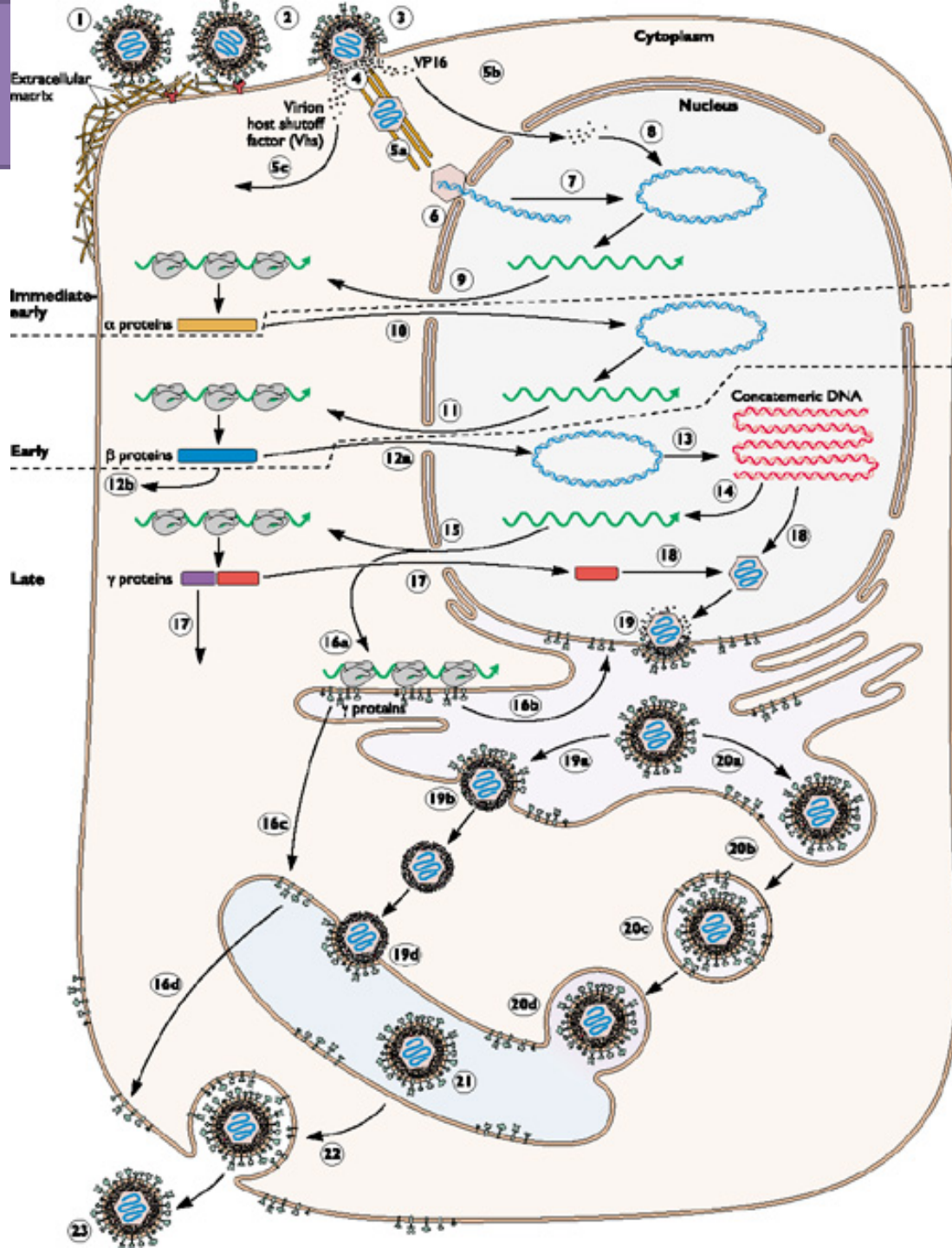
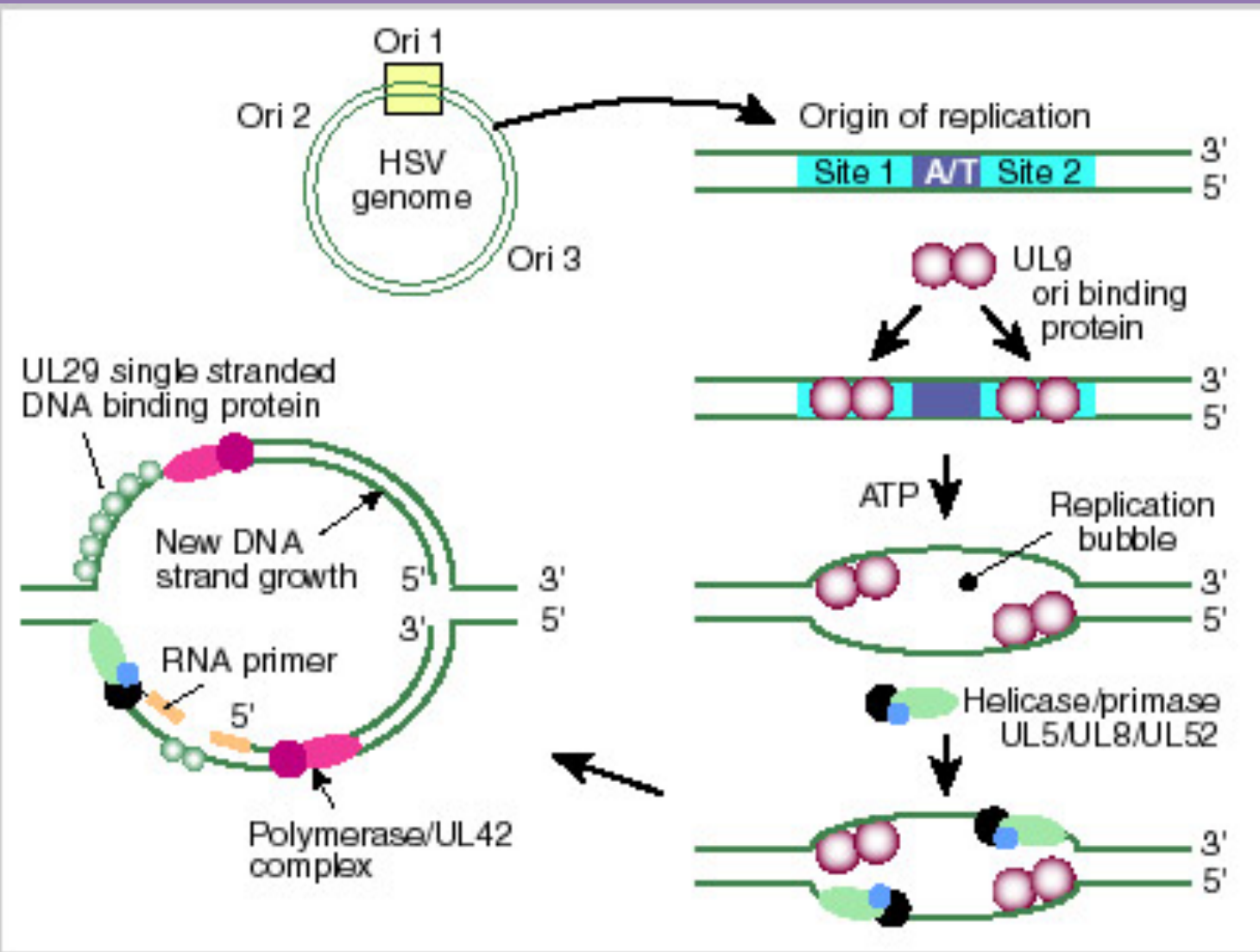


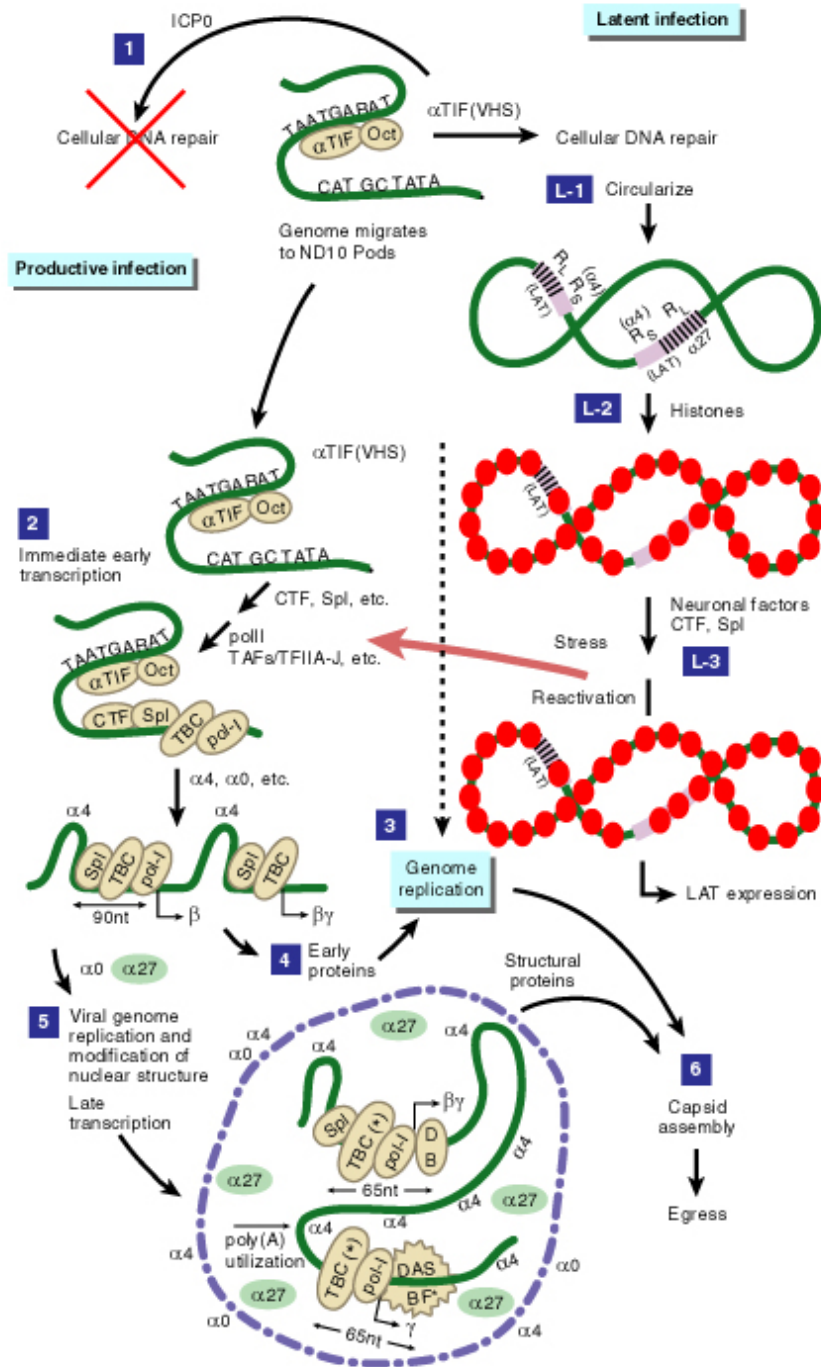
# Structural Virology

Lecture 6

Pavel Plevka







# Parvoviruses

**Hosts:** mammals

birds

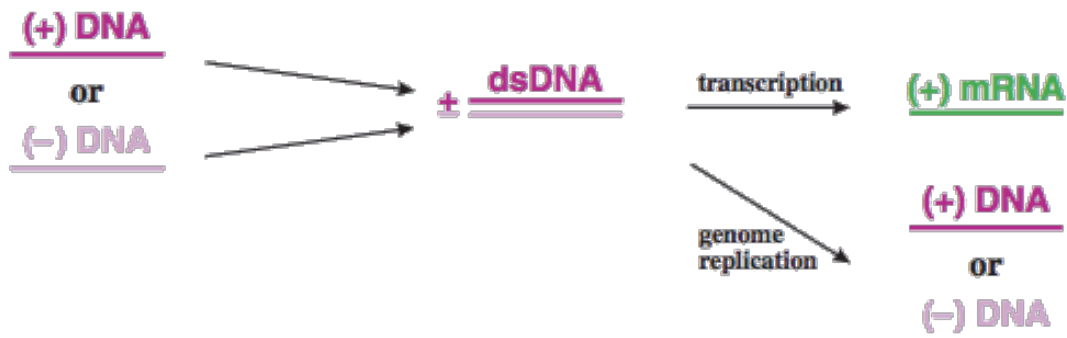
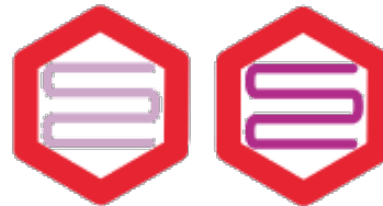
insects

**Disease:** erythema infectiosum (B19 virus)

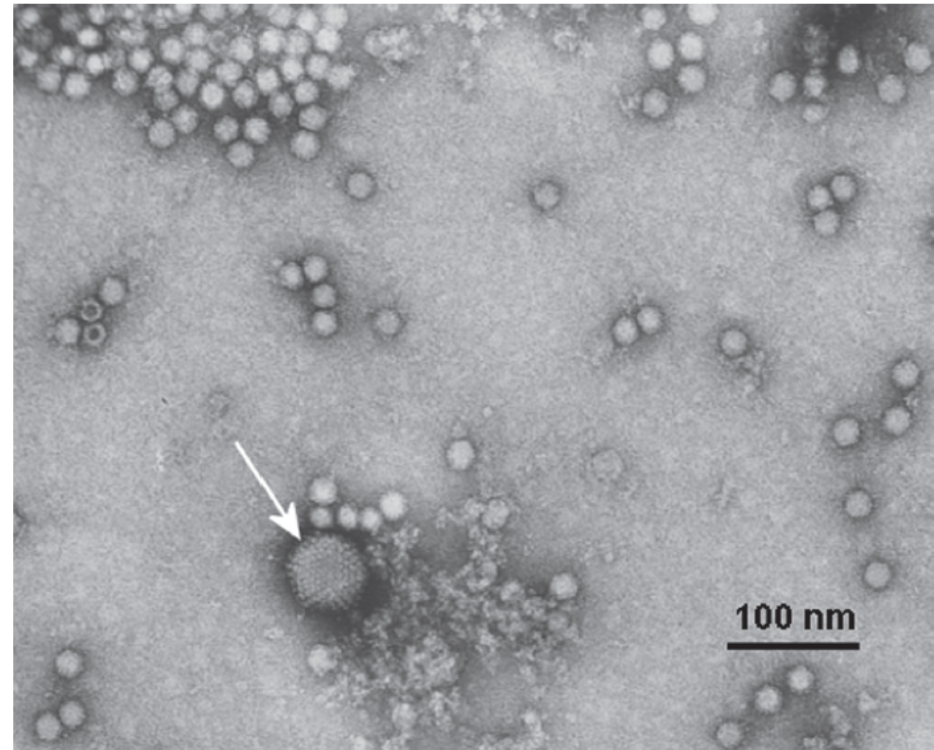
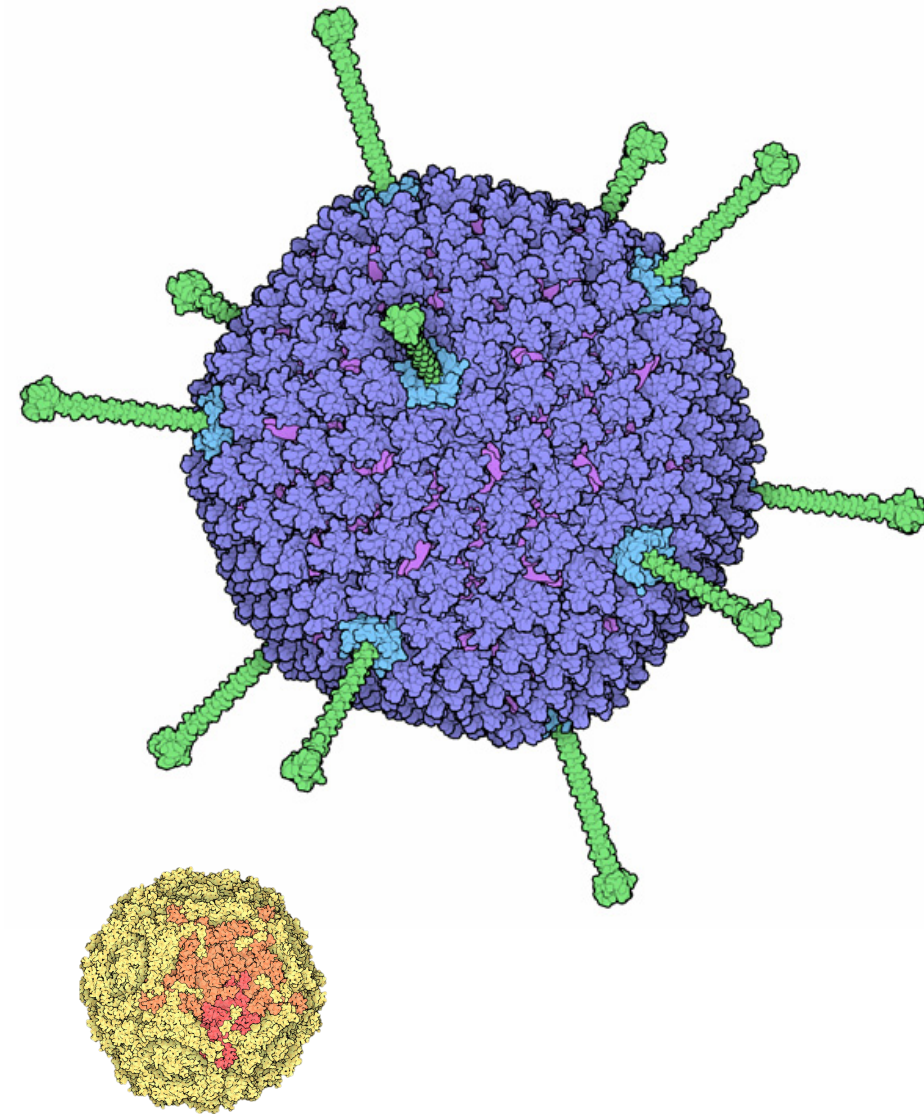
**Used as:** gene vectors (dependoviruses)

## Virion

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



# Parvoviruses

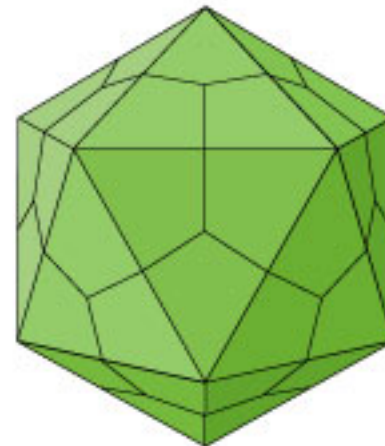
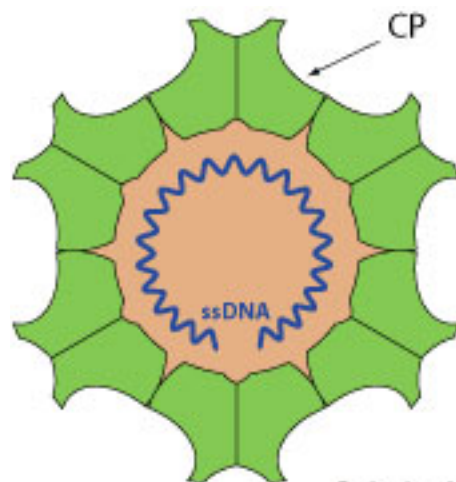
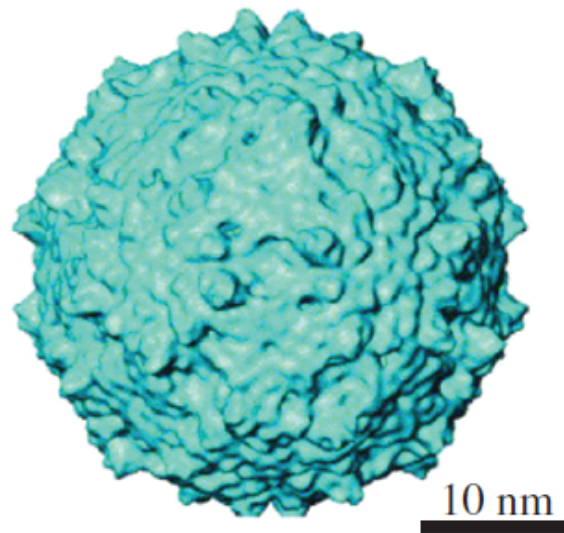
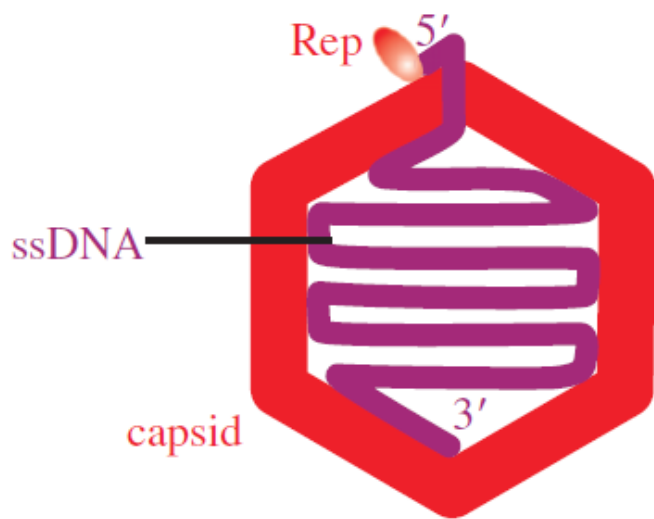


**Figure 12.1** Virions of adenovirus (arrowed) and dependovirus.

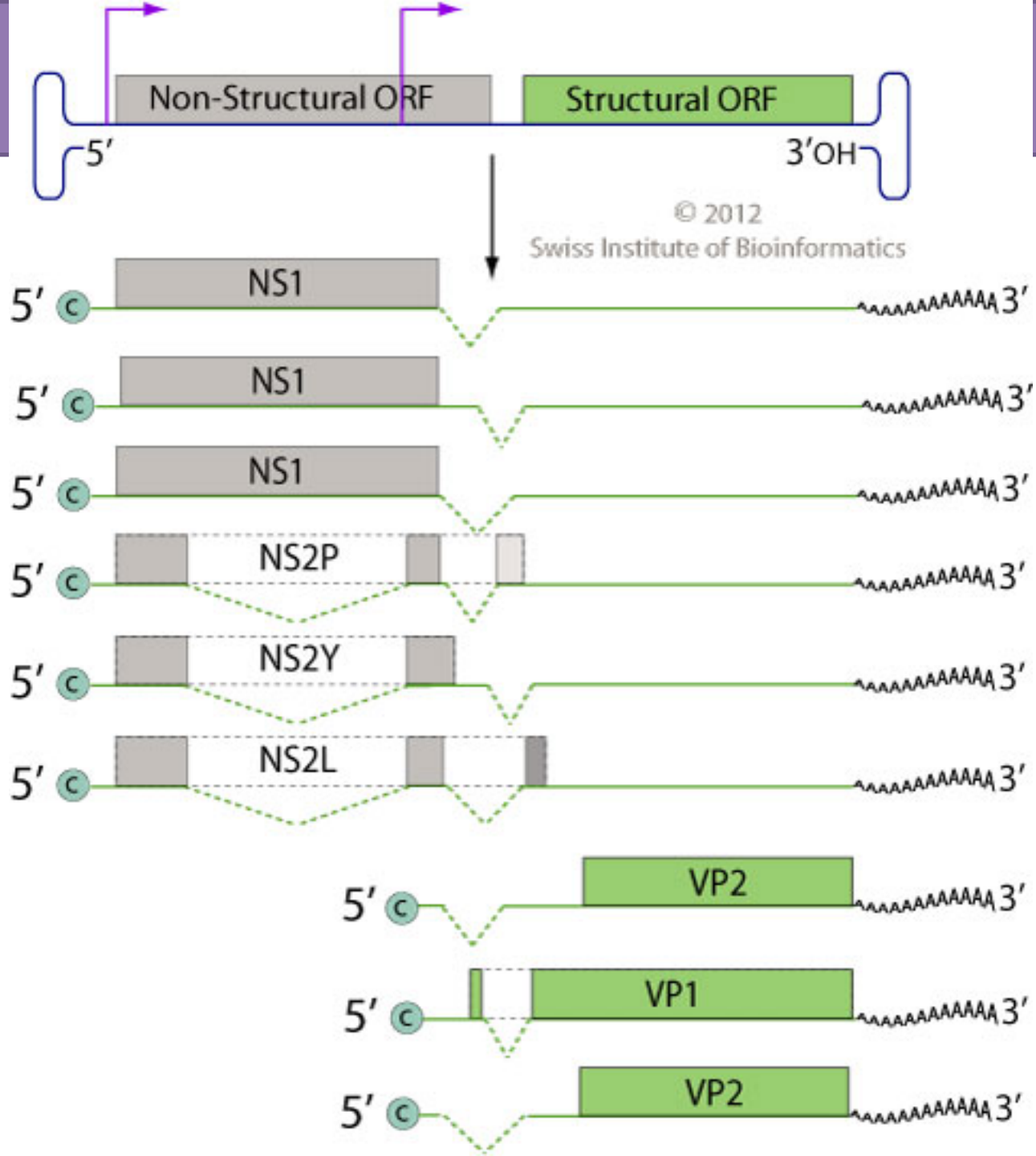
*Source:* Reproduced with permission of Professor M. Stewart McNulty and The Agri-Food and Biosciences Institute.



