VIRUSES

BC530

Fall Quarter 2011
(Slide set # 2)

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VIRUSES

- **Are nucleo-protein or lipid-nucleo-protein complexes which use living cells for their proliferation.**
- **Affect bacterial, plant and animal cells. Those attacking bacteria are called "bacteriophages" or "phages".**
- **Are very diverse in content: they contain either ds or ss DNA or RNA.**
- **Have EITHER a protein outer shell and contain NO lipids, OR contain lipids which surround as a membrane a core of nucleic acids and proteins. These membranes contain specialized surface proteins.**
- **Have very different sizes and shapes. Some form long rod-like structures, others are spherical with high symmetry and again others can assume a number of different shapes.**

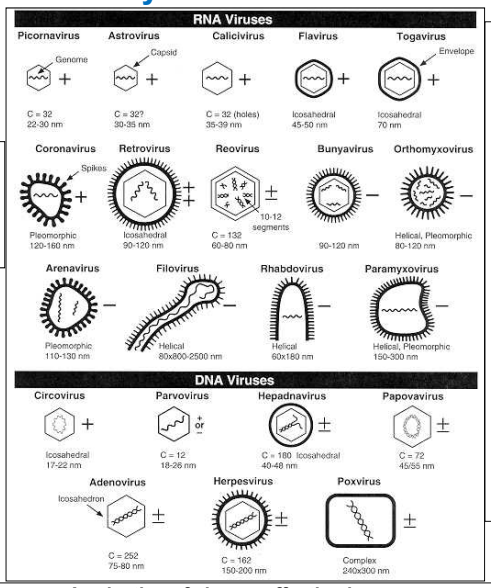
VIRUSES

HAVE VERY DIFFERENT SIZE GENOMES

- ✓ Tobacco Mosaic Virus (TMV) has about 4 genes
- ✓ Hepatitis C Virus (HCV) has about 10 protein-encoding genes
- ✓ Rotavirus codes for 11 proteins
- ✓ Influenza virus has ~ 8 genes encoding ~10 proteins
- ✓ Picornaviruses (like TBSV, SBMV, Poliovirus, Foot and Mouth Disease Virus (FMDV), Rhino virus) have about 12 protein products
- ✓ Bacteriophage T4 has ~ 300 protein encoding genes
- ✓ Some large icosahedral algae-infecting viruses, like the *Emiliania huxleyi* Virus-86 from the English channel, has just over 400 Kbases and is predicted to encode 472 proteins (Wilson, Science 309,1090-1092 (2005)
- ✓ Mimivirus is even larger: 1.2 Mb with 1262 open reading frames. It infects amoebae (Raoult, Science 308, 1114- (2004))

A general website with info about viruses:
http://www.microbiology.wustl.edu/training/med/micpath99/04huang/

The Diversity of Viruses is Enormous



http://www.ncbi.nlm.nih.gov/books/bv.fcgi?rid=mmed.figgrp.2270

Book Edited by Samuel Baron.
Title: Medical Microbiology
Medical Microbiology Section 2.
Virology
41. Structure and Classification of Viruses

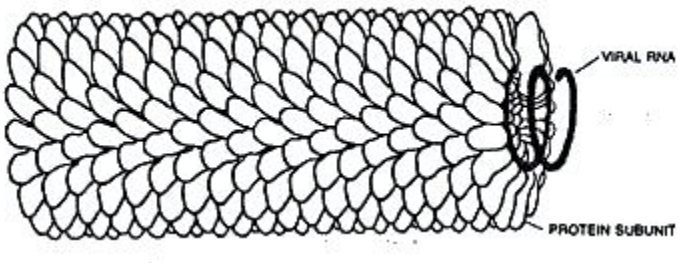
Figure 41-6. Schemes of 21 virus families infecting humans showing a number of distinctive criteria: presence of an envelope or (double-) capsid and internal nucleic acid genome.

+, Sense strand; -, antisense strand; ±, dsRNA or DNA; 0, circular DNA; C, number of capsomeres or holes, where known; nm, dimensions of capsid, or envelope when present; the hexagon designates the presence of an isometric or icosahedral outline.

A selection of viruses affecting humans.
For formal classification see:
The International Committee on Taxonomy of Viruses (http://www.ncbi.nlm.nih.gov/ICTVdb/Images/)
(And: http://www.mcb.uct.ac.za/ictv/ICTV.html)

Tobacco Mosaic Virus (TMV)

A Rod-shaped virus



HELICAL STRUCTURE of the tobacco-mosaic virus is apparent in this drawing, which shows about a sixth of the entire length of the rod-shaped virus particle.

The virus consists of a single long strand of RNA (black), representing perhaps four genes, packed between the turns of a helical protein coat made up of 2,130 identical protein subunits.

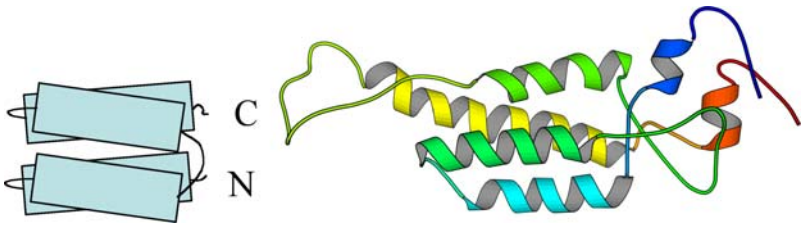
The rod is about 3000 Å long and 90 Å in radius, with a central hole of 20 Å diameter.

The final length of the rod is determined by the length of the RNA. The viral RNA is 6,400 nucleotides long.

Until the virus infects its host cell the protein helix protects the RNA from damage; after infection the RNA is released from the protein and the viral genes are expressed by the host's enzymes.

The central hole in the rod of the virus particle, once thought to be a trivial consequence of protein packing, plays an essential role in assembly of the virus.

TMV: The coat protein



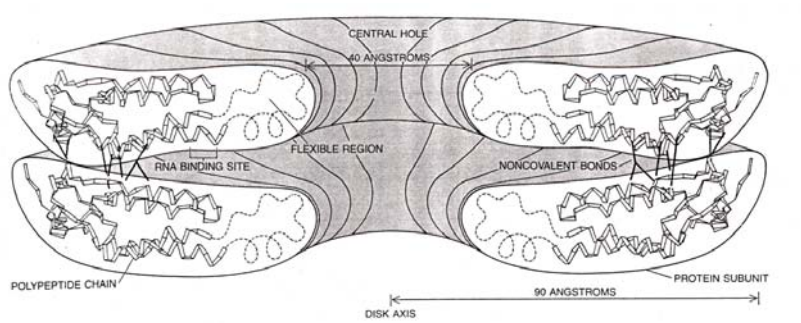
Left: Schematic drawing of an up-and-down four-helix bundle.

Right: The coat protein of tobacco mosaic virus (PDB: 2TMV).

Each subunit consists of 158 residues (17,500 daltons)

FIG. 2.23 from Liljas textbook of Structural biology.

TMV : DOUBLE DISK without RNA



CROSS SECTION THROUGH A DISK was reconstructed from the results of an X-ray diffraction analysis to a resolution of 2.8 Å.

Each ring of a disk contains 17 subunits.

