

Structural Virology

Lecture 6

Pavel Plevka

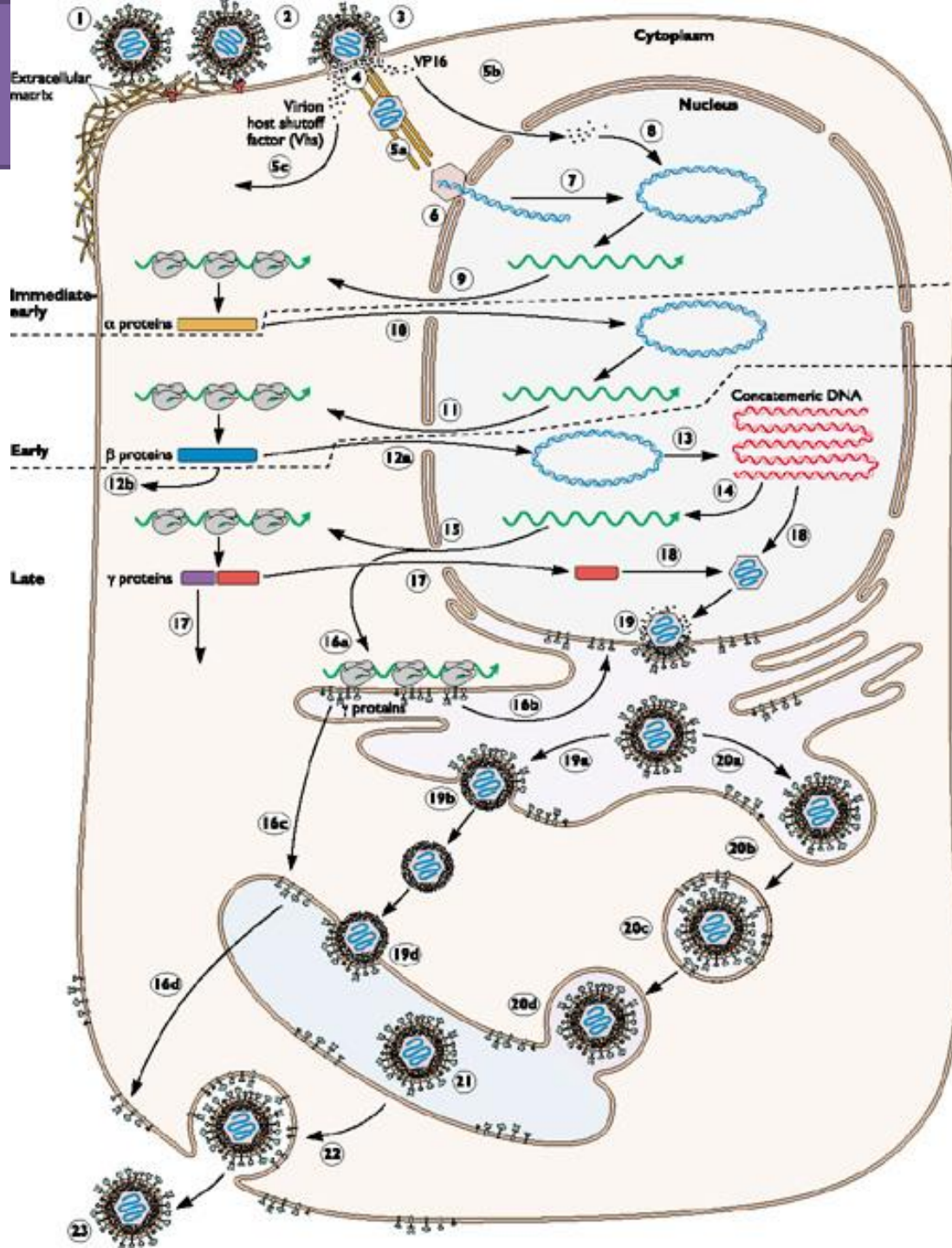


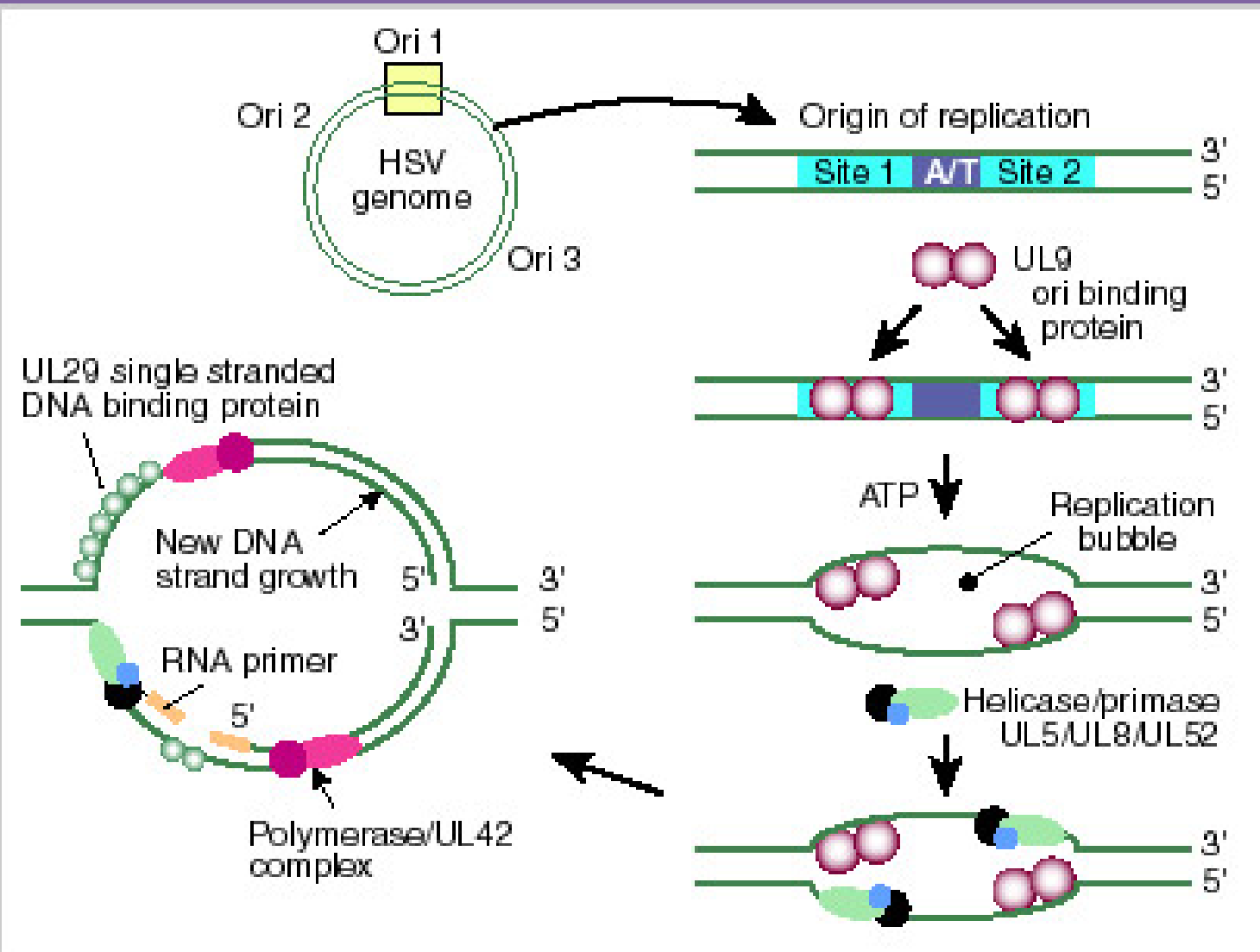
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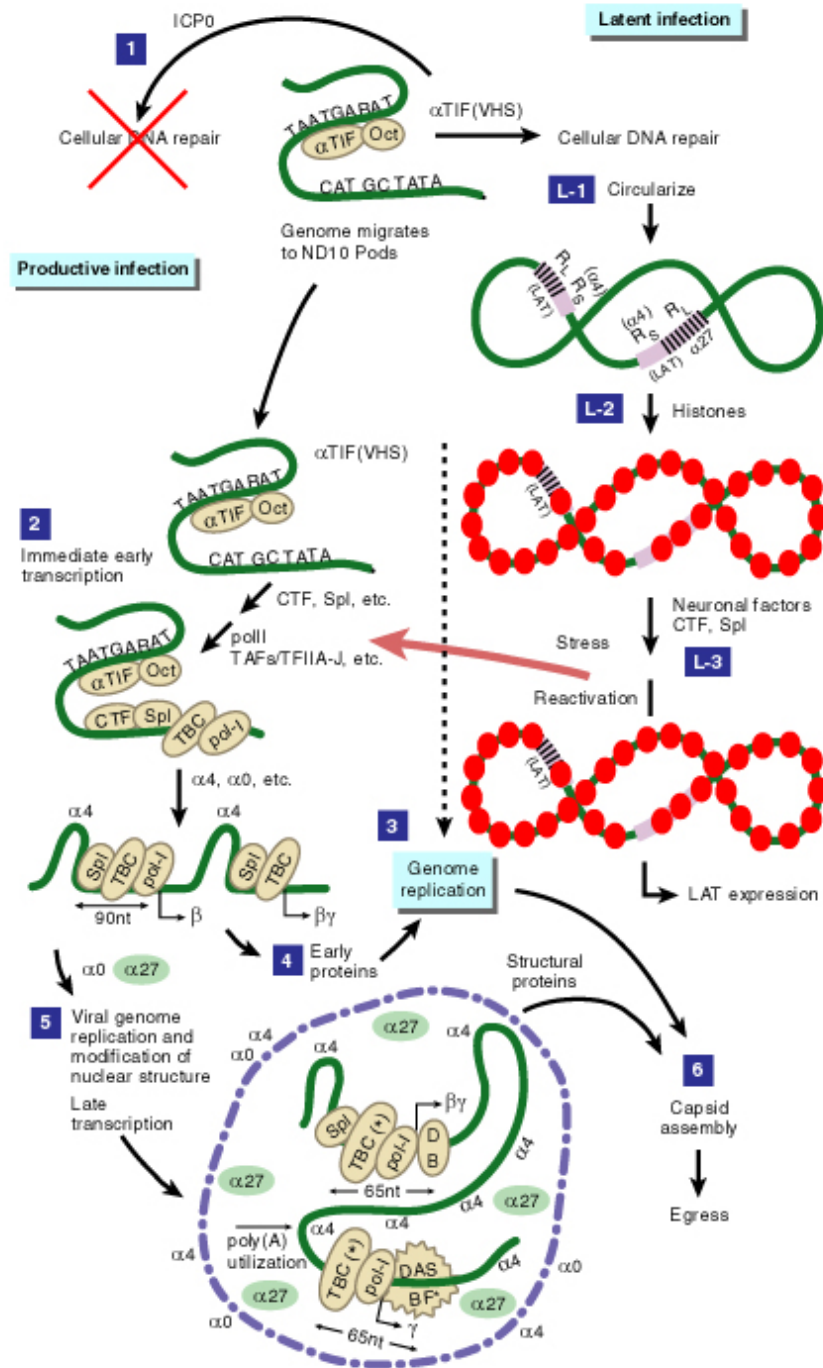


NÁRODNÍ
PLÁN OBNOVY

MŠMT
MINISTERSTVO ŠKOLSTVÍ,
MLÁDEŽE A TĚLOVÝCHOVY







Parvoviruses

Hosts: mammals

birds

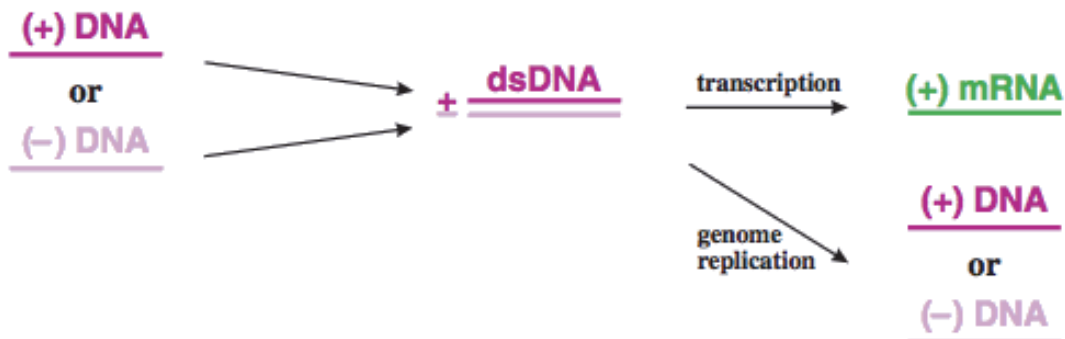
insects

Disease: erythema infectiosum (B19 virus)

Used as: gene vectors (dependoviruses)

Virion

- Icosahedral
- 18–26 nm diameter
- Genome: single-stranded DNA
4–6 kb
linear



Parvoviruses

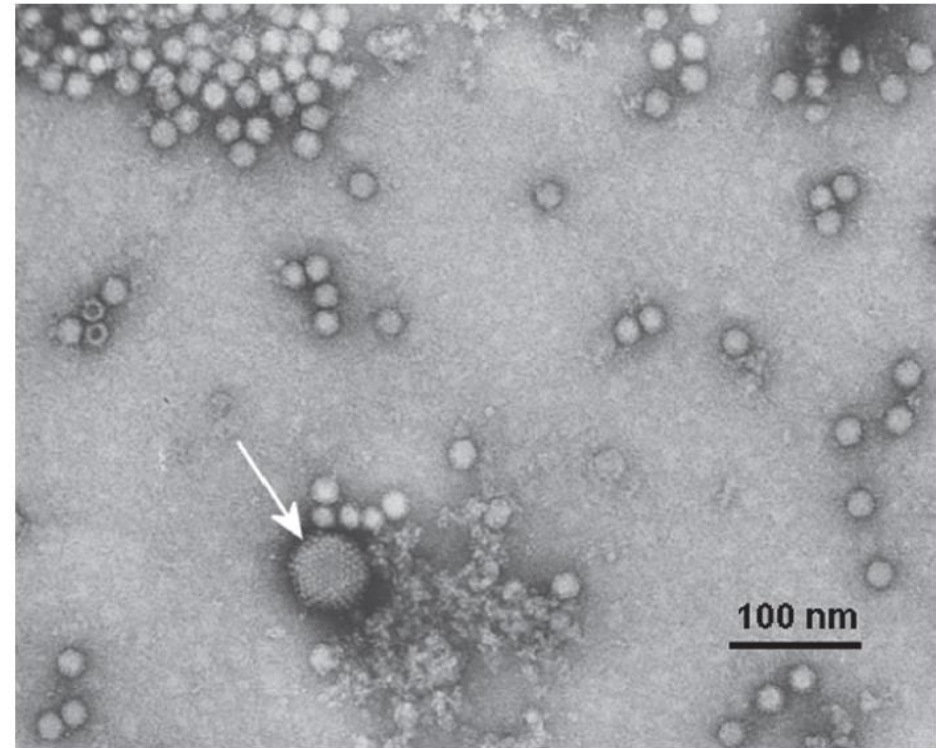
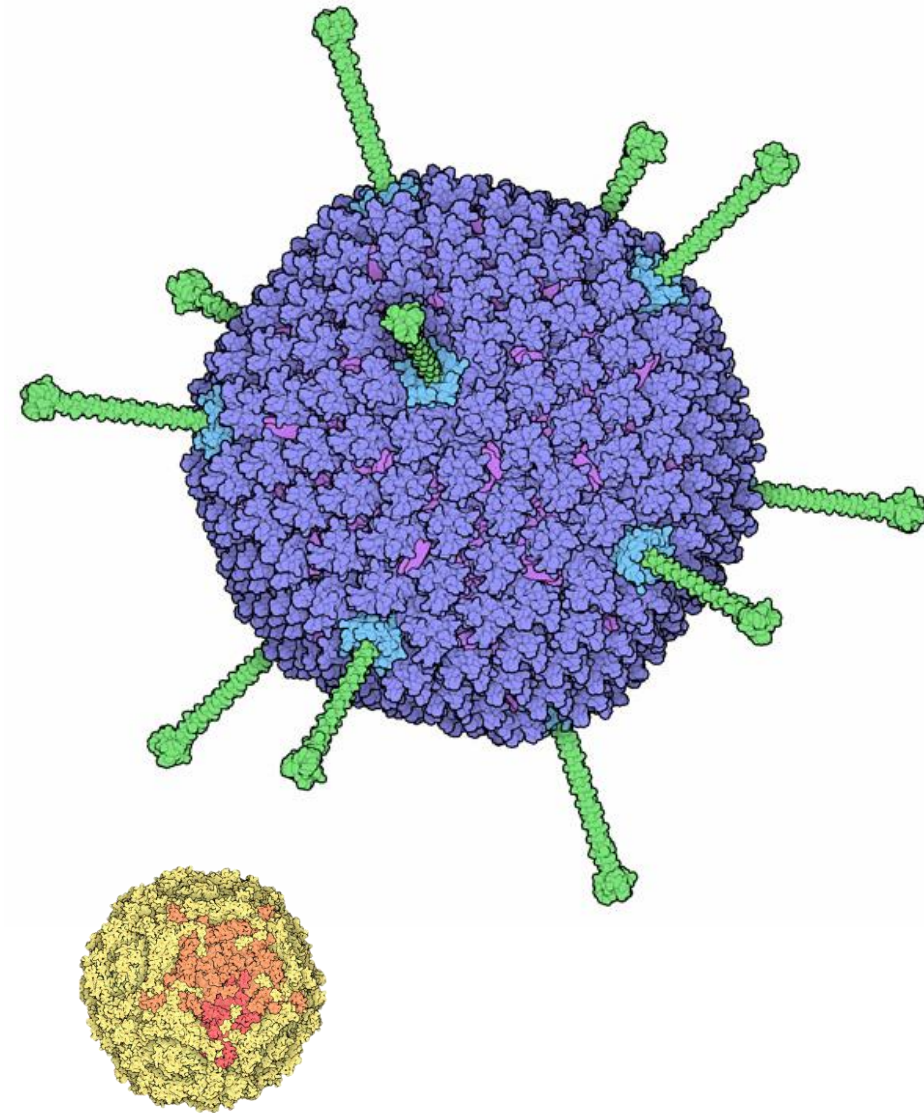
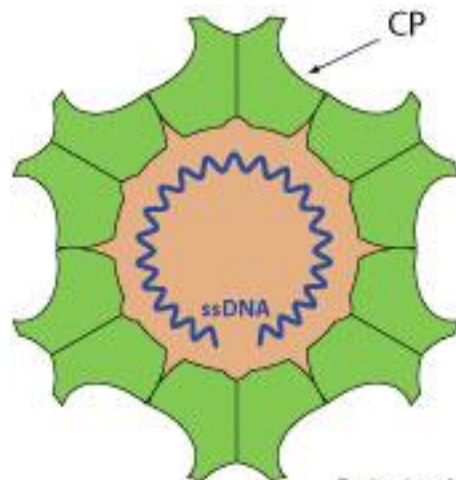
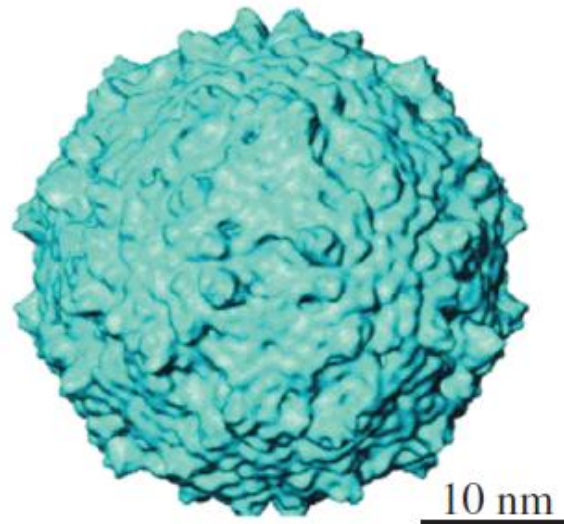
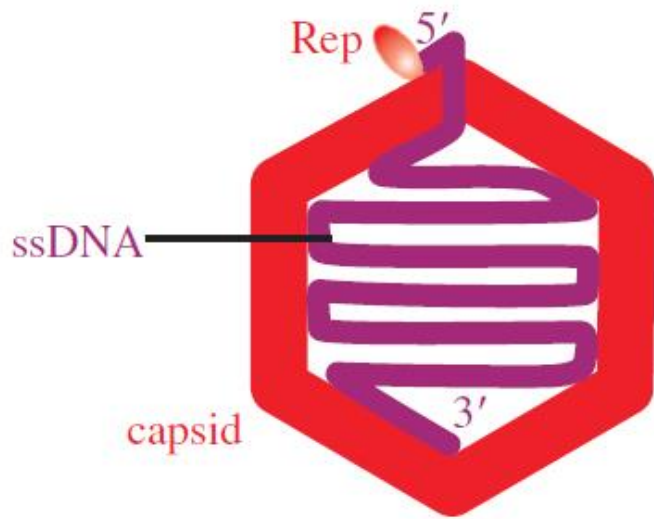


