Physics of Virus Self-Assembly and Virus-like Biological Nanostructures

V.L. Lorman

Laboratoire Charles Coulomb
Département de Physique Théorique
CNRS - Université de Montpellier, France

UNIVERSITÉ DE MONTPELLIER

OLIM COUS
NUNC MONSPELIENSIS

Established in 1289
(Medical School since 1150)

In the frame of the Program

"IPOLS - International Physics

of Living Systems" - **NSF (USA) + CNRS & INSERM (France)**

Laboratory of Excellence "NUMEV":
*Modeling for Life Sciences*

3 health & biotechnology programs

- Struggle against emergent infectious diseases

- Controlled drug delivery

- Bio-inspired nanotechnology

Viruses, alive or not ?

Cell attachment

Activation

Release of genome

Transcription and translation

Pro-assembly

Maturation

Release
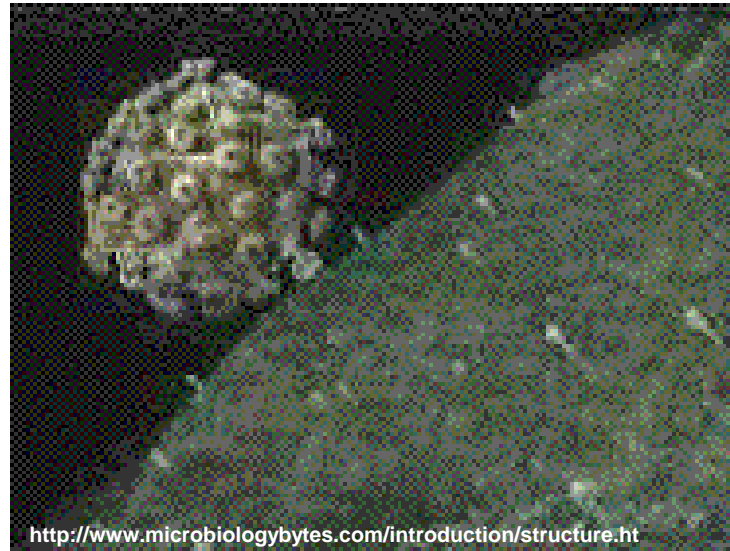
Transmission and host defense

All viruses require a host cell to replicate

Follow some basic pattern

- Deliver viral genomic material into host cell
- Subvert cell's biosynthetic machinery into producing new viral particles
- New virus particles self-assemble in the infected cell
- New virus particles leave infected cell to infect others

Adsorption

Entry

Replication

Assembly

Release
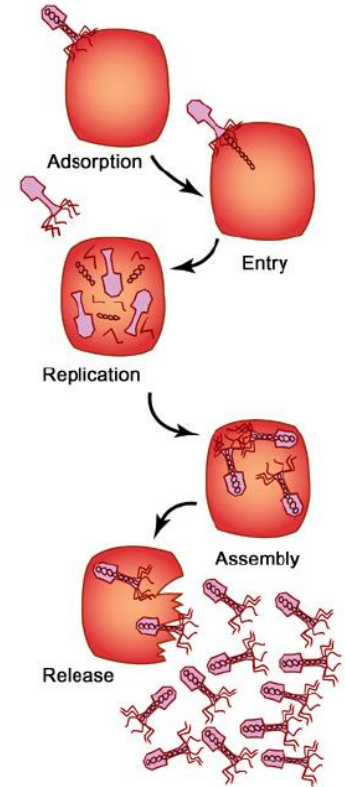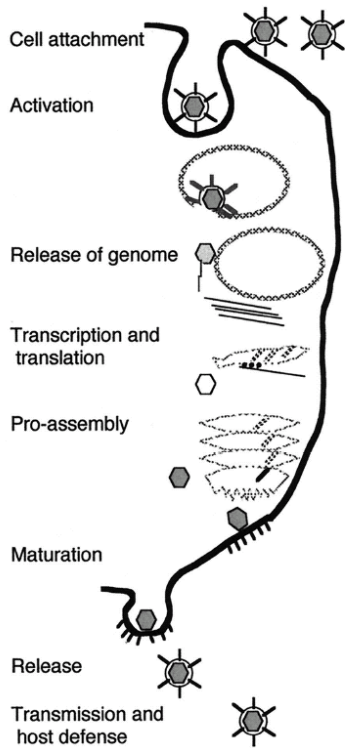
Lytic cycle

Virus structure

- Genomic material
    - DNA or RNA (both "+" and "-")
    - single- or double-stranded
    - linear or circular
    - one or several copies

- Capsid – Protective protein shell
    - regular organization
    - high symmetry
    - made of many identical subunits
    - enveloped with lipid membrane
      or not