Bent ribbons indicate the polypeptide chains that make up the protein subunits. The two-layered structure of the disk is evident. The subunits of the two stacked rings touch over a small area near the outer rim of the disk but open up toward the center like a pair of jaws. During the assembly of the virus the viral RNA binds within the jaws.

The broken lines indicate the flexible portion of the protein chains extending up from the RNA binding site. Because this chain segment is in constant motion its structure cannot be resolved.

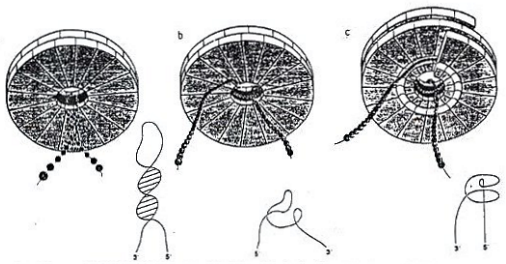
TMV-assembly

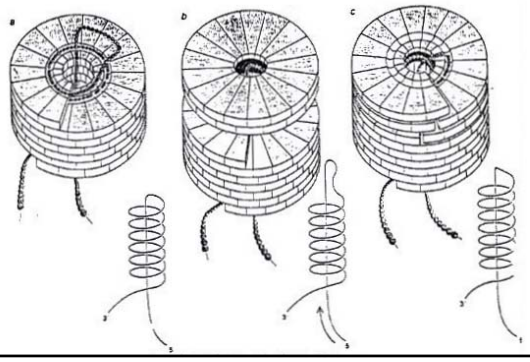
NUCLEATION of Tobacco Mosaic Virus

a. **RIGHT: It begins with the insertion of the hairpin loop formed by the initiation region of the viral RNA into the central hole of the between the two layers of subunits and binds to the protein disk**

b. **The loop intercalates around the first turn of the disk, opening up the base-paired stem as it does so**

c. **some feature of the interaction causes the disk to dislocate into the helical lock-washer form. This structural transformation closes the jaws made by the rings of subunits, trapping the viral RNA inside.**





LEFT: ELONGATION of the virus

proceeds by the addition of protein disks.

a. As a result of the mode of initiation the longer RNA tail is doubled back through the central hole of the growing rod, forming a traveling loop at the growing end of the particle

b. The loop inserts itself into the center of an incoming disk and binds within open jaws of the rings

c. This interaction converts the new disk into a helical lock washer.

d. Once all RNA is inserted into disks the assembly is complete.

References TMV:

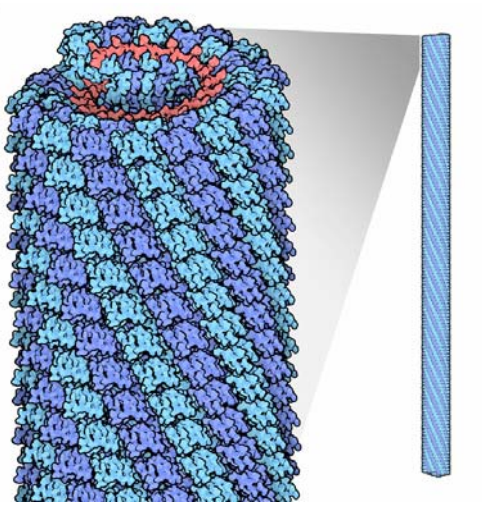
Structural Biology of Viruses (Eds. W. Chiu, R.M. Burnett & R. L. Garcia), Oxford University Press (1997).

P.J.G. Butler and A. Klug, *Scientific American* 239, 62-69 (1978).The assembly of a virus.

A.C. Bloomer, J.N. Champness, G. Bricogne, R. Staden and A. Klug, *Nature* 276, 362-373 (1978). Protein disk of tobacco mosaic virus at 2.8 Å resolution showing the interactions within and between subunits.

G. Stubbs, S. Warren and K. Holmes, *Nature* 267, 216-221 (1977). Structure of RNA and RNA binding site in tobacco mosaic virus from 4 Å map calculated from X-ray fibre diagrams.

A nice impression of the TMV disk and the TMV particle can be found on a Website from the Protein Data Bank: http://www.rcsb.org/pdb/101/motm.do?momID=109 (See e.g. Figure at the right)



TMV in the PDB

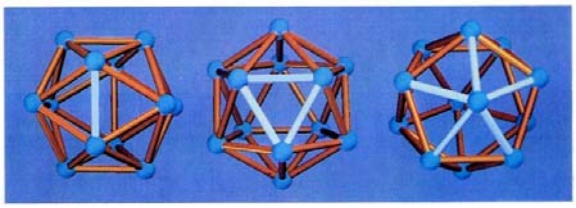
The helix contains 49 subunits in three turns, or 16 1/3 subunit per turn.

ICOSAHEDRAL SYMMETRY

Underlies the architecture of several important viruses

ICOSAHEDRON

- **20 equilateral triangles as its faces**
- **12 five-fold axes – at the corner of each triangle**
- **20 three-fold axes**
- **30 two-fold axes**
- **Generates an object with 60 "units" (e.g. gold L's)**

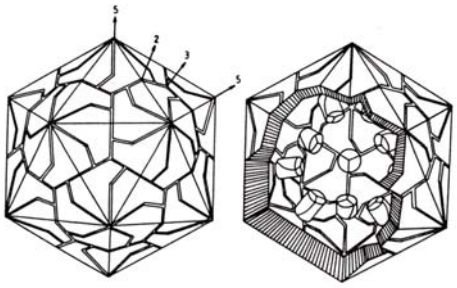


View (almost) along a 2-fold

View along a 3-fold

View (almost) along a 5-fold

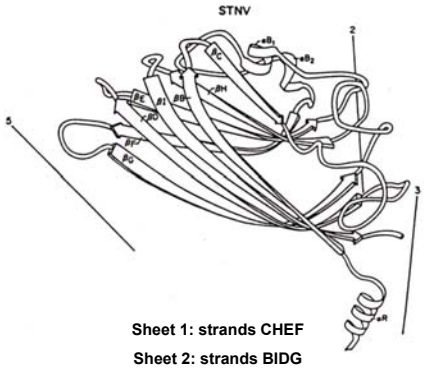
Satellite Tobacco Necrosis Virus (STNV)



Drawing of the subunit packing in STNV.

There are 60 subunits per STNV capsid.

This is a T=1 virus capsid.
T is the "triangulation number"
The geometric meaning of "T" will be explained in the next slides.



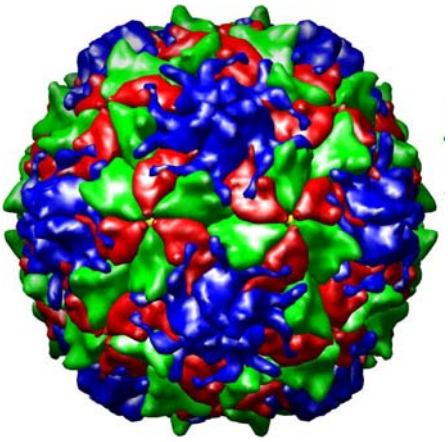
Sheet 1: strands CHEF

Sheet 2: strands BIDG

Schematic drawing of the STNV protein subunit.

The fold is similar to the capsid proteins of plant viruses like TBSV and SBMV.

