- **Small DNA genome virus cycles**

Bacteriophages with DNA genomes, viruses of mycoplasmas and Archea

*Polyomaviridae*

*Papillomaviridae*

*Parvoviridae*, including genus *Dependovirus*

*Geminiviridae*

*Circoviridae* – the smallest viruses in general (17 nm, 1760 bases of cssDNA)

Genome organization is more versatile than in viruses with big DNA genomes!

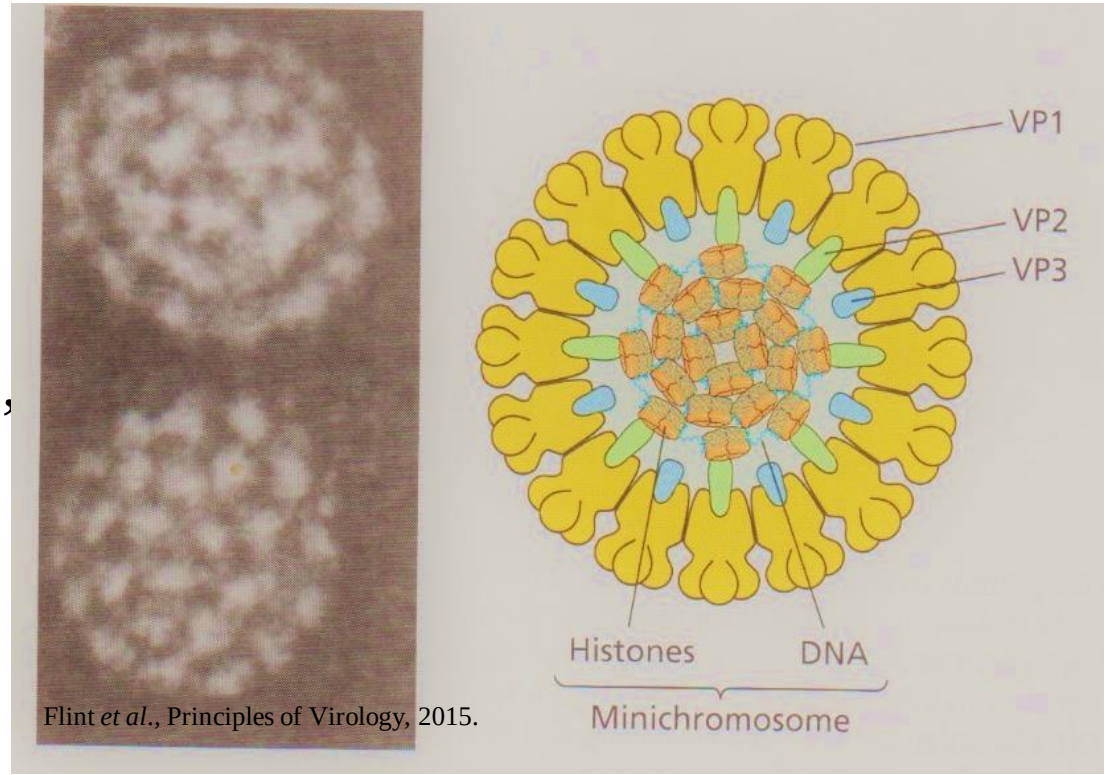
***Polyomaviridae***:

- It used to ba a subfamily in *Papovaviridae* (papilloma virus/polyoma virus/simian vacuolating virus (SV40)),

-Bird and mammal hosts

- human viruses, mainly asymptomatic, widespread: BKPyV (nephropathy), JCPyV (progressive multifocal leukoencephalopathy (PML) in immunocompromised patients), SV40, new viruses (MCPyV, etc.).

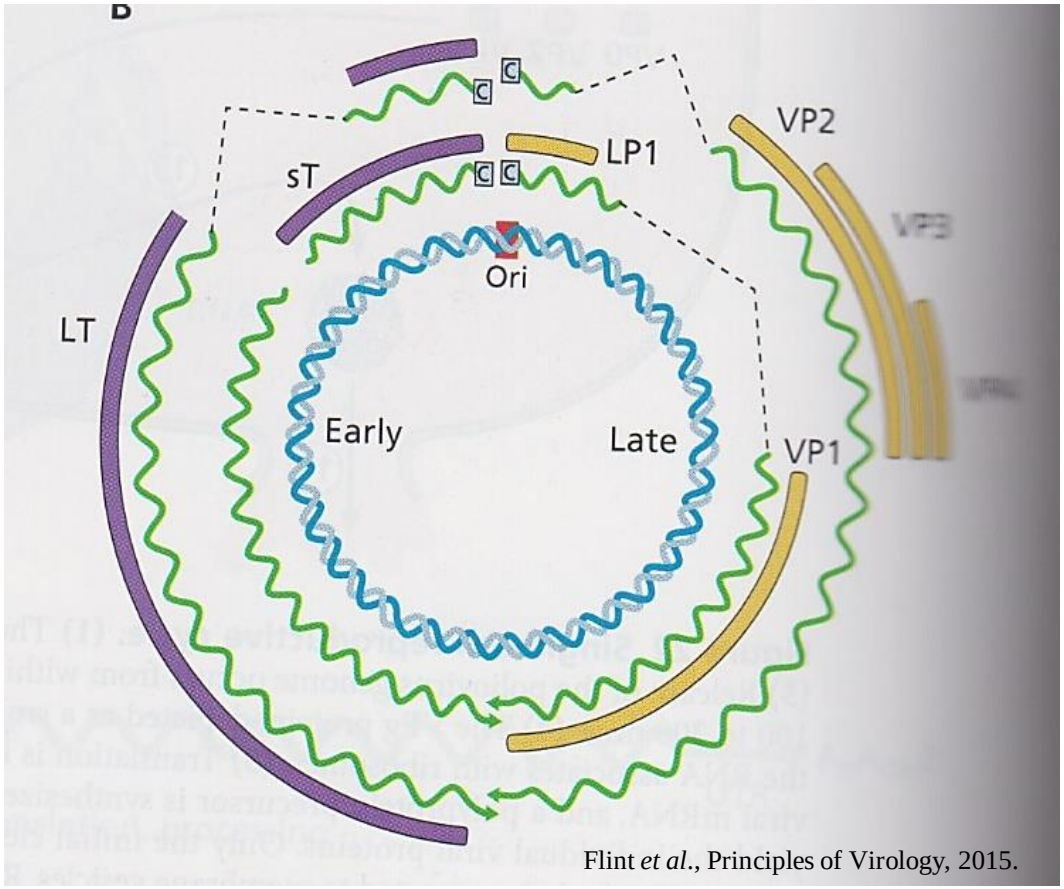
- Genome is cdsDNA, about 5kbp as a minichromosome in isometric virion of 45 nm (25 nucleosomes in SV40), θ – replication of the genome in nucleus, virion assembly too. Infection is lytic.



Flint *et al*., Principles of Virology, 2015.

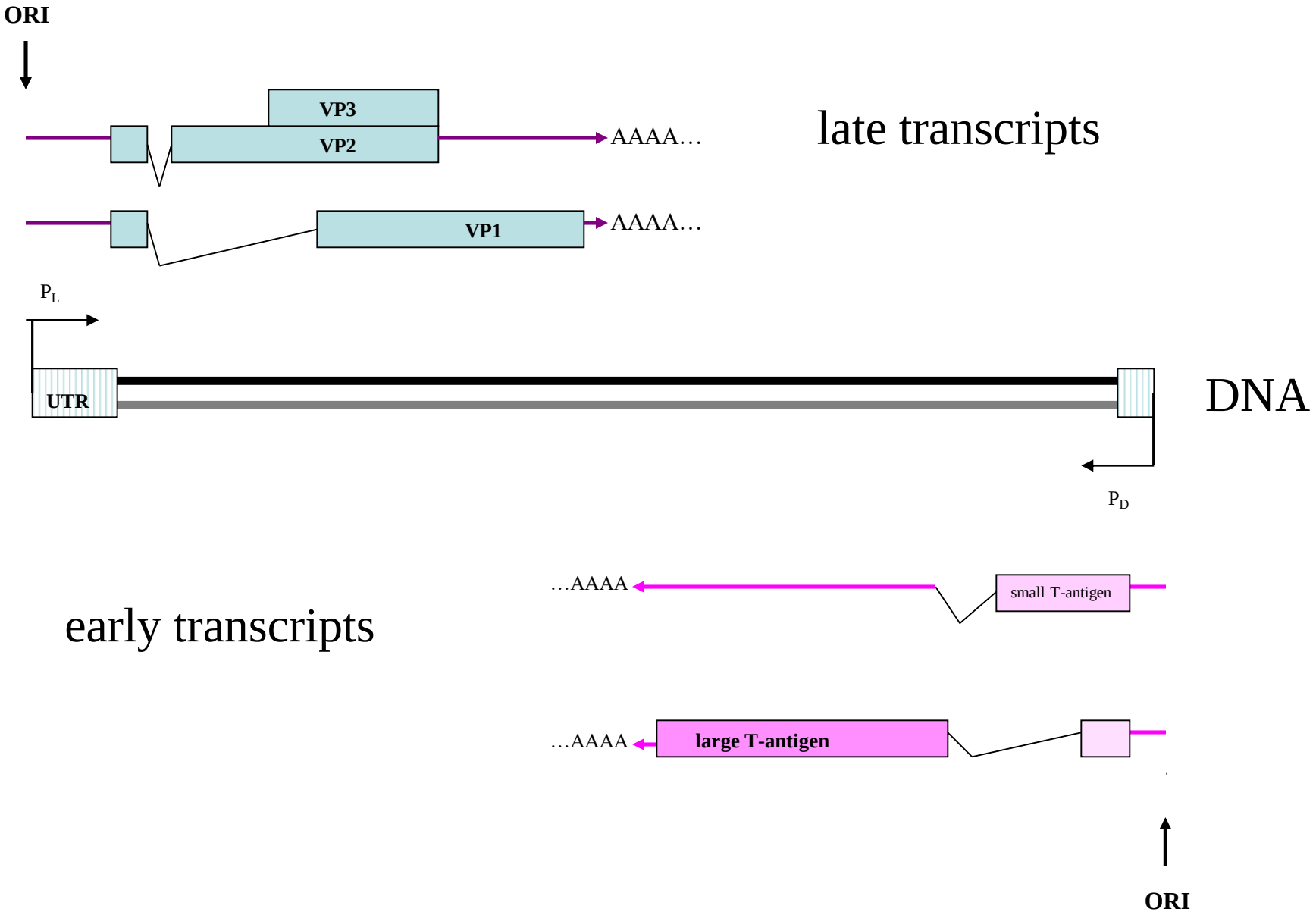
Temporally regulated transcription – early and late genes.