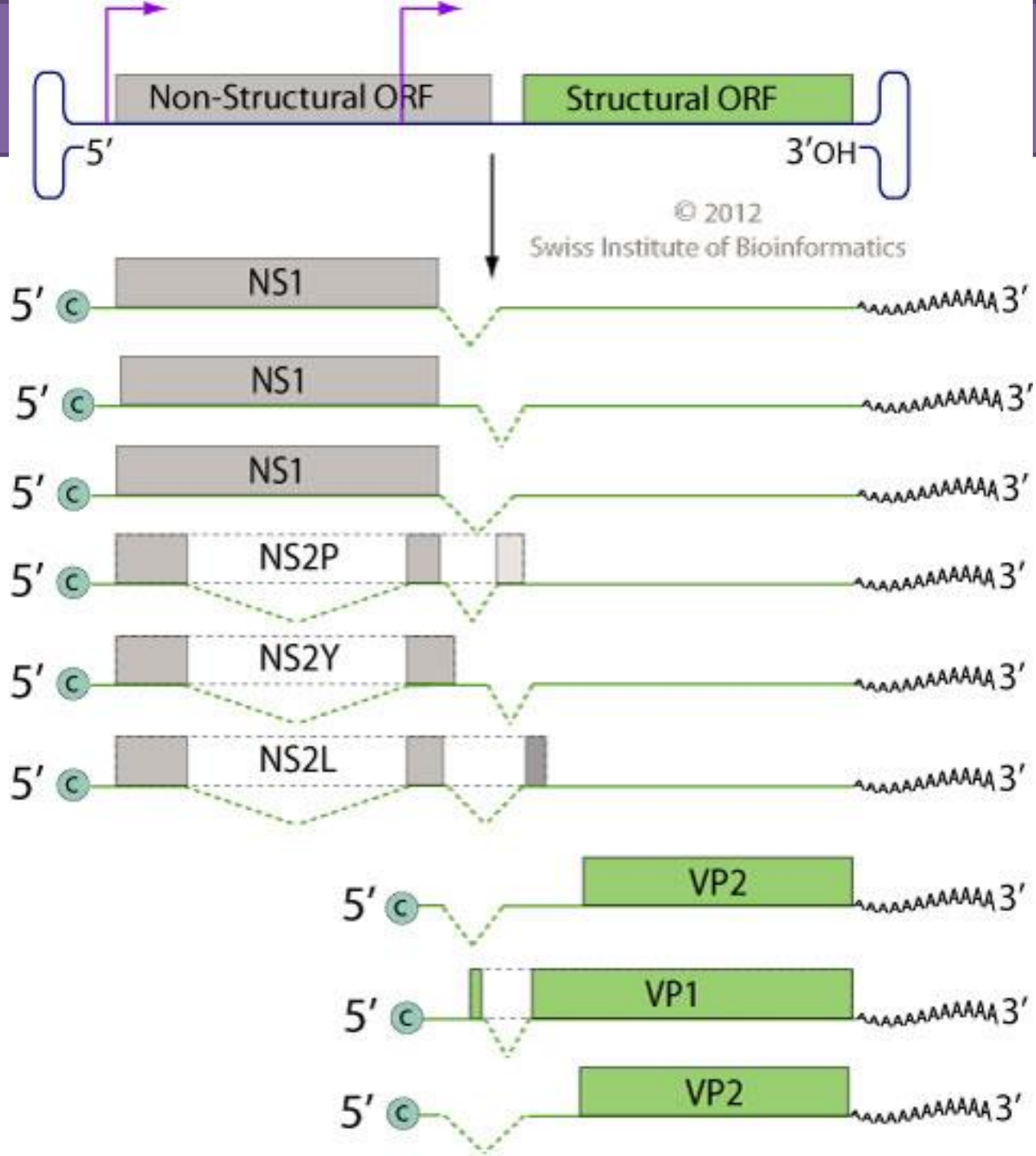
Figure 12.1 Virions of adenovirus (arrowed) and dependovirus.

Source: Reproduced with permission of Professor M. Stewart McNulty and The Agri-Food and Biosciences Institute.

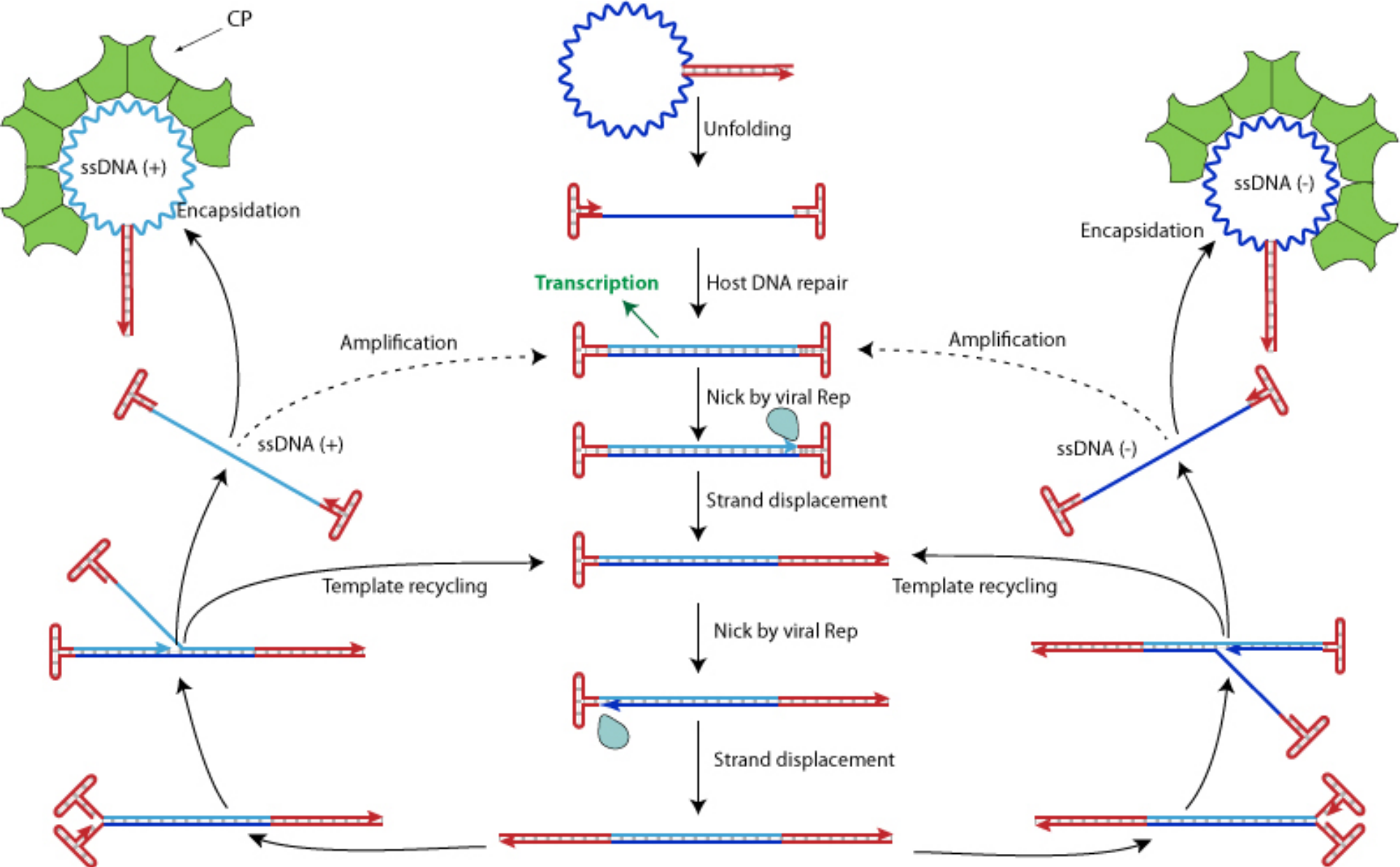


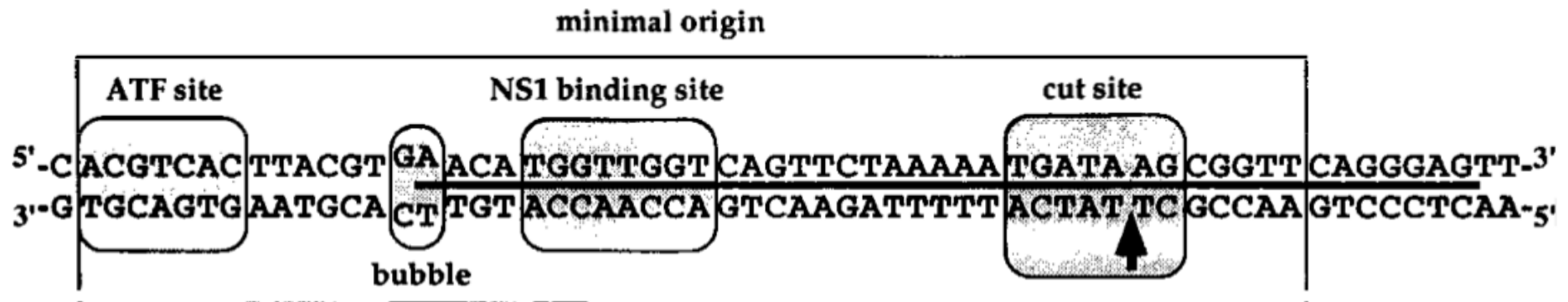
Figure 12.2 Child with fifth disease.



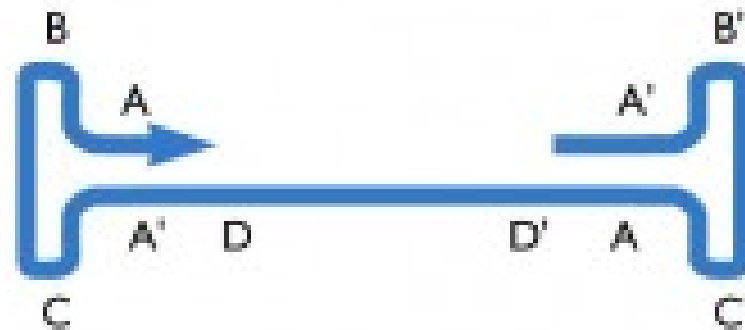


Rolling hairpin Replication (AAV)





Parvoviridae (4–6 kb)



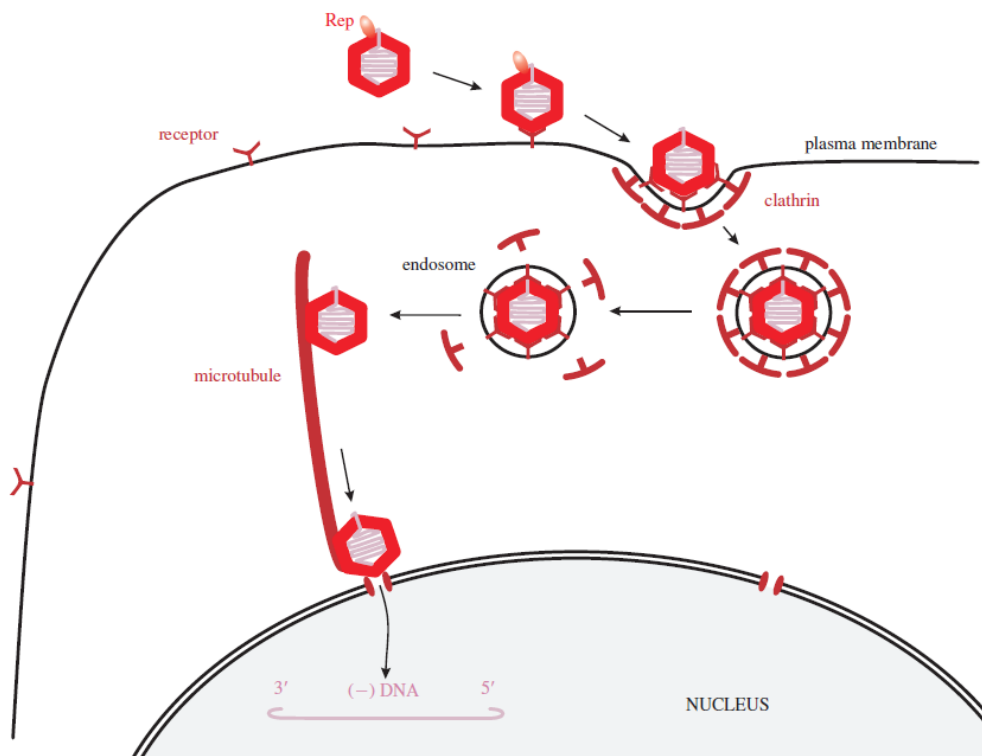


Figure 12.6 Parvovirus attachment and entry. A virion is taken into the cell by clathrin-mediated endocytosis. After release from the endosome it is transported on a microtubule to a site close to the nucleus. It is uncertain whether uncoating of the virus genome occurs at a nuclear pore (as shown here) or within the nucleus.

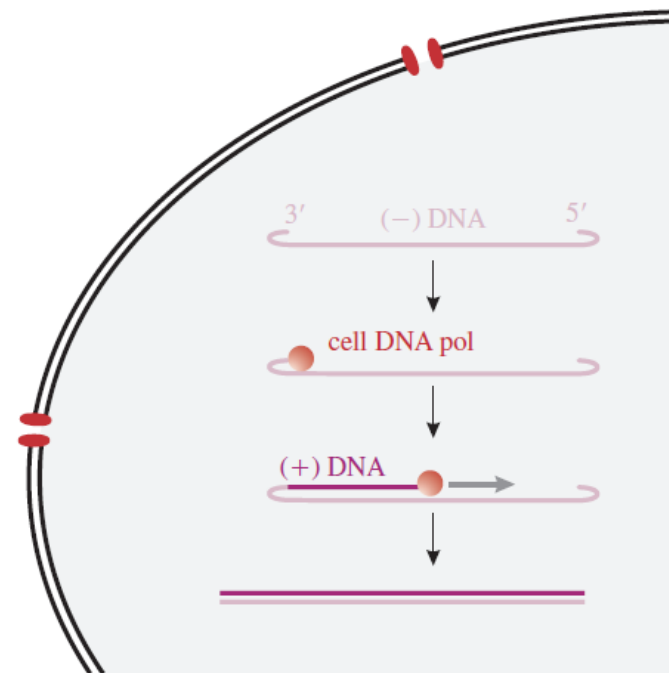
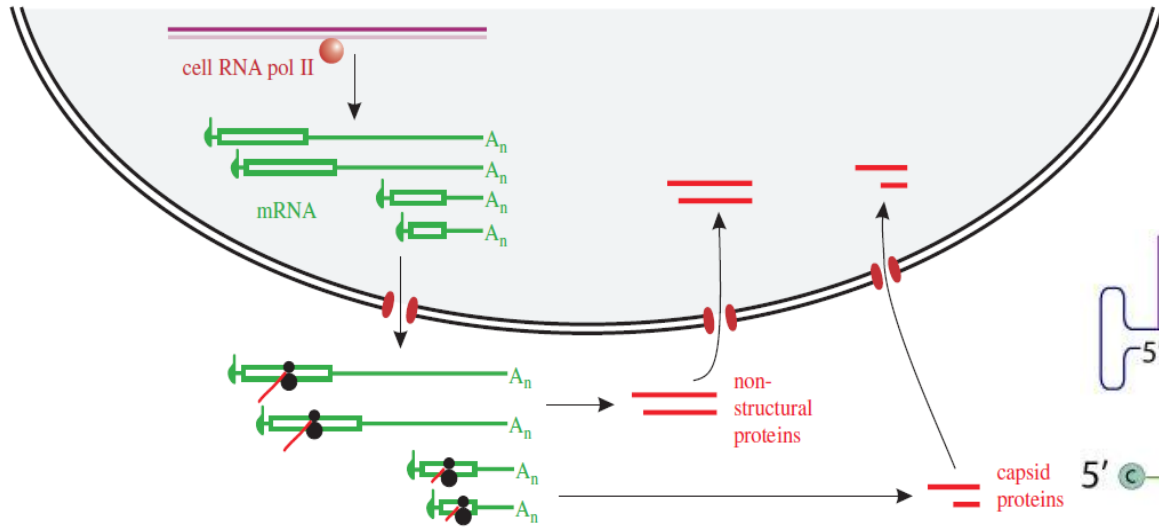
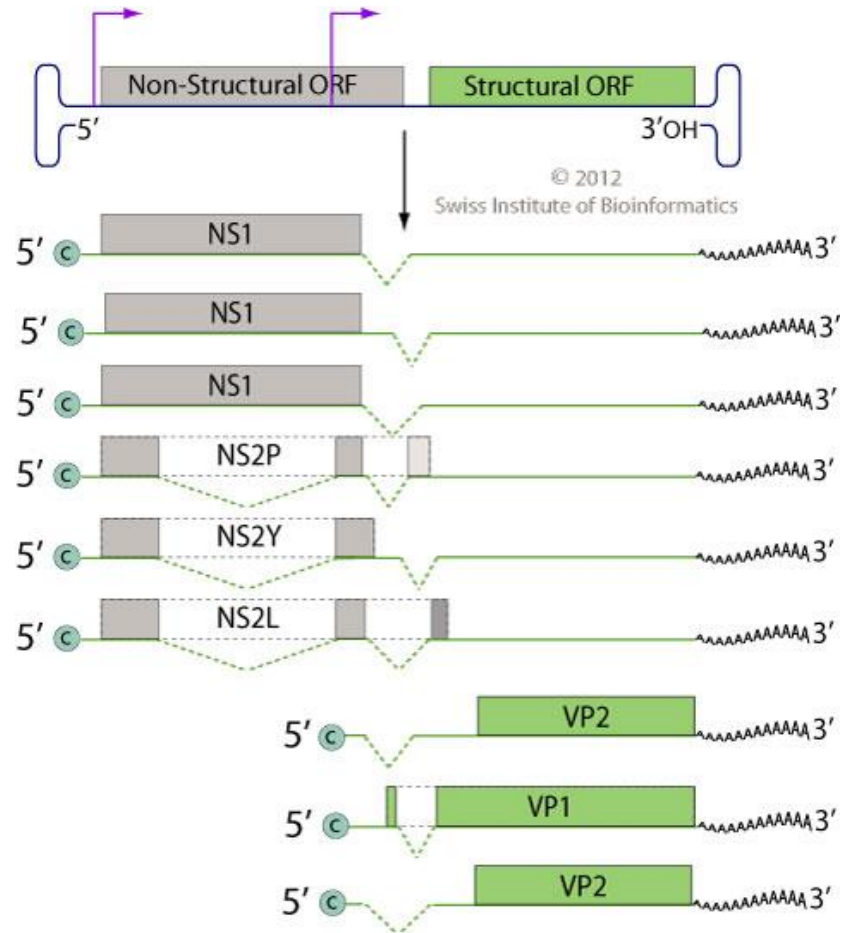


Figure 12.7 Conversion of ssDNA to dsDNA by a cell DNA polymerase. Not all steps are shown.