Poliovirus capsid



Poliovirus, a simple icosahedral virus with a diameter of about 300 Å.
The blue subunits form a pentamer. The red and green subunits form a hexamer.

There are 60 copies of three different proteins called VP1, VP2 and VP3, i.e. 180 subunits in total per capsid.
This is a T=3 capsid but with three different subunits with a similar fold.
From VIPER (http://viperdb.scripps.edu/).

FIGURE 15.1 from Liljas Textbook of Structural Biology

Icosahedral Viruses

Icosahedral symmetry and "quasi-equivalence"

Small spherical virus particles appear to contain numerous subunits.

The number of subunits can be 60 but also often multiples of 60.

An icosahedron has "point group symmetry" **532.**

That means that it contains five-fold, three-fold, and two-fold symmetry axes which all intersect in one point.

That point is the center of the icosahedron.

The symmetry operations are such that 60 "equivalent positions" are generated which means that assemblies consisting of 60 identical protein subunits are likely to have icosahedral symmetry.

But how are spherical viruses with multiples of 60 subunits organized?
Well, before any information at the atomic level was obtained, Caspar and Klug, in 1962, came up with a possible explanation based on "quasi-equivalence."

Reference:
D.L.D Caspar and A. Klug, Cold Spring Symposium on Quantitative Biology 27, 1-24 (1962). Physical principles in the construction of regular viruses.

Quasi Equivalence

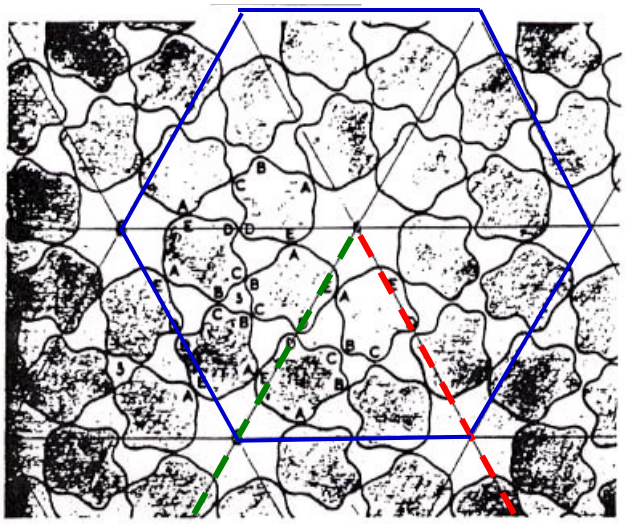
Quasi-equivalence is based on the assumption that the protein shell of an icosahedral virus is held together by the same type of subunit-subunit interactions throughout, but that these interactions may differ slightly in different, non-symmetry related, environments.

Caspar and Klug (1962) proposed that hexamers deviate sufficiently little from pentamers, so that by a judicious mixture of hexamers and pentamers at the surface of the icosahedron each subunit could be given an environment which was almost the same everywhere.

The Caspar and Klug theory implies that only spherical icosahedral viruses with 1 x 60, 3 x 60, 4 x 60, 7 x 60, 9 x 60, etc. identical subunits should occur, but that e.g. 2 x 60 and 5 x 60 would *not* occur.

In their terminology, this means that viruses with so-called "triangulation numbers" T = 1, 3, 4, 7 and 9 do exist, but not with T=2 or 5.

Triangulation



Asymmetric units arrayed in an equilateral-triangular plane net. Besides having translations, *a* along the hexagonal axes, the lattice has 6-fold rotational axes of symmetry. Each unit here is equipped with five "bond" sites, A, B, C, D and E, forming three different "bonds", namely a hexamer bond AE, a trimer bond BC, and a dimer bond DD.

Cut the paper along the red line, then bend so that red touches green=> a pointed five-fold arrangement is obtained

The AE, EA and DD contacts in the original hexamer and in the new pentamer are "quasi-equivalent".

The sixfold axis at the center of the current blue hexamer shown becomes a five fold axis.

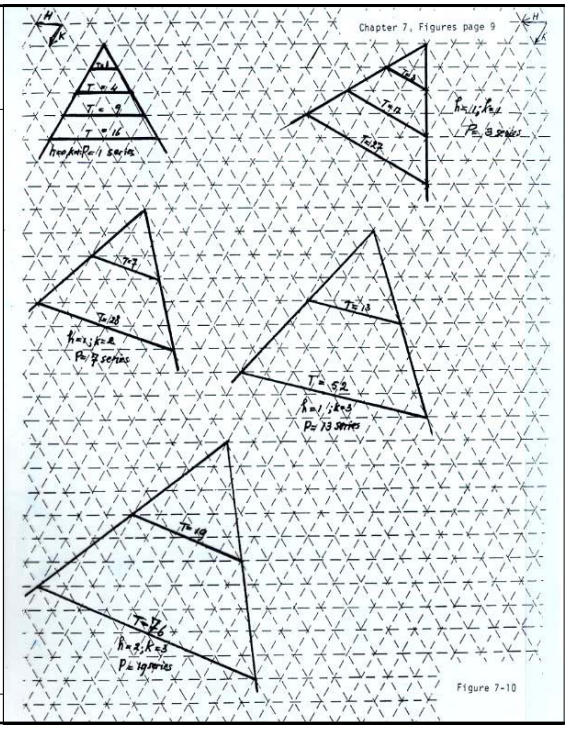
Triangulation

At the corners of each triangle, the sixfolds in the plane depicted are:

1. altered into fivefold axes which then are

2. made to coincide with the fivefold axes of the icosahedron.

The sixfolds in the two-dimensional plane become "quasi sixfolds" in three dimensions.



Triangulation

T=1: 60 units

T=3: 180 units

T=4: 240 units

T=7: 420 units

T=13: 780 units

Etc.

The Triangulation number "T" is the number of structurally quasi-equivalent "initial" triangles (i.e. for T=1) per new icosahedral triangle (also called "icosahedral asymmetric unit")

$T=H^2+HK+K^2$

Where H and K are steps along the hexagonal axes of the grid.

Triangulation

Triangular nets where points of six-fold symmetry have been selected in a regular manner to be replaced by five-folds.

Twenty triangles (in green; tough to find except for T=1!) correspond to the surfaces of the icosahedron, where each corner of the triangles corresponds to a five-fold axis.

The icosahedral asymmetric unit is shown as the blue-ish triangle.

The arrangements for triangulation numbers 1, 3, 4 and 7 are shown.

The six-fold symmetry becomes a quasi-six-fold that coincides with the icosahedral three-fold (T = 3) or two-fold (T = 4).

In T = 1, only five-fold symmetry is found and in T = 7 the quasi-six-fold does not coincide with any of the icosahedral symmetry axes.

Bottom: The *h*, *k* coordinate system in the net, showing one triangle for each of these triangulation numbers (orange: T = 1, blue: T = 3, green: T = 4, red: T = 7).

