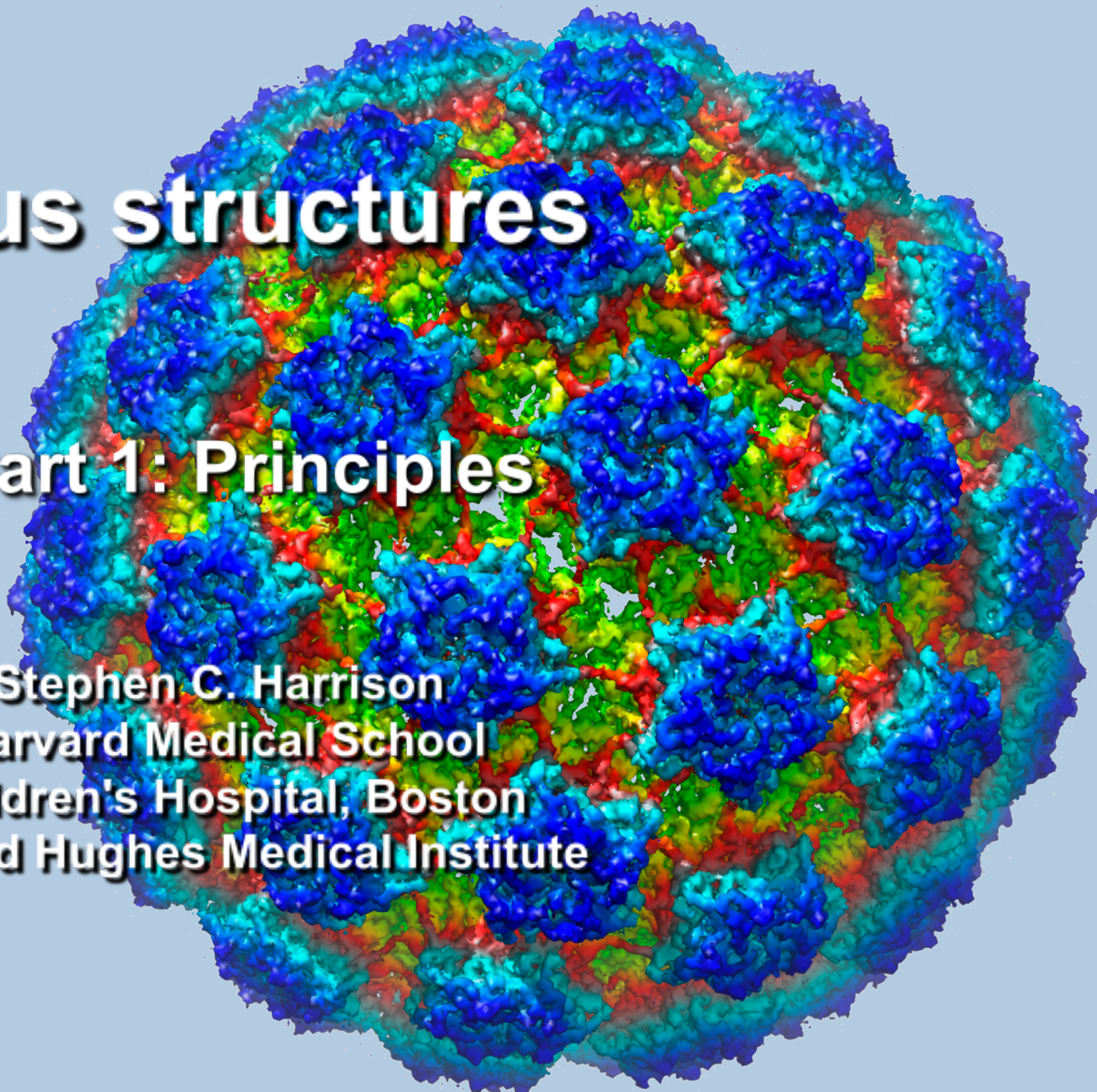
Virus structures



Part 1: Principles

Stephen C. Harrison
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Viruses:

Carriers of genetic information from cell to cell: "extracellular organelles"

Infectious virus particle ("virion") is a molecular machine that:

- packages viral genome
- escapes from infected cell
- survives transfer from one cell to another
- attaches, penetrates, initiates replication in new host cell

Viruses as pathogens:

- virus bears the genetic information needed to harness cellular biosynthetic machinery and replicate itself

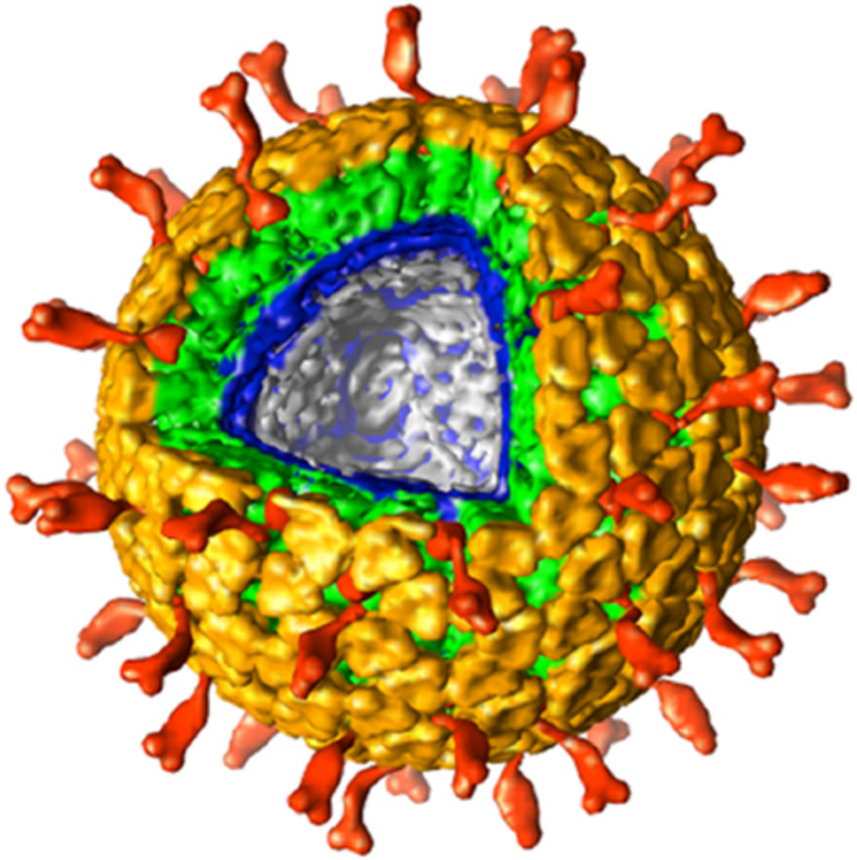
- hence, selective advantage for virus may be selective disadvantage for host

- evolution of host defense (immunity)

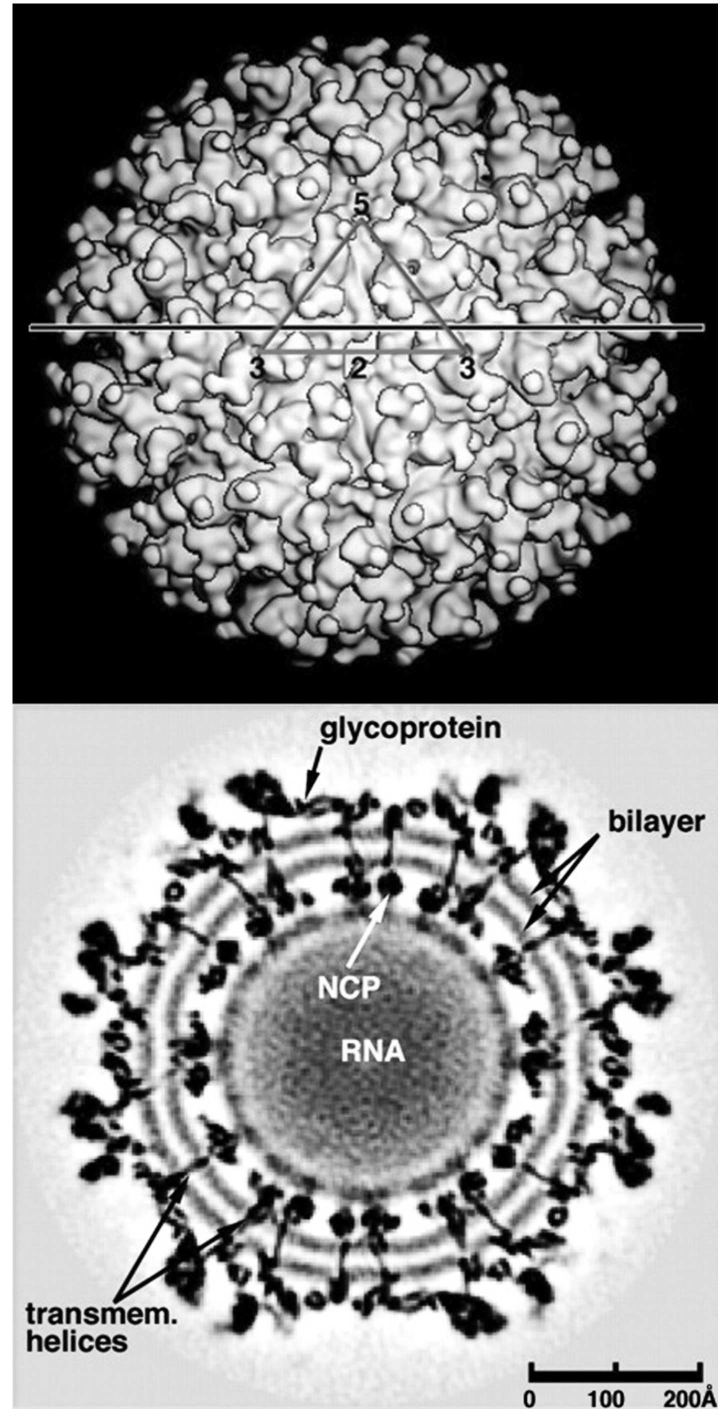
Two types of virus particles:

- Enveloped viruses: infectious virus particle has a lipid-bilayer membrane (derived from a host-cell membrane) as part of the coat that surrounds its genome

- Non-enveloped viruses: no lipid-bilayer membrane,protective coat is protein only



Rotavirus
based on work by
Yeager; Prasad; Grigorieff & Harrison



Sindbis virus
Zhang W, Mukhopadhyay S, Pletnev SV, Baker TS, Kuhn RJ, Rossmann MG.
J Virol. (2002)76:11645-58.

Sizes and distance scales:

Both the rotavirus and Sindbis virus outer shells have a diameter of about 700 Å (70 nm)

~ one millionth the size of a tennis ball

recall that chemical bonds are ~1-2 Å long

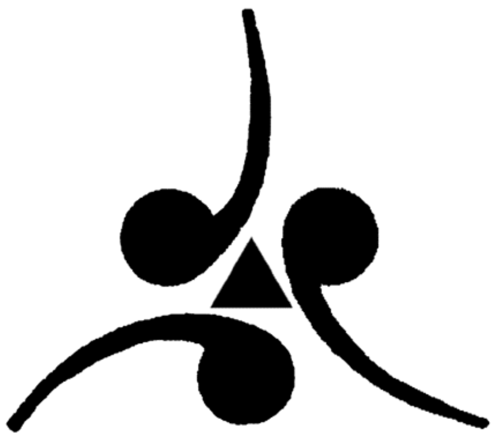
This lecture:

- Why do most non-enveloped viruses and a number of smaller enveloped viruses have symmetric structures?

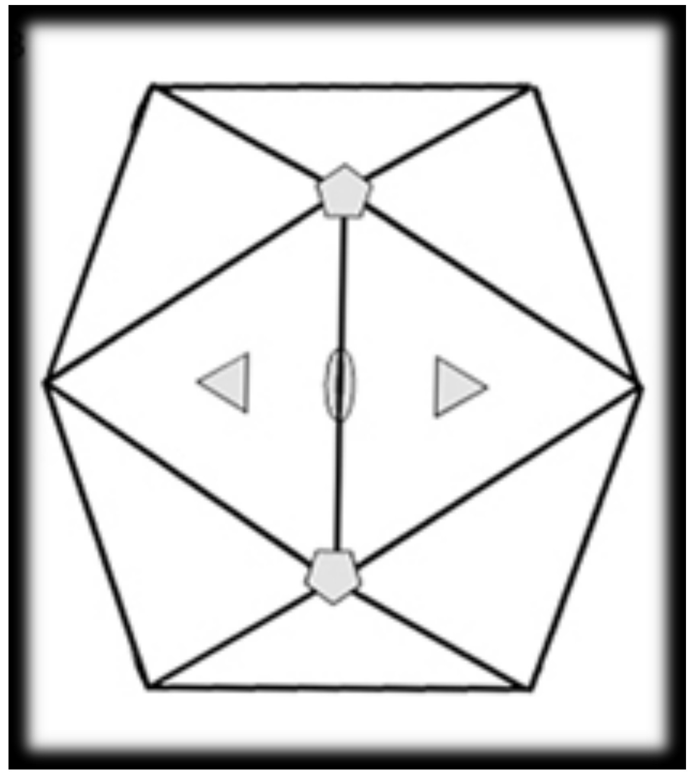
- What do the building blocks of these particles look like?

- What do the outer proteins of some enveloped viruses look like?

