Structural Virology

Lecture 10

Pavel Plevka

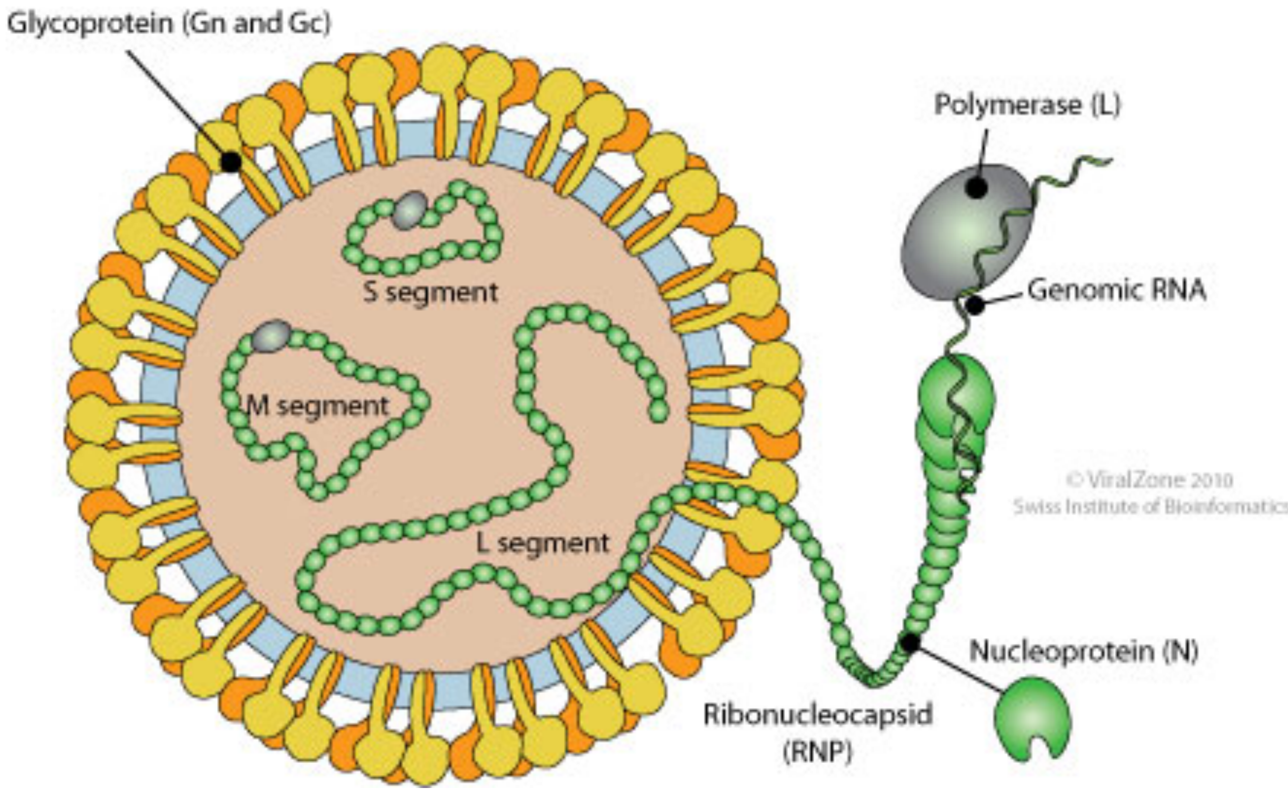
Lecture on 12.12. will take place in A35

- excursion to virology, cryo-EM and X-ray lab
- demonstration of structural-biology approaches used in virology

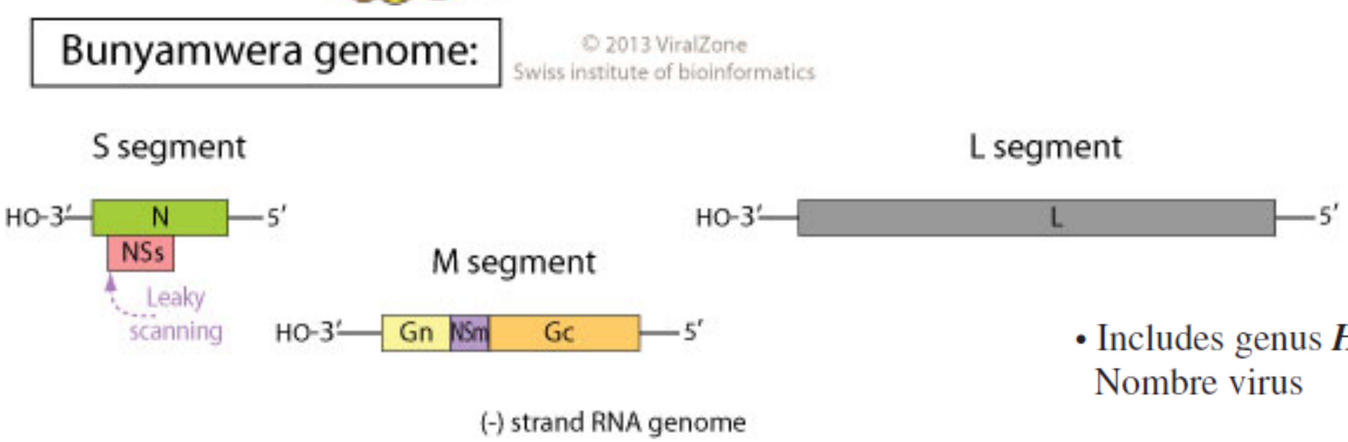
Emerging viruses

Emerging Viruses	Examples
• Viruses in new hosts	Nipah virus in pigs and humans
• Viruses in new areas	West Nile virus in North America
• Newly evolved viruses	Influenza virus reassortants
• Recently discovered viruses	Human metapneumovirus
• Re-emerging viruses	Mumps virus

Bunyaviridae

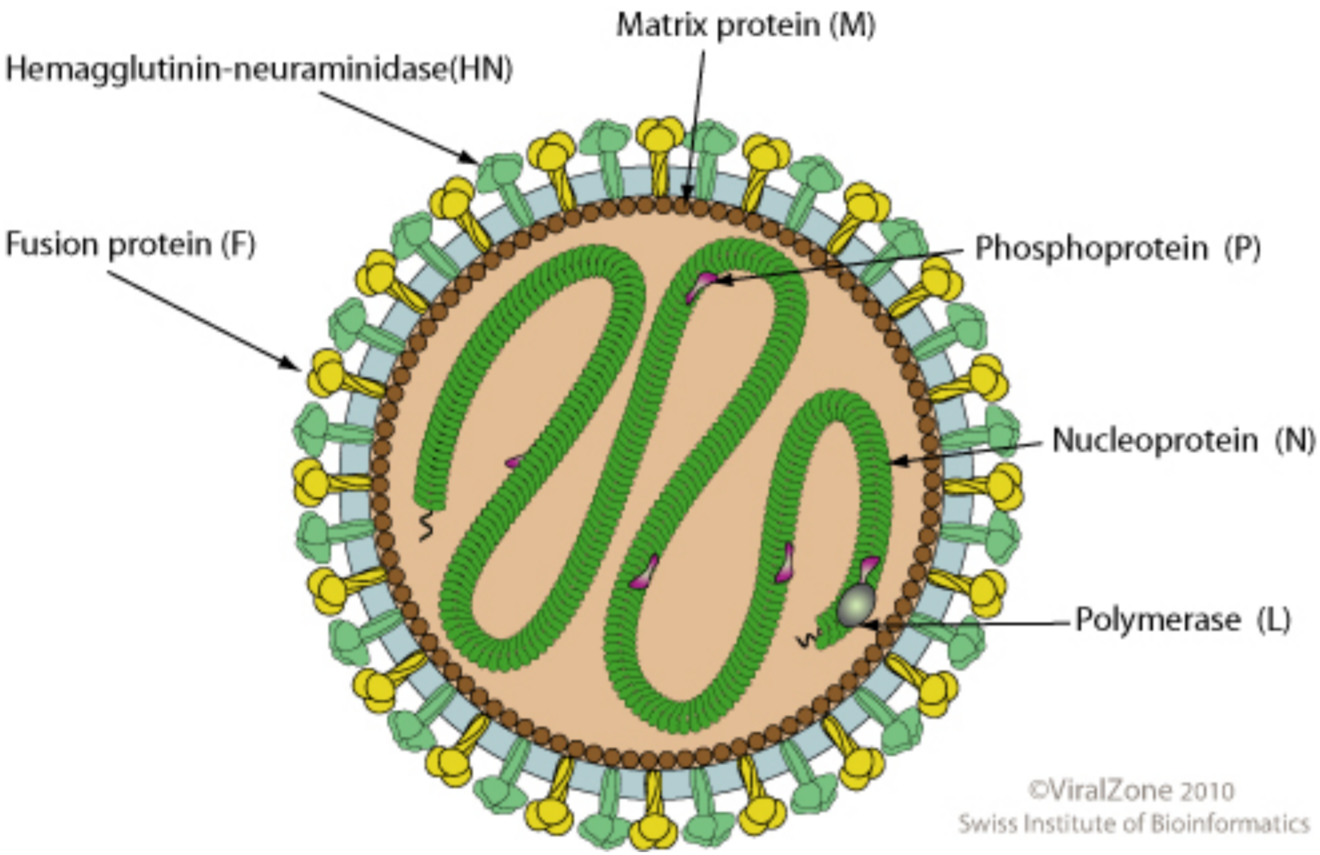


Segmented -ssRNA linear genome, L segment is between 6.8 and 12 kb, M segment between 3.2 and 4.9 kb and S segment between 1 and 3 kb. Encodes for four to six proteins.



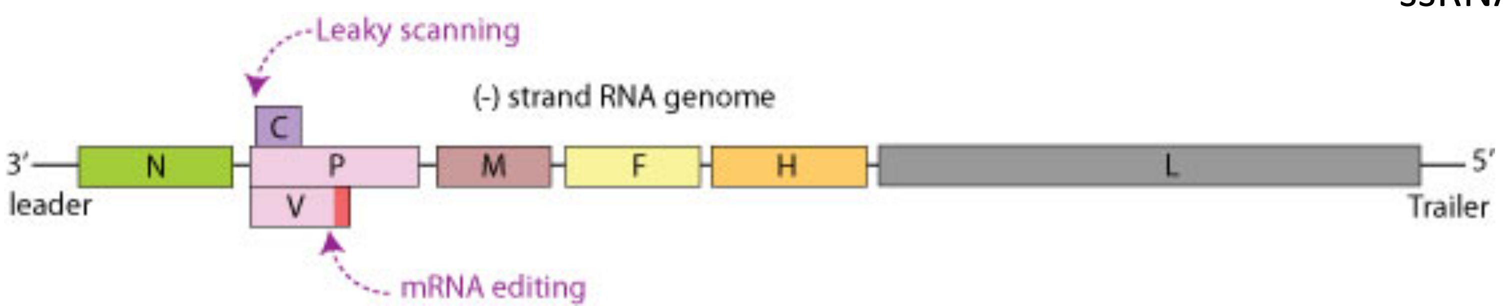
- Includes genus ***Hantavirus***, e.g. Sin Nombre virus

Paramyxoviridae

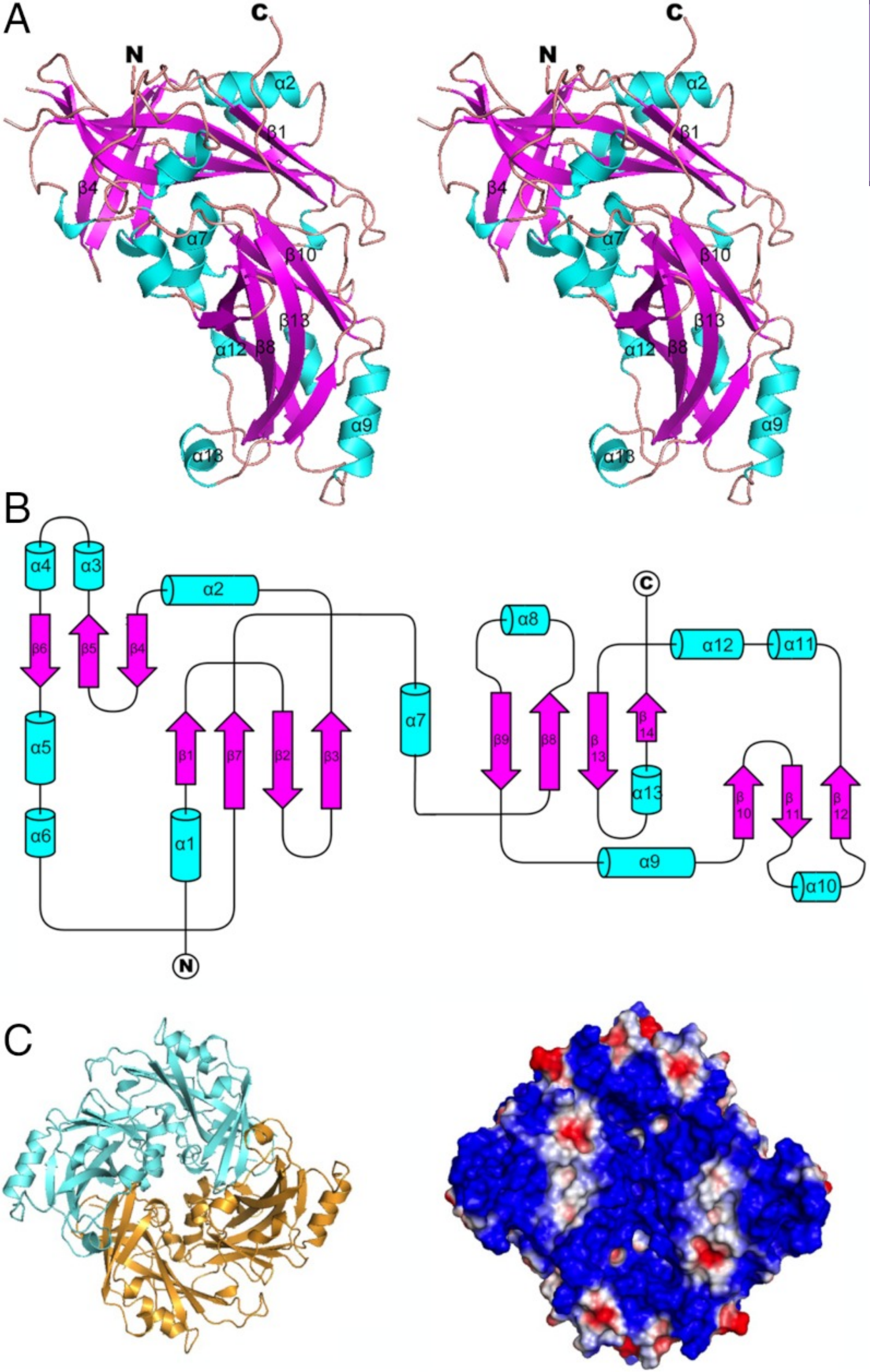


- Nucleocapsid symmetry: helical
- Enveloped, with glycoprotein spikes
- Includes Hendra, Nipah, measles, mumps, and human metapneumoviruses