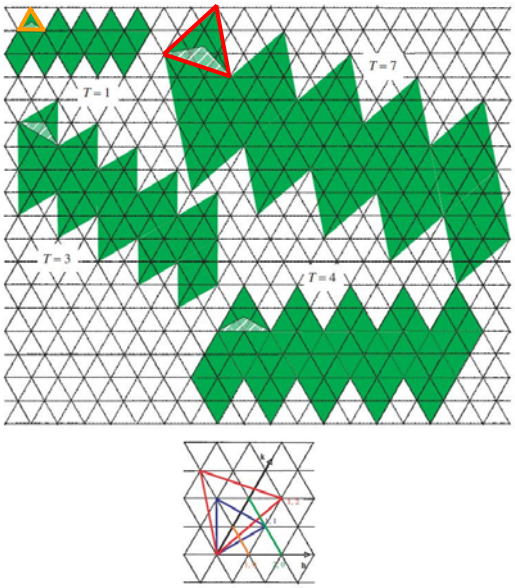
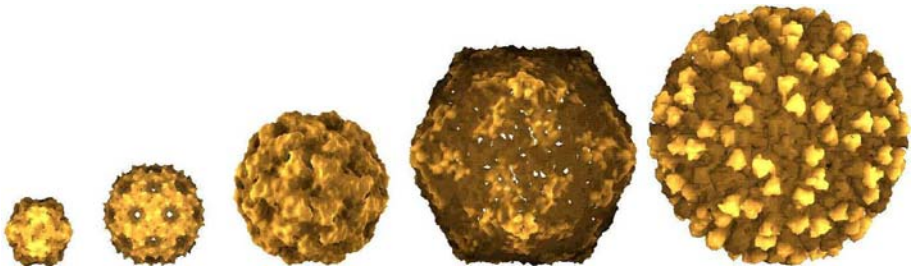


FIGURE 15.3 from Liljas Textbook of Structural Biology

Triangulation



Viruses with triangulation numbers 1, 3, 4, 7 and 13 showing their relative sizes. The surface of the virus particles is shaded according to its distance from the center, darker being closer.

Some particles have an icosahedral shape, but the particles all have icosahedral symmetry.

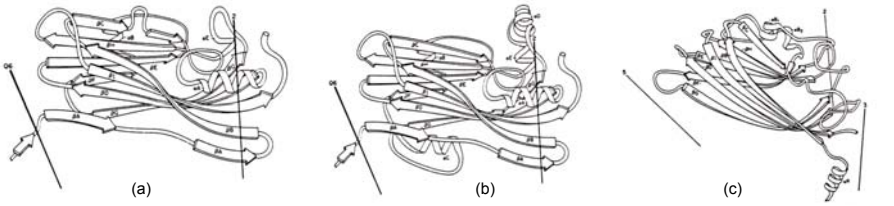
The drawings are based on the crystal structures (from *left* to *right*) of satellite tobacco necrosis virus (STNV), phage MS2, *Nudaurelia capensis* ω virus, phage HK97 and the bluetongue virus. From VIPER (http://viperdb.scripps.edu/).

FIGURE 15.4 from Liljas Textbook of Structural Biology

Plant icosahedral virus capsid subunits/domains

A constant CHEF-BIDG two-sheet framework plus a considerable variation in loops.

TBSV **SBMV** **STNV**



(a) (b) (c)

Tomato Bushy Stunt Virus (TBSV) (T=3)

Southern Bean Mosaic Virus (SBMV) (T=3)

Satellite Tobacco Necrosis Virus (STNV) (T=1)

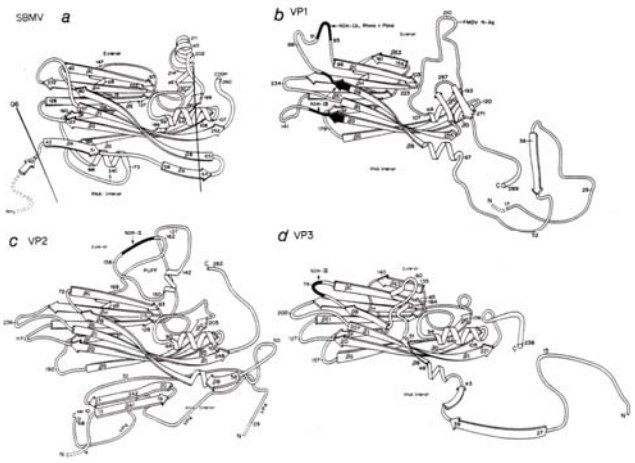
Diagrammatic representation of the backbone folding for (a) TBSV, (b) SBMV and (c) STNV shown in roughly comparable orientations.

In all three cases: β-sheet 1: strands CHEF, and β-sheet 2: strands BIDG

In all three cases the capsid of these viruses is made up of IDENTICAL subunits.

RHINO VIRUS

Human common cold virus



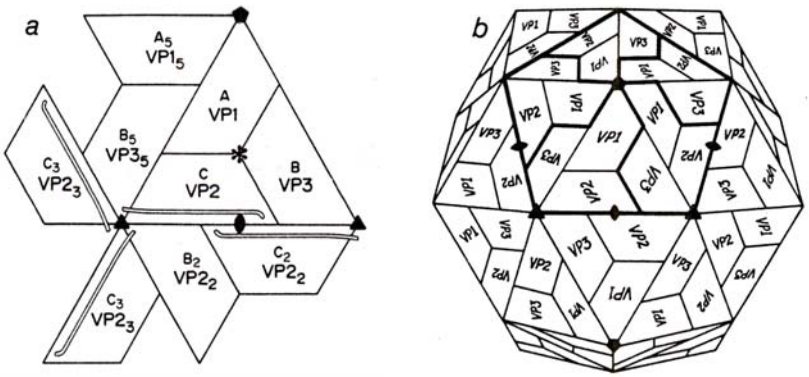
The three different subunits of Rhinovirus are each related to Plant Viruses.

Rhino virus and related viruses have molecular weights of ~8.5 million daltons of which ~30 is RNA. They form icosahedral particles with diameters of roughly 300 Å.

In size and in RNA-to-protein ratio they do not differ too much from the previously discussed plant viruses.

RHINO VIRUS compared to TBSV and SBMV

Architecture of the Icosahedron



The VP1, VP2 and VP3 subunits of Rhinovirus are pseudo-equivalent to, respectively, the quasi-equivalent subunits A, C and B in TBSV and SBMV.

(a) Icosahedral asymmetrical unit showing the ordered amino-terminal arm βA (thin wire) present only in the C subunit of the plant viruses and in VP2 of Rhinovirus HRV14. Asterisk indicates the position of the quasi-3-fold axis in SBMV and TBSV analogous to the pseudo-3-fold axis in HRV14. Subscripts designate the symmetry operation required to obtain the given subunit from the basic triangle.

(b) Icosahedral capsid of rhinovirus.

Functions of Viral Coat Proteins

(Sometimes these functions are performed by one protein, sometimes distributed over several different coat proteins)

1. **Assembly**
   - **RNA/DNA recognition**
   - **Protein-protein recognition**
2. **Protection**
   - **Sufficient stability**
3. **Immune evasion**
4. **Receptor recognition**
5. **Disassembly and delivery of RNA/DNA to other side of target cell membrane**

Dengue Virus

Dengue virus is a major threat to health in tropical countries around the world. It is limited primarily to the tropics because it is transmitted by a tropical mosquito, but even with this limitation, 50-100 million people are infected each year. Most infected people experience dengue fever, with terrible headaches and fever and rashes that last a week or two. In some cases, however, the virus weakens the circulatory system and can lead to deadly hemorrhaging. Researchers are now actively studying the virus to try to develop drugs to cure infection, and vaccines to block infection before it starts.