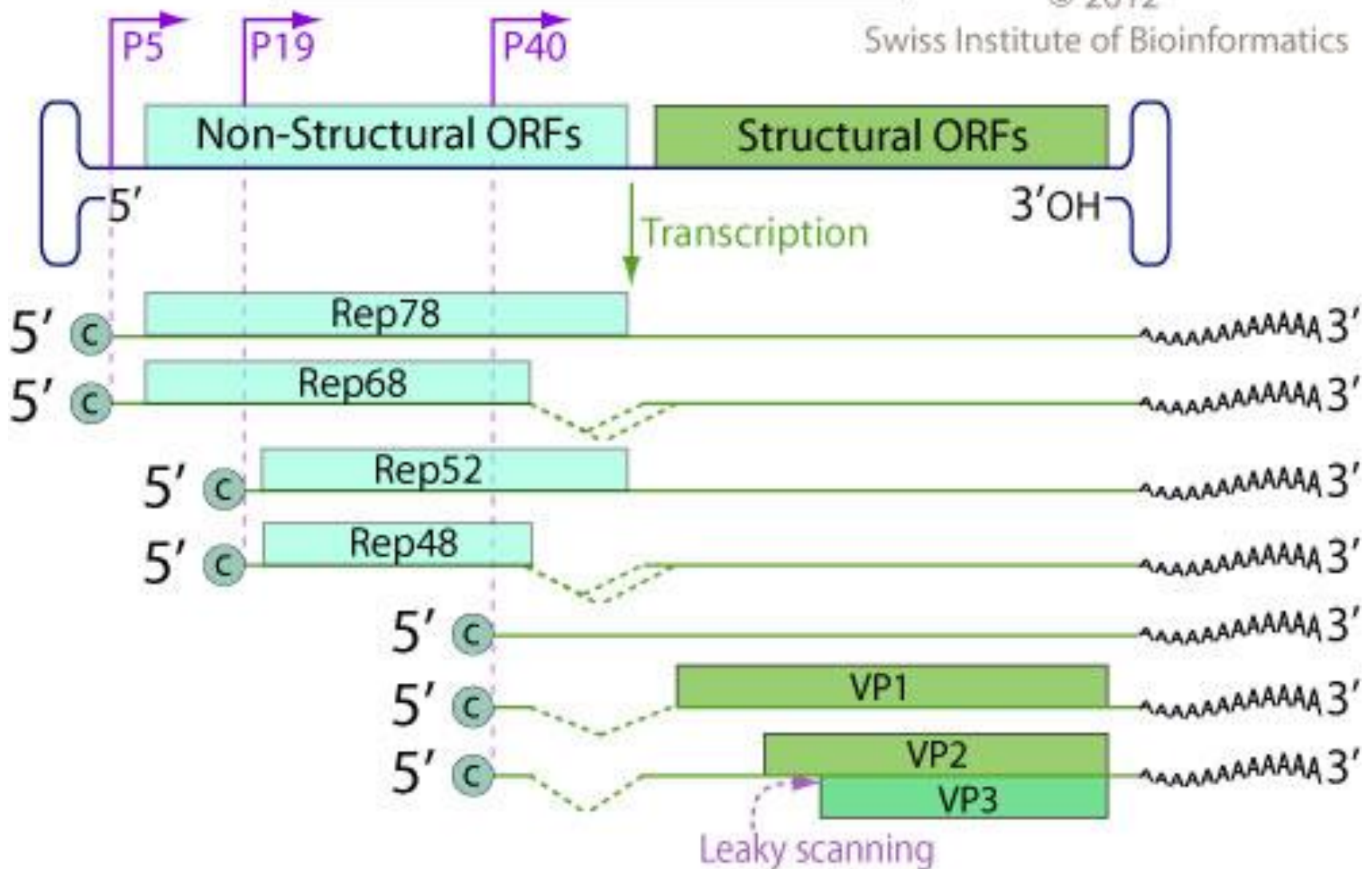
Minute virus of mice genome organization



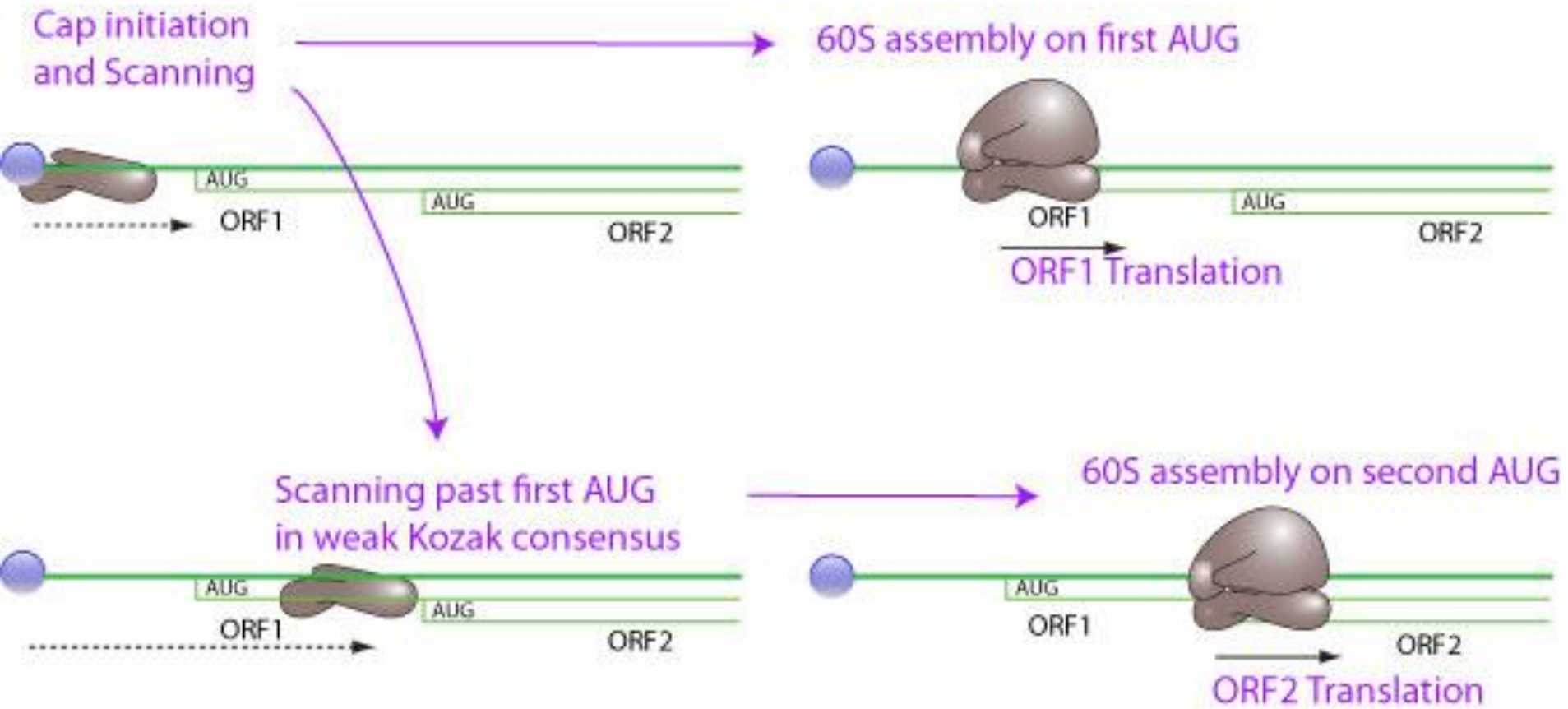
Adeno-associated virus-2

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Kozak's sequence: gccRccAUGG



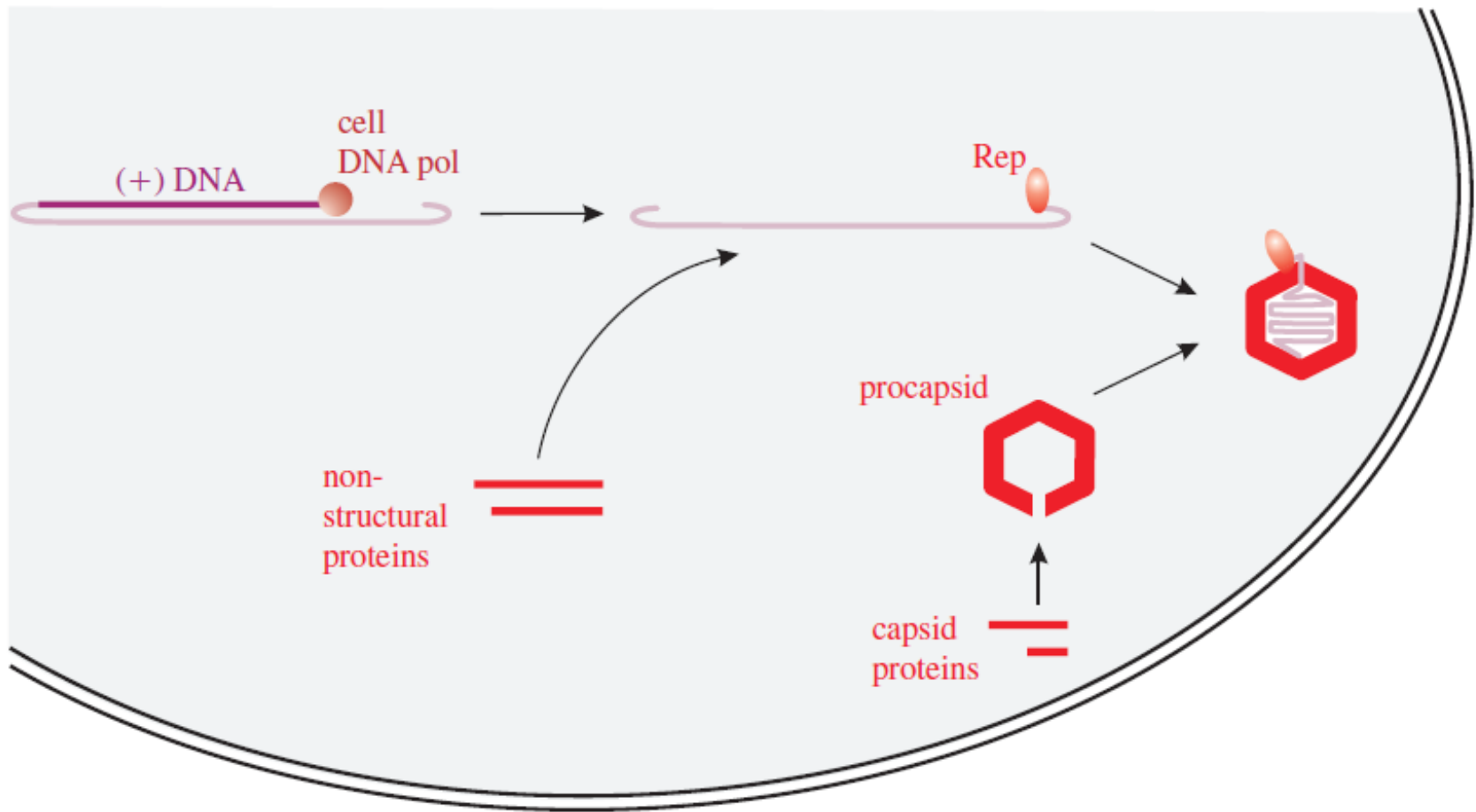
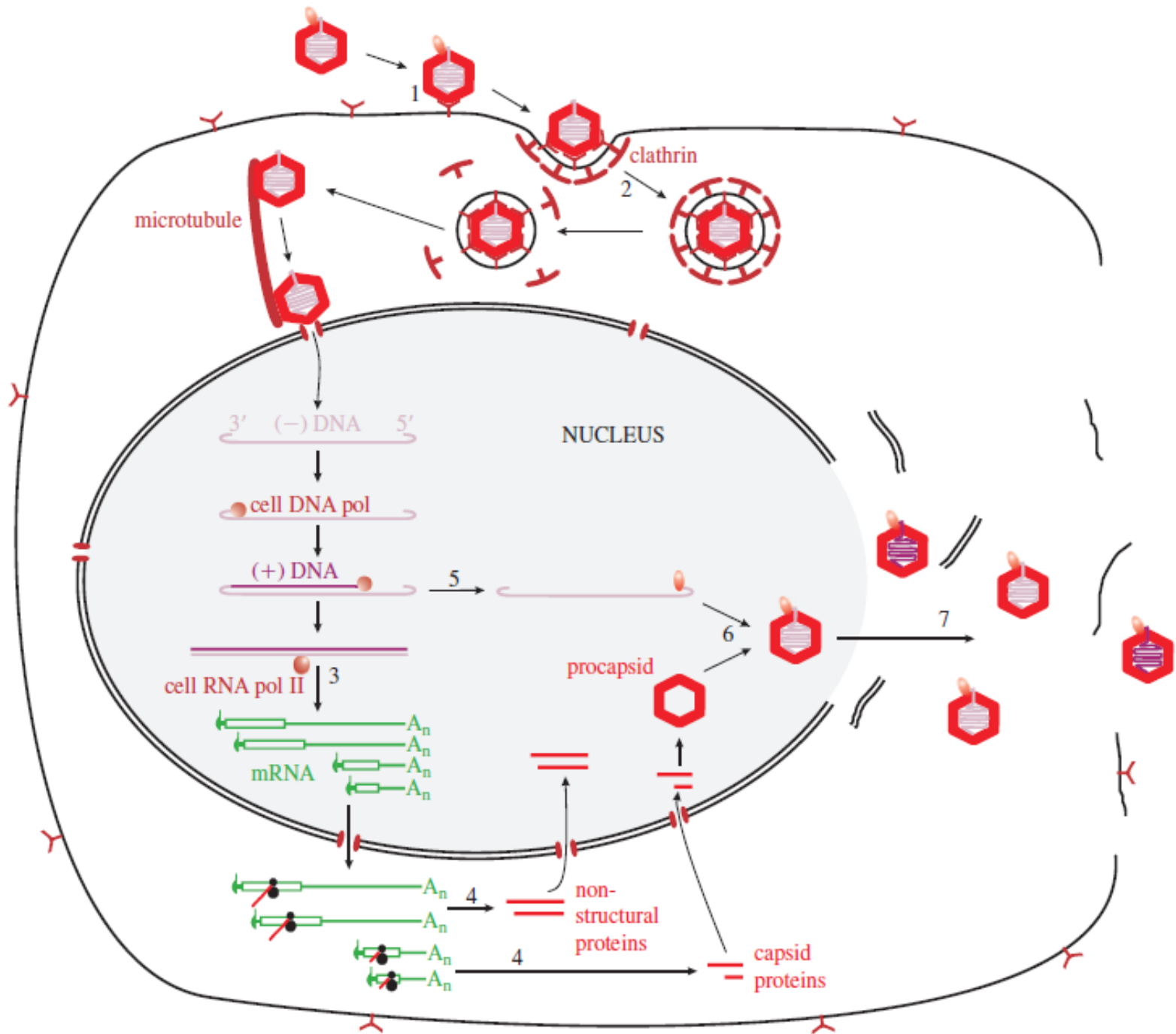
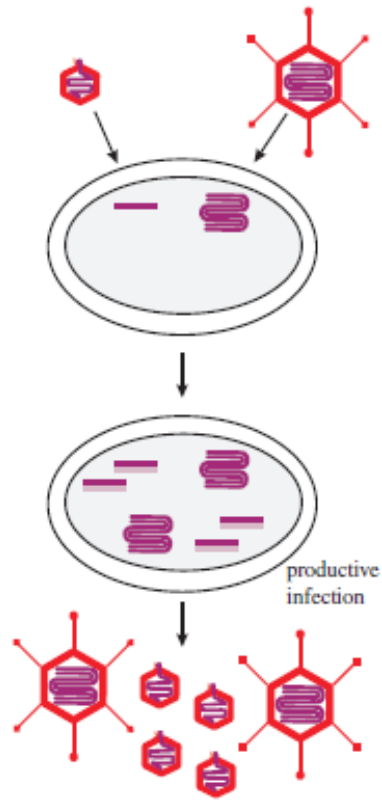


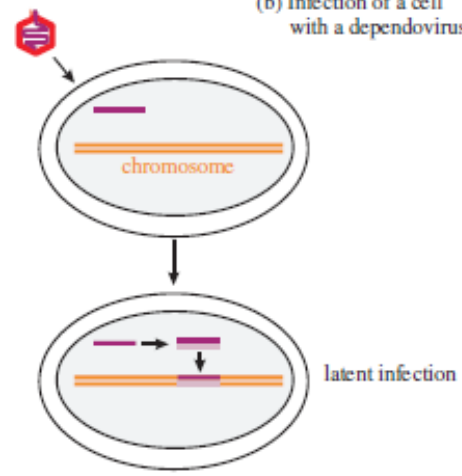
Figure 12.9 Parvovirus virion assembly.



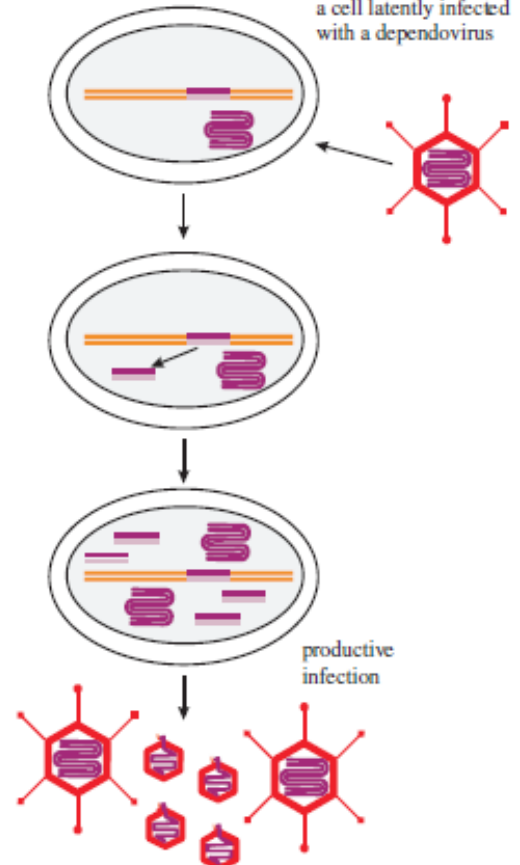
(a) Co-infection of a cell with a dependovirus and an adenovirus



(b) Infection of a cell with a dependovirus



(c) Adenovirus infection of a cell latently infected with a dependovirus



Learning outcomes

- give examples of parvoviruses and explain their importance;
- describe the parvovirus virion;
- outline the main features of the parvovirus genome;
- describe the replication cycle of parvoviruses;
- explain the difference between autonomous and defective parvoviruses.

Reoviridae

Hosts: mammals
birds
fish
insects
plants
fungi

Respiratory
Enteric
Orphan

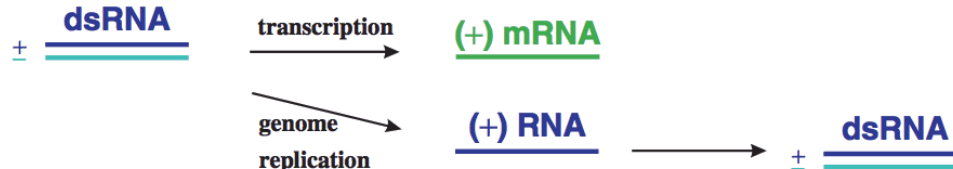
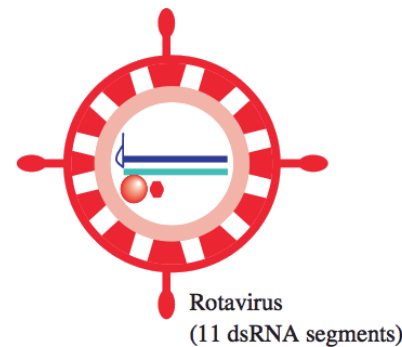
Disease: gastroenteritis in humans and animals (rotaviruses)

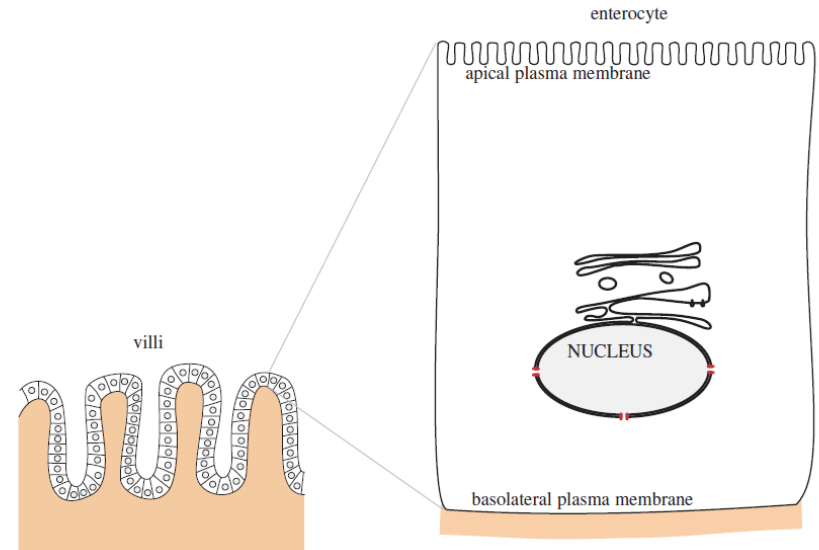


'Diarrhoea On Wheels'

Virion

- Icosahedral
- 60–80 nm diameter
- Genome: double-stranded RNA
10–12 segments
18–32 kbp



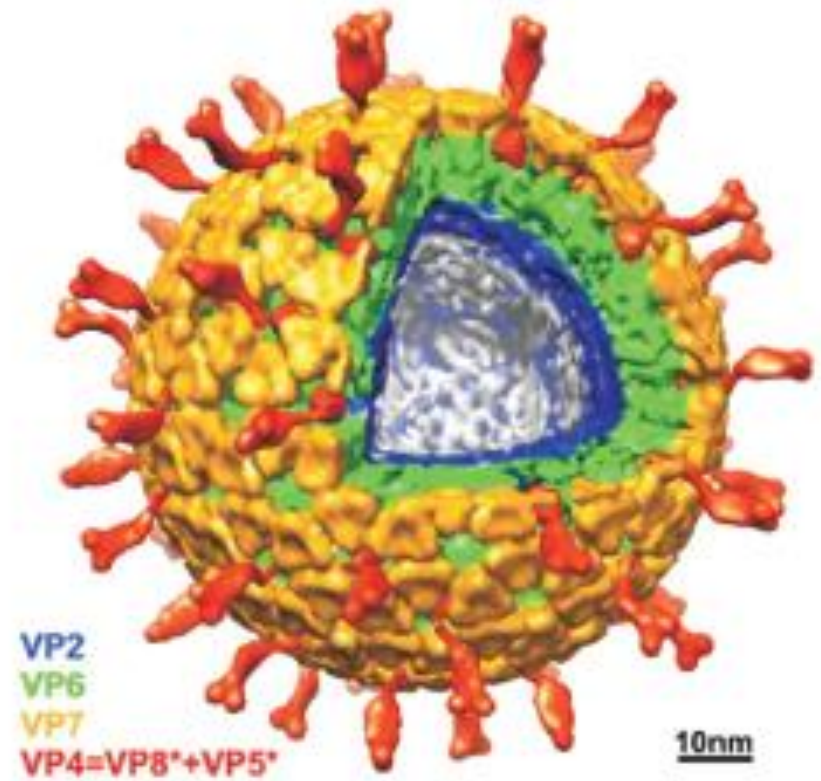
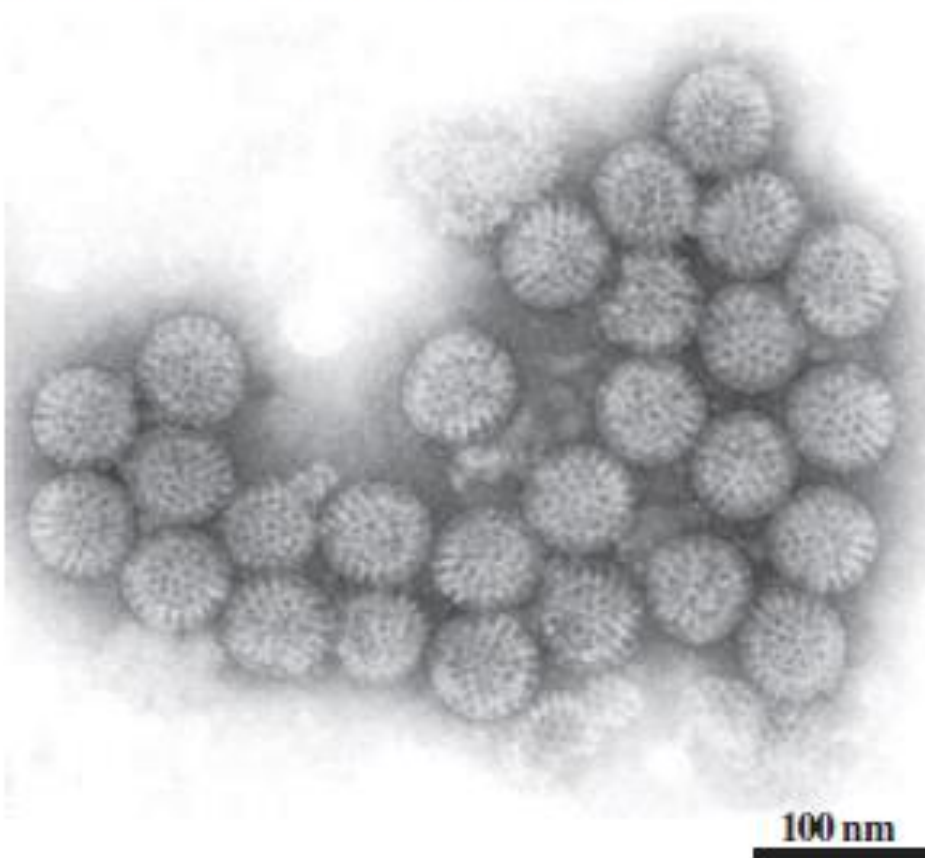