Symmetry: rotation axes

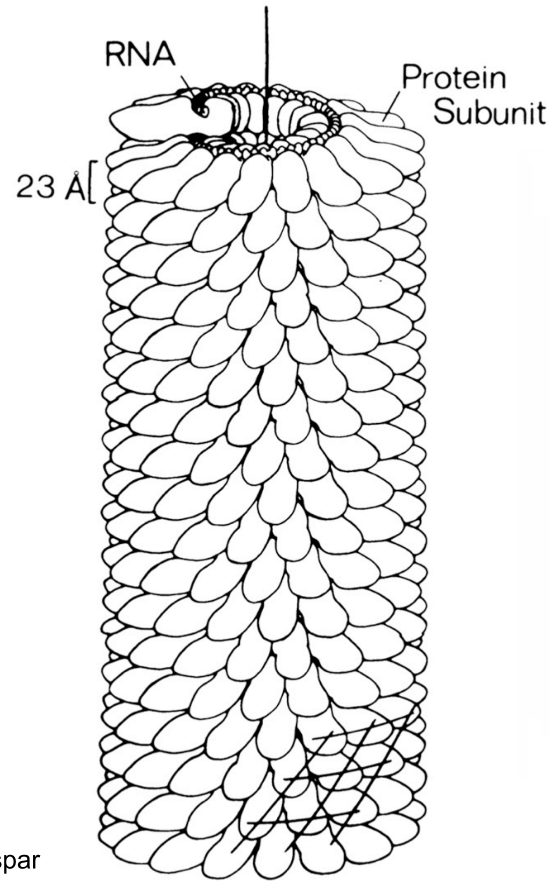


Threefold axis



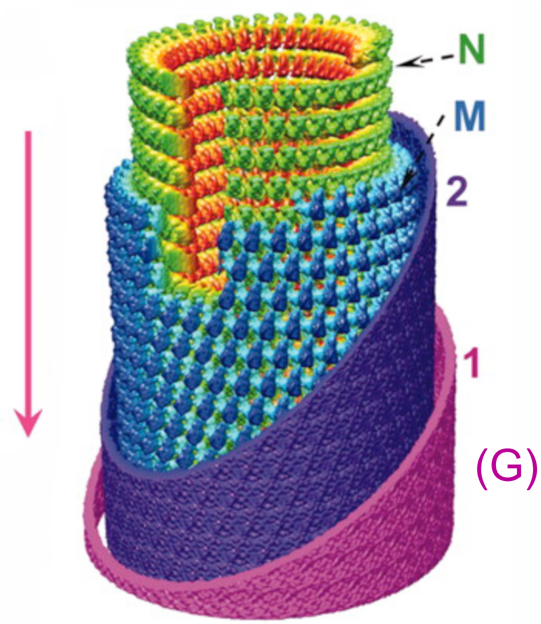
Twofold, threefold
& fivefold axes

Helical symmetry: screw axes



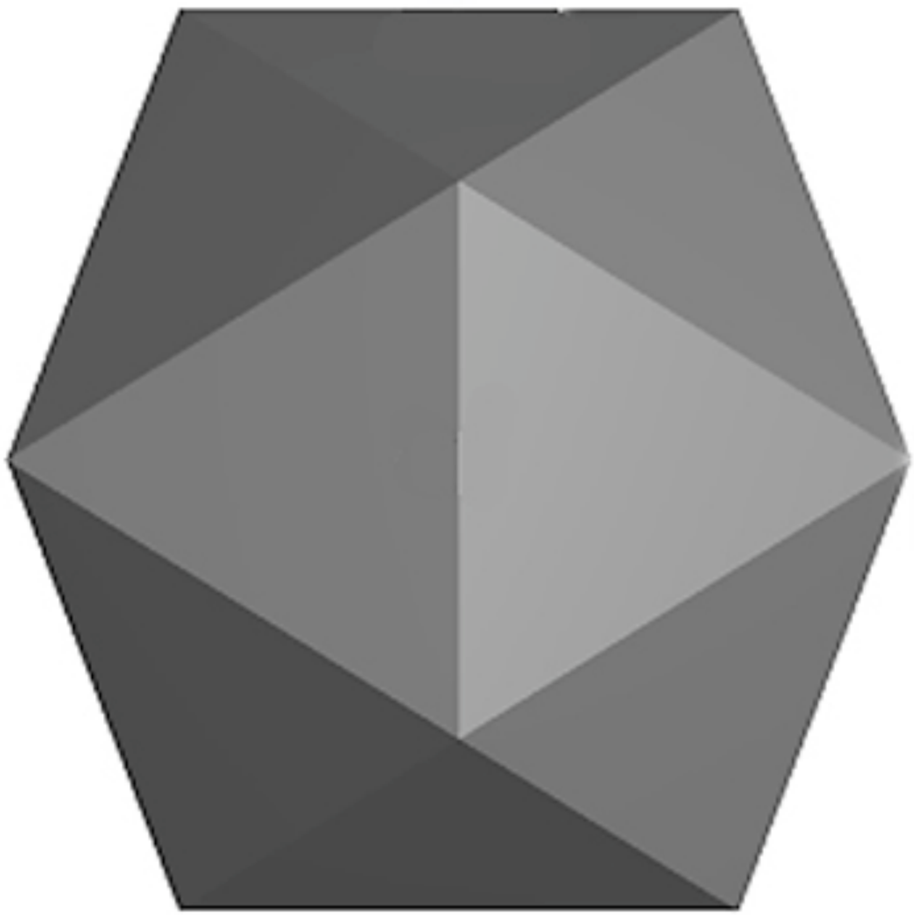
D.L.D. Caspar

TMV

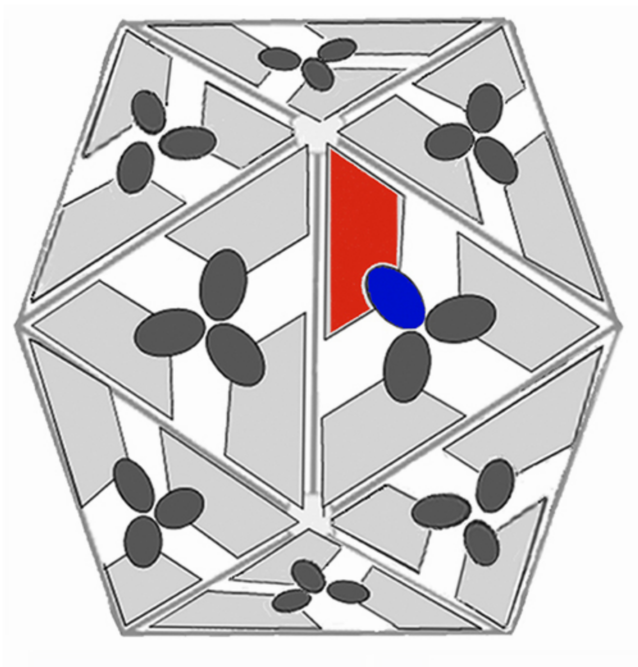


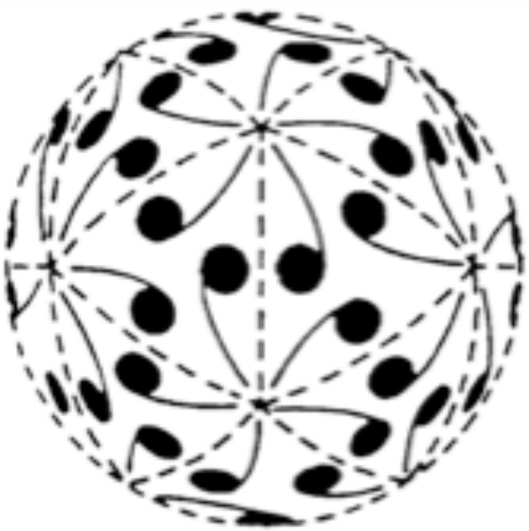
P Gee et al 2010 Science 327:689.

VSV



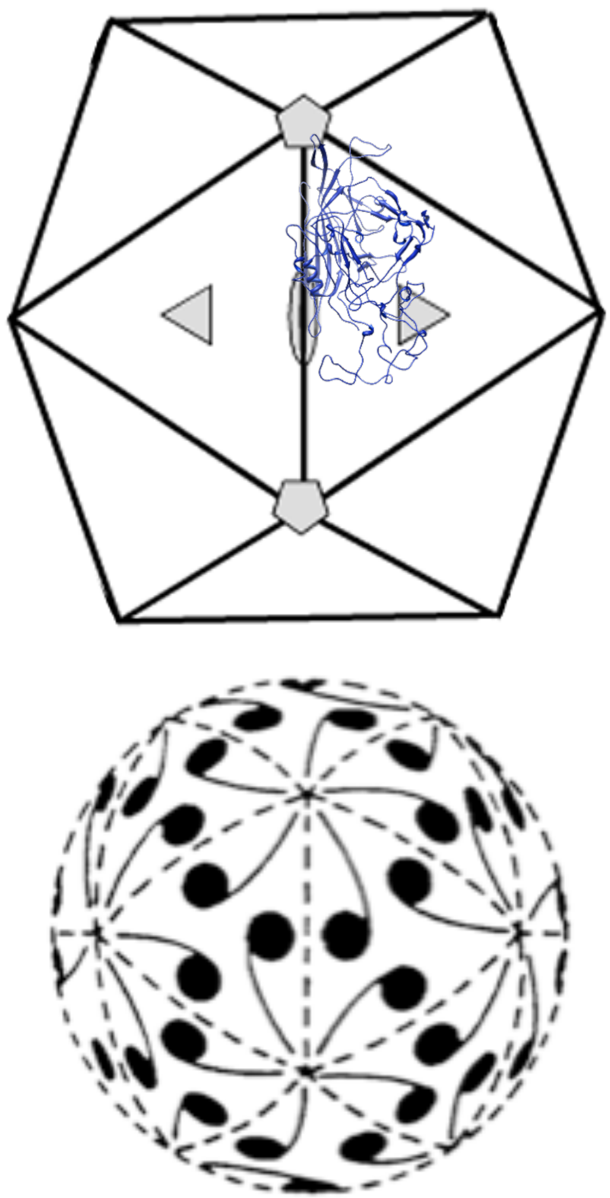
Icosahedral symmetry



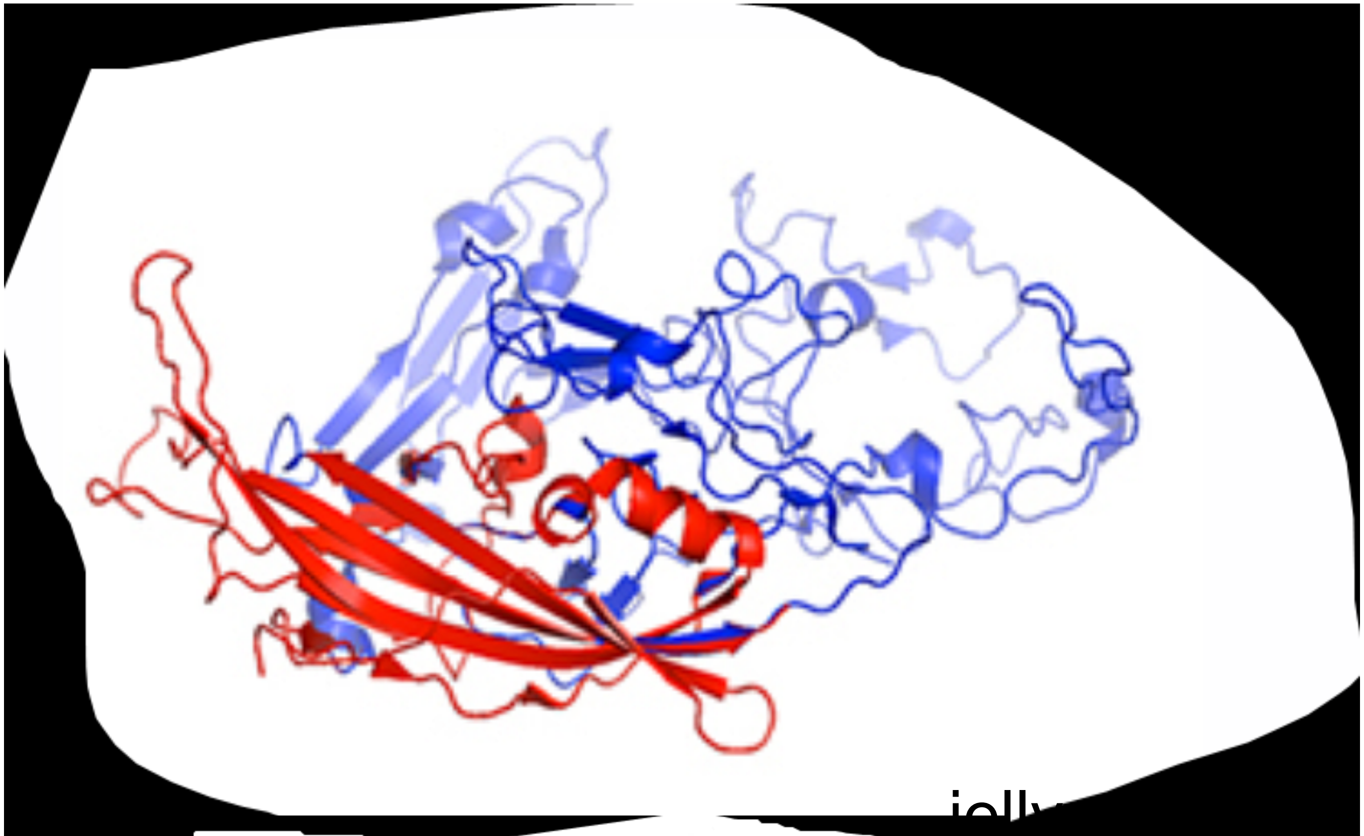


60 subunits

Icosahedral symmetry

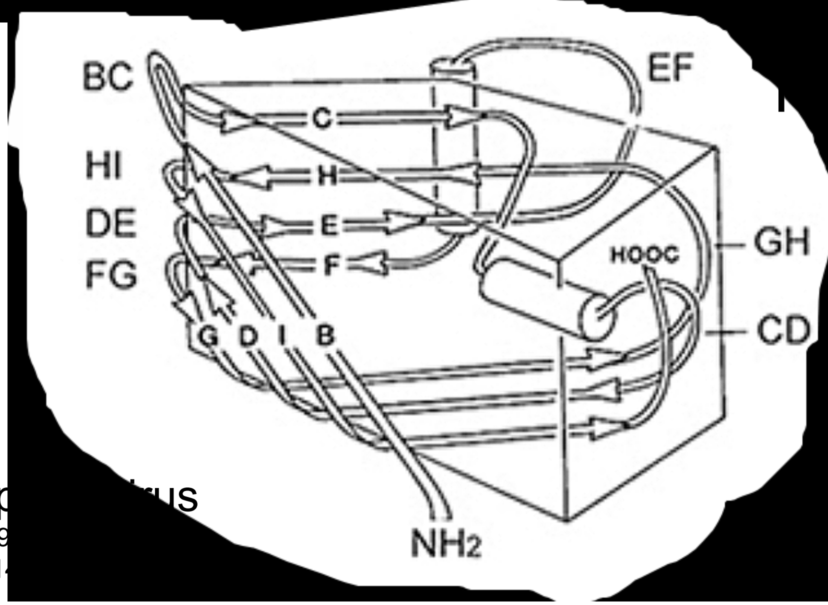


Parvovirus



jelly

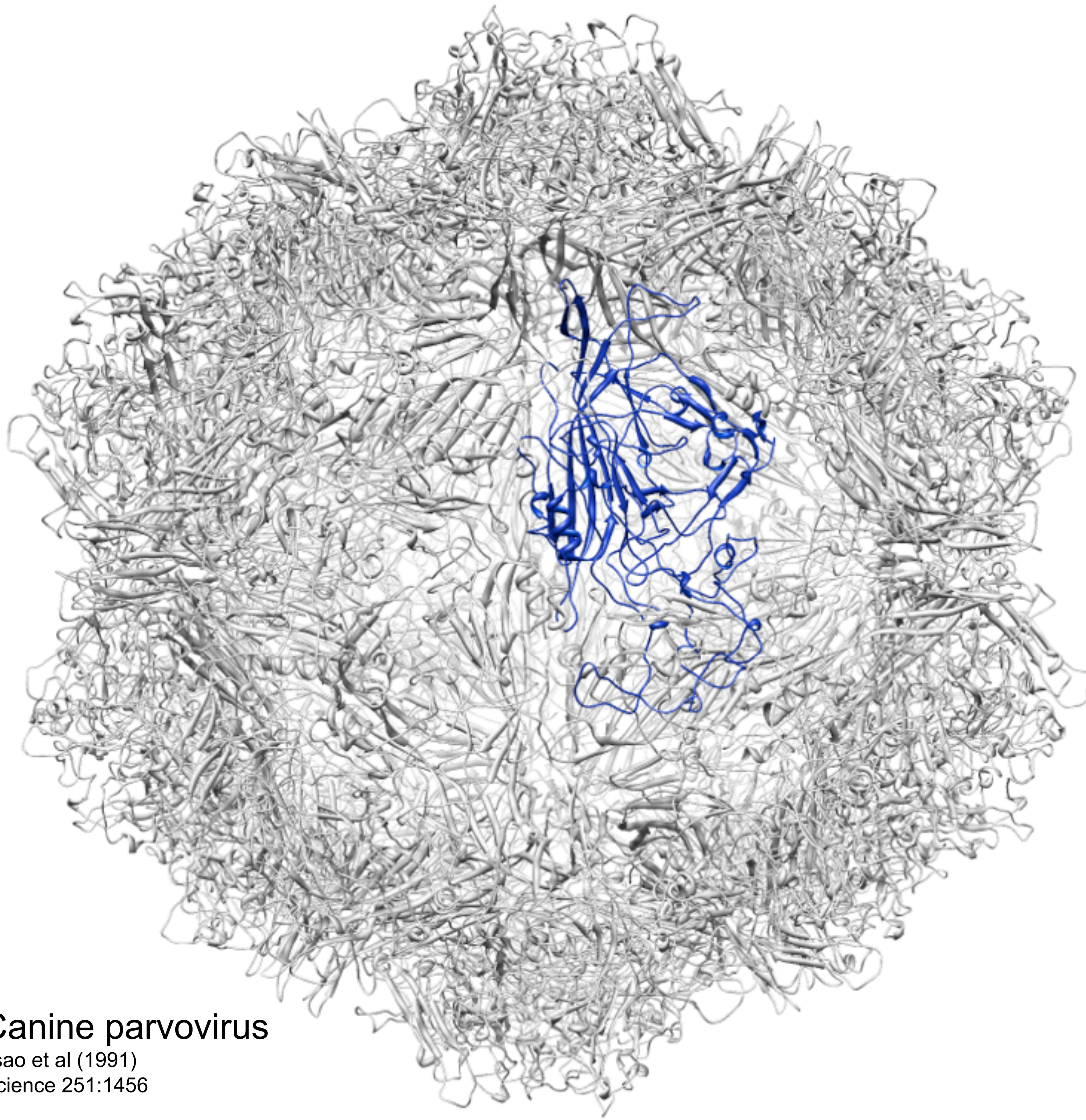
barrel



Canine p rus

Tsao et al (199

Science 251:14



Canine parvovirus

Tsao et al (1991)
Science 251:1456

Parvoviruses:

~ 5kb ssDNA genome
50 kDa molecular mass coat protein
inner radius of shell: 80 Å

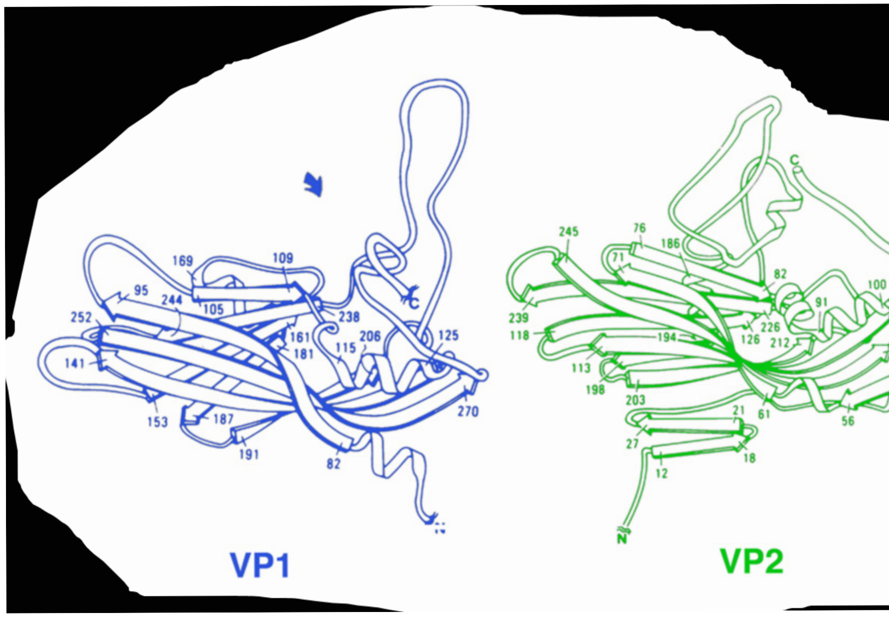
=> just enough volume to package
a 5 kb genome, of which about 1/3
dedicated to coding for coat protein

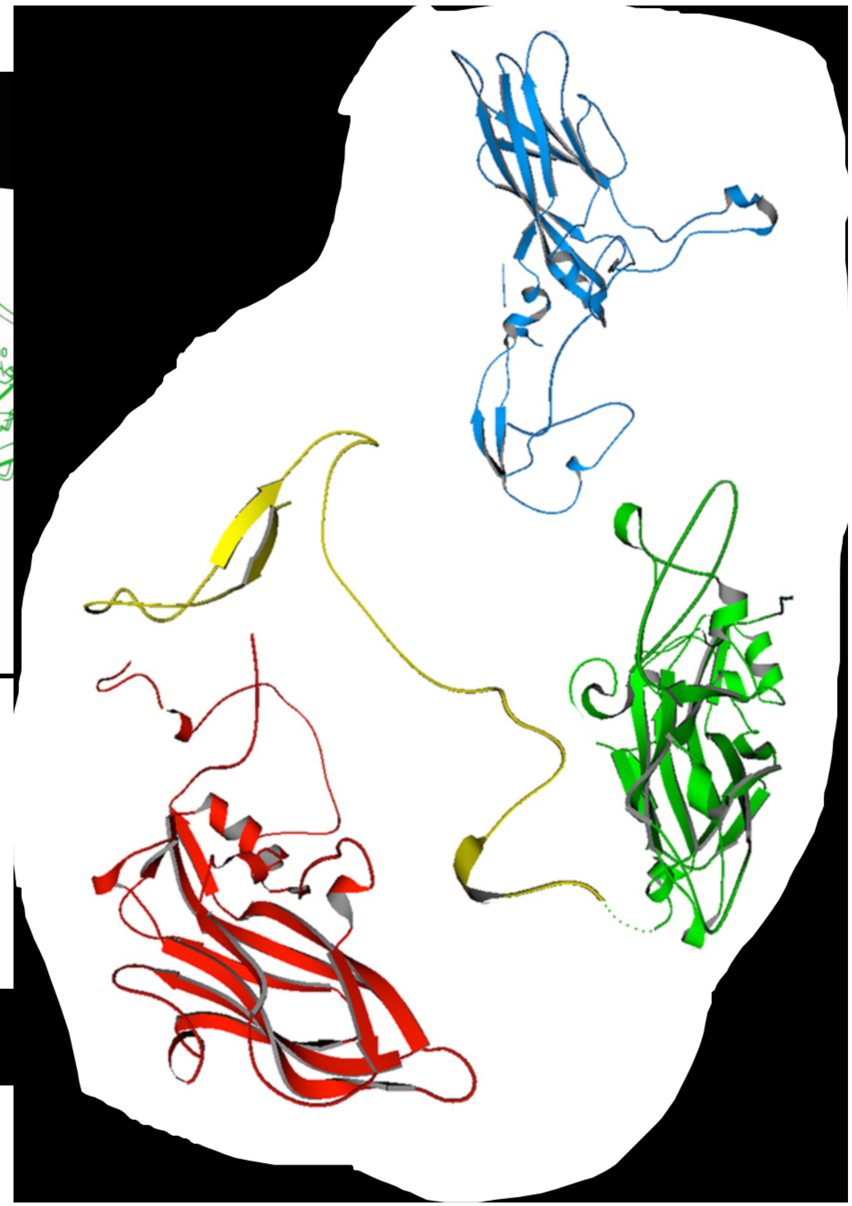
What about larger genomes?