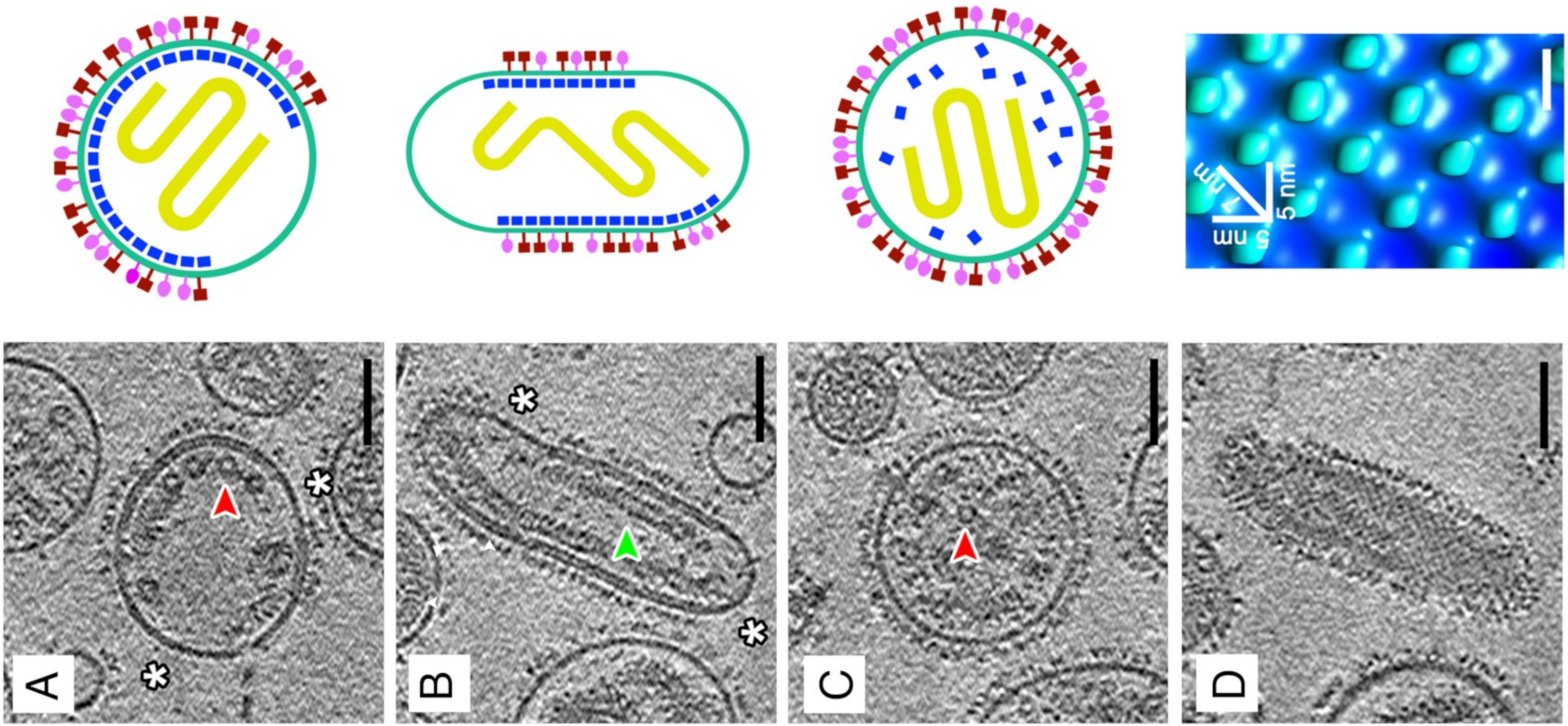
-ssRNA ±15kB



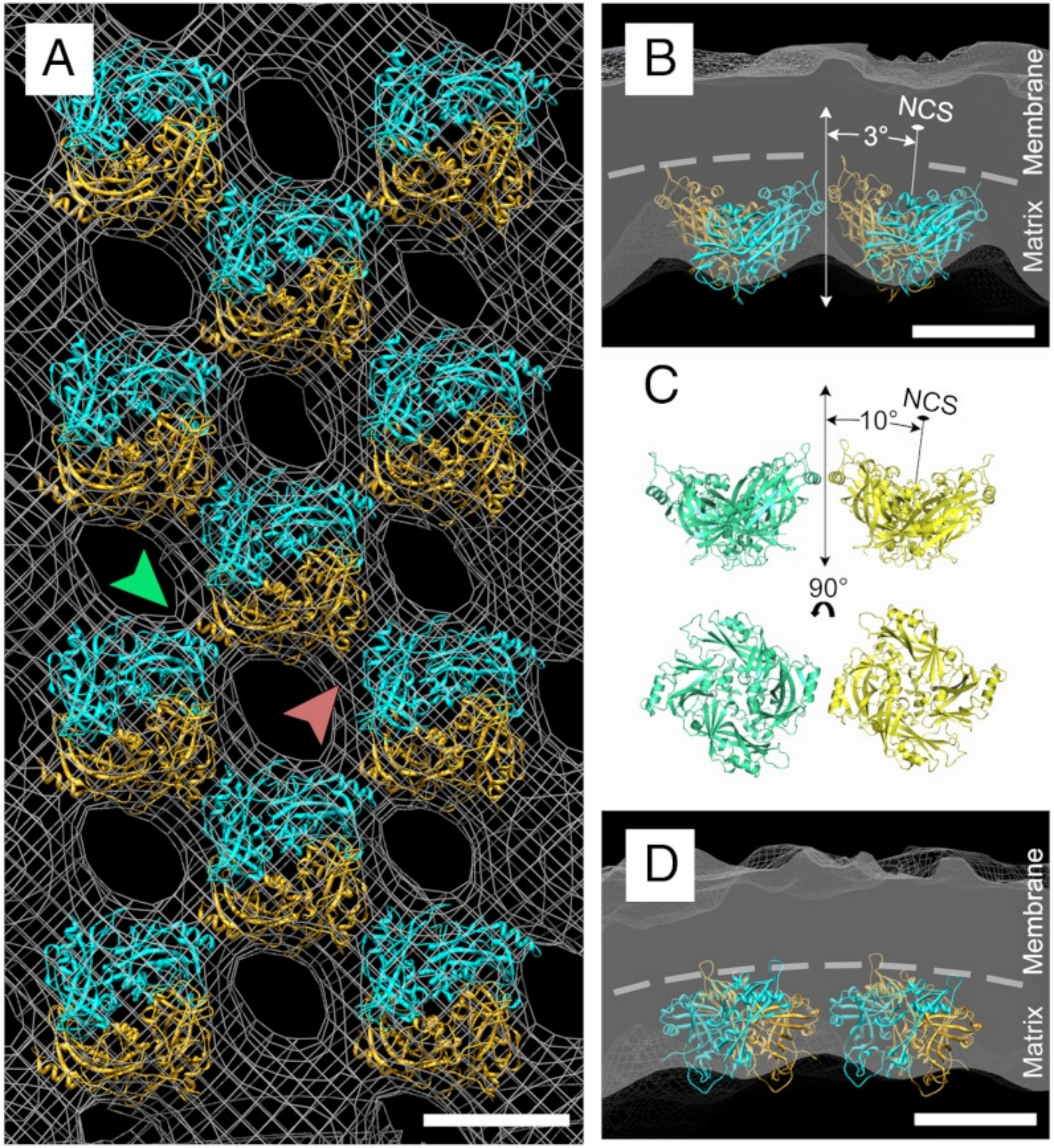
Newcastle disease virus matrix protein

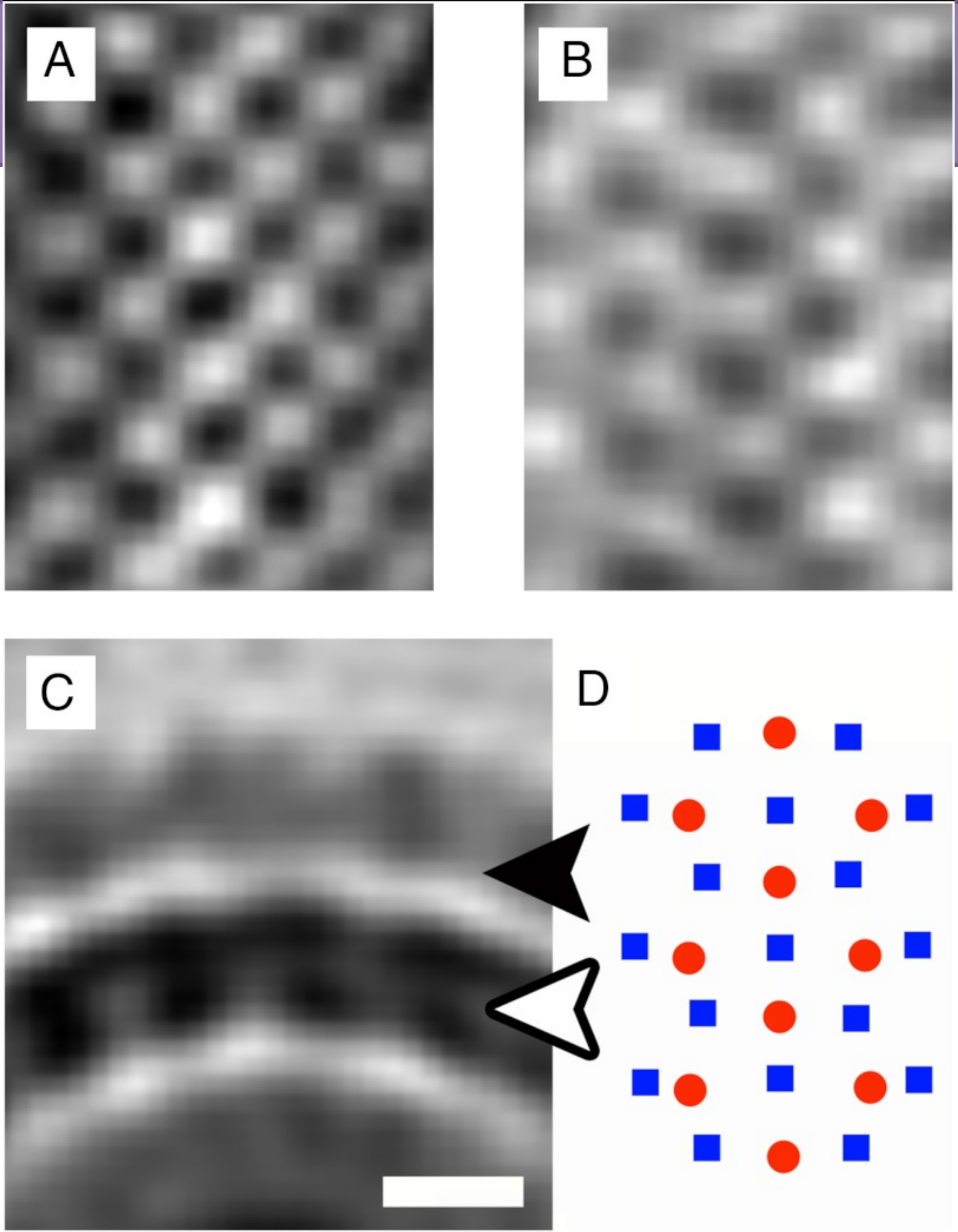


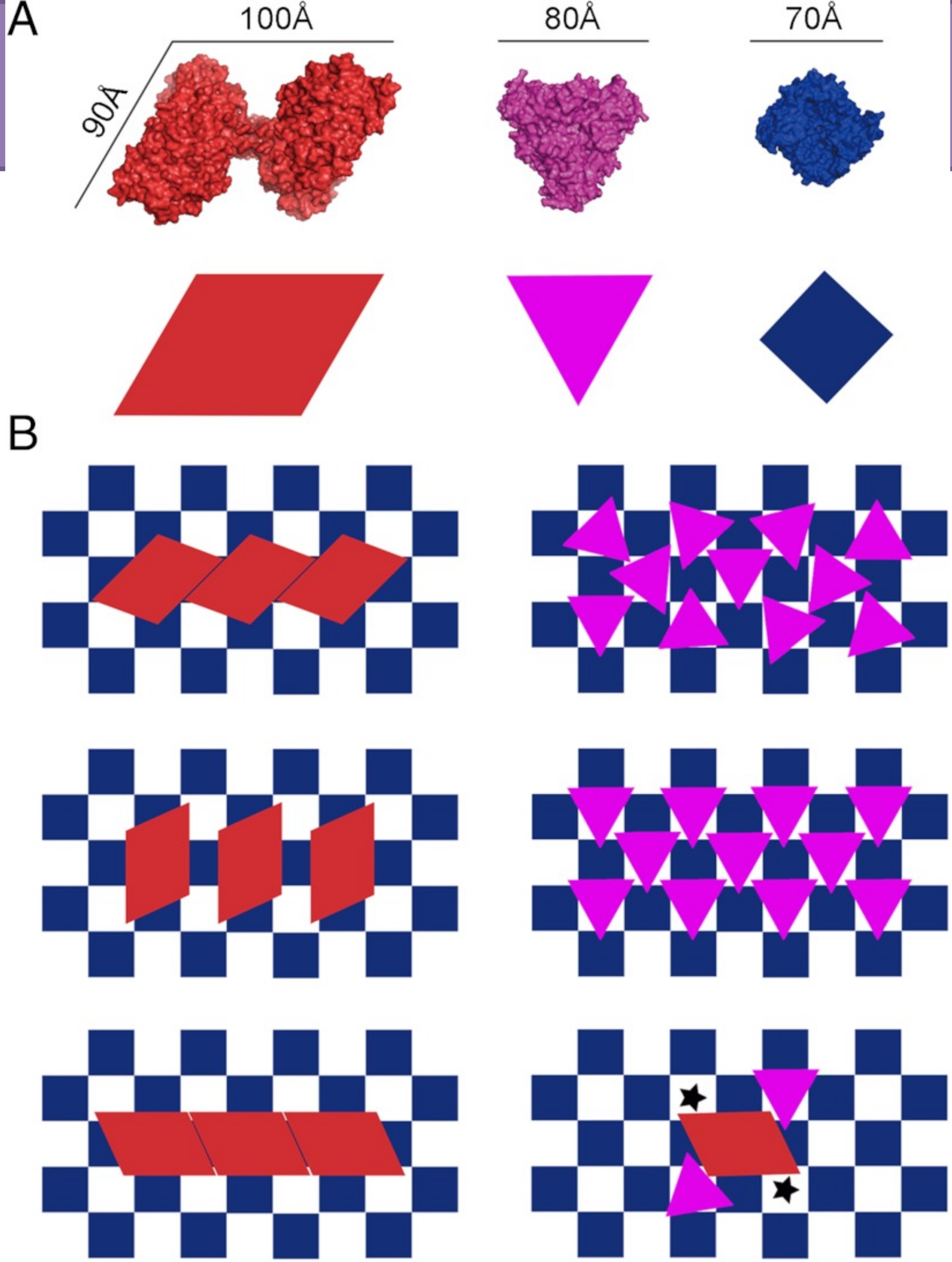
Newcastle disease virus – matrix protein