Ori – regulatory region between early and late, origin of DNA replication, strong enhancers, strong SV40-promoters (the basis for commercial expression vectors).

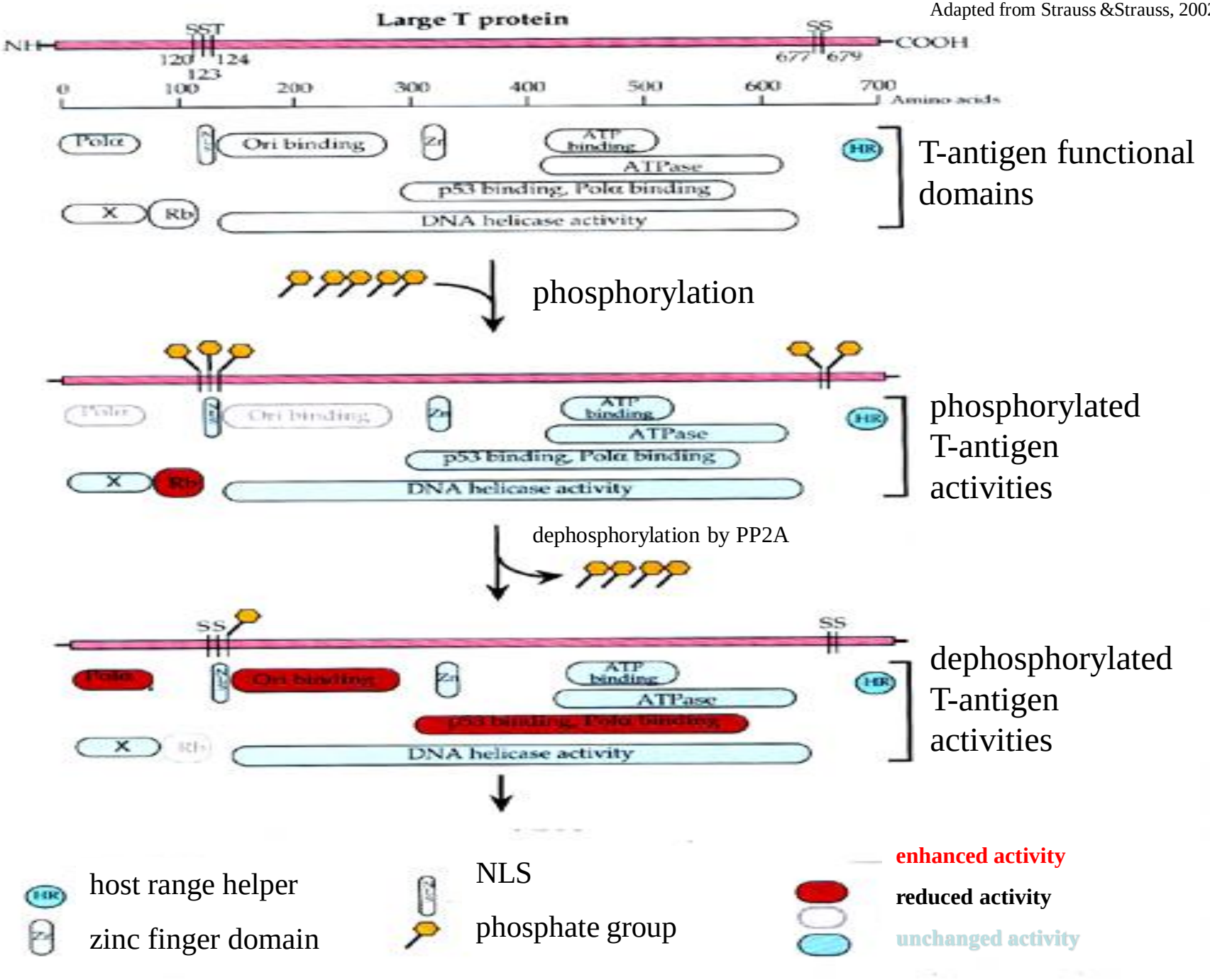



Flint *et al*., Principles of Virology, 2015.

# Linearized transcriptome of SV40 (5243 bp)



Adapted from Strauss &Strauss, 2002



T is tumor antigen. Its expression, even without productive infection, transforms the cell and leads into tumor formation in animals.

The simplest example in SV40, but there are T antigens of different sizes.
Multifunctional protein – interaction with viral promoters and cell proteins.
Differentially regulated by Ser and Thr aa-residue phosphorylation.

Large T-antigen binds p53 and Rb (tumor suppressor proteins).

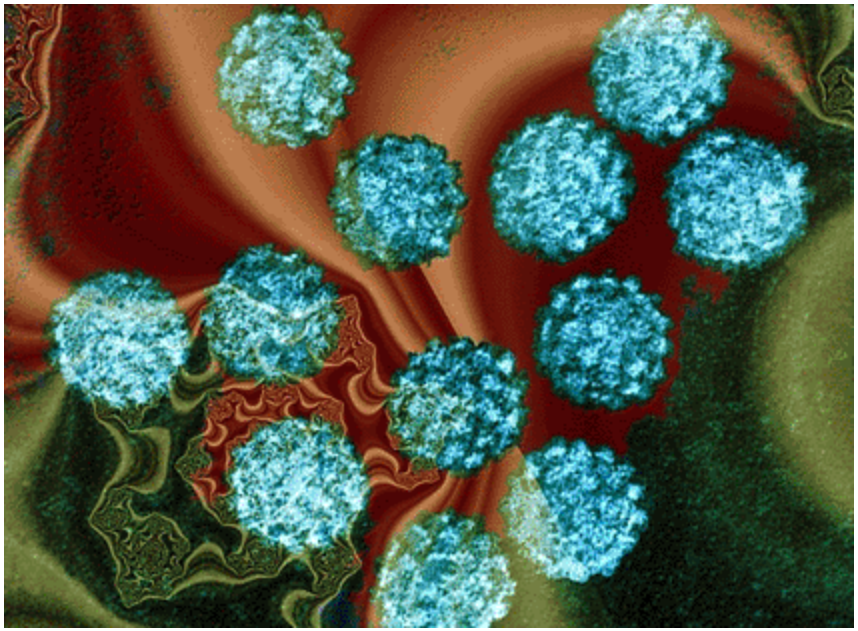
***Papillomaviridae***:

Structurally similar to polyomaviruses,

somewhat bigger (55nm, cdsDNA 8 kbp),

primarily infect mammals, some found in birds,

host specificity limited to the species level (very narrow host range), cell tropism also very narrow.