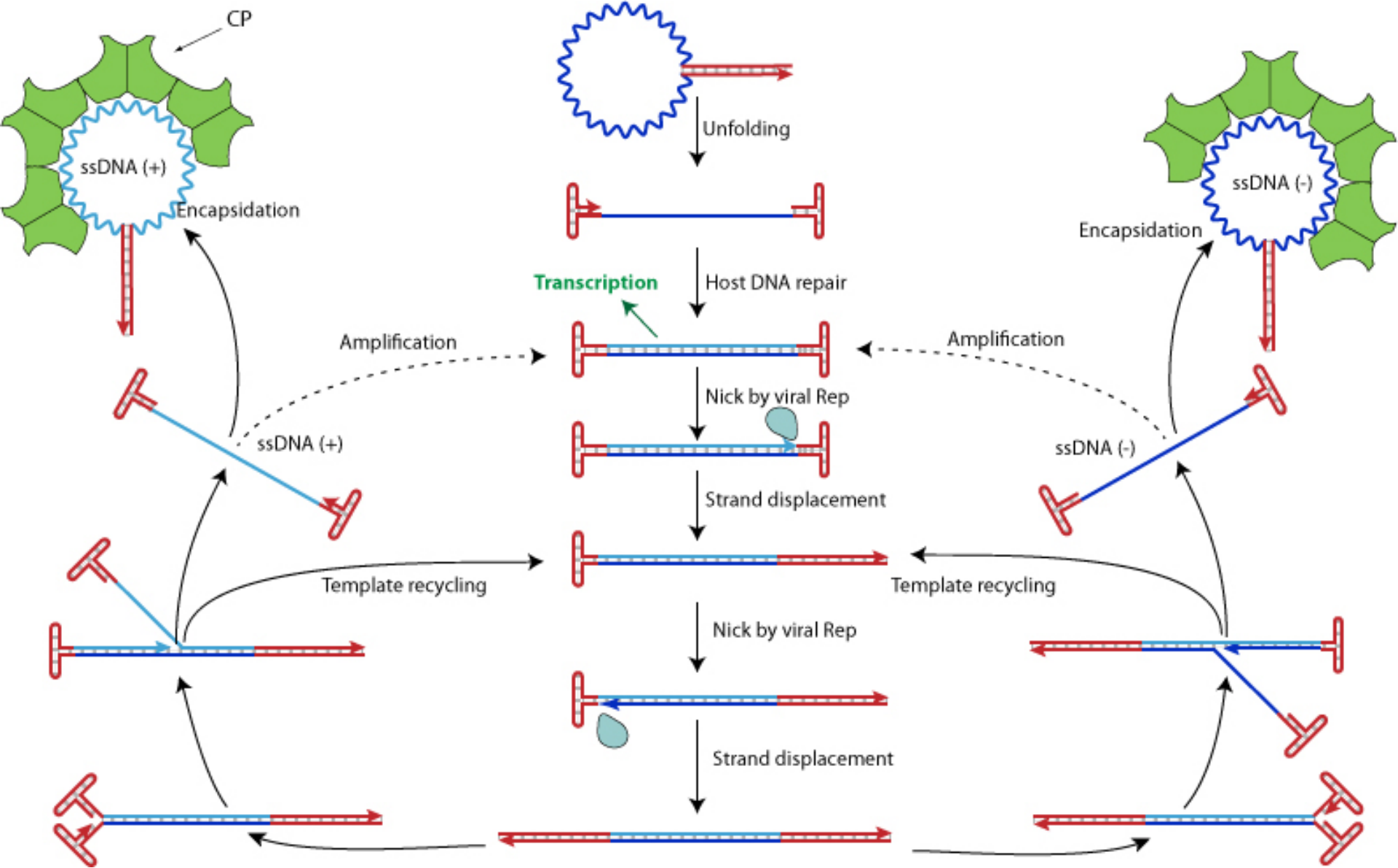
Figure 12.2 Child with fifth disease.



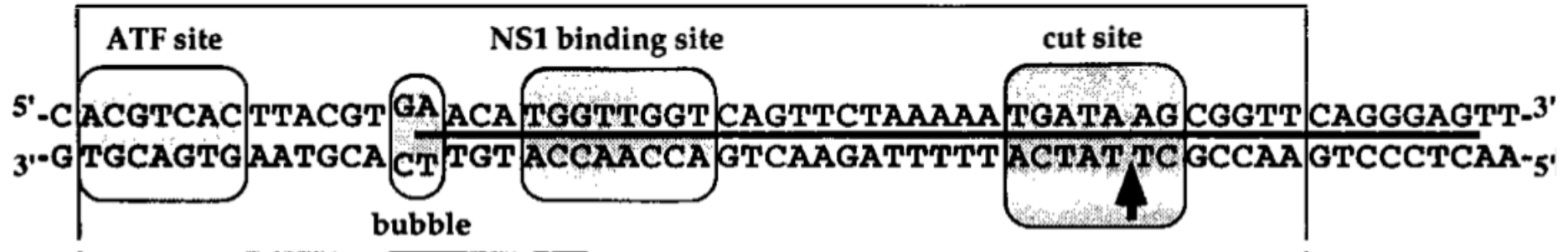




# Rolling hairpin Replication (AAV)

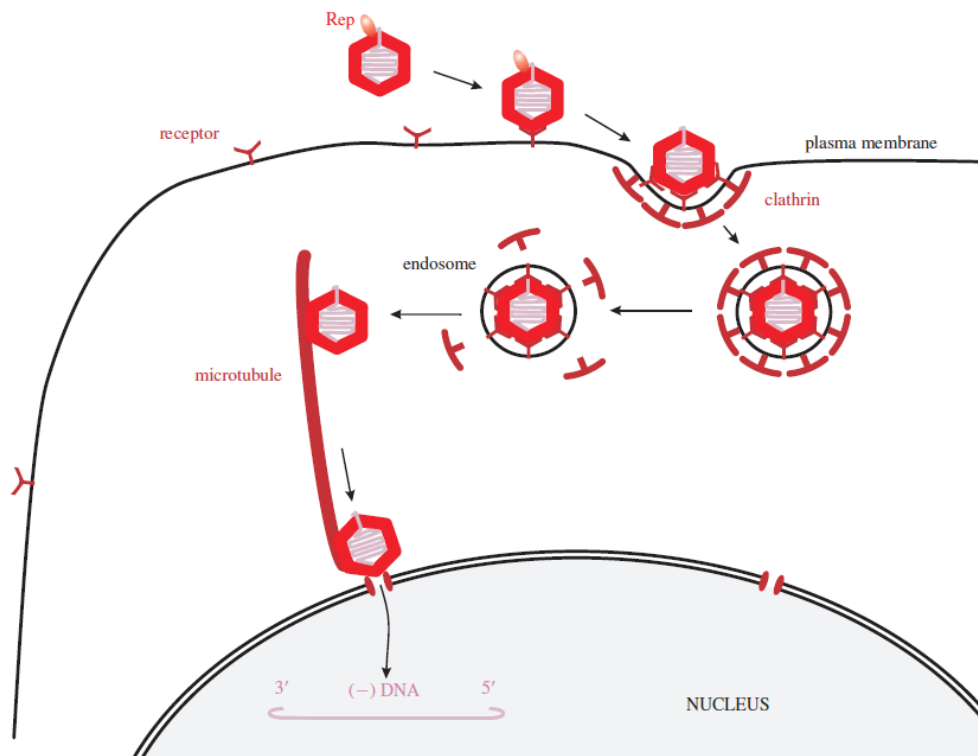


minimal origin

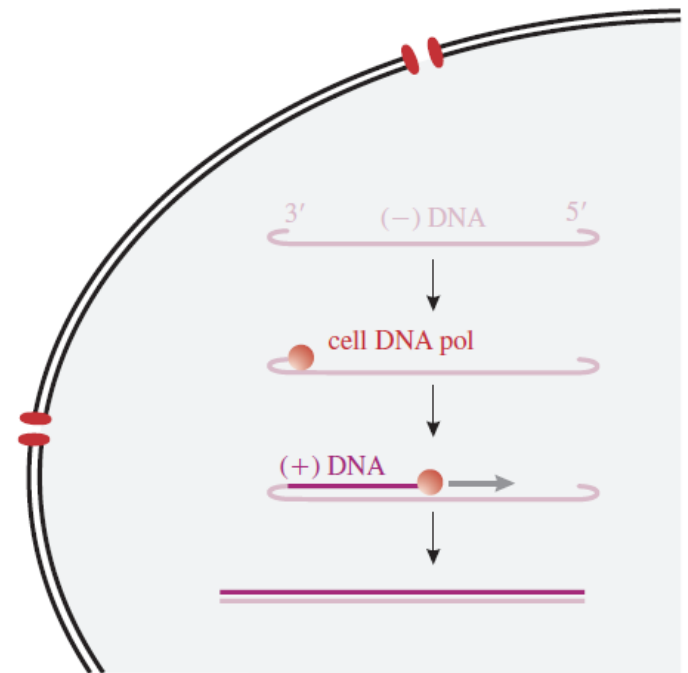


*Parvoviridae* (4–6 kb)

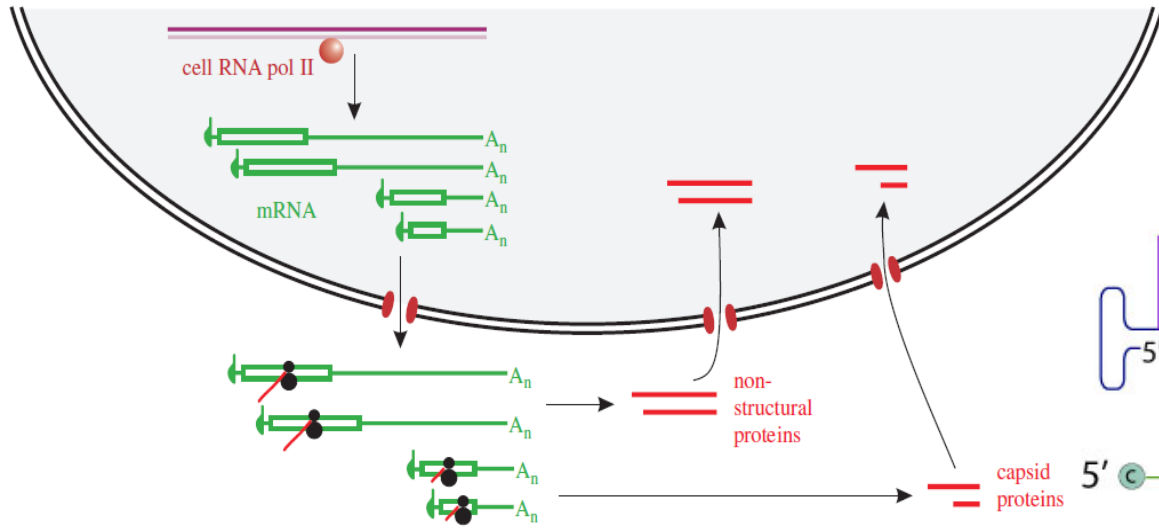




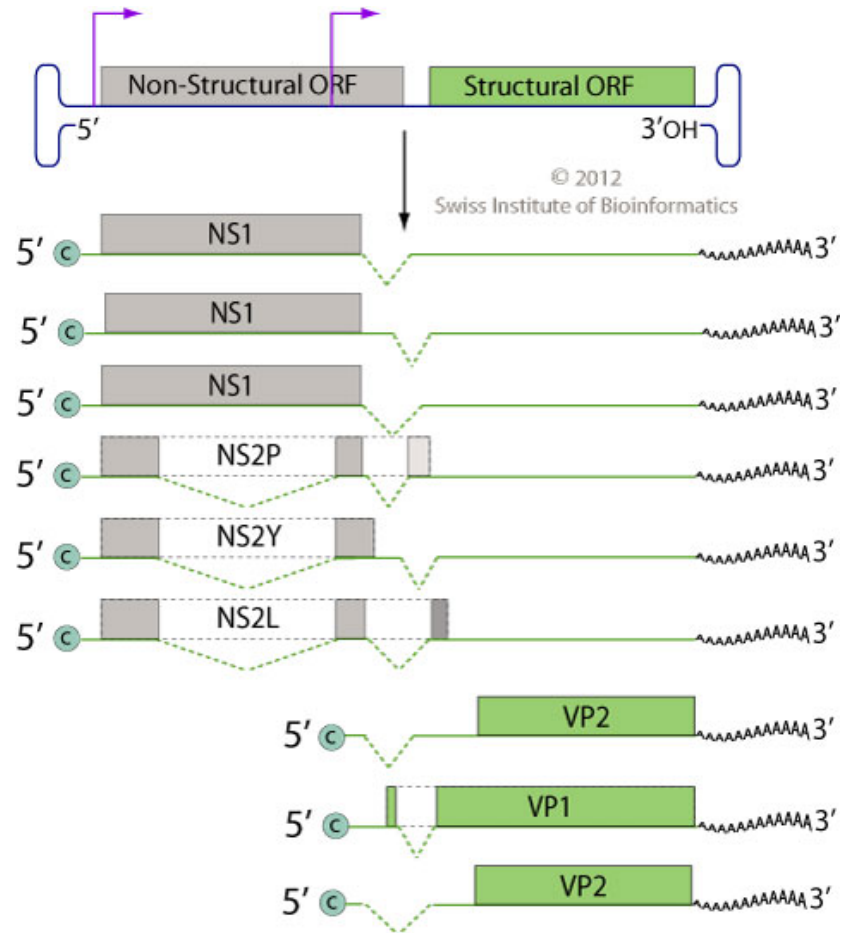
**Figure 12.6** Parvovirus attachment and entry. A virion is taken into the cell by clathrin-mediated endocytosis. After release from the endosome it is transported on a microtubule to a site close to the nucleus. It is uncertain whether uncoating of the virus genome occurs at a nuclear pore (as shown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



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



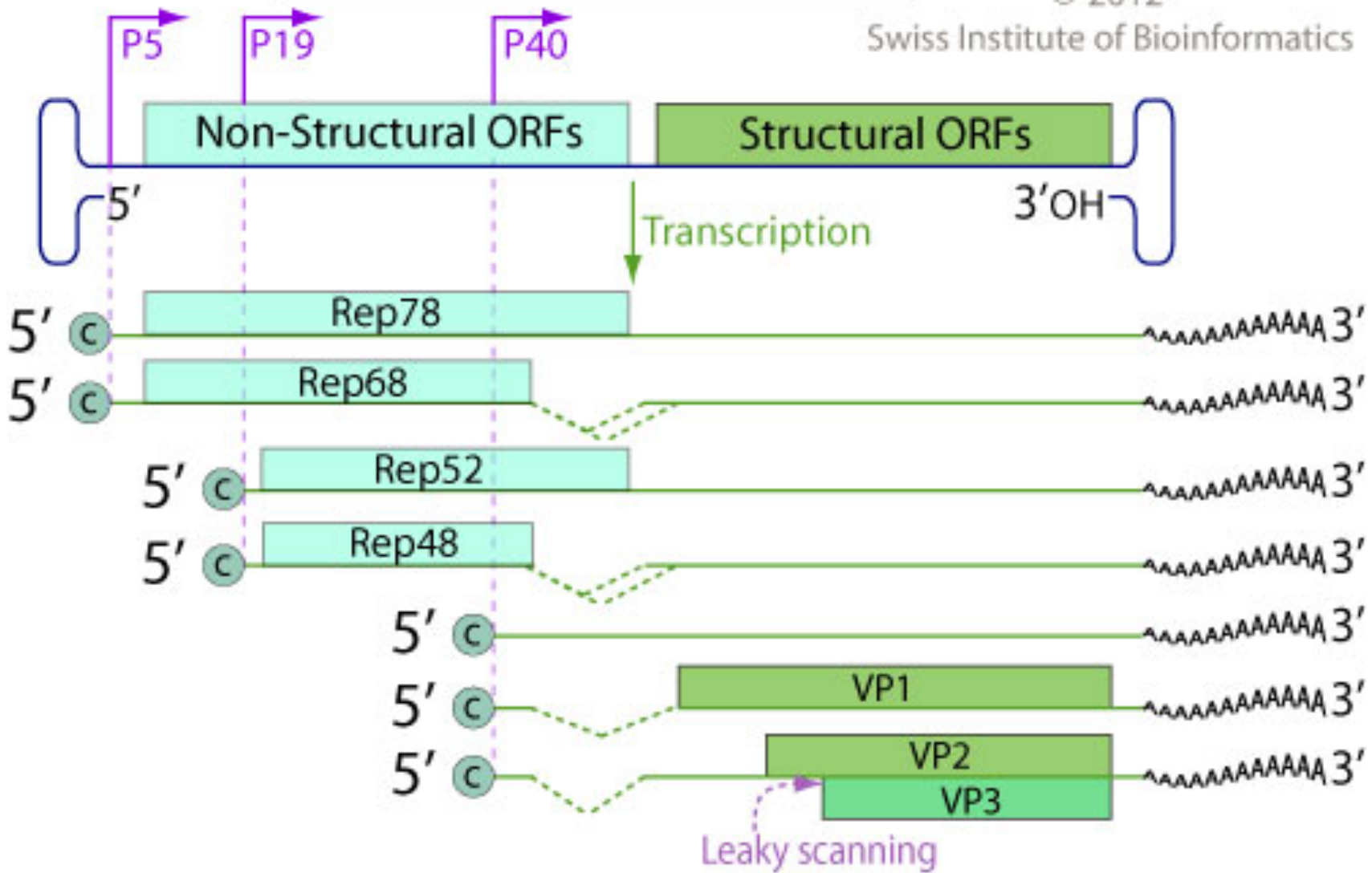
## Minute virus of mice genome organization



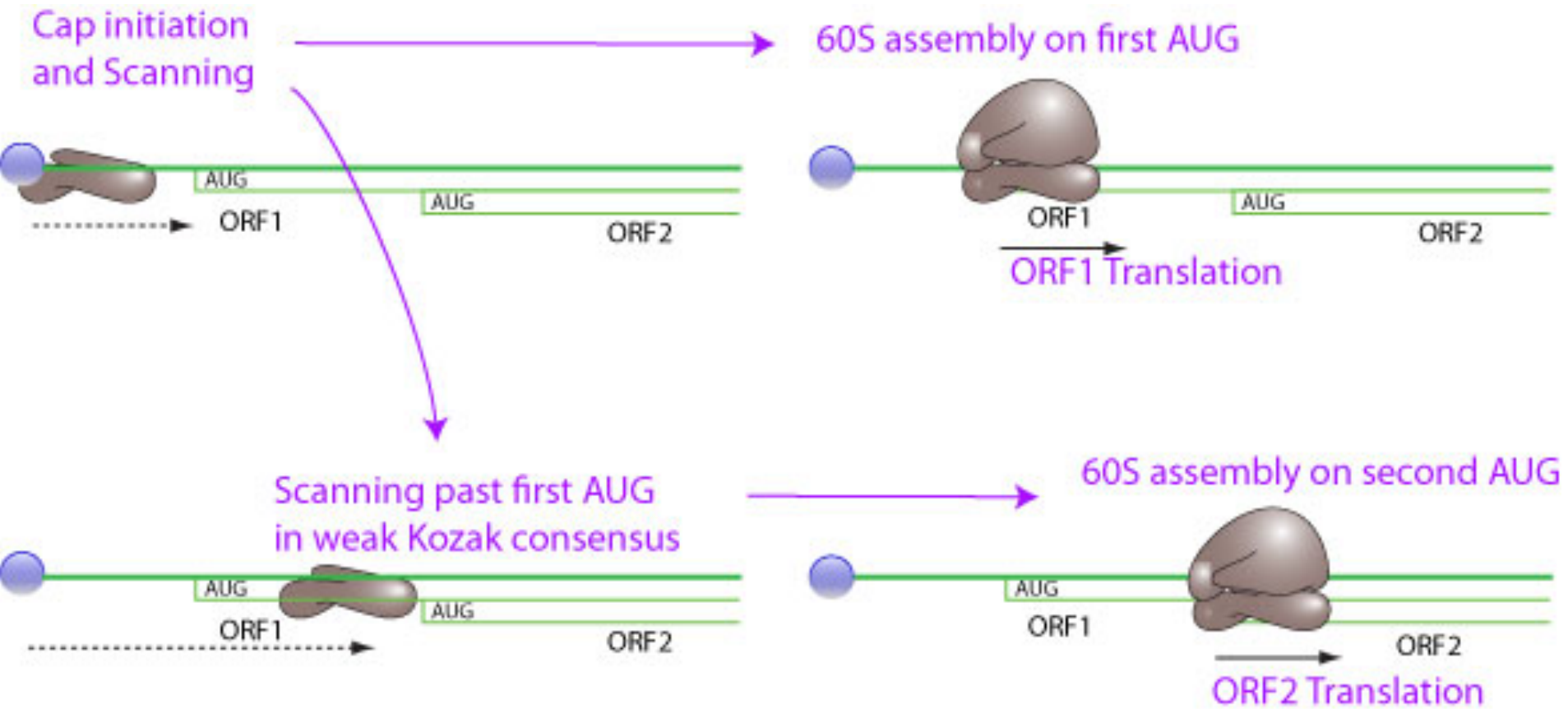
# Adeno-associated virus-2

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Swiss Institute of Bioinformatics