The Dengue Virus Genome

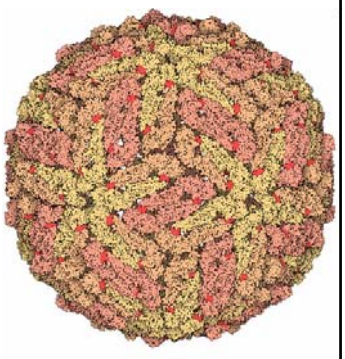
Dengue virus is a small virus that carries a single strand of RNA as its genome. The genome encodes only ten proteins. Three of these are structural proteins that form the coat of the virus and deliver the RNA to target cells, and seven of them are nonstructural proteins that orchestrate the production of new viruses once the virus gets inside the cell. The outermost structural protein, termed the envelope protein, is shown a few slides later from PDB entry 1k4r. The virus is enveloped with a lipid membrane, and 180 identical copies of the envelope protein are attached to the surface of the membrane by a short transmembrane segment. The job of the envelope protein is to attach to a cell surface and begin the process of infection.

Dengue Virus

A Surprising capsid

180 subunits with icosahedral symmetry.

Yet: no T=3 organisation!



A three-dimensional image reconstruction shows that the virion has a well-organized outer protein shell, a lipid bilayer membrane, and a less-well-defined inner nucleocapsid core.

The known atomic structure of the homologous E protein dimer of (TBEV) (Rey et al., 1995) has been fitted into the outer layer of density in the cryoelectron microscopy (cryoEM) reconstruction.

The icosahedral scaffold consists of 90 such dimers with three monomers in the icosahedral asymmetric unit but lacking *T*= 3 quasi-equivalent environments (Caspar and Klug, 1962).

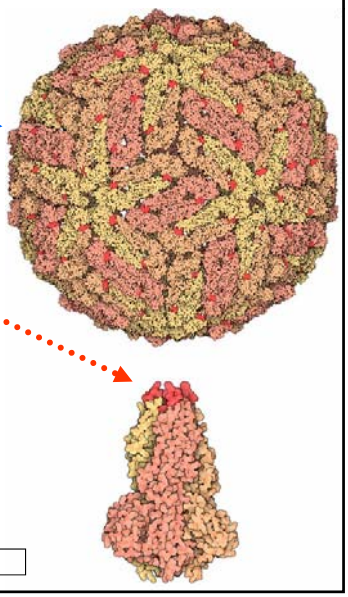
Kuhn et al, Cell 108: 717-725 (2002) . Also: doi: 10.2210/rcsb_pdb/mom_2008_7

Dengue Virus: A Deadly Switch

In the infectious form of the virus, the envelope protein lays flat on the surface of the virus, forming a smooth coat with icosahedral symmetry.

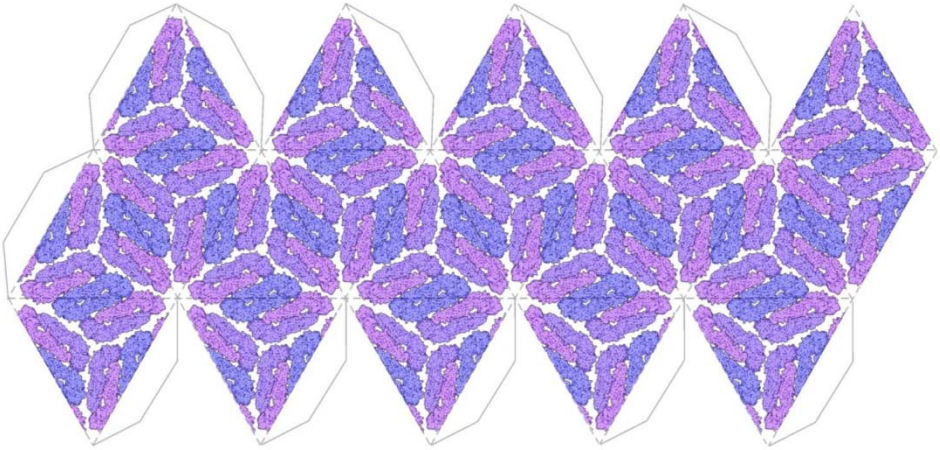
However, when the virus is carried into the cell and into lysozomes, the acidic environment causes the protein to snap into a different shape, assembling into trimeric spike, as shown at the right (PDB entry 1ok8).

Several hydrophobic amino acids at the tip of this spike, colored bright red here, insert into the lysozomal membrane and cause the virus membrane to fuse with lysozome. This releases the RNA into the cell and infection starts.



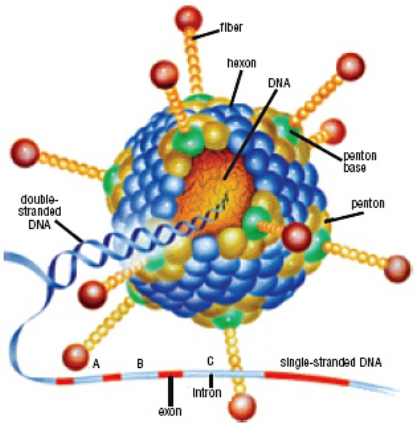
Kuhn et al Cell 108: 717-725 (2002) . Also: doi: 10.2210/rcsb_pdb/mom_2008_7

Make a Dengue Virus Structure



Kuhn et al Cell 108: 717-725 (2002) . Also: doi: 10.2210/rcsb_pdb/mom_2008_7

Adenoviruses



Non-enveloped, double-stranded DNA viruses

Some are human pathogens

Vectors for gene therapy

Icosahedral symmetry

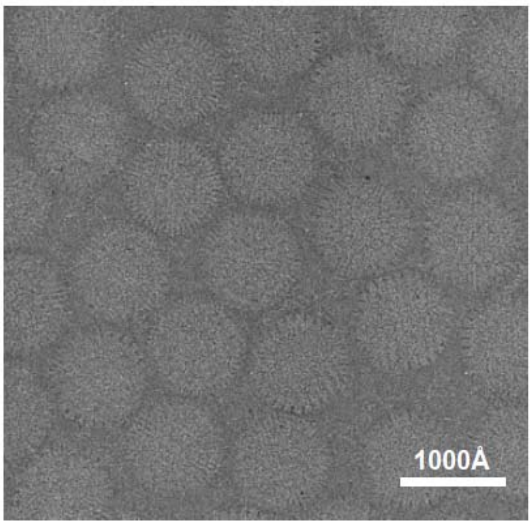
Diameter 900 Å (not including spikes)