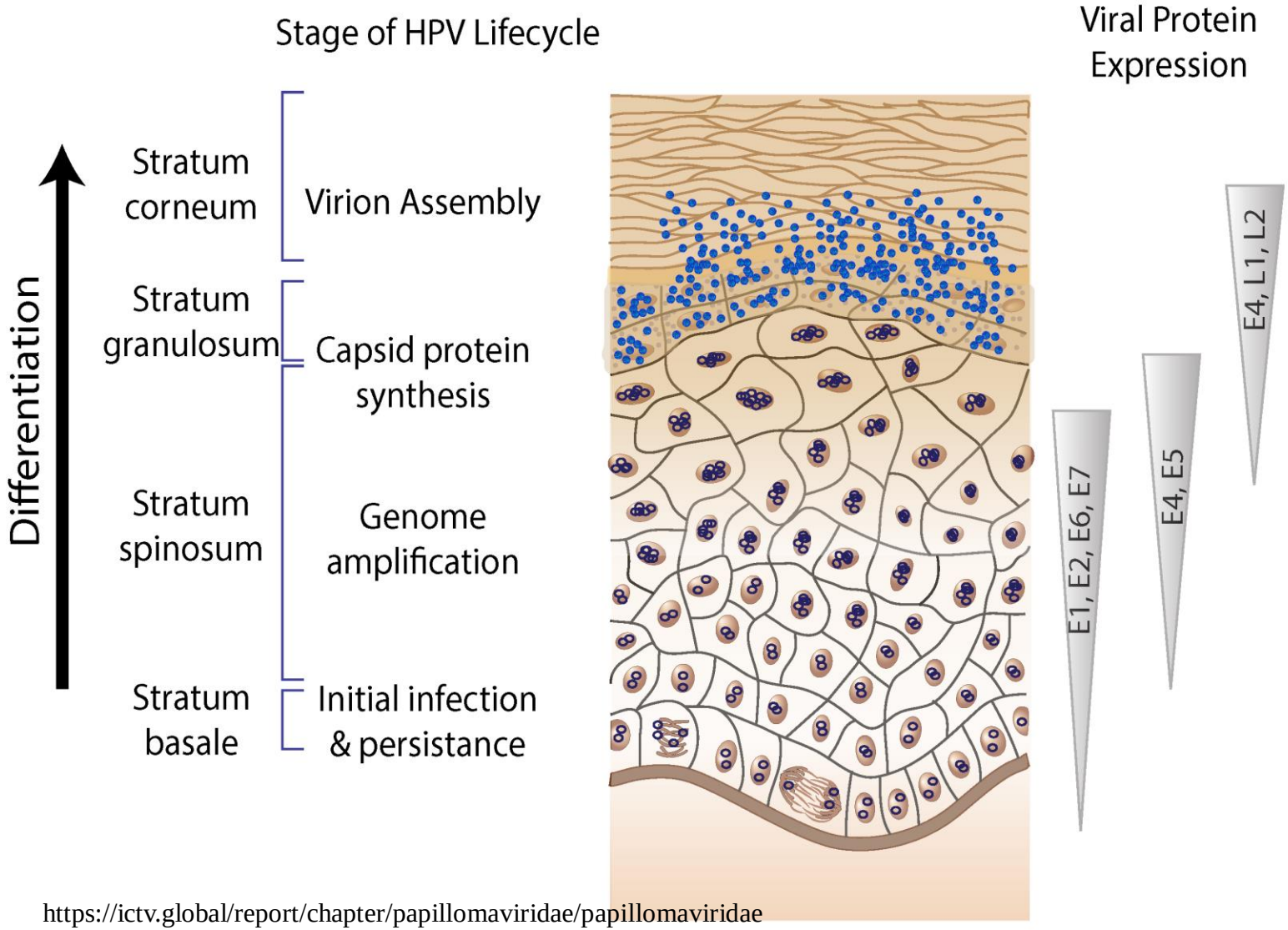


Dr. Linda Stannard, UCT-SPL

Human papilloma viruses (HPV)

They induce cell proliferation – warts (papilloma), occasionally malignant tumors.

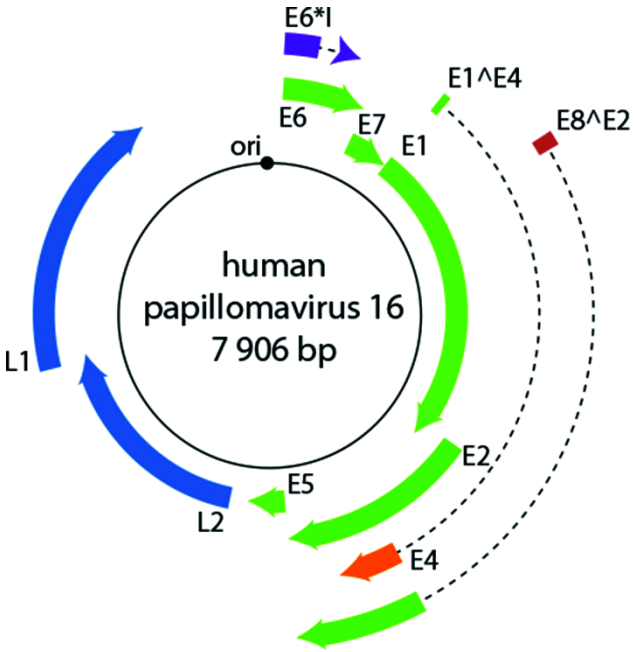
- Complete replication cycle only in the skin layer with fully differentiated cells, mostly epithelial, cultivation is difficult.

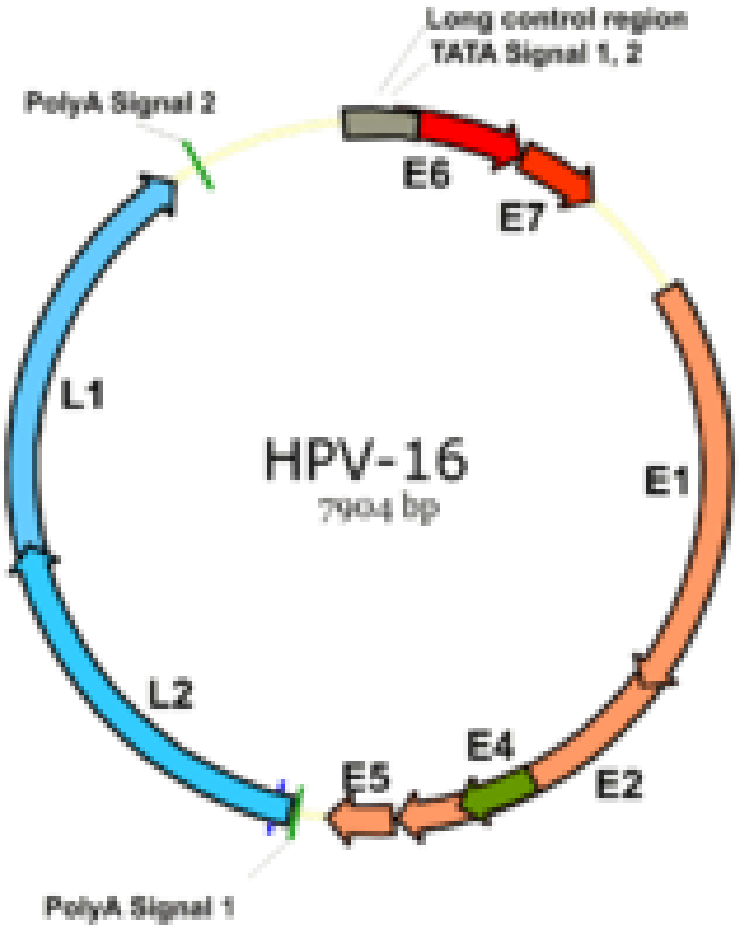



https://ictv.global/report/chapter/papillomaviridae/papillomaviridae

# HPV (human papilloma virus)

All genes are transcribed from one DNA chain! Some genes overlap, alternative splicing, posttranslational processing.




In cells with unproductive cycle, virus exists as an episome (number of episome copies 50-400).

E6 binds p53 and E7 binds Rb – the basis of oncogenicity.

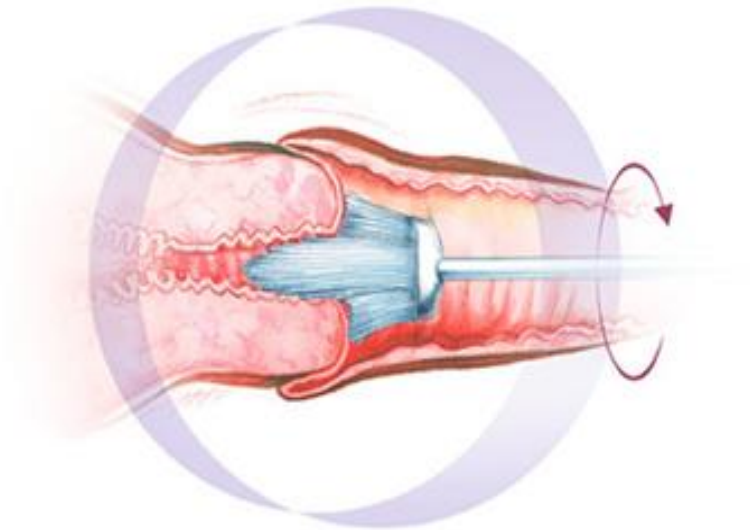
HPV – about 100 types/viruses (different species now e.g. HPV18 is *Alphapapillomavirus 7* ), 30-40 infect genital mucosa.

HPV16 and HPV18 - high risk viruses (found in 70% of women with cervical cancer). HPV16 integrates in the cellular DNA!

In 99% cervical cancer cases, some high risk HPV-type was found.

PAPA – test (*PAP smear*)

It allows identification of abnormal cells.
Precancerous cells – transformation potential.
Lesions – clusters of precancerous cells.



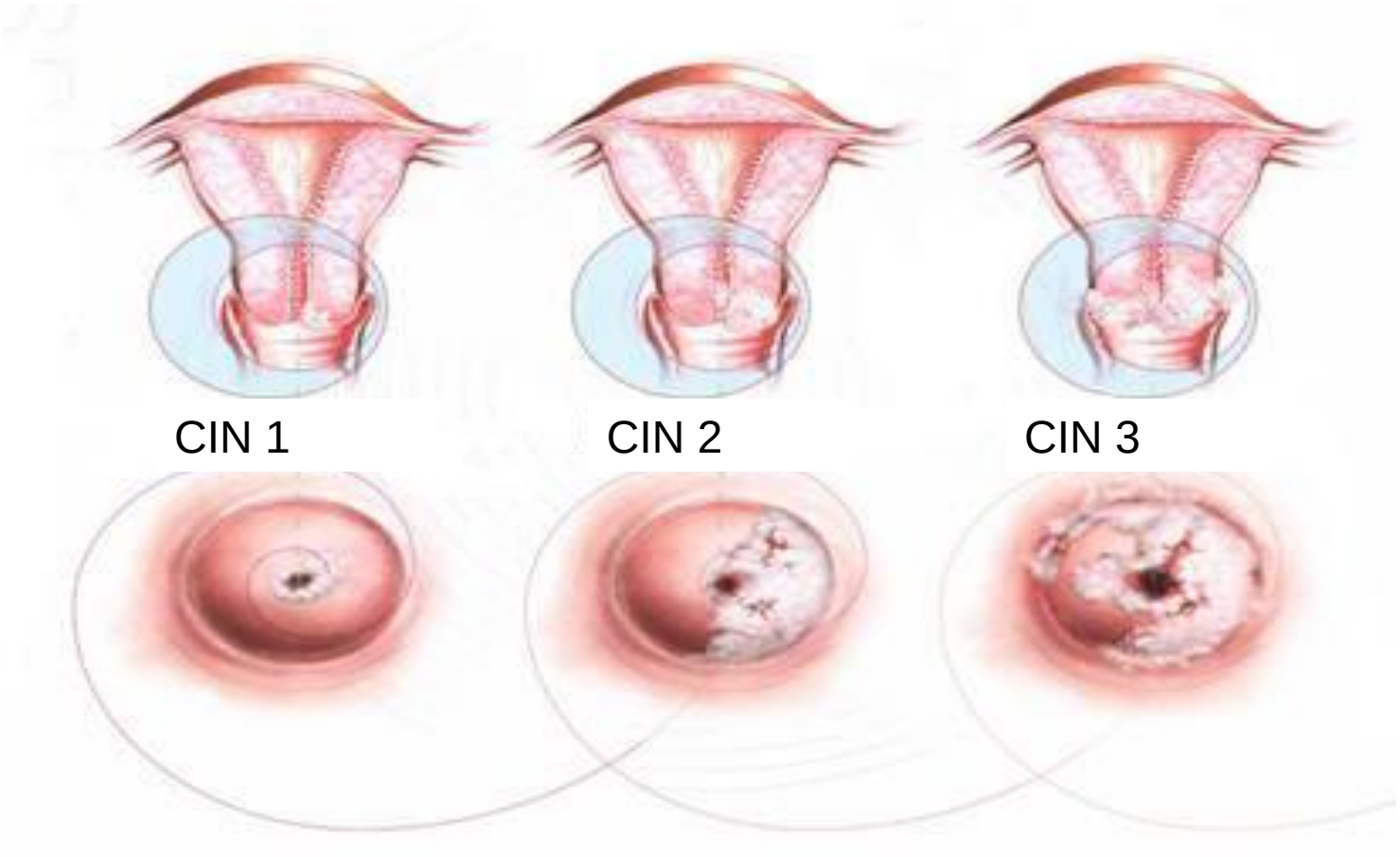
New HPV test types – include screening tests based on the viral DNA analyses.