# Kozak's sequence: gccRccAUGG



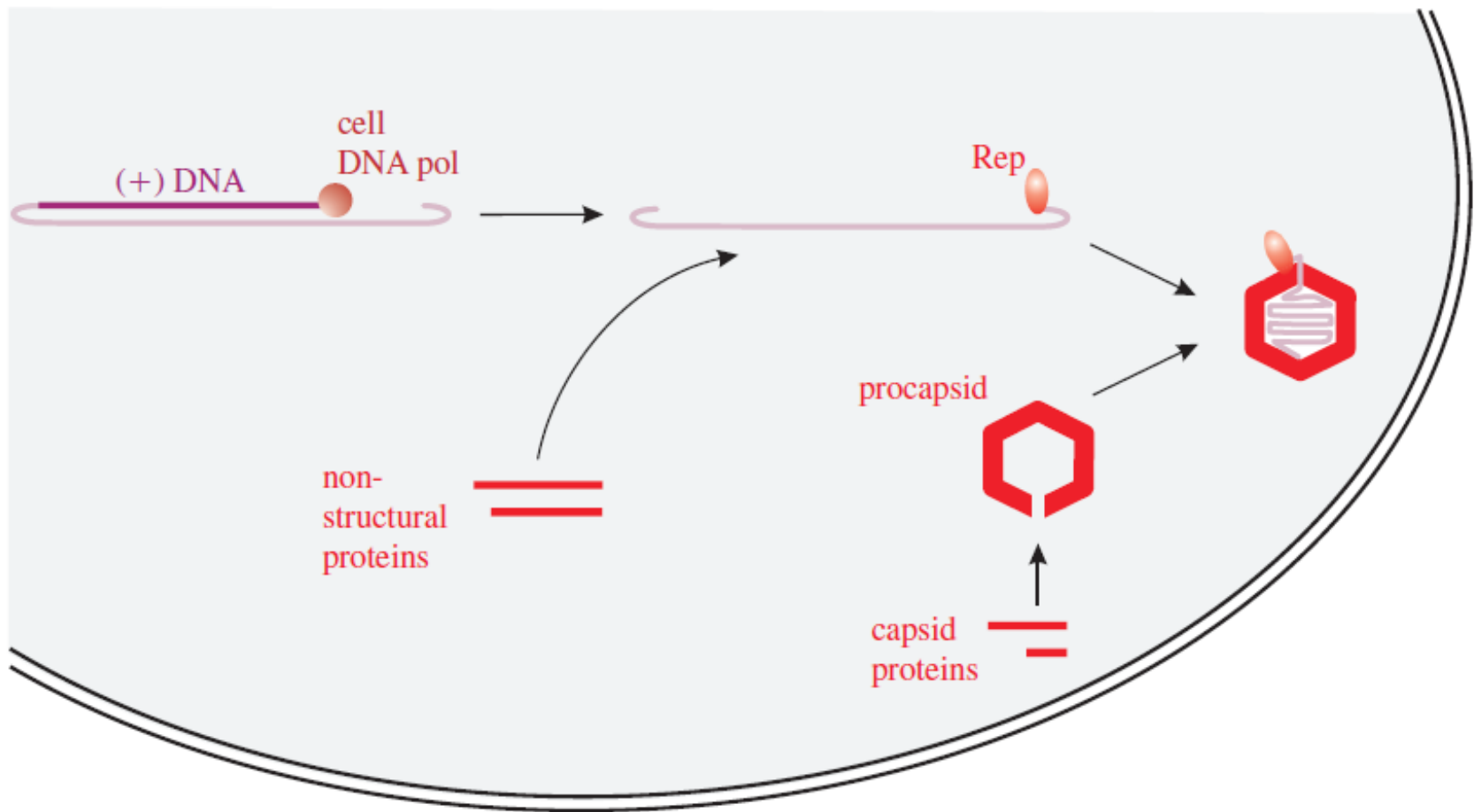
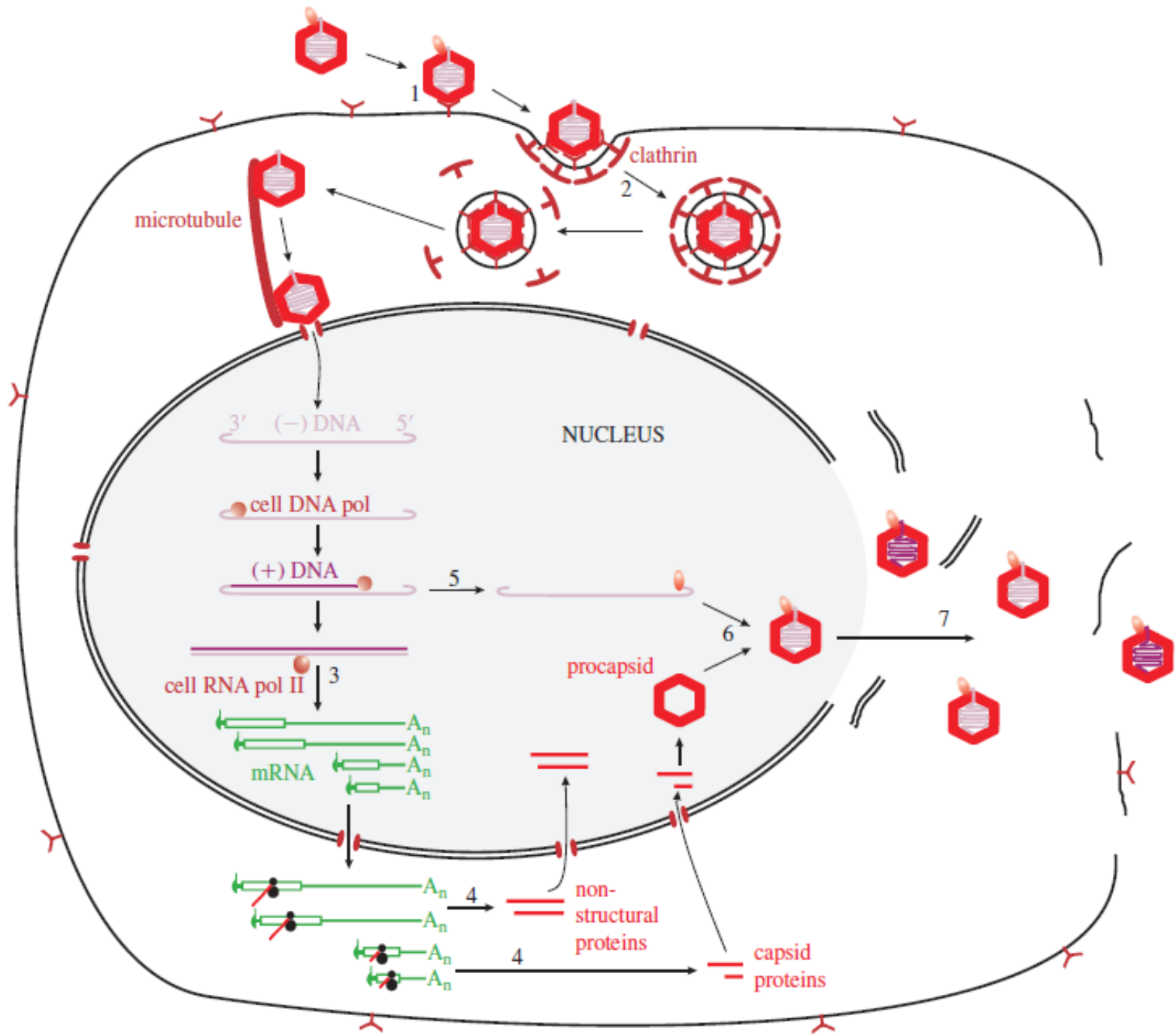
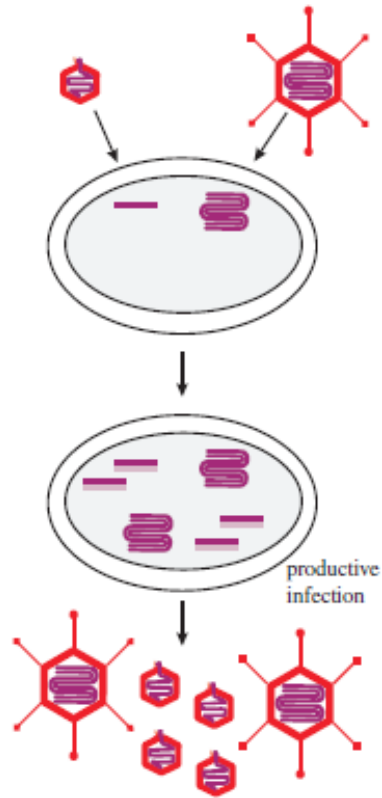


Figure 12.9 Parvovirus virion assembly.

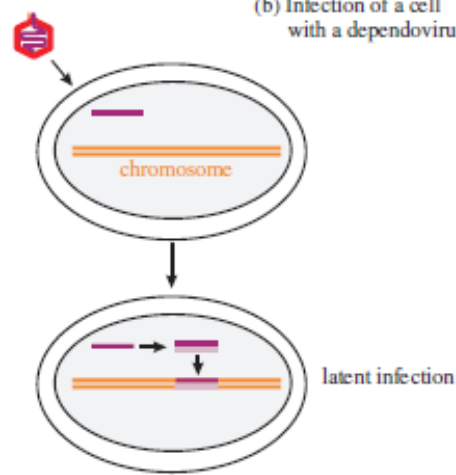




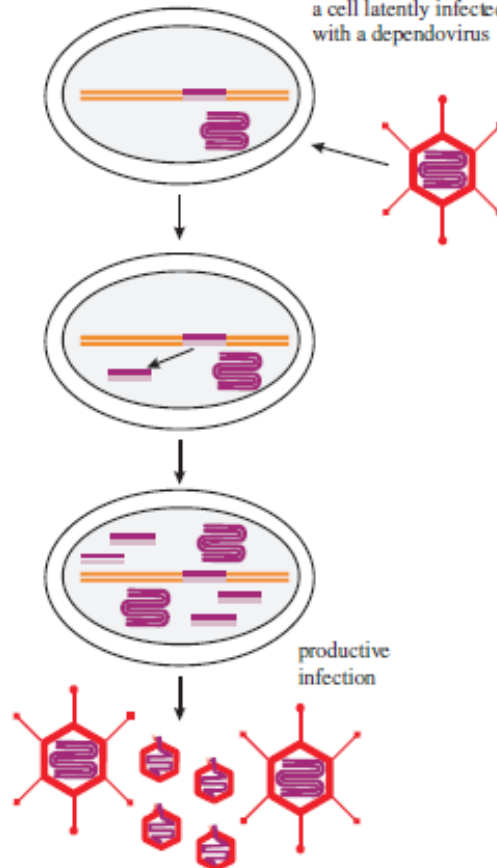
(a) Co-infection of a cell with a dependovirus and an adenovirus



(b) Infection of a cell with a dependovirus



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



# Learning outcomes

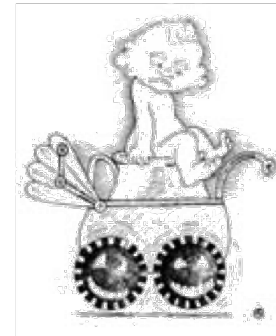
- give examples of parvoviruses and explain their importance;
- describe the parvovirus virion;
- outline the main features of the parvovirus genome;
- describe the replication cycle of parvoviruses;
- explain the difference between autonomous and defective parvoviruses.

# Reoviridae

**Hosts:** mammals  
birds  
fish  
insects  
plants  
fungi

**Respiratory**  
**Enteric**  
**Orphan**

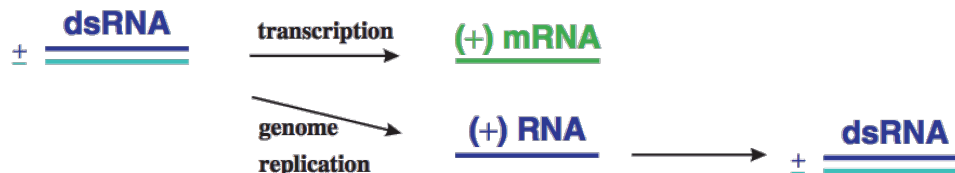
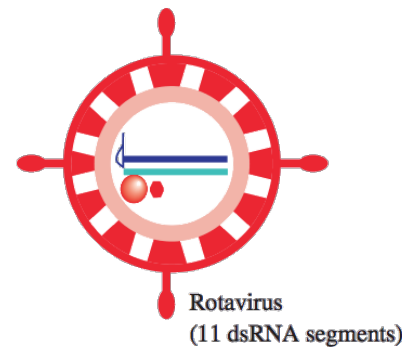
**Disease:** gastroenteritis in humans and animals (rotaviruses)

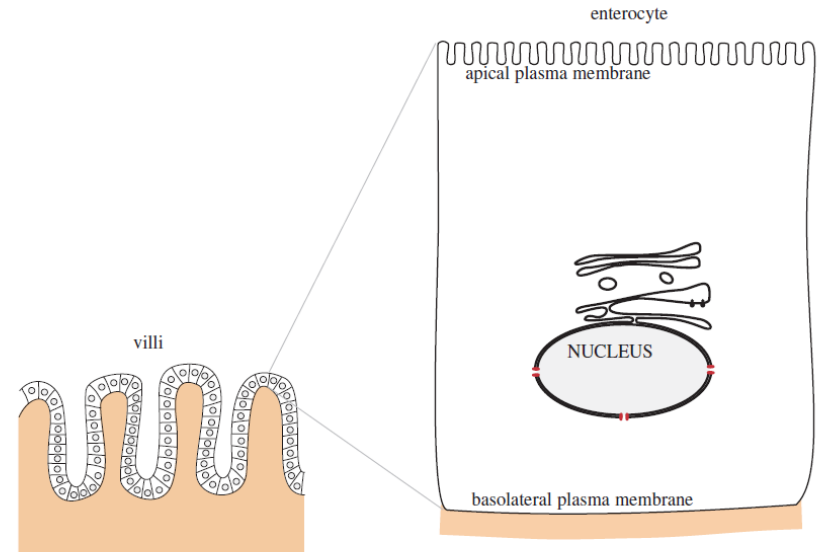


**'Diarrhoea On Wheels'**

## Virion

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



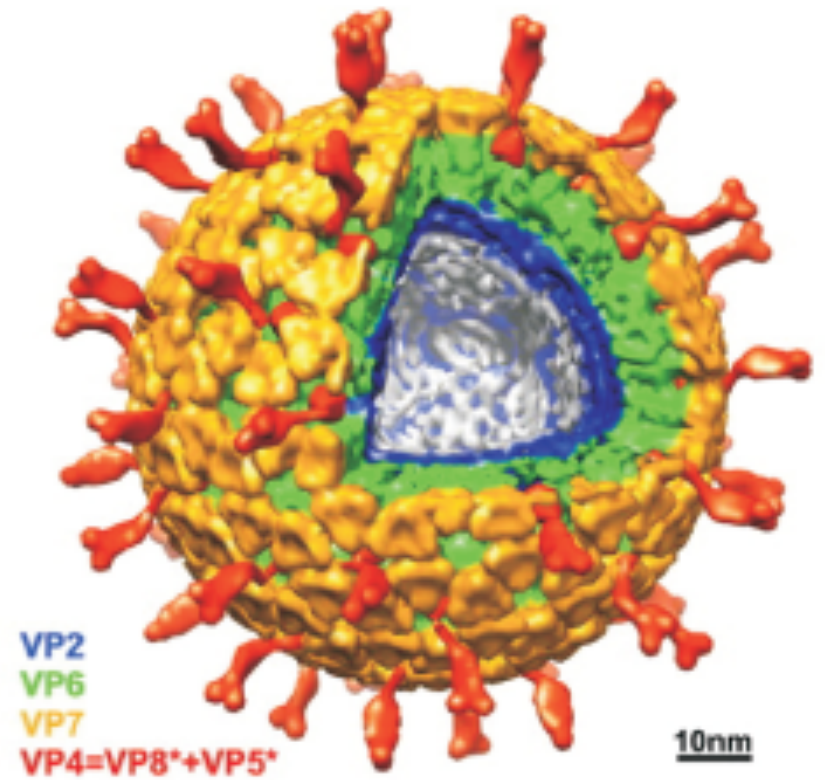
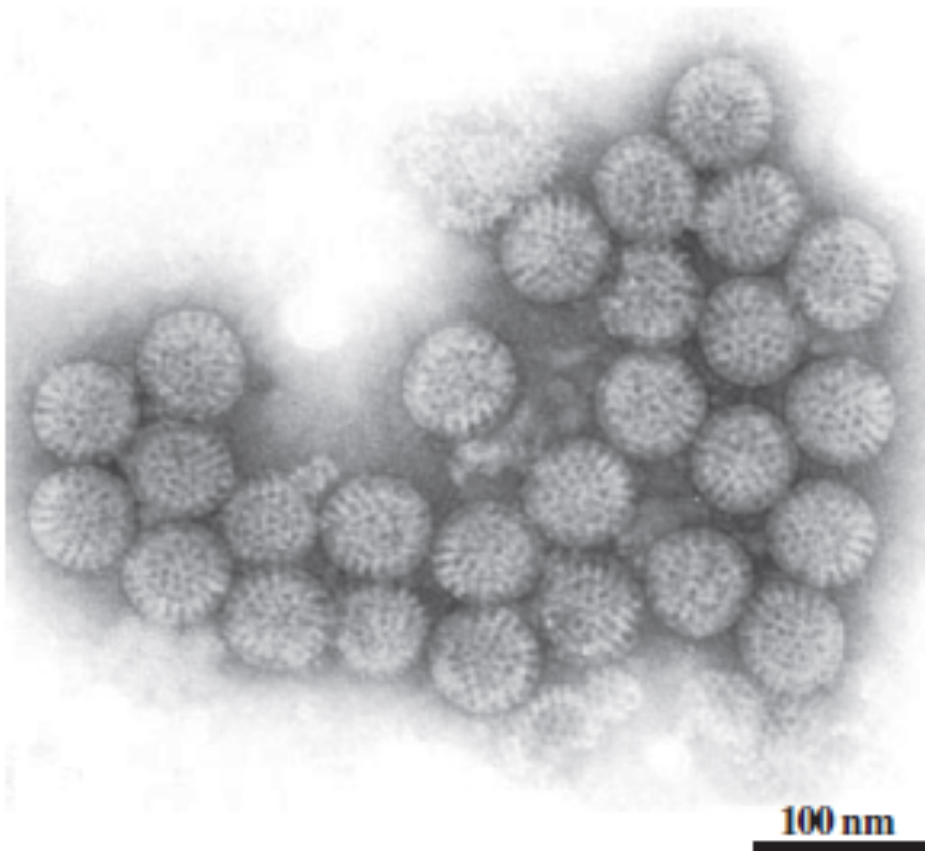


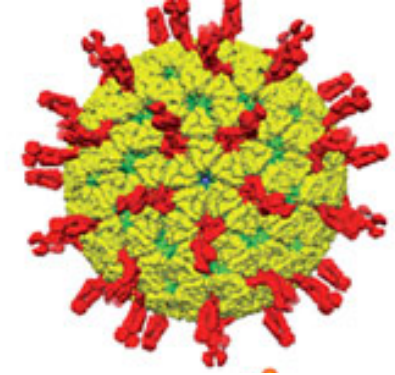
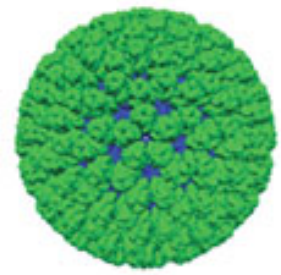
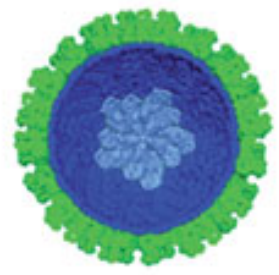
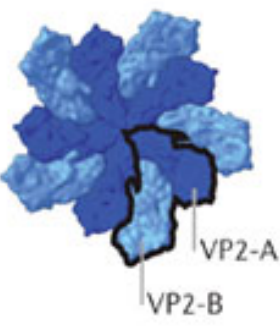
NSP4 induces:

- 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

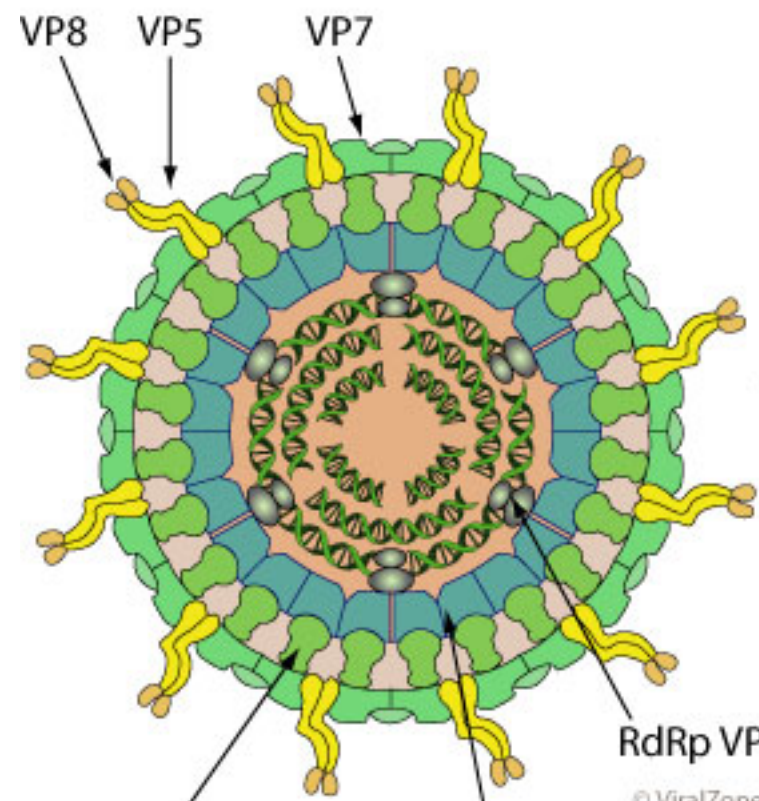
Electron micrograph of negatively stained virions