Picornaviruses

Poliovirus (Hogle et al)

Rhinoviruses (Rossmann et al)

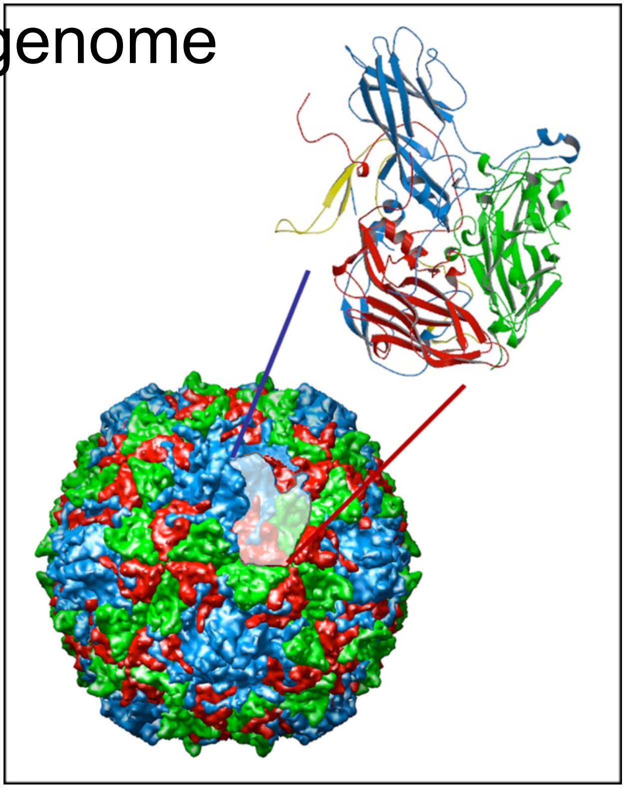




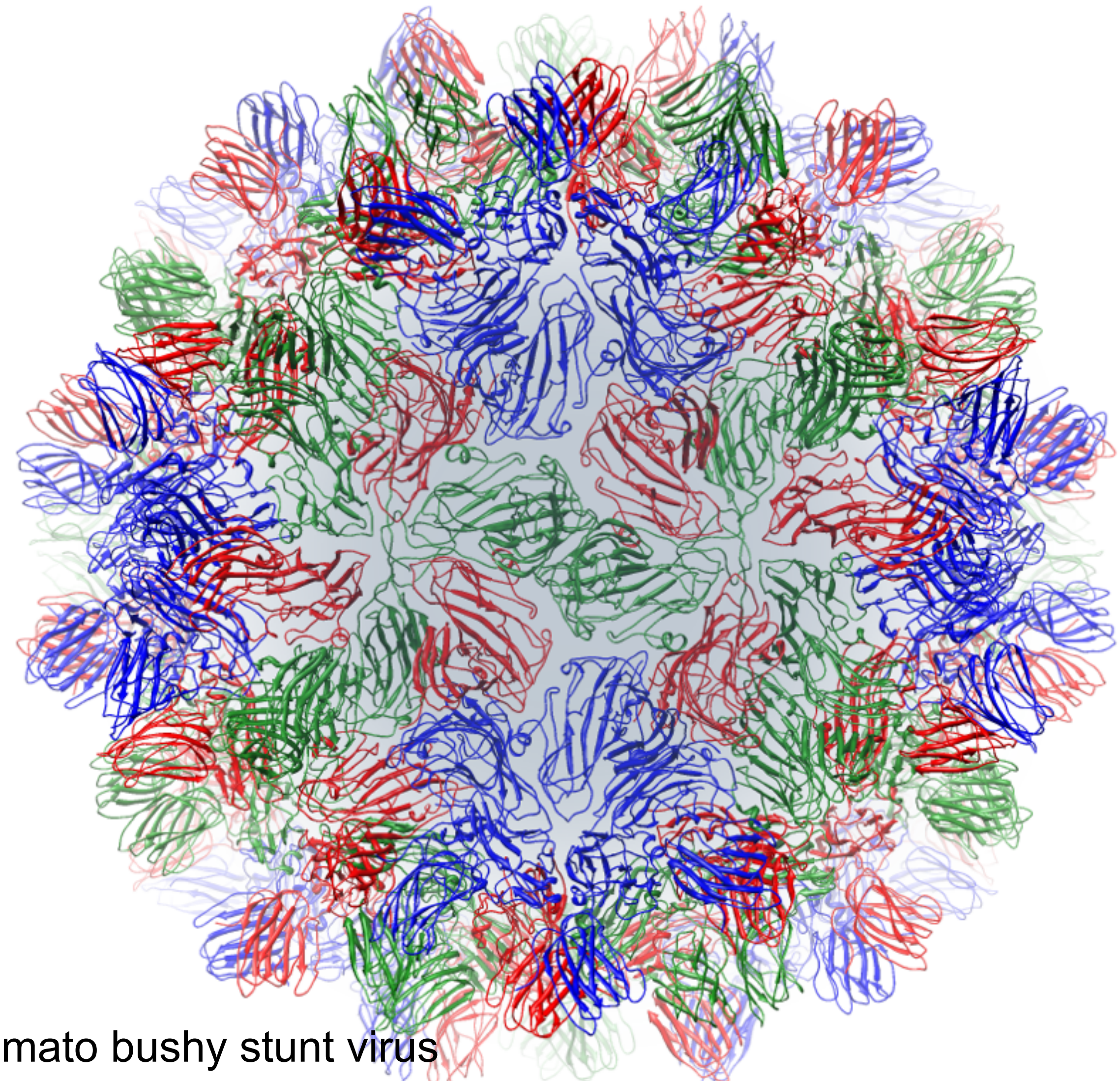
Picornaviruses:

~ 9kb ssRNA genome
30 kDa molecular mass each coat protein
inner radius of shell: 100 Å

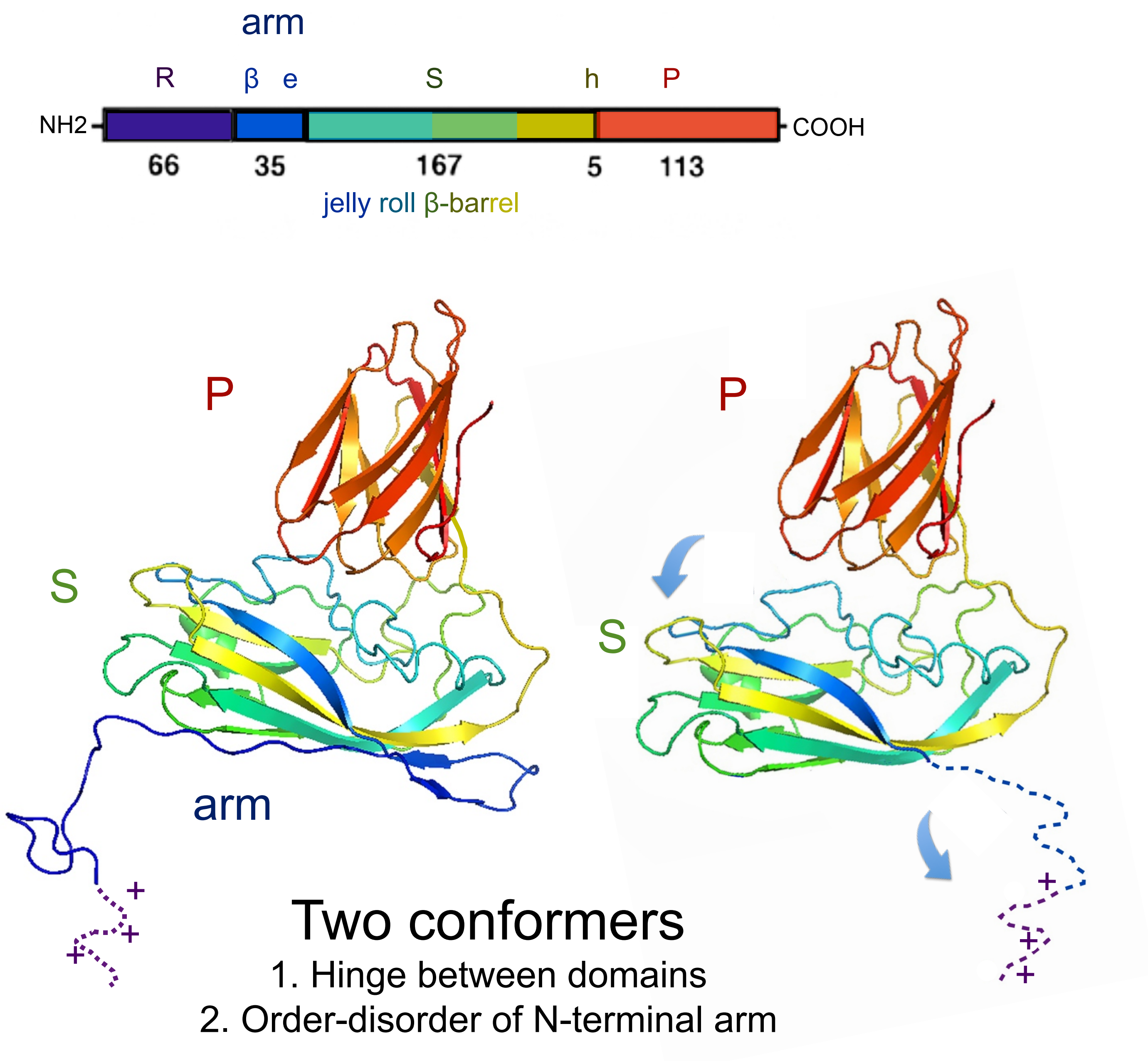
=> just enough volume to accommodate RNA, using 1/3 of genome to encode coat



Multiple conformations of a single kind of subunit can save coding capacity

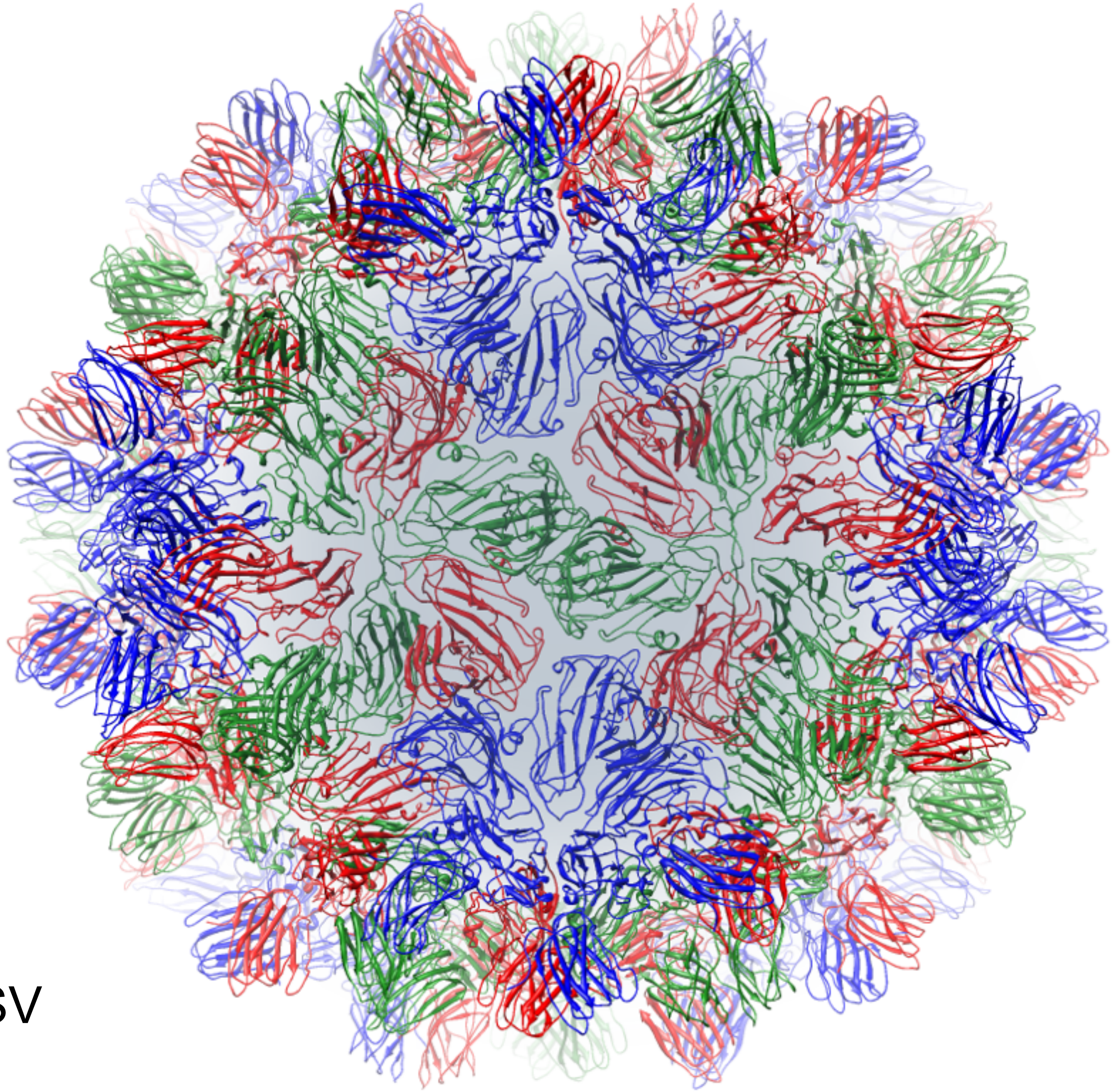


Tomato bushy stunt virus
(TBSV)