- Basic shape
    - helical rod-like
    - spherical

- Typical size
    - 30 ÷ 50 nm
    - nearly 1000 nm for some big ones
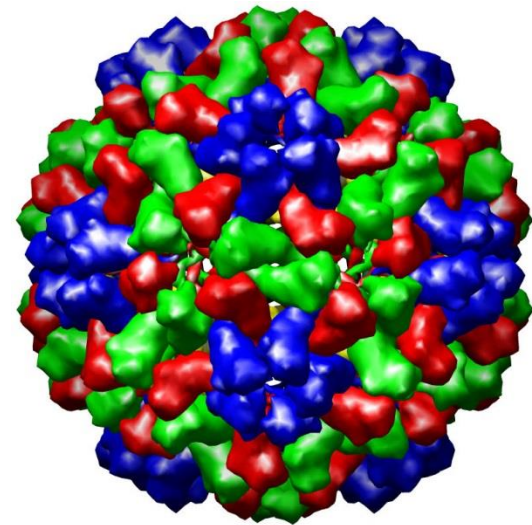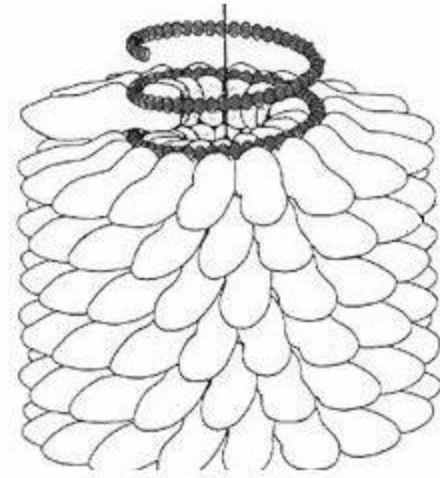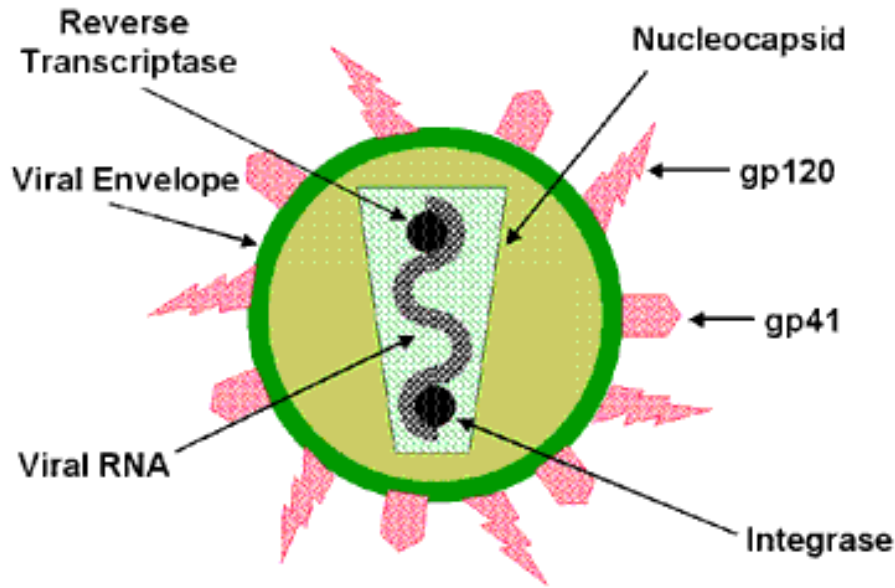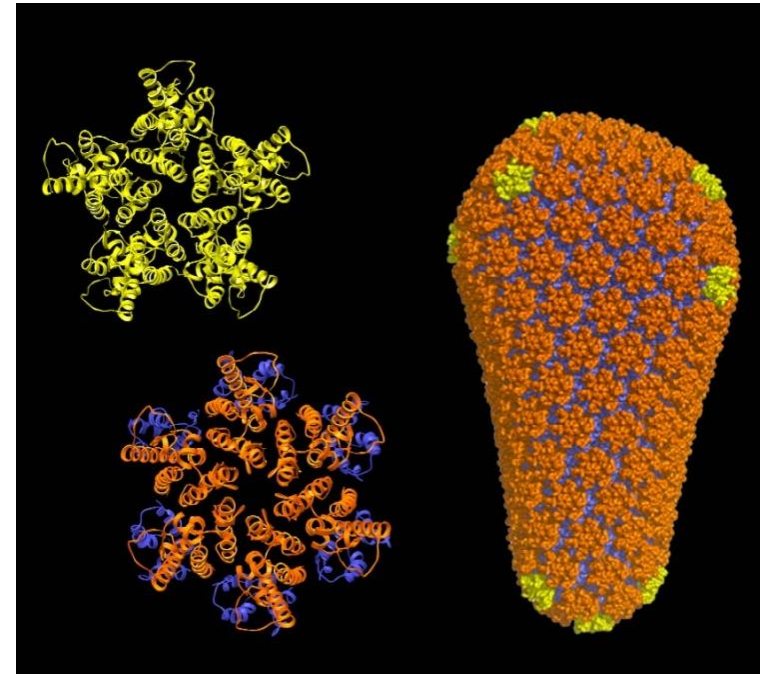
Exceptional shape viruses
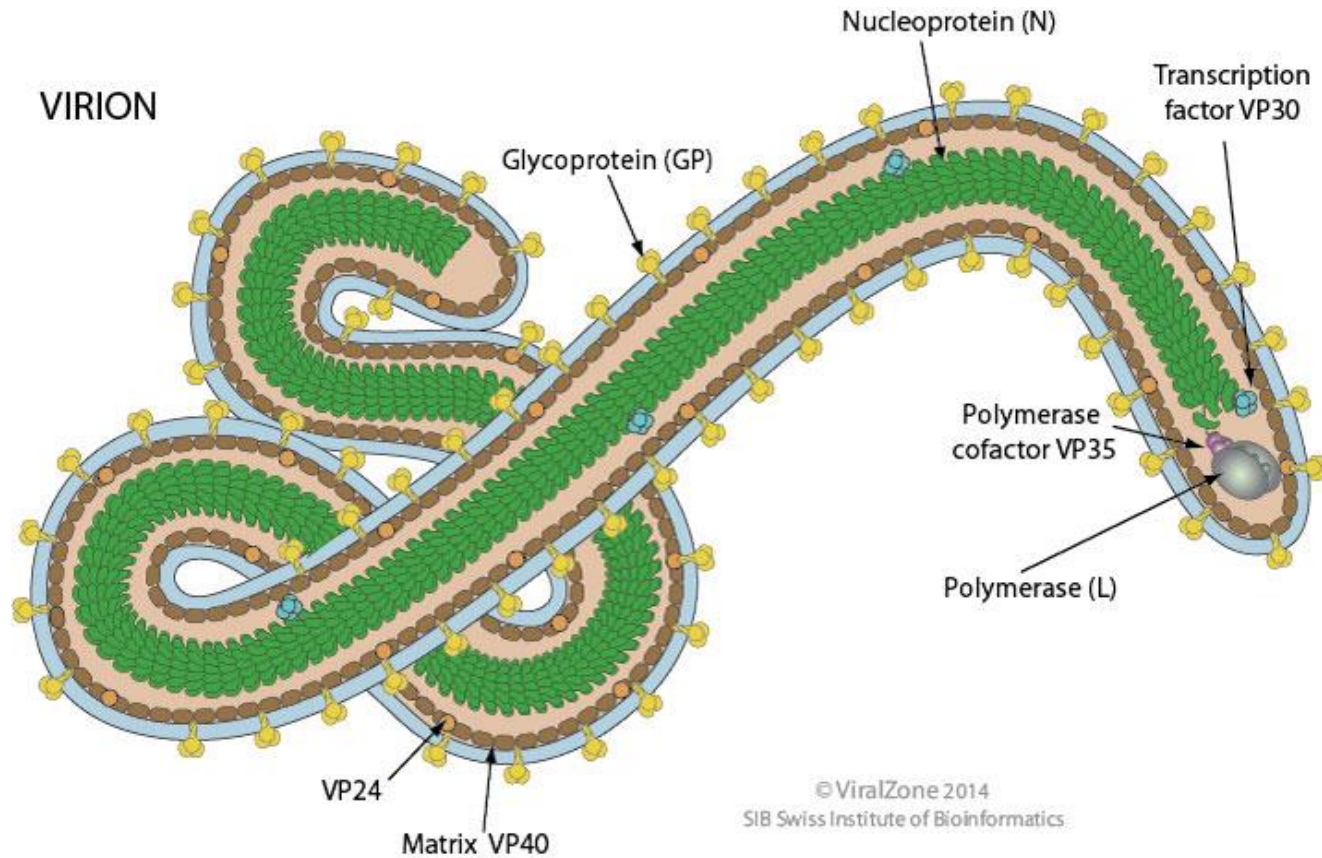