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

**OUTER CAPSID**

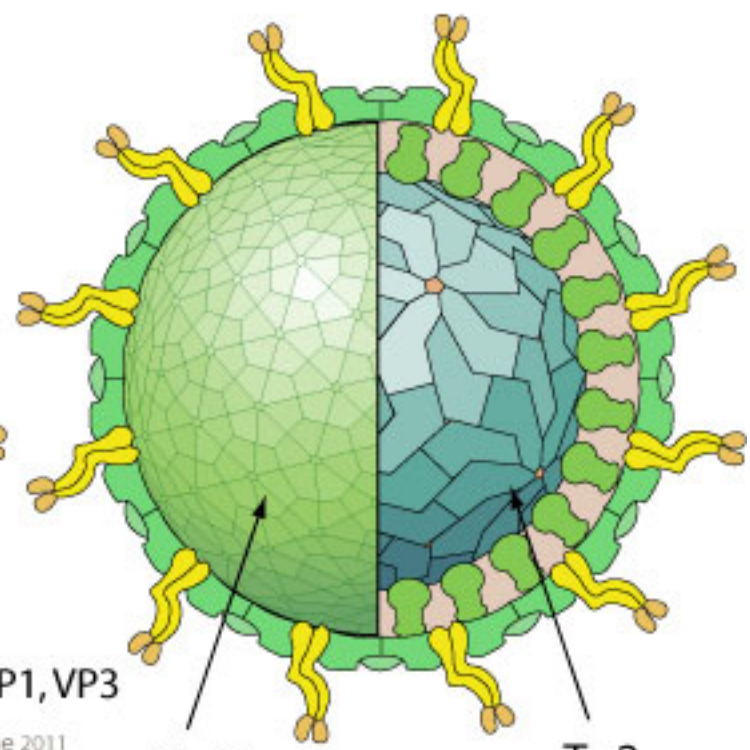


VP6  
**INTERMEDIATE CAPSID**

VP2  
**INNER CAPSID**

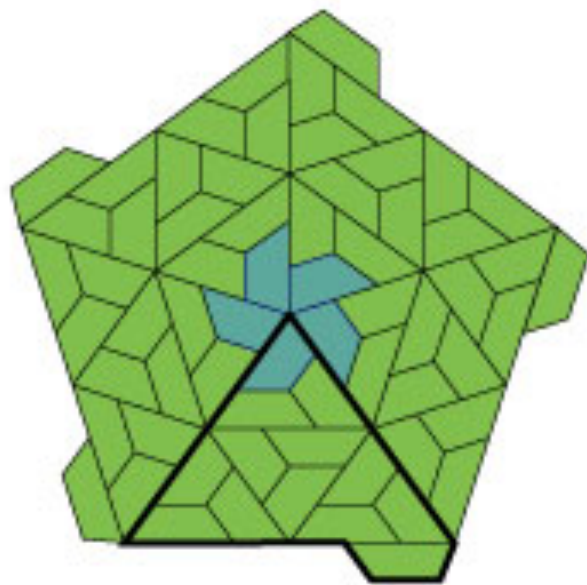
RdRp VP1, VP3

© ViralZone 2011  
Swiss Institute of Bioinformatics

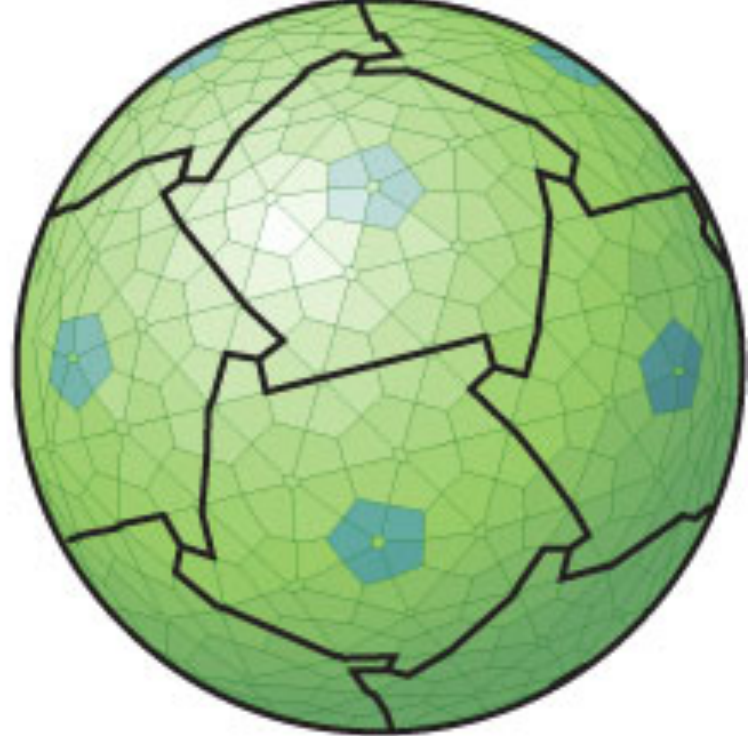




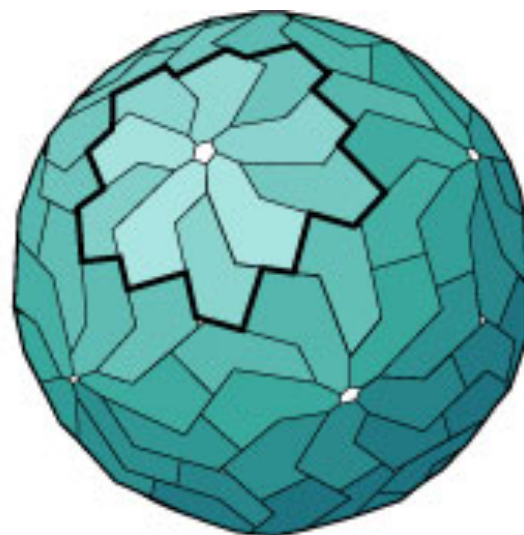
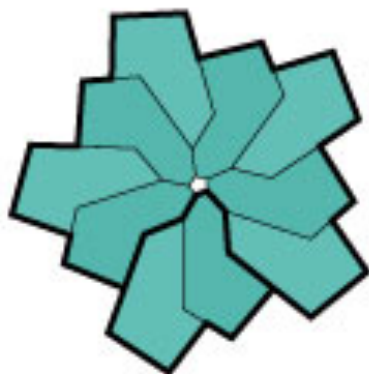
x60



x12



© 2010

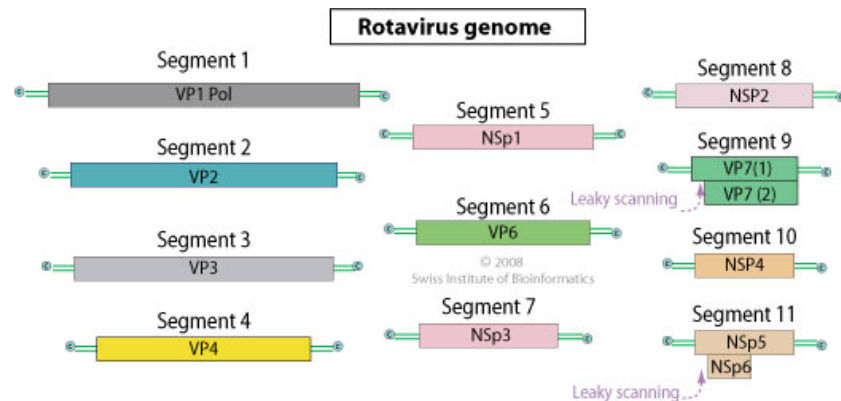
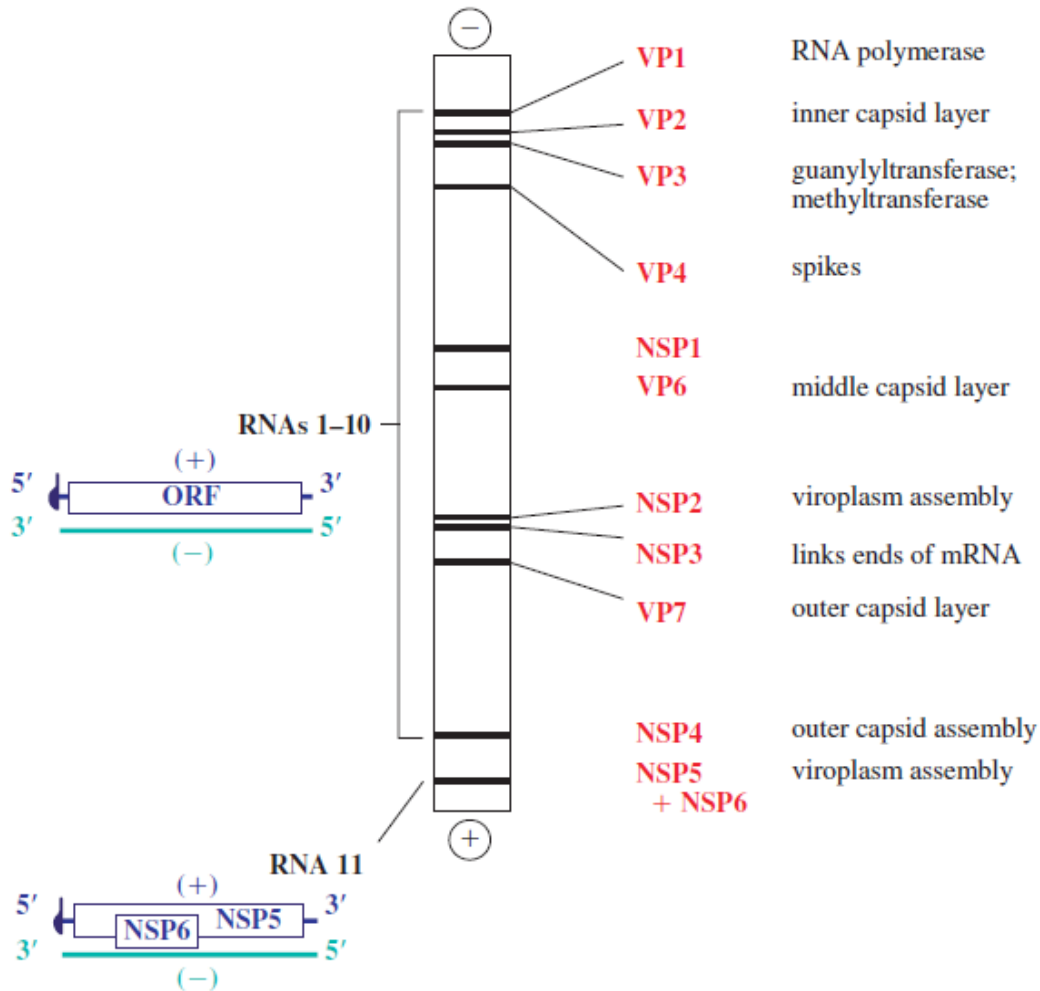




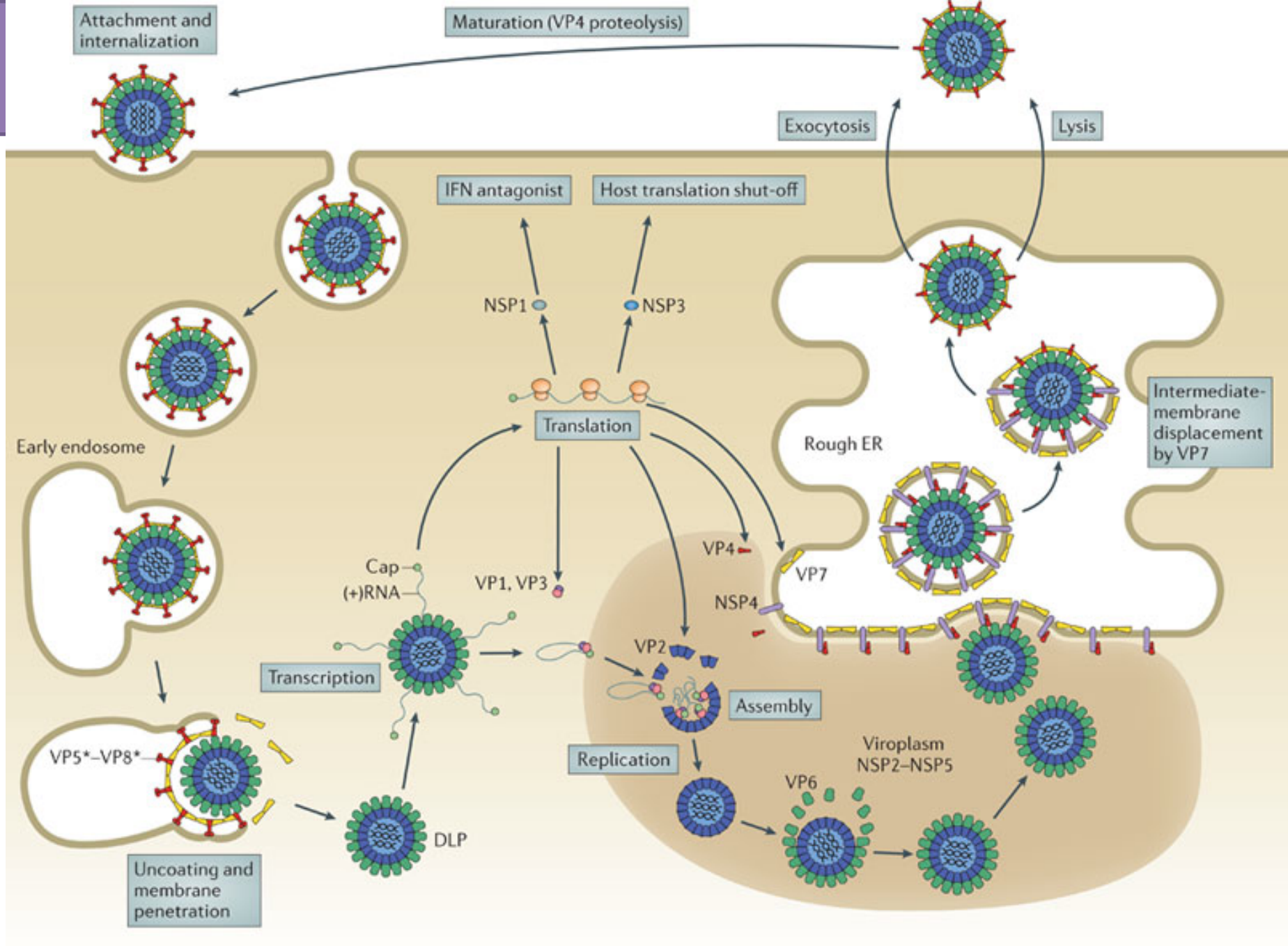
RNA bands  
in gel after  
separation by  
electrophoresis

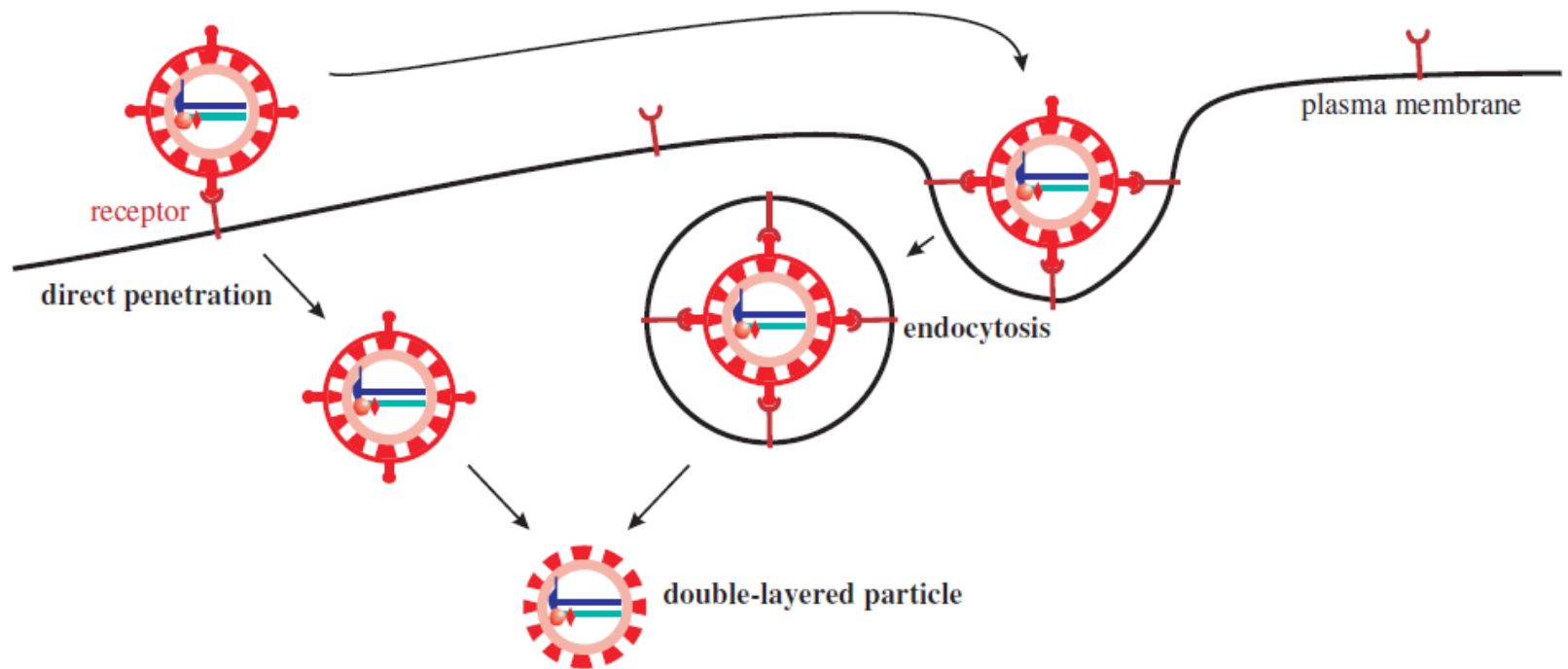
Gene  
product(s)

Function

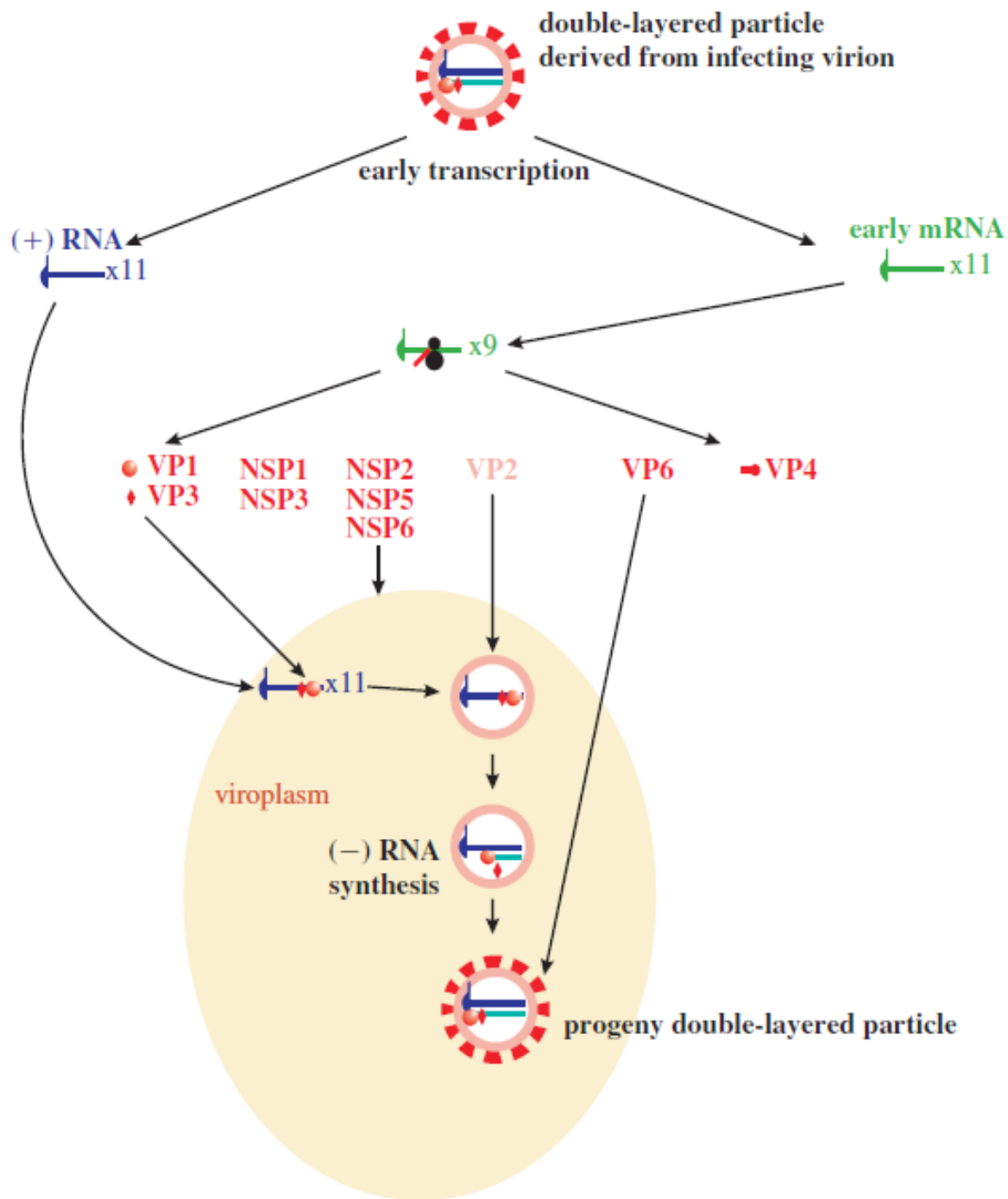


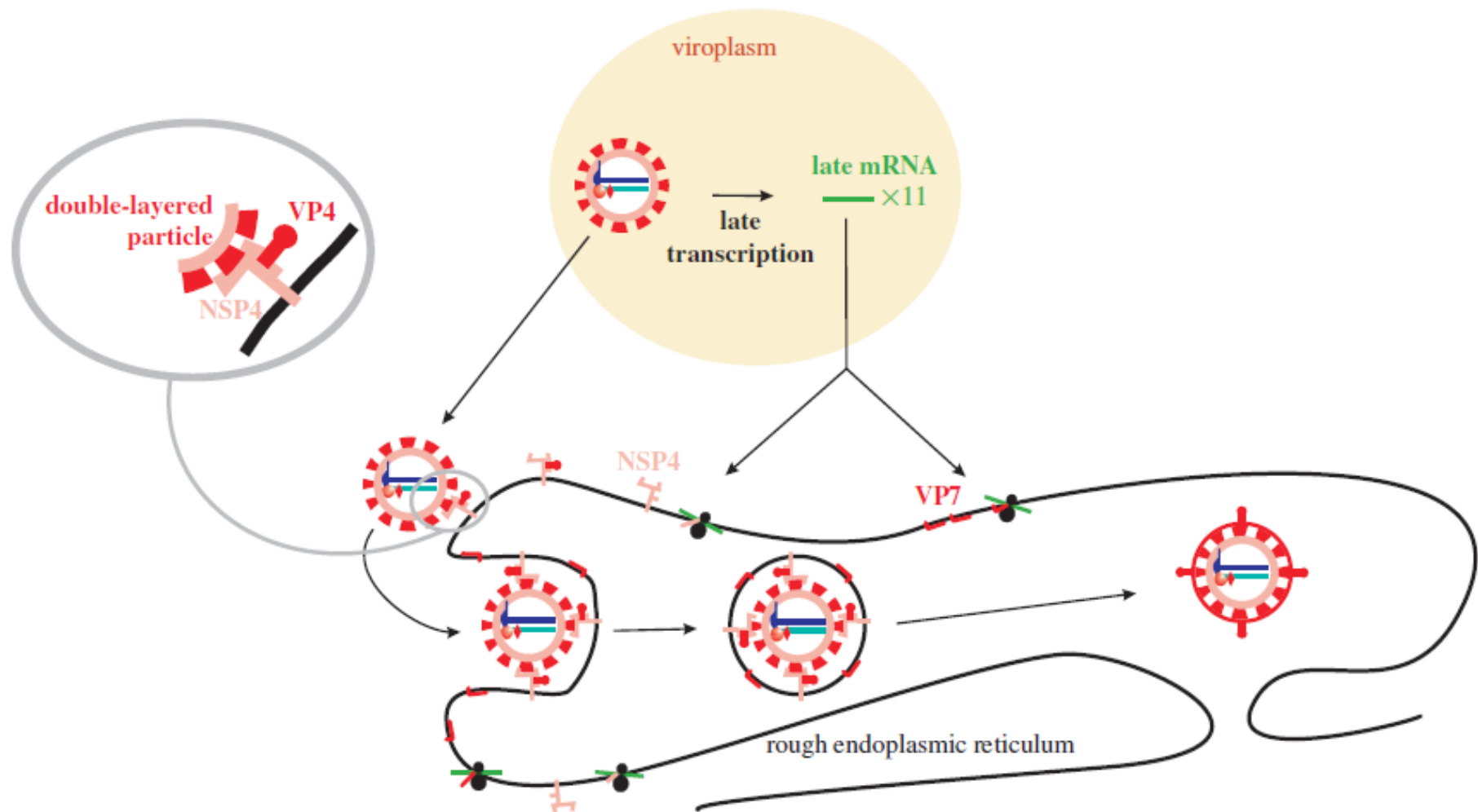
Key: ORF open reading frame  
VP virus protein (structural protein)  
NSP non-structural protein



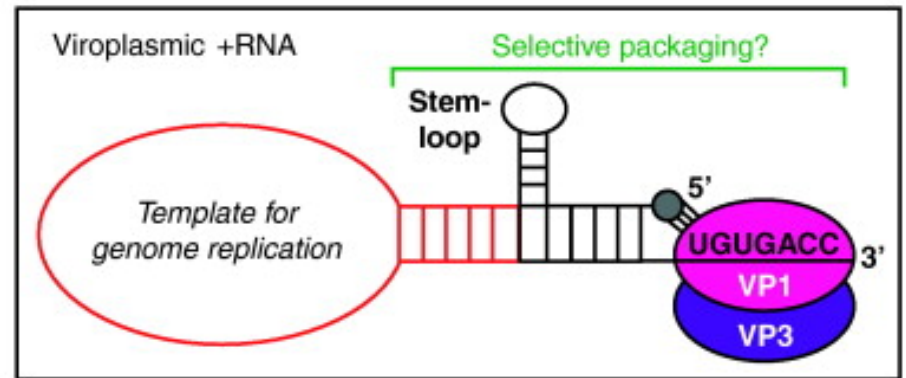
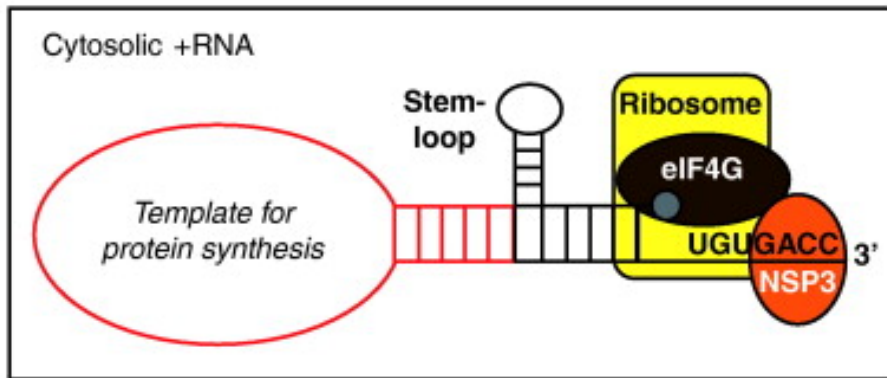


**Figure 13.5** Modes of rotavirus entry into the host cell. A rotavirus virion may either penetrate the plasma membrane or it may be endocytosed. Only one of the 11 dsRNA molecules in the virion is shown.

