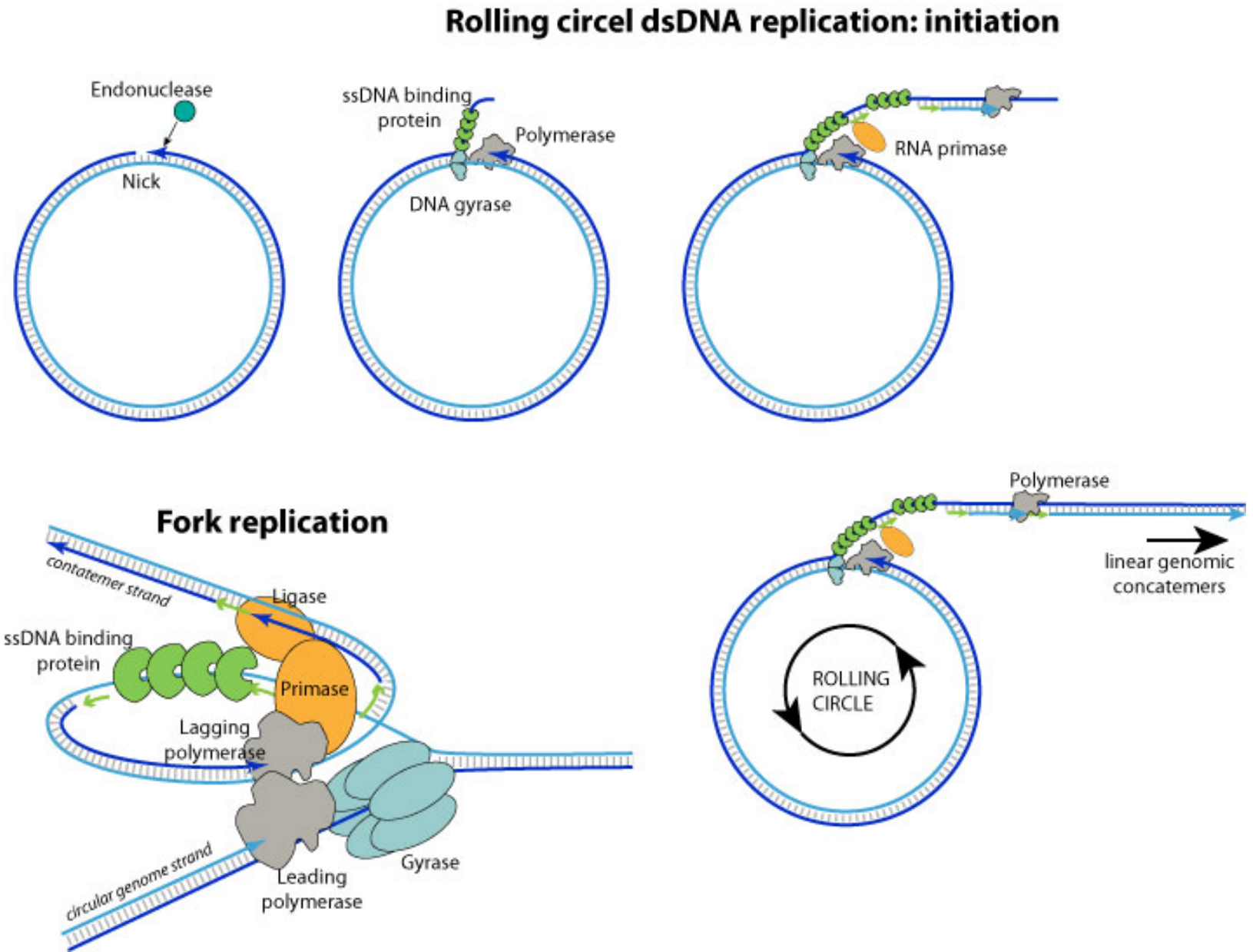


Siphoviridae – theta replication





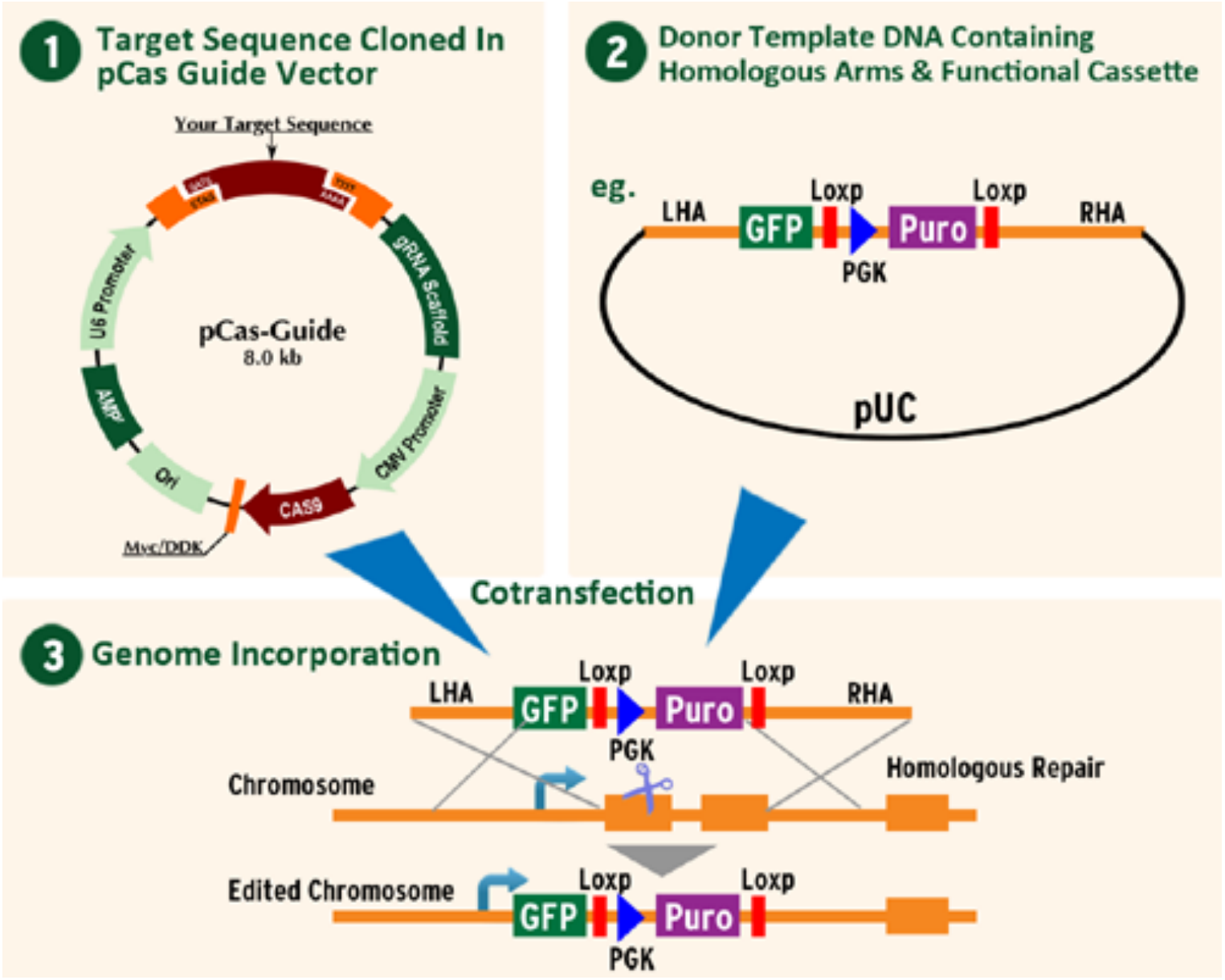
Siphoviridae – rolling circle replication



Learning outcomes

- discuss the replication cycle and control of gene expression in ssRNA coliphages
- outline the infection process of dsRNA phages
- review the biology of the filamentous and icosahedral ssDNA phages