Newcastle disease virus



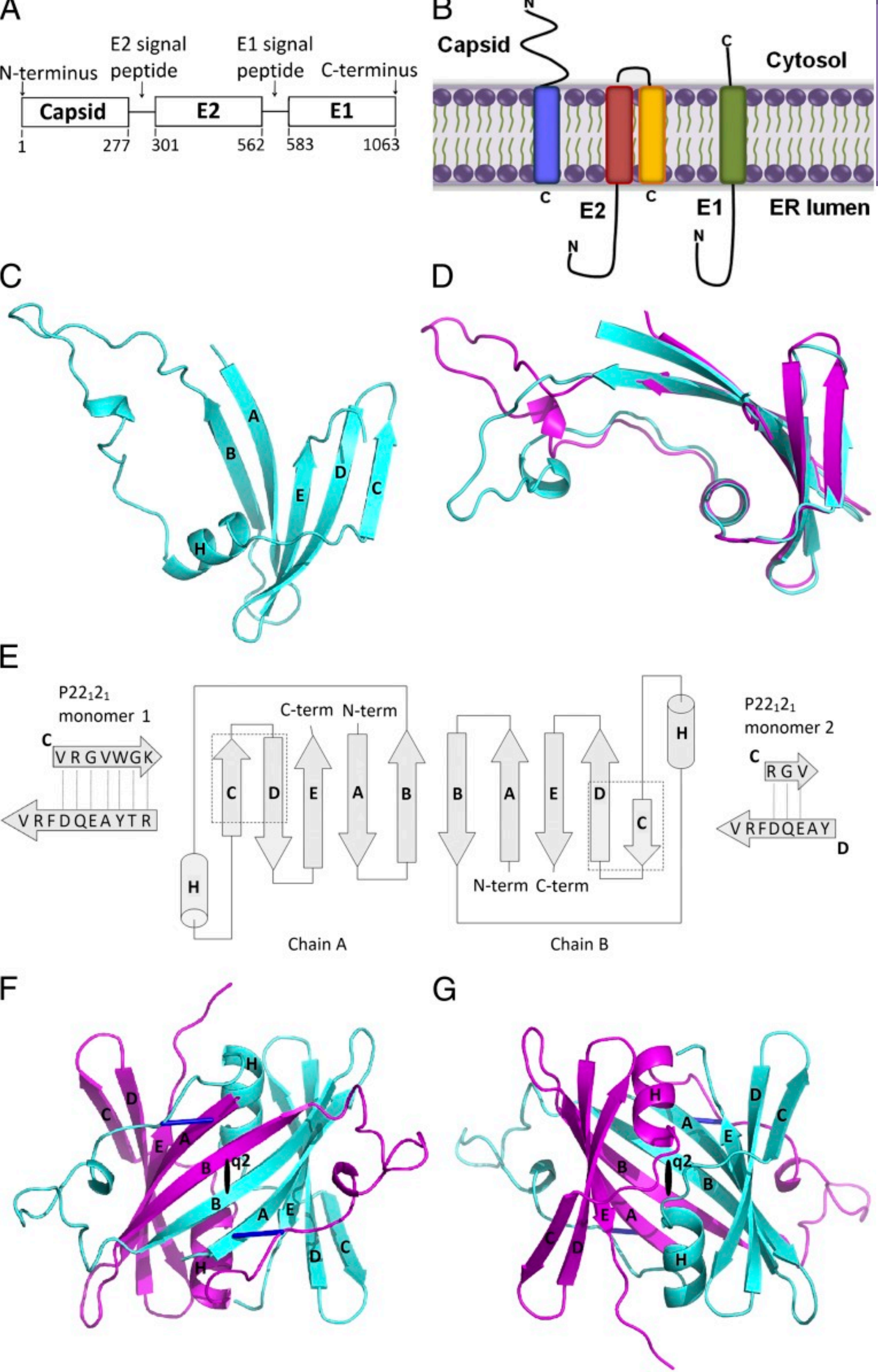

A
B
C
D

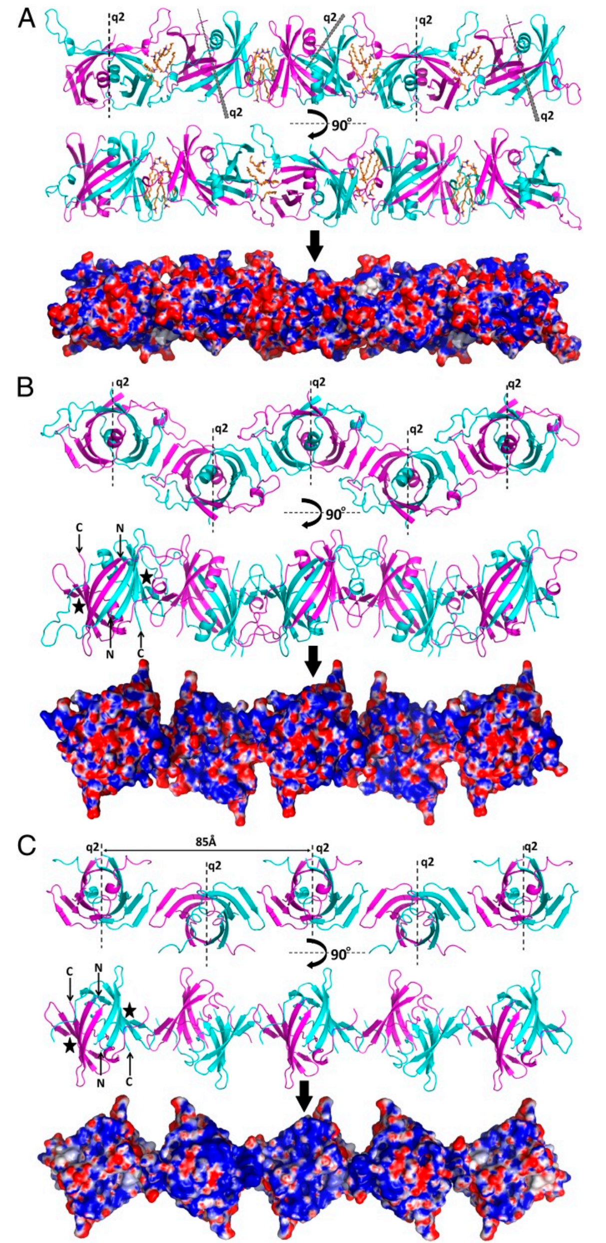

A
100Å
90Å
80Å
70Å
B

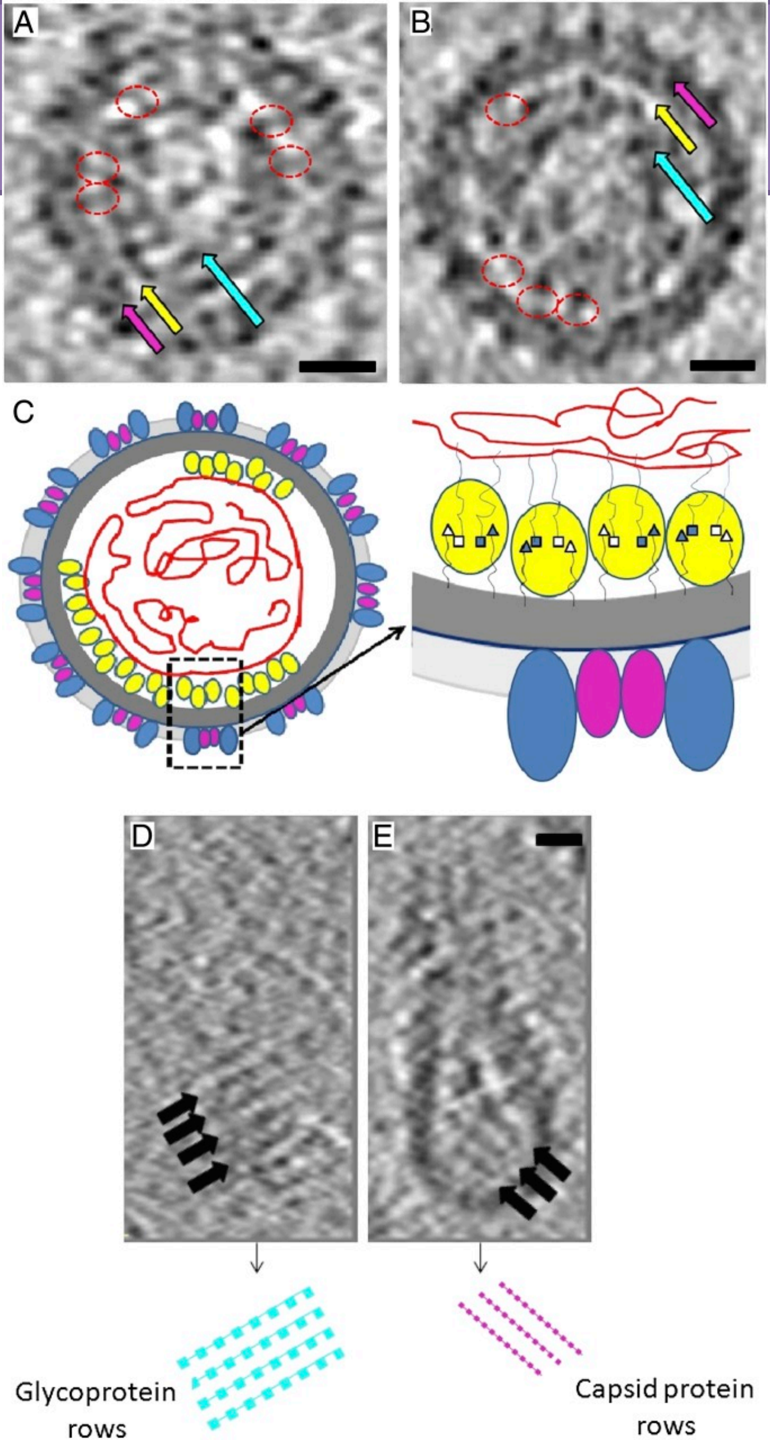
Paramyxoviridae - rubulavirus

Mumps

Rubella – capsid protein structure

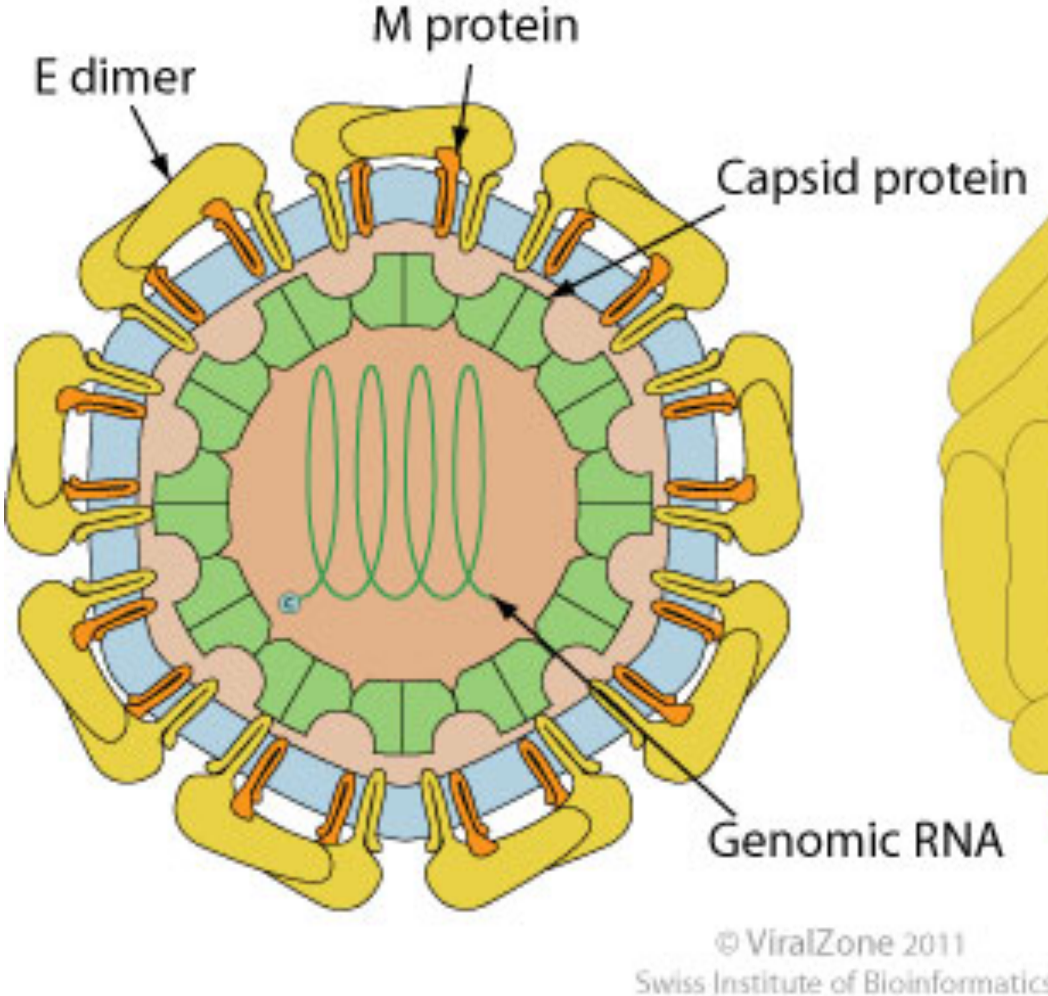


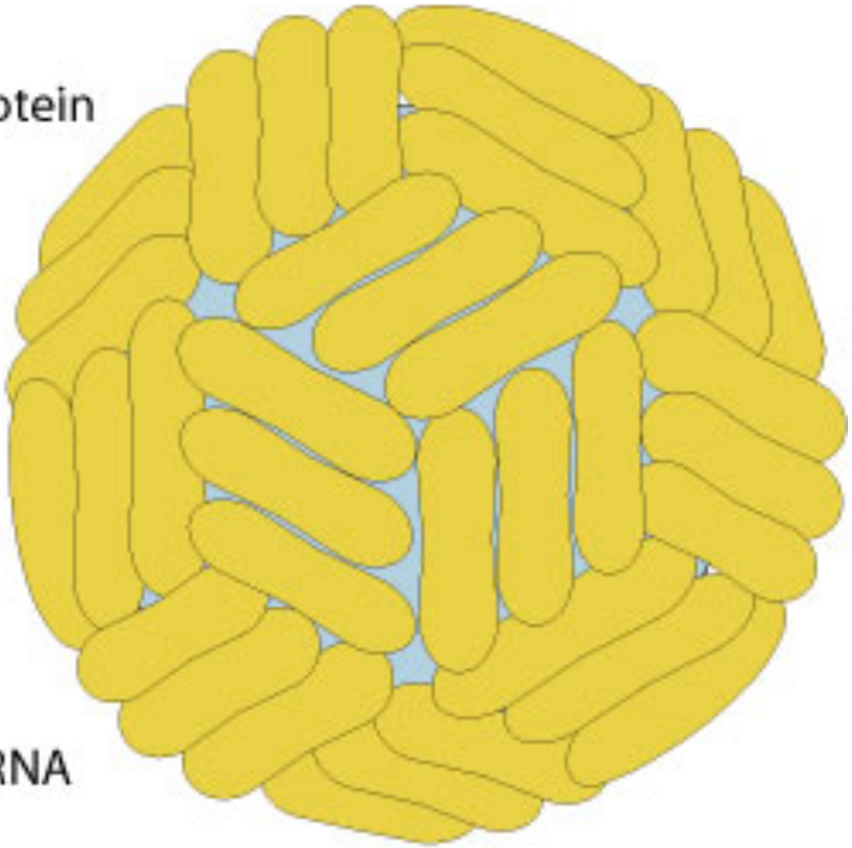




A
B
C
D
E
Glycoprotein rows
Capsid protein rows

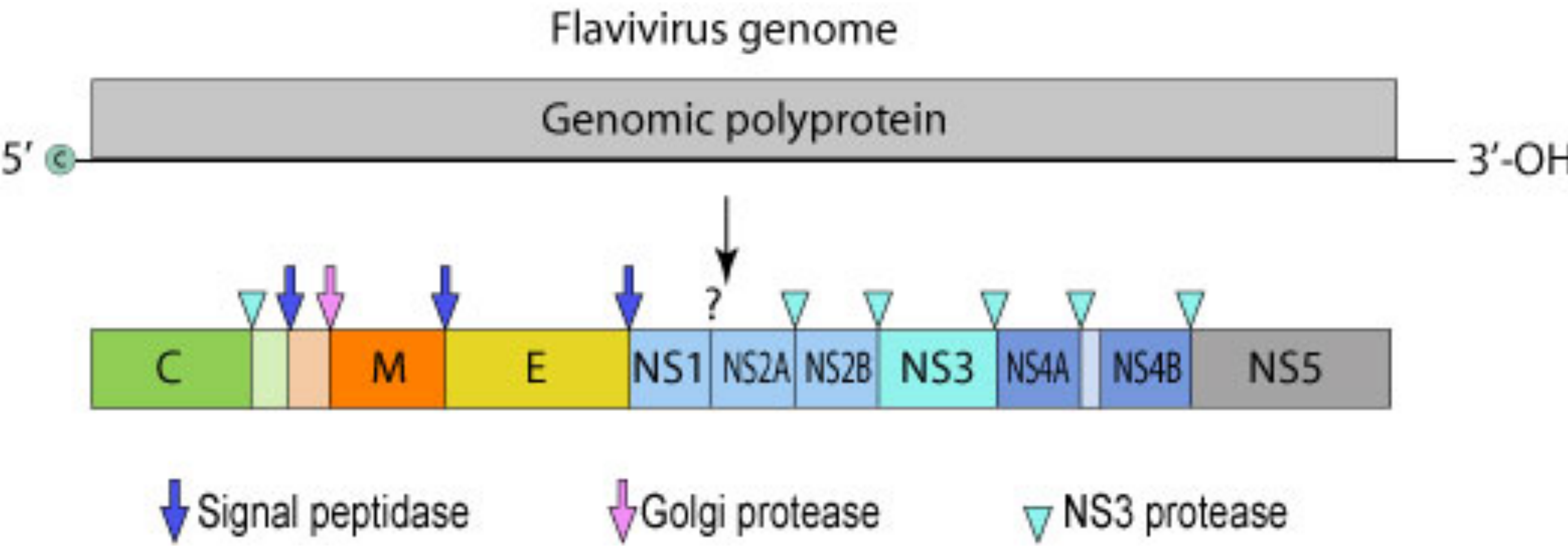
Flaviviridae





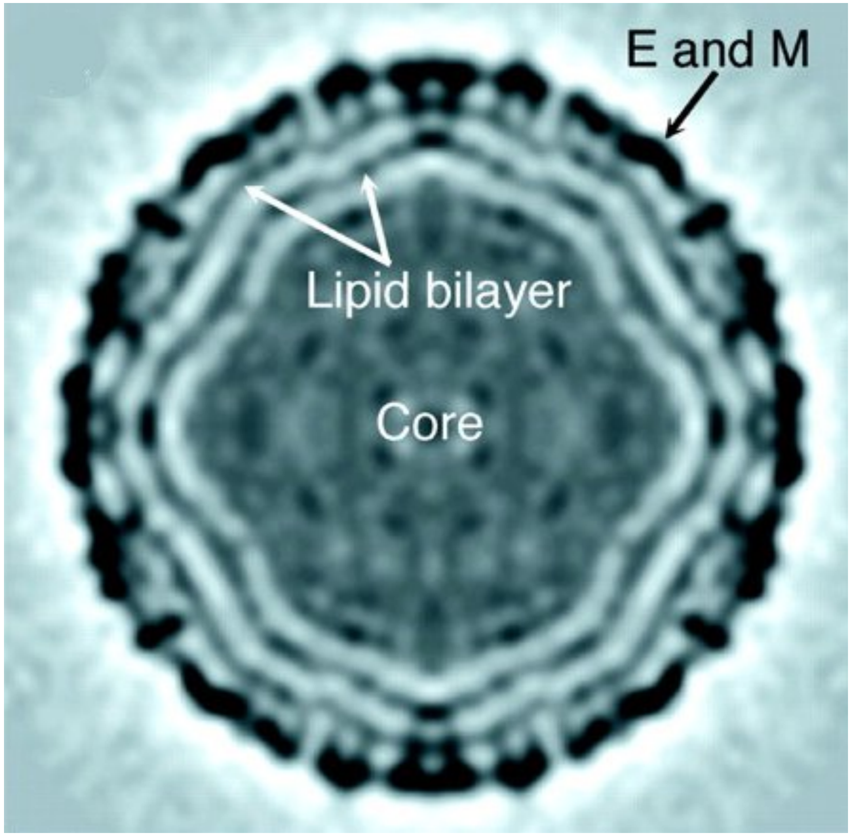
T=3-like organization of surface dimers

Flaviviridae - genome

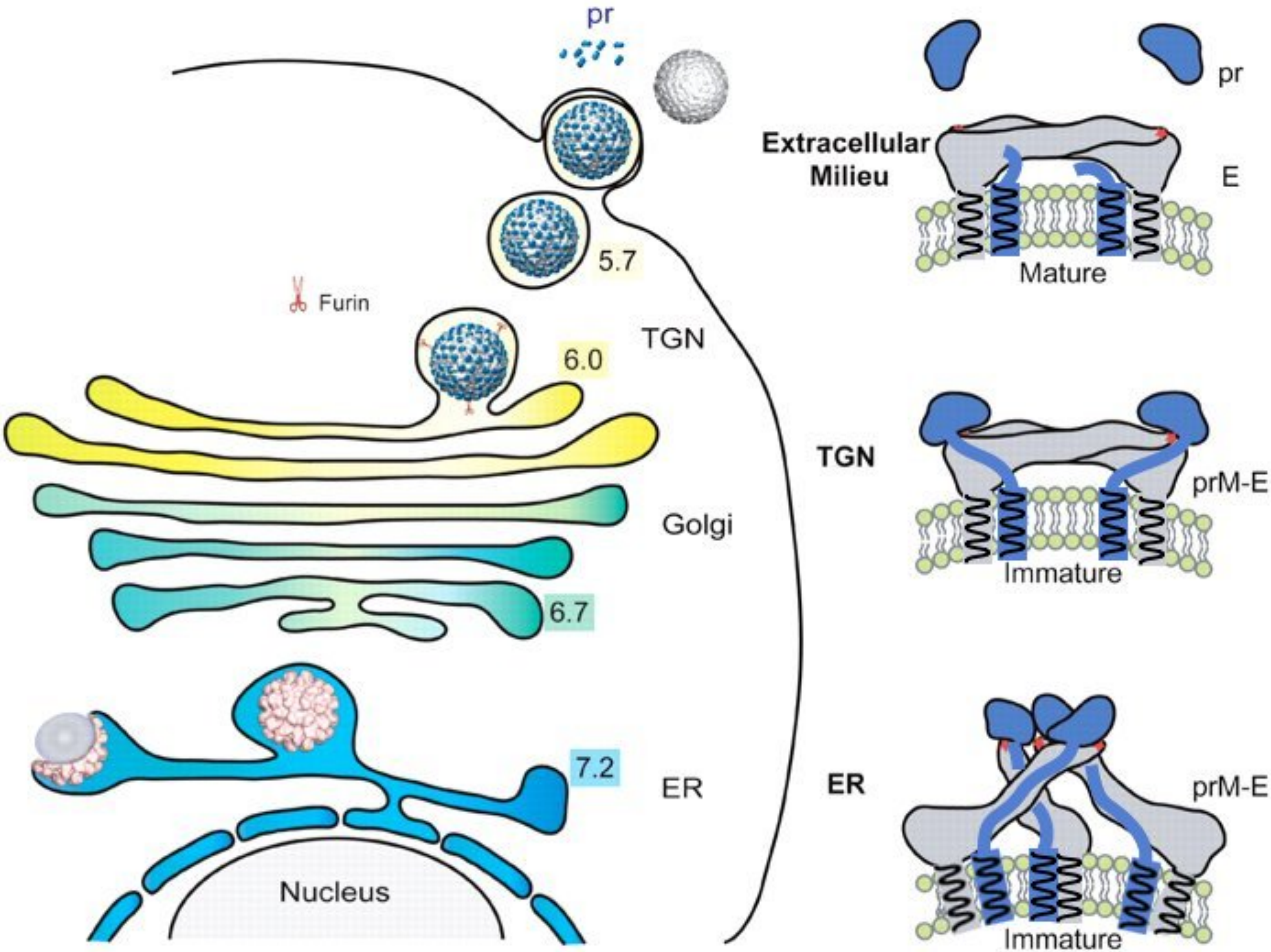


Flaviviruses

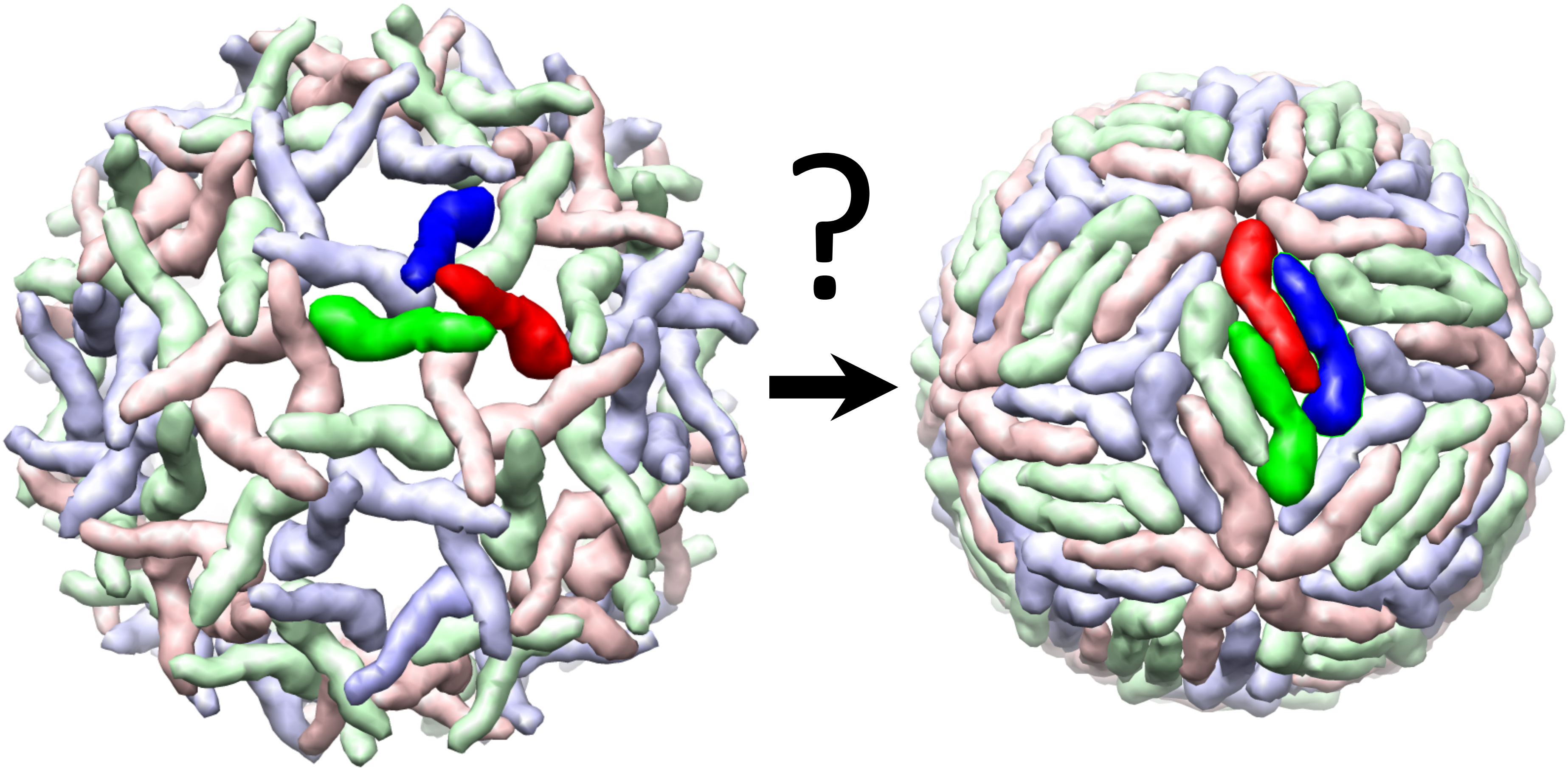
- Tick-borne encephalitis
- West Nile
- Yellow fever
- Dengue (strains 1-4)