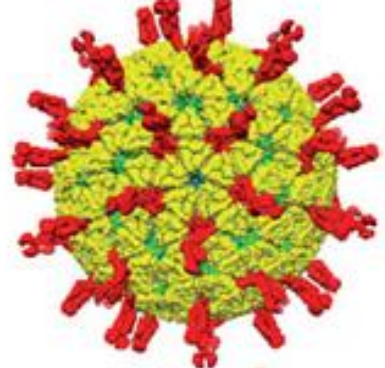
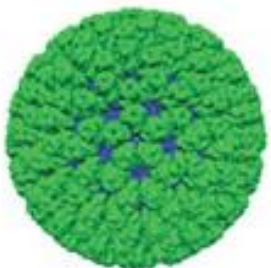
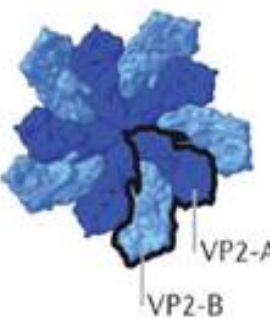
NSP4 induces:

- calcium ion-dependent chloride secretion, disrupts SGLT1 transporter-mediated reabsorption of water
- reduces activity of brush-border membrane and possibly limits activity of enteric nervous system

Reoviridae

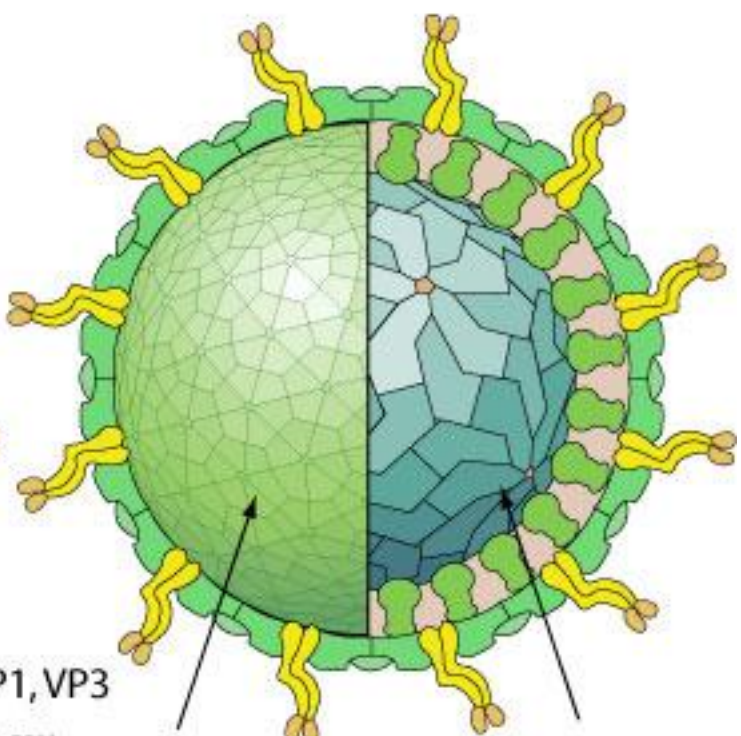
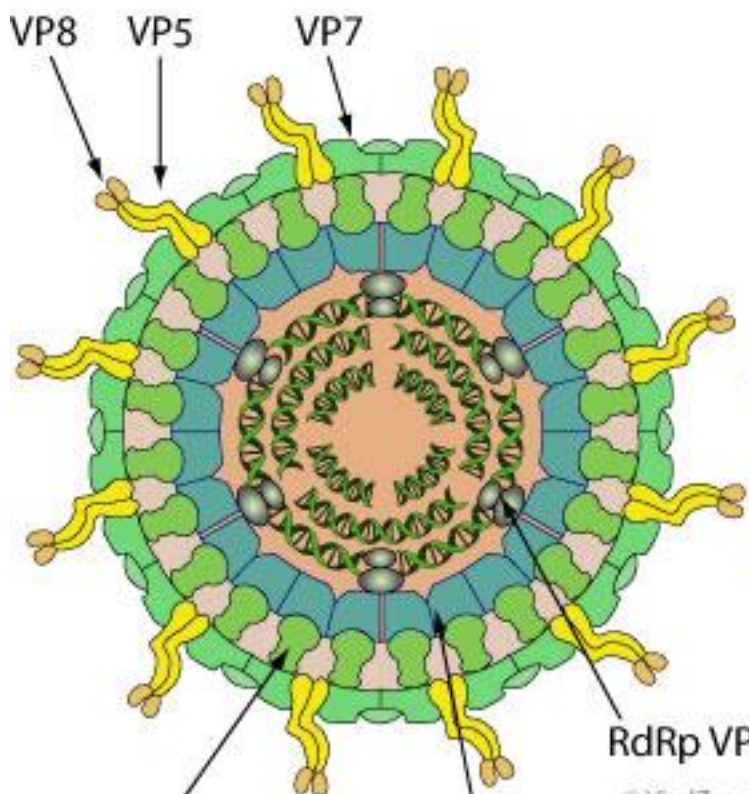
Electron micrograph of negatively stained virions





- VP2 Core shell
- VP5* Membrane penetration and receptor binding
- VP6 Middle layer
- VP7 Sensor

OUTER CAPSID



VP6
INTERMEDIATE CAPSID

VP2
INNER CAPSID

RdRp VP1, VP3

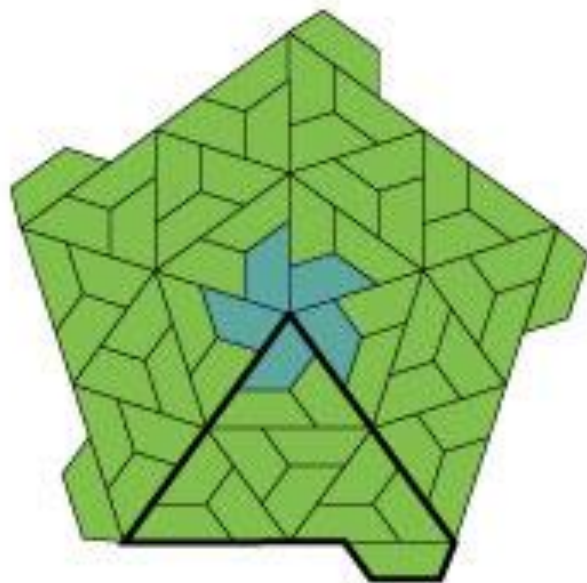
T=13
INTERMEDIATE CAPSID

T=2
INNER CAPSID

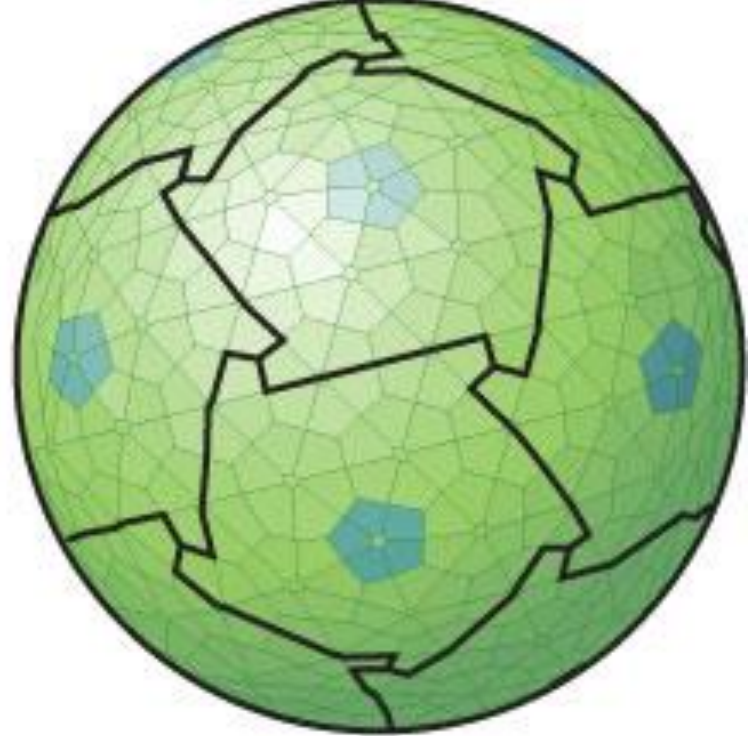
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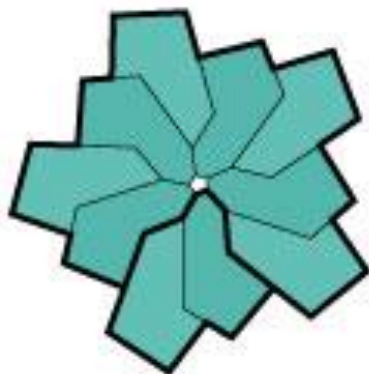
x60



x12



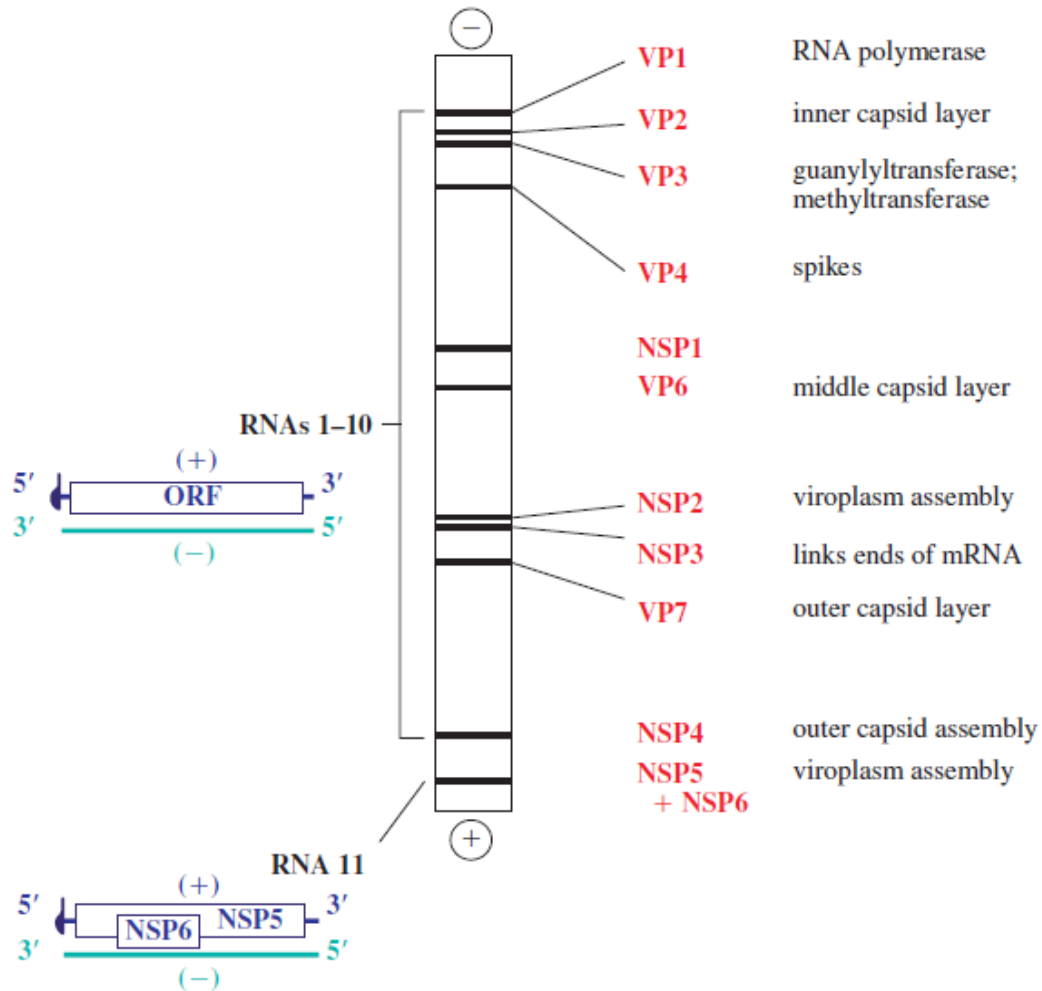
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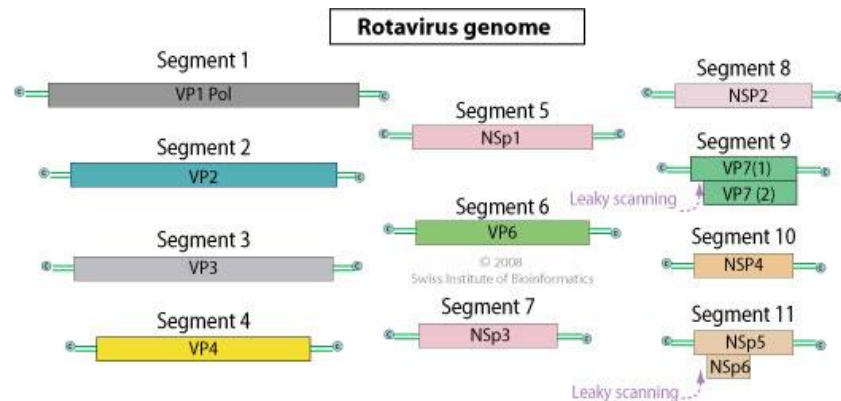
RNA bands
in gel after
separation by
electrophoresis

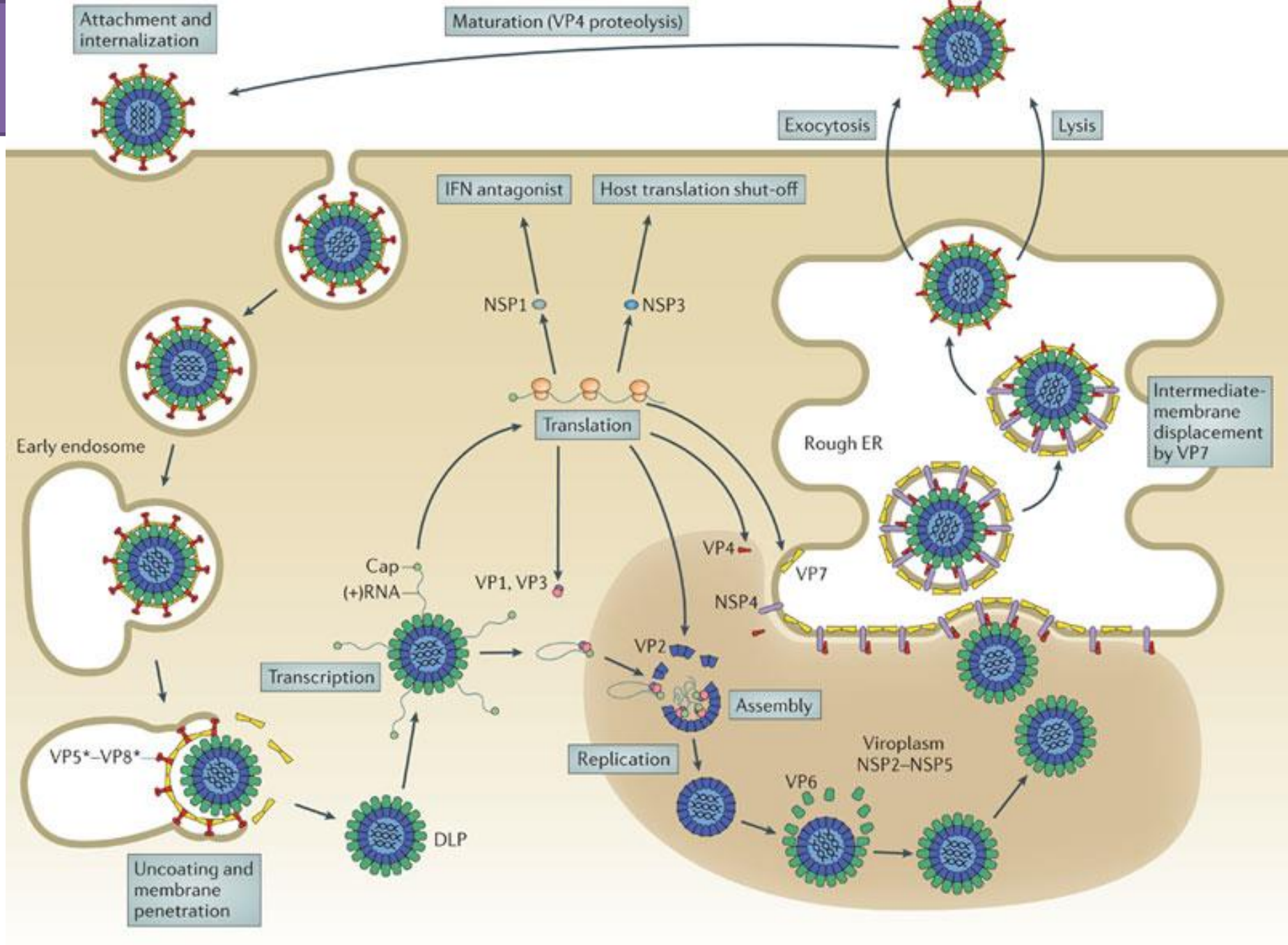
Gene
product(s)

Function



Key: ORF open reading frame
VP virus protein (structural protein)
NSP non-structural protein