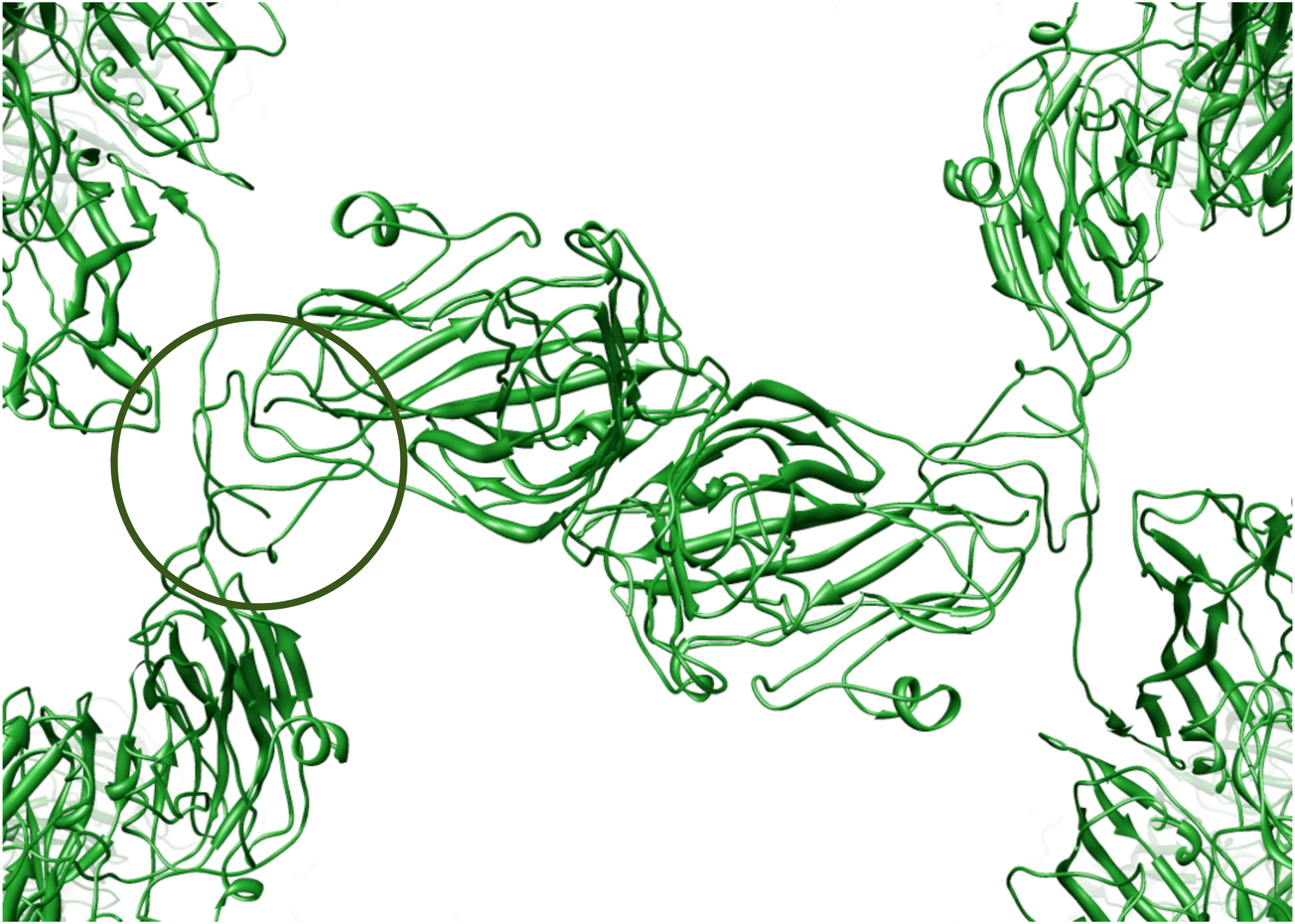


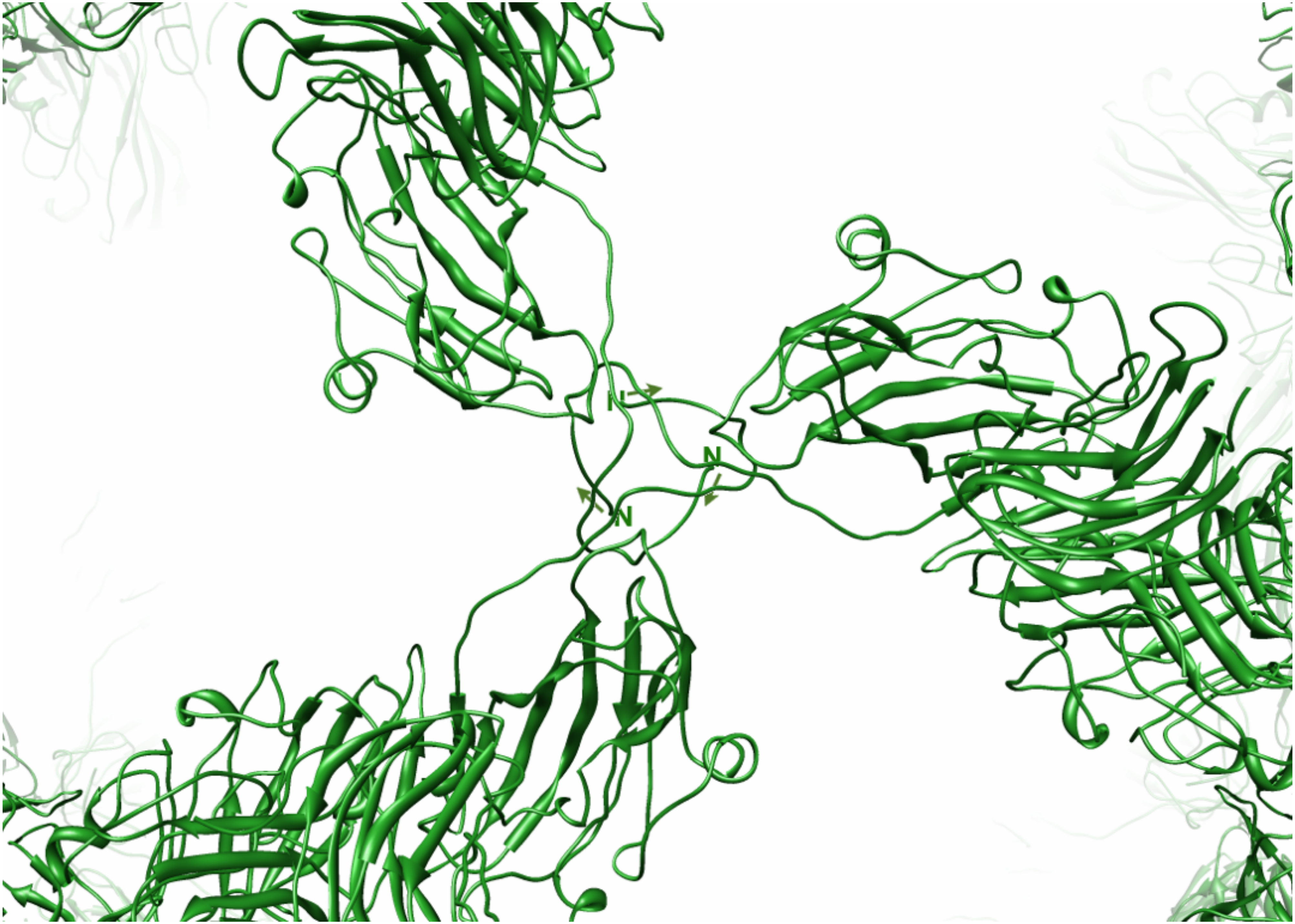
Two conformers

1. Hinge between domains
2. Order-disorder of N-terminal arm



TBSV

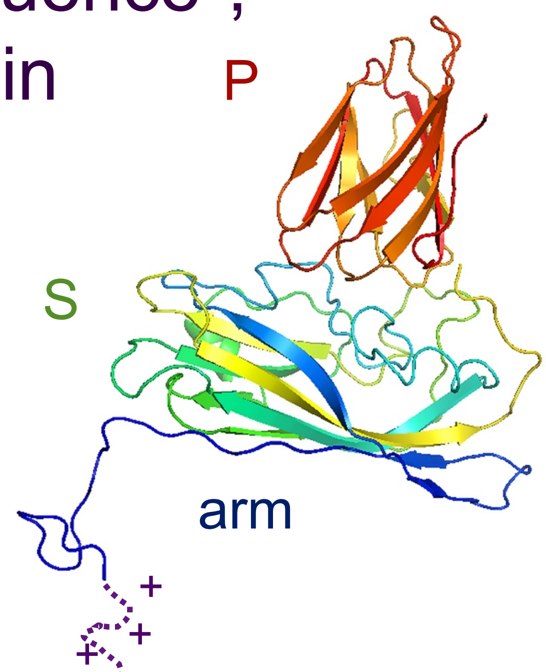



N
N
N

Arm-like extensions fold together
to form an inner scaffold

Flexible links to RNA: "undemanding"
packaging of genome

=> "Packaging sequence",
assembly origin



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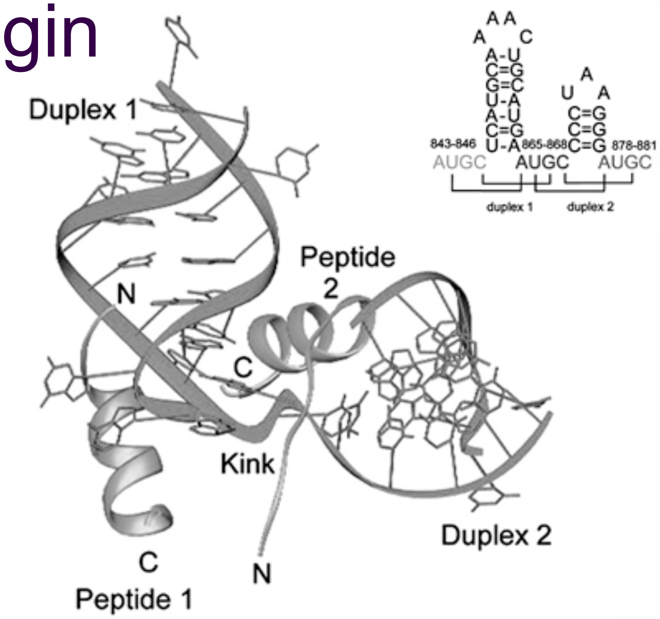
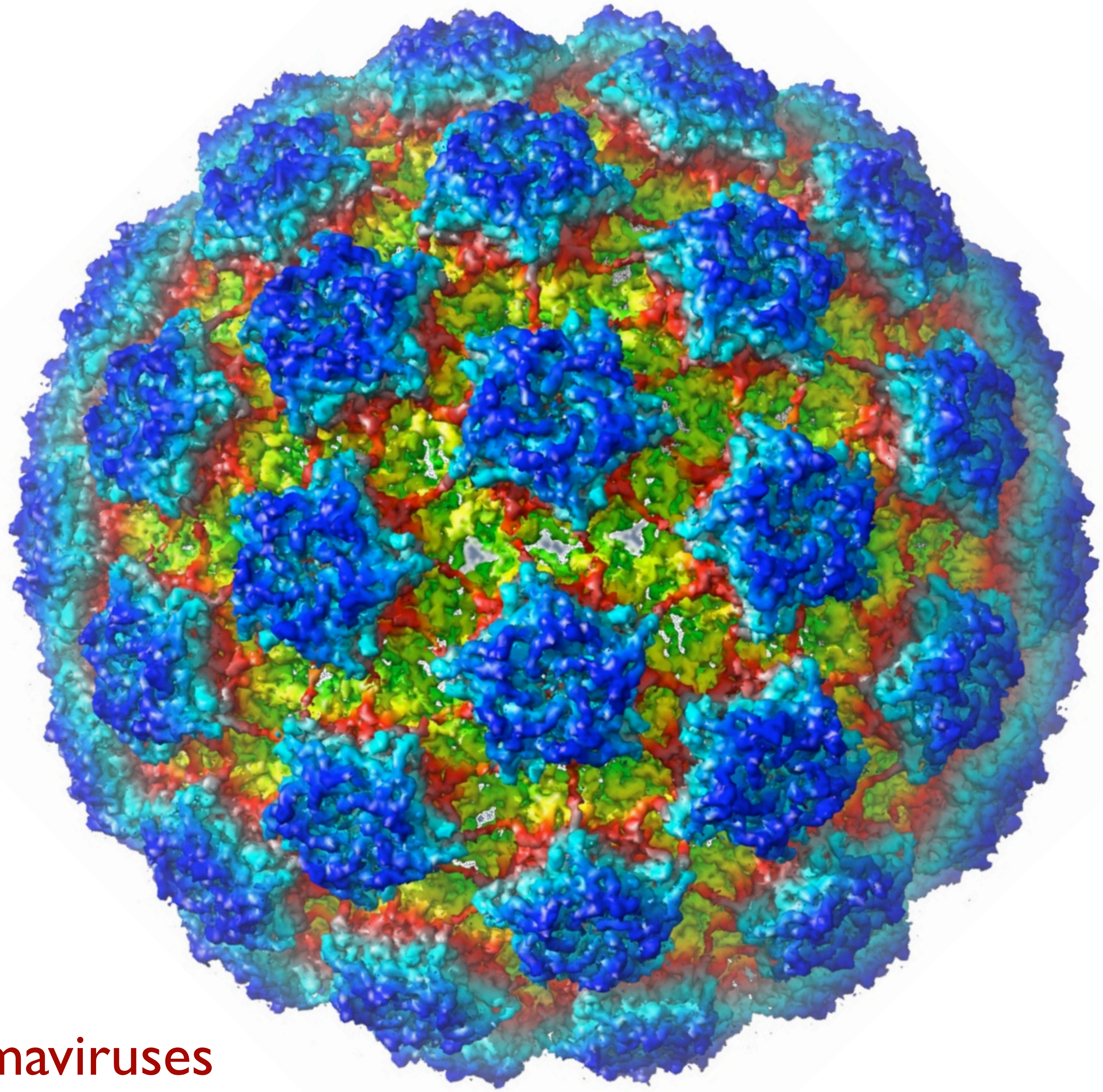
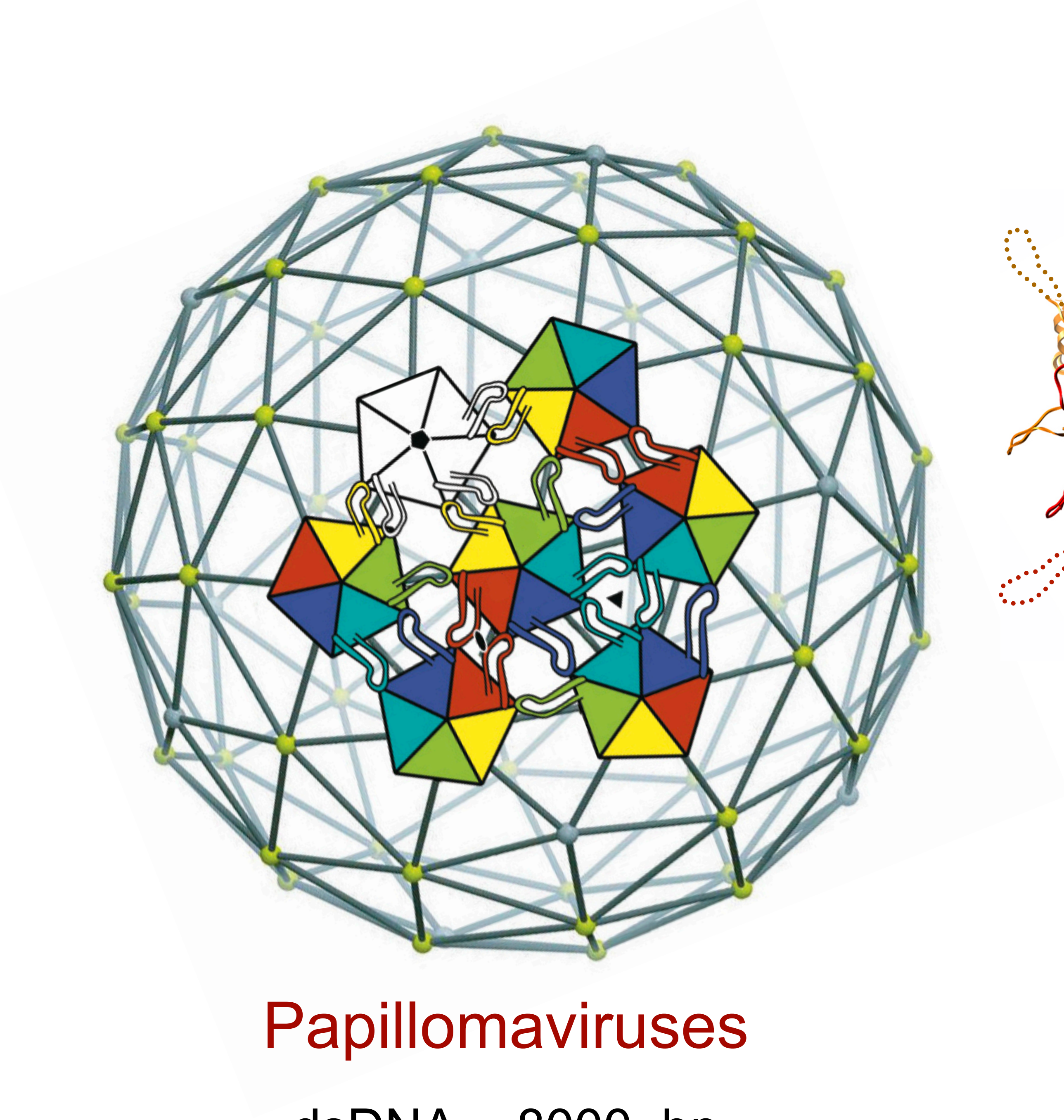


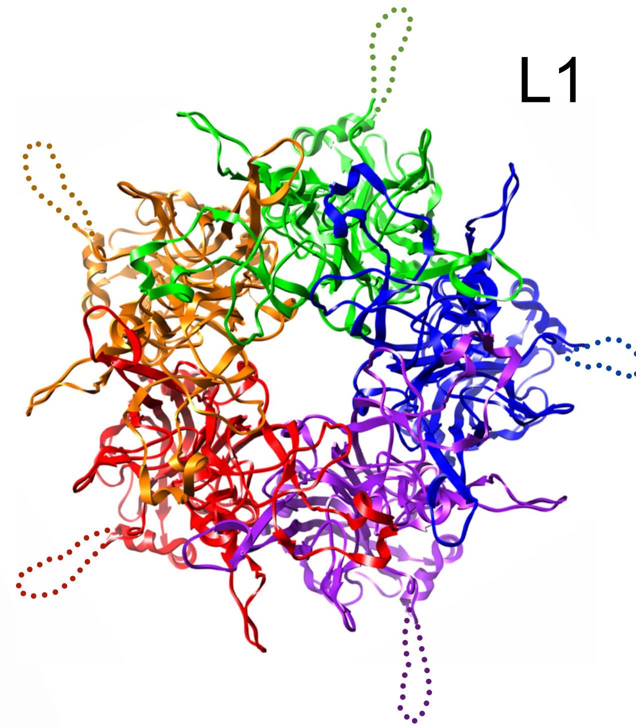
AMV packaging interaction

Co-folding of N-terminal "R-domain"
and RNA packaging sequence
Guogas LM, Filman DJ, Hogle JM,
Gehrke L. Science. 2004 306:2108-11.