Mukhopadhyay et al. Science, 2003

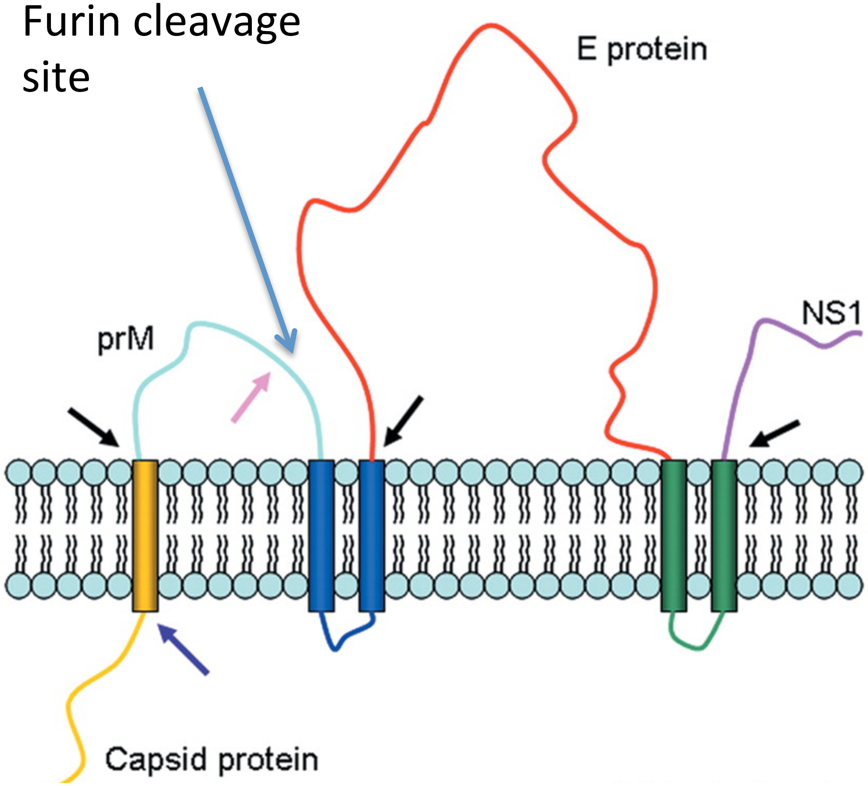


I Yu et al. Science 2008

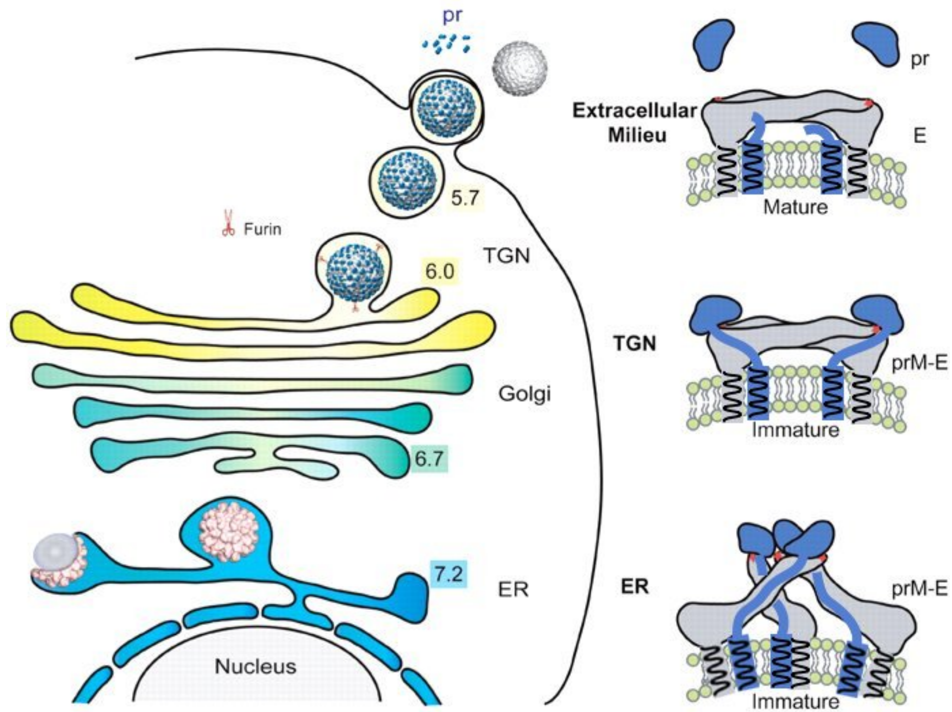


Dengue2 prR201A maturation mutant

Furin cleavage site



L Li et al. Science 2008

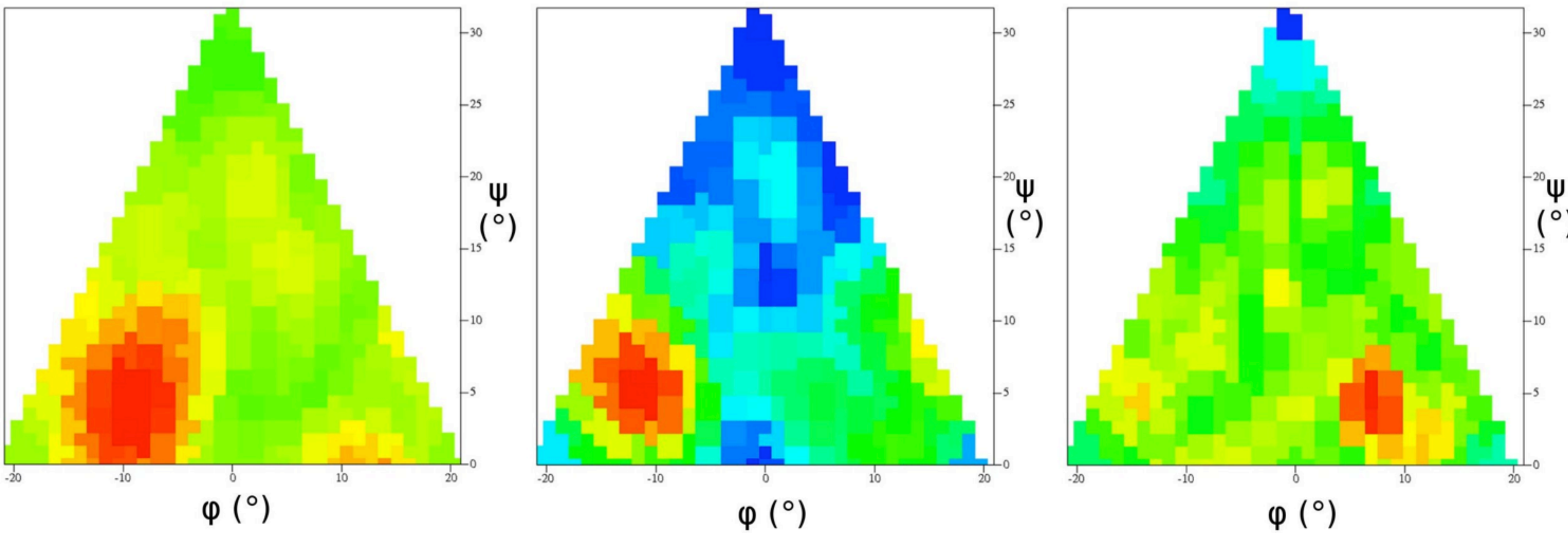


I Yu et al. Science 2008

Immature dengue virus structure in tomogram

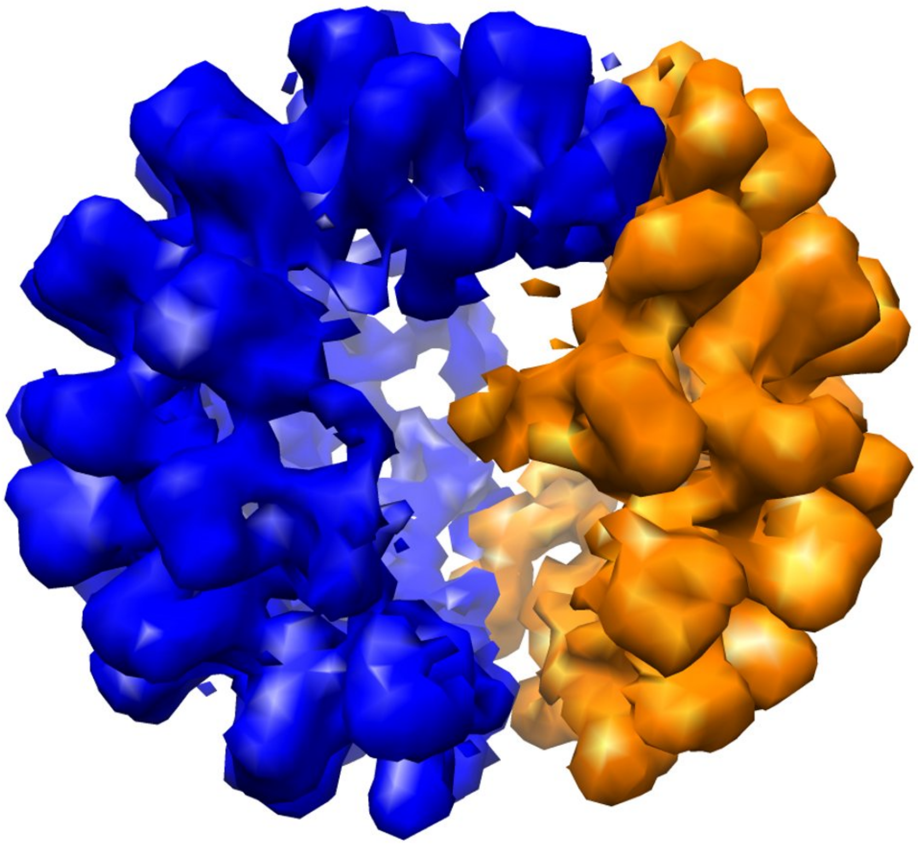
Immature dengue virus structure in projection image

Low pH-immature dengue virus structure structure in projection image

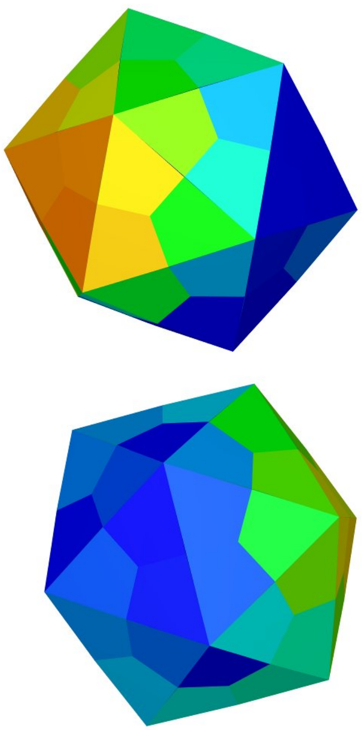


orientation of immature structure from tomogram: .... psi = 240°, theta = 28°, phi = 160°
orientation of low immature structure from projection: ..... psi = 246°, theta = 28°, phi = 152°
orientation of low pH-immature structure from projection: psi = 197°, theta = 26°, phi = 196°
(Euler angles in ZYZ convention relative to icosahedron in standard orientation.)

prR201A particles with “double” symmetry



Correlation with model in orientation 1

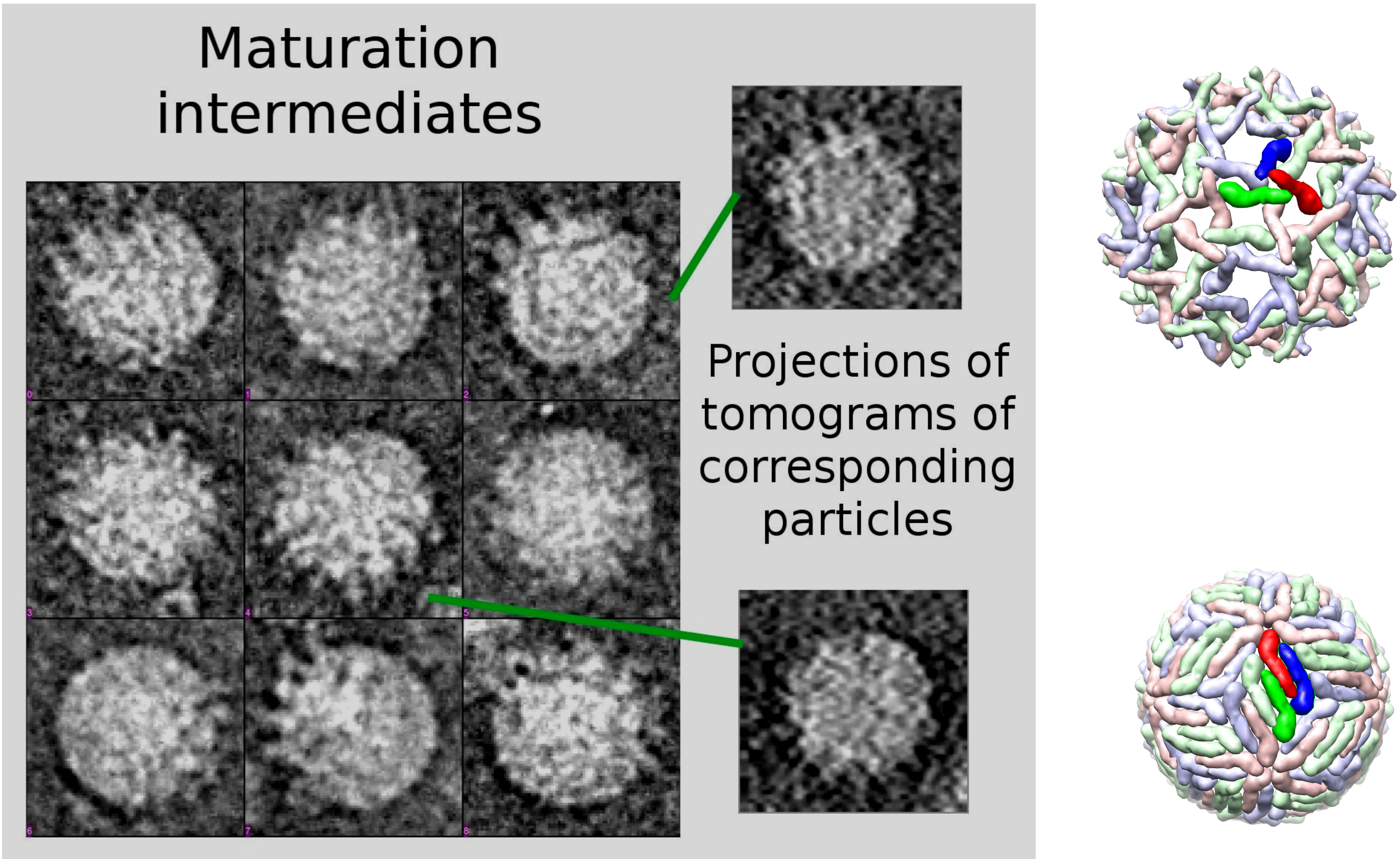


Correlation with model in orientation 2

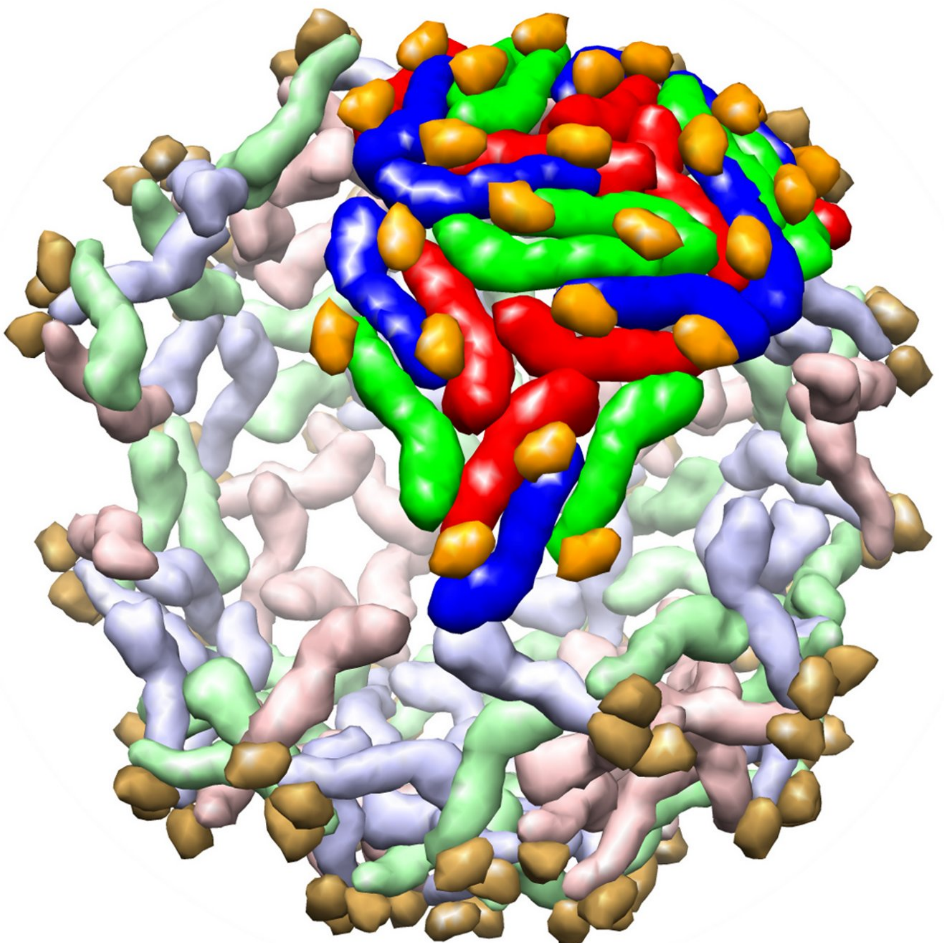
0.0 0.7

Corr. coeff. scale:

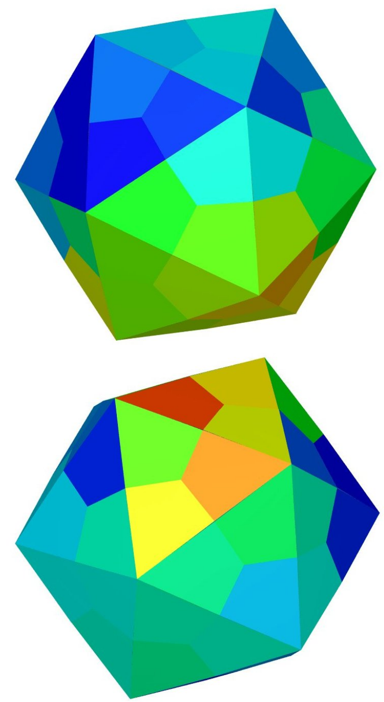
Combination of tomography and single particle data