Figure 1. **Human Immunodeficiency Virus**

O. Pornillos *et al., Nature*, **469**, 424 (2010)

The capsid of HIV is a ***conical*** shell, with *continuously varying "lattice" curvature*,
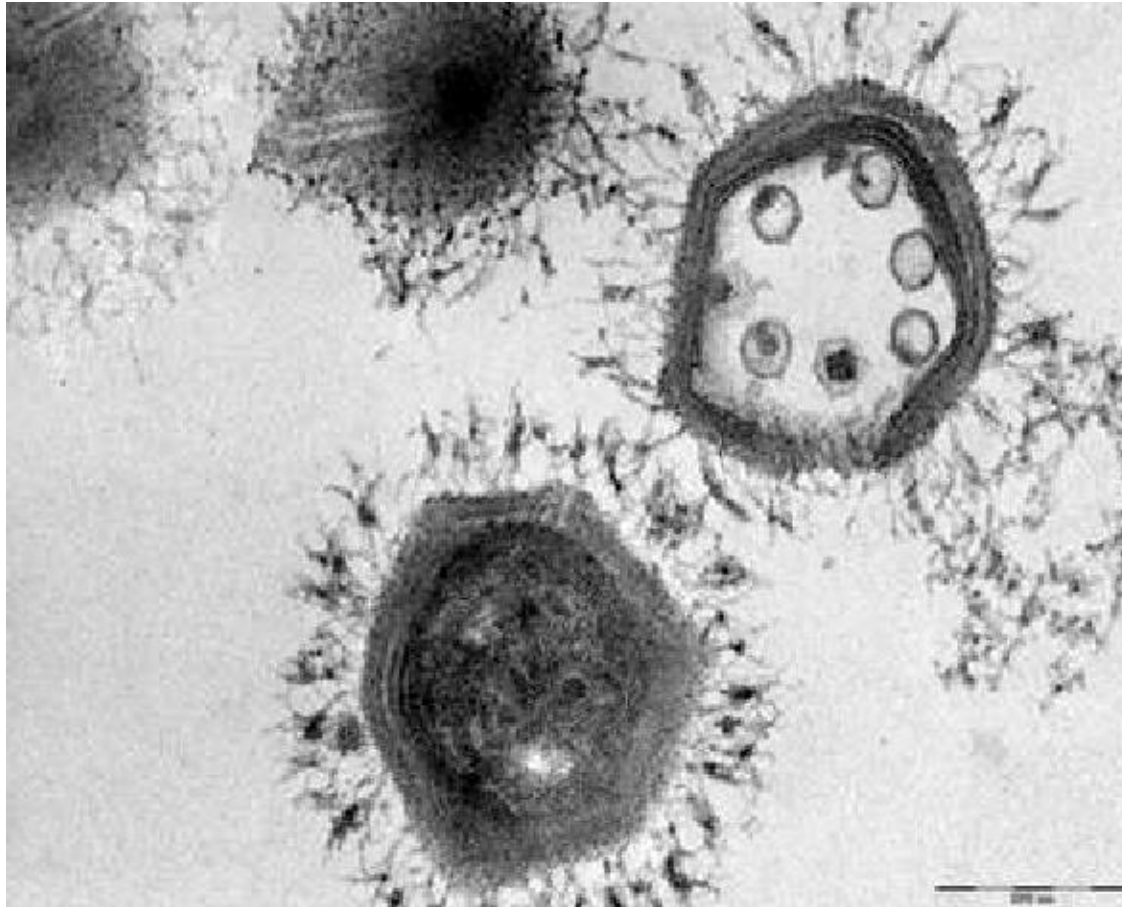
Exceptional shape viruses

Filoviridae (Ebola virus)

Filamentous: compact and flexible . Mean diameter is about 80nm.