***CIN (Cervical Inthraepithelial Neoplasia)***

**CIN 1 -** spontaneous recovery expected, more than 50% of women with CIN1 do not need treatment.

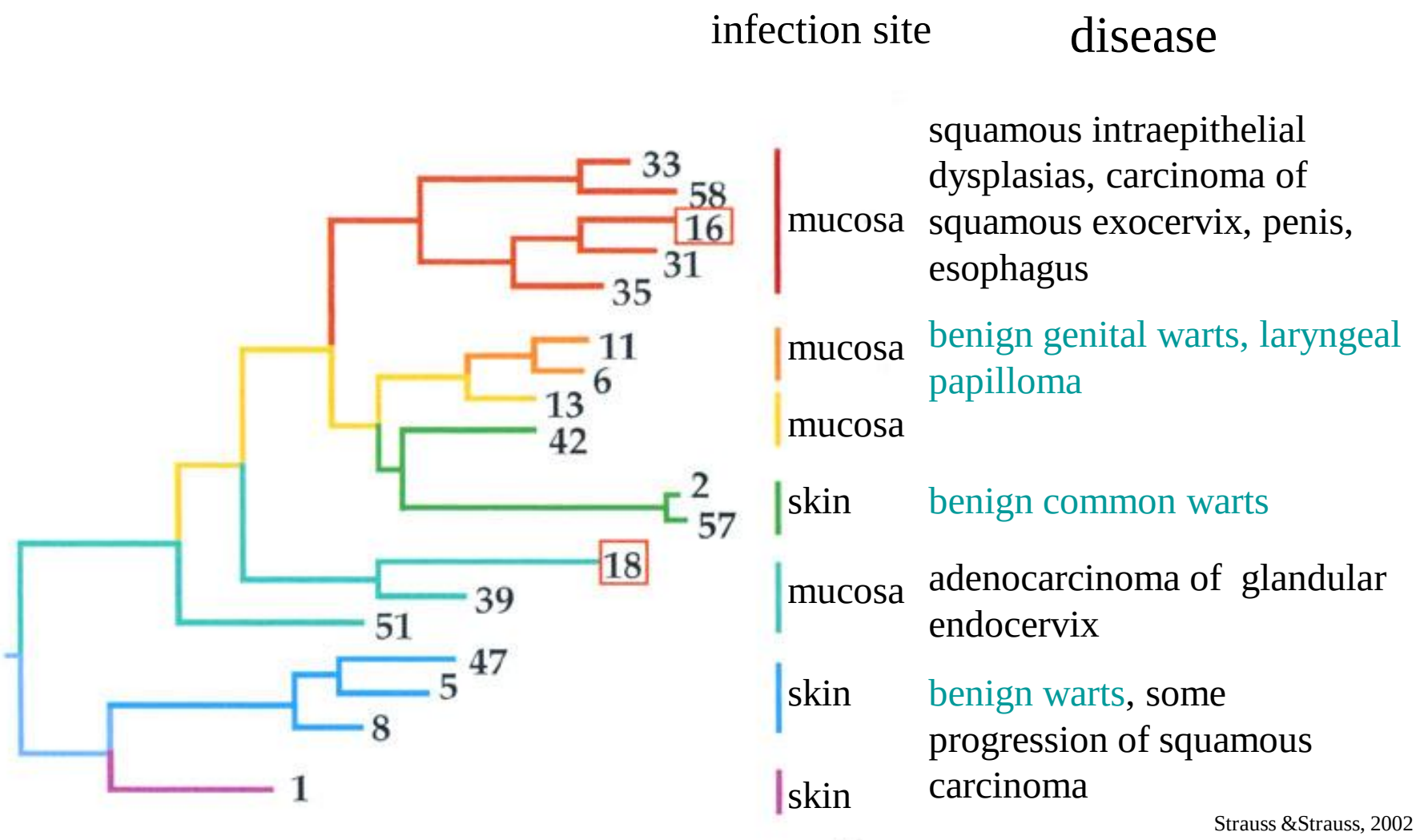
**CIN 2** – higher probability of transformation. Treatment – part of the cervix removed to prevent the disease.

**CIN 3 - surgical treatment is always needed in this case**.




www.cybermed.hr

# Human papilomavirus phylogeny- N-terminal part of E2




Strauss &Strauss, 2002

HPV VLP vaccines – e.g. Gardasil 9 (Merck) protects form HPV6, 11, 16, 18, 31, 33, 45, 52 and 58.

***Parvoviridae***:

- small (lat. *parvus*) isometric 18-26 nm, ssDNA, 4-6 kb, few genes, complicated splicing

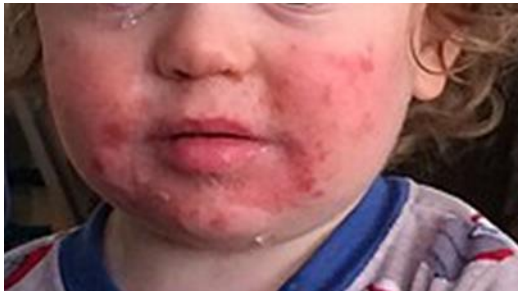
- viruses of mammals, birds, reptiles; insects (*Bombyx mori*), crustaceans, echinoderms

- B19V (*Erythroparvovirus primate1*) – infects erythrocyte precursors (*erythema infectiosum = fifth disease*), dangerous for fetuses (hydrops, stillbirth or abortion), arthritis in adults

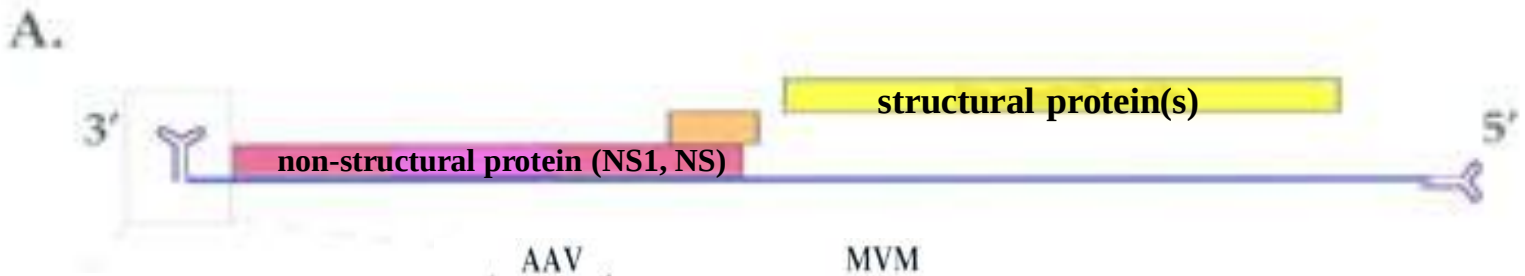
- replicate only in dividing cells

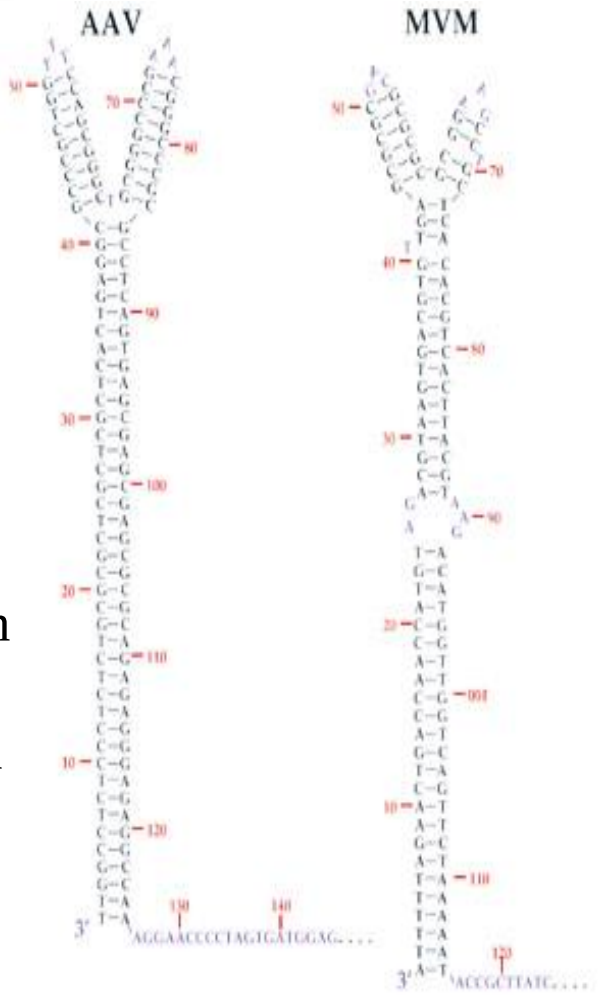
- (pseudo)satellitism - genus *Dependovirus*