Structure of Dengue 2 maturation intermediate



Correlation with immature model



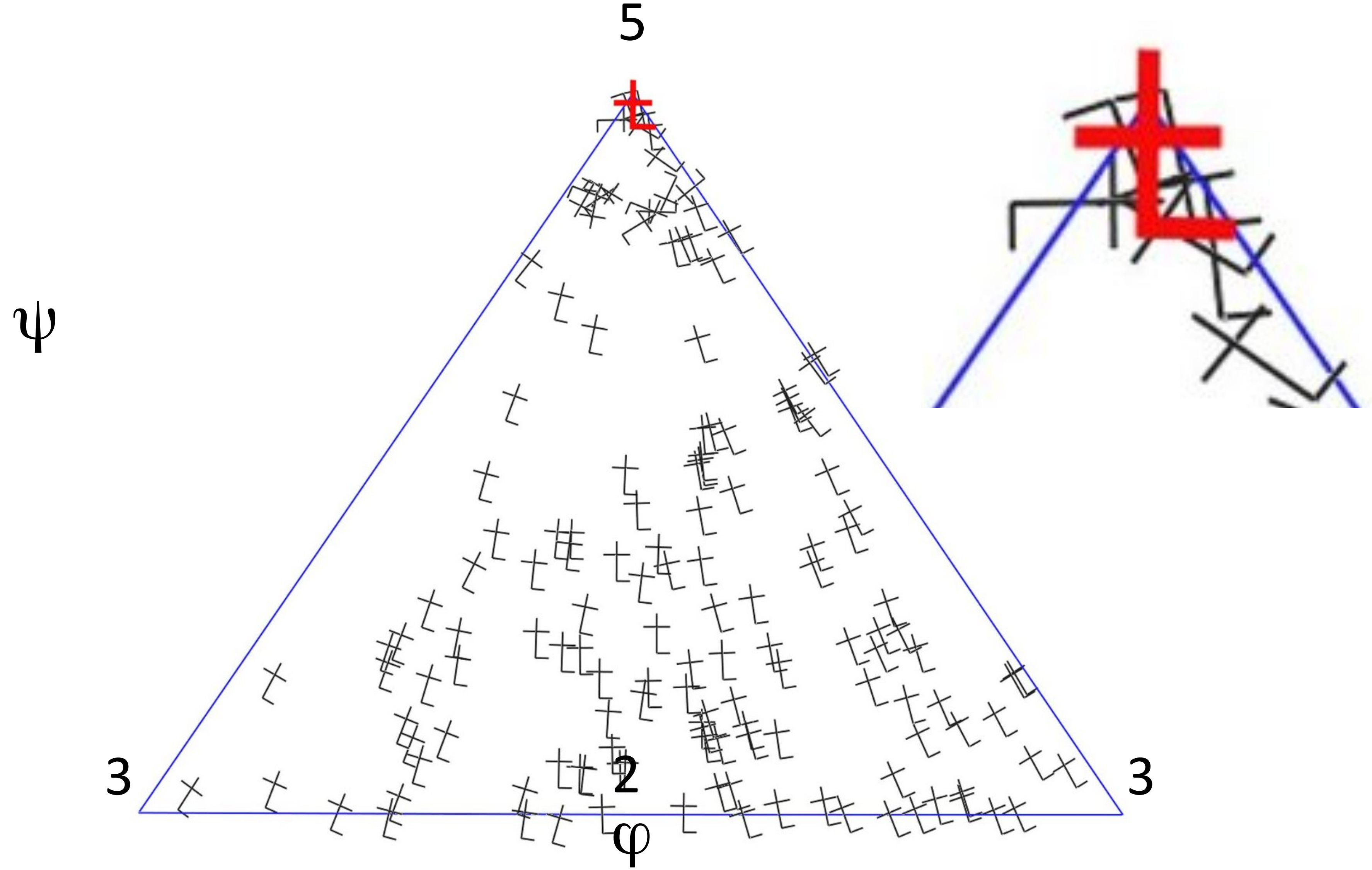
Correlation with low-pH immature model

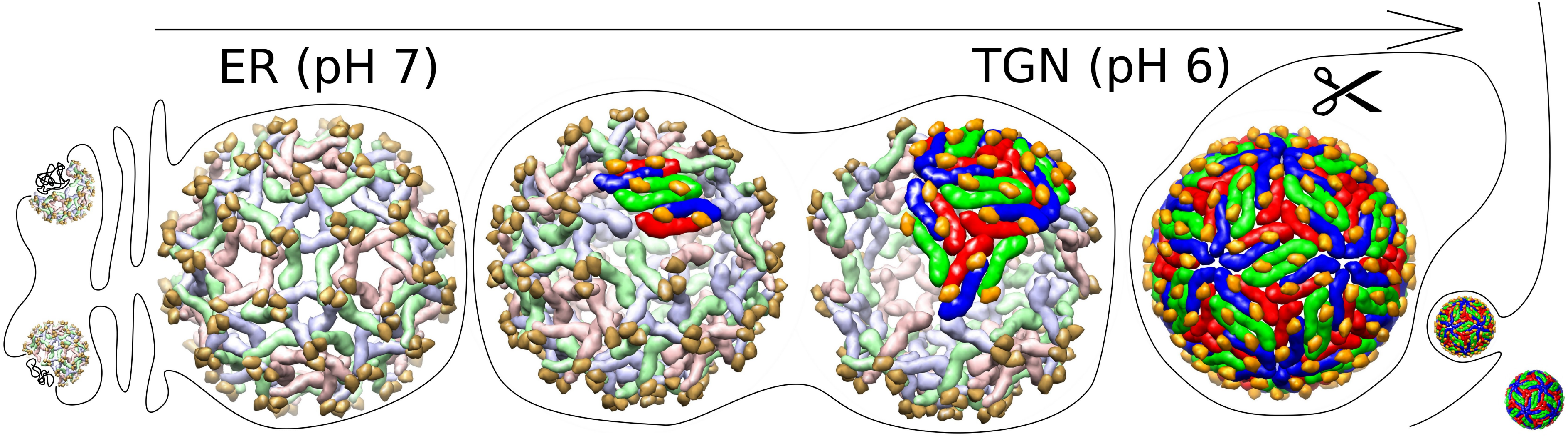
0.0 0.7

Corr. coeff. scale: 

Relative orientations of immature and low-pH

immature domains




ER (pH 7)
TGN (pH 6)

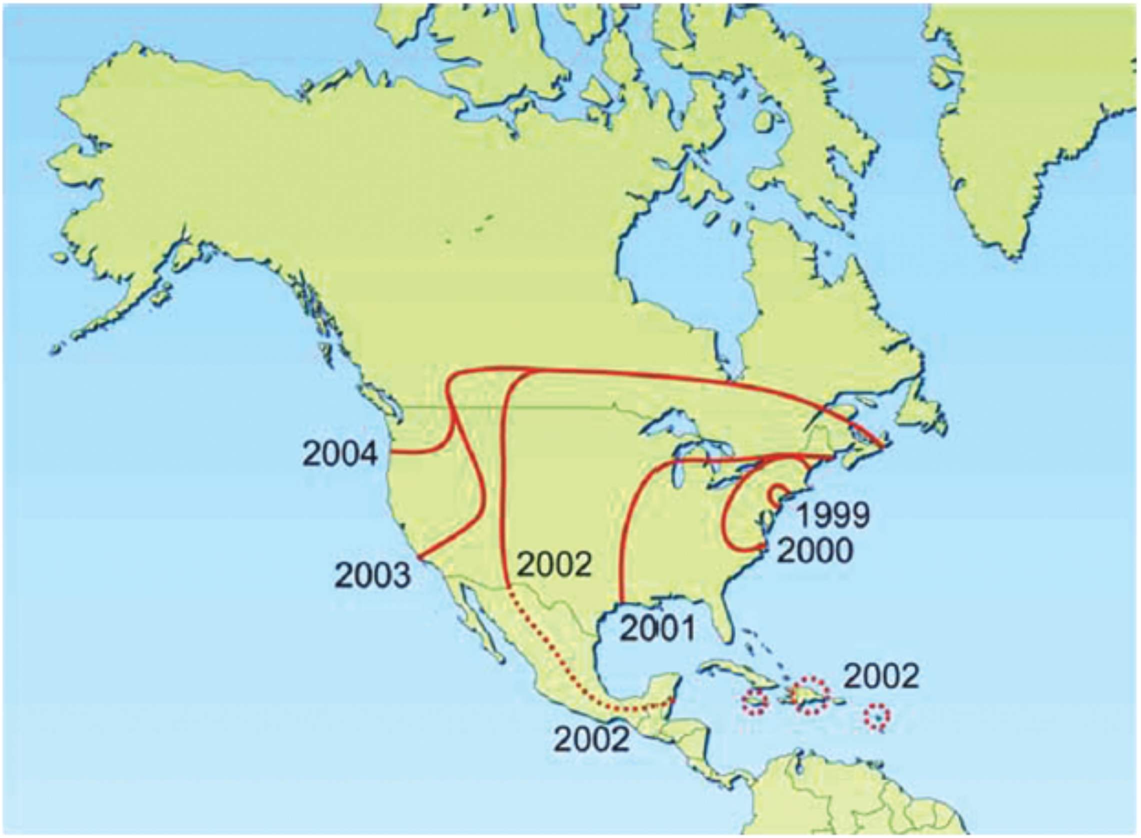


Figure 22.7 **Approximate distribution of West Nile virus in the Americas 1999–2004.**

Source: Mackenzie *et al.* (2004) *Nature Medicine*, **10**, S98. Reproduced by permission of Nature Publishing Group and the author.

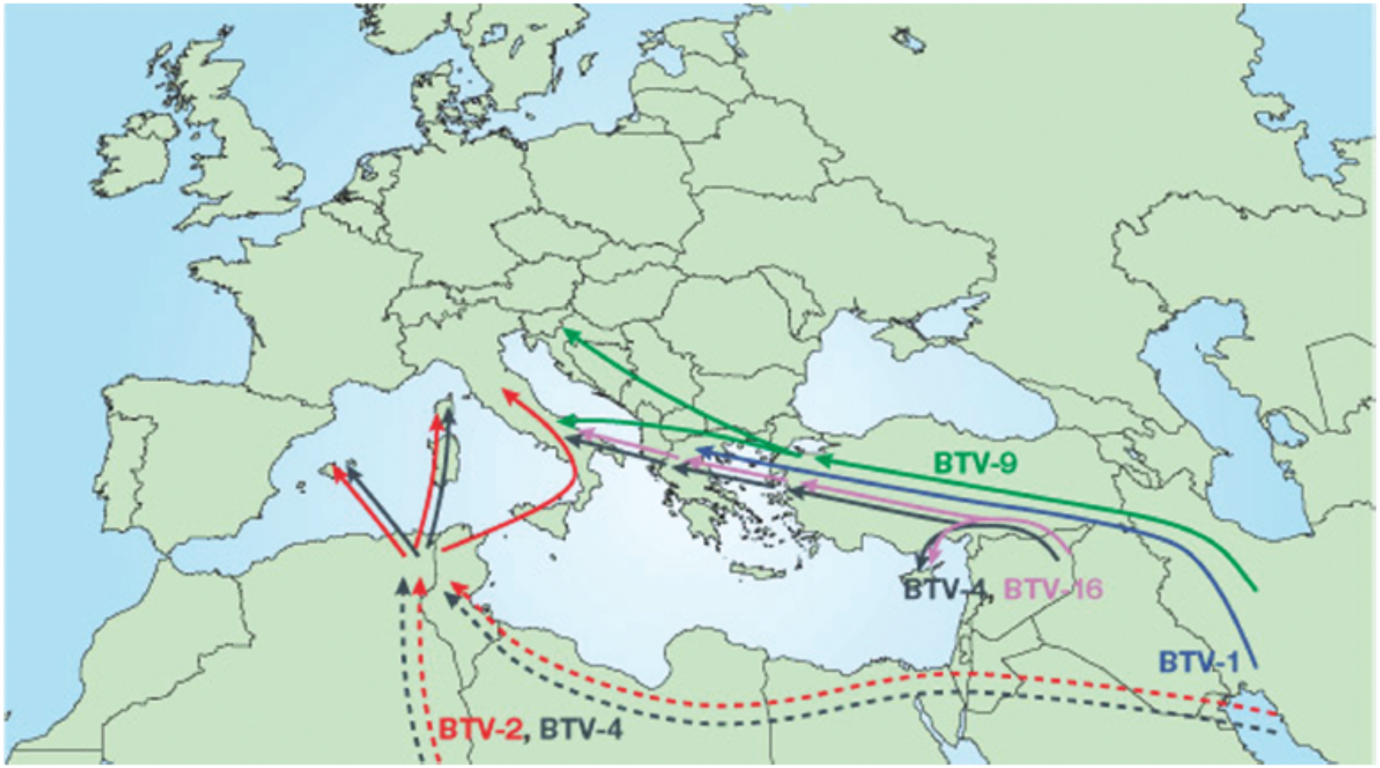
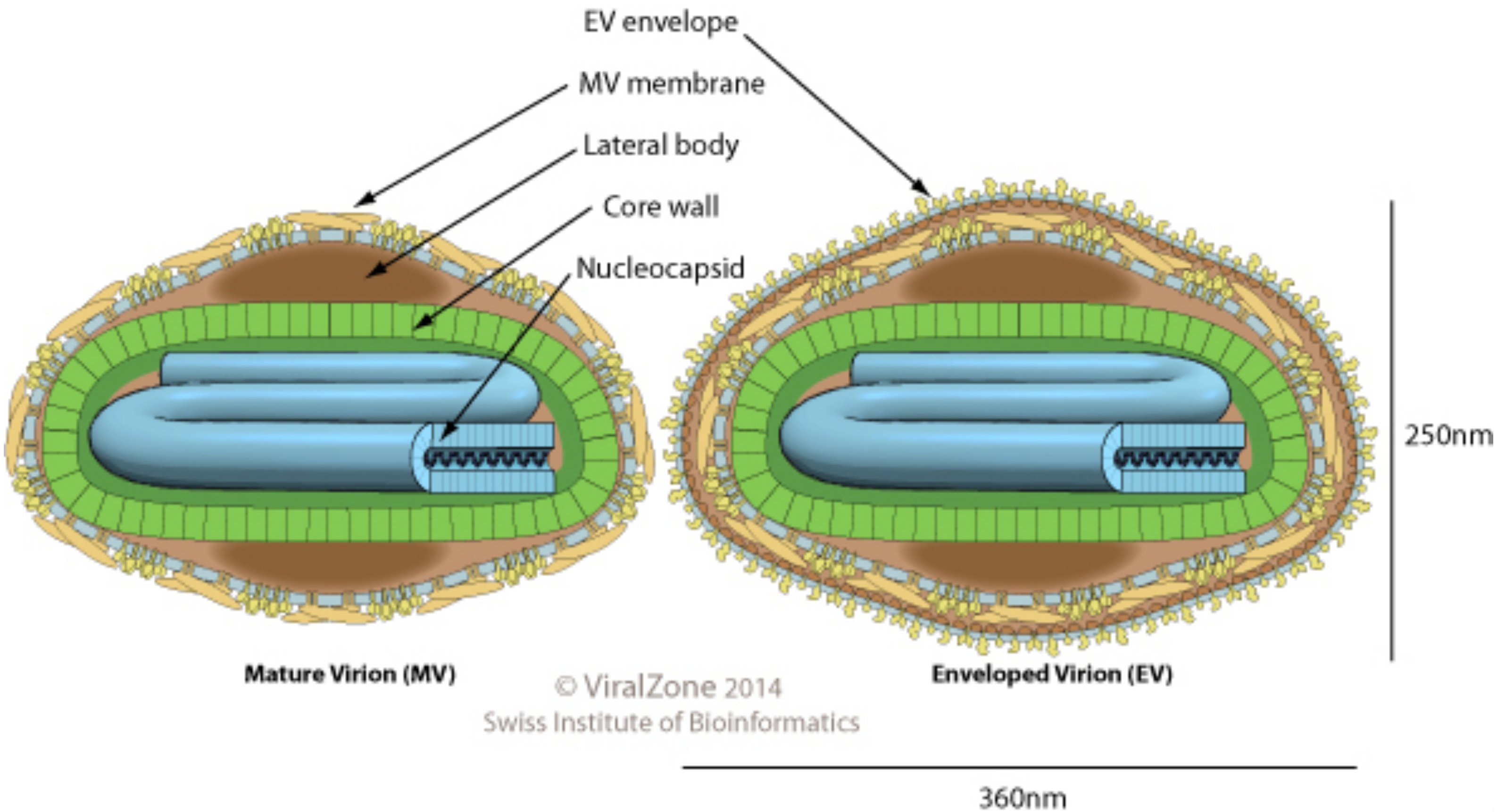


Figure 22.10 Spread of bluetongue virus serotypes in Europe 1998–2004.

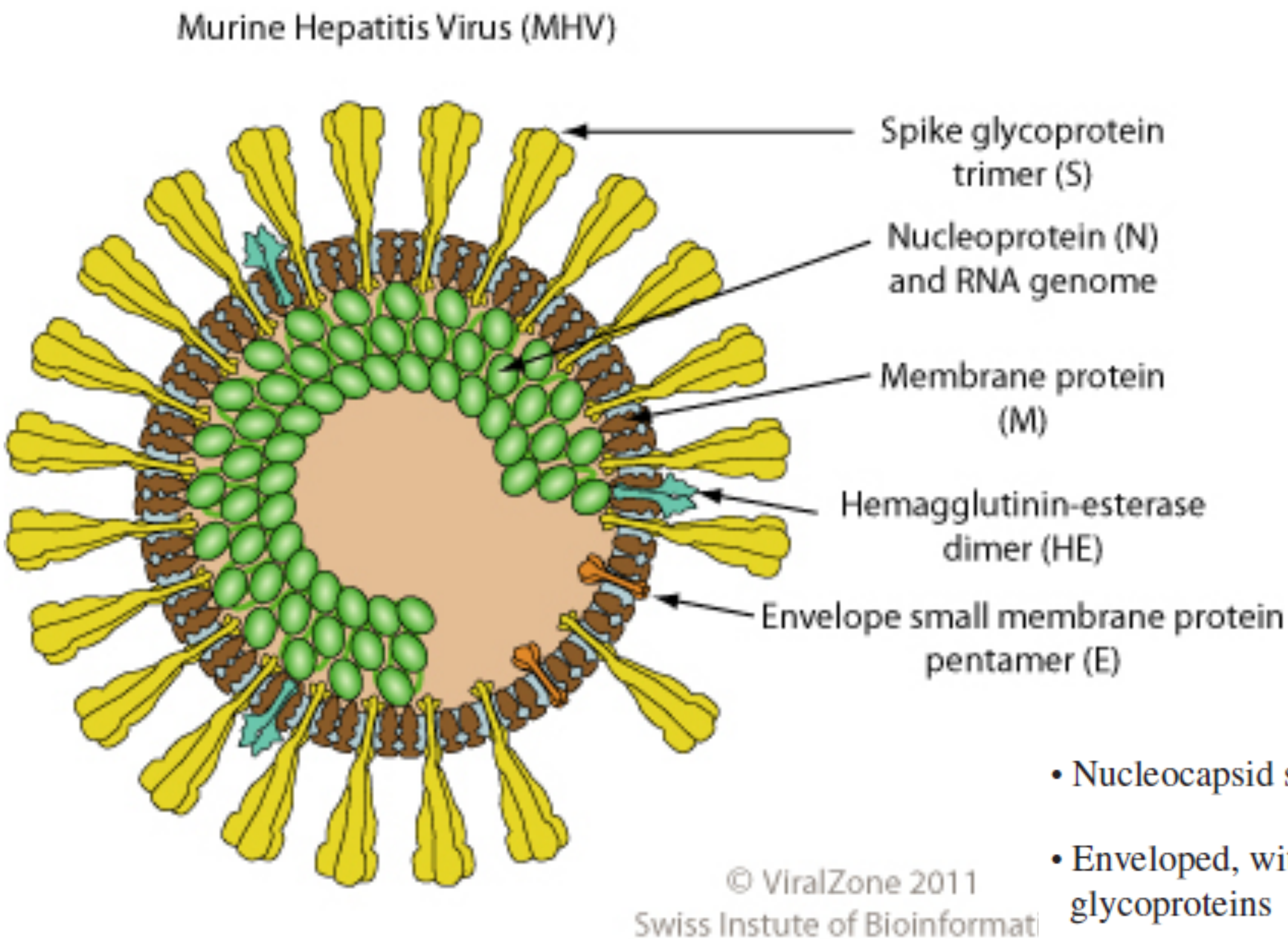
Source: Purse *et al*. (2005) *Nature Reviews Microbiology*, 3, 171. Reproduced by permission of Nature Publishing Group and the authors.