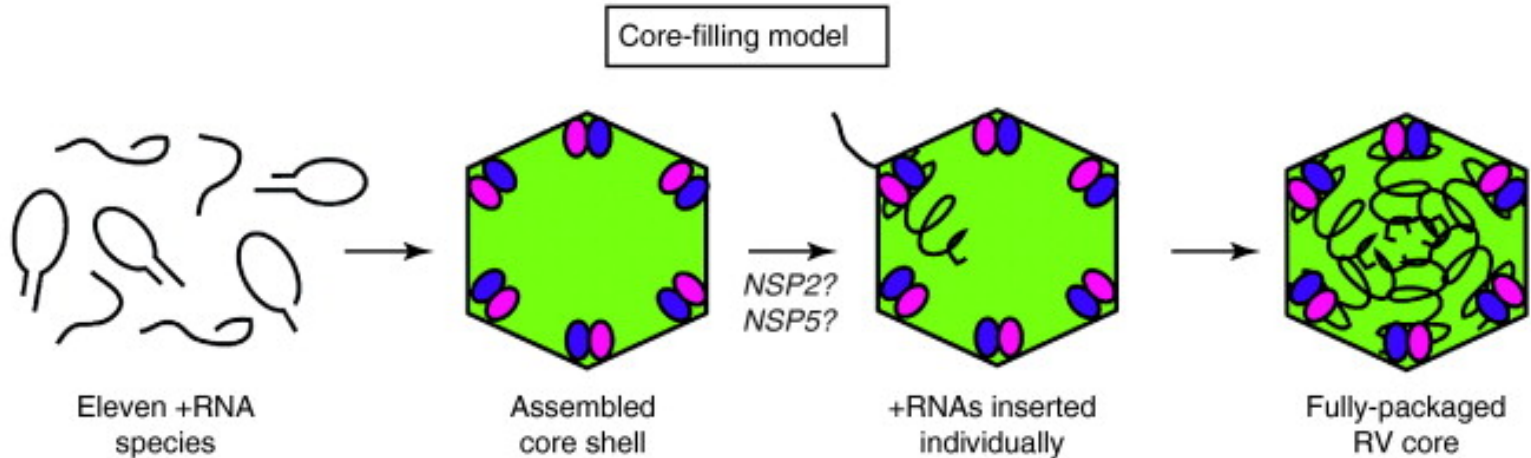
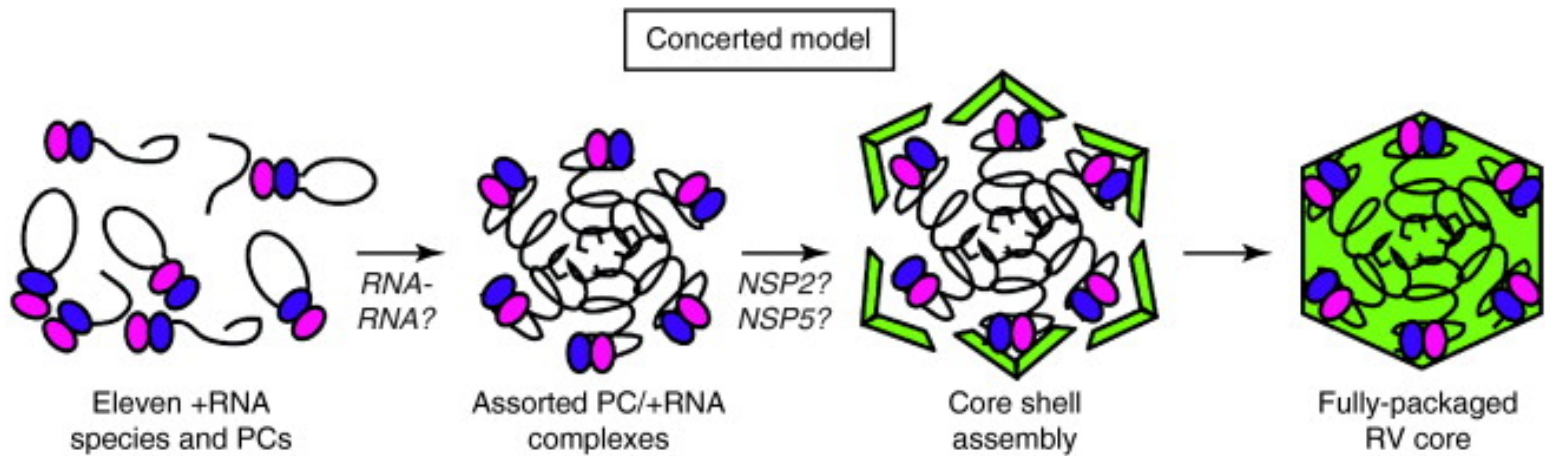




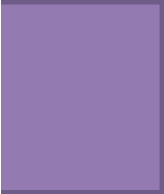
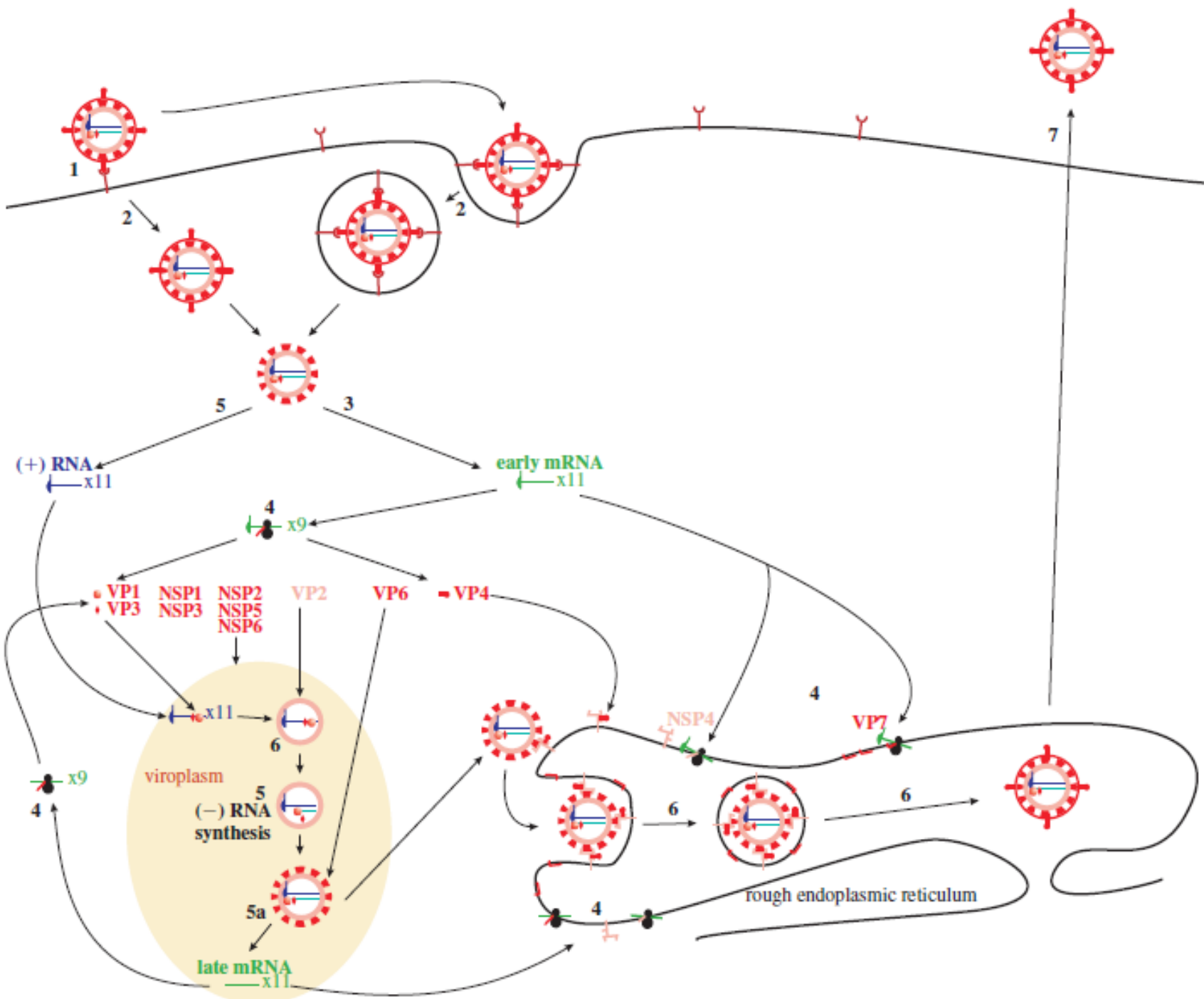
**Figure 13.7** Late events in rotavirus replication. Secondary transcription takes place in progeny double-layered particles and results in the synthesis of uncapped mRNA. The 12 virus proteins are translated; only NSP4 and VP7 translation are shown here (both are synthesized in the endoplasmic reticulum). 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.



TRENDS in Microbiology



*TRENDS in Microbiology*





# Learning outcomes

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

# Picornaviruses

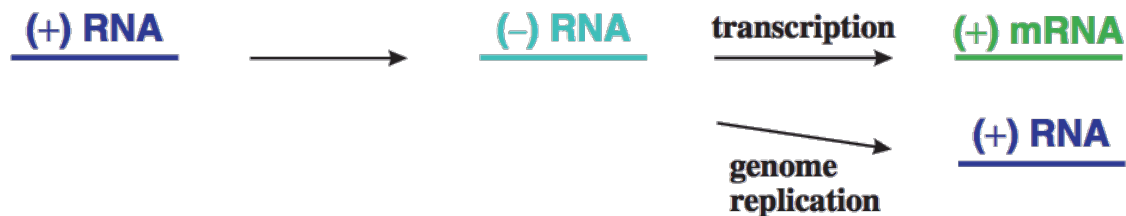
**Pico** (= small) **RNA** viruses

**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



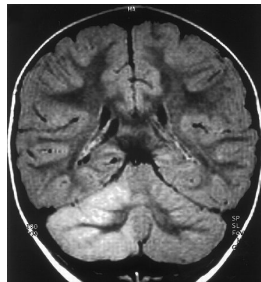
# Human picornaviruses

## 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

## 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.



GETTY IMAGES

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

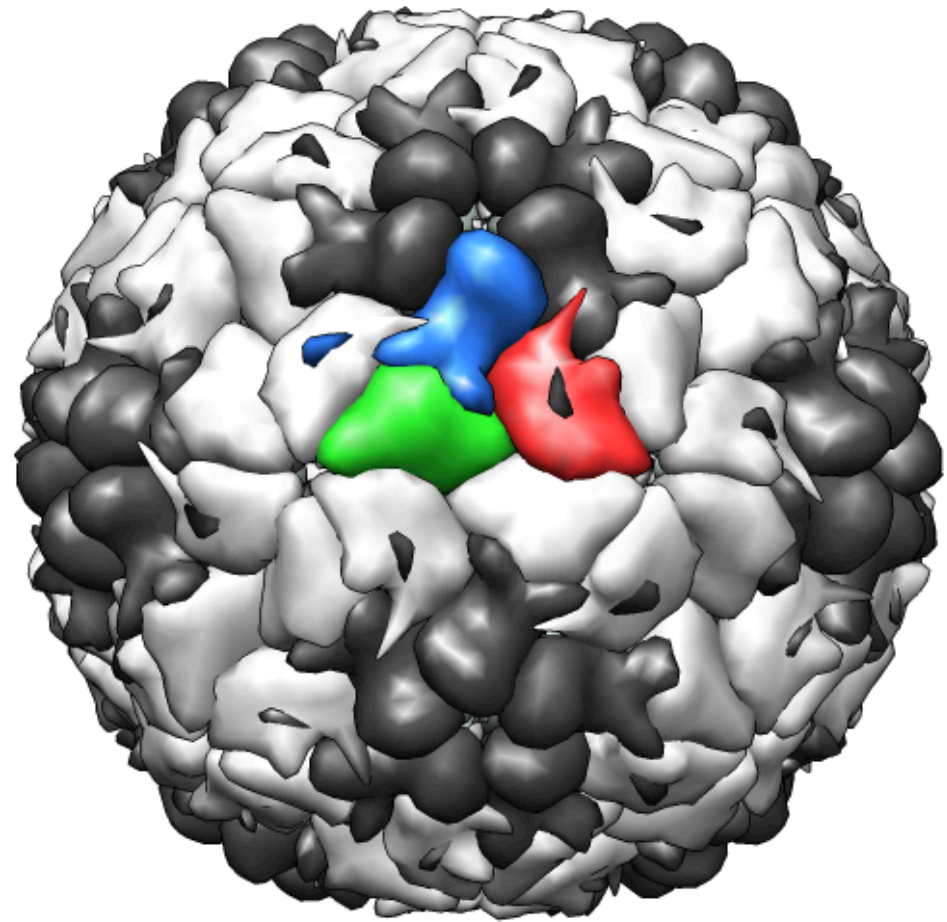
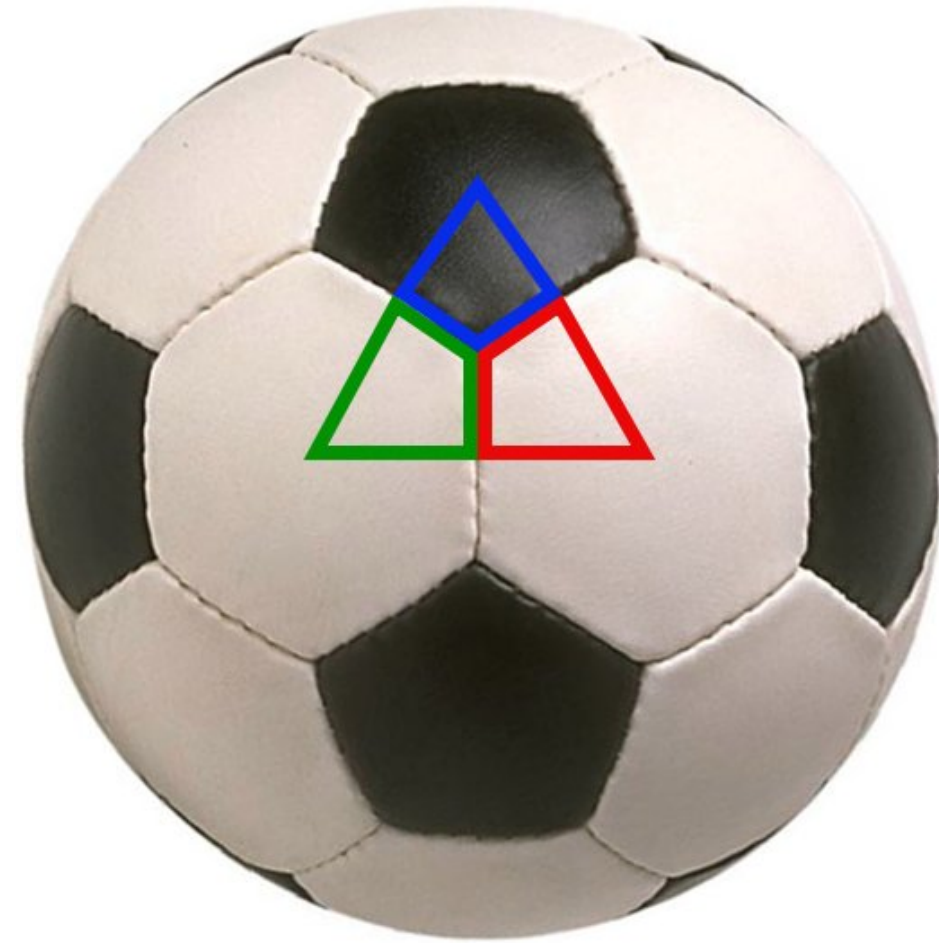
The number of reported cases of the virus in children rose to 3,736 early Saturday in the hardest-hit city of Fuyang, according to the state-run news agency. There were 3,321 reported cases Friday in Fuyang.

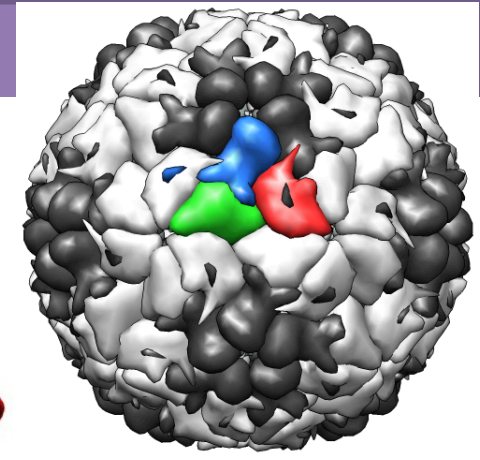
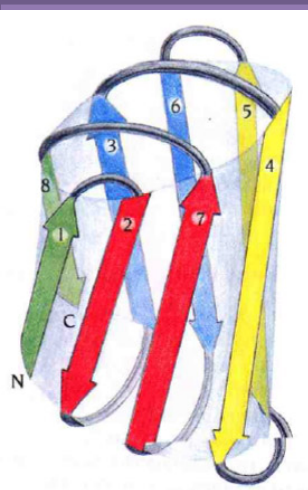
Xinhua reported that 4,529 children have been sickened in 15 cities in Anhui province.

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.

# Picornavirus virion

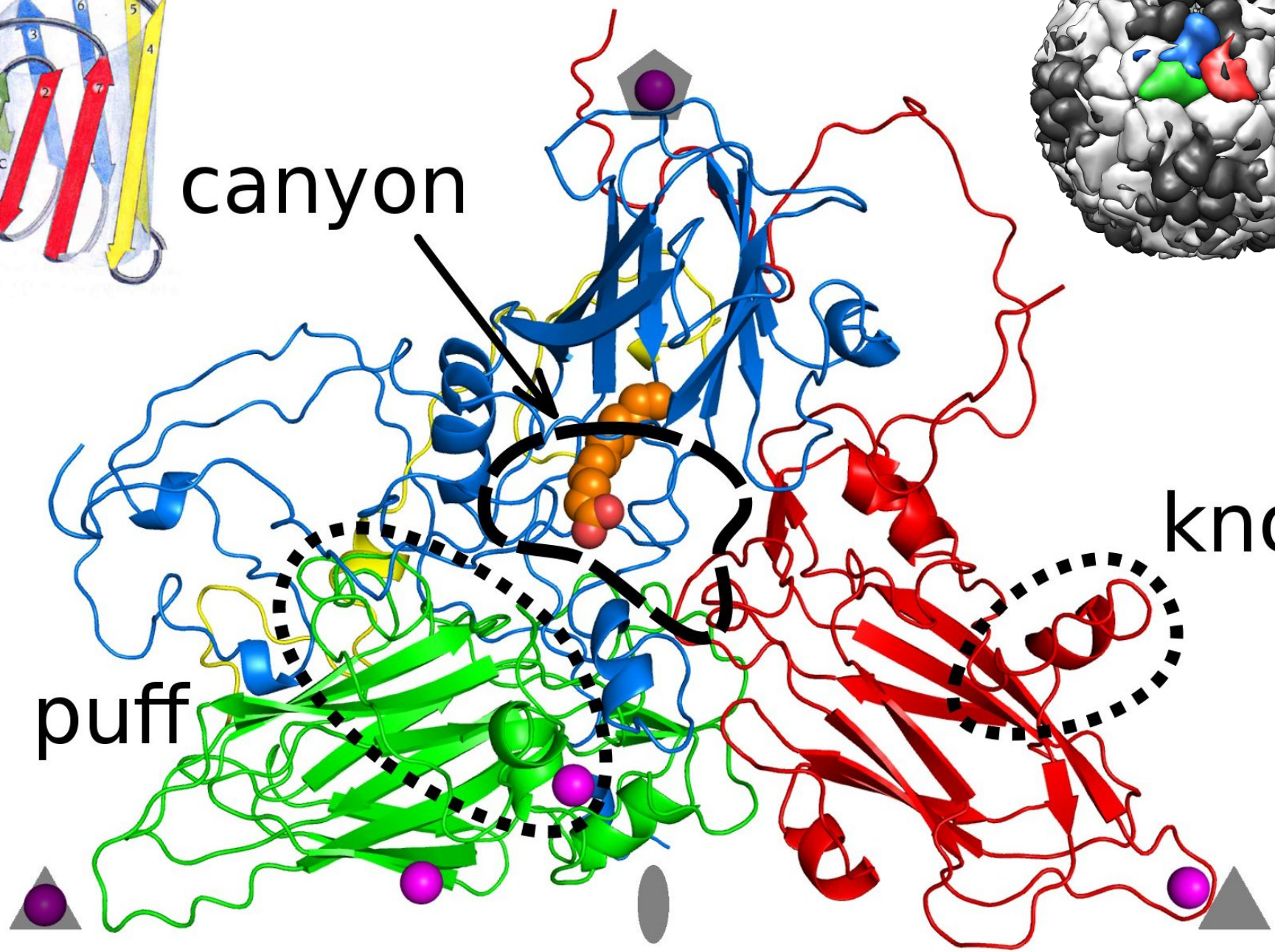




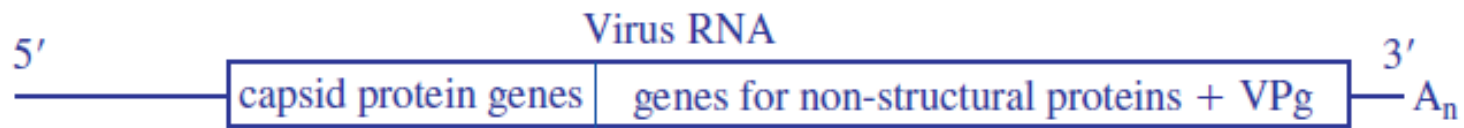
canyon

knob

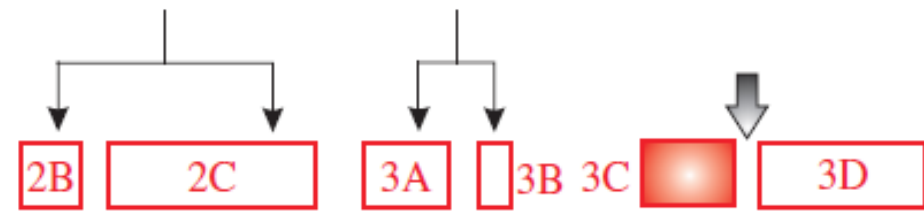
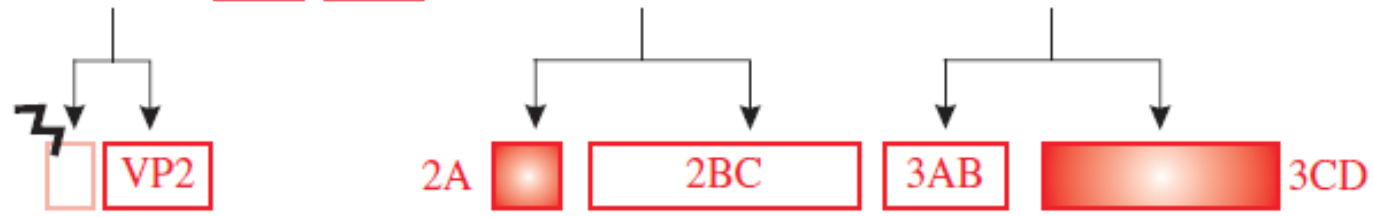
puff