- viral vectors (adeno associated virus, AAV)



# Parvoviral genome (ssDNA, 4-6 kb)



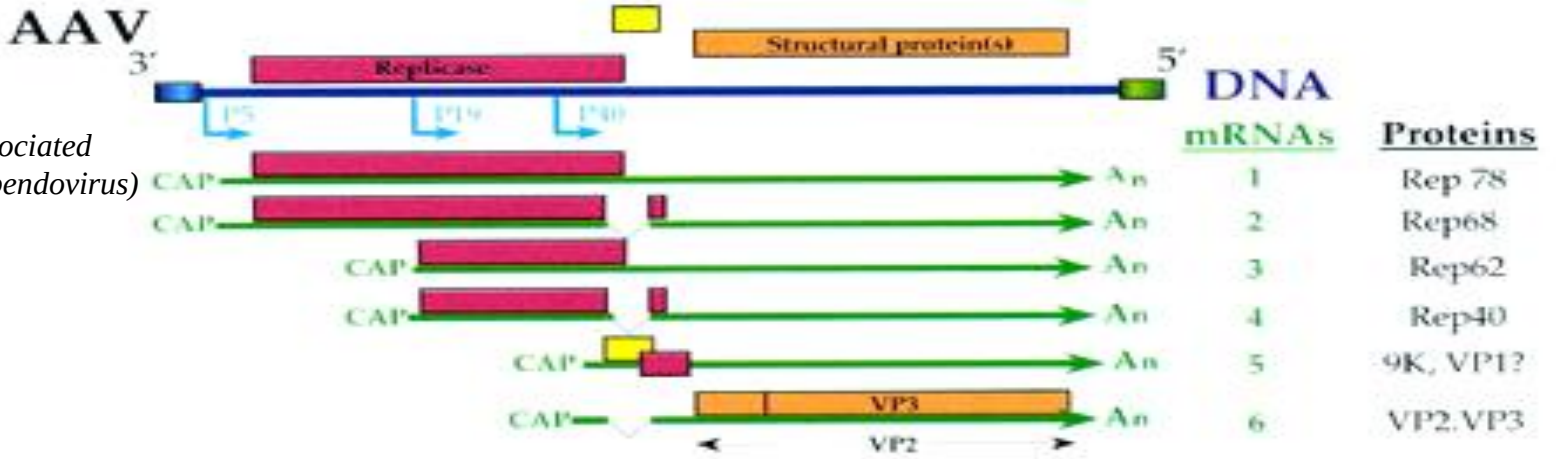




Homotelomeric genome B19 (5596 nt) with long (383 nt) terminal repeats (TRs) ending in imperfect palindromic hairpins (365 nt).

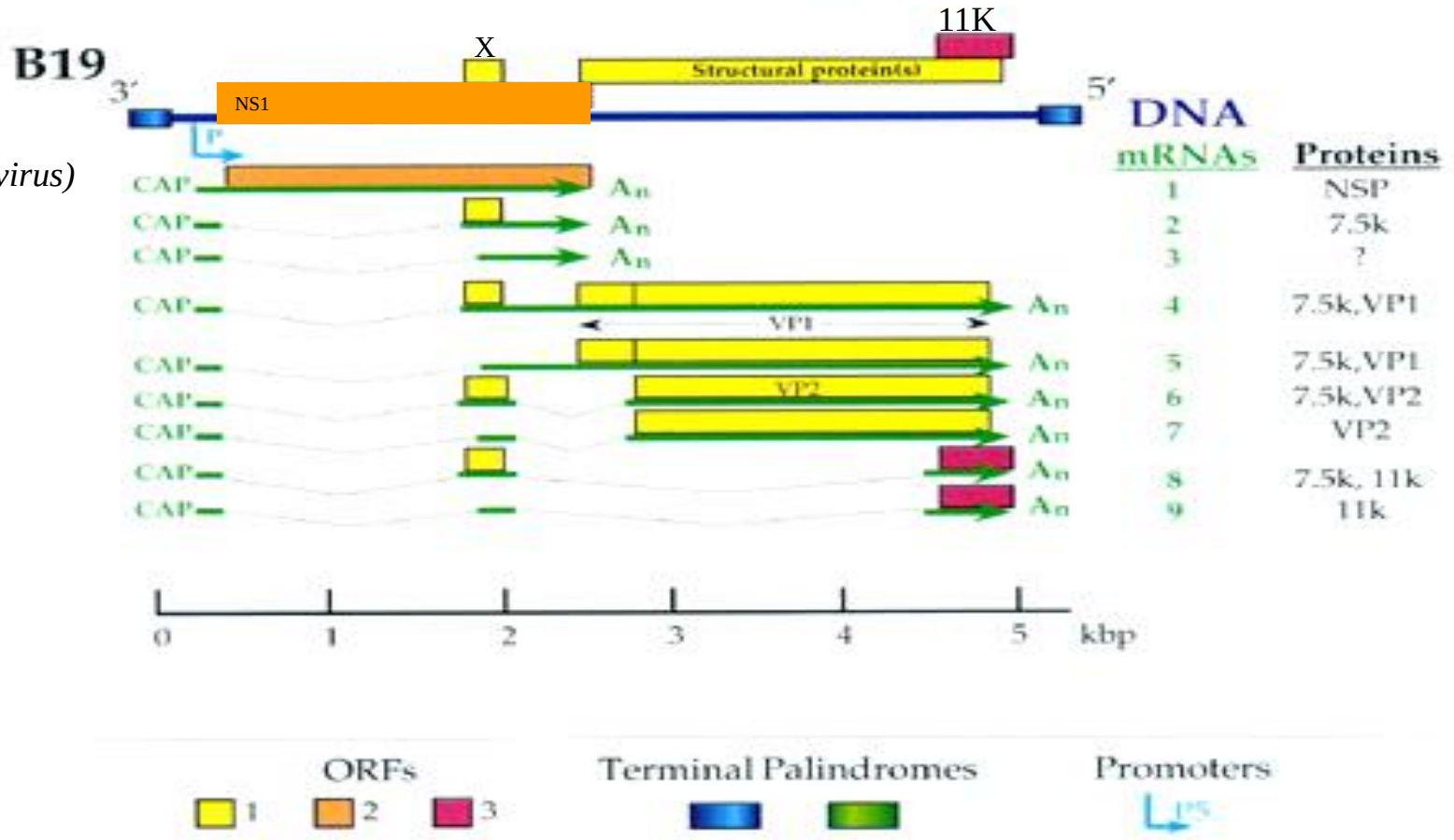
Hairpin integrity id essential for infectivity, specific interactions with signal transducer and activator of transcription 5 (STAT5).