150 MDa

http://www.iavireport.org

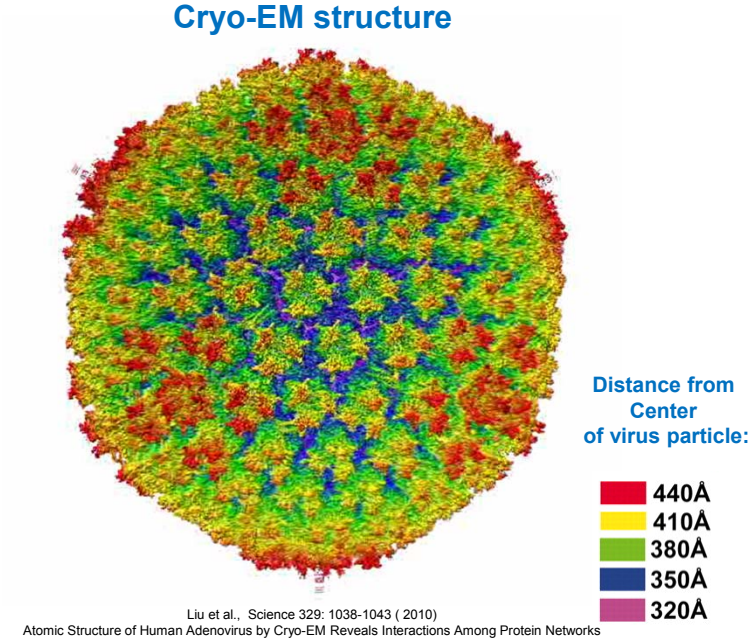
Adenovirus
Cryo-EM structure

The human adenovirus particle (HAdV) is composed of more than 2700 polypeptide molecules, with a total mass of approximately 150 MDa



Liu et al., Science 329: 1038-1043 (2010)
Atomic Structure of Human Adenovirus by Cryo-EM Reveals Interactions Among Protein Networks

Adenovirus
Cryo-EM structure



Liu et al., Science 329: 1038-1043 (2010)
Atomic Structure of Human Adenovirus by Cryo-EM Reveals Interactions Among Protein Networks

References spherical viruses

S.C. Harrison, *Trends in Biochemical Sciences* 9, 345-351 (1984).
Multiple modes of subunit association in the structures of simple spherical viruses.

S.C. Harrison, A.J. Olson, C.E. Schutt and F.K. Winkler, *Nature* 276, 368-373 (1978).
Tomato bushy stunt virus at 2.9 Å resolution A.J. Olson, G. Bricogne and S.C. Harrison, *J. Mol. Biol*. 171, 61-93 (1983).
Structure of tomato bushy stunt virus IV. The virus particle at 2.9 Å resolution.

C. Abad-Zapatero, S.S. Abdel-Meguid, J.E. Johnson, A.G.W. Leslie, I. Rayment, M.G. Rossmann, D. Suck and T. Tsukihara, *Nature* 286, 33-39 (1980).
Structure of southern bean mosaic virus at 2.8 Å resolution.

M.G. Rossmann, E. Arnold, J.W. Erickson, E.A. Frankenberger, J.P. Griffith, H.J. Hecht, J.E. Johnson, G. Kamer, M. Luo, A.G. Mosser, R.R. Ruekert, B. Sherry and G. Vriend, *Nature* 317, 145-153 (1985).
Structure of a human common cold virus and functional relationship to other picornaviruses.

References Poliovirus
J.M. Hogle, M. Chow and D.J. Filman, *Science* 229, 1358-1365 (1985).
Three-dimensional structure of poliovirus at 2.9 Å resolution.

J.M. Hogle, M. Chow and D.J. Filman, *Scientific American* 256, 42-49 (1987).
The structure of poliovirus.

Membrane-enveloped viruses

Example: Influenza virus

INFLUENZA VIRUS

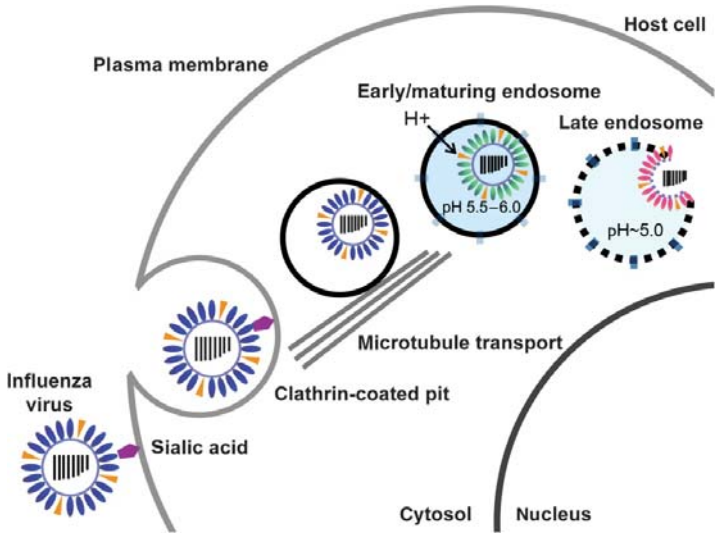
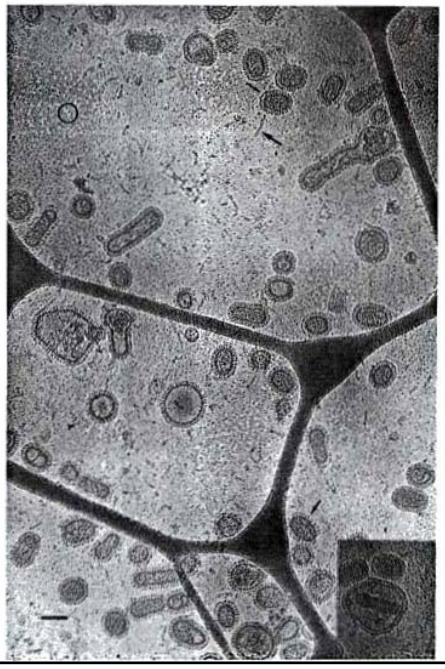


Figure 1 from Kelly K Lee (2010) *EMBO Journal* (2010)

INFLUENZA VIRUS



Well underfocused electron micrograph of an unstained, frozen, hydrated specimen of A/X31 influenza virus. Some free haemaglutinin spikes are ringed.

The arrows (you have to look really well) point to free ribonucleoprotein material from disrupted virions and also to virions in which an indication of the ribonucleoprotein is seen.

The inset shows an example of a large coiled structure within a virion. The bar represents 1000 Å.

The virus can obviously adopt many different shapes. In other words it is pleiotropic.

INFLUENZA VIRUS

The surface contains about ~500 haemagglutinin spikes and ~100 neuraminidase spikes.

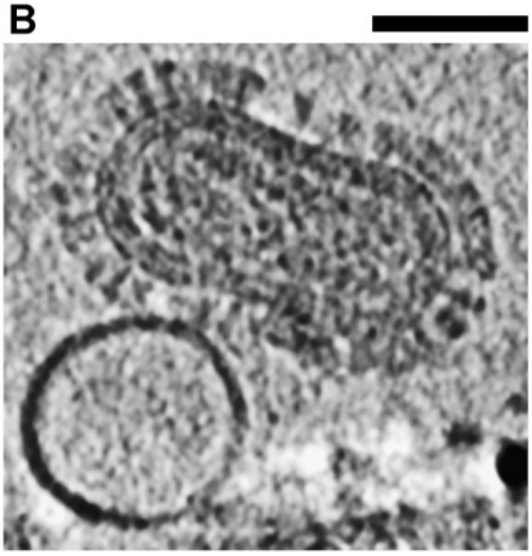


Figure 3 from Kelly K Lee (2010) *EMBO Journal* (2010)

Influenza Virus Haemagglutinin

Haemagglutinin (HA) of influenza virus is an integral membrane protein which is a trimer with a molecular weight of 224,640. By proteolytic cleavage, a large fragment can be solubilized. This releases this fragment from a 24-28 residues long peptide which spans the membrane and from the small hydrophilic domain of 10-55 residues in the internal side of the membrane. Each monomer contains two chains, HA1 with 328 amino acids, and HA2 with 221 amino acids. These two chains are obtained by post-translational removal of arginine329.