Poxviridae



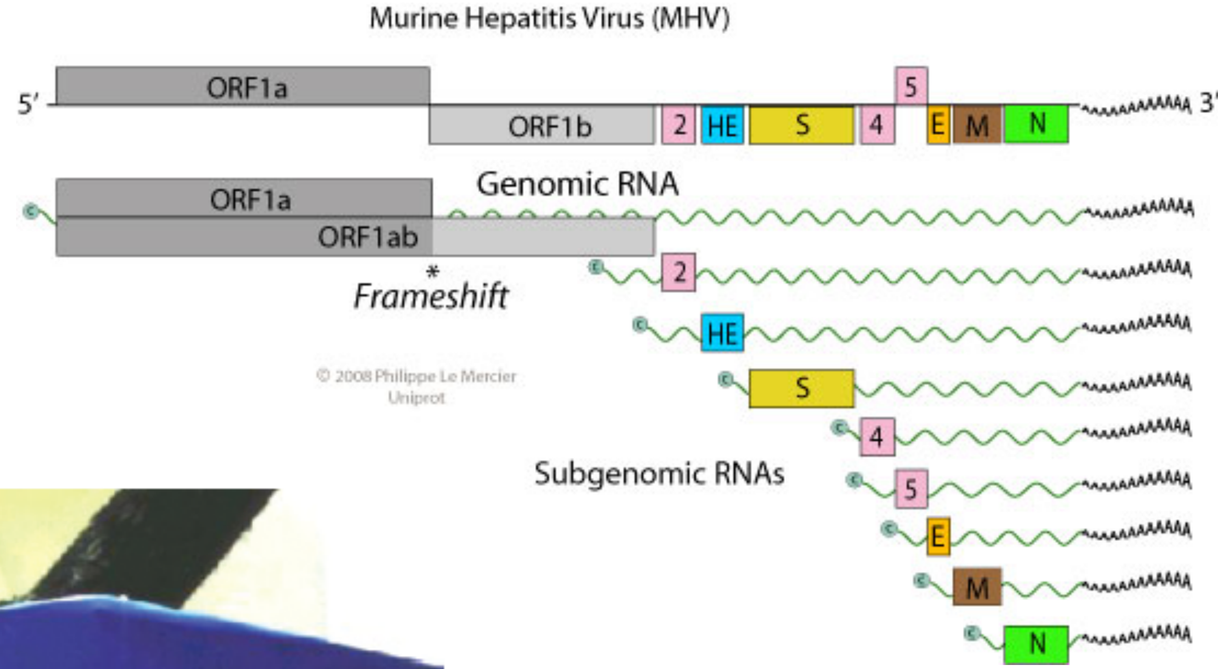
- Large, complex virion, ovoid or brick-shaped
- Members include smallpox, vaccinia, and monkeypox

Coronaviridae



- Nucleocapsid symmetry: helical
- Enveloped, with a corona of glycoproteins
- Includes SARS coronavirus

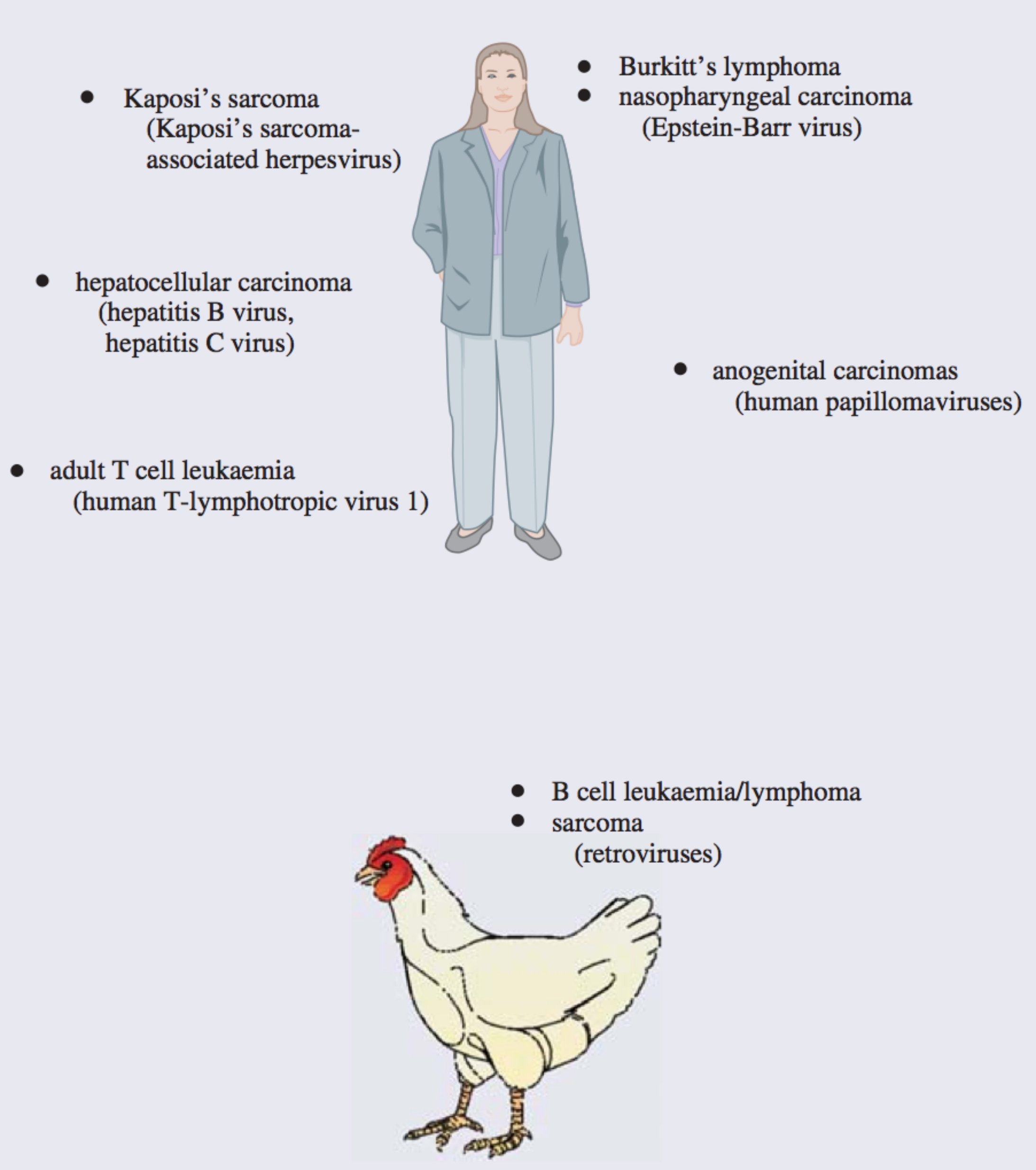
Coronaviridae



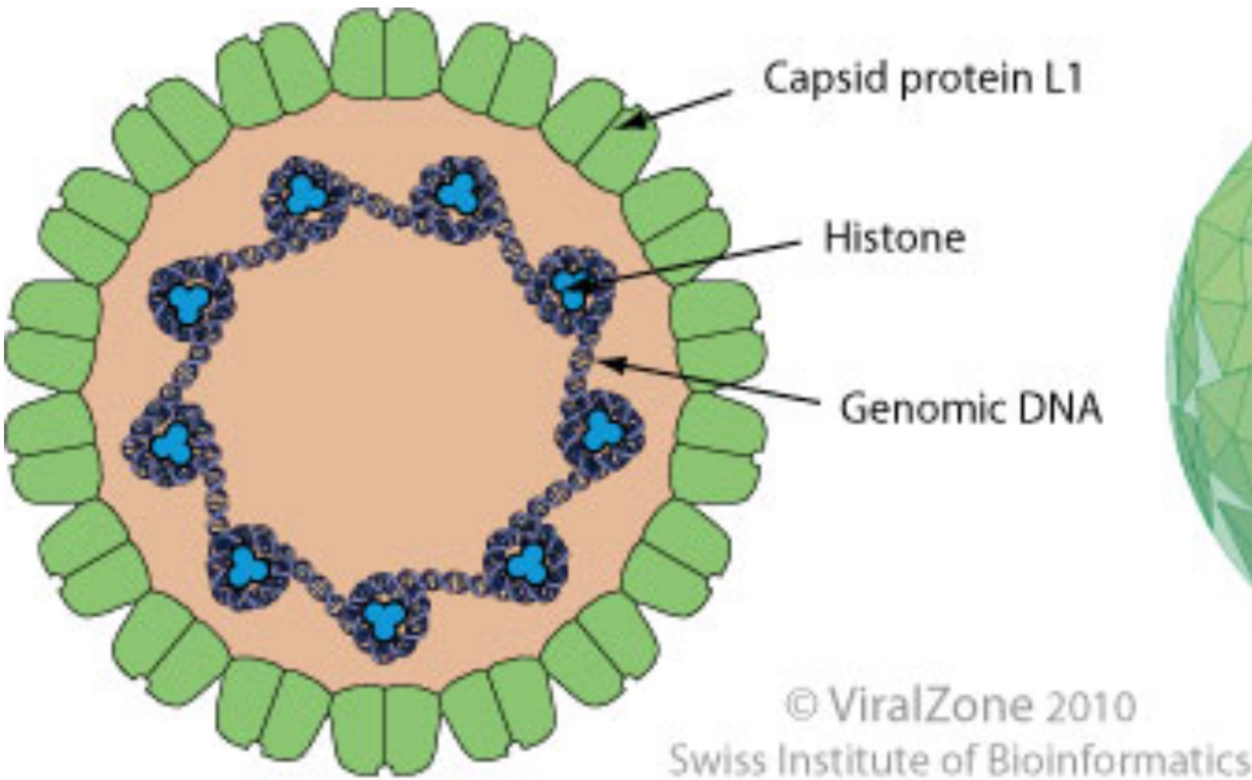
Learning outcomes

- know the term ‘emerging virus’
- discuss examples of viruses that have recently appeared in new host species
- discuss examples of viruses that have recently appeared in new parts of the world
- discuss examples of new viruses
- discuss examples of re-emerging viruses
- assess measures that can be taken to prevent and contain outbreaks of infectious disease

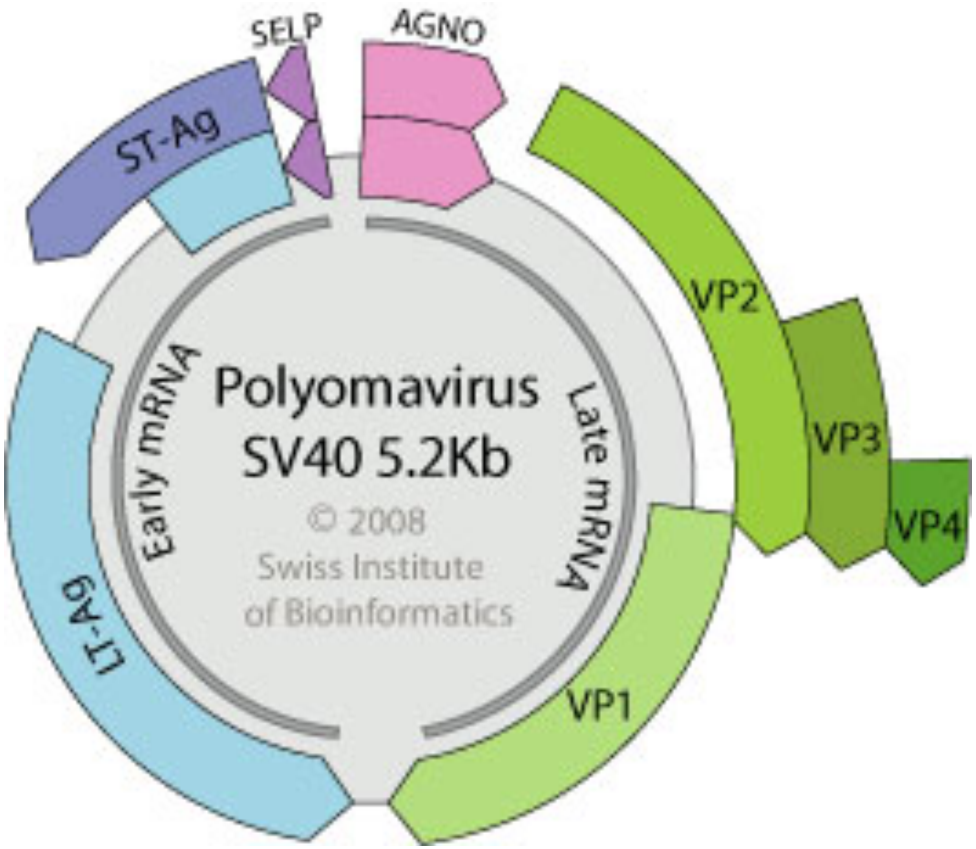
Viruses and cancer

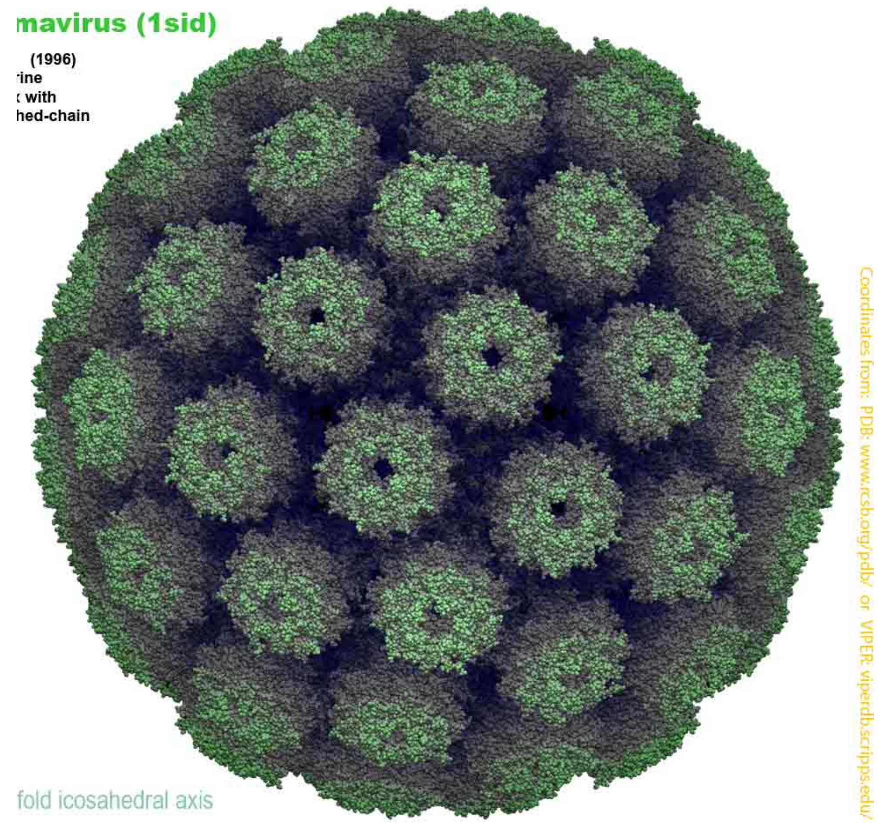


Papillomaviruses



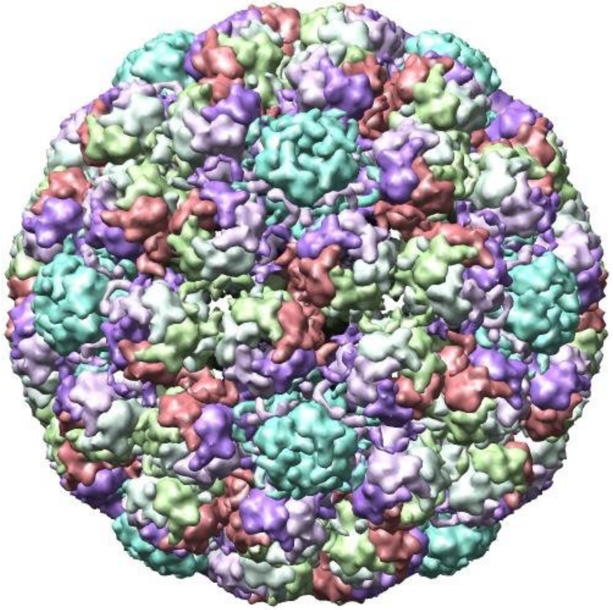
T=7d


SELP
AGNO
ST-Ag
VP2
VP3
VP4
Early mRNA
Polyomavirus
SV40 5.2Kb
© 2008
Swiss Institute
of Bioinformatics
Late mRNA
LT-Ag
VP1

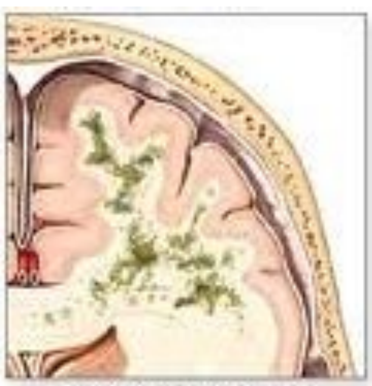

mavirus (1sid)
(1996)
hed-chain
fold icosahedral axis
Coordinates from: PDB: www.rcsb.org/pdb/ or VIPER: viperdb.scripps.edu/