- describe the structure and replication cycle of dsDNA phages

CRISPR-cas genome editing



Virus origins

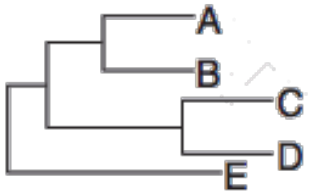
Possible Virus Origins:

- RNA molecules that existed before cells
- cell components
- micro-organisms.

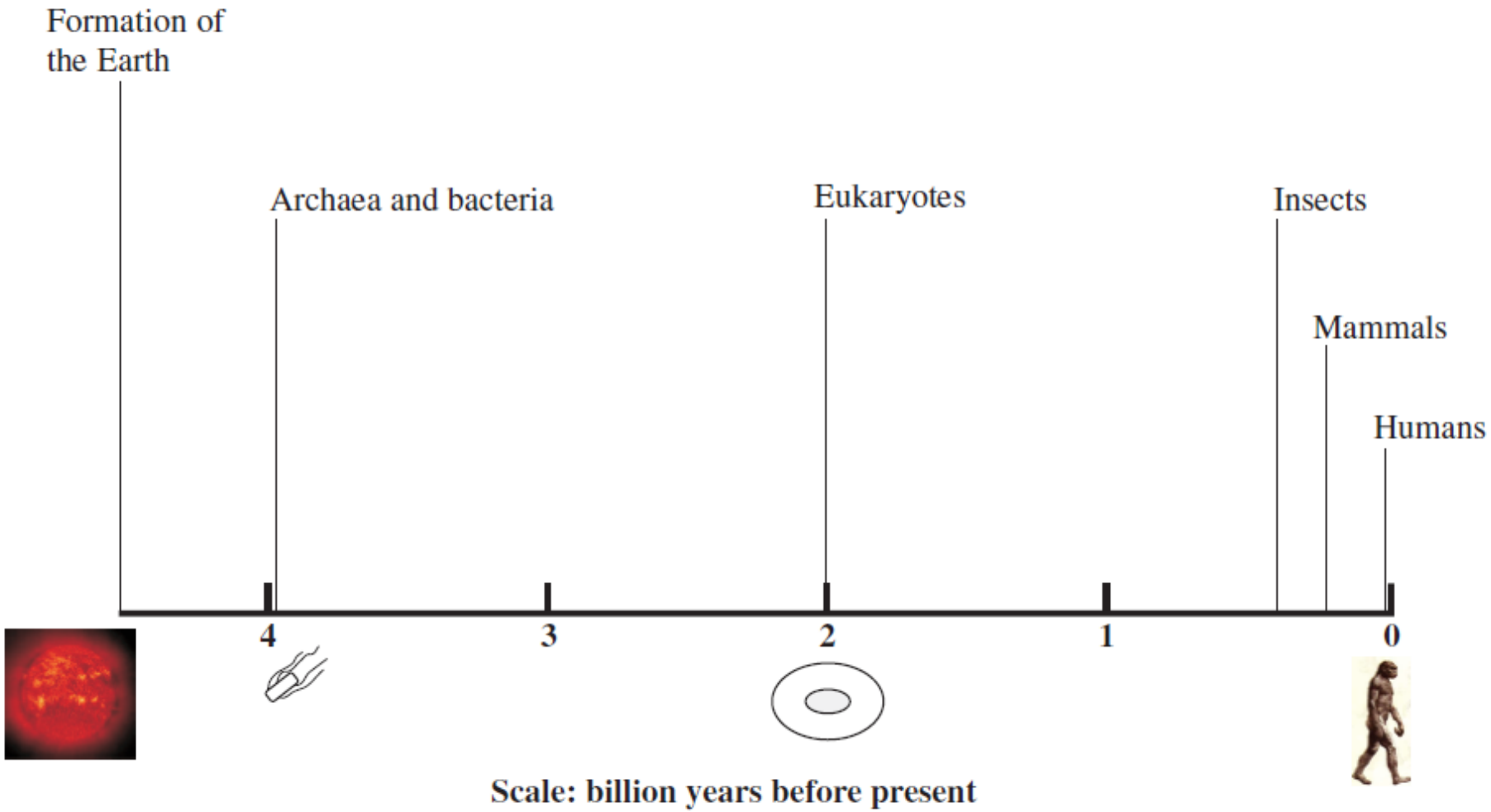
Viruses evolve as a result of:

- errors during nucleic acid replication;
- recombination between virus strains;
- reassortment between virus strains;
- acquisition of cell genes.

Evolution of viruses can be monitored by sequencing their genomes and creating phylogenetic trees:

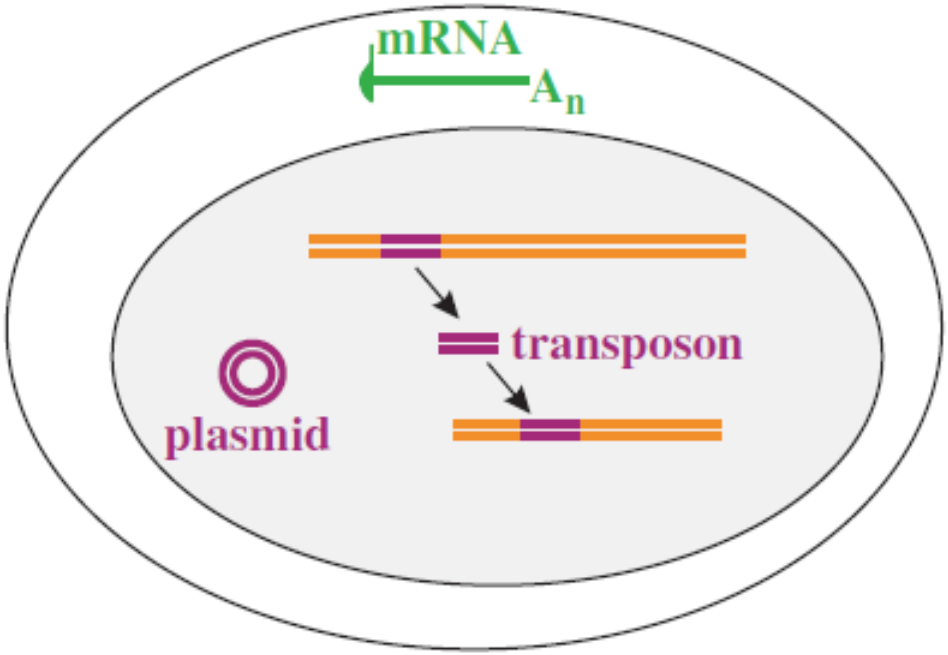


New viruses may evolve as a result of viruses infecting new host species, e.g. HIV-1 and HIV-2.