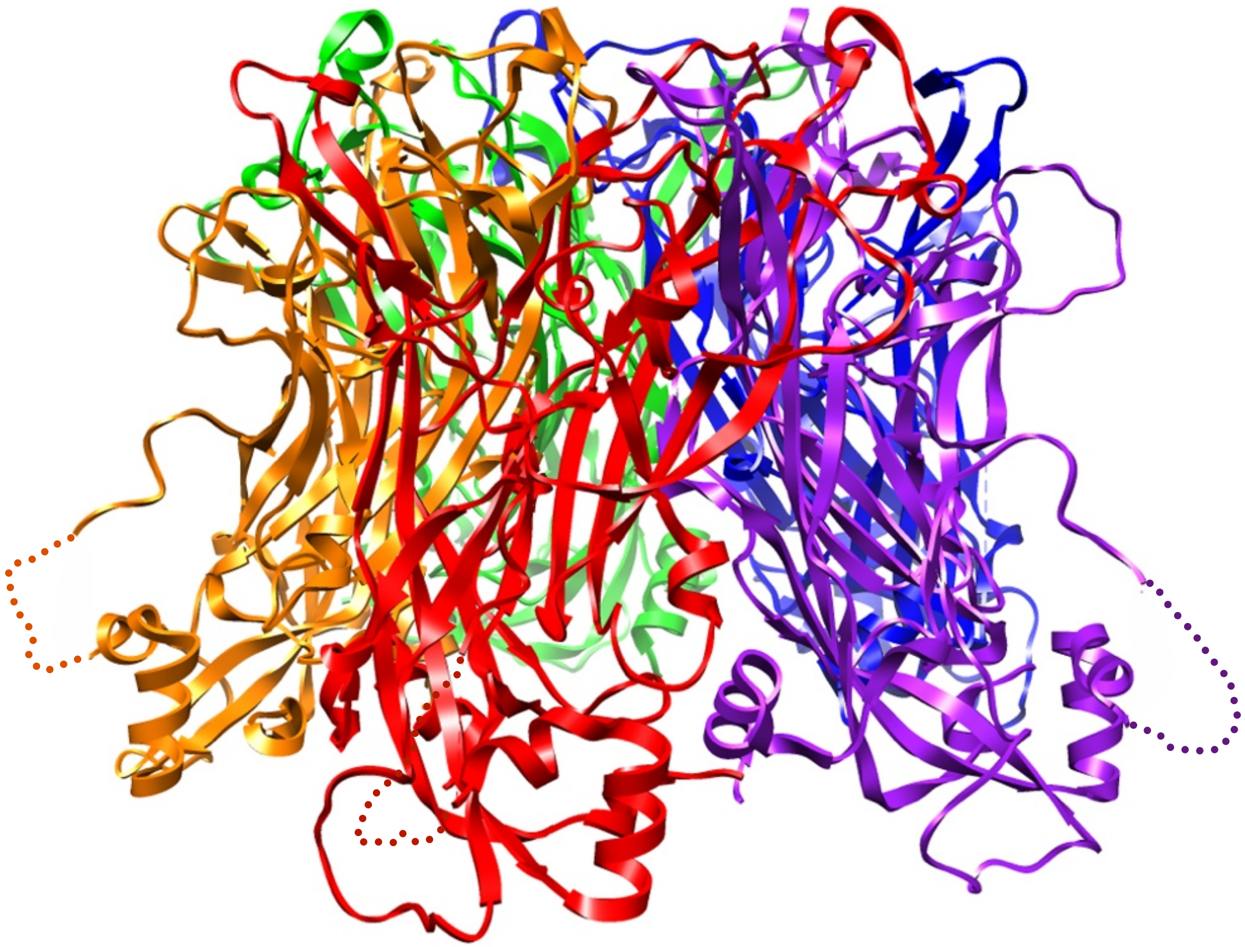
Papillomaviruses



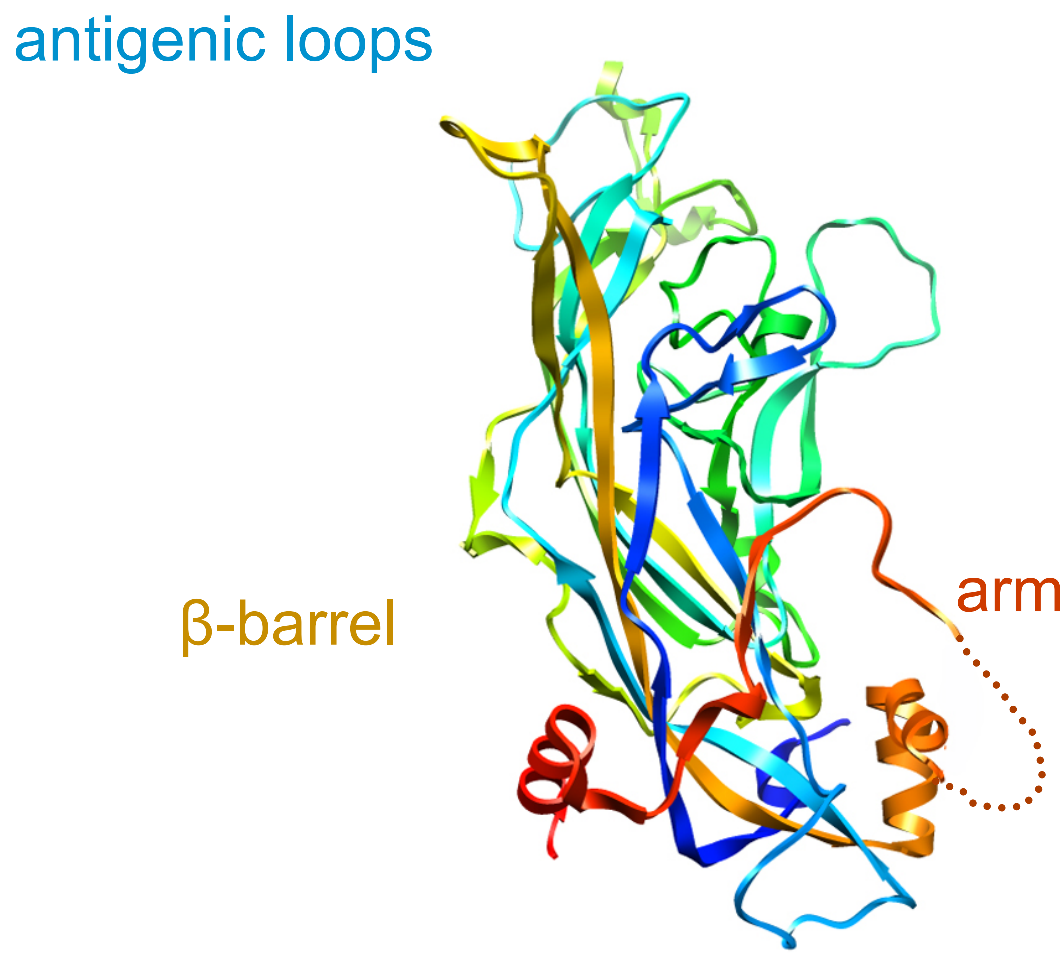


Papillomaviruses

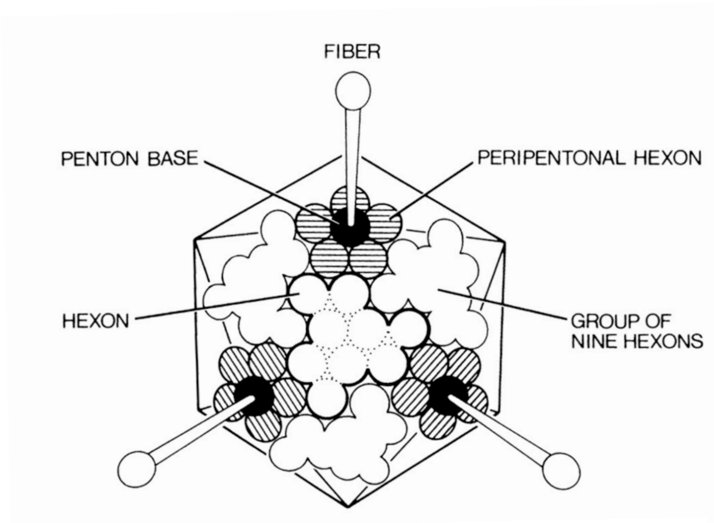
dsDNA, ~8000 bp



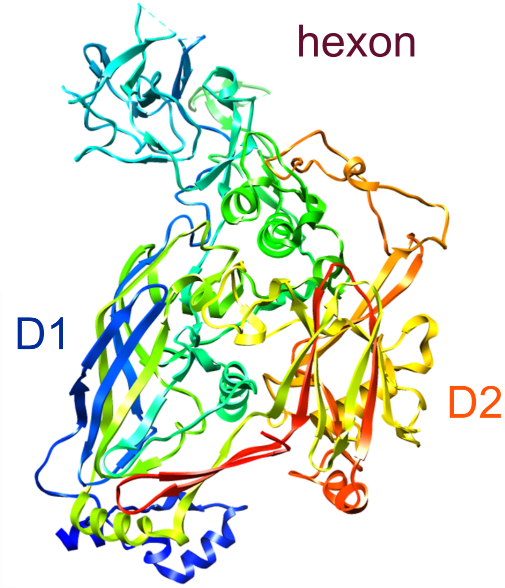
L1 pentamer

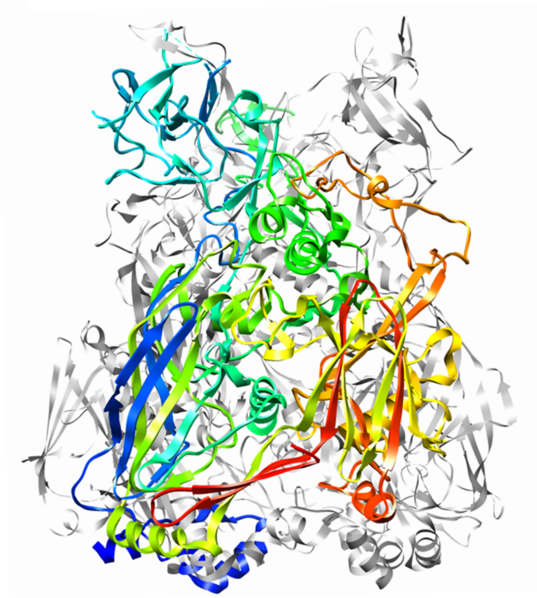

antigenic loops
β-barrel
arm

Adenoviruses

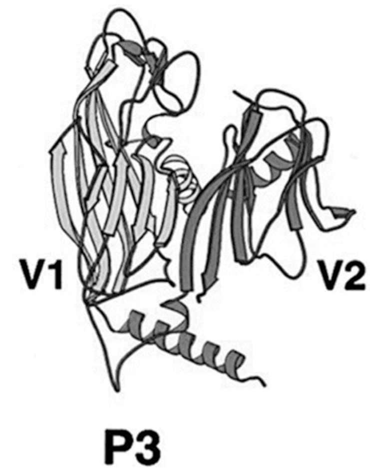


hexon



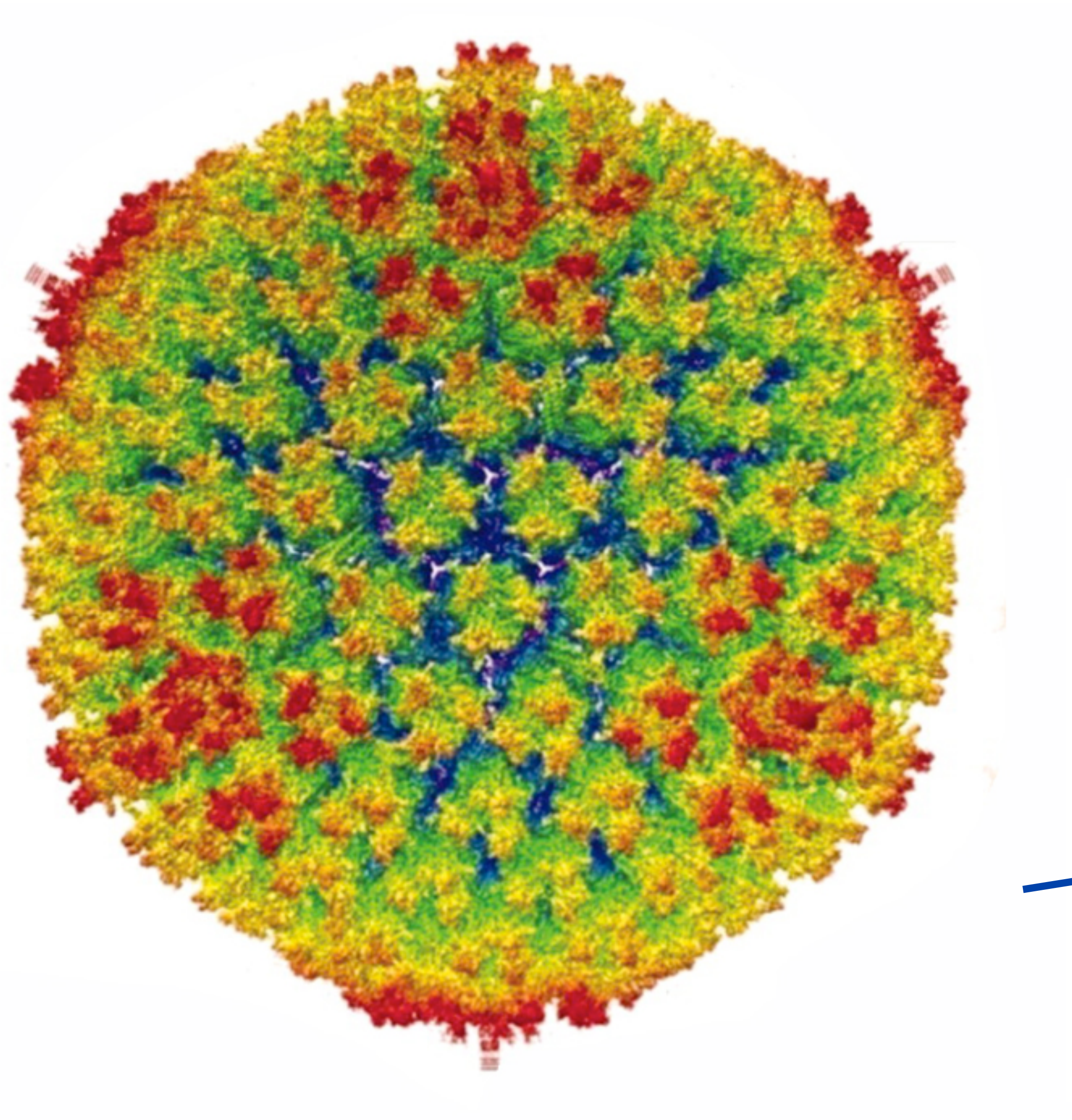


Phage PRD1
protein P3



Adenoviruses

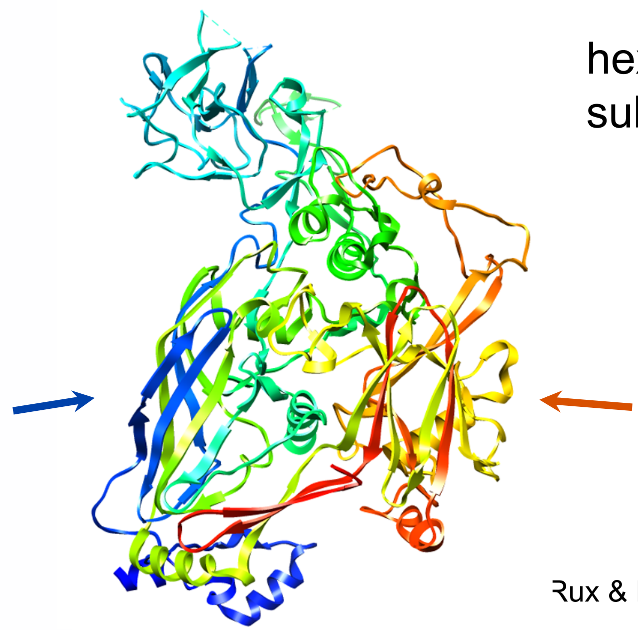
~ 35 Kbp dsDNA genome



H Liu et al. Science 2010;329:1038-1043

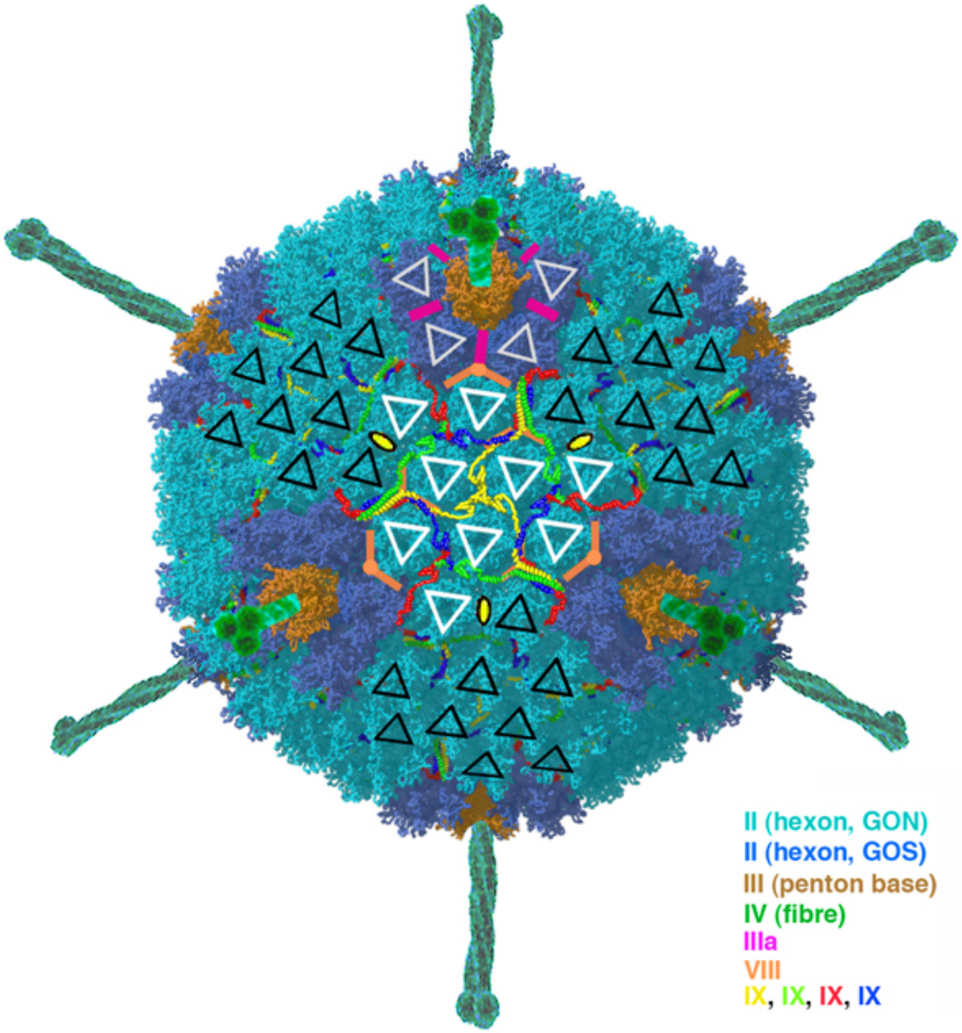
penton subunit

Cusack & coworkers

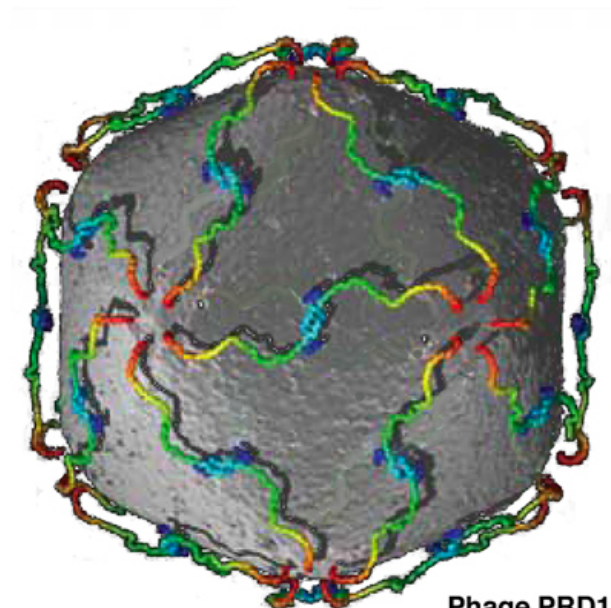


hexon subunit

Rux & Burnett



H Liu et al. Science 2010;329:1038-1043



Phage PRD1
(internal “tape measure” protein)