Human Polyomaviruses

Merkel cell carcinoma



Mouse polyomavirus

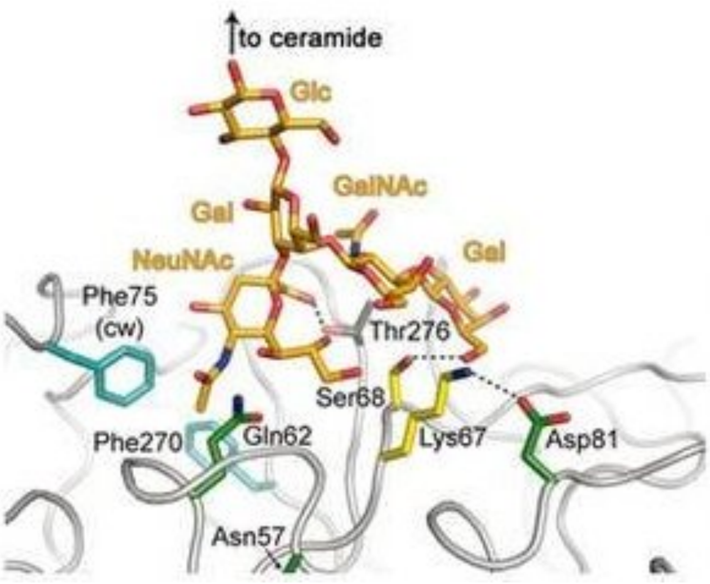


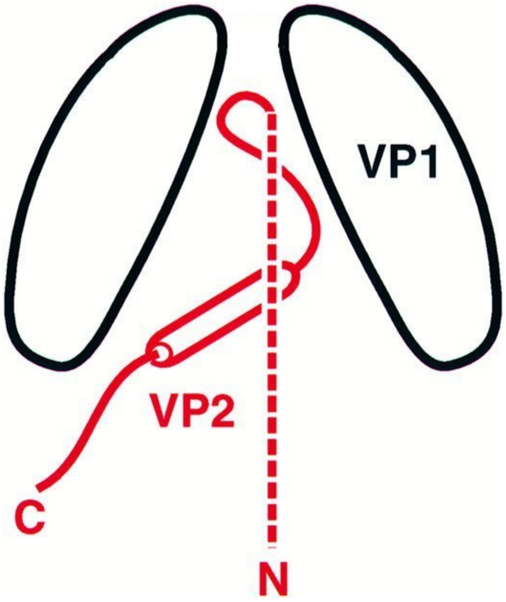
Progressive Multifocal Encephalopathy (JCV)

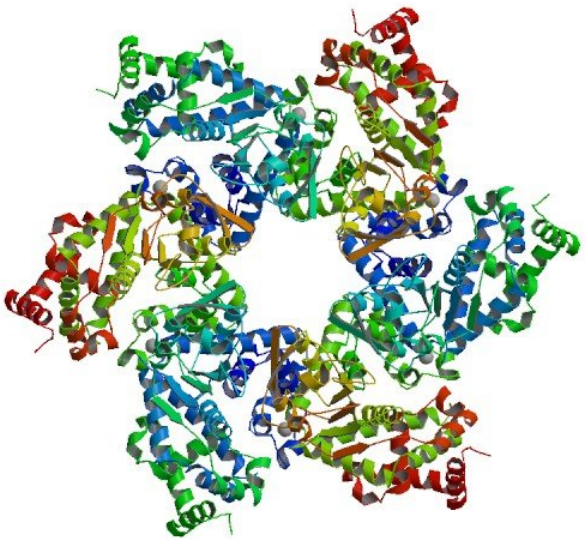
	MCV	BKV	JCV	KIV	WUV
Inf. pop. (%)	42	82	39	55	69
SI to Mouse PyV	52	51	51	26	25
SI to SV40	48	81	76	26	27

Feng et al. Science, 2008; Koralnik. A Neur. 2006; Stehle et al. Nature, 1994;

Human Polyomaviruses







Stehle et al. Nature, 1994

Liddington et al. Nature, 1991

Li et al. Nature, 2003

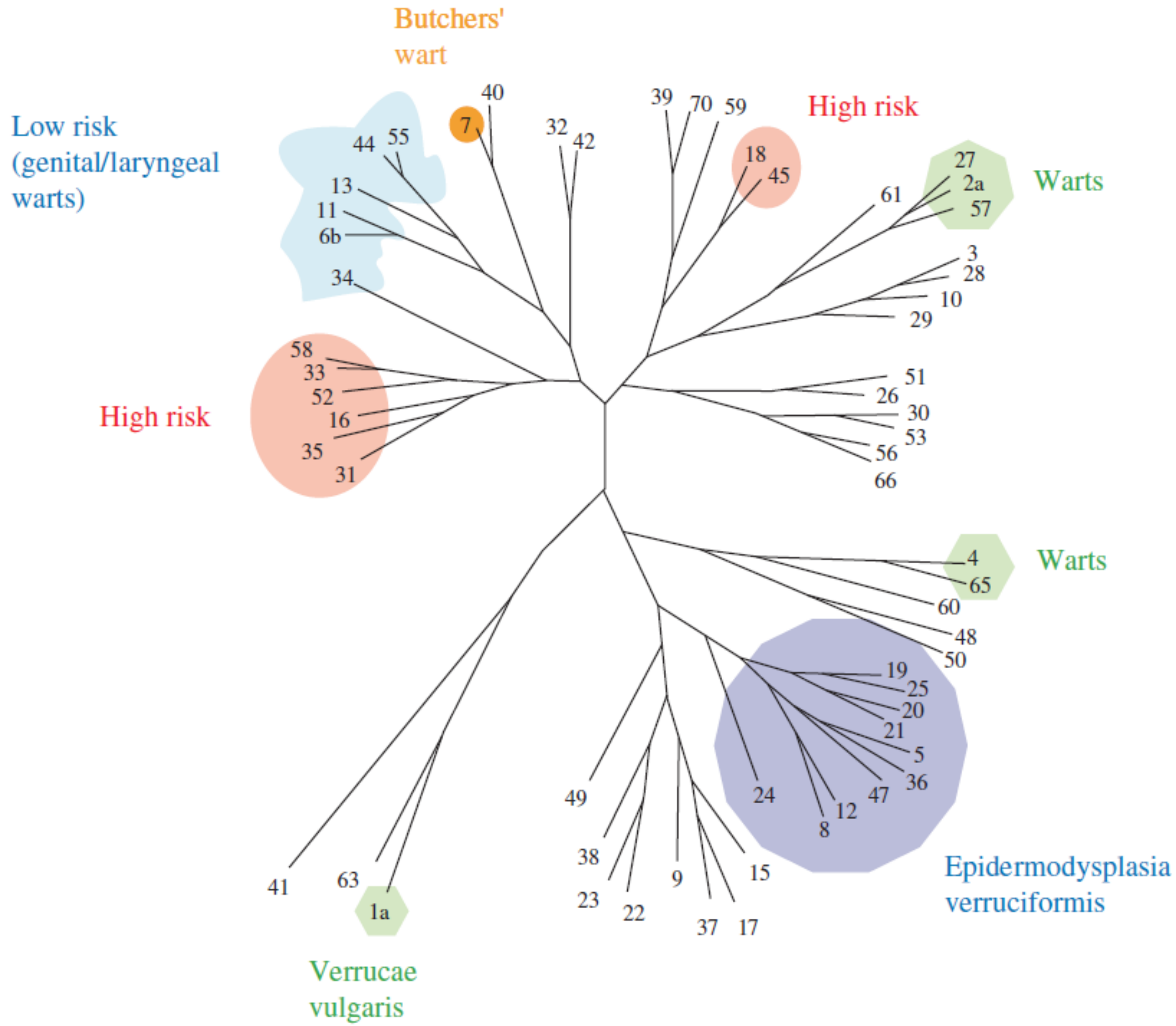


Figure 23.3 Phylogenetic tree showing relationships between some HPVs. The high-risk HPVs cluster in two regions of the tree.
Source: Modified from *Microbiology Today*, August 2005, with the permission of Professor N. J. Maitland (University of York) and the Society for General Microbiology. Data from Los Alamos National Laboratory HPV website (http://hpv-web.lanl.gov).

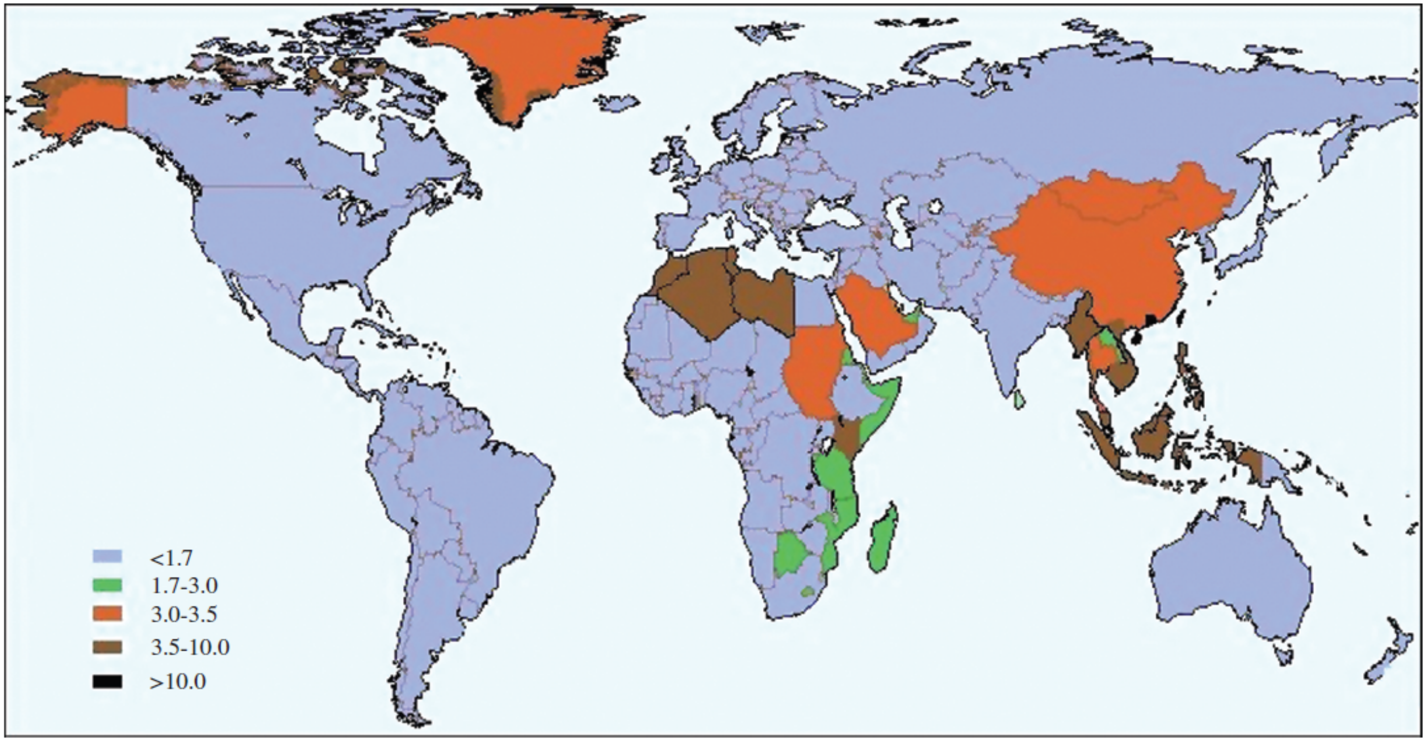


Figure 23.4 Incidence rates of nasopharyngeal carcinoma in males.

Source: Data (age standardized incidence rates per 100 000) published by Busson *et al*. (2004) *Trends in Microbiology*, **12**, 356. Map drawn by V. Gaborieau and M. Corbex (Genetic Epidemiology Unit, International Agency for Research on Cancer). Reproduced by permission of Elsevier Limited and the authors.

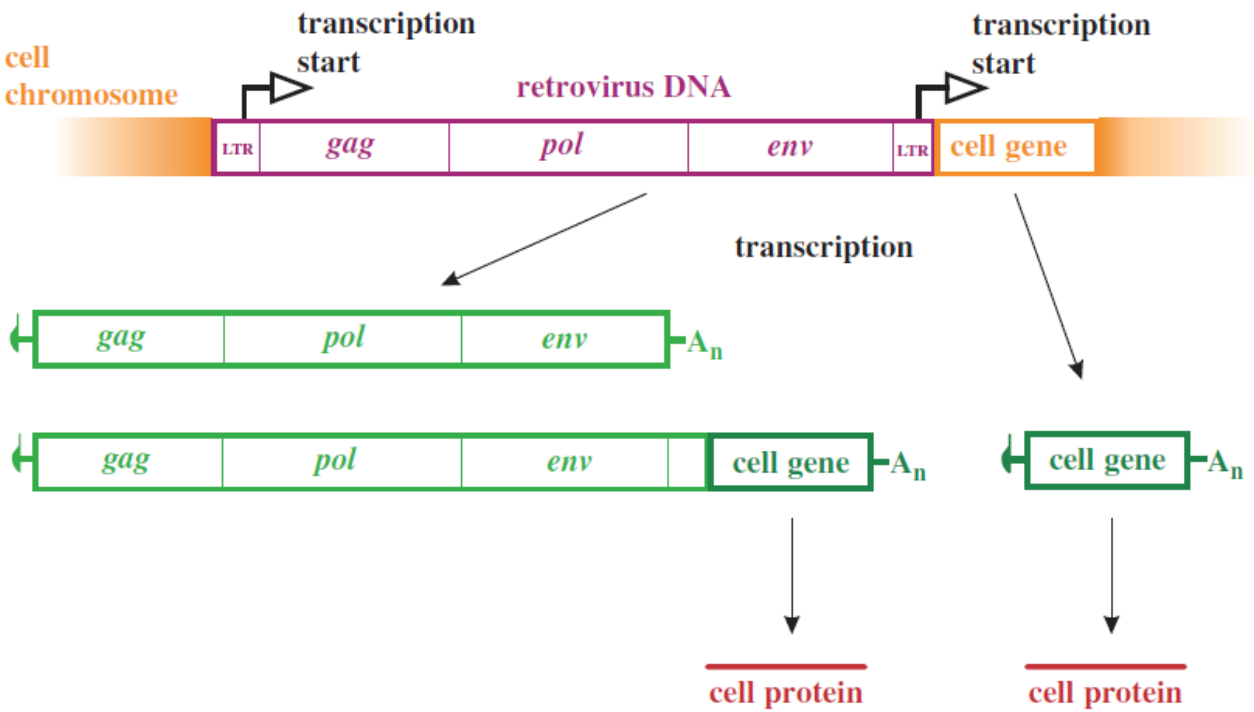


Figure 23.5 Activation of a cell gene by insertion of a retroviral provirus. Initiation of transcription at either of the provirus LTRs may lead to expression of the cell gene.

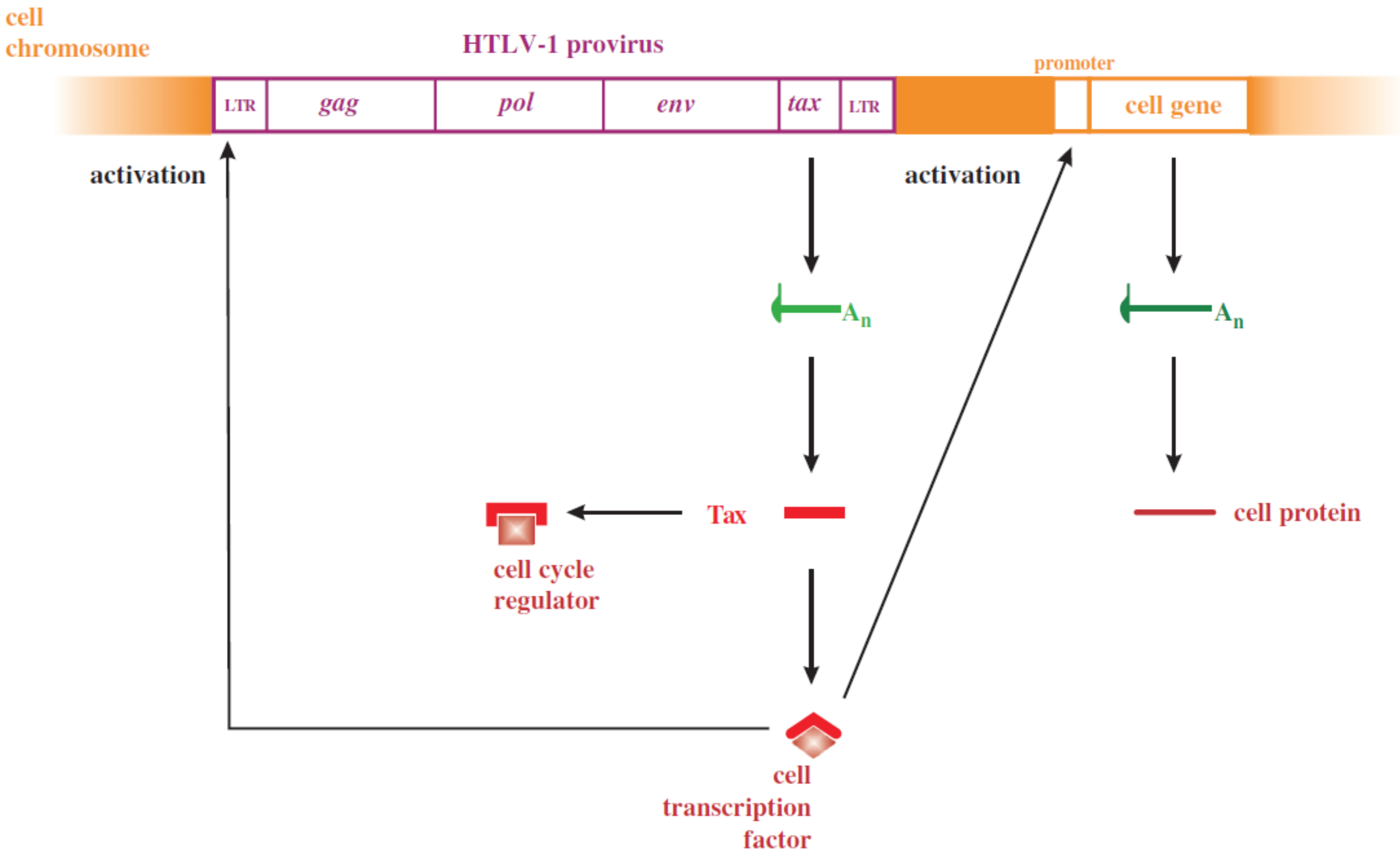


Figure 23.6 **HTLV-1 oncogenesis.** The virus Tax protein, complexed with cell proteins, activates transcription of the provirus and may also activate transcription of cell genes. Tax can also influence the cell cycle by binding to cell cycle regulators such as p53.