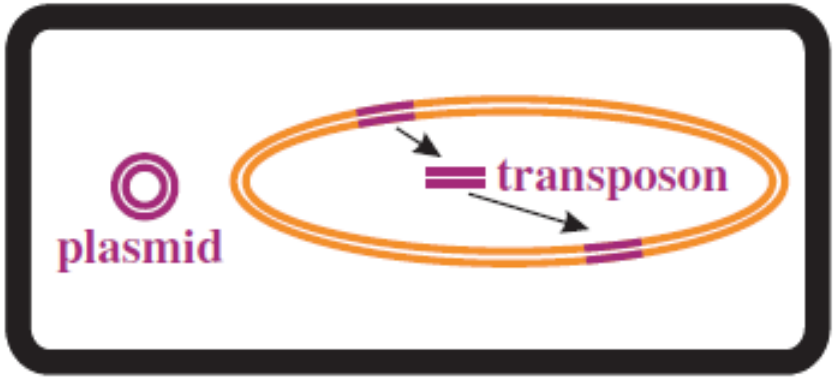


Potential virus precursors

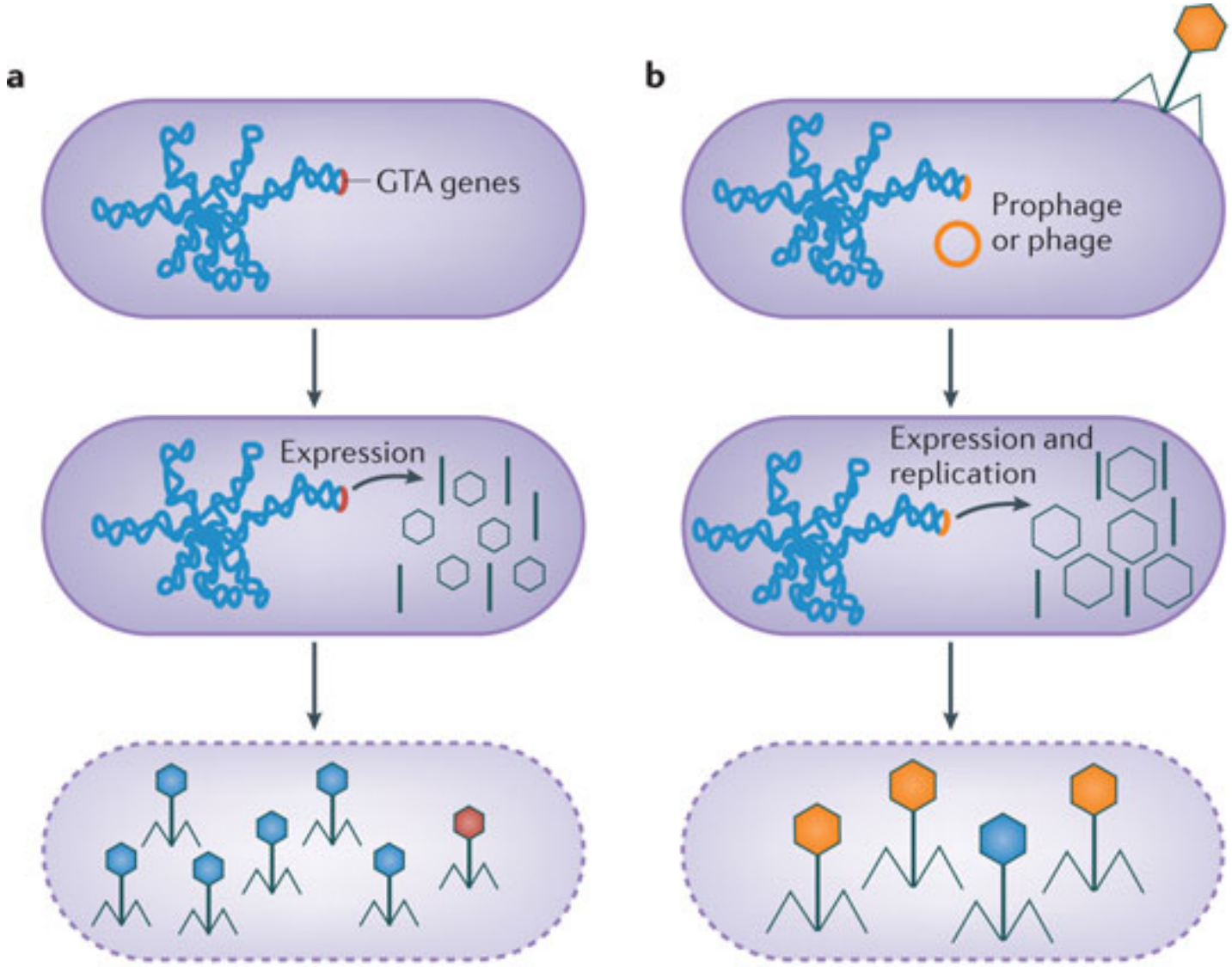
eukaryotic cell



prokaryotic cell



Gene transfer agents



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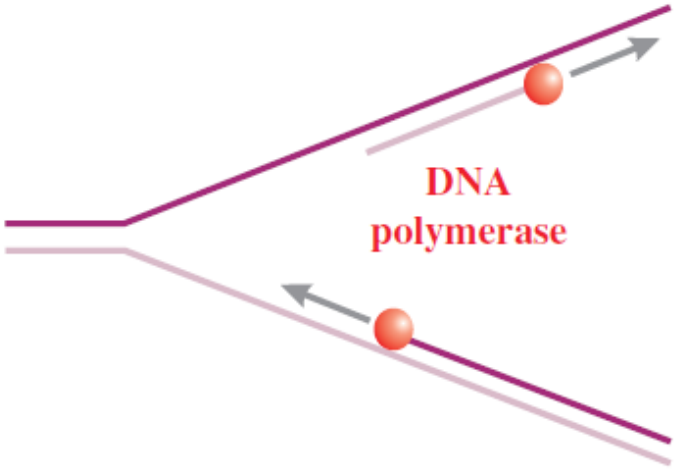
Polymerase error rates