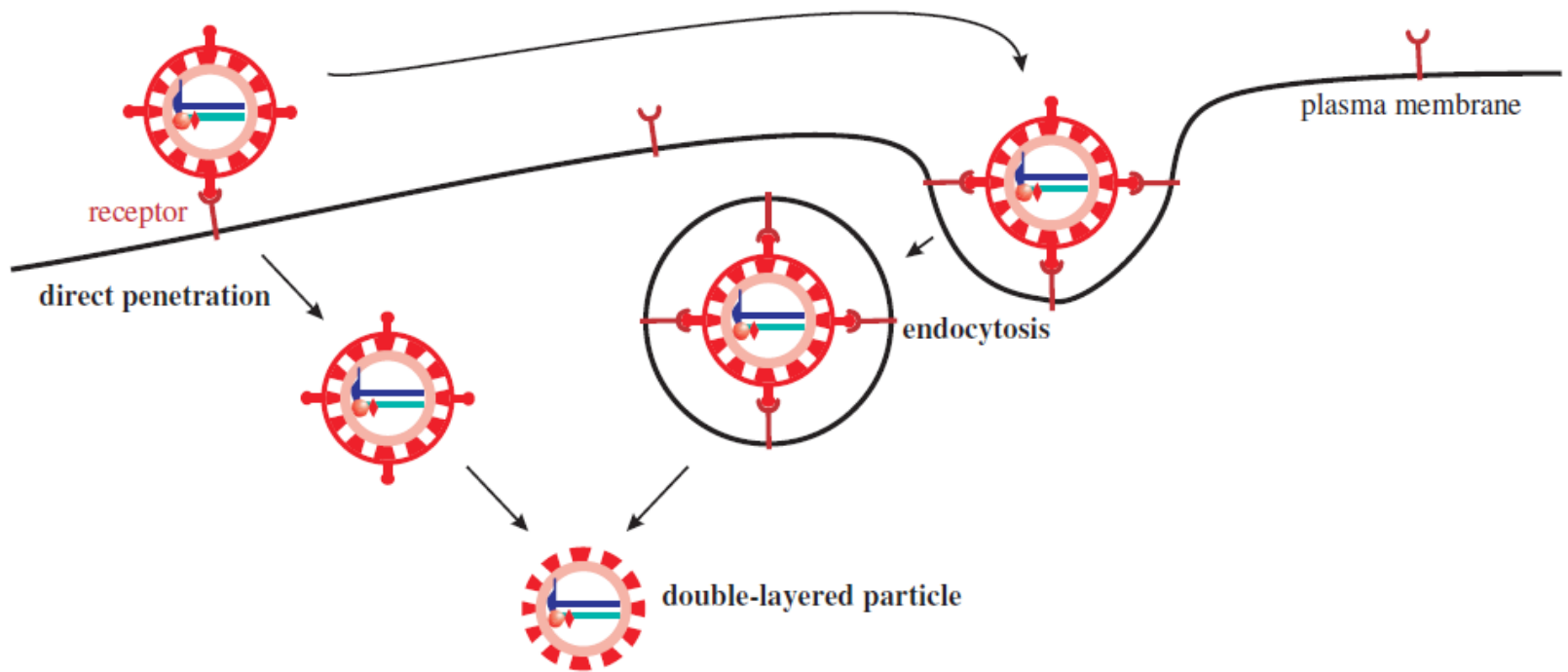
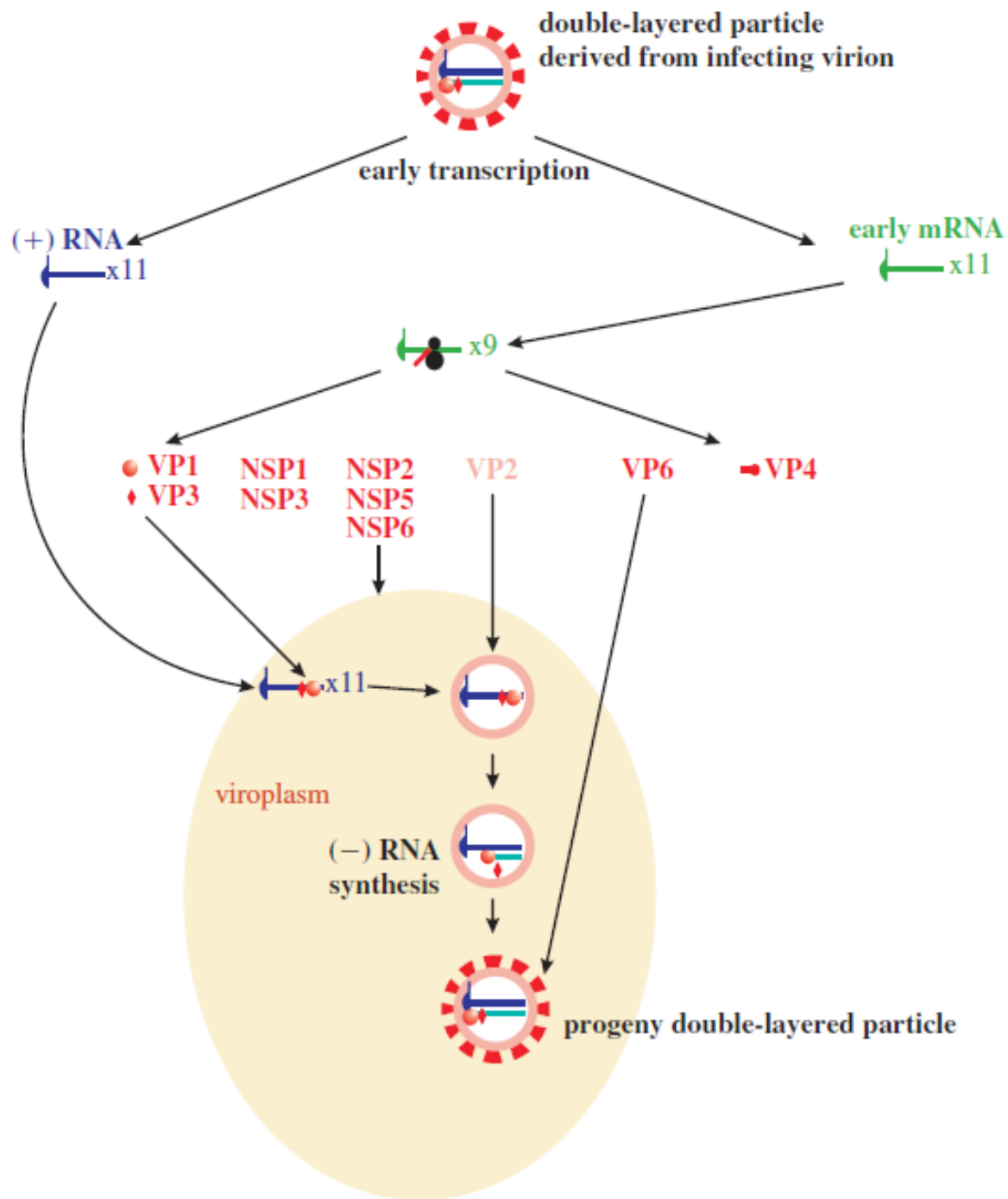


Figure 13.5 Modes of rotavirus entry into the host cell. A rotavirus virion may either penetrate the plasma membrane or it may be endocytosed. Only one of the 11 dsRNA molecules in the virion is shown.



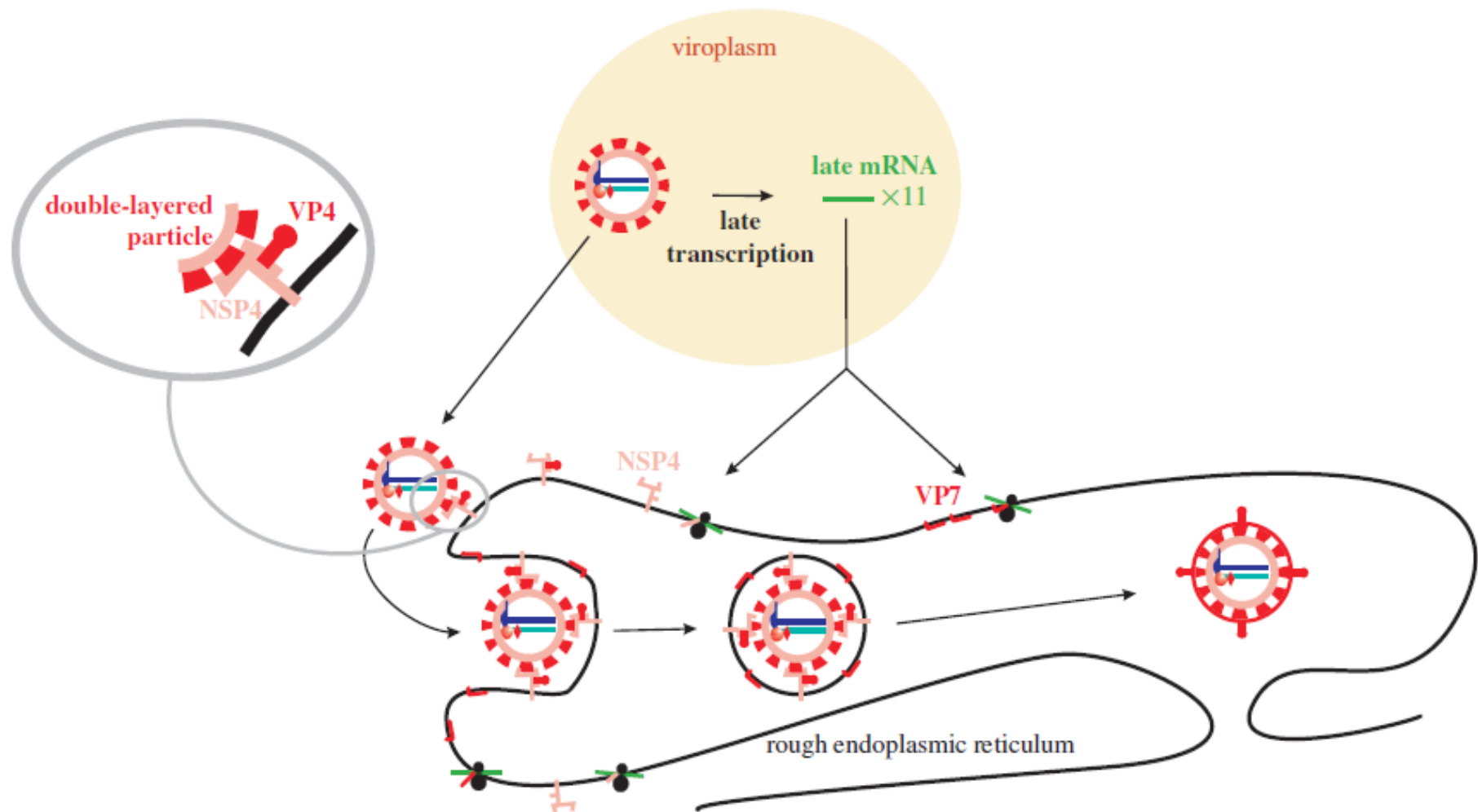
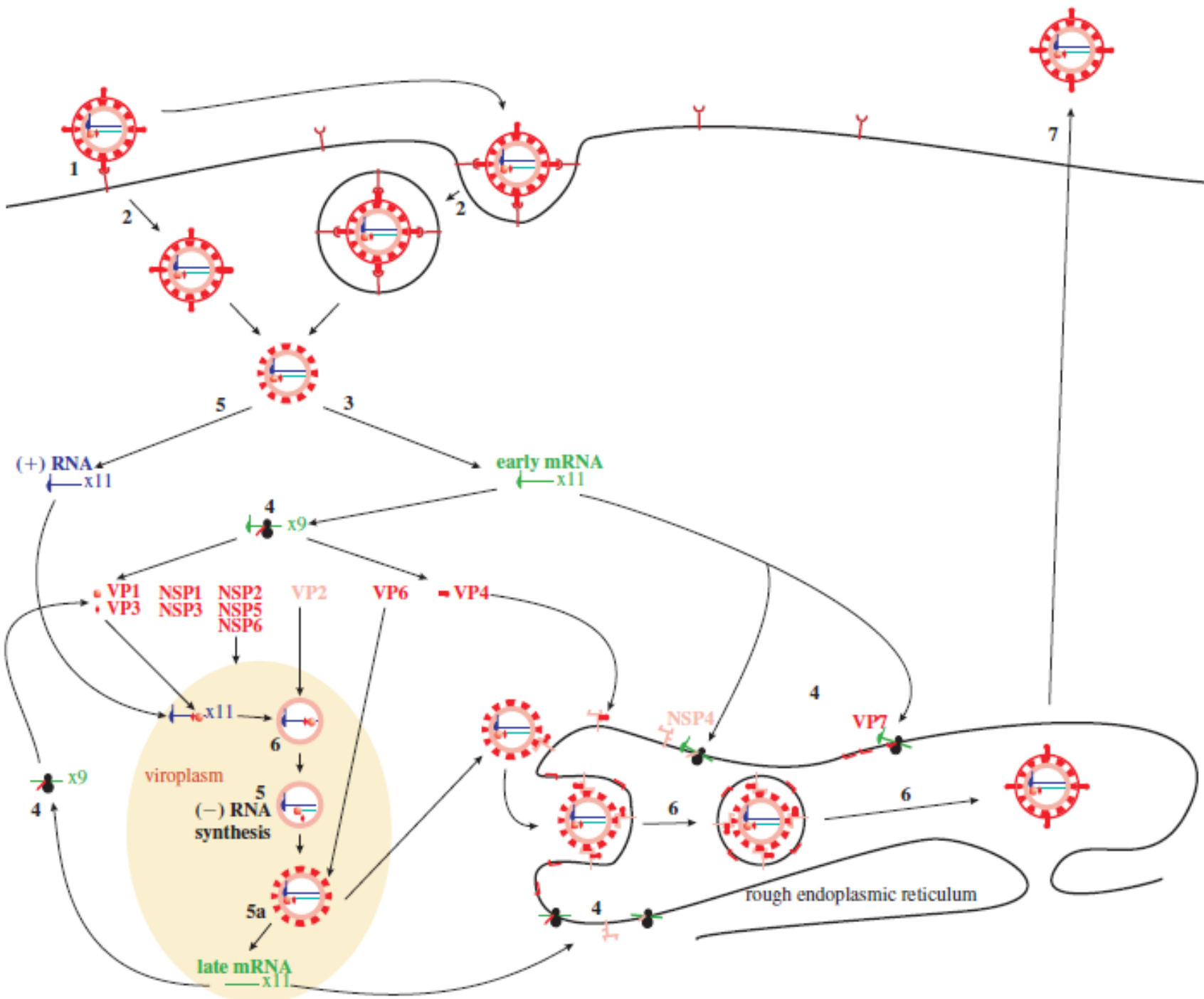


Figure 13.7 Late events in rotavirus replication. Secondary transcription takes place in progeny double-layered particles and results in the synthesis of uncapped mRNA. The 12 virus proteins are translated; only NSP4 and VP7 translation are shown here (both are synthesized in the endoplasmic reticulum). NSP4 binds VP4 and a double-layered particle (inset), and this complex buds into the endoplasmic reticulum. The VP4 spikes and the VP7 outer layer of the capsid are added.



Learning outcomes

- describe the rotavirus virion;
- discuss the main events of the rotavirus replication cycle;
- explain how rotaviruses cause disease.

Picornaviruses

Pico (= small) **RNA** viruses

Hosts: mammals
birds

Diseases: common cold
polio
hepatitis A
foot and mouth disease

Virion

- icosahedral
- 25–30 nm diameter
- genome: single-stranded RNA
 - Plus polarity
 - 7–8 kb
 - Covalently linked protein (VPg)



The virus genome can function as mRNA.



FMDV



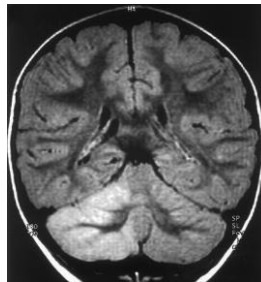
Human picornaviruses

Rhinoviruses

- 40% of common cold cases
- economic losses \$16bn/year in USA & EU

Enteroviruses (EV71)

- hand-foot-and-mouth-disease
- encephalitis



China on alert over deadly child virus

STORY HIGHLIGHTS

NEW: Virus seen in 3,736 cases in kids in city of Fuyang, 4,529 in Anhui province

STORY HIGHLIGHTS

- **NEW:** Xinhua says 3,736 cases in kids in city of Fuyang, 4,529 in Anhui province
- **NEW:** Province south of Beijing upgrades health emergency to allow quarantines
- **NEW:** Virus can cause polioliike paralysis; death toll at 22

reported.



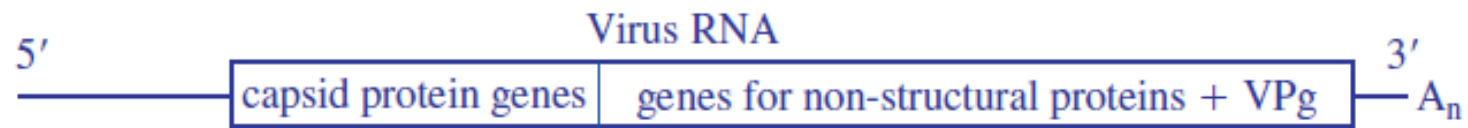
A girl suffering from an Enterovirus 71 infection receives treatment this week in a Fuyang, China, hospital.

The number of reported cases of the virus in children rose to 3,736 early Saturday in the hardest-hit city of Fuyang, according to the state-run news agency. There were 3,321 reported cases Friday in Fuyang.

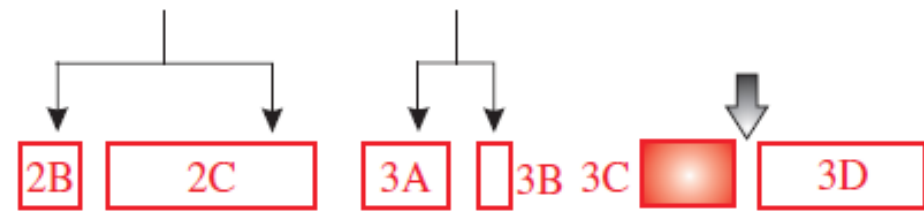
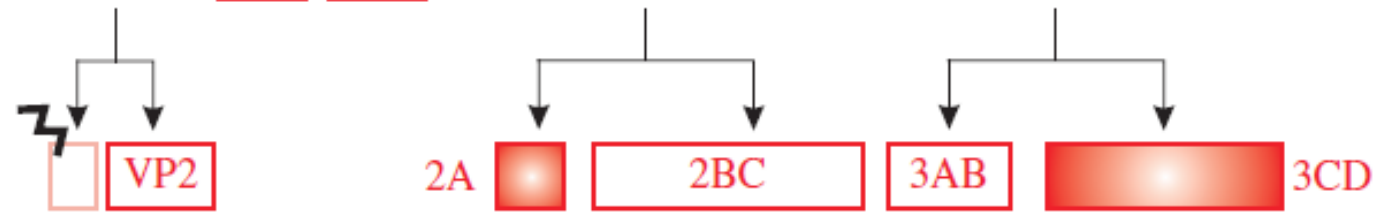
Xinhua reported that 4,529 children have been sickened in 15 cities in Anhui province.

The virus – called Enterovirus 71, or EV71 – can cause hand, foot and mouth disease. It's often confused with foot-and-mouth disease in livestock, but the diseases aren't the same, according to the U.S. Centers for Disease Control and Prevention.

An Anhui province official, Wang Yan, told Xinhua that 978 children are hospitalized, including 48 in critical condition.