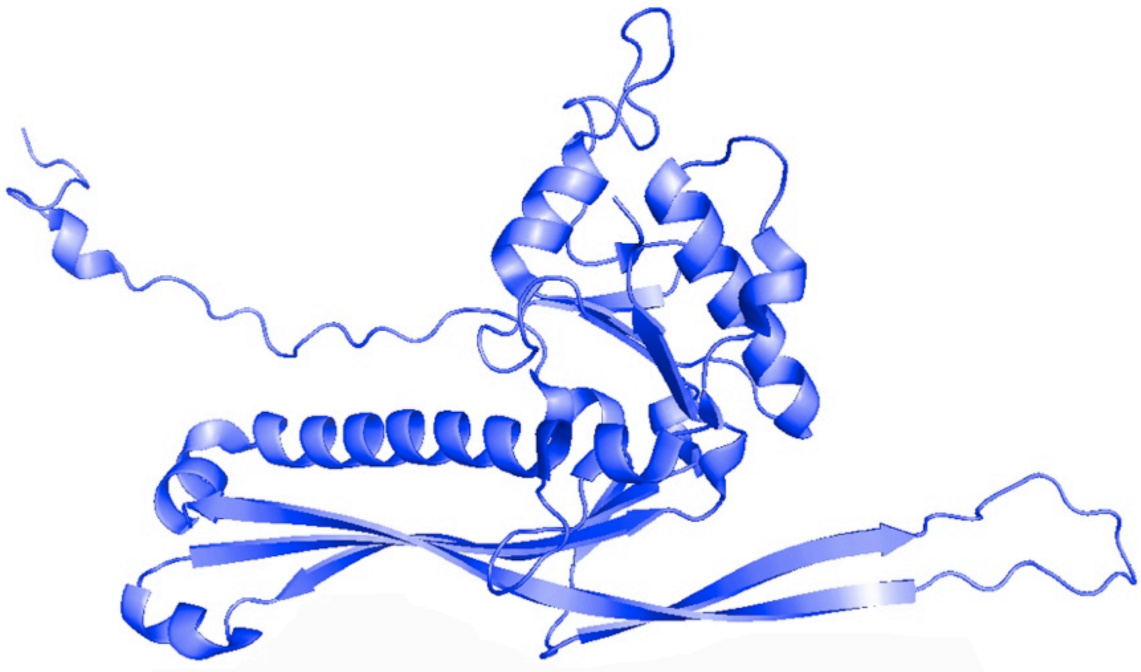
Adenovirus and phage PRD1

Fixed assembly unit ("assembly line")
TBSV coat protein dimer
Papillomavirus L1 pentamer
Adenovirus hexon

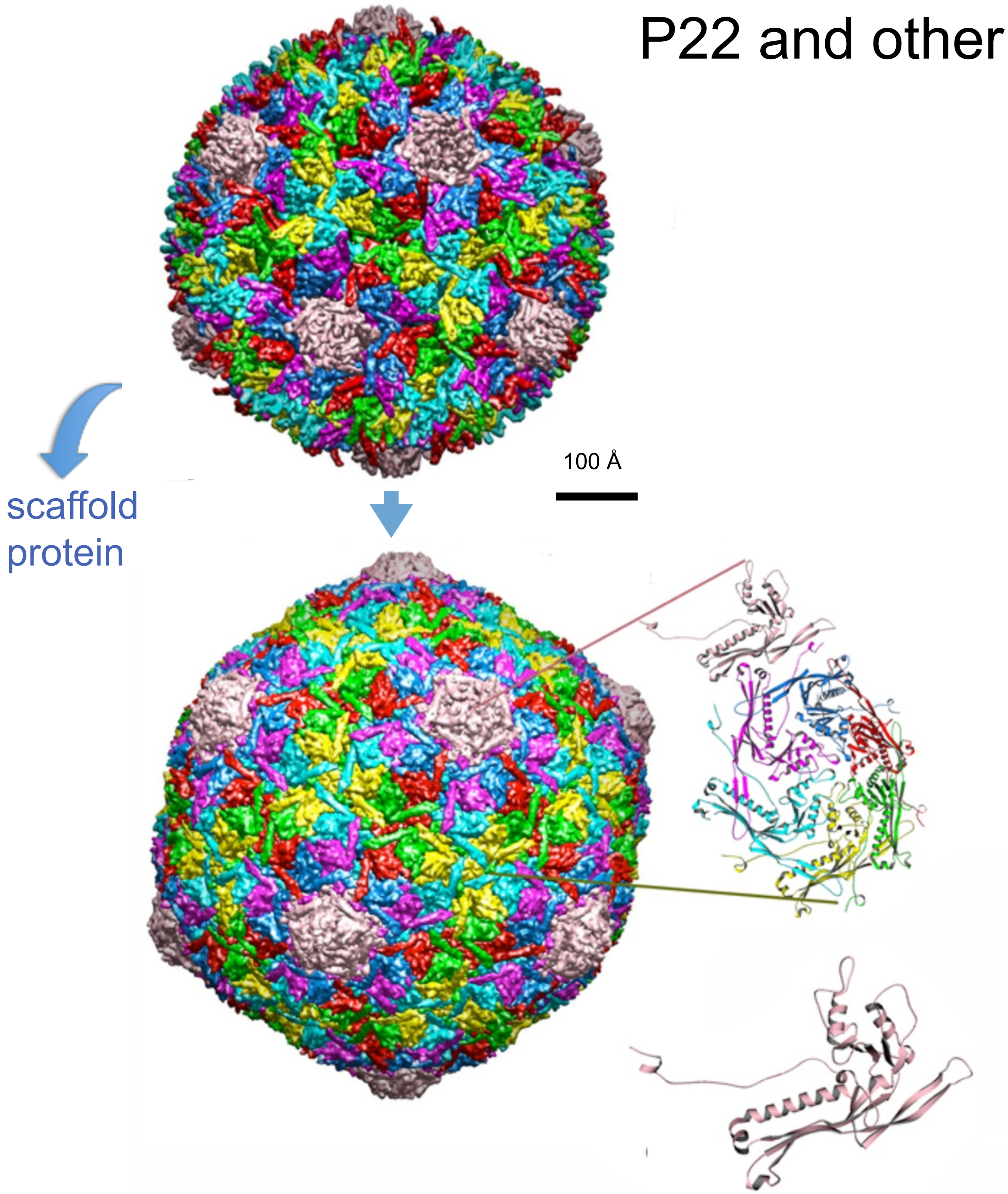
A framework or scaffold to ensure accurate placement of "mass produced" assembly units

Recurring architectural motif (jelly-roll β-barrel)

"HK97" fold



P22 and other dsDNA bacteriophage

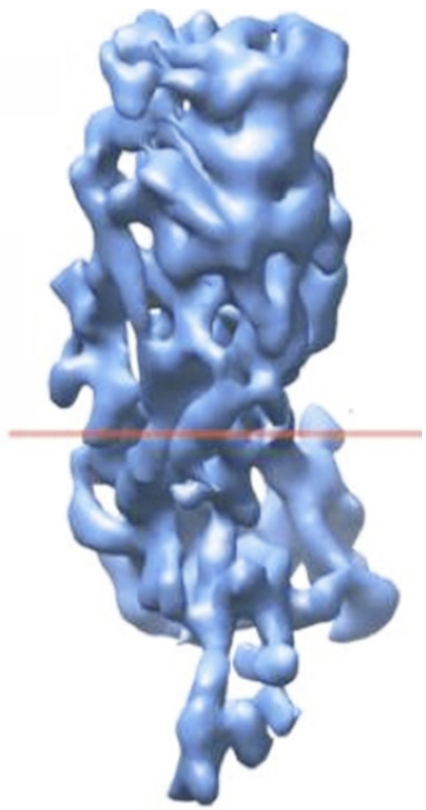


"HK97" fold

phage HK97

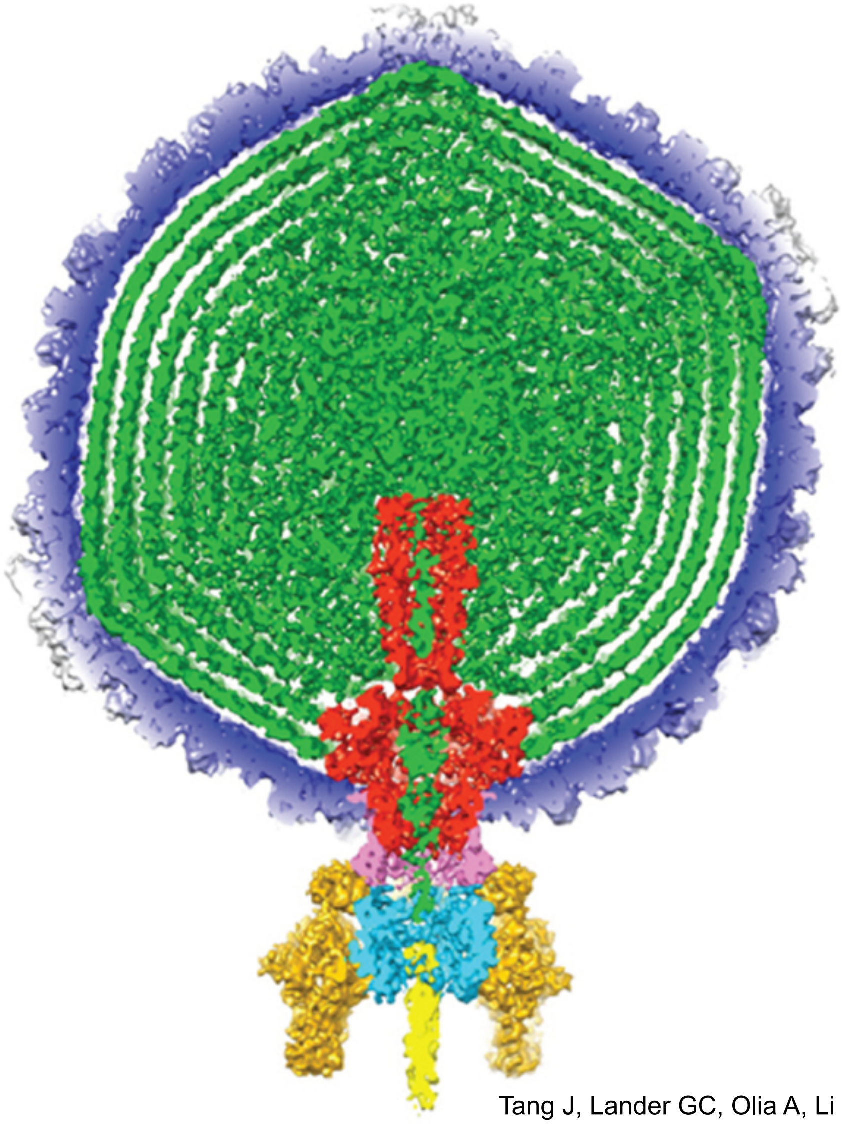
phage T4

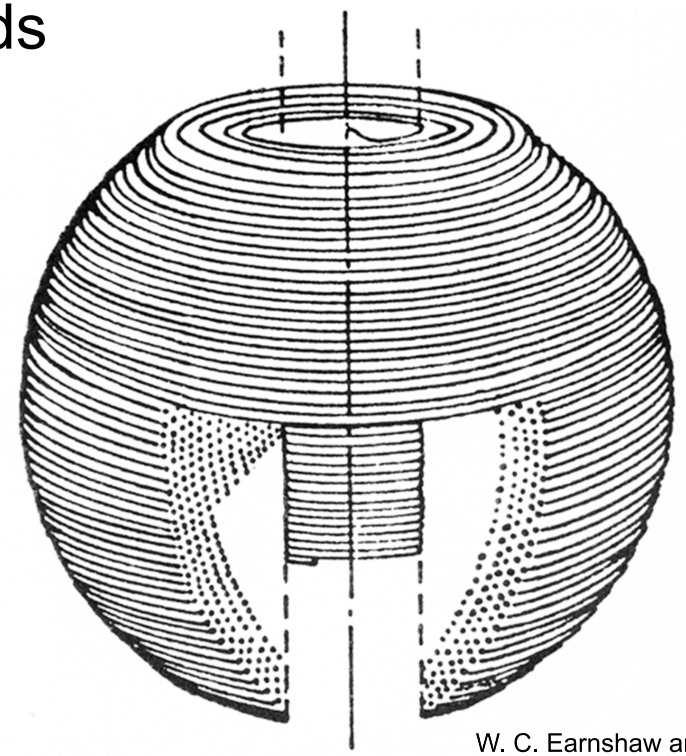
herpes simplex virus
type 1



Baker ML, Jiang W, Rixon FJ, Chiu W. 2005

Coiling of double-strand nucleic acids in DNA phage





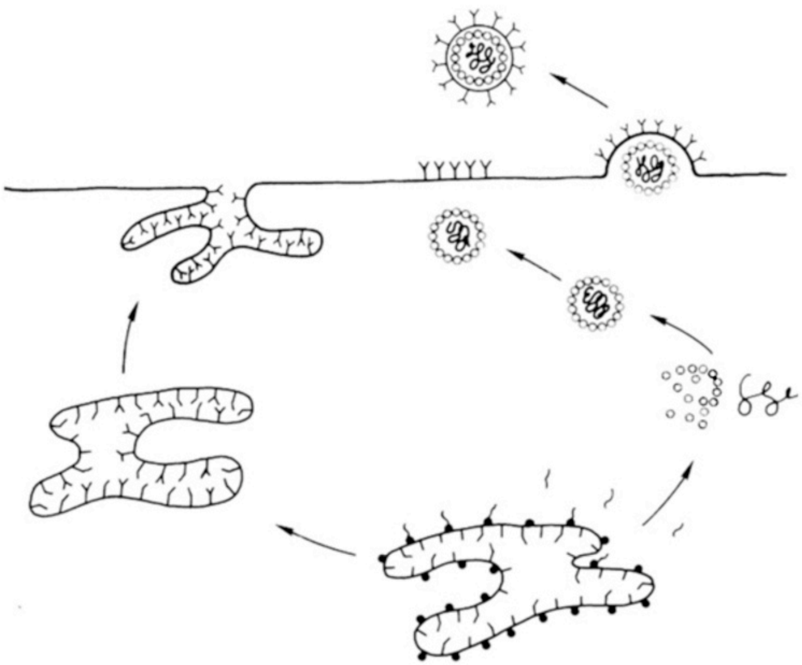
W. C. Earnshaw and S.C. Harrison. Nature 268, 598 (1977).

Tang J, Lander GC, Olia A, Li R, Casjens S, Prevelige P Jr, Cingolani G, Baker TS, Johnson JE. Structure. 2011 19:496-502.