Adapted from Strauss &Strauss, 2002

*Adeno associated virus (Dependovirus)*

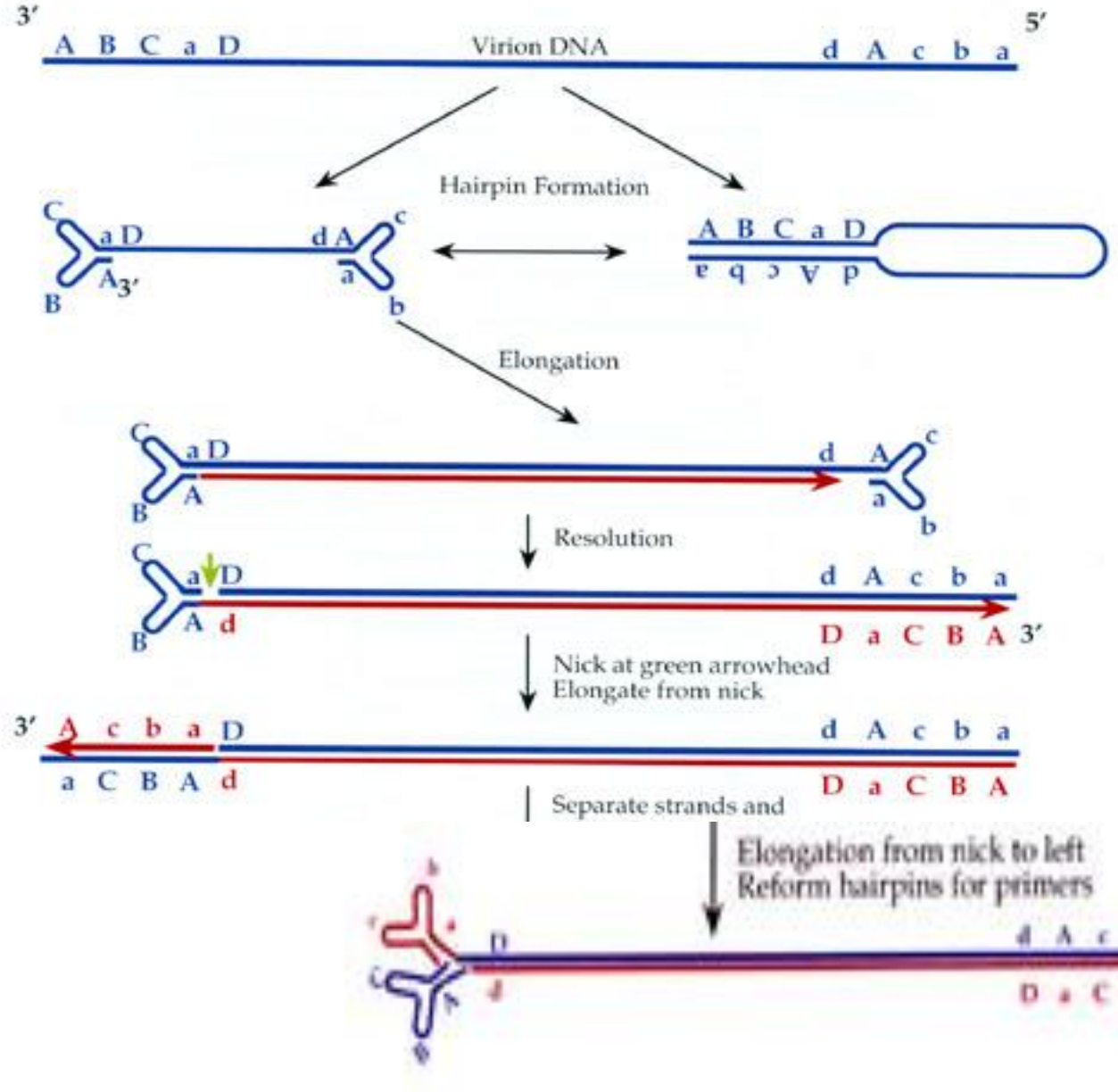



*(Erythrovirus)*




Prerađeno iz Strauss &Strauss, 2002

# Replikacija genoma parvovirusa – model kotrljajuće ukosnice

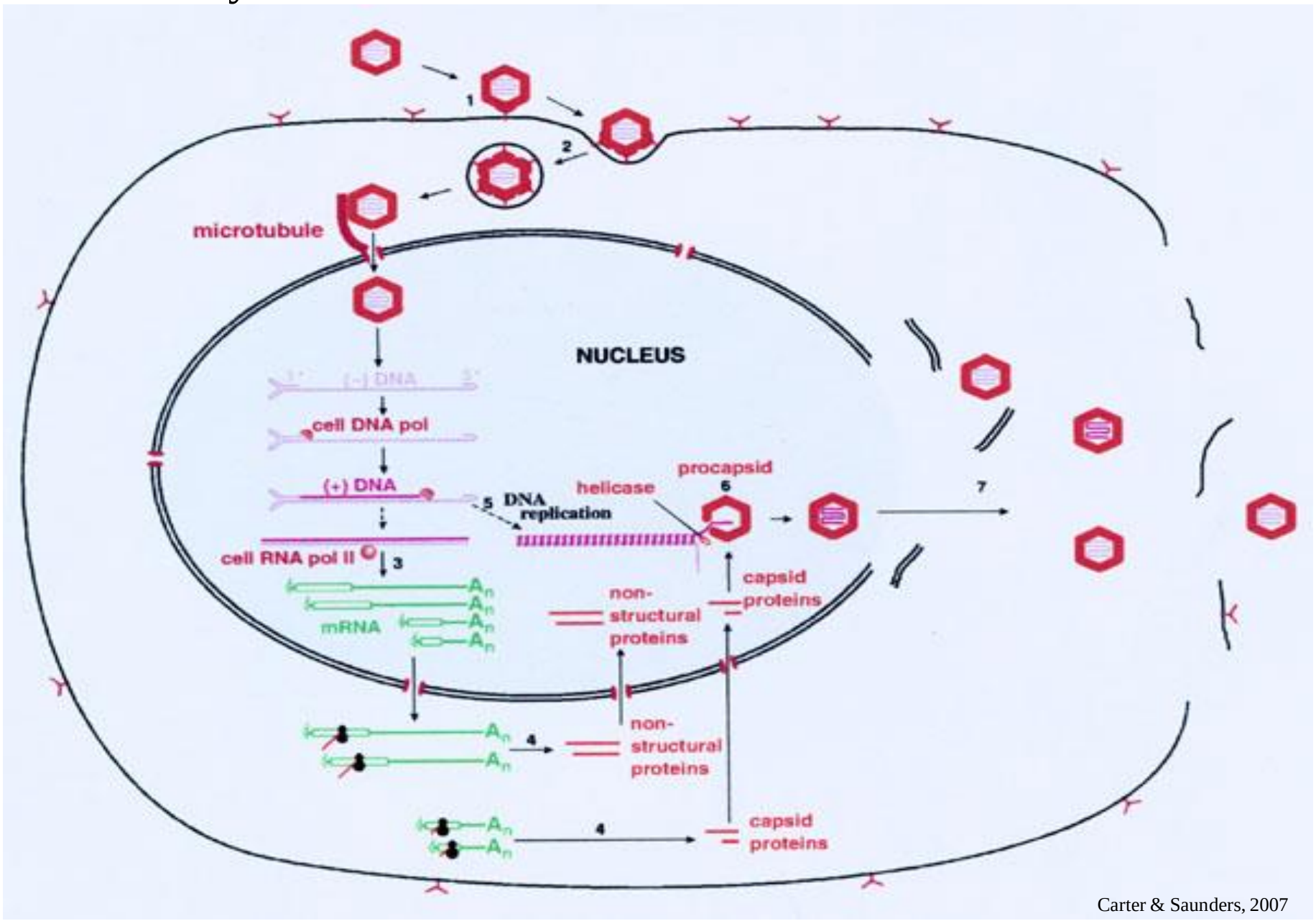



non-structural protein (NS1)

non-structural protein (NS1)