polyprotein

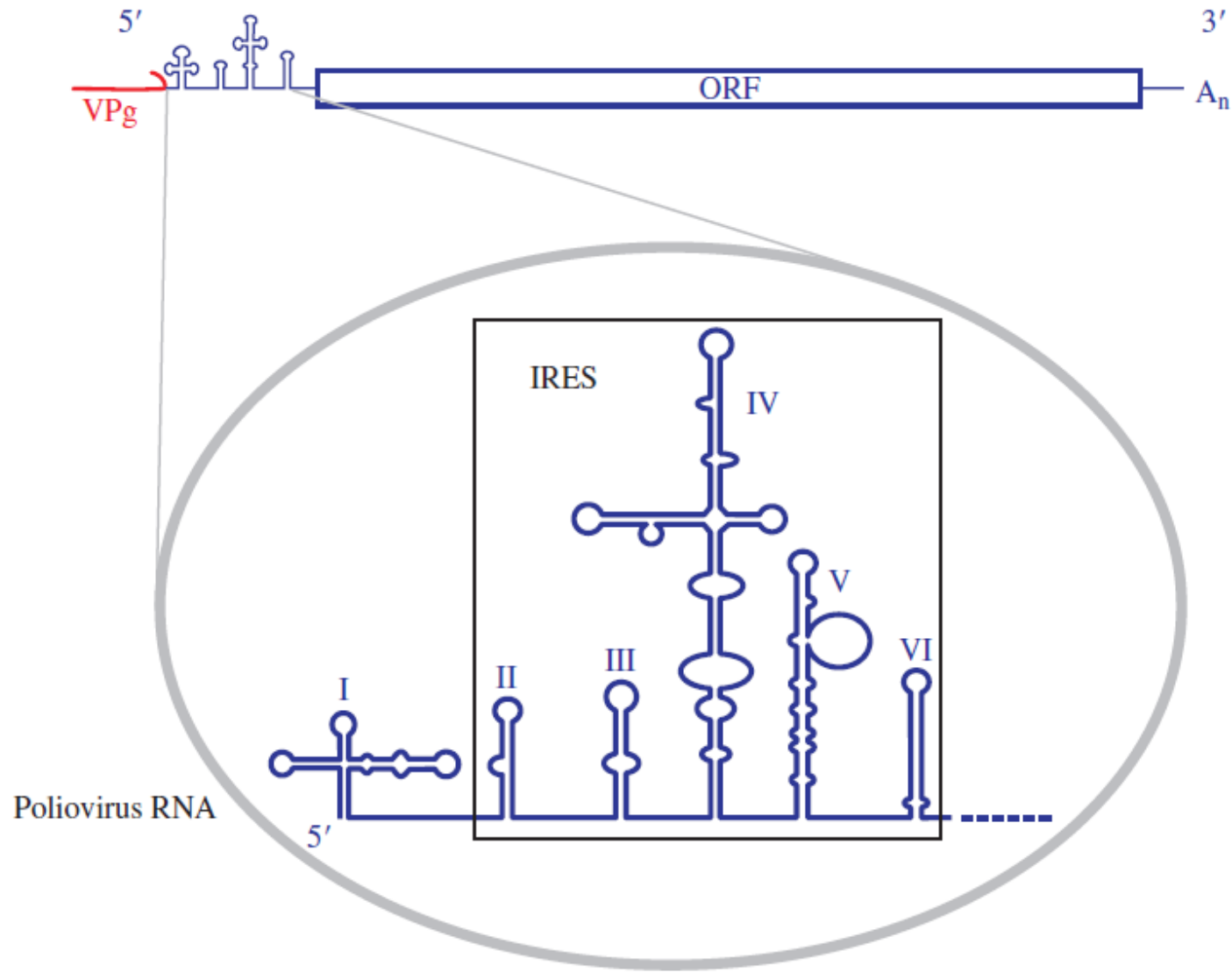


ATPase

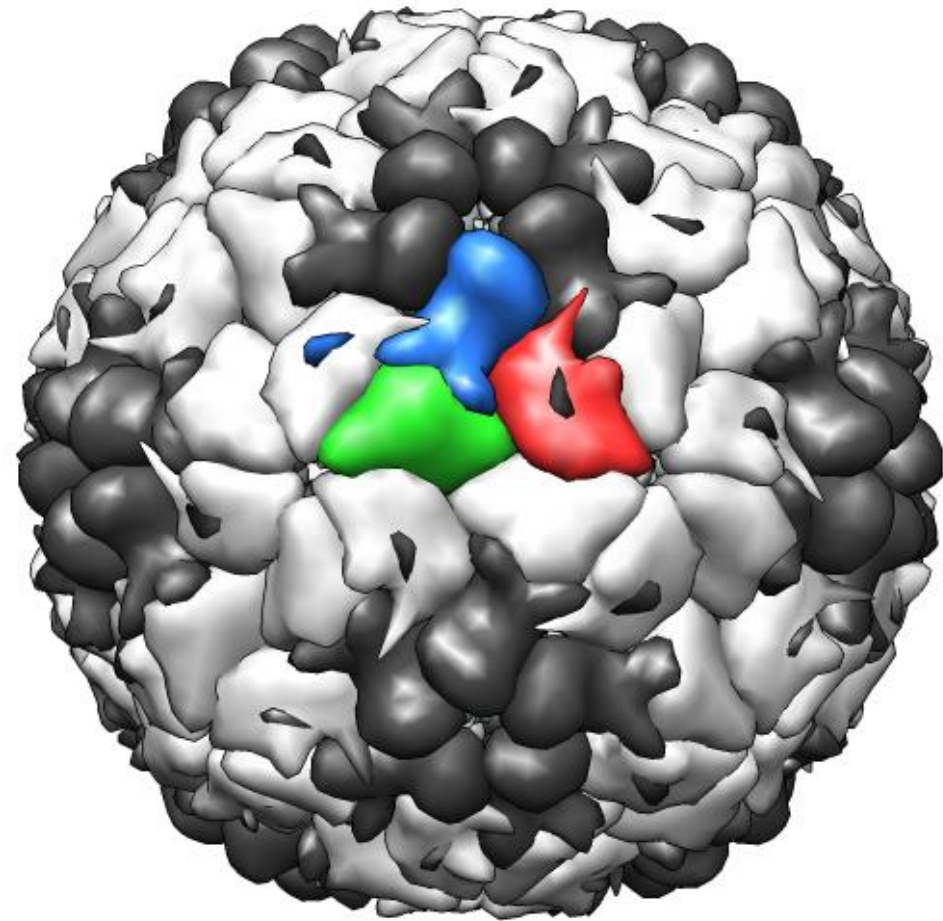
VPg

RNA polymerase

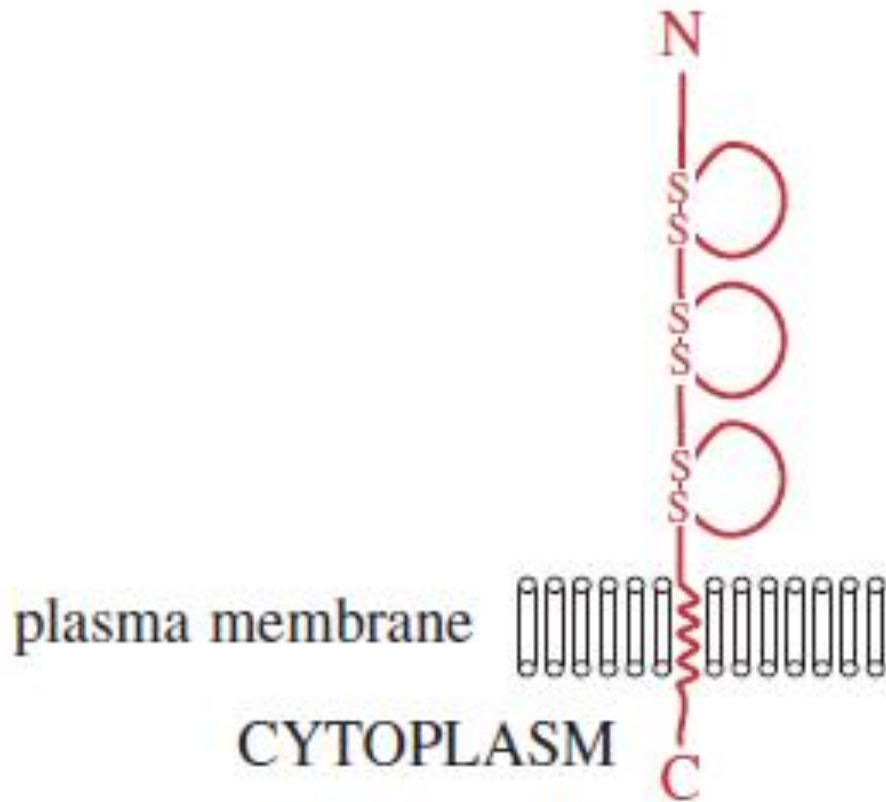
Picornavirus genome organization



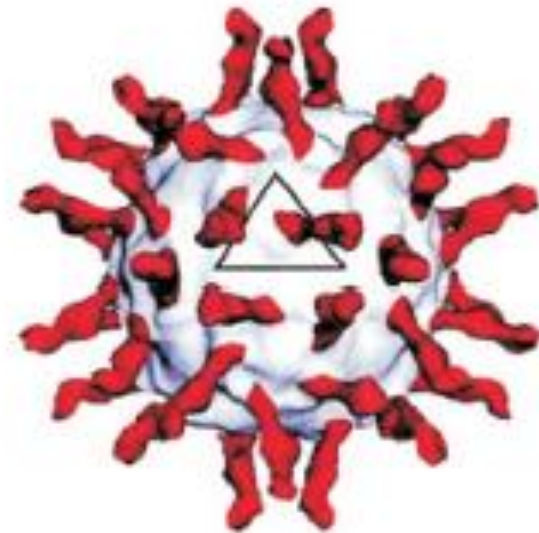
Picornavirus virion

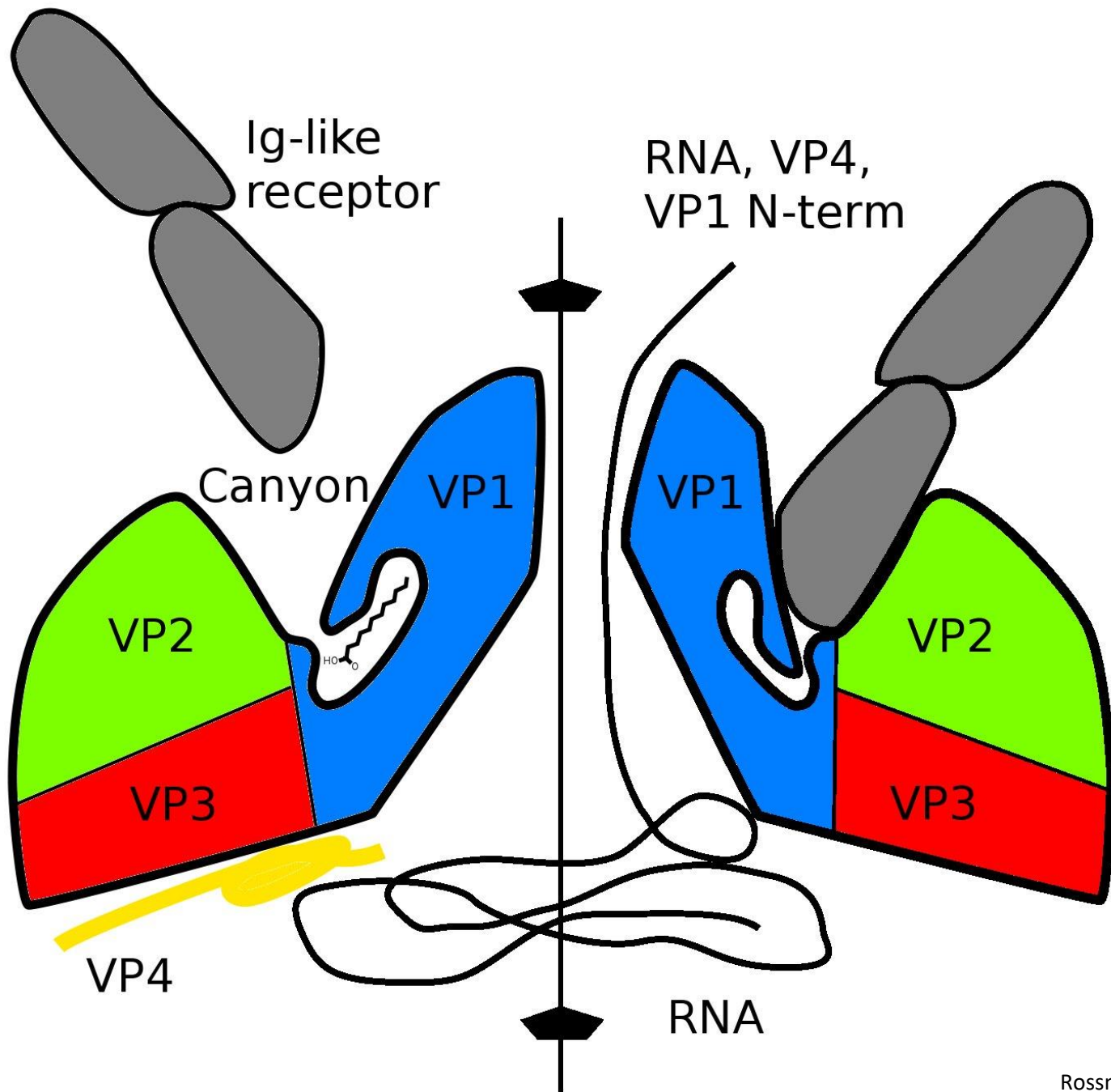


(a) CD155 structure

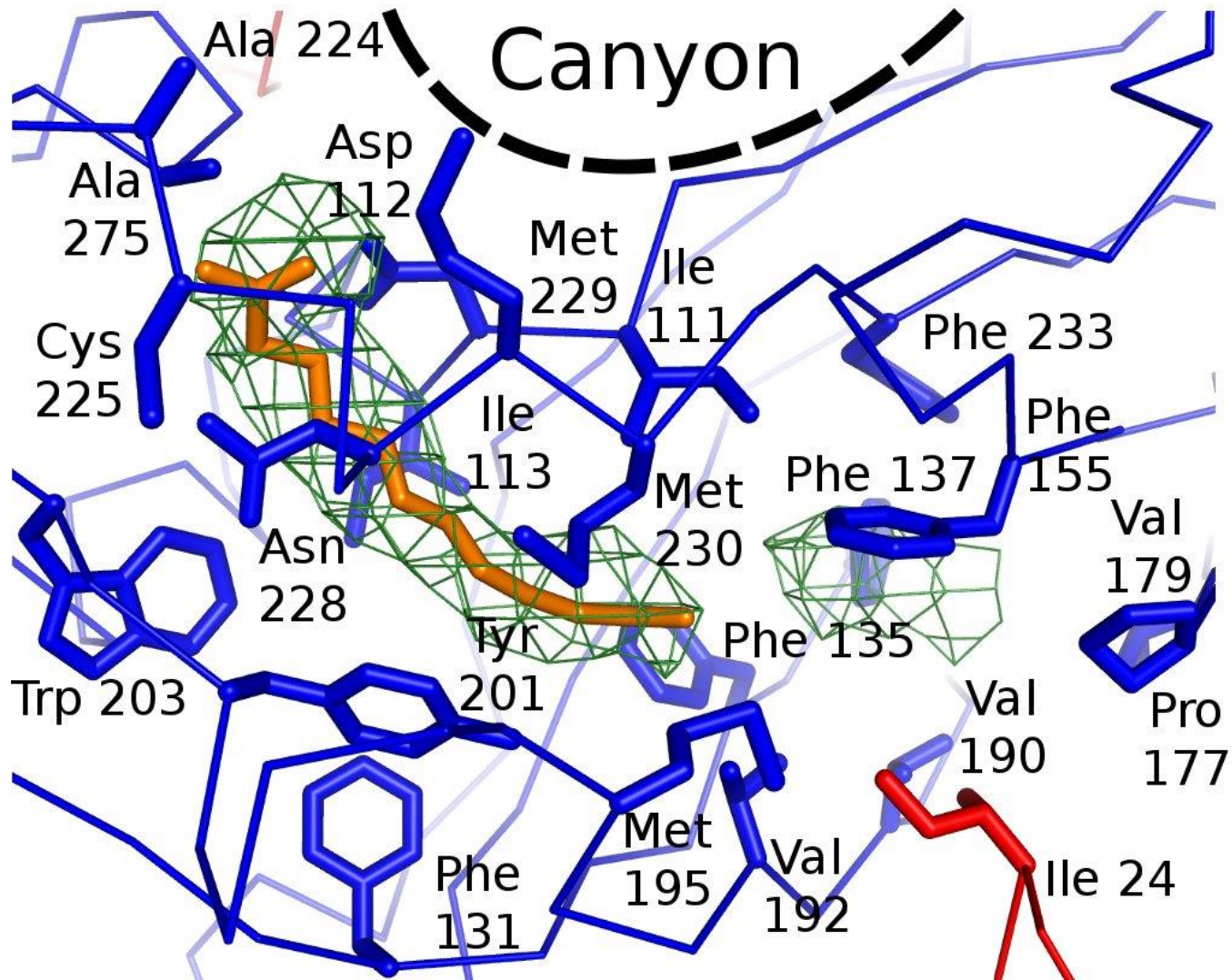


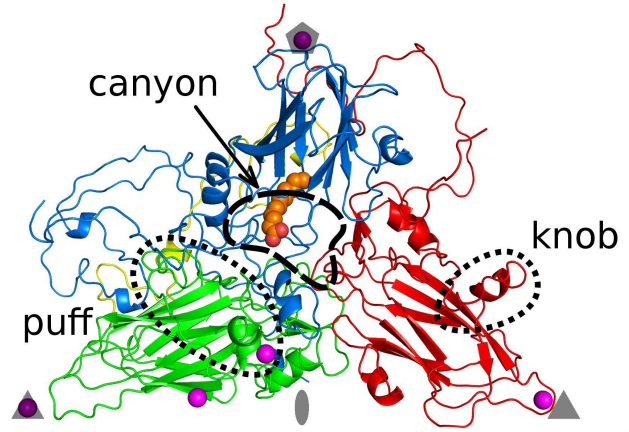
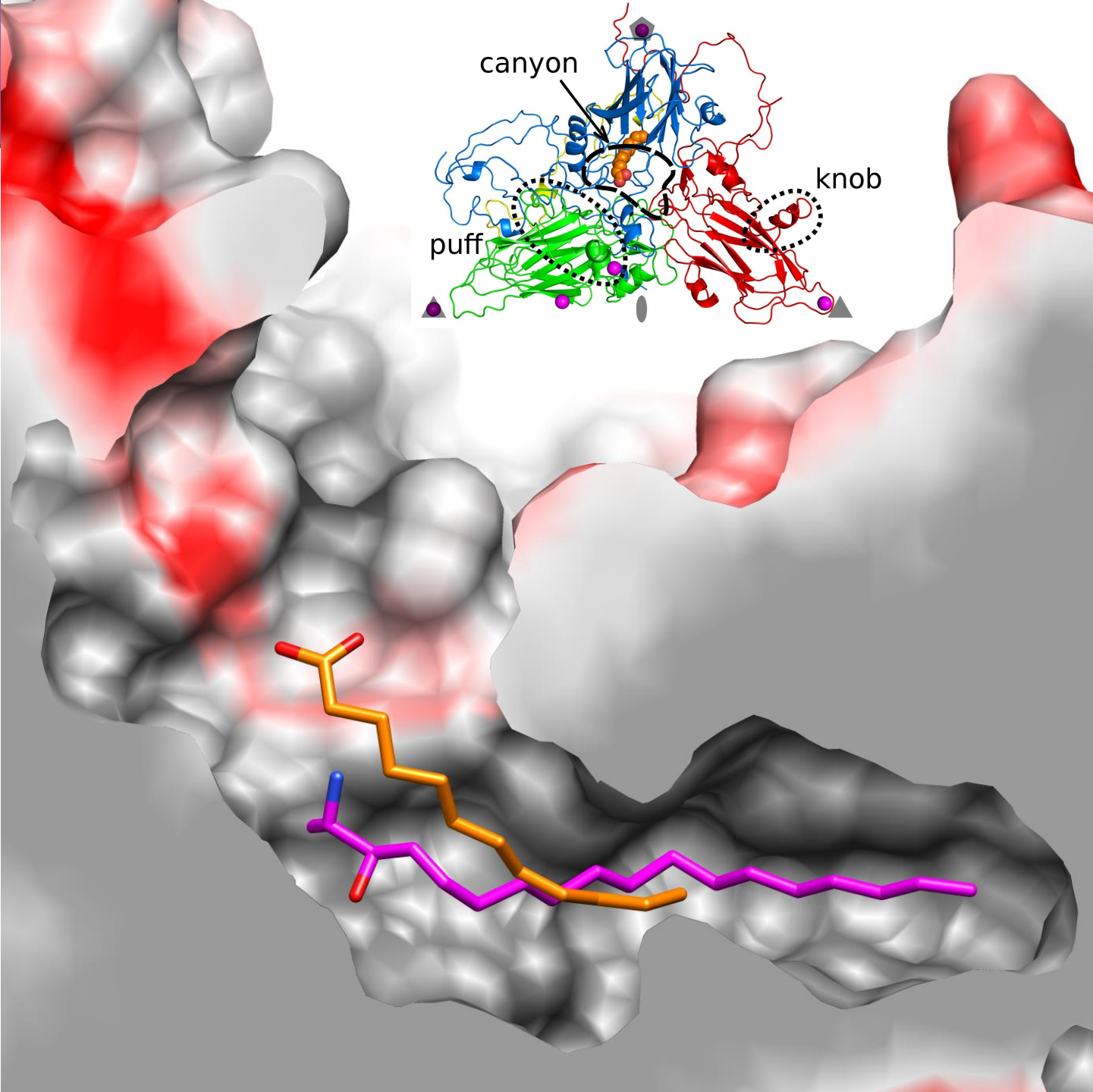
(b) CD155 molecules complexed with a poliovirus particle