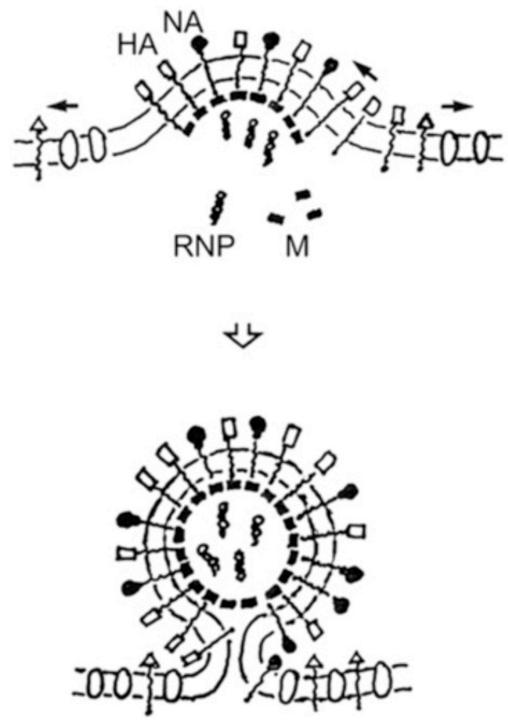
Enveloped viruses

1. Budding
2. Smaller, icosahedrally symmetric enveloped viruses (dengue)
3. Larger, less regular enveloped viruses (HIV; influenza)