Exceptional size viruses

© CNRS Photothèque/URMITE/IRD 198 / RAOULT Didier,
ESPINOSA Leon, CAMPANA Bernard

Giant Mamavirus infecting amoeba
Mamavirus itself is infected by small Sputnik viruses

Virus structure

- Genomic material
 - DNA or RNA (both "+" and "-")
  - single- or double-stranded
  - linear or circular
  - one or several copies

- Capsid – Protective protein shell
  - regular organization
  - high symmetry
  - made of many identical subunits
  - enveloped with lipid membrane
    or not

- **Basic shape**
  - helical rod-like
  - **spherical**

- **Typical size**
  - 30 ÷ 50 nm
  - nearly 1000 nm for some big ones
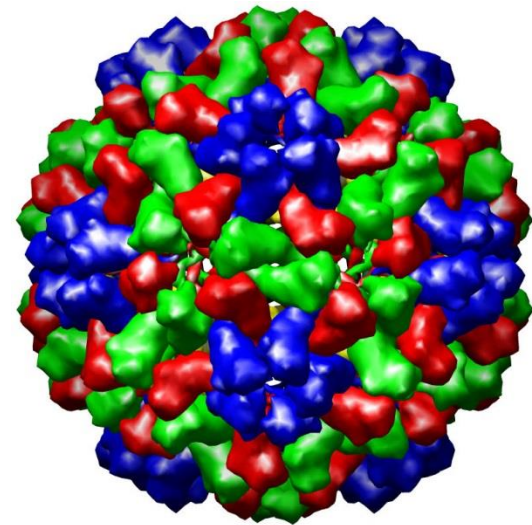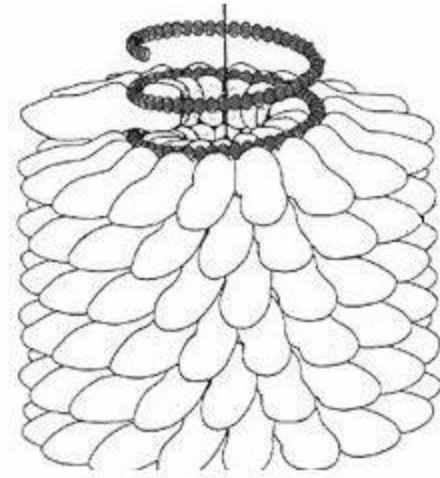
Virus Self-Assembly Process: Physicist's View

A.C. Steven et al., Curr. Opinion Struct. Biol. **15**, 227 (2005)
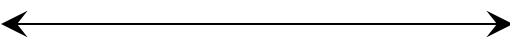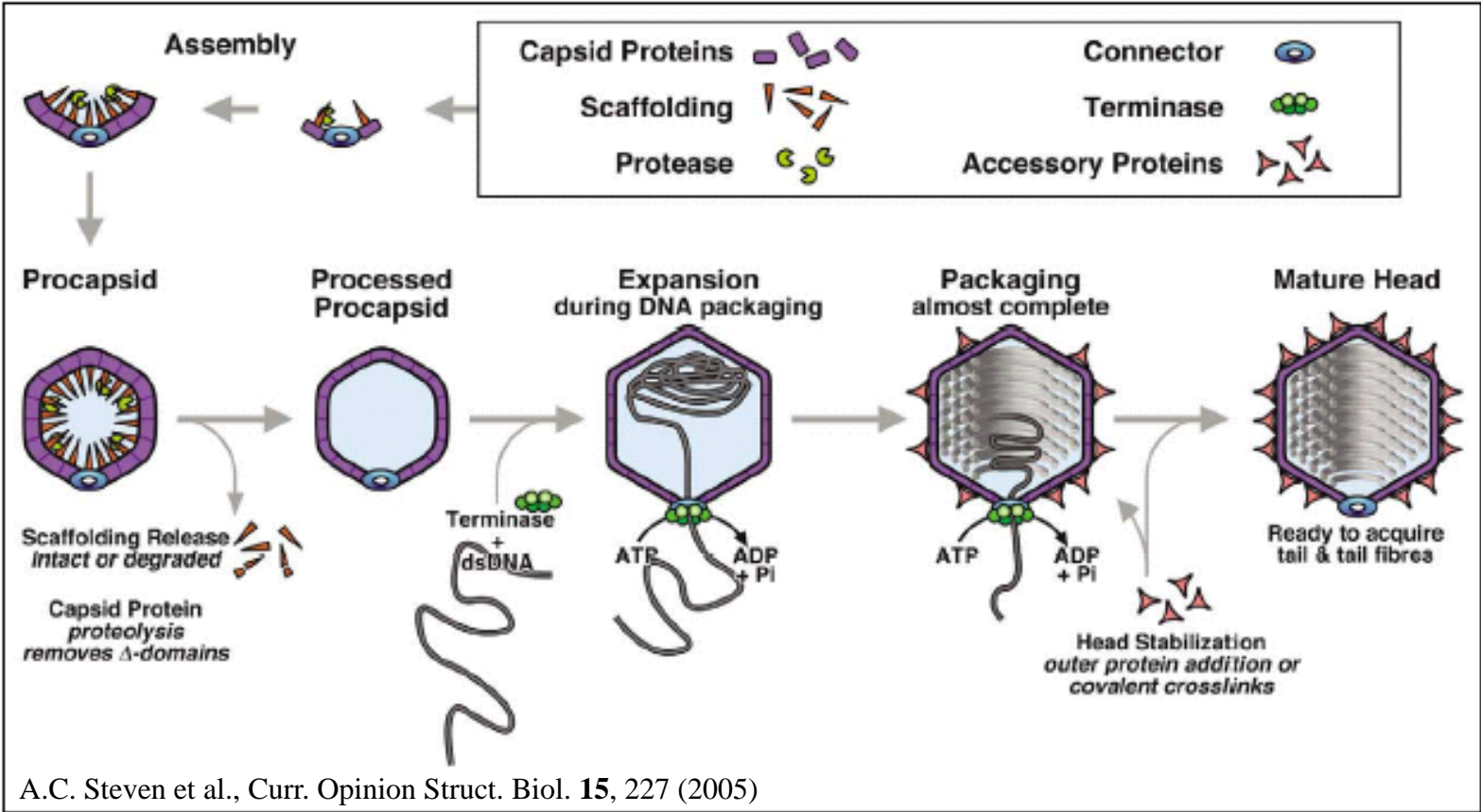
Procapsid Assembly
from the Isotropic Solution
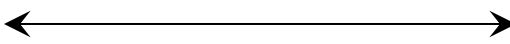
Procapsid-to-Capsid
Transformation during Maturation