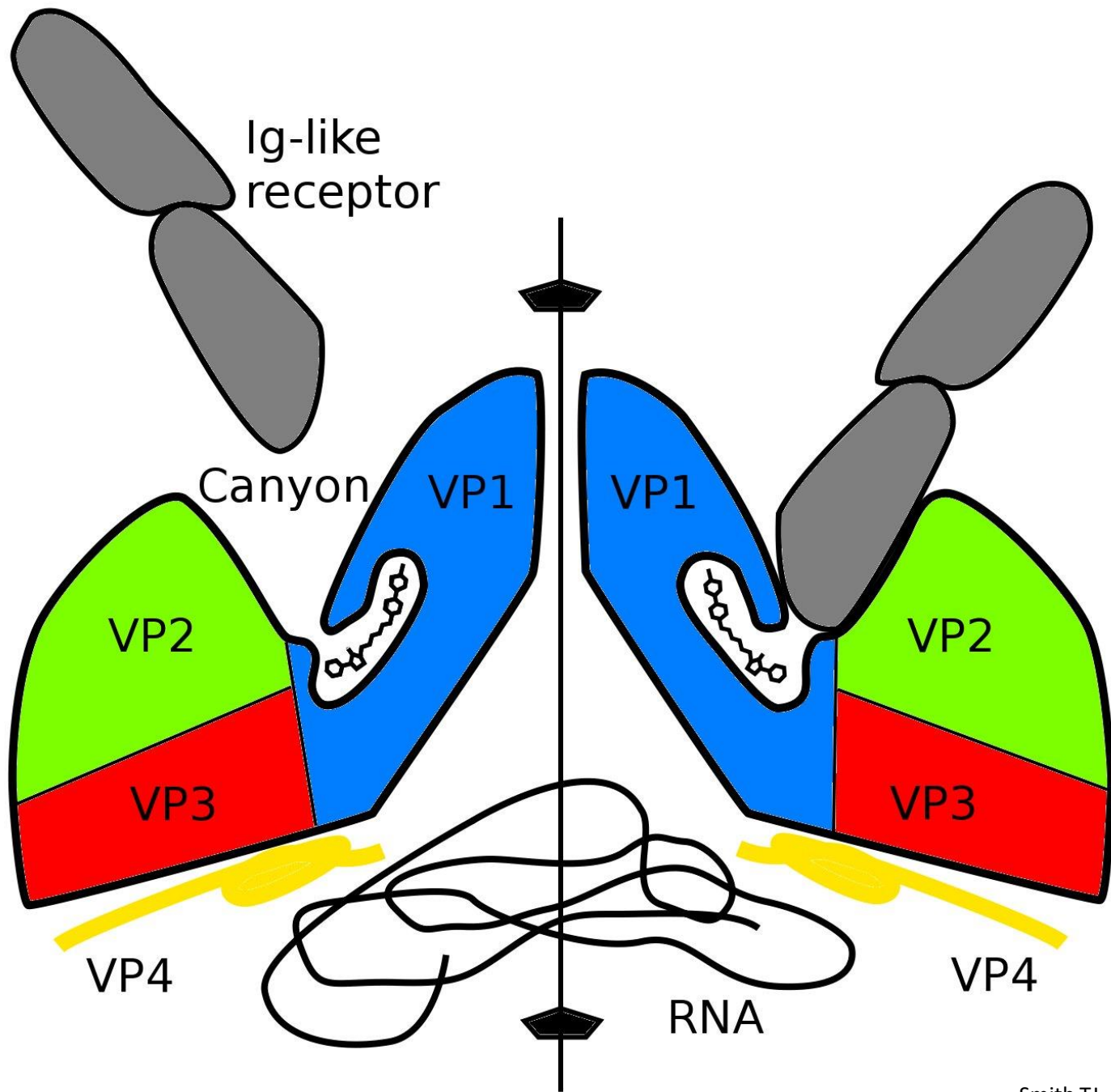




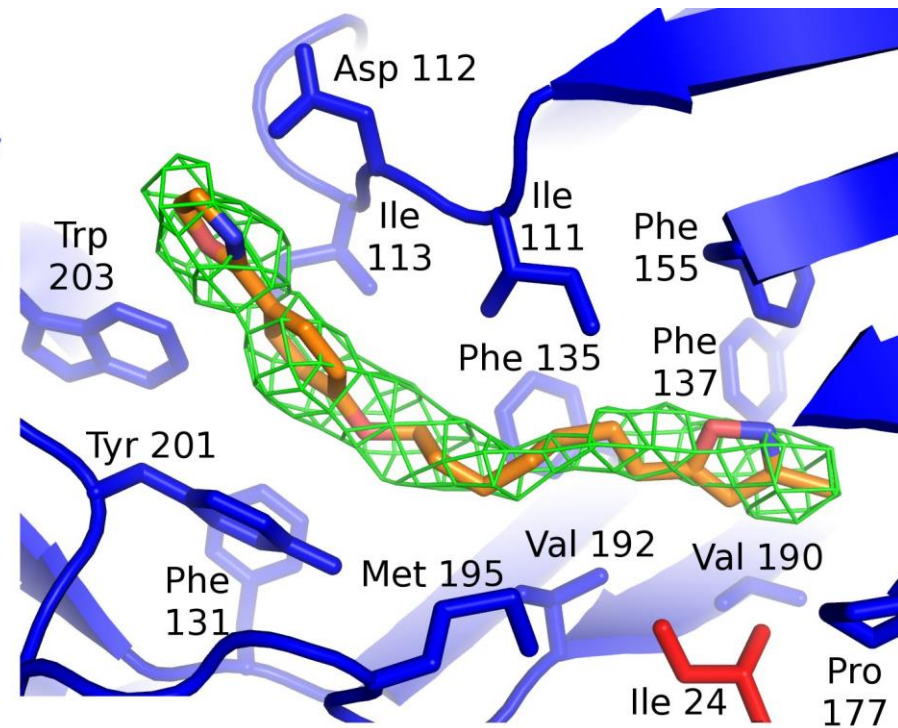
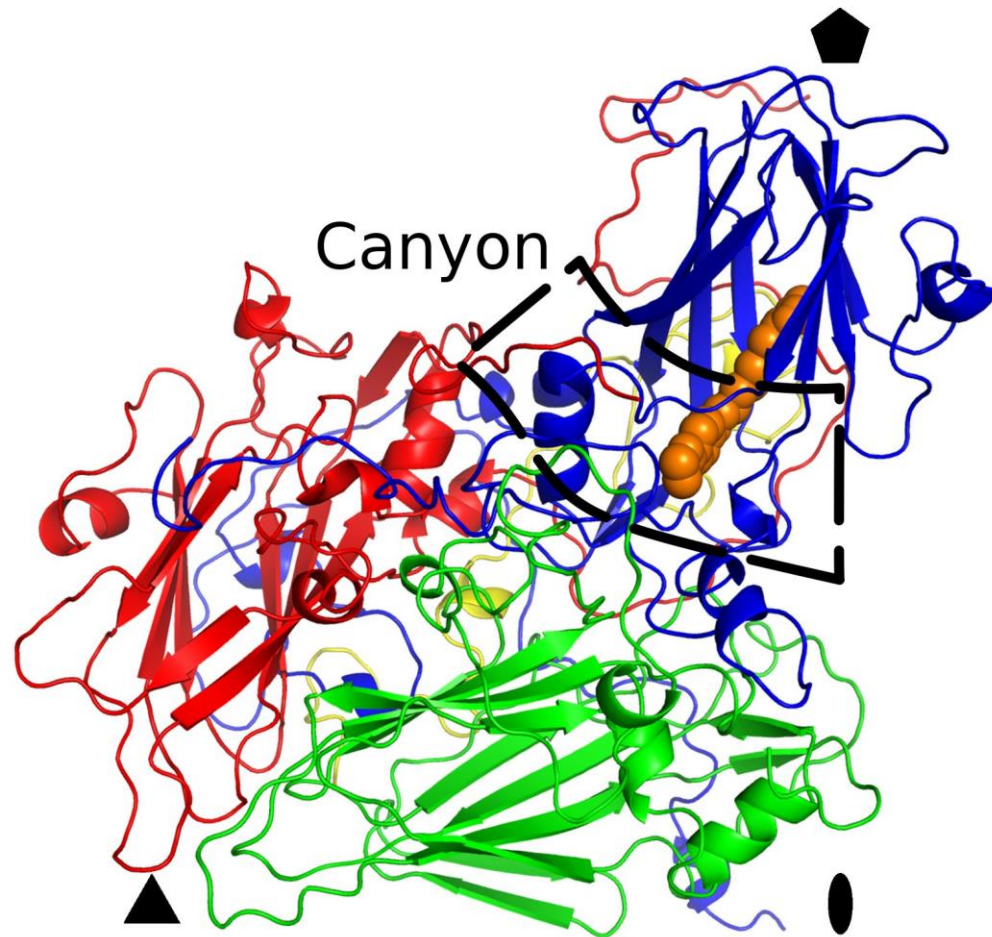
Pocket factor in EV71