DNA Replication



One error per
10^6 to 10^8 bases added

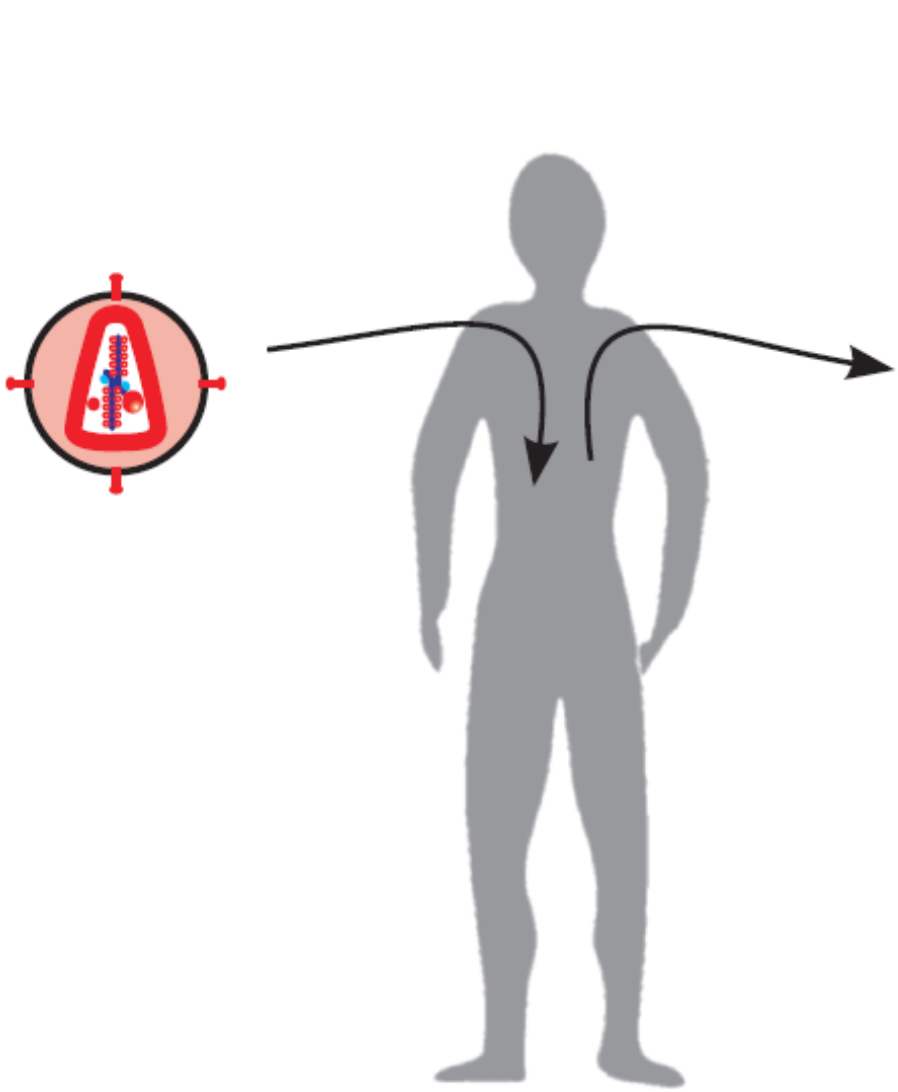
RNA Replication

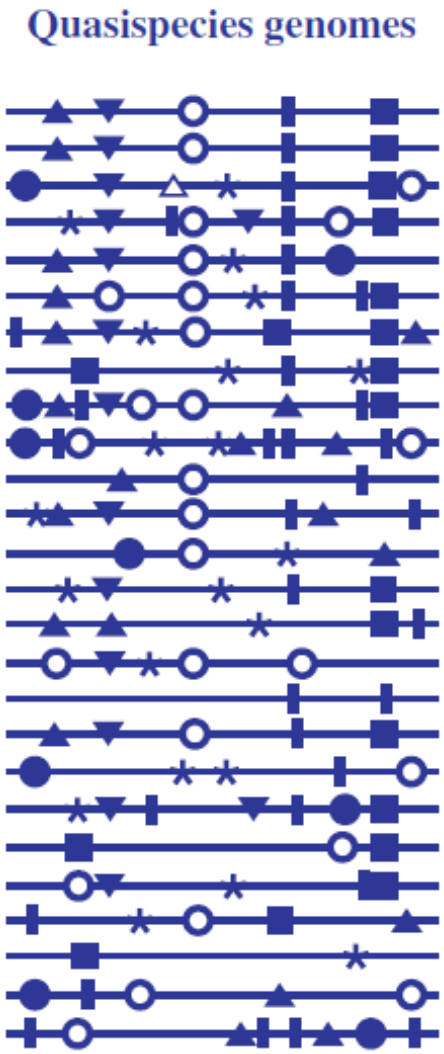
One error per
10^4 to 10^6 bases added

Reverse
Transcription

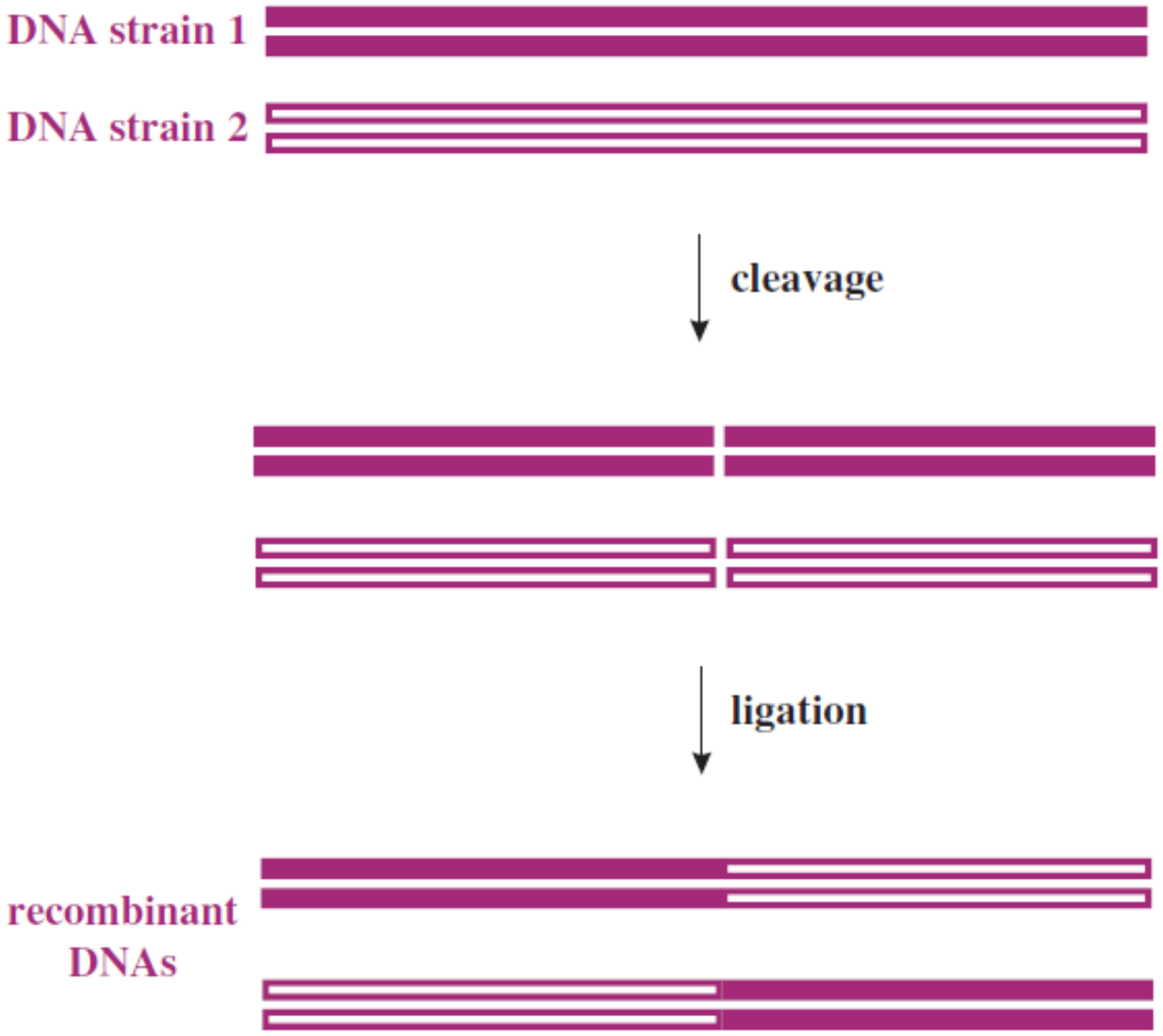