polyprotein

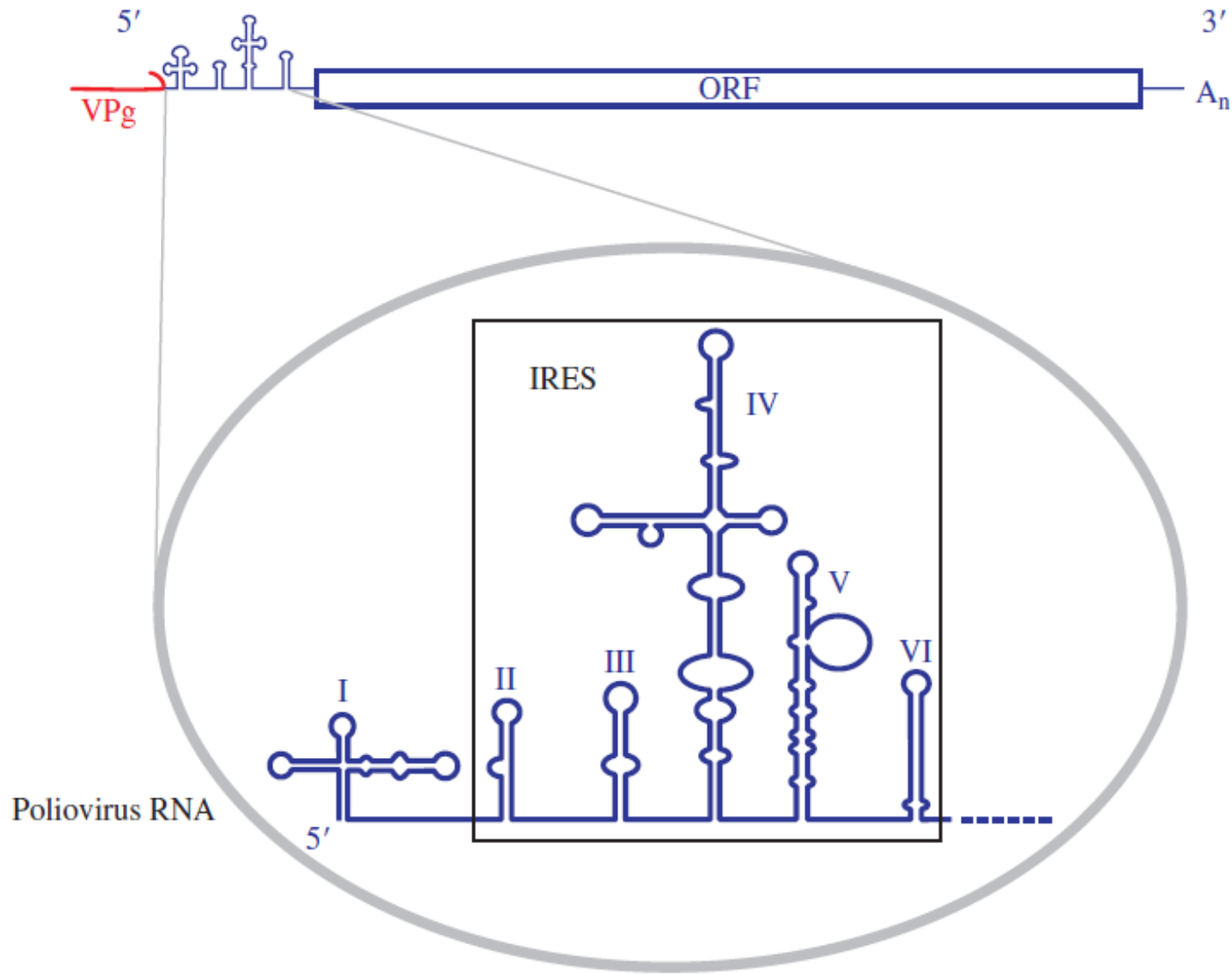


ATPase

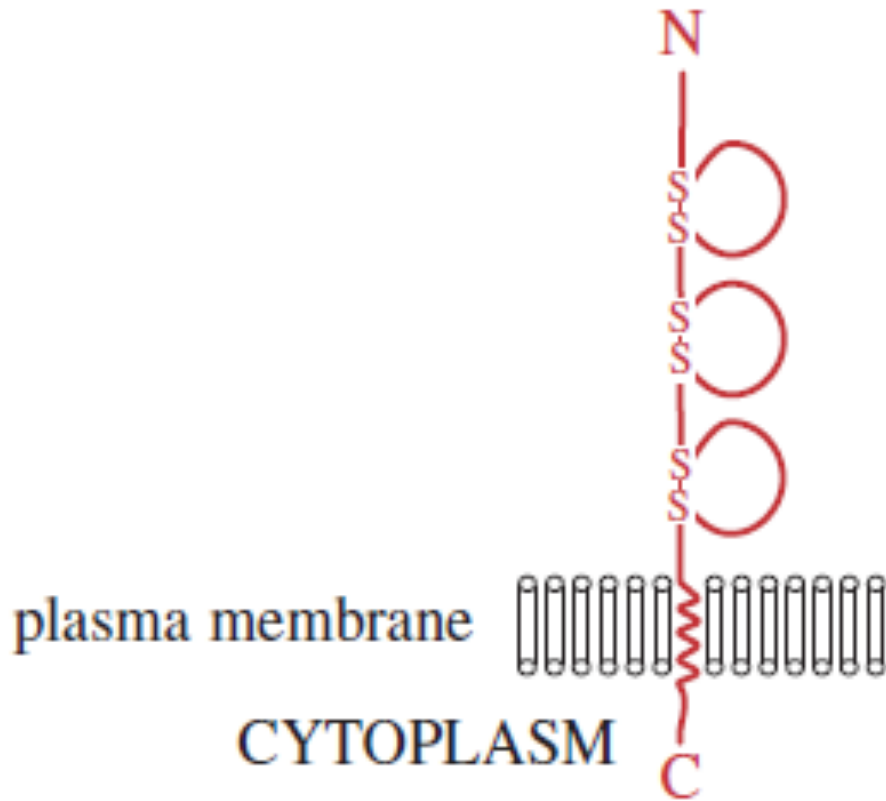
VPg

RNA polymerase

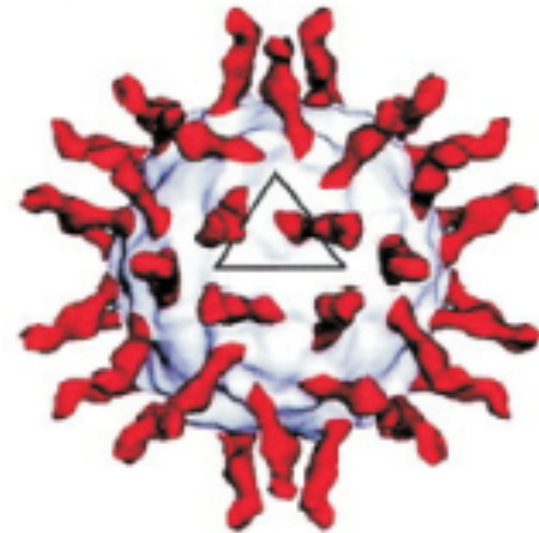
# Picornavirus genome organization



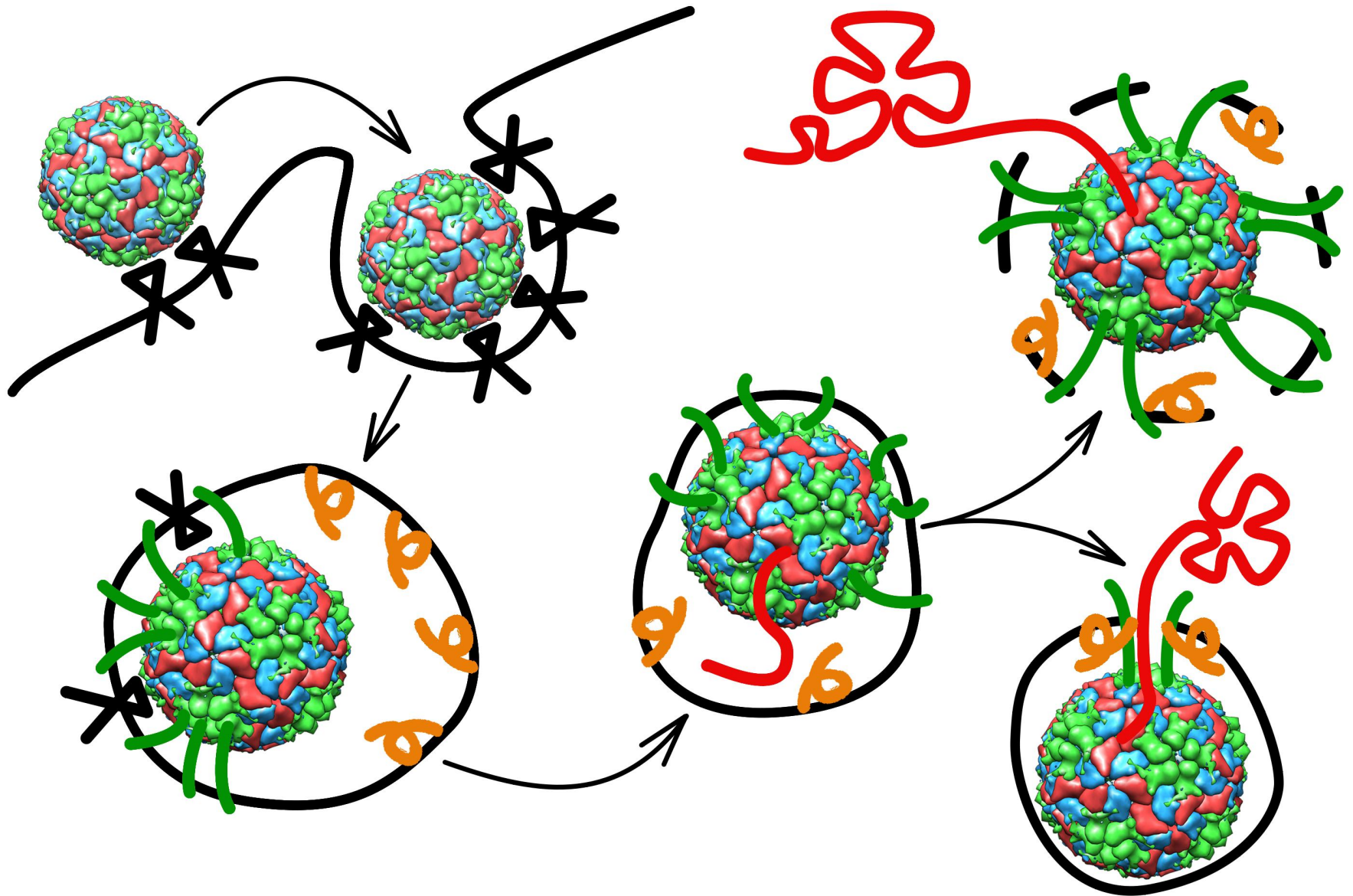
(a) CD155 structure

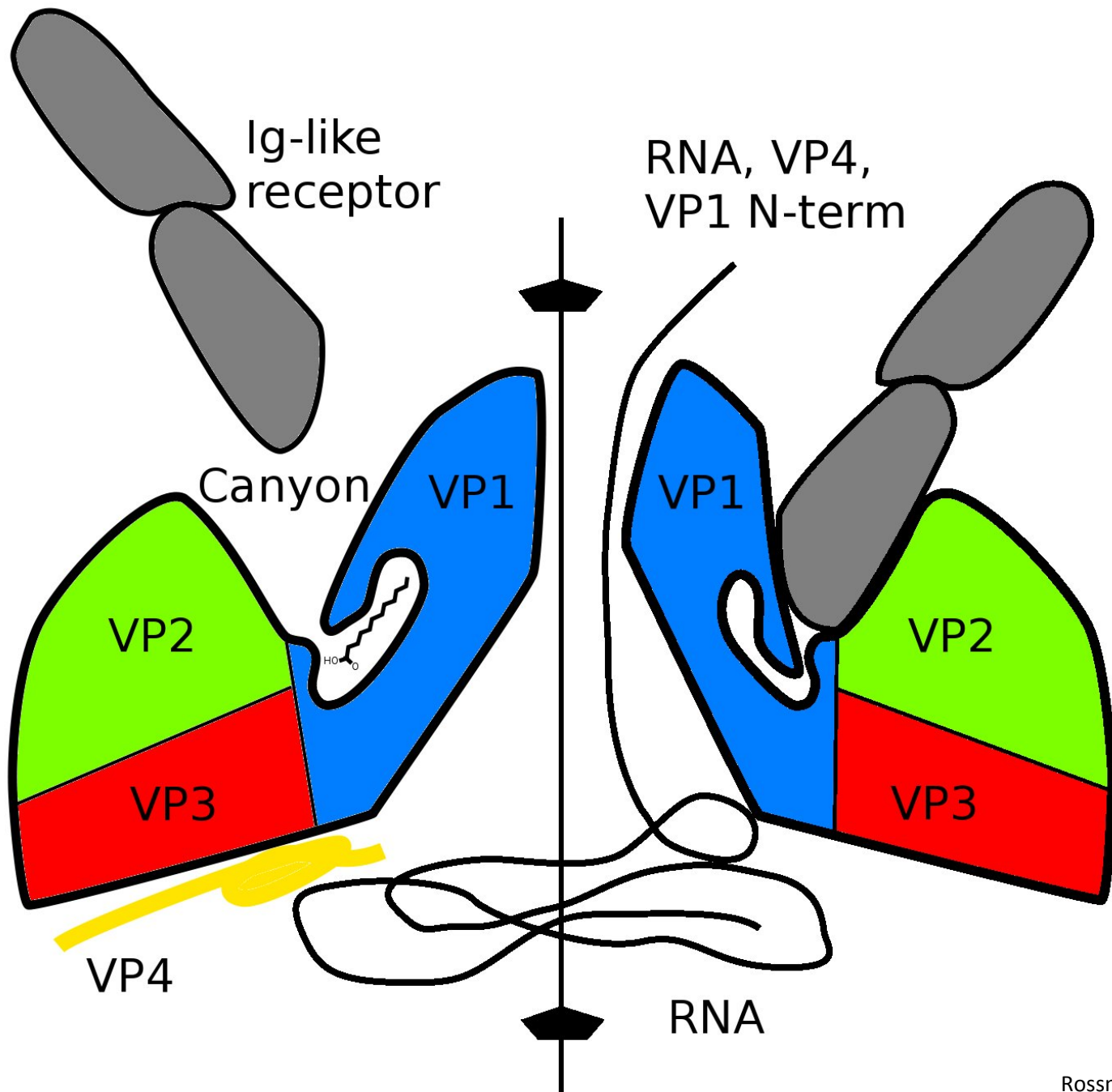


(b) CD155 molecules complexed with a poliovirus particle

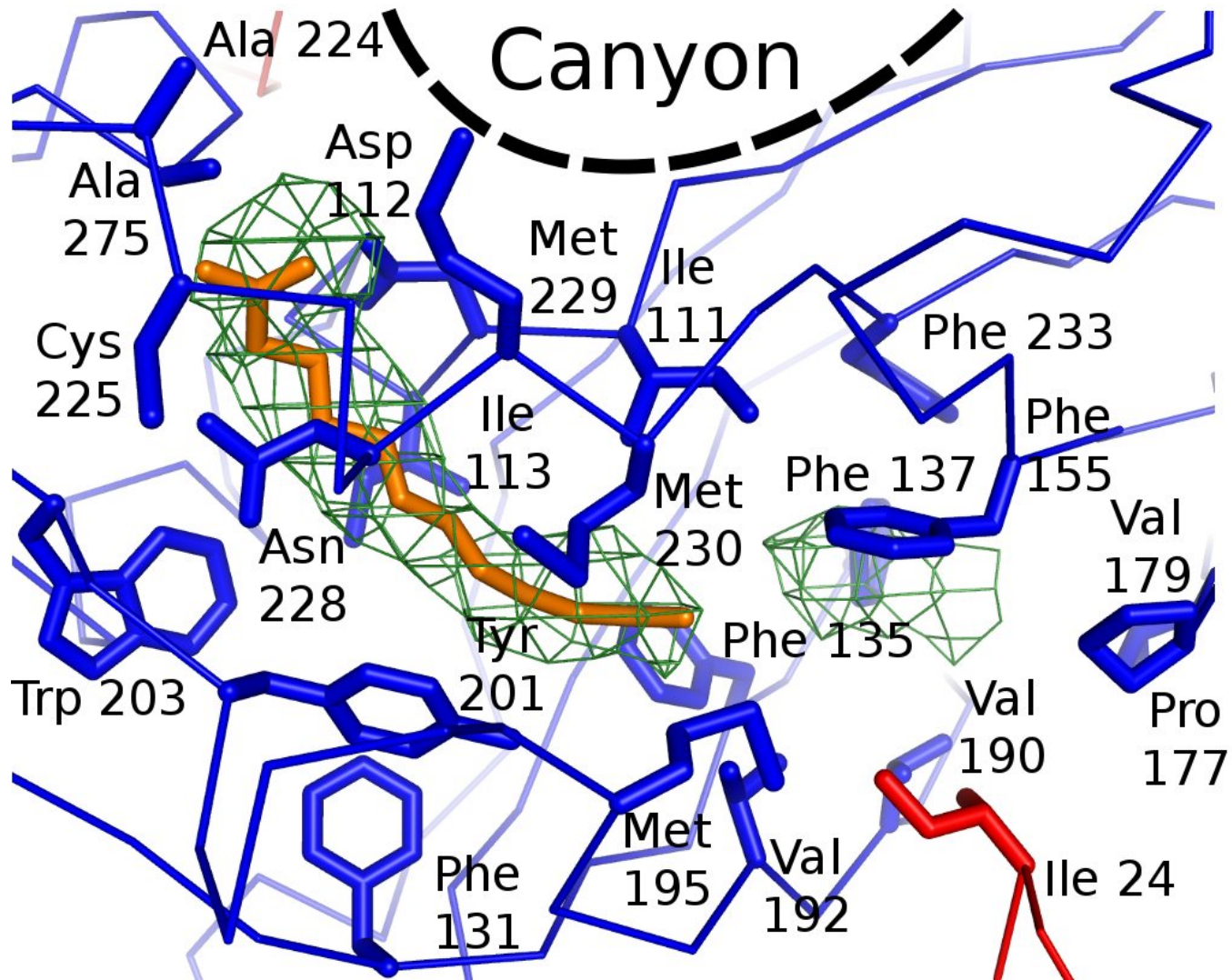


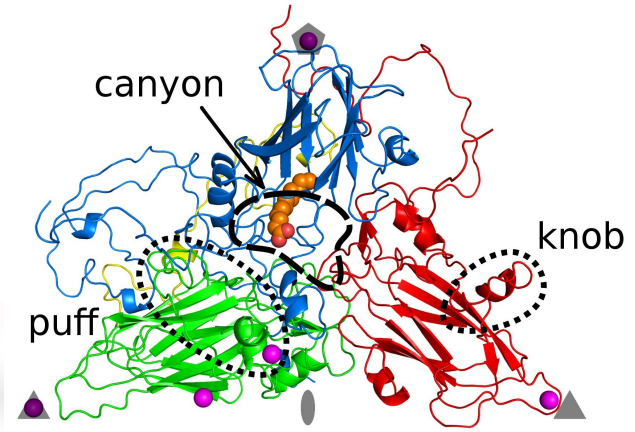
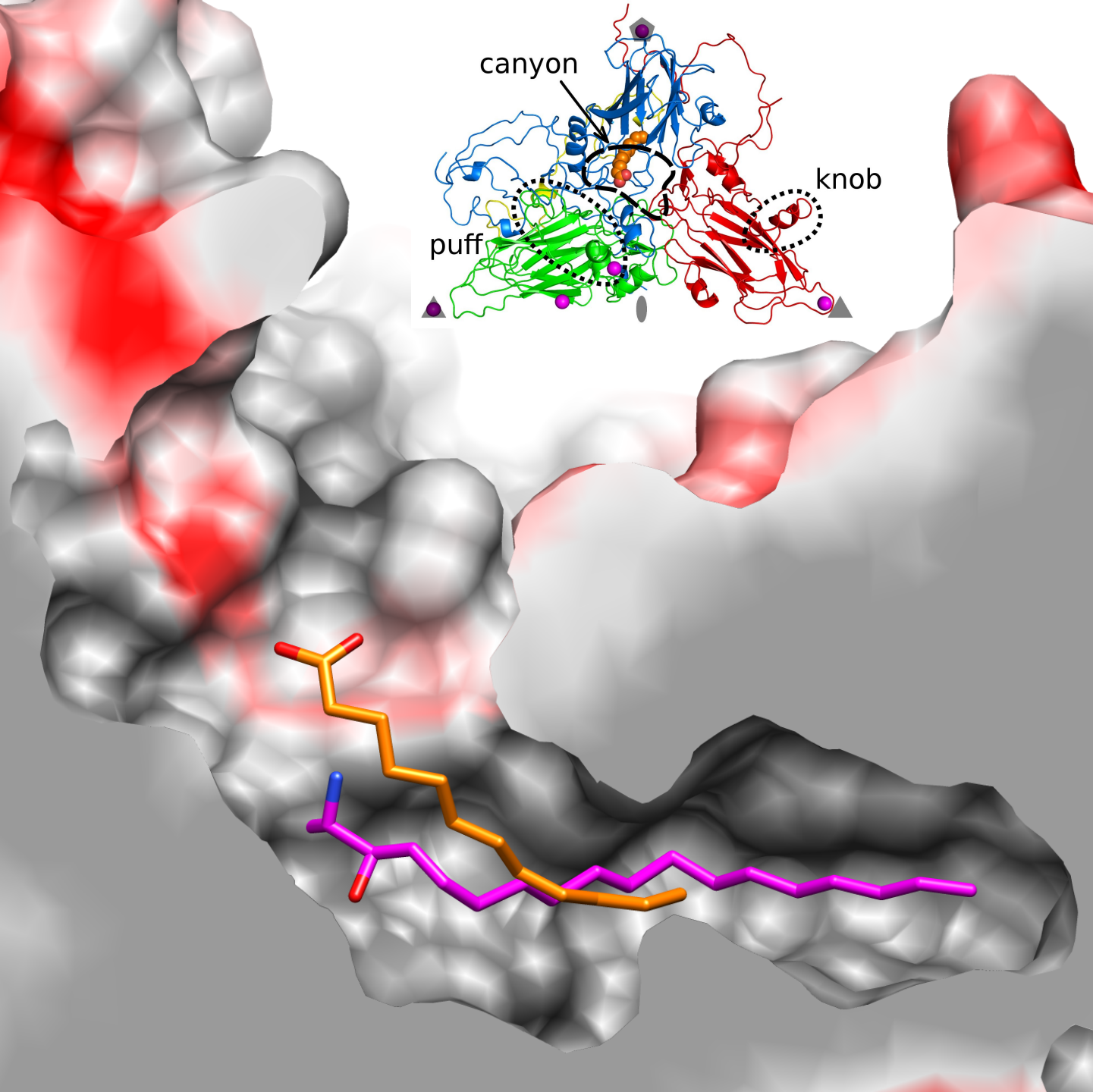
# 1. Genome delivery into cytoplasm