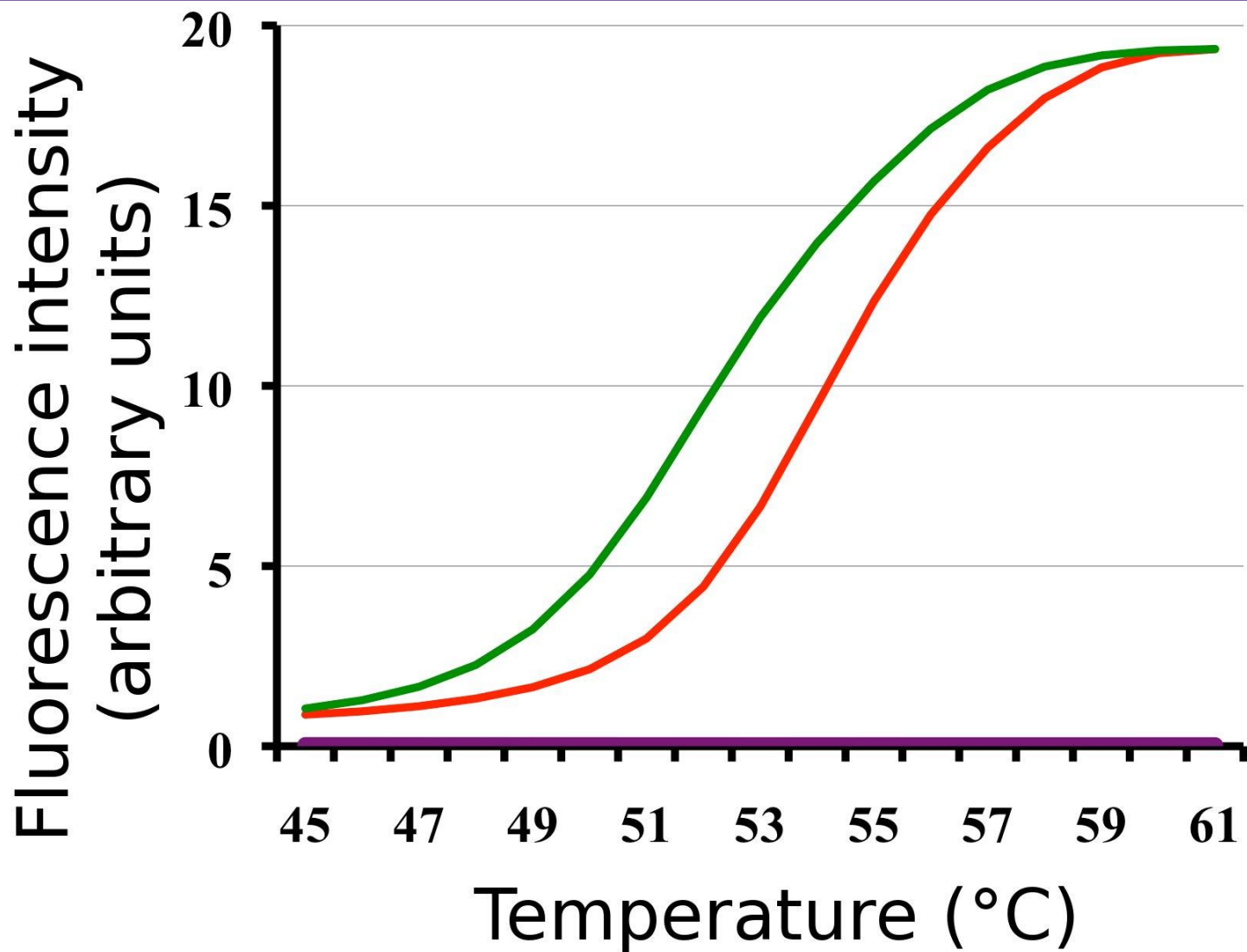




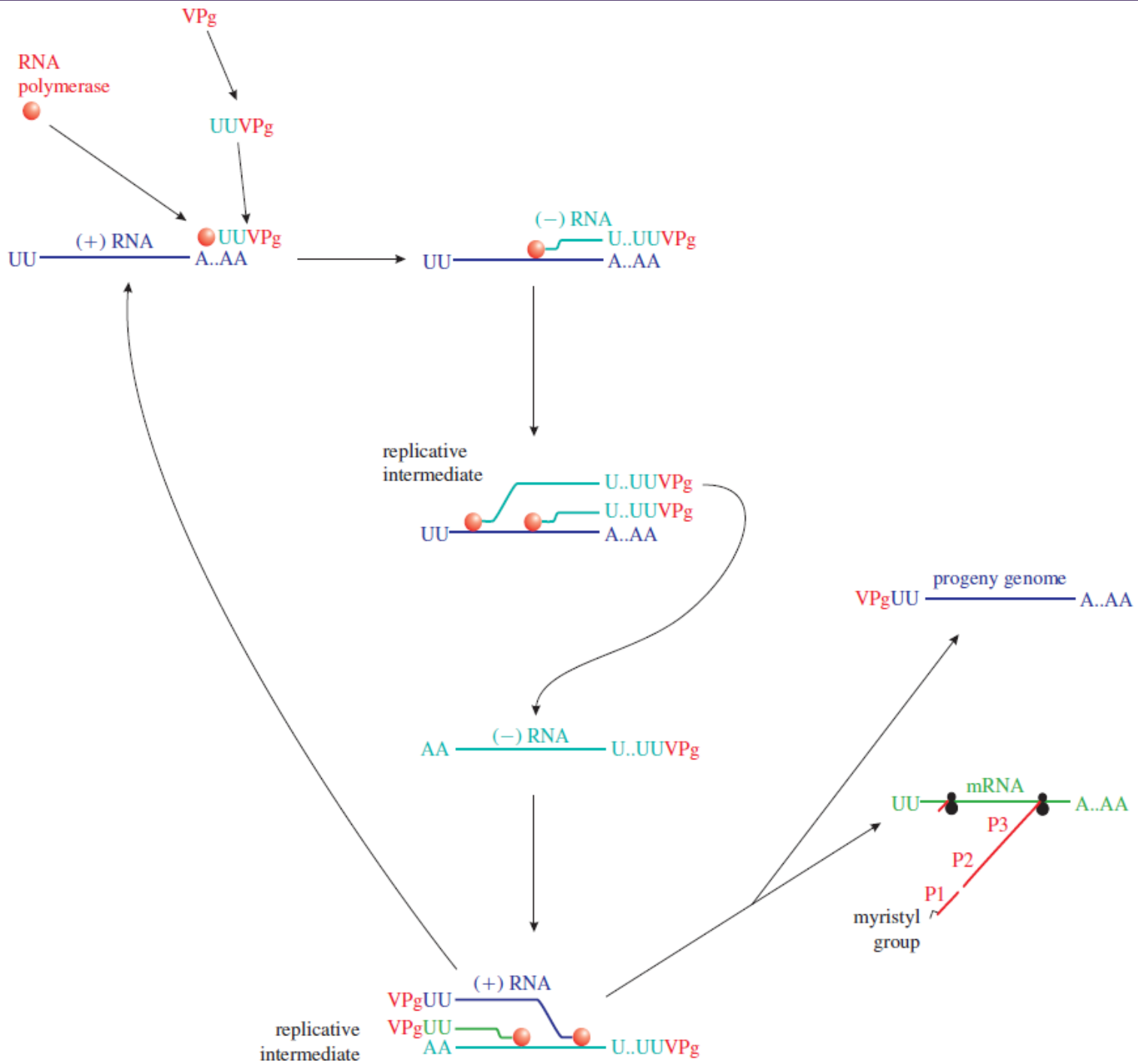


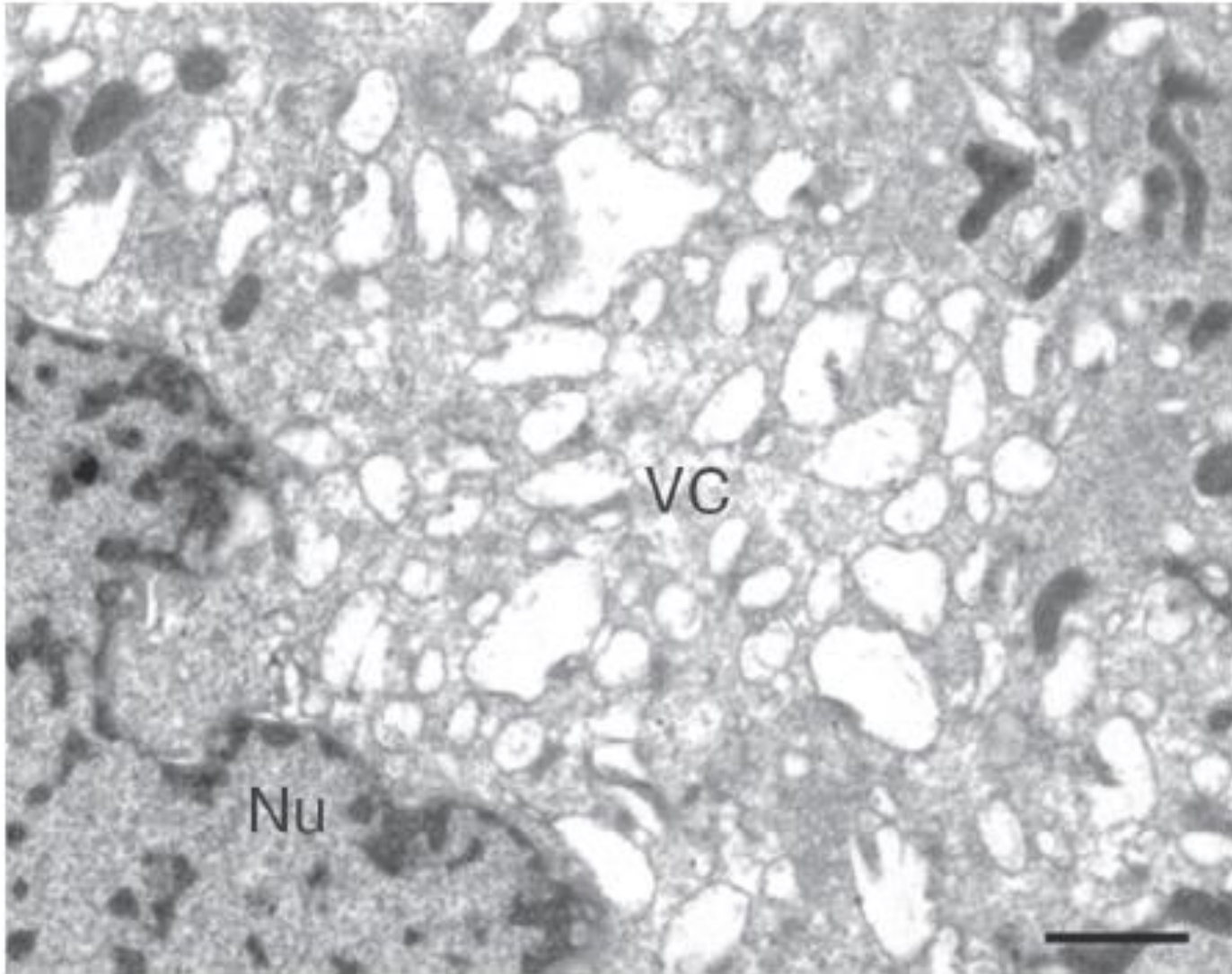
Inhibition of EV71 by WIN 51711

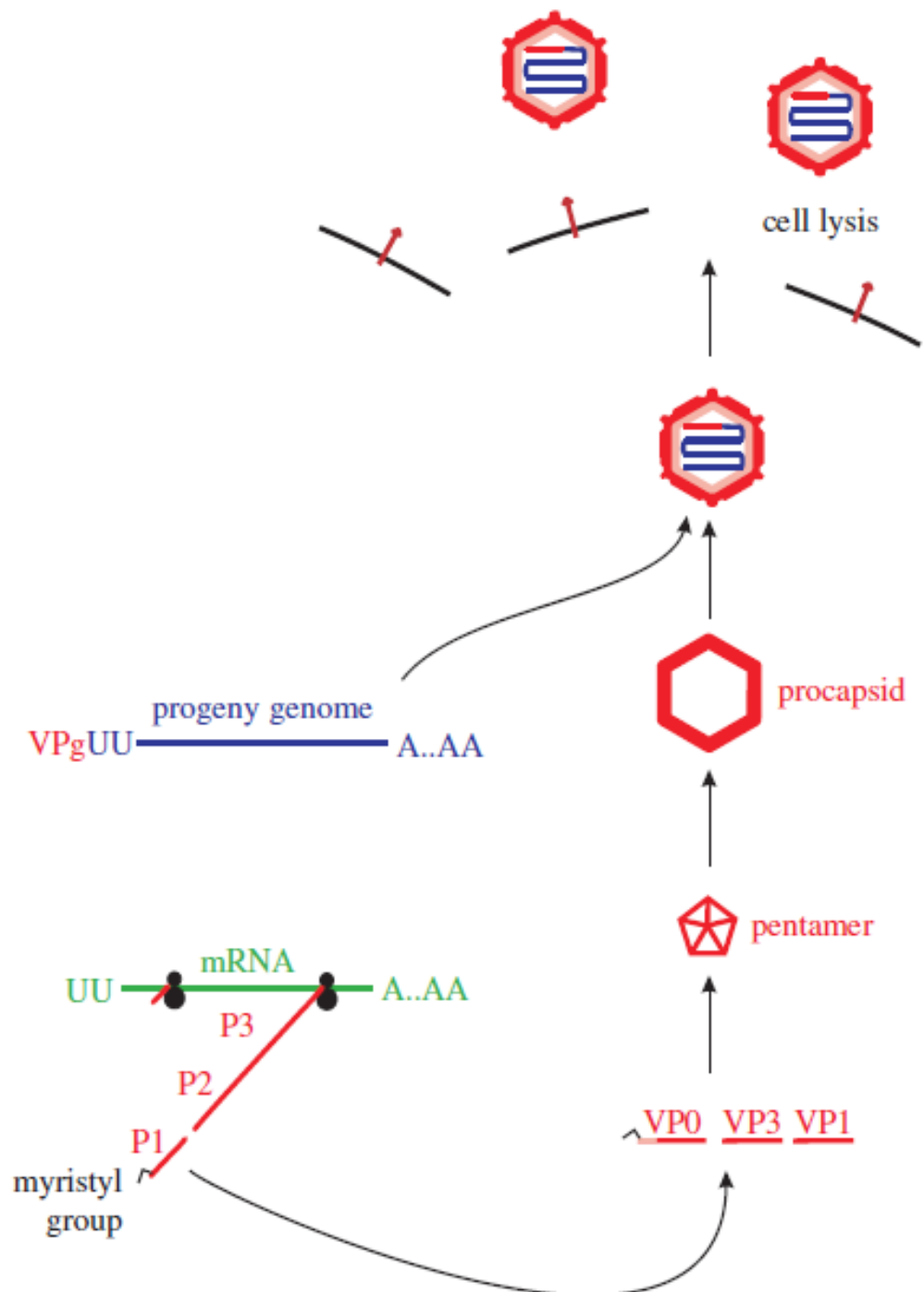




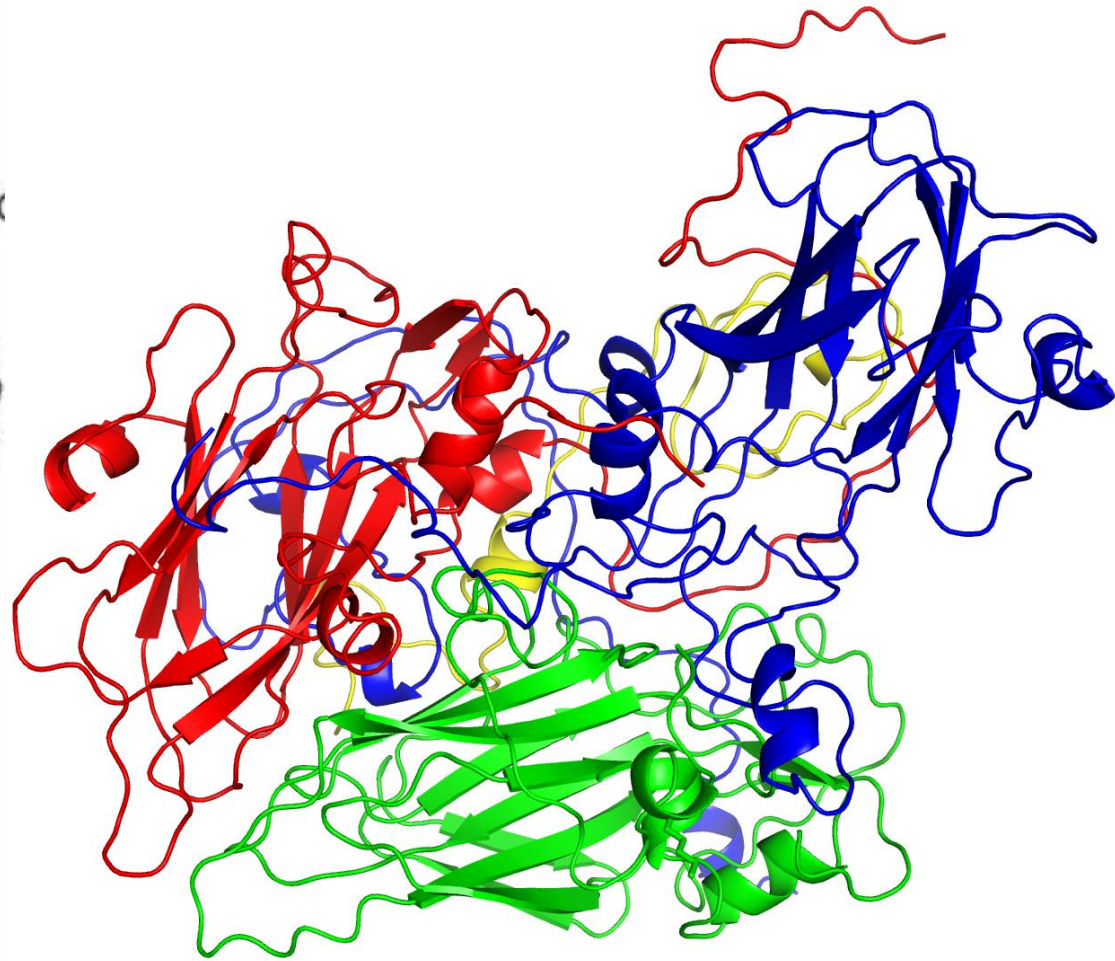
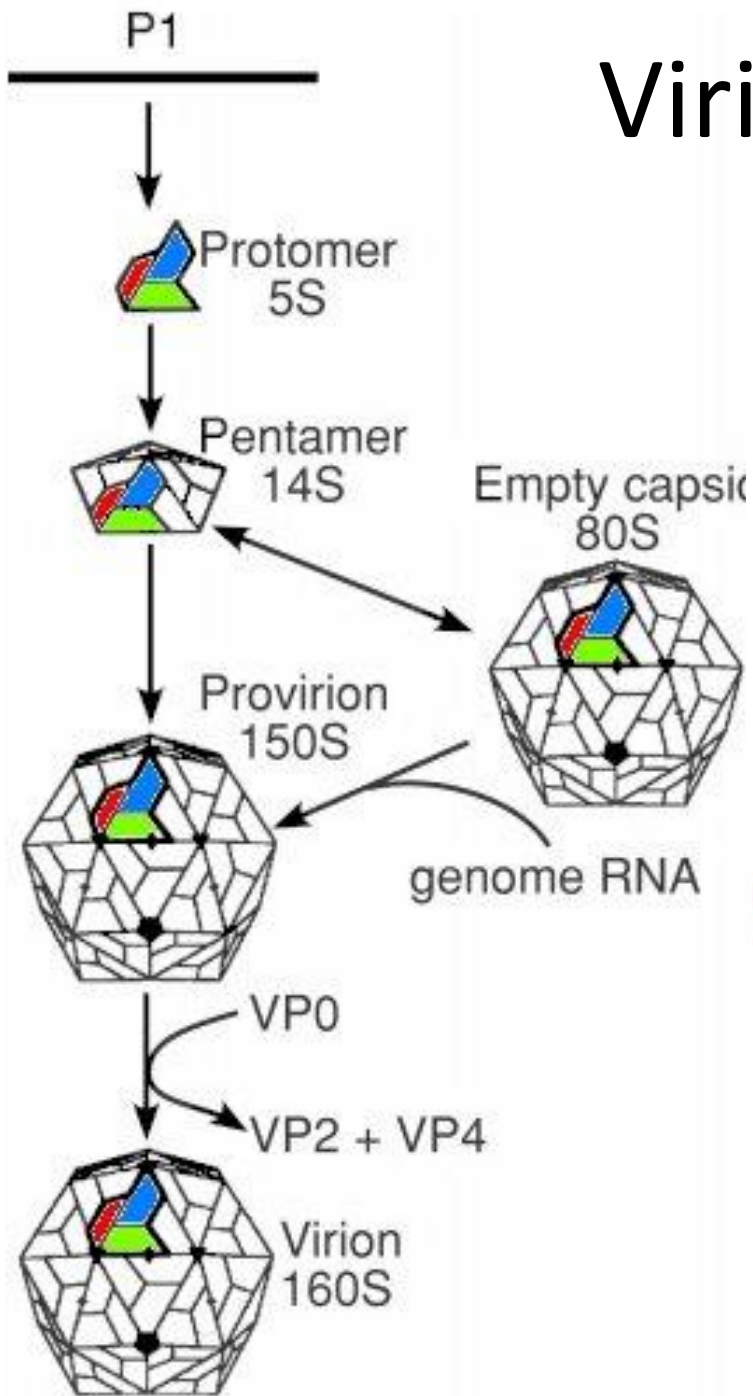
- no virus
- EV71
- EV71 + 300µM WIN 51711





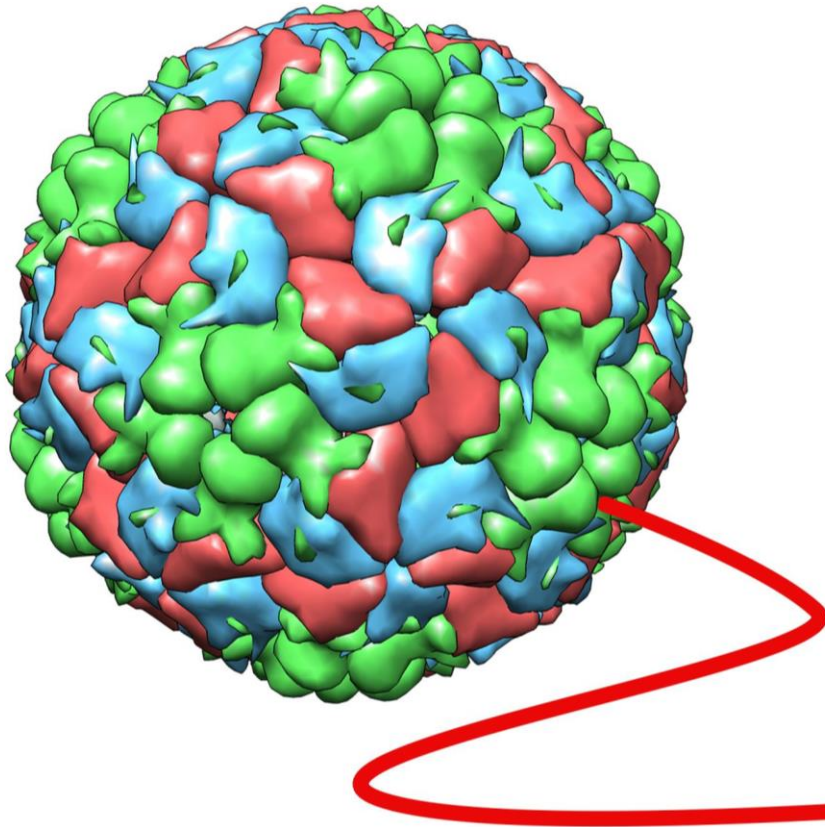


Virion assembly

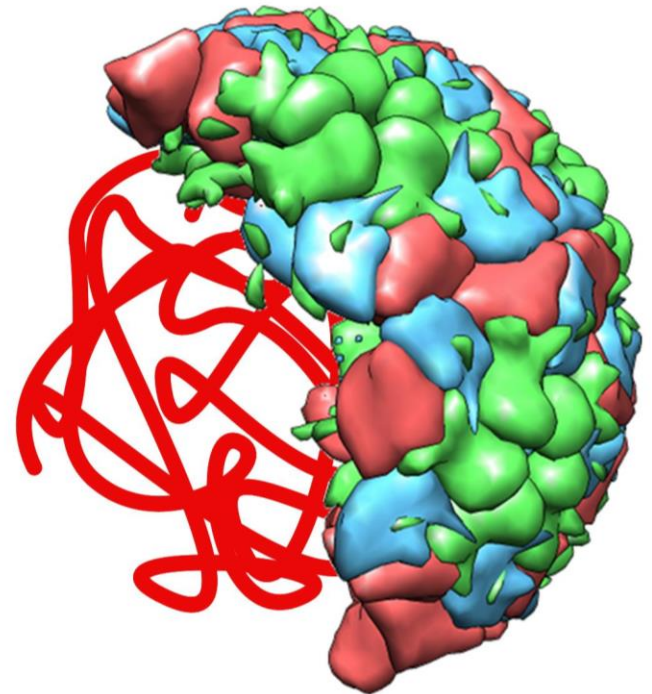


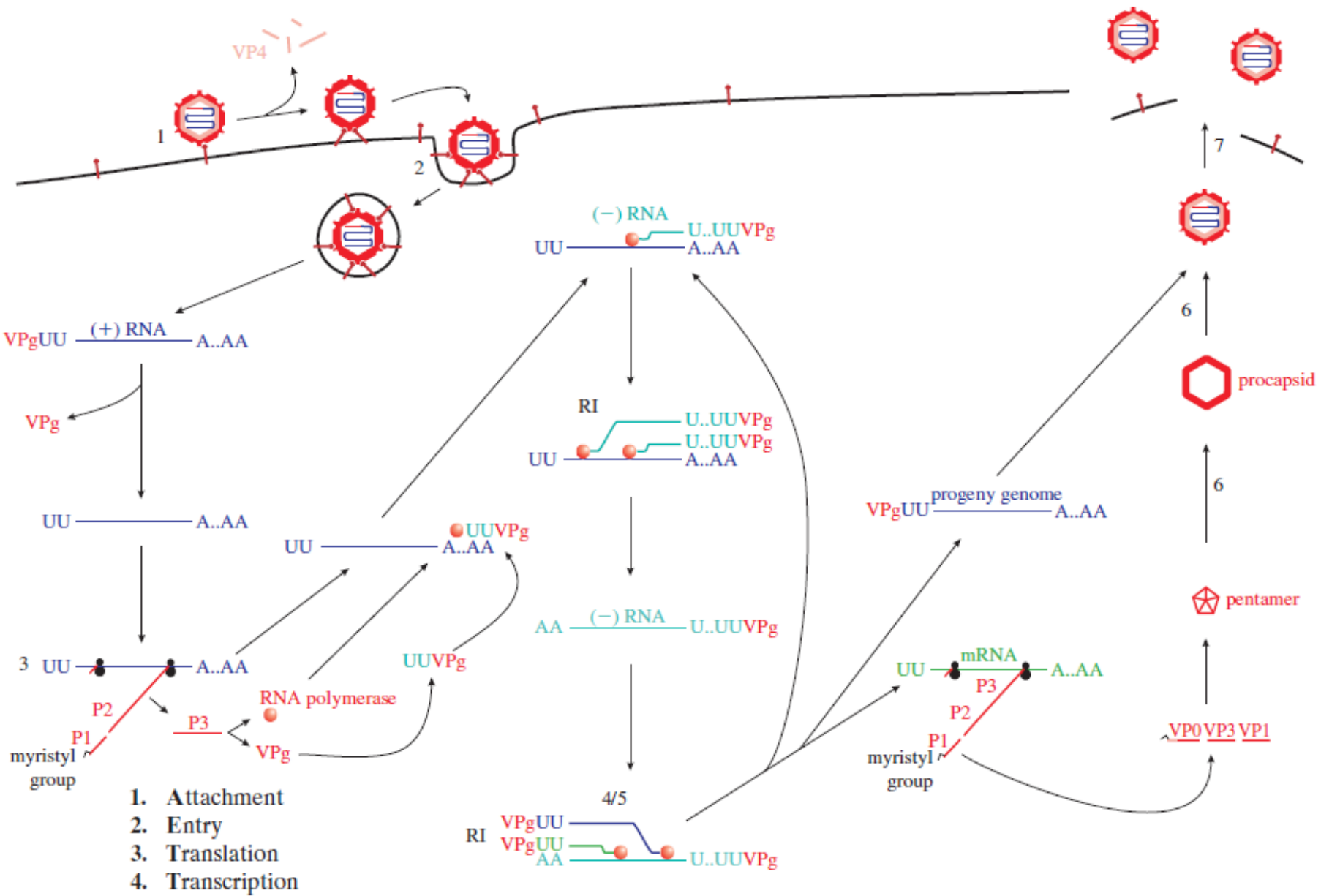
4. Virion assembly mechanism

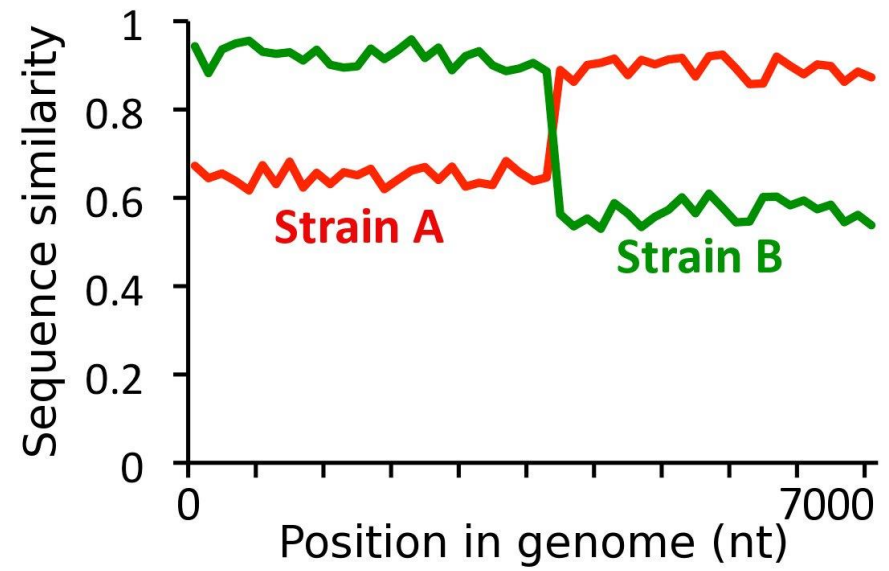
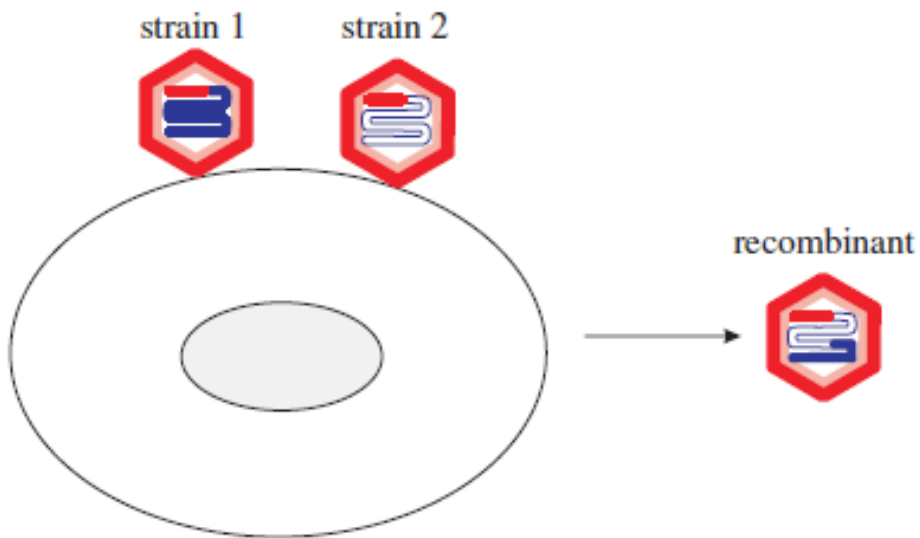
Genome packaging into pre-formed capsids

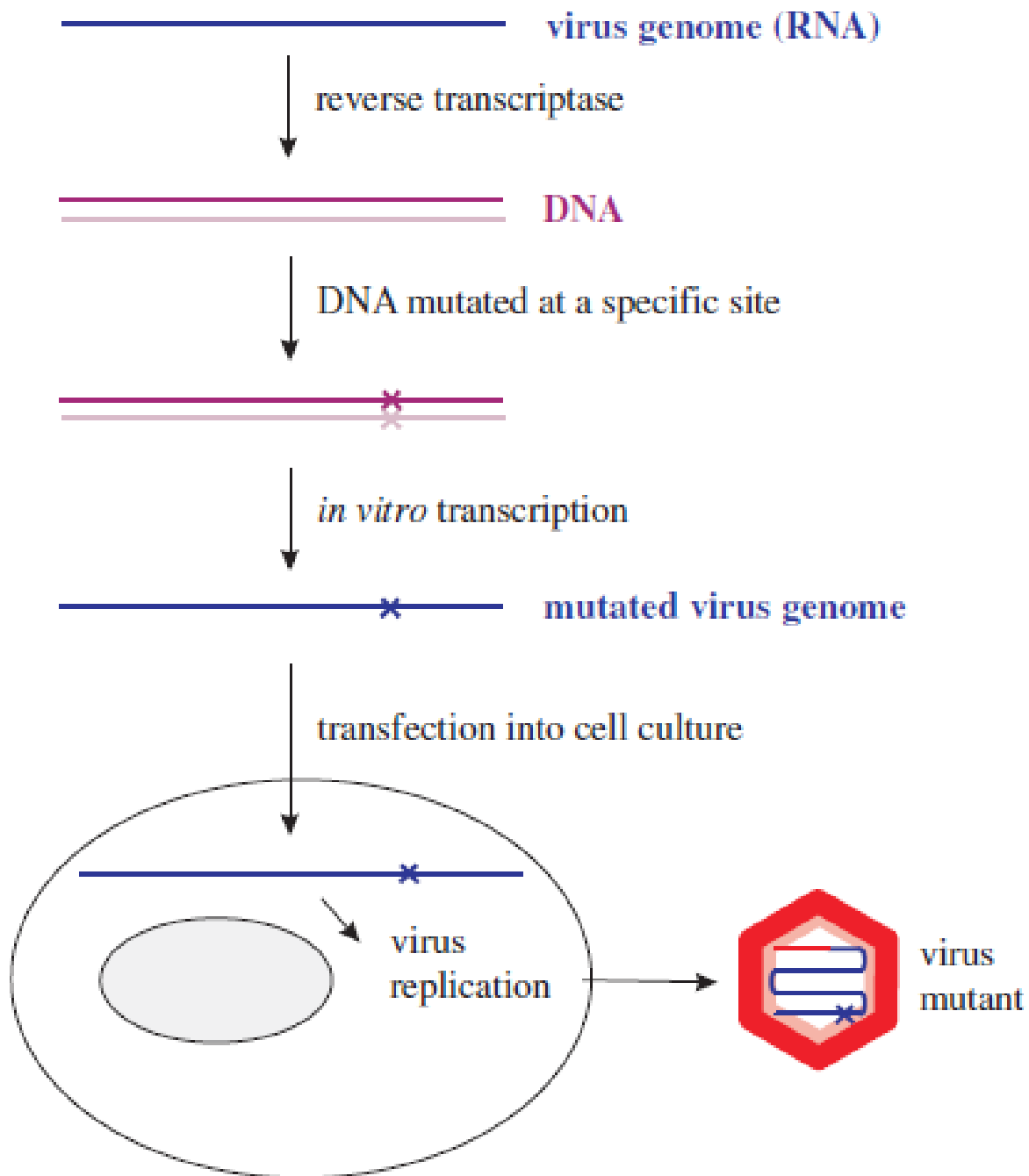


Capsid assembly around condensed genome









deoxyribonucleotides



poliovirus cDNA sequences



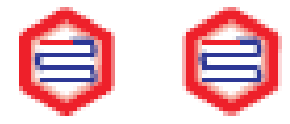
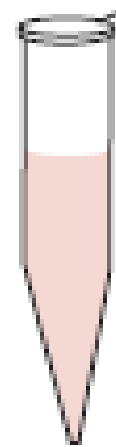
poliovirus cDNA



poliovirus RNA



cell extract



infectious poliovirus

Learning outcomes

- give examples of picornaviruses and explain their importance;
- describe the picornavirus virion;
- describe the picornavirus replication cycle;
- discuss picornavirus recombination;
- describe experimental systems used for picornavirus studies.