One error per
10^4 to 10^6 bases added

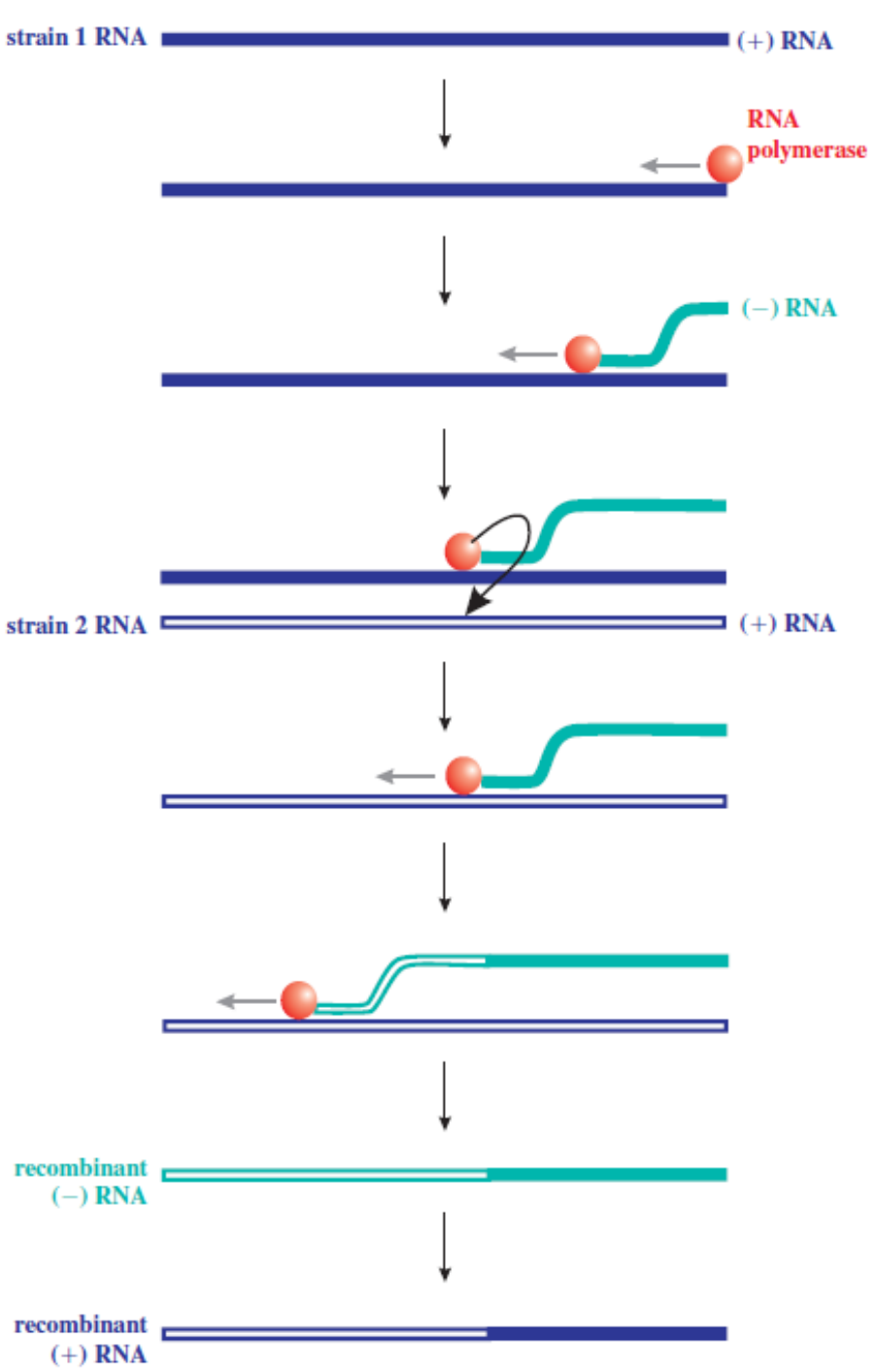
Quasispecies



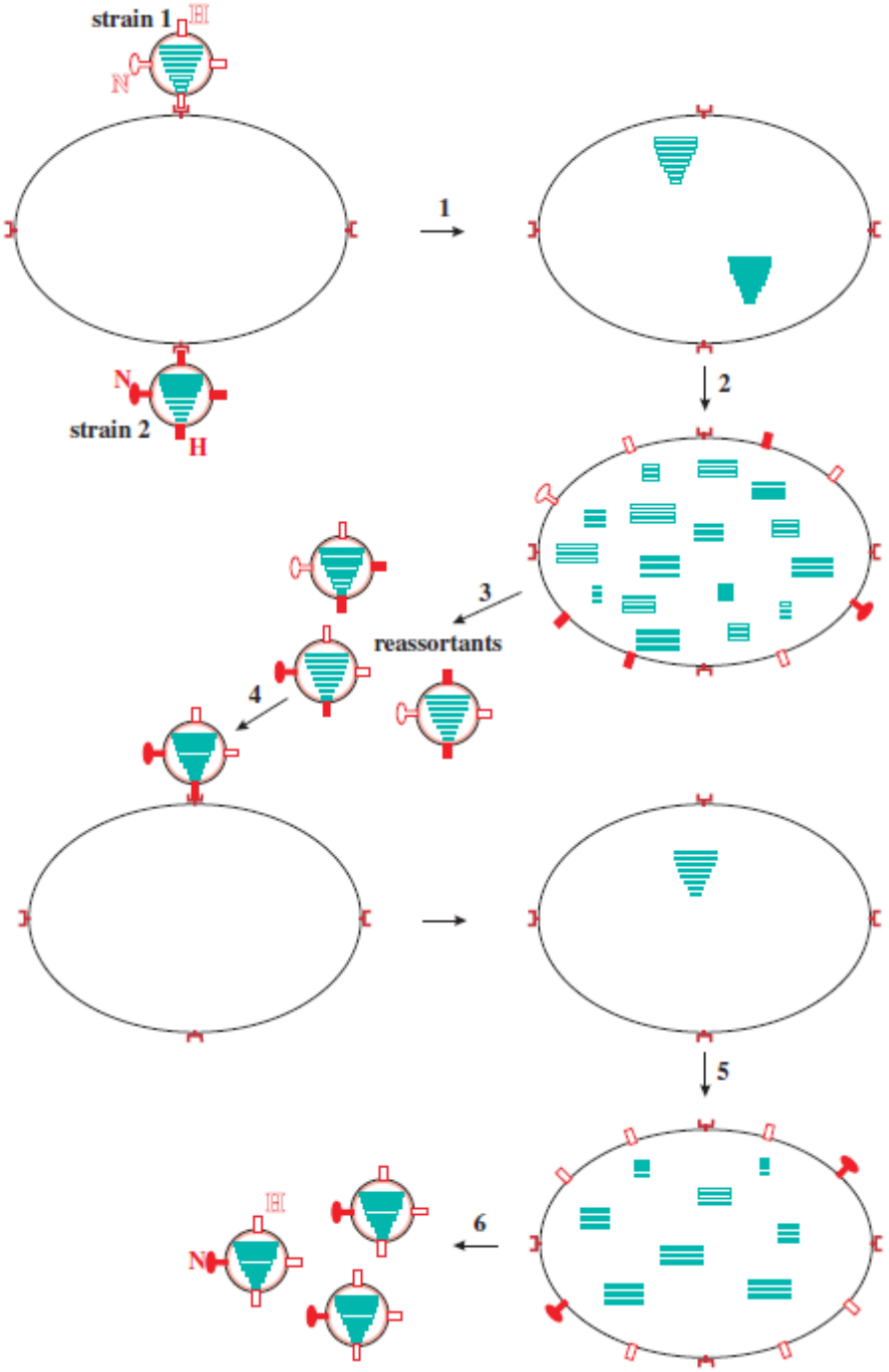


Recombination



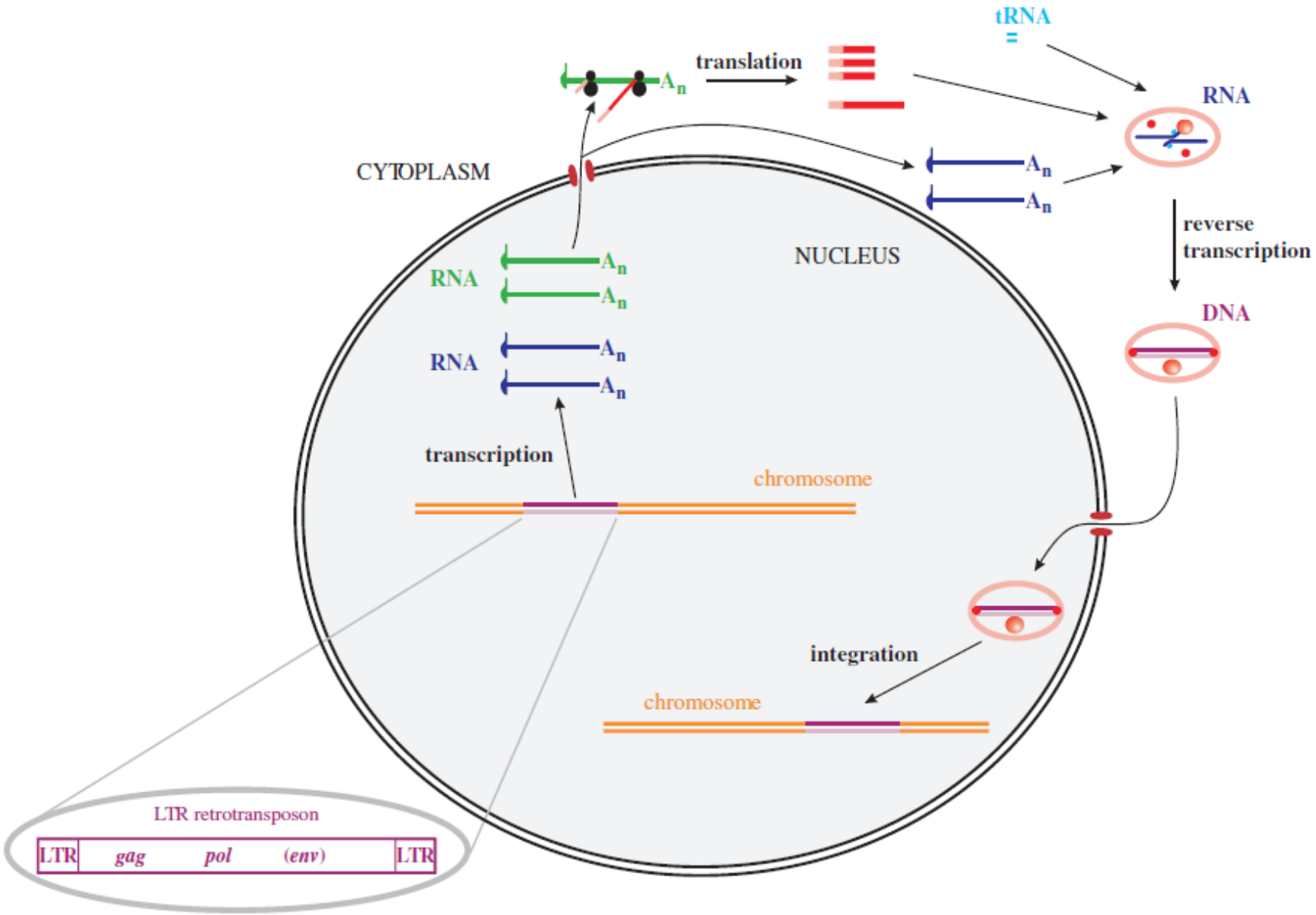


Copy-choice recombination



Genome fragment re-assortment

LTR retrotransposons



- Progressive hypothesis
- Regressive hypothesis
- Virus-first hypothesis
- Nucleocytoplasmic large DNA viruses as precursors of nuclei in eukaryotes

Learning outcomes

- evaluate theories on the origins of viruses
- explain how virus evolution occurs through mutation, recombination and re-assortment
- assess the value of virus genome sequencing in studies of virus origins and evolution
- assess the threats posed to man and animals by rapid virus evolution
- discuss the co-evolution of viruses and their hosts