### Proteins and symmetry

<table>
<thead>
<tr>
<th>Protein</th>
<th>Rotational symmetry</th>
<th>Composition*</th>
<th>Buried surface†</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuraminidase</td>
<td>4</td>
<td>α₄</td>
<td>14</td>
<td>1953</td>
</tr>
<tr>
<td>β-subunit pentamer of AB₅ toxins</td>
<td>5</td>
<td>α₅</td>
<td>39</td>
<td>2941</td>
</tr>
<tr>
<td>Serum amyloid IP component</td>
<td>5</td>
<td>α₅</td>
<td>15</td>
<td>1547</td>
</tr>
<tr>
<td>Aerolysin</td>
<td>7</td>
<td>α₇</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>GroEL</td>
<td>7</td>
<td>α₇ / α₇</td>
<td>15</td>
<td>3702</td>
</tr>
<tr>
<td>20S proteasome</td>
<td>7</td>
<td>α₇β₇ / β₇α₇</td>
<td>15</td>
<td>3702</td>
</tr>
<tr>
<td>Bacterial LH2</td>
<td>9</td>
<td>α₉β₉</td>
<td>48</td>
<td>3833</td>
</tr>
<tr>
<td>*trp RNA-binding attenuating protein</td>
<td>11</td>
<td>α₁₁</td>
<td>49</td>
<td>2383</td>
</tr>
<tr>
<td>Portal protein from bacteriophage SPP1</td>
<td>13</td>
<td>α₁₃</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Bacterial LH1</td>
<td>16</td>
<td>α₁₆β₁₆</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Tobacco mosaic virus disk</td>
<td>17</td>
<td>α₁₇α₁₇</td>
<td>30</td>
<td>4541</td>
</tr>
</tbody>
</table>

*Composition: α = alpha, β = beta, and †Buried surface in Å².
Viruses (symmetry)

Viruses come in many shapes, sizes and compositions
All carry genomic nucleic acid (RNA or DNA)

Structurally and genetically the simplest are the spherical viruses
Purpose of protein viral capsid

Assembly
Subunits must recognize each other to form a stable capsid (non-covalent interactions)
>> self assemble

Infection
Must be able to transfer nucleic acid from one host to another
>> stable and recognize receptor

Small genome

Genetic economy - few structural proteins
symmetry - identical building blocks
Simple Spherical Viruses

Protein

RNA/DNA

30 nm
From geometry considerations

Two 3D solid objects use a single point symmetry operator to produce the theoretical maximum possible identical units to build a solid object

Icosahedron and

Dodecahedron

Identical symmetry
(point group 5.3.2)

Enclose maximum volume
Spherical Virus Shells have Icosahedral Symmetry

- Built from 20 identical equilateral triangles.
- Triangles are arranged to enclose the volume inside.

5-fold axis at each corner

3-fold at each face

2-fold at each edge

5 triangles

10 triangles

5 triangles
Icosahedral Symmetry Axes

3-fold

5-fold

2-fold
Icosahedral Symmetry

Each triangle is divided into 3 asymmetric units related by 3-fold axis.

Minimum number of protein subunits that can form a virus shell with icosahedral symmetry is therefore equal to 60.

>> Since there are 20 faces and each face has three subunits the total number of subunits is $3 \times 20 = 60$
Triangulation numbers, $T$

There are constraints preserving specificity of interactions within an icosahedron

-Caspar and Klug (1962)
Showed that only certain multiples $(1, 3, 4, 7)$ of 60 subunits are likely to occur

The more subunits used to build the virus the larger the volume it encloses

$T = h^2 + hk + k^2$

where $h$ and $k$ are any integers

Satellite viruses, STNV are $T=1$
Bromo viruses, $T=3$
Icosahedral Symmetry - Slightly More Complicated arrangements

T=3

3-fold view
Hexamer
pentamer
One AU

T=4

2-fold view
One AU

180 proteins
60 x T = # of subunits in a capsid. Can get up to T=217 (Iridoviridae)

240 proteins
Coat protein (capsid)

Capsid Proteins - Bacterial, Plant, insect and animal viruses have a similar motif - an eight-stranded antiparallel $\beta$-barrel

Inside is hydrophobic

Wedge-shaped arrangement seen in virus structures
Examples of Viral β-barrels

Satellite tobacco necrosis virus

Polio Virus VP1

Human rhinovirus 14 VP2

All proteins in a given virus have very similar motifs even when there are no amino acid similarities
Virus life cycle (structure/function)

Attachment to host cell
   >> Host cell receptor recognition
       Protein/ligand interaction

Transfer of genetic material
   >> transport to nucleus

Nucleic acid and protein syntheses

Assembly

Release from host cell

Avoid immune system
**Picornaviruses**

Examples common cold, polio, hepatitis
Small RNA virus (300Å diameter)
Contains 4 structural proteins VP1-4

<table>
<thead>
<tr>
<th>Protein</th>
<th>MW</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>VP1-3</td>
<td>30,000</td>
<td>different aa sequences P=3</td>
</tr>
<tr>
<td>VP4</td>
<td>7,000</td>
<td>(interior)</td>
</tr>
</tbody>
</table>

![Diagram of Picornavirus structure](image)
Surface of virus
>> function
canyon 25Å deep and 12-30Å wide

Receptor the adhesion molecule ICAM I
Anti-body binding sites decoys
Anti viral drug design

Base of VP1 hydrophobic pocket

WIN compounds bind deep in the β-barrel motif.

Prevent uncoating

>> spin off vaccine stability
Virus Structure - Exceptions to the $\beta$-barrel motif

Bacteriophage MS2
ssRNA genome

5-stranded anti-parallel sheet, small hairpin and two $\alpha$-helices.

Dimer is the basic building block of the capsid - 10 $\beta$-strands with interchanged $\alpha$-helices
Virus Structure - Exceptions to the β-barrel motif

Alphaviruses

Example Sinbis virus
enveloped RNA genome
cause encephalitis

T=4 capsid
Virus Structure - Other arrangements, e.g. Retroviruses

Cryo-Electron Micrograph HIV-1

Nucleocapsid

Envelope

Core

Type B

Lentiviruses

Type C
Parvoviridae
Family Portrait

CPV
AAV5
B19
AMDV
AAV5

2-fold 3-fold 5-fold

Future: Gene therapy …..