Main control parameters: protein concentration, ionic force, pH-level

Genome packaging mechanisms
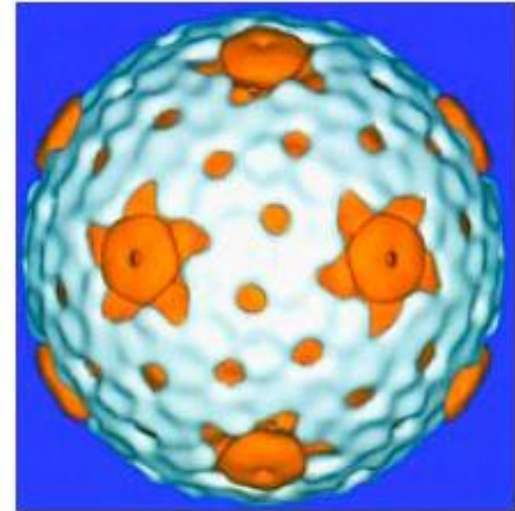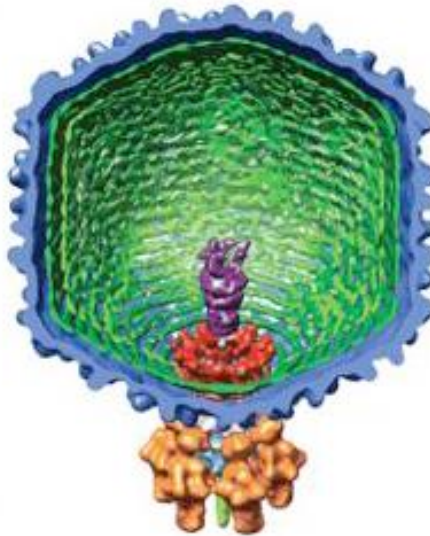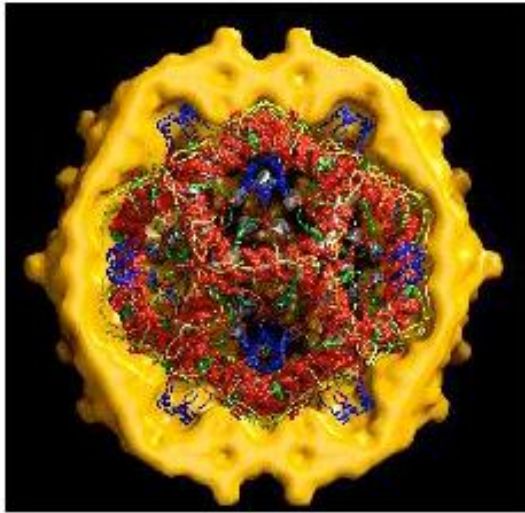
RNA Virus capsids assemble around their RNA genome.
Flock House Virus with its RNA structured as a dodecahedral cage.

dsDNA bacteriophage, packages its genome into a pre-assembled capsid through a portal.