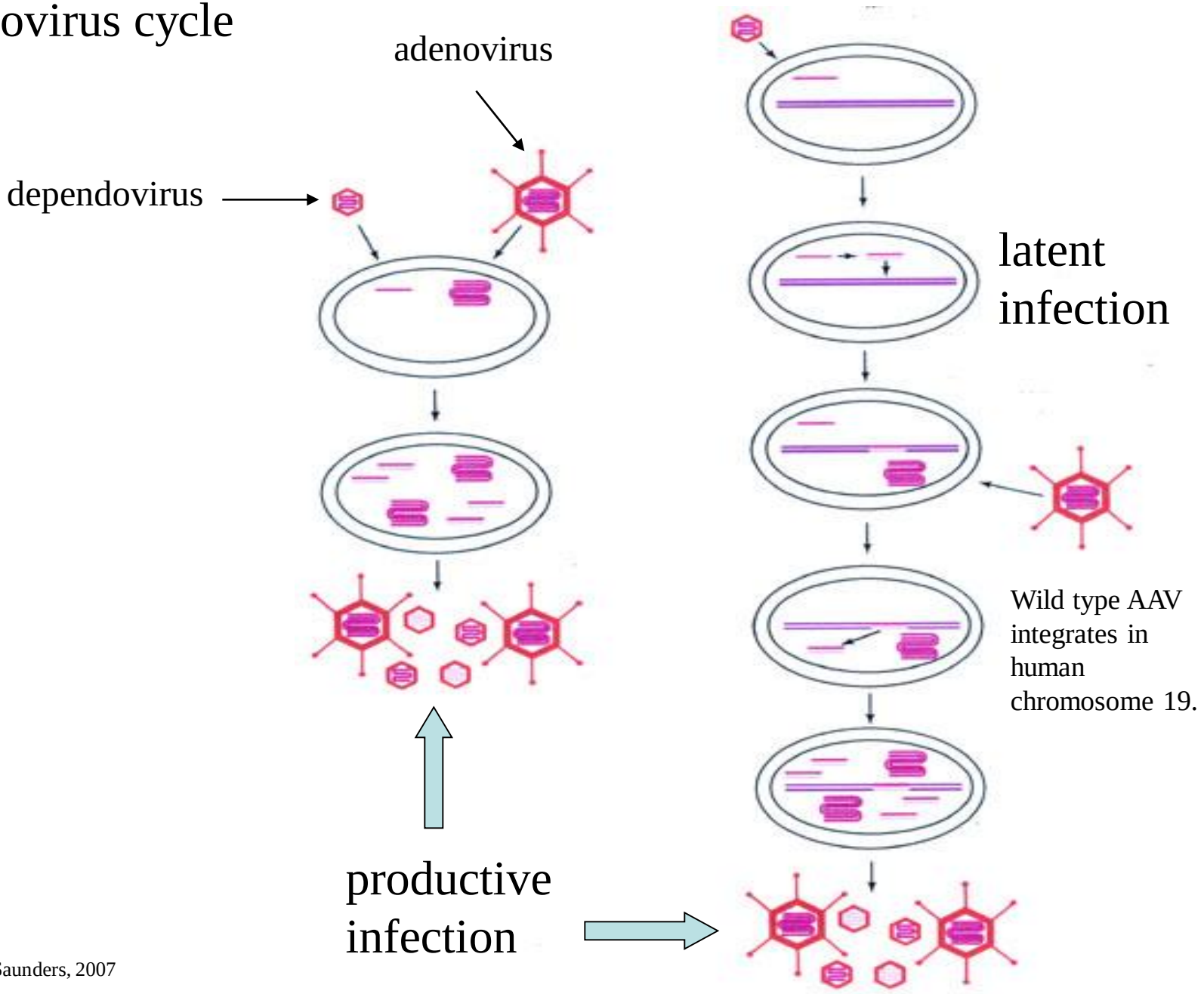
Strauss &Strauss, 2002

# Parvoviral cycle




Carter & Saunders, 2007

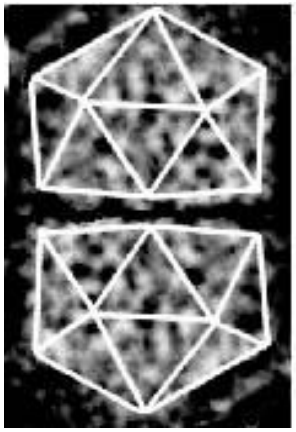
# Dependovirus cycle

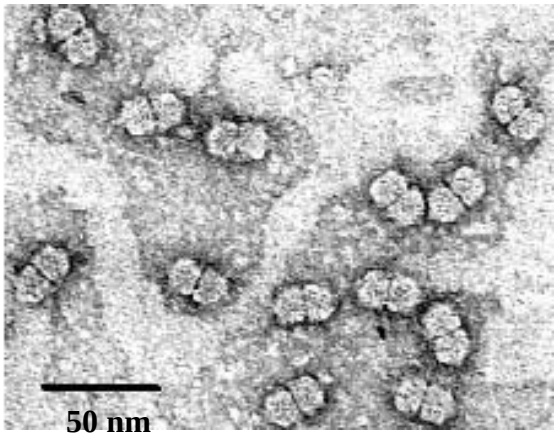



Carter & Saunders, 2007

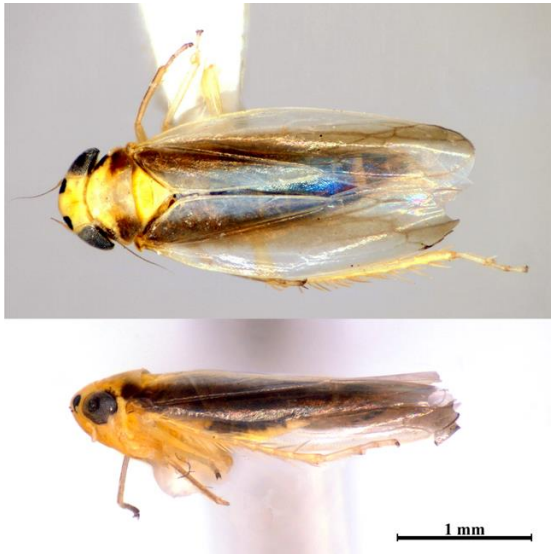
Geminiviruses – plant pathogenic,

economically important, emerging, invasive vectors!





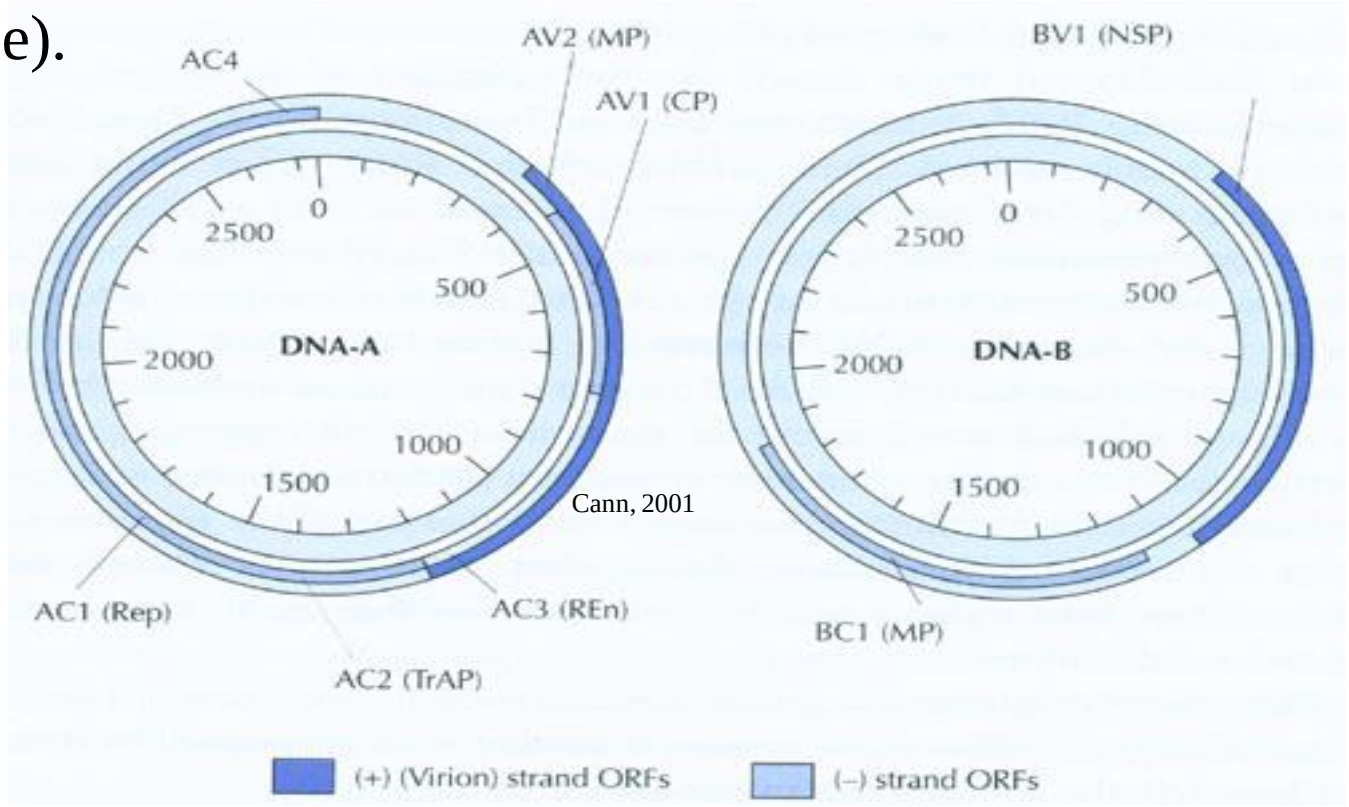

**maize streak virus, 18x30 nm**




*Cicadulina mbila* – maize leafhopper, maize streak virus vector.

*Bemisia tabaci* – vectors tomato, pepper, other plants geminiviruses.

# Geminiviral genomes are monopartite or bipartite, sscDNA (ambisense).




Cann, 2001

Segment A

V1 (R1) - positive orientation: coat protein, 29.7 kDa
V2 - positive orientation: movement protein, 12.8 kDa
C1 (L1) - negative orientation: replication initiation protein (Rep) 40.2 kDa
C2 (L2) - negative orientation: transcription activator protein (TrAP), 19.6 kDa
C3 (L3) - negative orientation: replication enhancer (REn), 15.6 kDa
C4 - negative orientation: symptom expression determ.?, 12.0 kDa

Segment B (movement!)

V1 (R1) - positive orientation: nuclear shuttle protein, 33.1 kDa
C1 (L1) - negative orientation: movement protein, 29.6 kDa

*Begomovirus* – genom components A and B each 2,7 kb in a separate particle (2 particle types = bipartite virus).

Both segments usually needed for infection, but B depends on A for replication.

V-proteins in + sense, C in - sense.