Budding of enveloped viruses

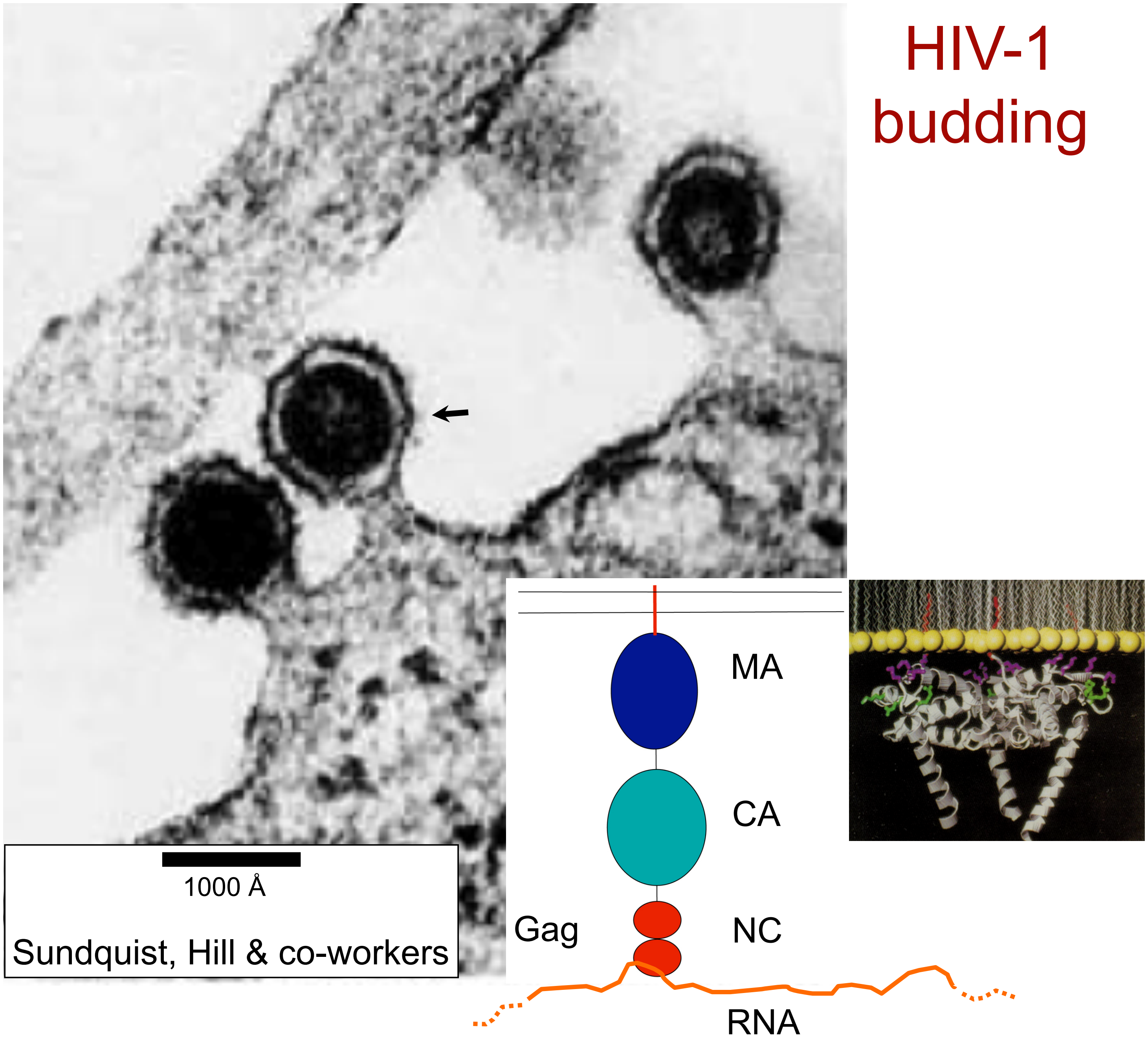


alphaviruses

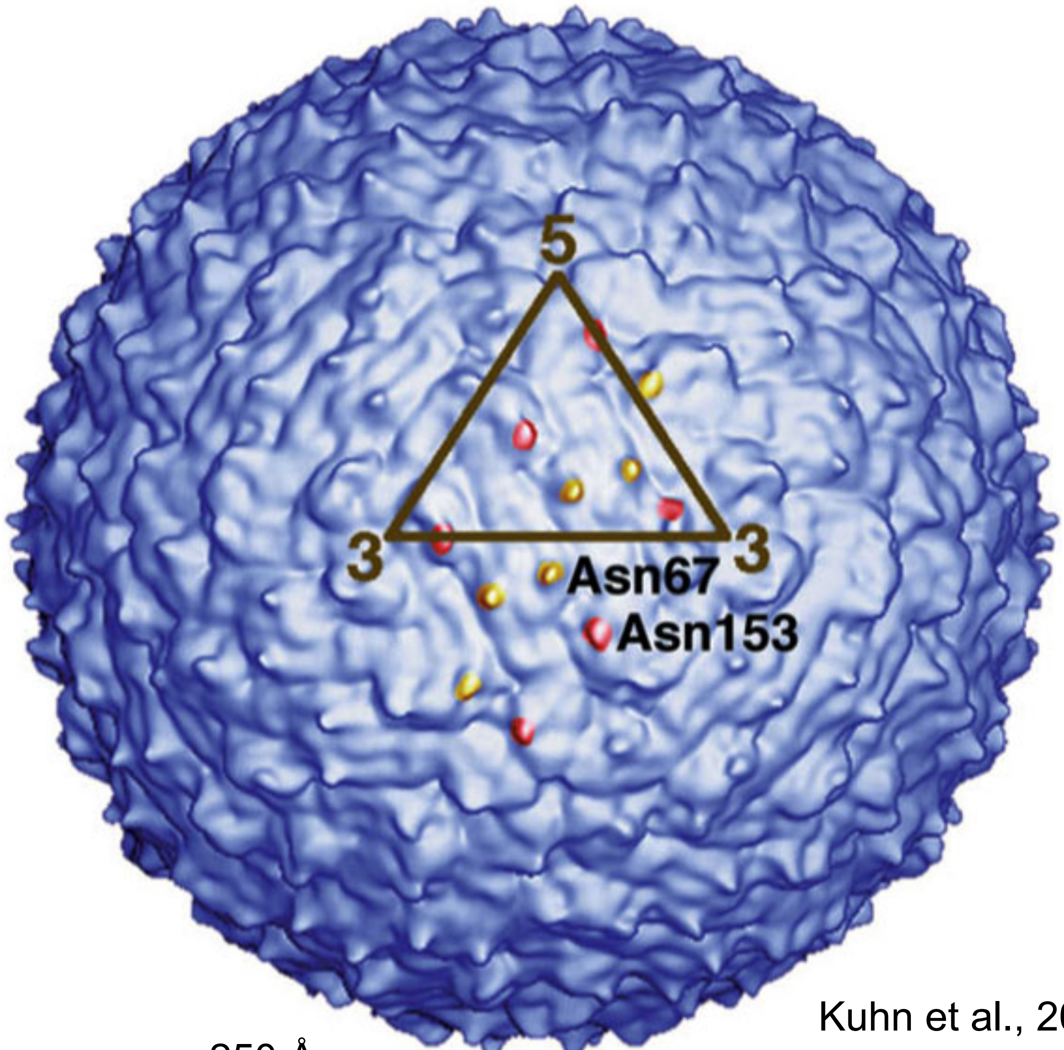


influenza virus

HIV-1 budding



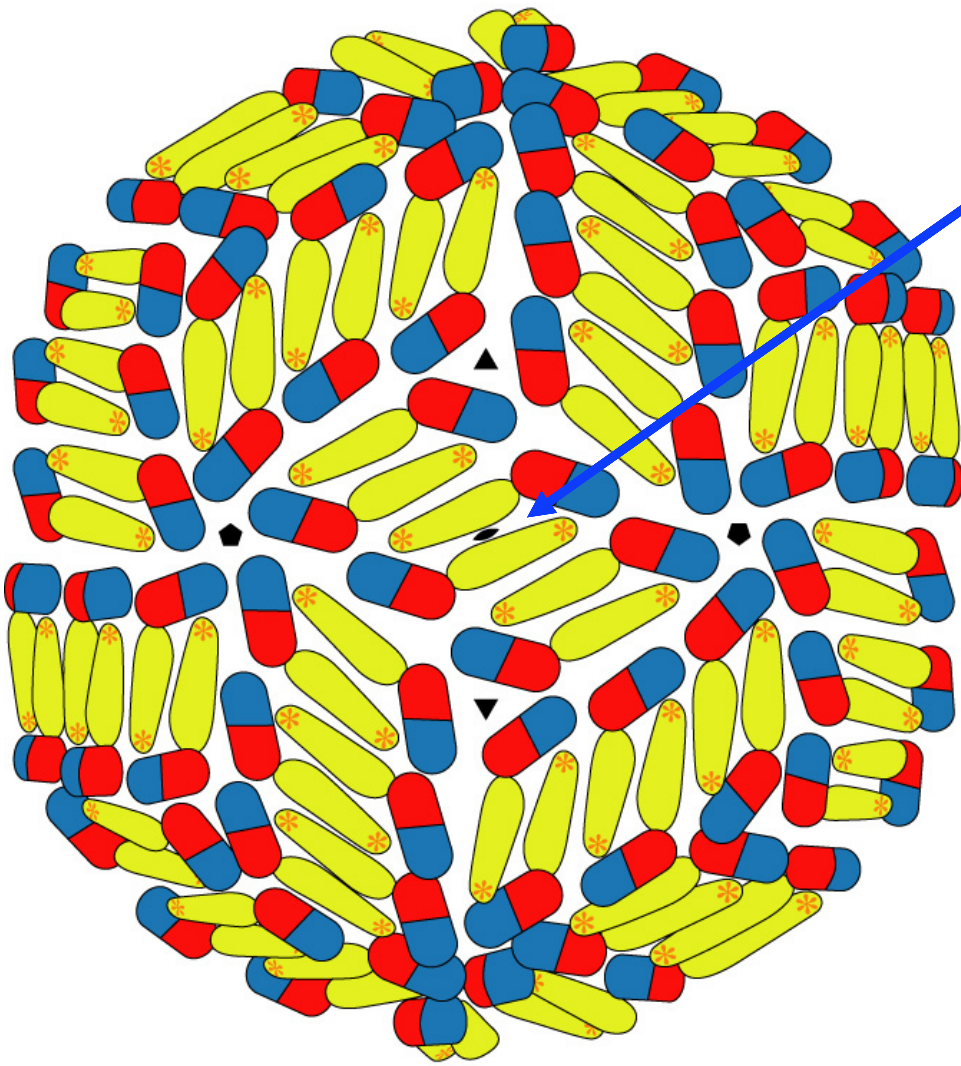
Dengue virus particle

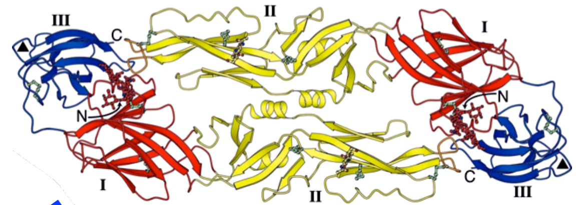


Kuhn et al., 2001

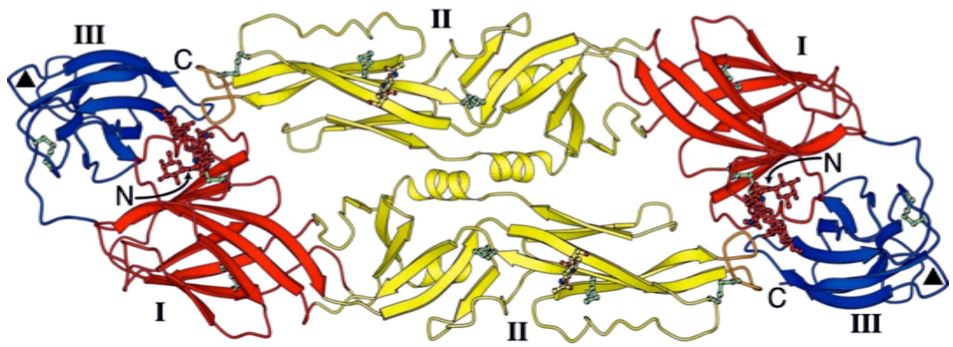
250 Å

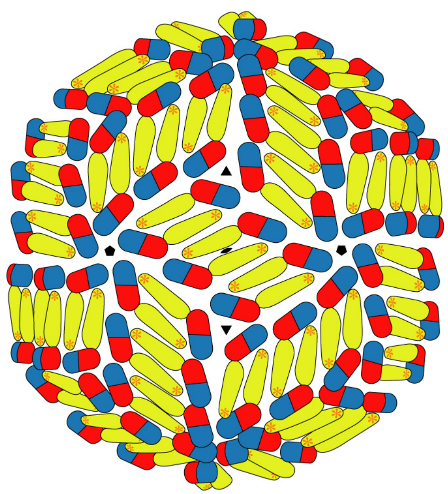
Dengue virus particle



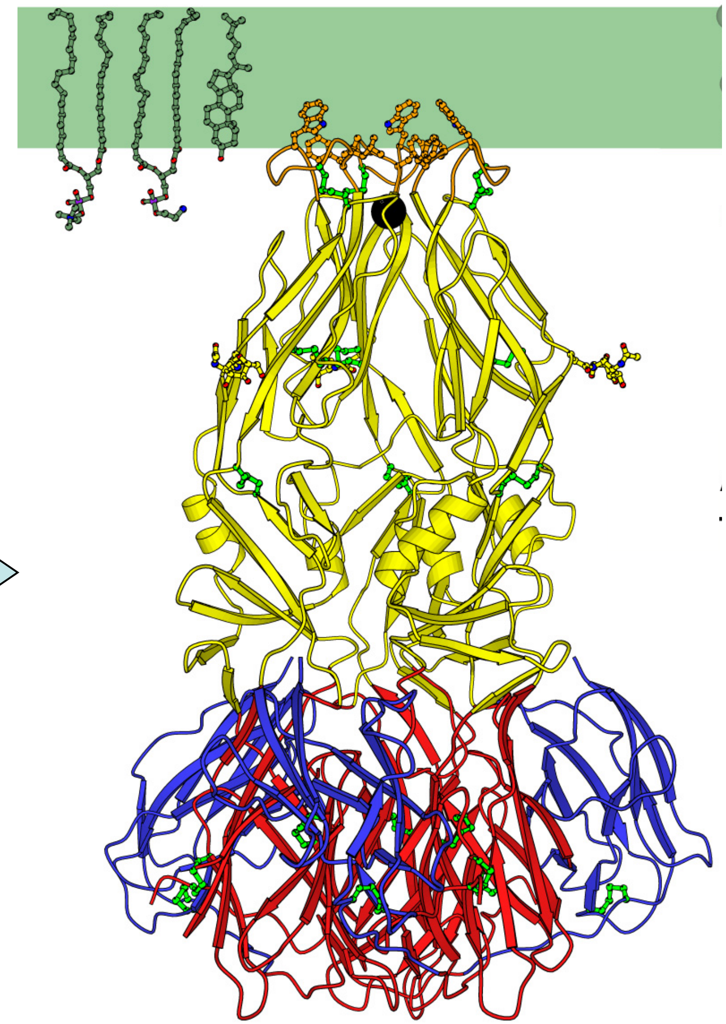


Fusion-promoting conformational change

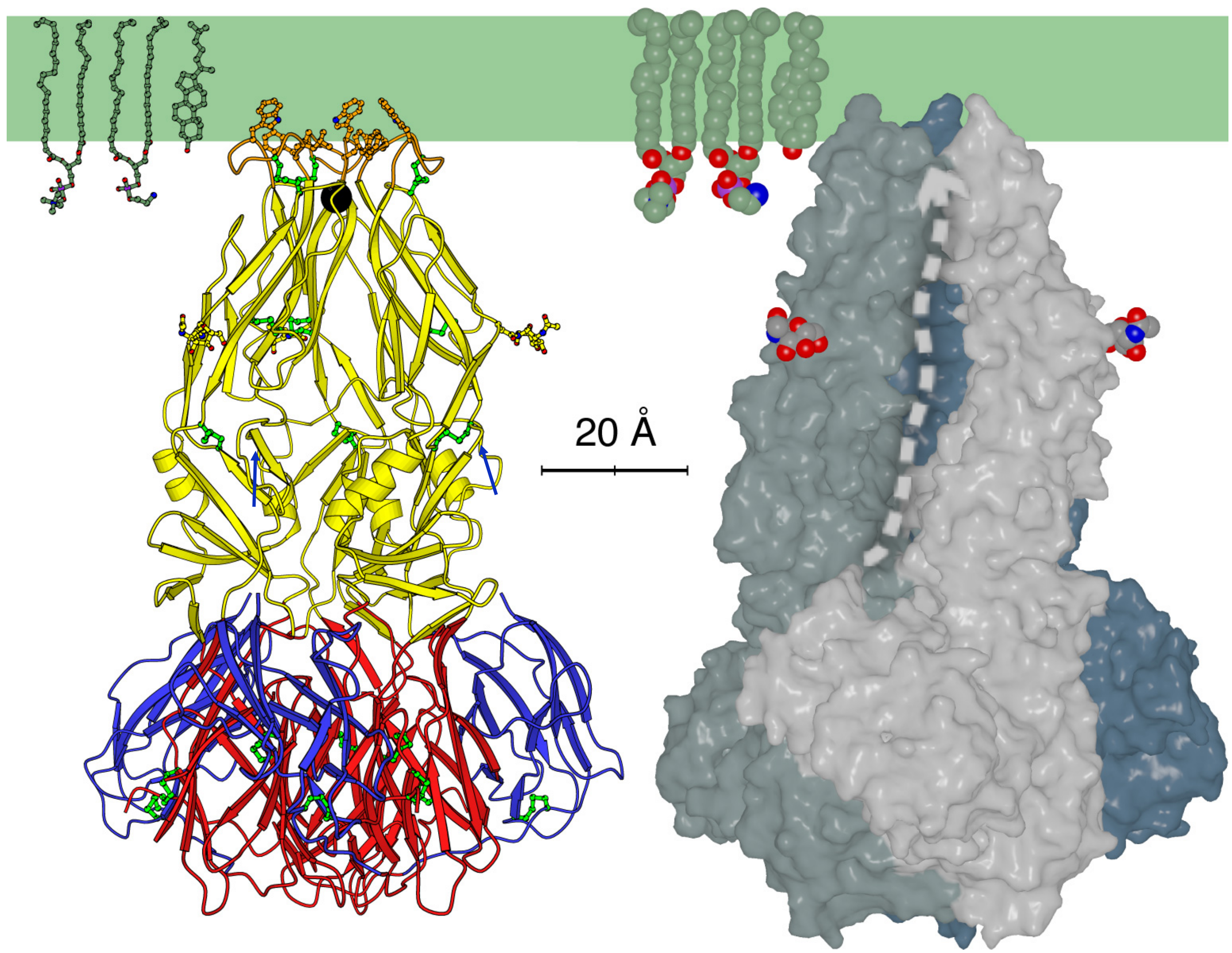




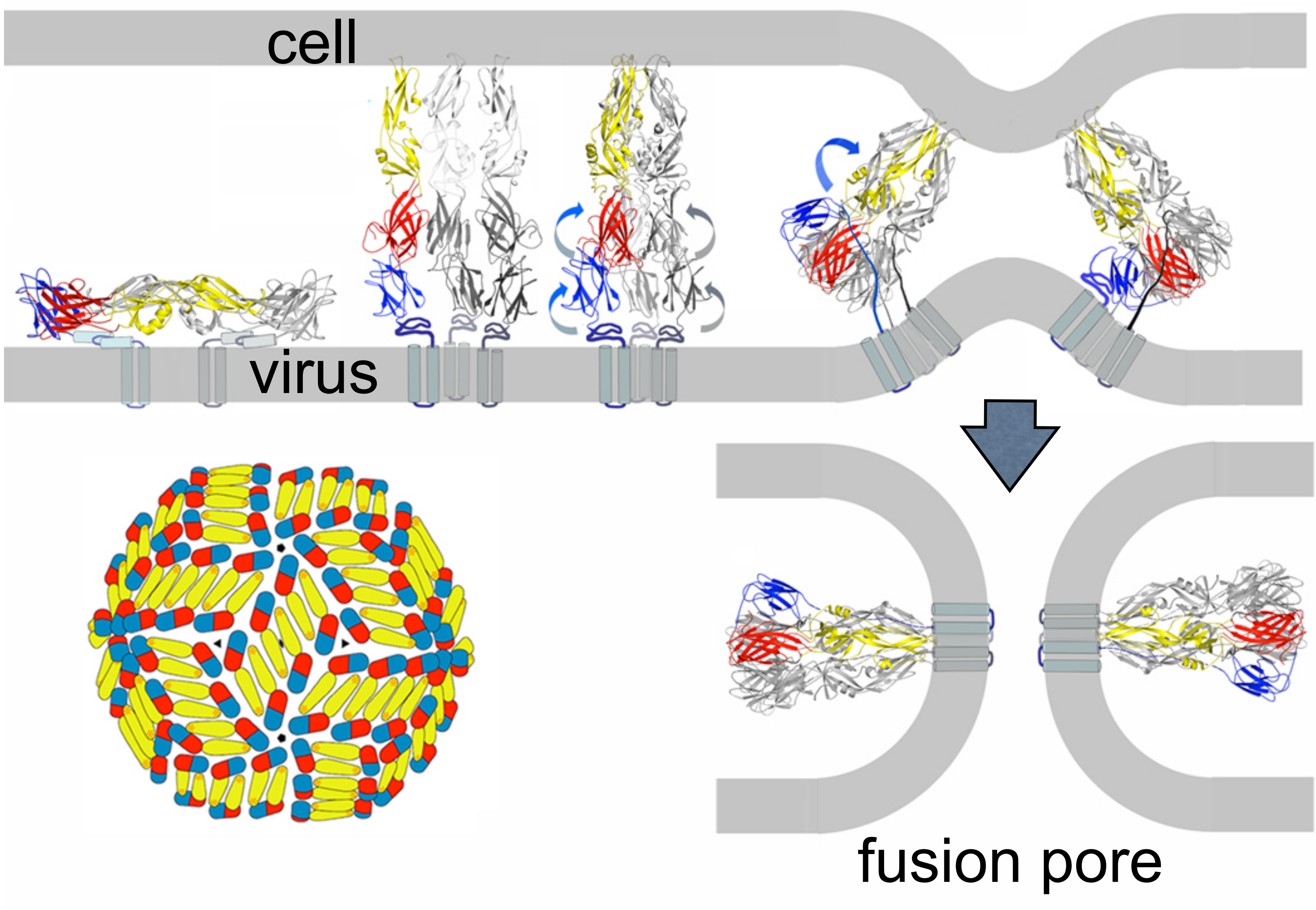
H^+



Modis & Harrison; Rey & co-workers


20 Å

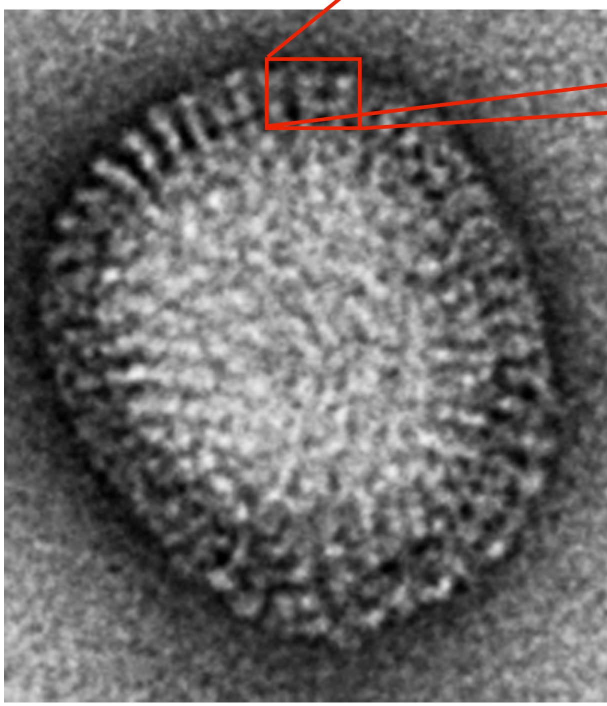
Dengue virus fusion mechanism



Influenza virus particle

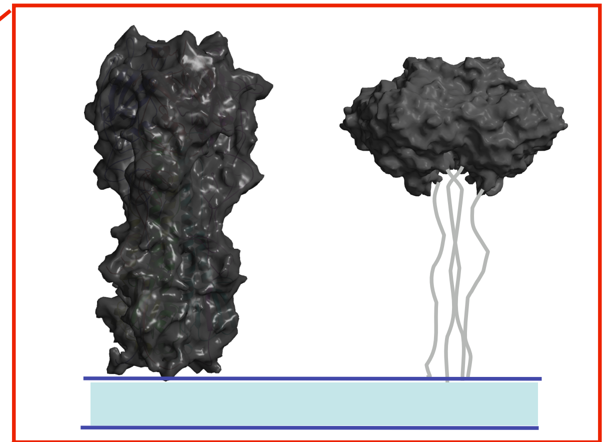
Electron micrograph

of influenza virus



500 Å

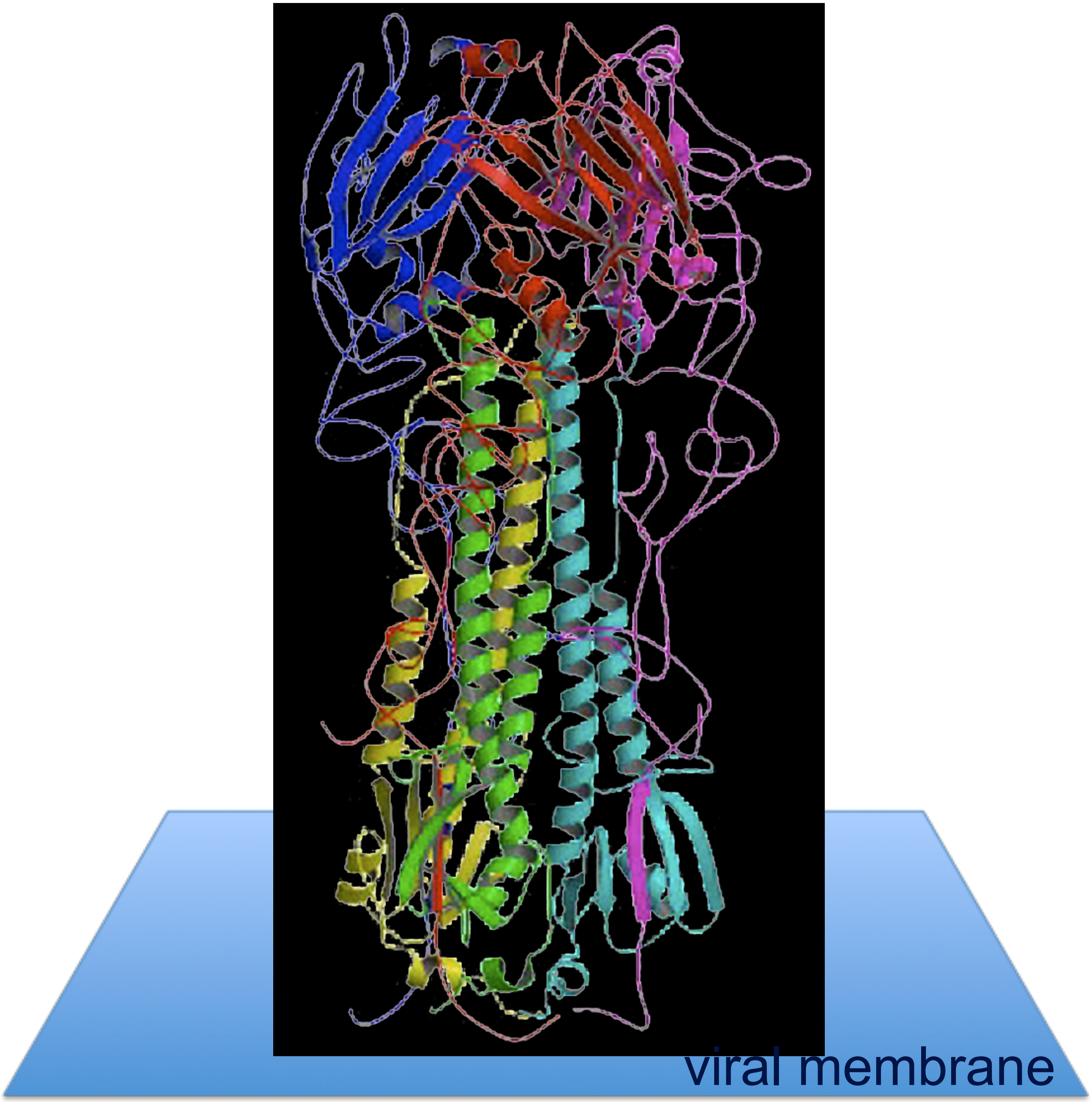
(X 1 million = golf ball)



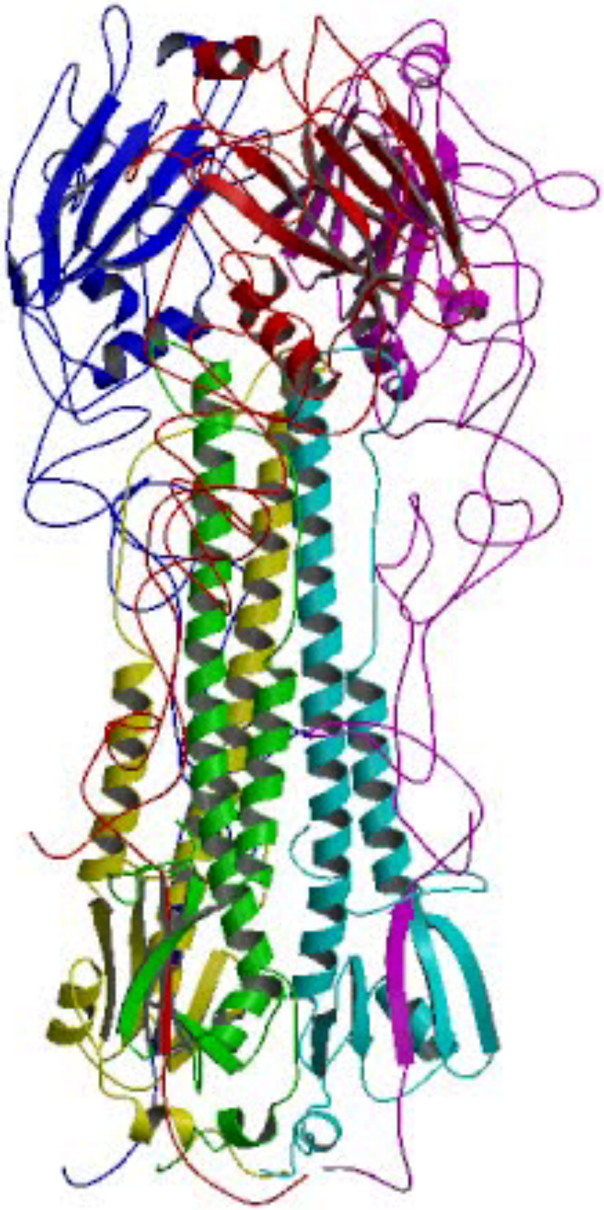
hemagglutinin (HA) neuraminidase (NA)

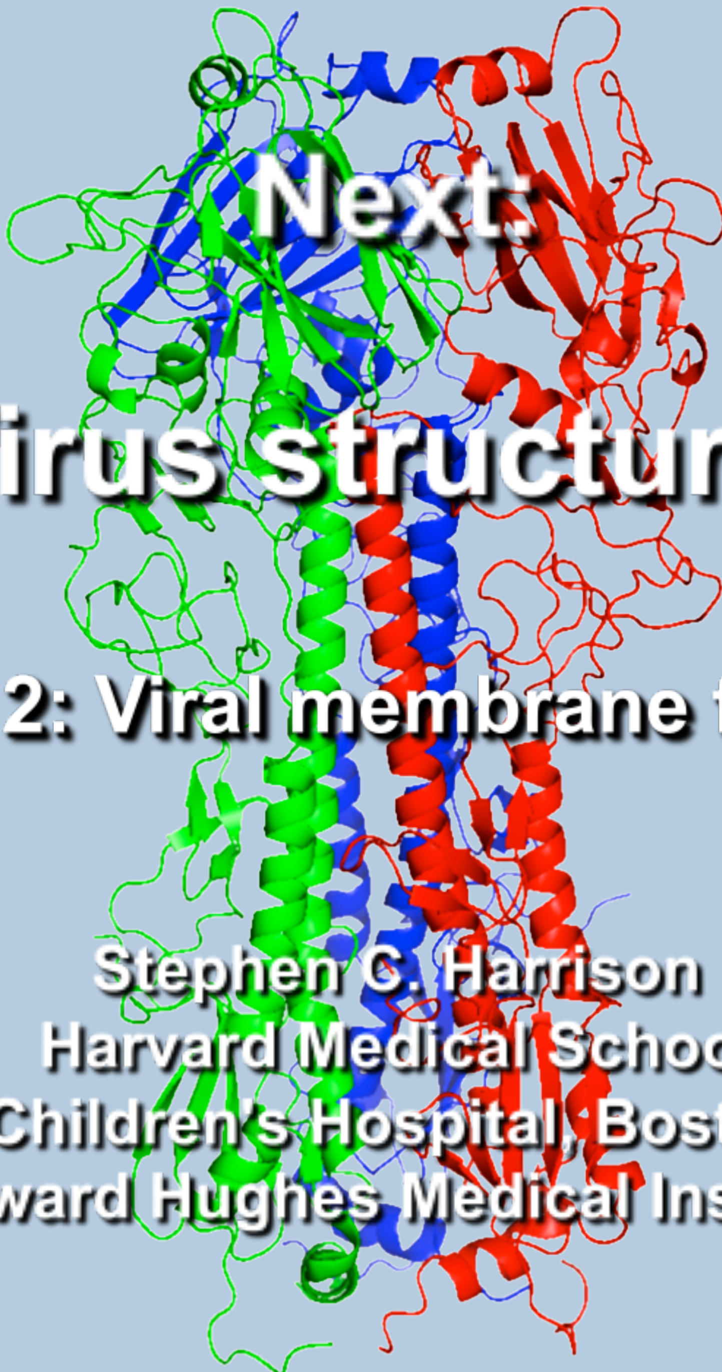
(X 5 million = golf tee)

Influenza virus hemagglutinin



Influenza virus hemagglutinin





Next:

Virus structures

Part 2: Viral membrane fusion

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