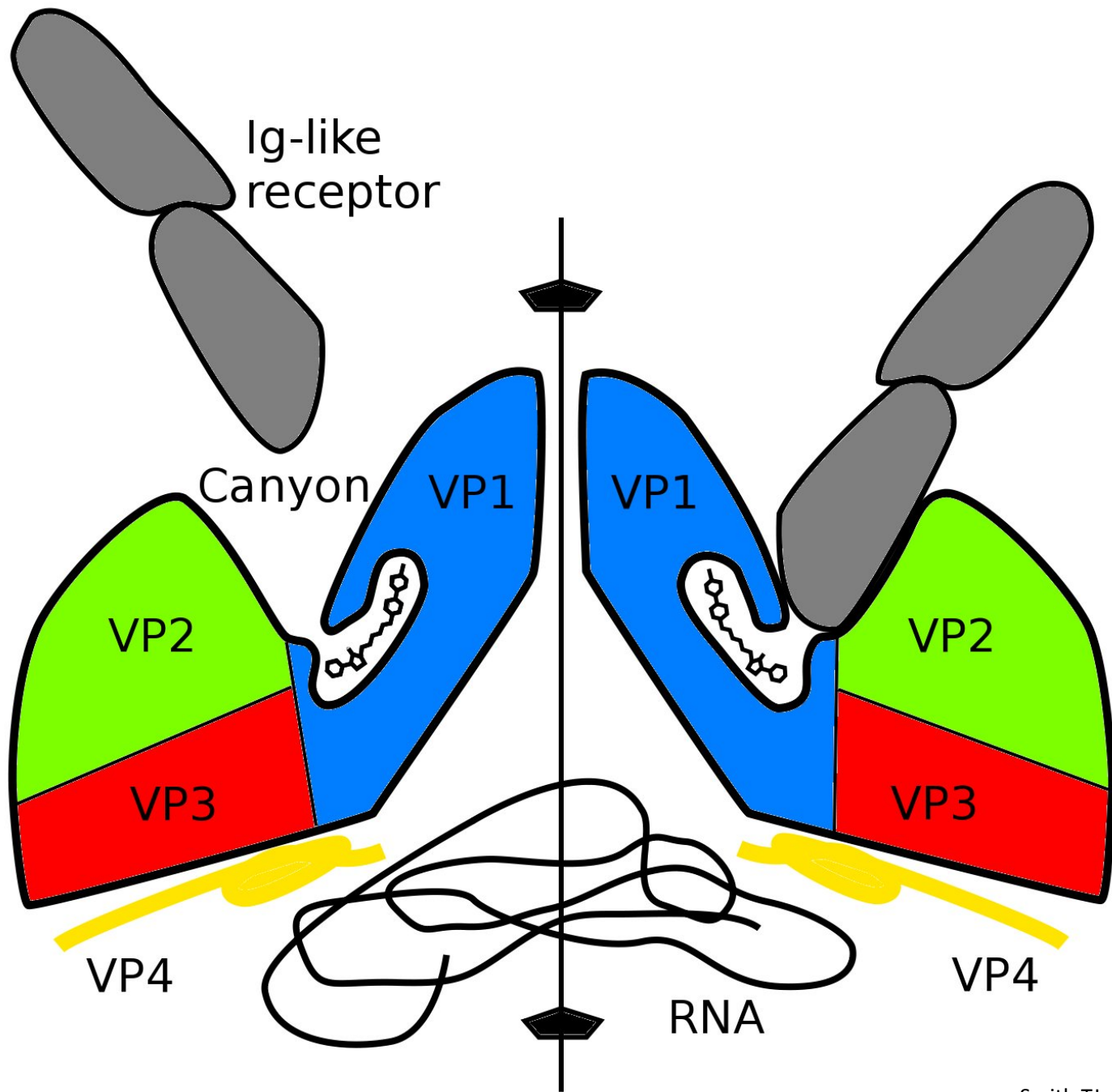




# Pocket factor in EV71

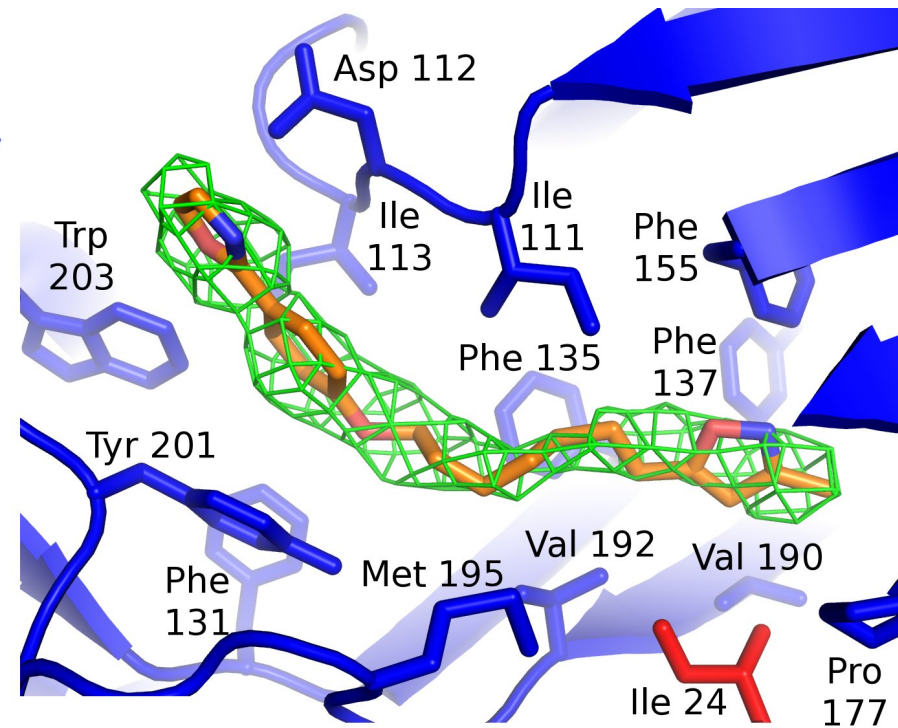
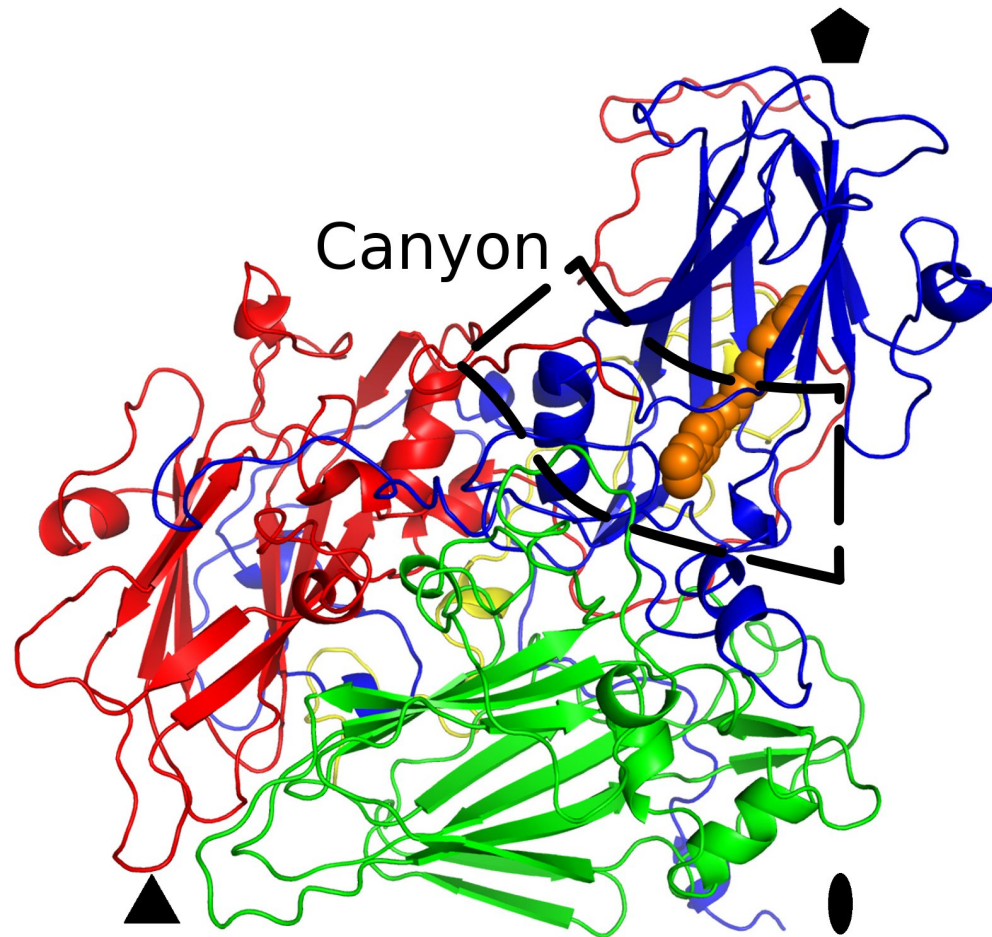


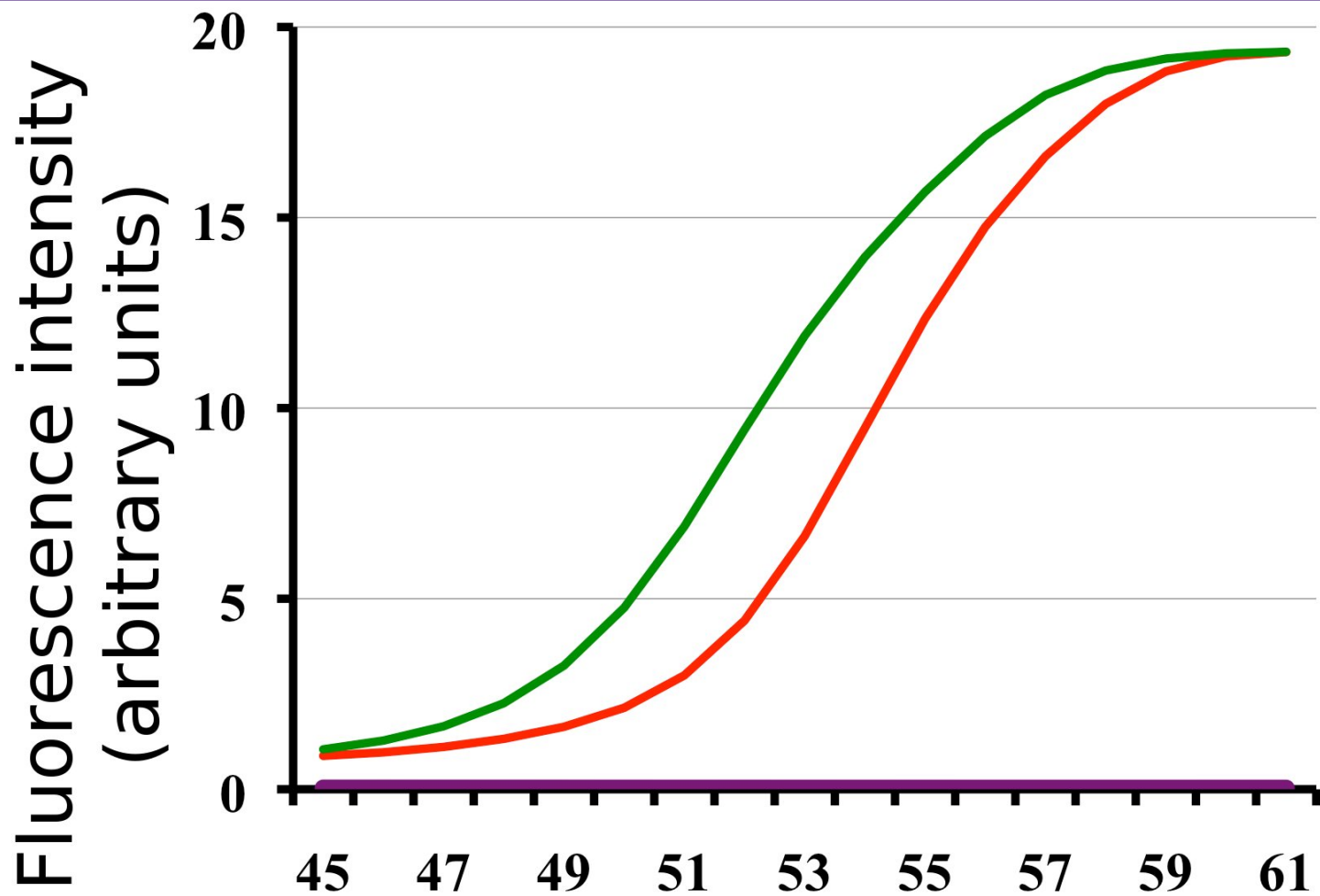




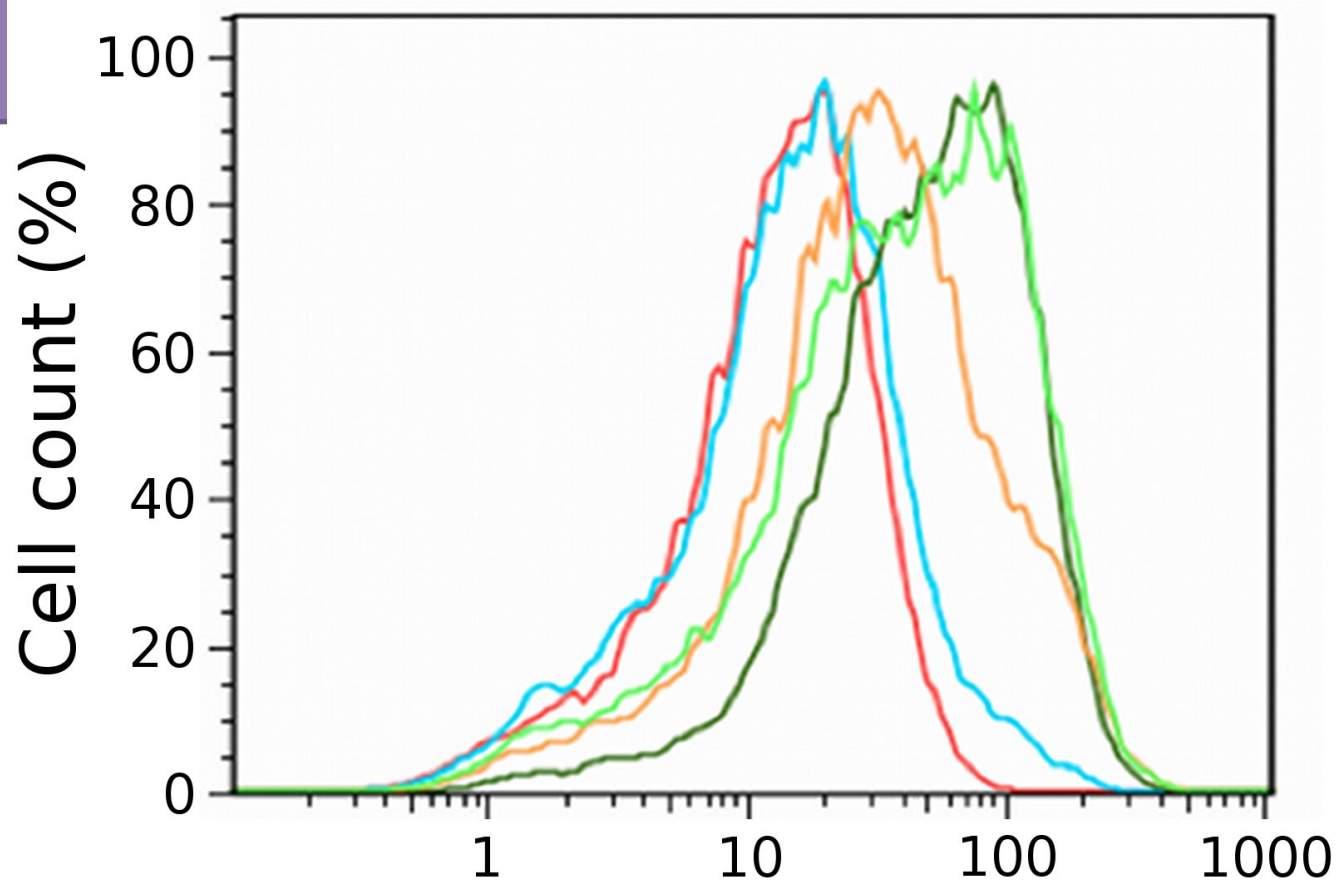


# Inhibition of EV71 by WIN 51711





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



Fluorescence intensity  
(arbitrary units)