# DNA - phages

lytic

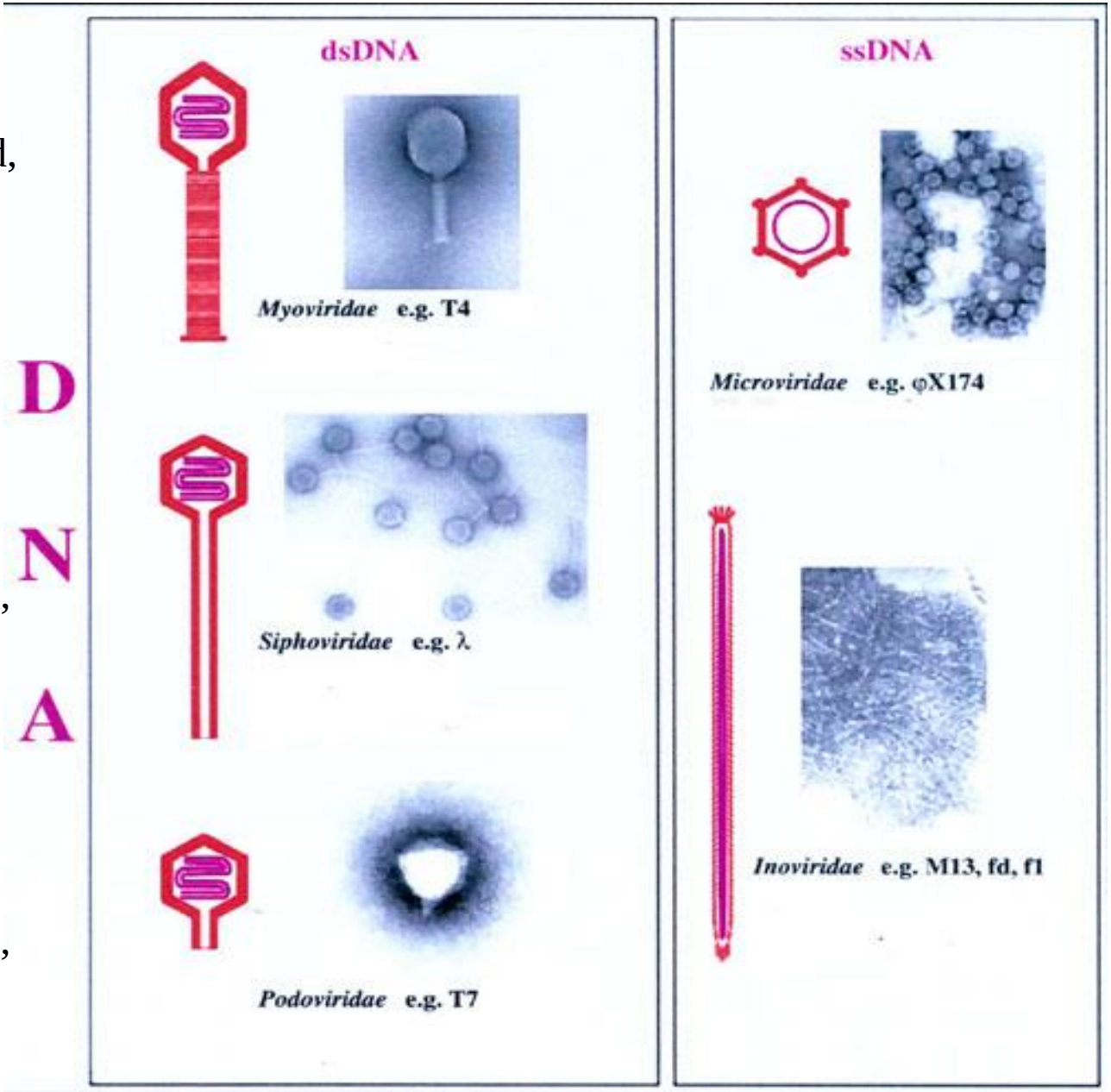
elongated head, contractile tail

lytic/lysogenic

isometric head, rigid long tail

lytic

isometric head, rigid short tail




lytic

isometric, minute

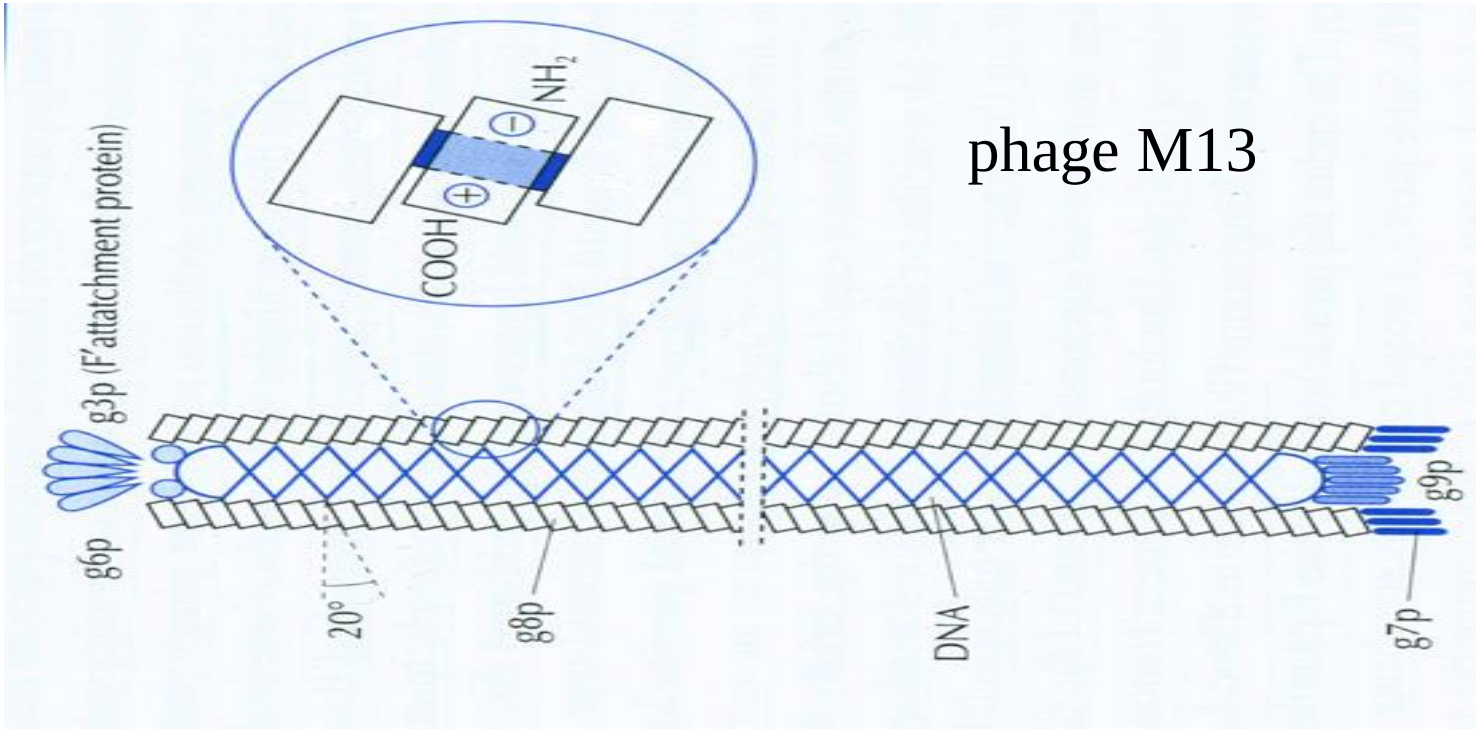
"chronic infections", filamentous

Carter & Saunders, 2007

Genome diversity in phages higher than in other virus groups.

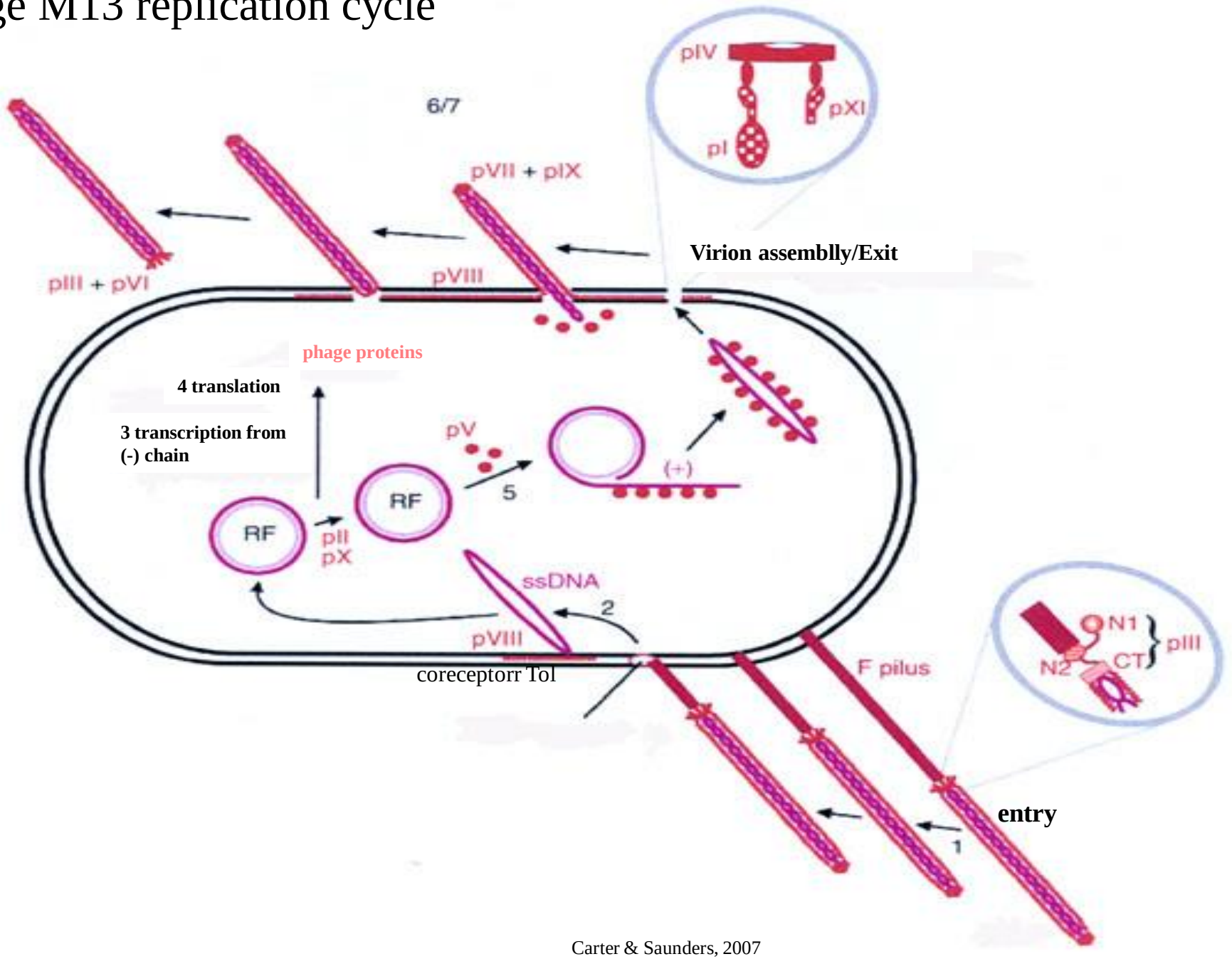
Generally, high density genomes and particles, different transcription and translation strategies, high applicability of related knowledge.

Regulations – temporal and spatial (other courses).




Cann, Principles of Molecular Virology, AP, 2001.

# Phage M13 replication cycle




Carter & Saunders, 2007

***Microviridae*** – first evidence of overlapping genes in prokaryotes, first sequenced DNA genome, second synthetic virus

***Inoviridae*** – androphages, high coding density, CPs are recycled, virion is assembled in the cell membrane, some can be integrated in the host genome (lysogeny).

M13-vectors, phagemids,

*phage display* – antibody production, protein-protein interaction research

CTXφ - codes cholera-toxin

Invasive meningococci have phages similar to M13.

***Myo-, Sipho-, Podoviridae*** :

T4 – first evidence of splicing, *phage display*, nanotechnology, potential therapy of diarrhea (*E. coli*),

T7-DNA-polymerase = Sequenase™

λ-vectors, *enzybiotics* (lytic phage enzymes), evolutionary (selective) advantages for bacteria.

Viruses with small DNA genomes are much more diverse regarding their genome replication strategies, transcription, translation. They include important cloning vectors, expression vectors, many are oncogenic, some can be integrated in the host genomes.