DNA packing in bacteriophages

Empty Virus Shell

DNA

ATP   ATP
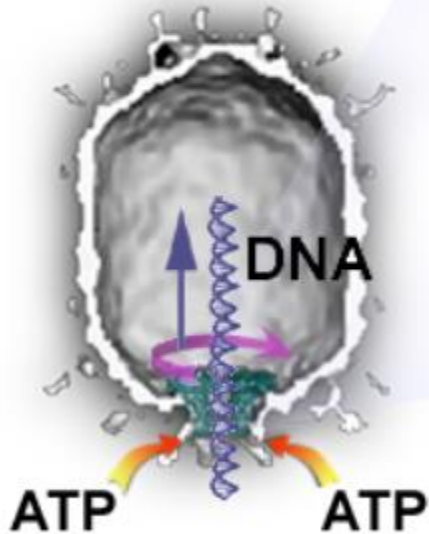
DNA Packaging Motor

DNA packing in bacteriophages
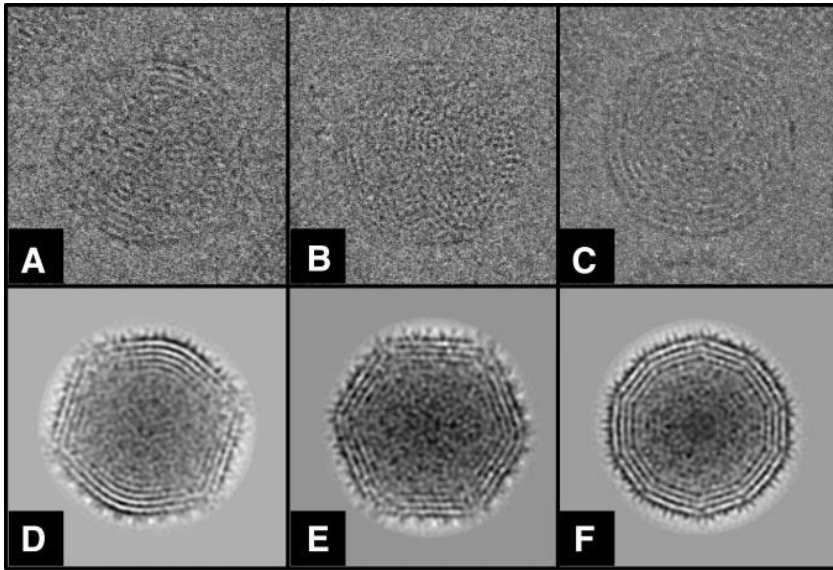
P22 phage
Z. Zhang *et al.*, *J. Mol. Biol.* **297**, 615 (2000)
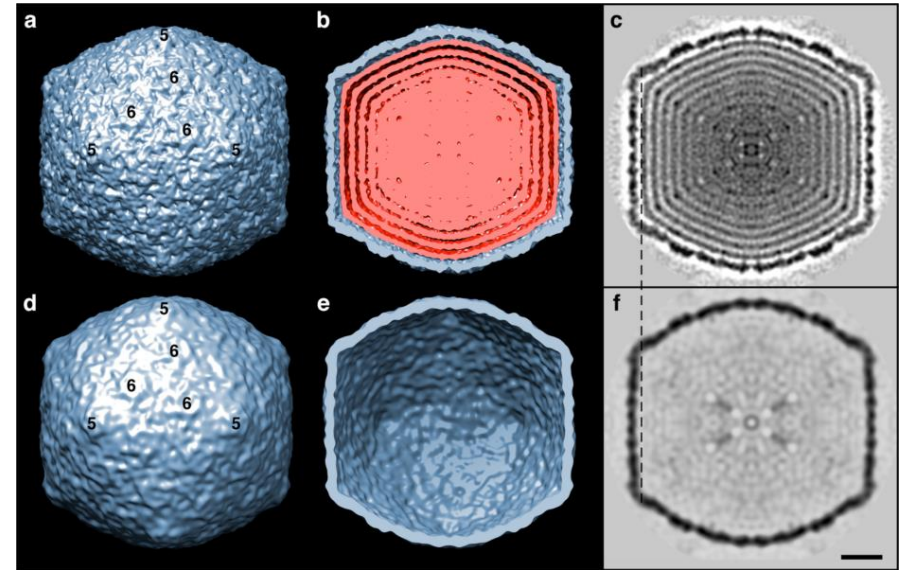
HK97 phage
R.L. Duda *et al.*, *J Mol Biol*. **391**, 471 (2009)

Nested shells of packaged DNA or compact structures akin to hexagonal lattice

Outwards pressure exerted by the DNA $\Delta P \approx$ up to 50 atm; enormous stock of elastic energy used then for genome injection.

Intracellular Viral Factories and DNA Packaging in Mimivirus
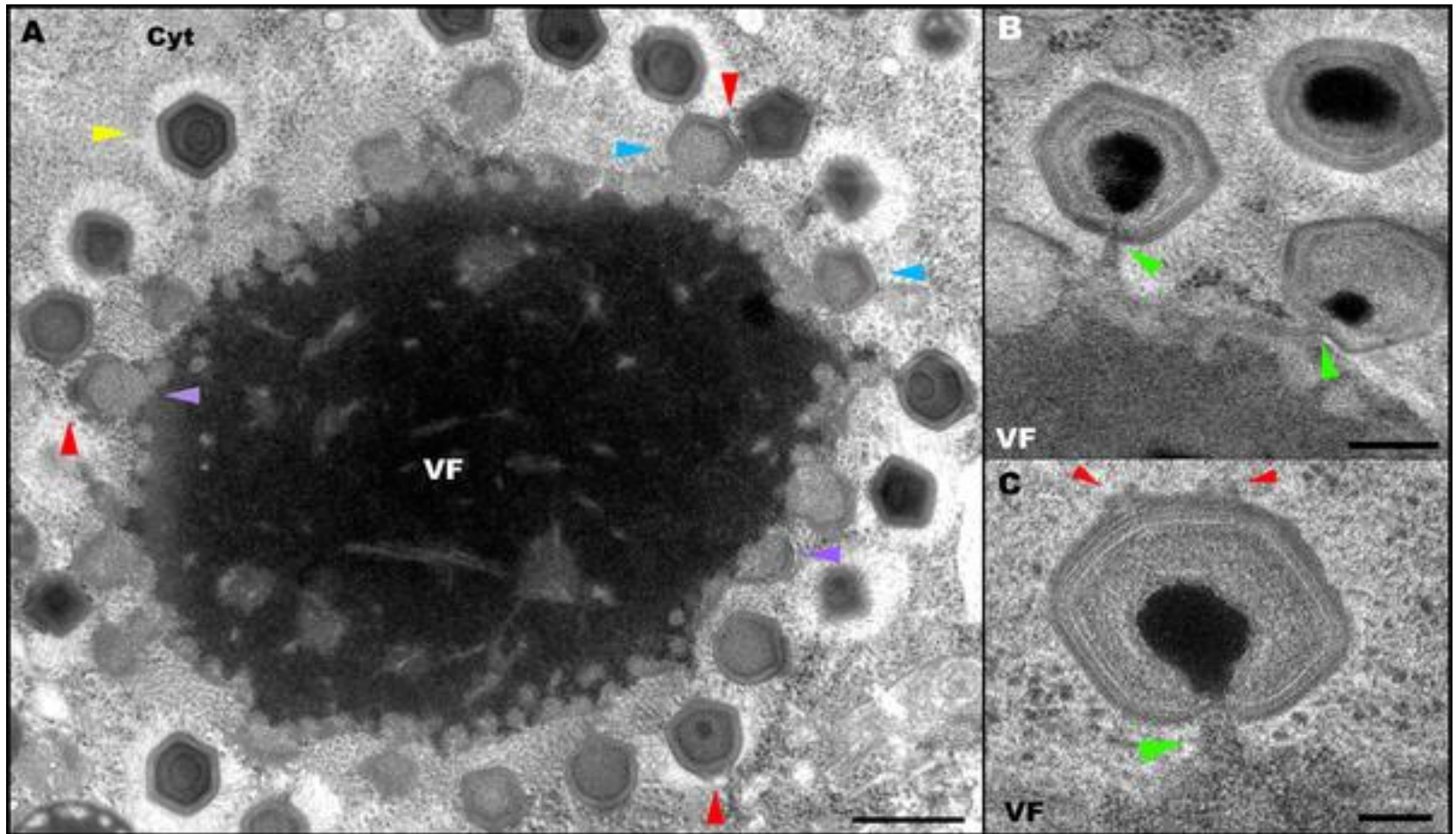
Zauberman N, Mutsafi Y, Halevy DB, Shimoni E, et al. (2008), PLoS Biol 6(5): e114