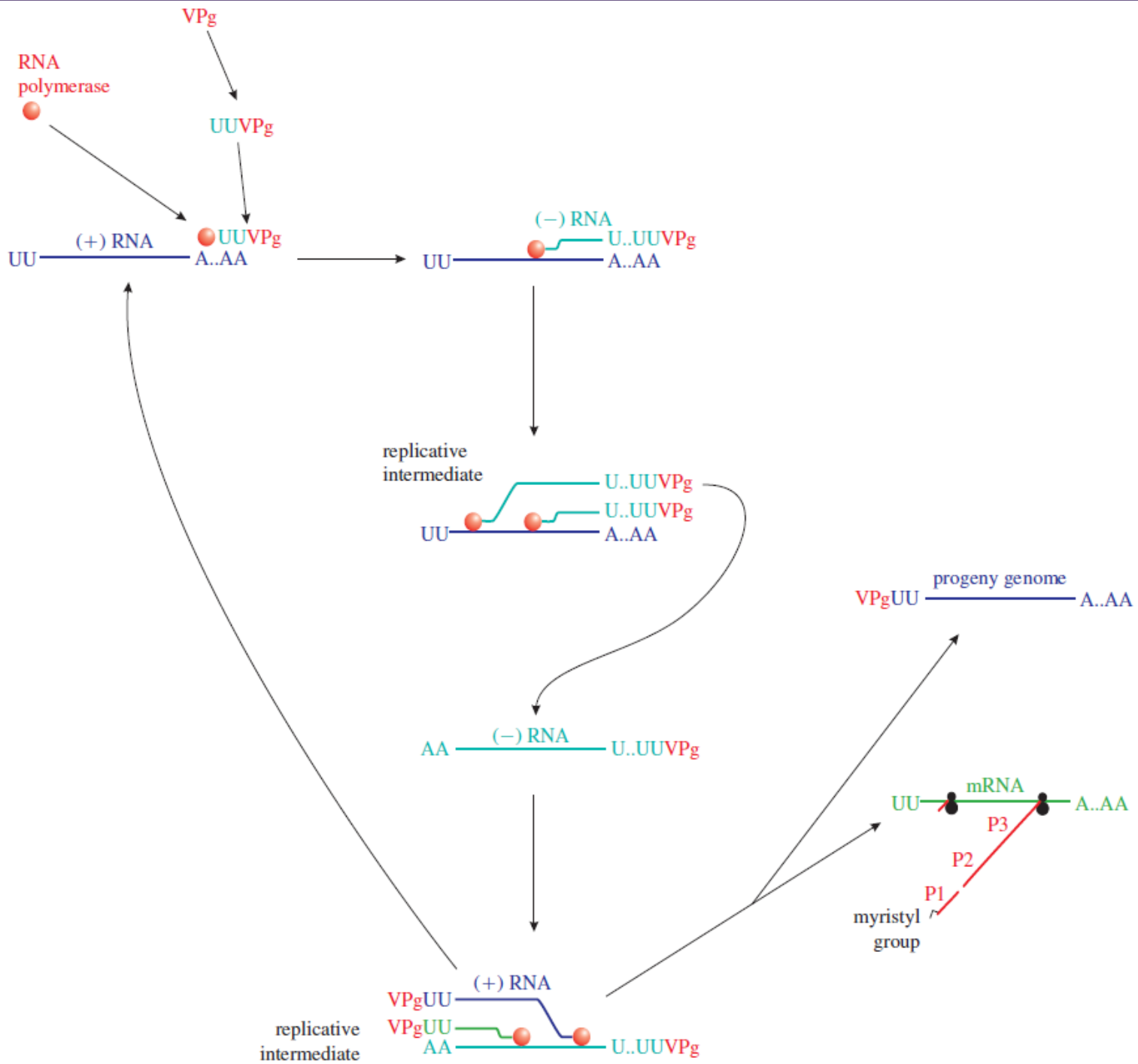
■ no virus

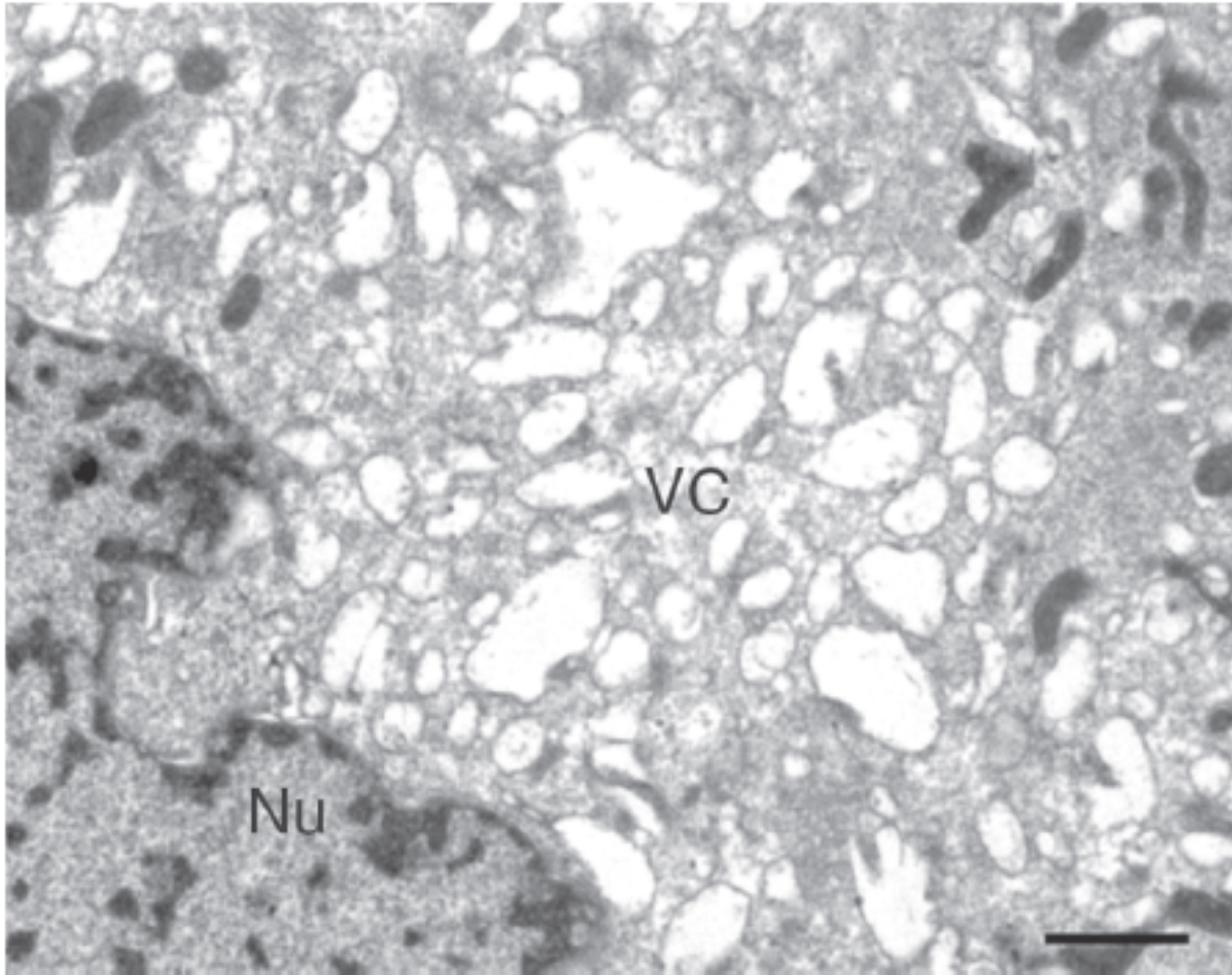
■ EV71

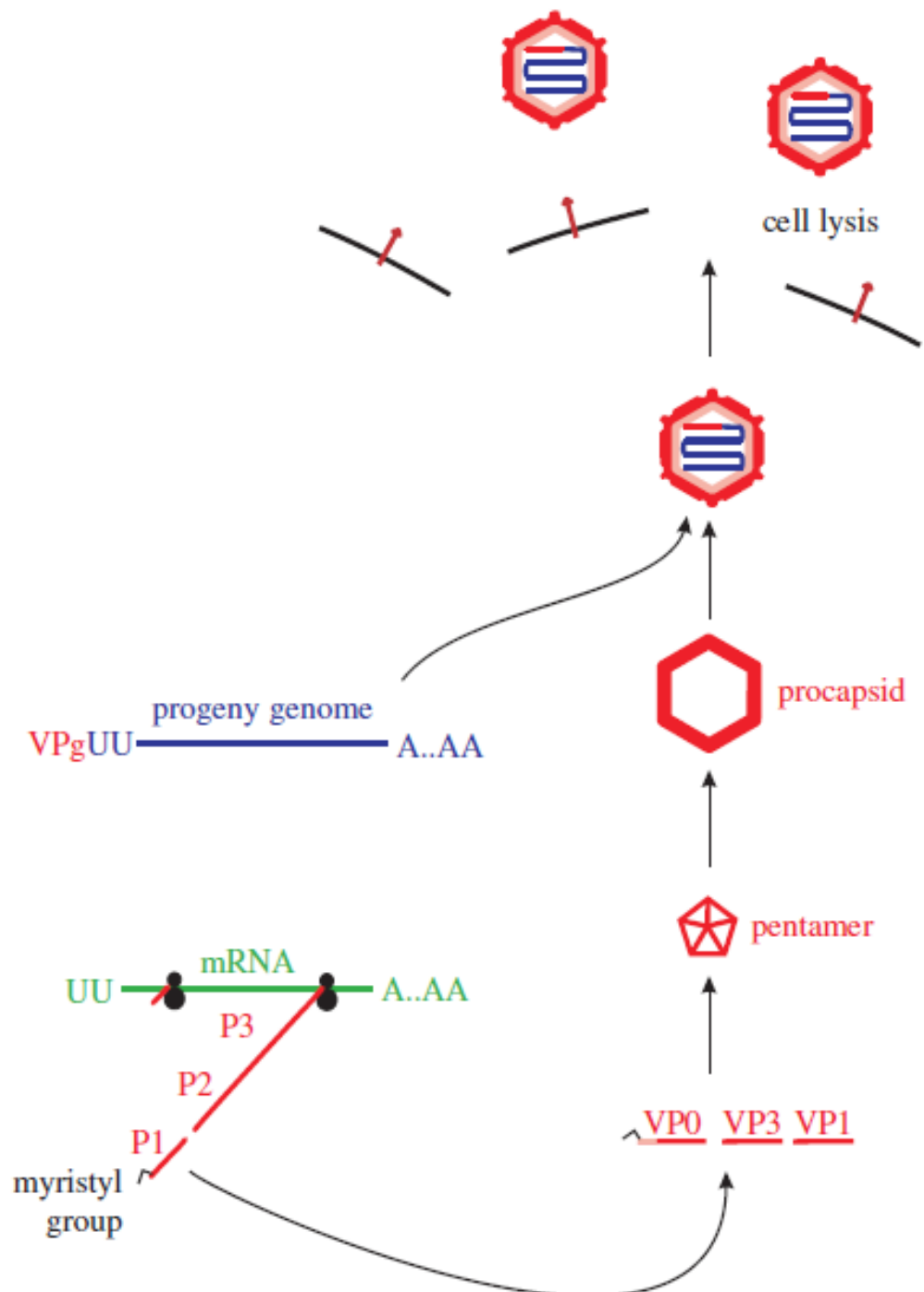
■ EV71 + 146 μM WIN 51711

■ EV71 + 291 μM WIN 51711

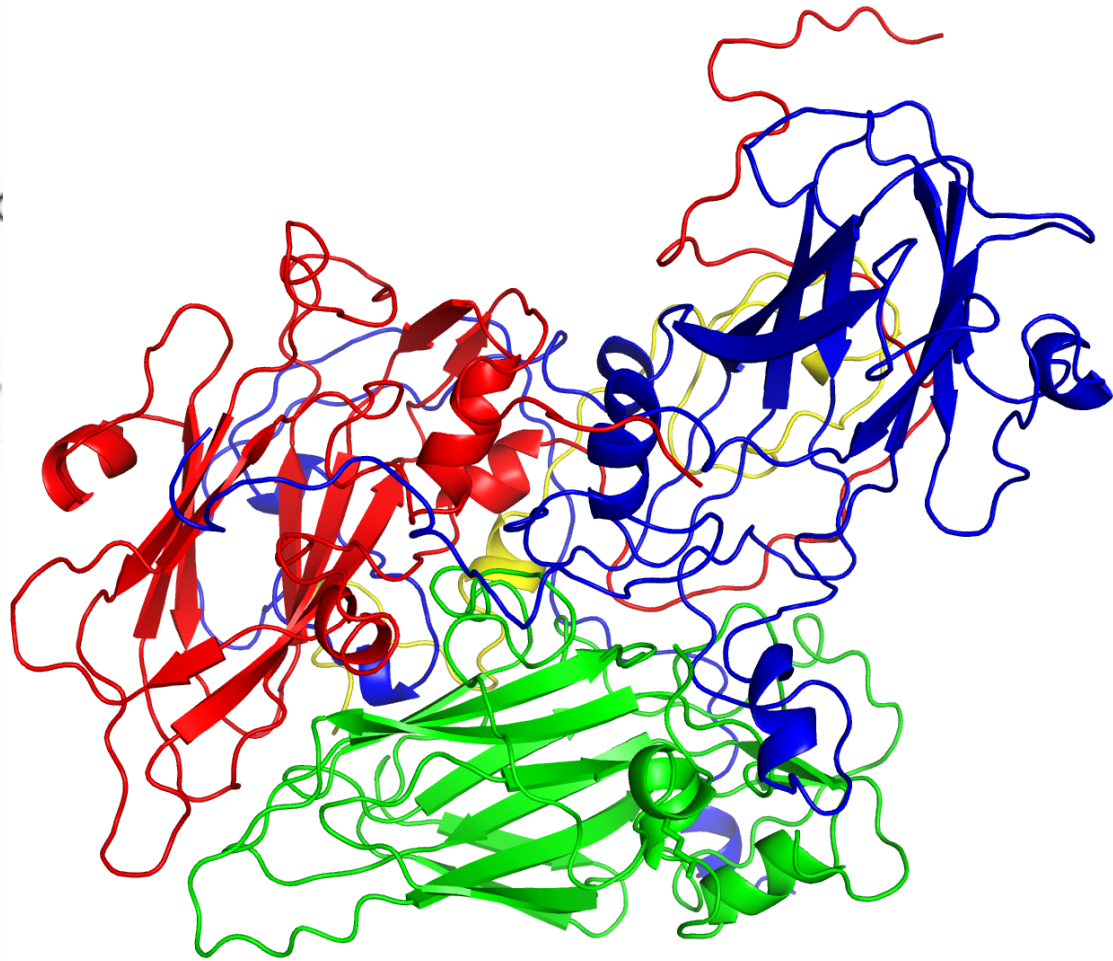
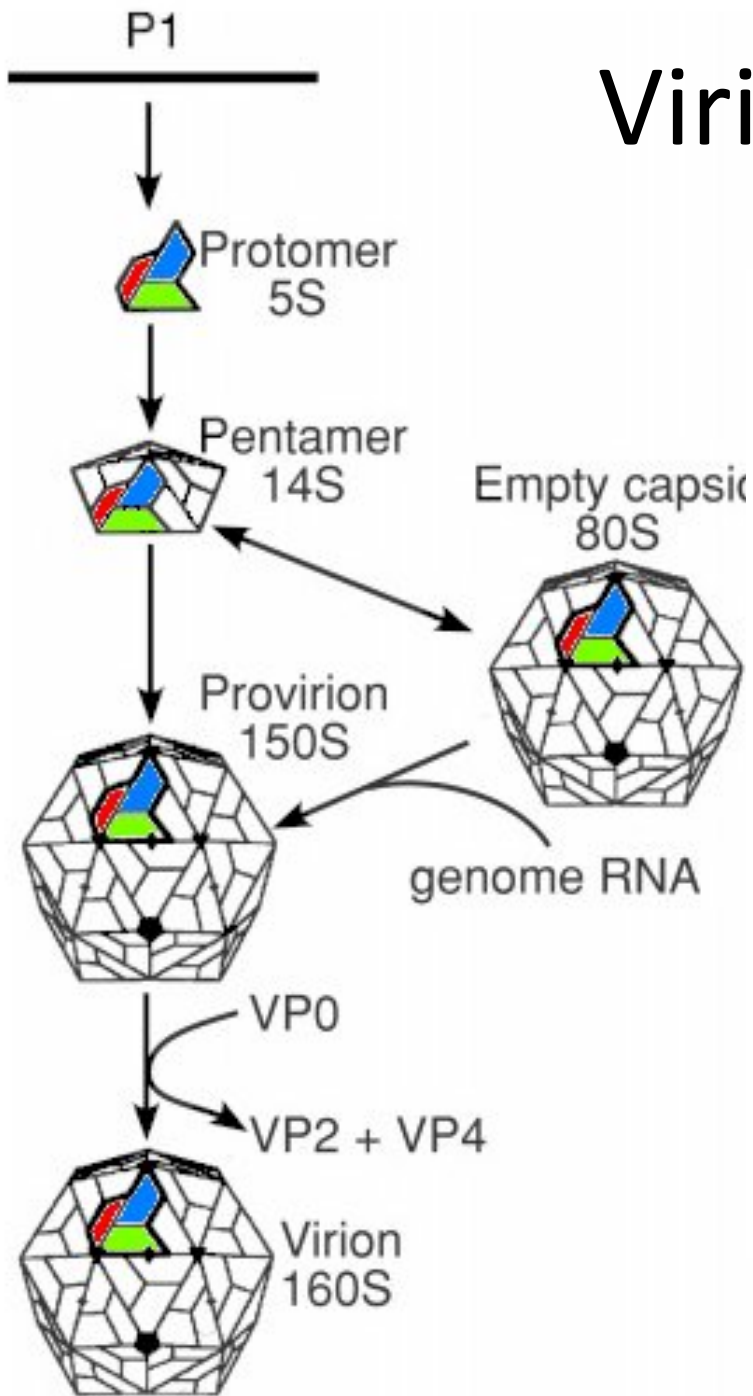
■ EV71 + 583 μM WIN 51711





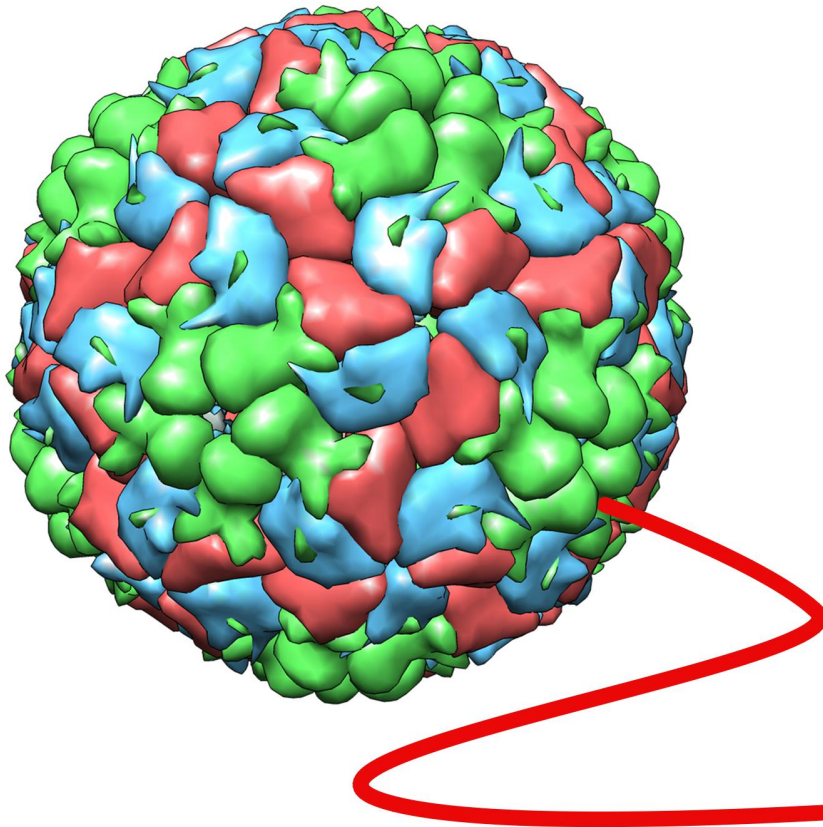


# Virion assembly

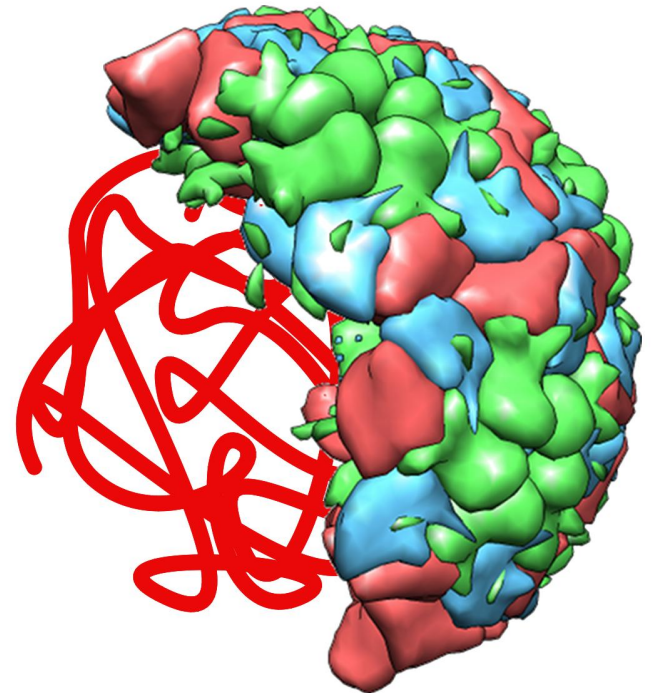


# 4. Virion assembly mechanism

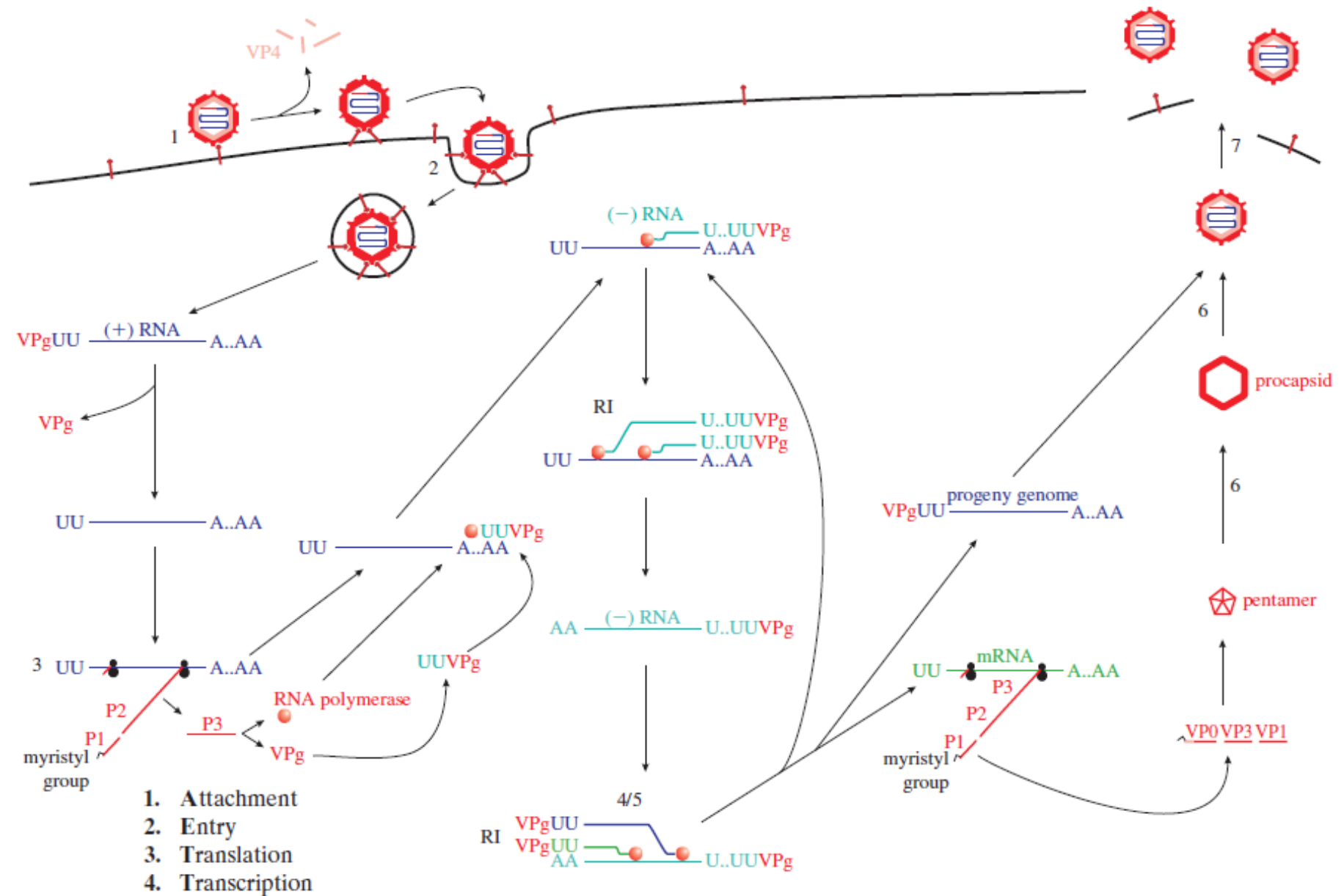
Genome packaging into pre-formed capsids

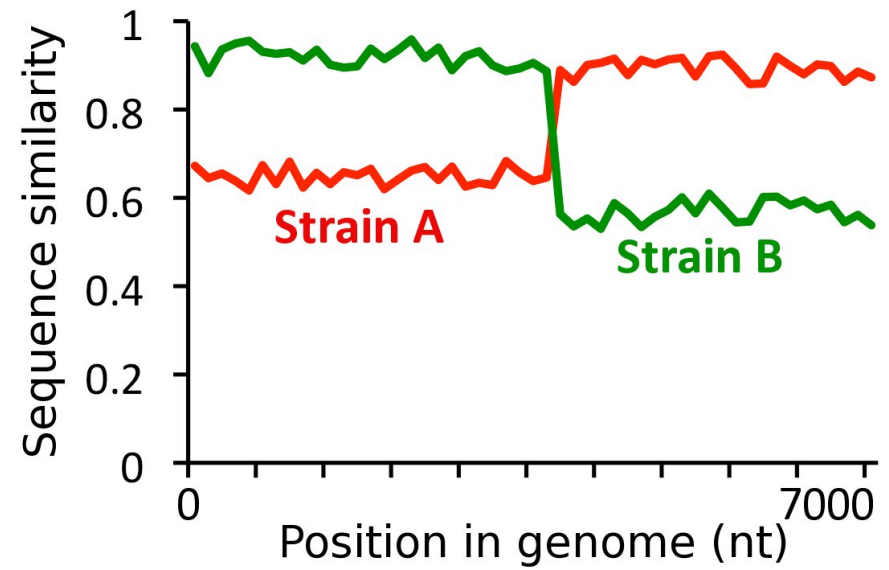
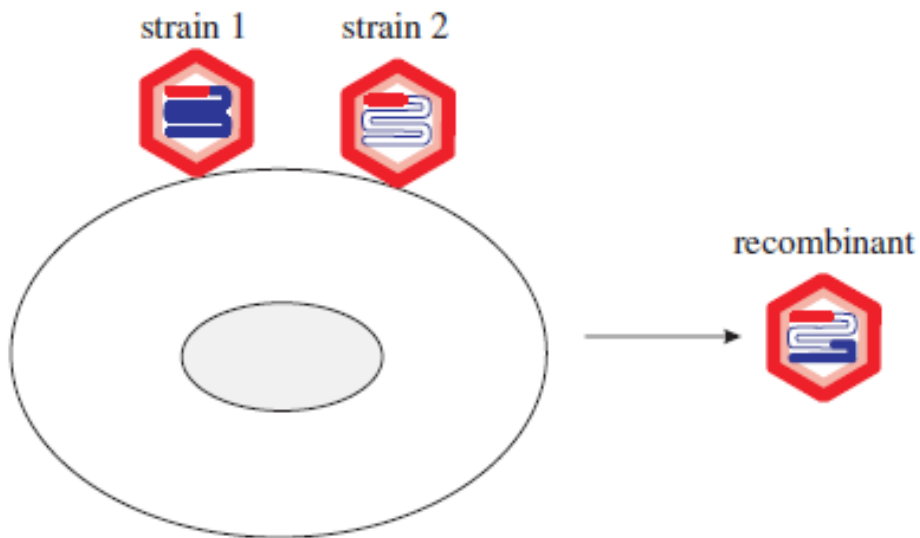


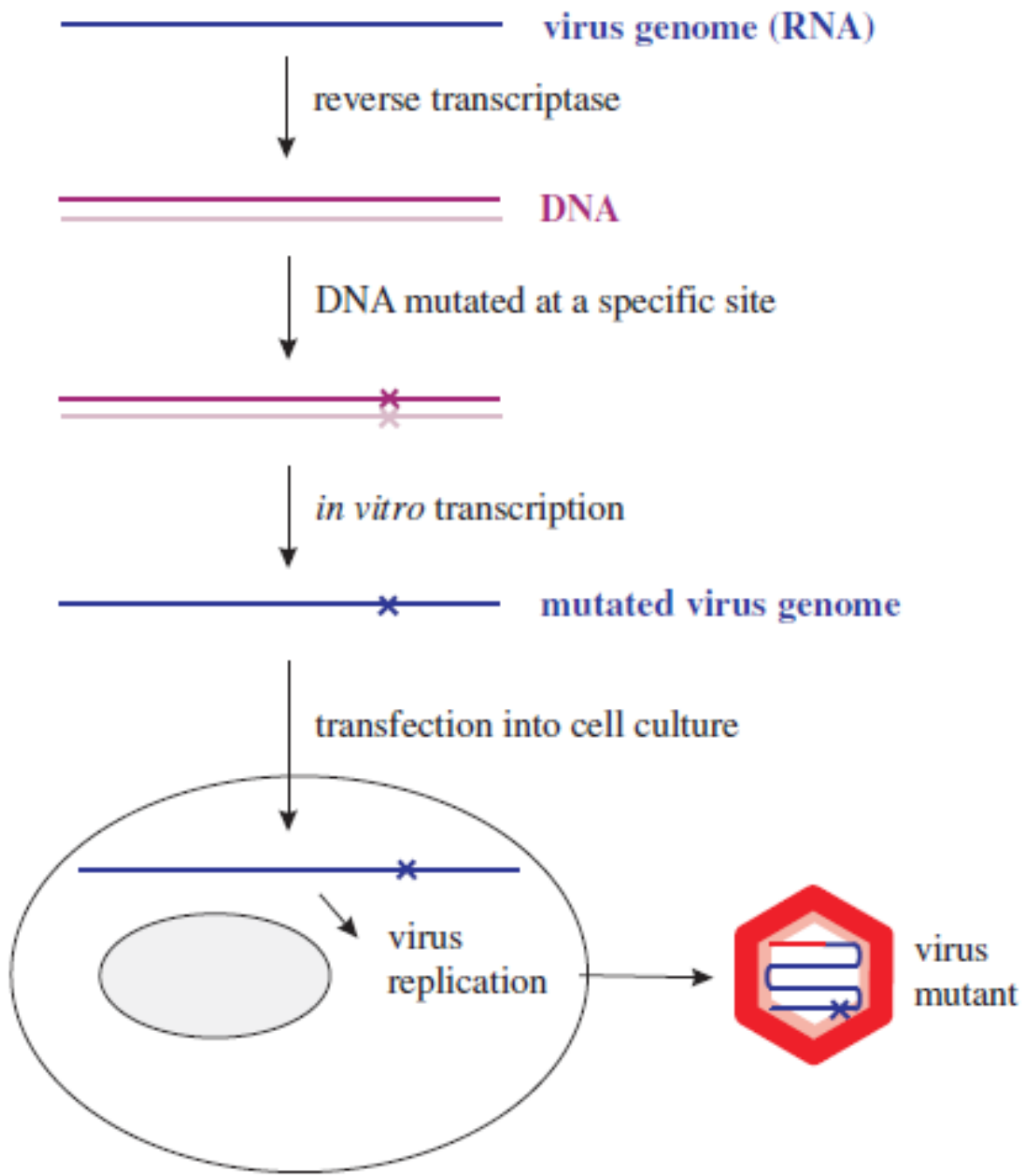
Capsid assembly around condensed genome











deoxyribonucleotides



poliovirus cDNA sequences

ligation



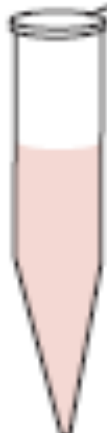
poliovirus cDNA



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.