The structure of HA is most remarkable as shown in several of the next slides. Each monomer contains one small globular domain near the membrane. This domain contains a 5-stranded anti-parallel beta-sheet. Quite remarkably, this sheet is formed by the first few residues of the HA1 chain coming out of the membrane plus four strands form the C-terminus of HA2, which are 350 residues further in the sequence. There is also a large globular domain faraway from the membrane where an 8-stranded anti-parallel beta structure dominates the fold.

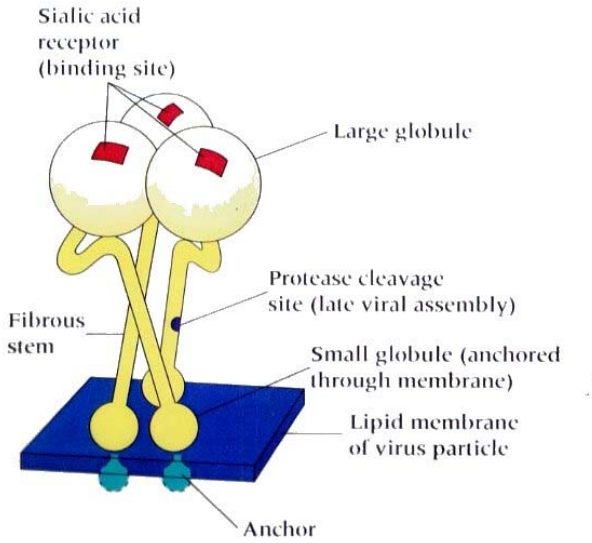
The most remarkable feature is a 14 turn, 53 amino acids long helix which comes back from the globular "head" to the membrane and spans a distance of 76 Å. In the trimer, this helix twists around two identical helices from other subunits to form the coiled-coiled core of the "fibrous" middle region of the trimer. The total extension from the membrane is ~135 Å, which is the reason why these haemagglutinin molecules appear in electron micrographs of the virus as "spikes".

Influenza Virus Haemagglutinin

There are numerous glycosylation sites on the protein, at seven positions, with a total molecular weight of 13,000 for the carbohydrate chains. These oligosaccharide chains are spread out over the entire molecule. Several antibody binding sites are known from immunological studies, and they appear to map on the part of the molecule which is furthest extended from the surface. Antigenic variation at these sites is responsible for the influenza epidemics which travel across the planet with irregular intervals.

The receptor binding site for sialic acid is located in the globular head of the trimer. This appears to be a logical location for receptor binding. After binding of the virus to the target cells, the virus is taken up in the endosome where the lower pH causes a major reorganization of the haemagglutinin molecule such that it can cross the membrane. Very recent studies are revealing that the conformational change includes a further elongation of the already impressively long helices of the trimer's coiled-coiled region.

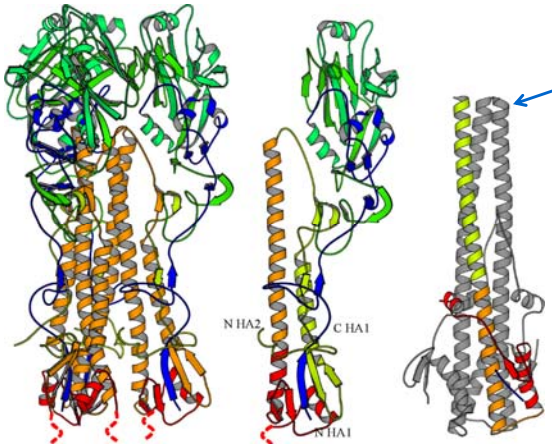
Influenza Virus Haemagglutinin



Schematic representation of the protein trimer that forms the hemagglutinin antigen on the surface of the influenza A virus: the HA spike.

Influenza Virus Haemagglutinin

Large Conformational Change in the Endosome with lower pH



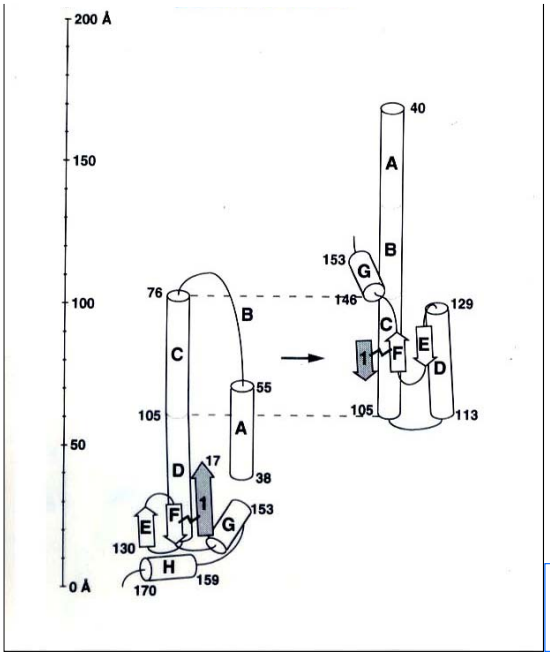
(Part of) a single HA subunit at lower pH.

Dramatic conformational changes occur: NOTE THAT ONLY THE ORANGE HELIX REMAINS THE SAME compared to the subunit at pH=7 shown in the middle…….

***Left*:** The trimer at neutral pH after cleavage into the HA1 and HA2 peptides (PDB: 1RU7). The membrane anchor if it were present would be attached to the C-terminus of HA2 (at the end of the dashed red lines).
***Middle*:** A monomer at neutral pH. The fusion peptide (N-terminus of HA2) is at the center of the molecule, hidden by interactions with the other proteins in the trimer.
***Right*:** The low pH form (PDB: 1HTM). The fusion peptide is disordered, but must be located on top of the three helices. Large conformational changes have occurred. The lower part of the long helix in the neutral pH form (red) is now bent and packed at the side of the long helix. The upper part of the long helix (green-yellow) forms a long loop and a helix in the neutral pH form.

FIG. 15.8 from Liljas textbook of Structural biology.

Influenza Virus Haemagglutinin's Conformational Change



This time with scale in Ångstroms

References Haemagglutinin

I.A. Wilson, J.J. Skehel and D.C. Wiley, *Nature* 289, 366-373 (1981).
Structure of the haemagglutinin membrane glycoprotein of influenza virus at 3 Å resolution.

P.A. Bullough, F.M. Hughson, J.J. Skehel and D.C. Wiley, *Nature* 371, 37-43 (1994).
Structure of influenza haemagglutinin at the pH of membrane fusion.

References Neuraminidase

J.N. Varghese, W.G. Laver and P.M. Colman, *Nature,* 303, 35-40 (1983).
Structure of the neuraminidase glycoprotein antigen Neuraminidase at 2.9 Å resolution.