DNA ejection into infected bacteria
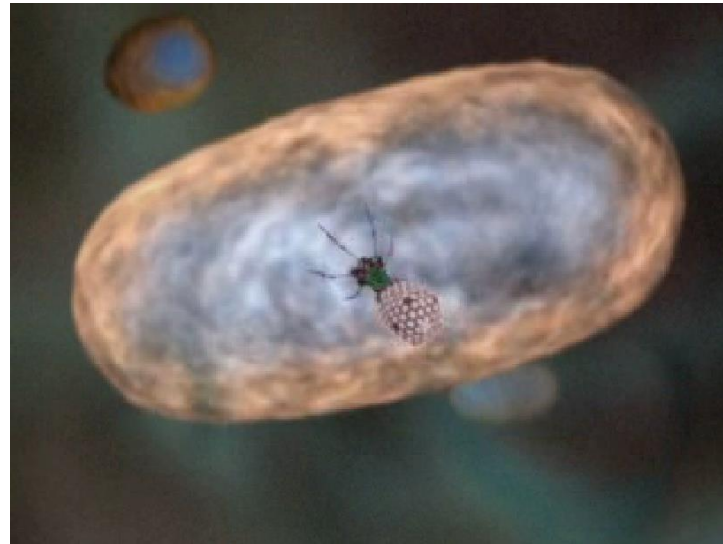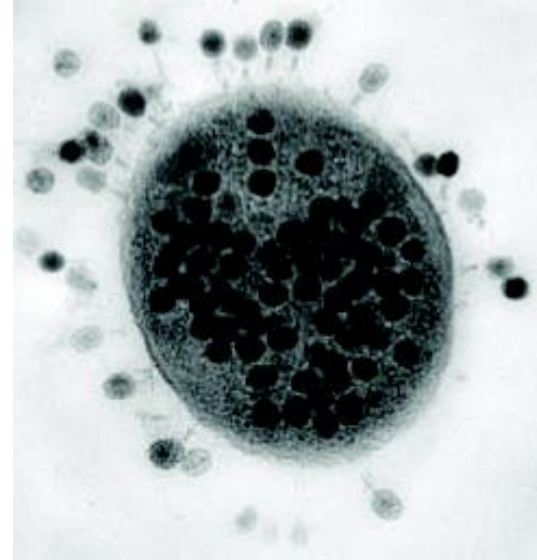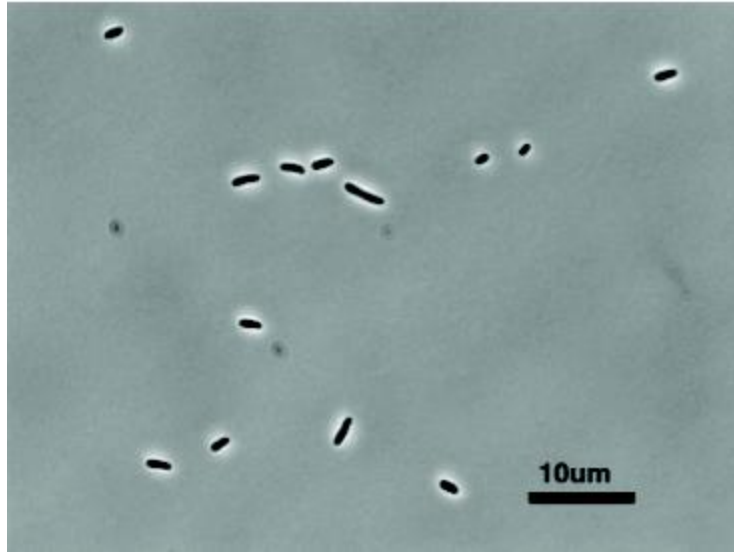
Drilling machine using commensurate shape transition