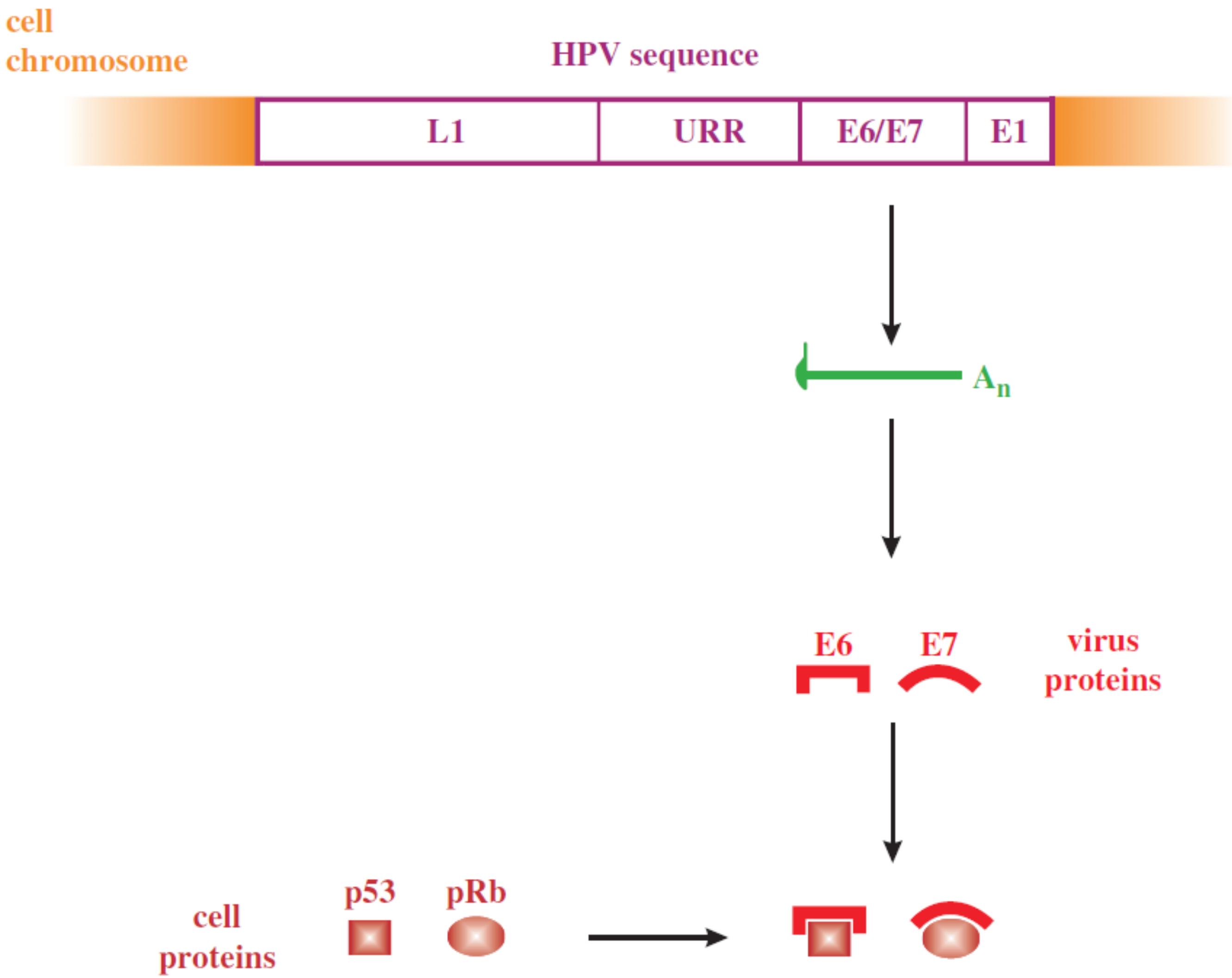


Figure 23.7 Expression of HPV genes from an integrated virus sequence. The HPV-18 sequence that is integrated into the HeLa cell genome is shown. The E6 and E7 proteins are synthesized and bind to the cell proteins p53 and pRb, respectively. E: early gene. L: late gene. URR: upstream regulatory region.

Learning outcomes

- outline the characteristics of viruses that are associated with cancers;
- evaluate the evidence for association of viruses with some cancers;
- discuss possible mechanisms for virus induction of cancer;
- suggest how virus-induced cancers may be prevented.

Figures
Chapter 24

Bacteriophages

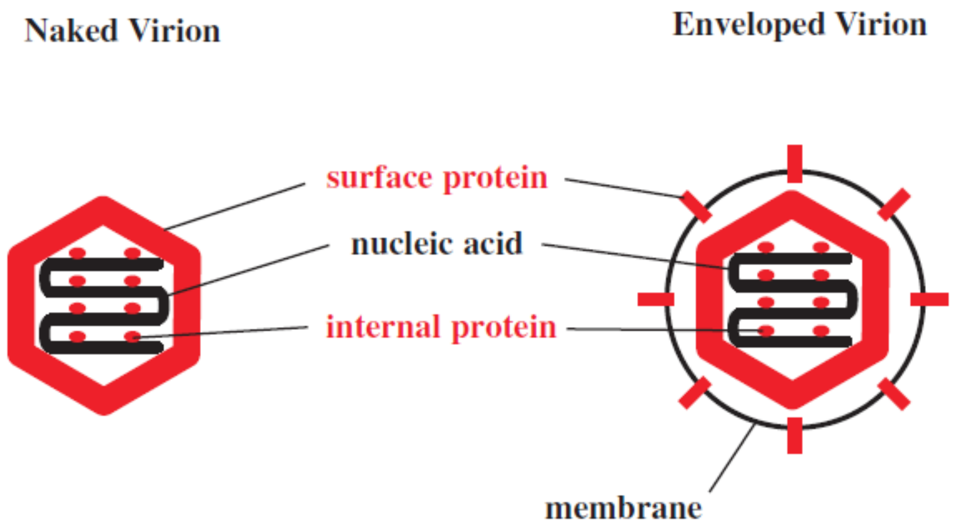


Figure 24.1 Inactivation targets in virions. Infectivity of a virion may be destroyed by damage to a nucleic acid, a protein, and/or a lipid membrane. Alteration of a surface protein might prevent a virion from attaching to its host cell and/or from entering the cell. Stripping the envelope from an enveloped virion removes the surface proteins and achieves the same outcome. Alteration of internal proteins can destroy properties, such as enzyme activities, essential for the replication of the virus.

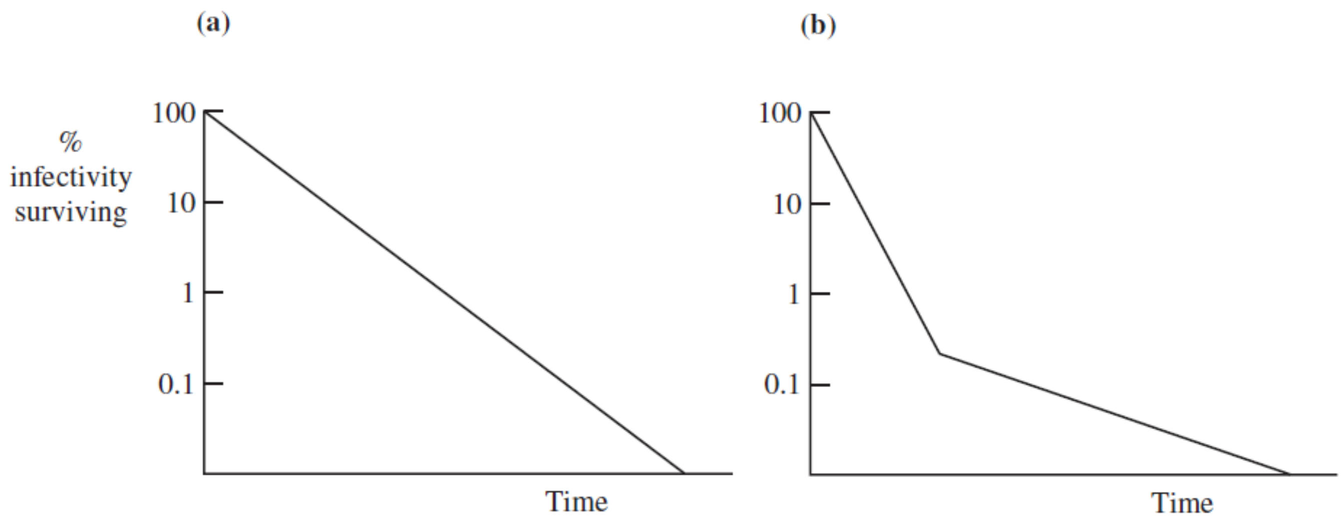


Figure 24.2 Loss of virus infectivity (a) at one rate and (b) at two rates.

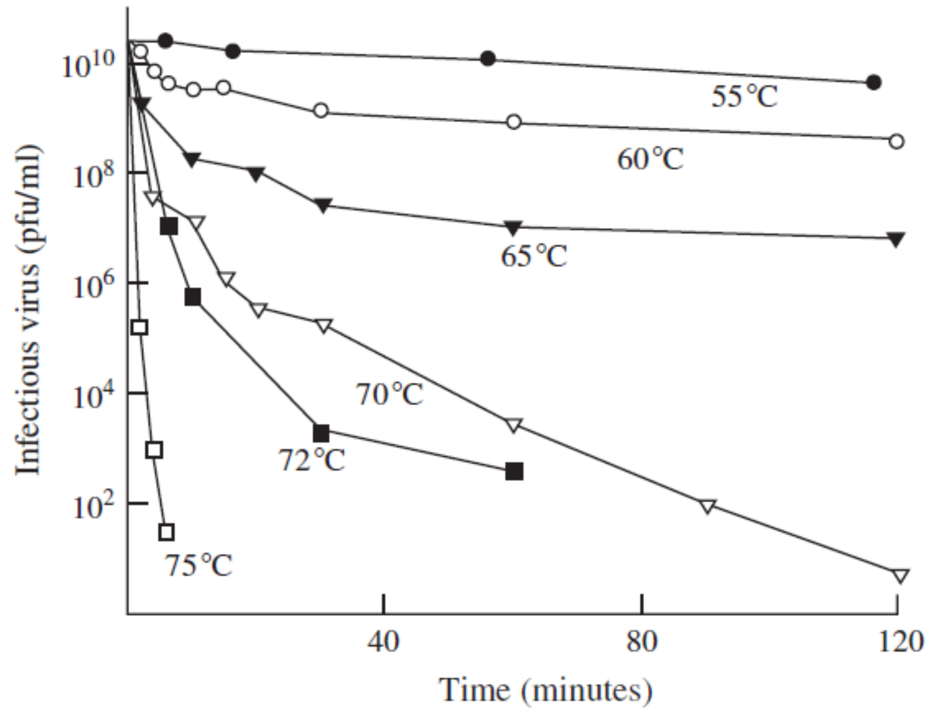


Figure 24.3 Inactivation of *Lactococcus lactis* phage P008 infectivity in a broth at temperatures between 55 and 75 °C.

Source: Data from Müller-Merbach *et al.* (2005) *International Dairy Journal*, 15, 777. Reproduced by permission of Elsevier Limited and the authors.

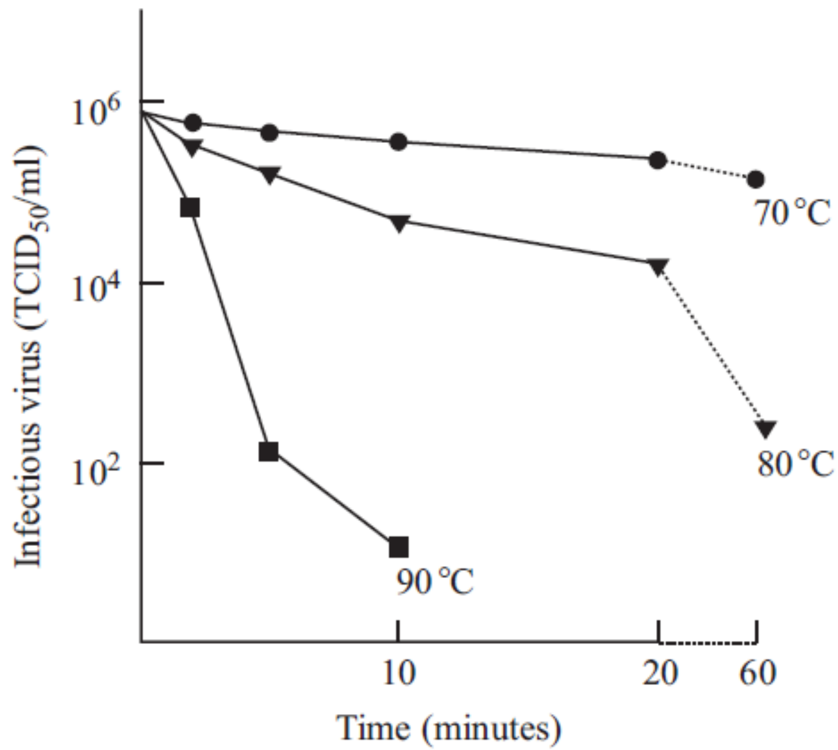


Figure 24.4 **Inactivation of minute virus of mice infectivity in water at 70, 80, and 90 °C.**

Source: Data from Boschetti *et al*. (2003) *Biologicals*, 31, 181. Reproduced by permission of Elsevier Limited and the authors.

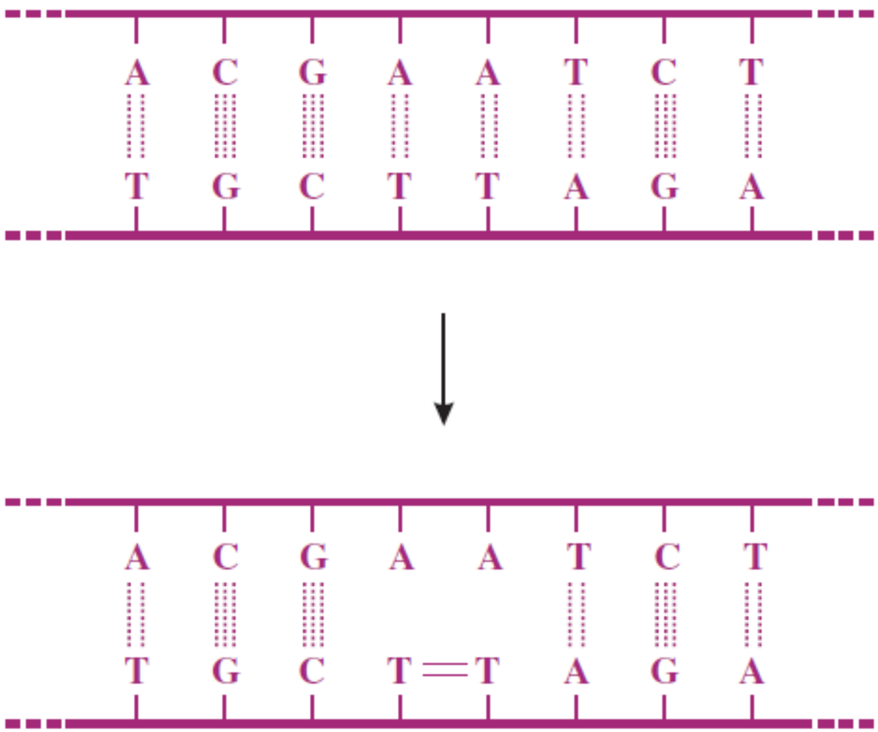


Figure 24.5 Formation of a thymine dimer in dsDNA.

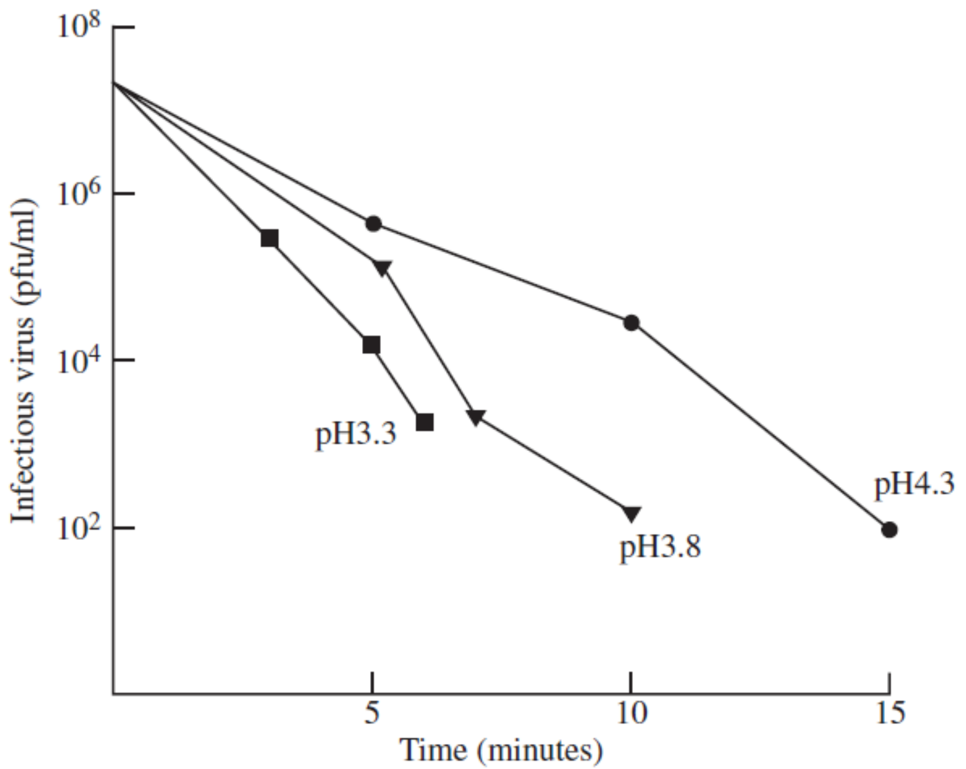


Figure 24.6 **Inactivation of hepatitis A virus infectivity at three pH values at 85 °C.**

Source: Data from Deboosere *et al.* (2004) *International Journal of Food Microbiology*, 93, 73. Reproduced by permission of Elsevier Limited and the authors.

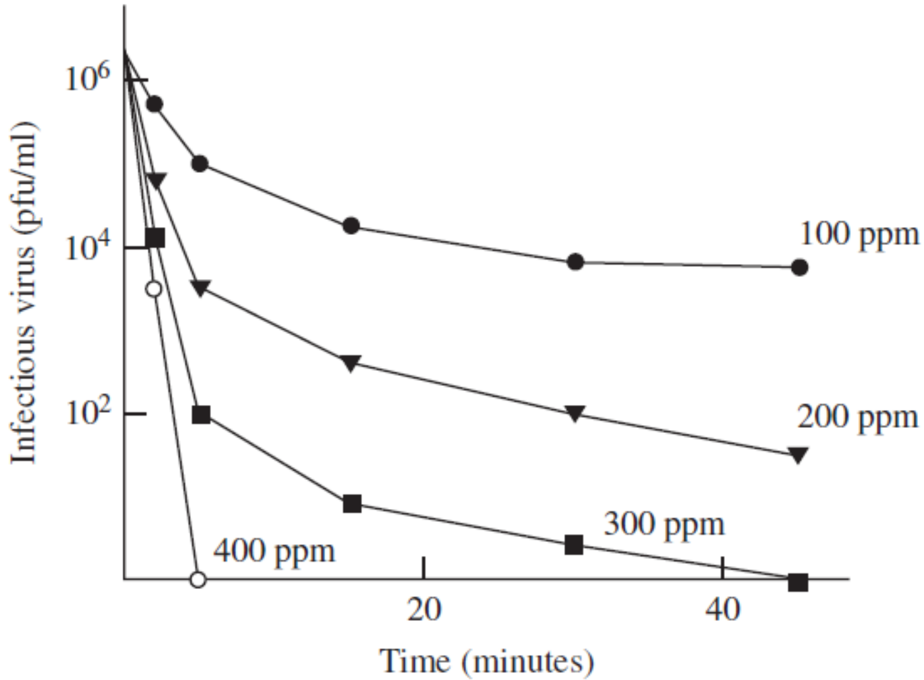


Figure 24.7 Inactivation of *Lactobacillus* phage BYM by hypochlorite. The concentrations are shown as parts per million (ppm) of free chlorine. The phage suspensions were at 25 °C and pH 7.

Source: Data from Quiberoni *et al*. (2003) *International Journal of Food Microbiology*, 84, 51. Reproduced by permission of Elsevier Limited and the authors.