P.M. Colman, et al., *Nature* 326, 358-363 (1987).
Three-dimensional structure of a complex of antibody with influenza virus neuraminidase.

W.R. Tulip, et al., *J. Mol. Biol*. 227, 122-148 (1992).
Refined crystal structure of influenza virus N9 neuraminidase - NC41 Fab complex.

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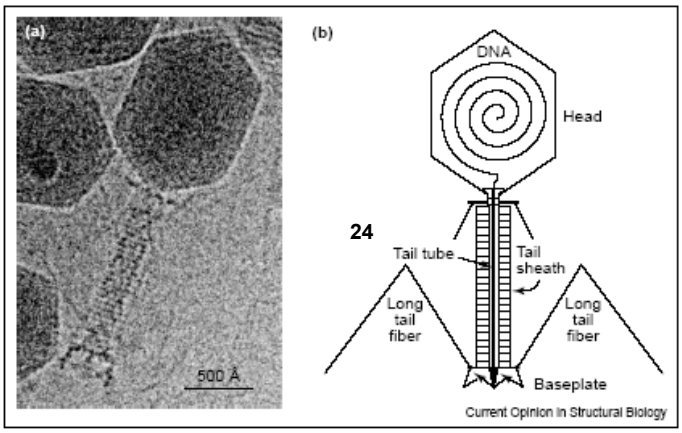
"The structure of a complex between the NC10 antibody and influenza virus neuraminidase and comparison with the overlapping binding site of the NC41 antibody."

Bacteriophage T4

its major components

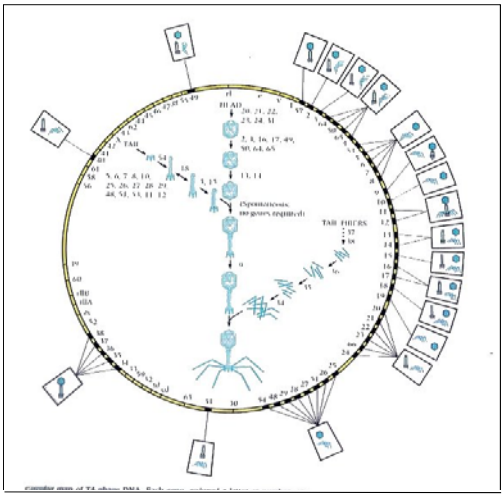


Belongs to the Myoviridae viral family.

(a) Cryo-EM micrograph of phage T4.

(b) Schematic of the major structural components of a Myoviridae phage. The black triangle in the center of the baseplate represents the cell-puncturing device. The short tail fibers are shown as bent arrow-like objects around the periphery of the baseplate.

Circular Map of T4 Phage DNA



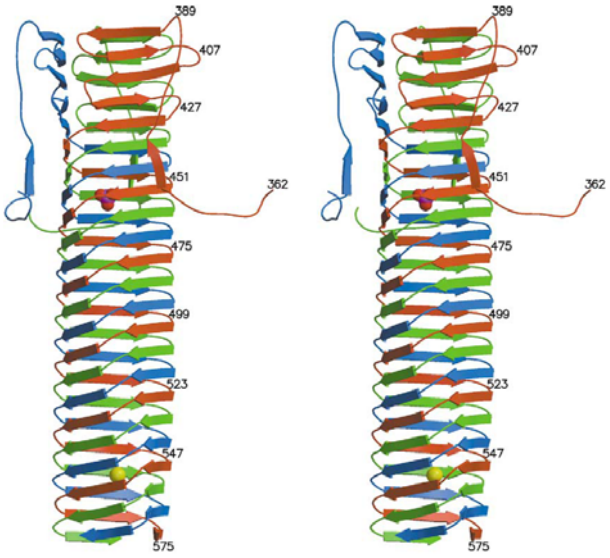
- Each gene, assigned a letter or number, encodes one protein.

- Genes for particle assembly – depicted inside the ring – are matched with the faulty structures produced when these genes are defective. For example, genes 34-38 (no tail fibers), gene 49 (no assembly), gene 9 (premature tail contraction).

- Mutations in genes 11-12 generate a complete but fragile bacteriophage.

Numbers next to arrows in the three branches of the assembly line indicate the genes crucial to each step.

The tail of T4: gp5, a most unusual structure



Stereo diagram of the gp5 C-terminal domain

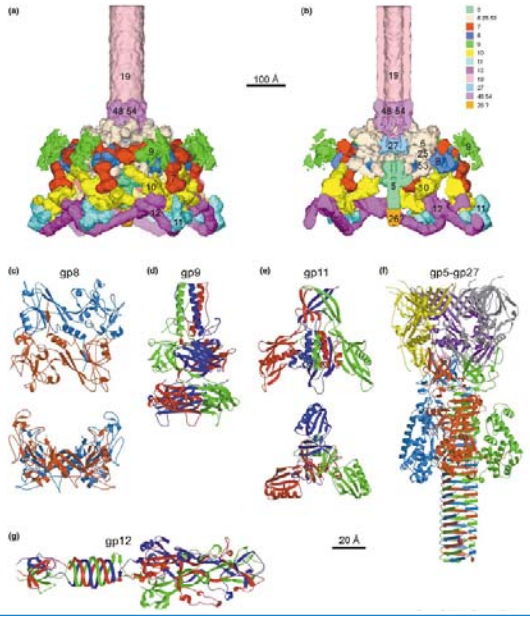
The three chains are colored red, green and blue.

The residue numbers are indicated in strategic locations.

The metal and phosphate ions, stabilizing the internal contacts in the beta-helix, are shown as yellow and magenta spheres, respectively.

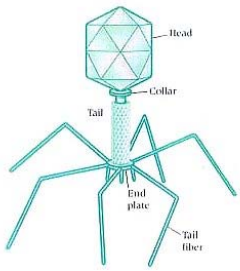
Rossmann, et al., Current Opinion in Structural Biology 2004, 14:171–180

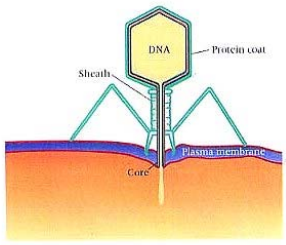
The tail of T4

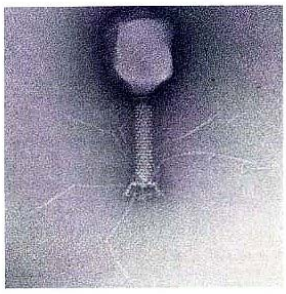


Combine Electron Microscopy and Crystallography to place Components in the T4 Tail

BACTERIOPHAGE T4 – A FABULOUS MACHINE







Above: Diagram of bacteriophage T4 (left); T4 attached to a bacterium and injecting its DNA (right). The tail contracts, forcing the injection tube through the wall and into the cytoplasm; the viral DNA travels from the head into the cell, while the coat proteins remain outside.

Right: EM of bacteriophage T4. The tail, which has a helical rod symmetry, is used as a syringe to inject the viral DNA contained in the head, which approximates an elongated icosahedron. The fibers that project from the end of the tail are proteins that attach the virus to a bacterial host.

The End

of

BC530

VIRUSES