Symmetry and Topology of Viral Capsids and their relation to the Self-Assembly

A.C. Steven et al., Curr. Opinion Struct. Biol. **15**, 227 (2005)
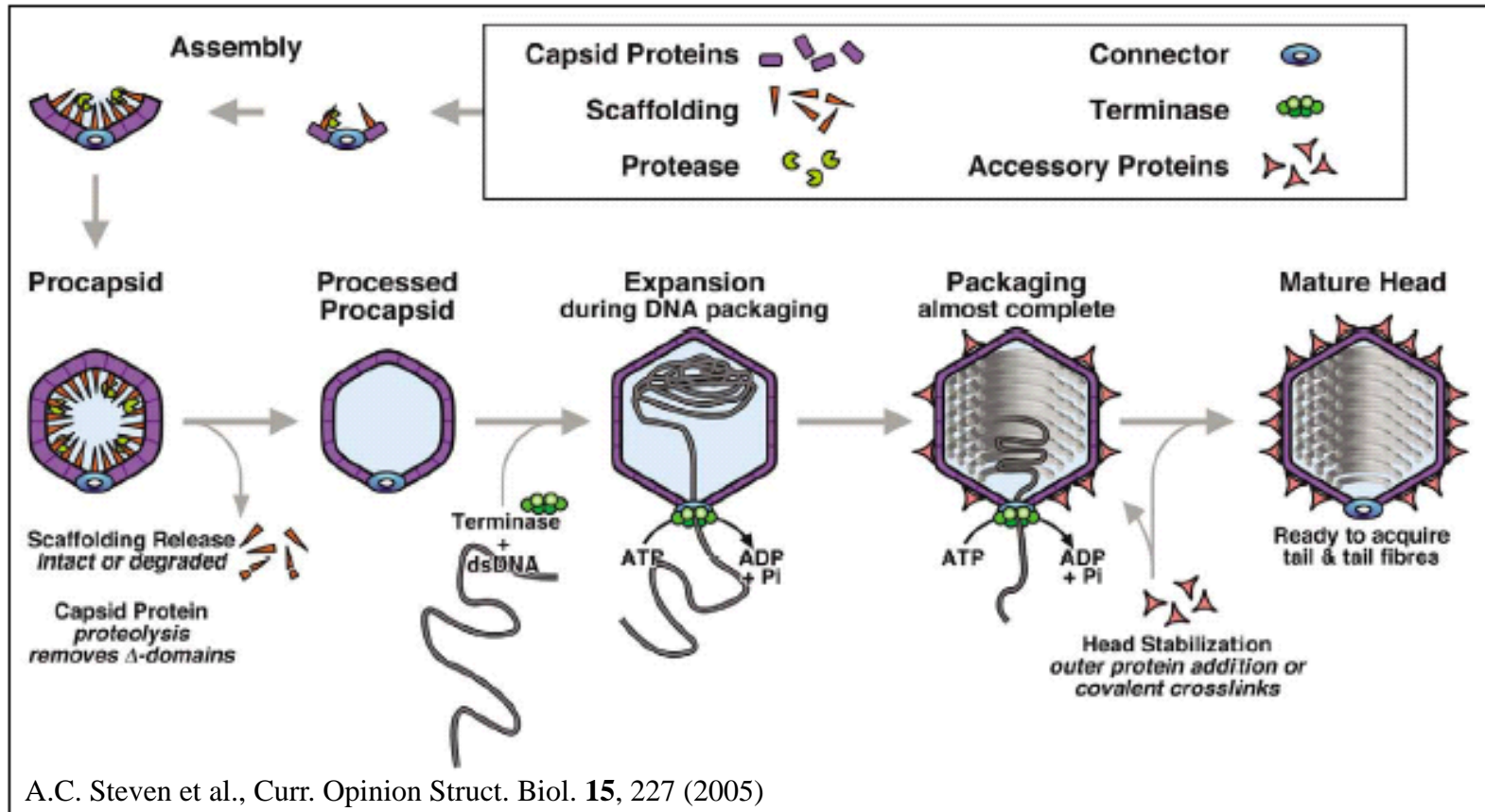
Procapsid Assembly
from the Isotropic Solution

Procapsid-to-Capsid
Transformation = Maturation

Main control parameters: protein concentration, ionic force, pH-level

Top-down approach in Condensed Matter Physics

Systems characterized by :
- regular organization
- high symmetry
- made of many identical subunits

Basic principles :
- relation between phenomenological thermodynamics and symmetry of the system
- order parameter notion, representations of symmetry groups
- **reliable structural data**

Simple systems :
- crystallization process (including molecular crystals)
- solid-solid phase transitions

More complex systems :
- ferroelectrics
- ferromagnetics
- superconductors
- liquid crystals

Structural Data

Symmetry of viral capsids make them uniquely well-suited to structural methods: X-Ray & CryoEM

$\Rightarrow$ Viruses are the largest aggregates of biological macromolecules whose structures have been determined at high resolution
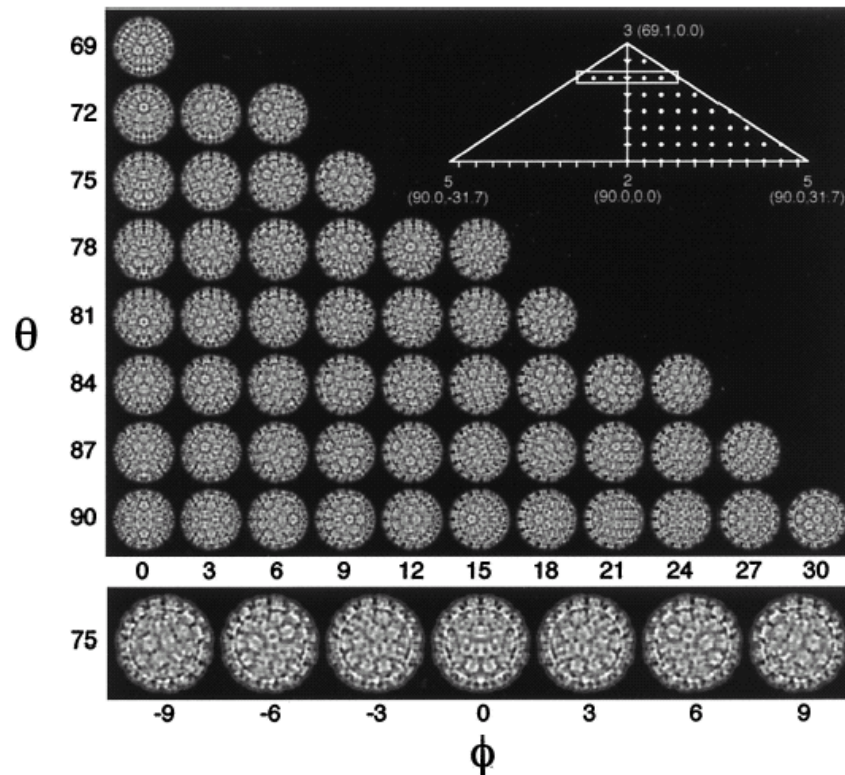
Structural Data

NωV (410Å) NβV (397Å) T=4 Ty Retro (392Å) SpV-4 (360Å) T=4 DHBc (340Å)

T=3 Ty Retro (338A) Bacteriophage φX174 (335Å) Flockhouse (330Å) Human rhino (320Å) Polio (320Å)

Cowpea mosaic (312Å) TBE-RSP (310Å) Cowpea chlorotic mottle (284Å) B19 parvovirus (260Å) Bacteriorhodopsin
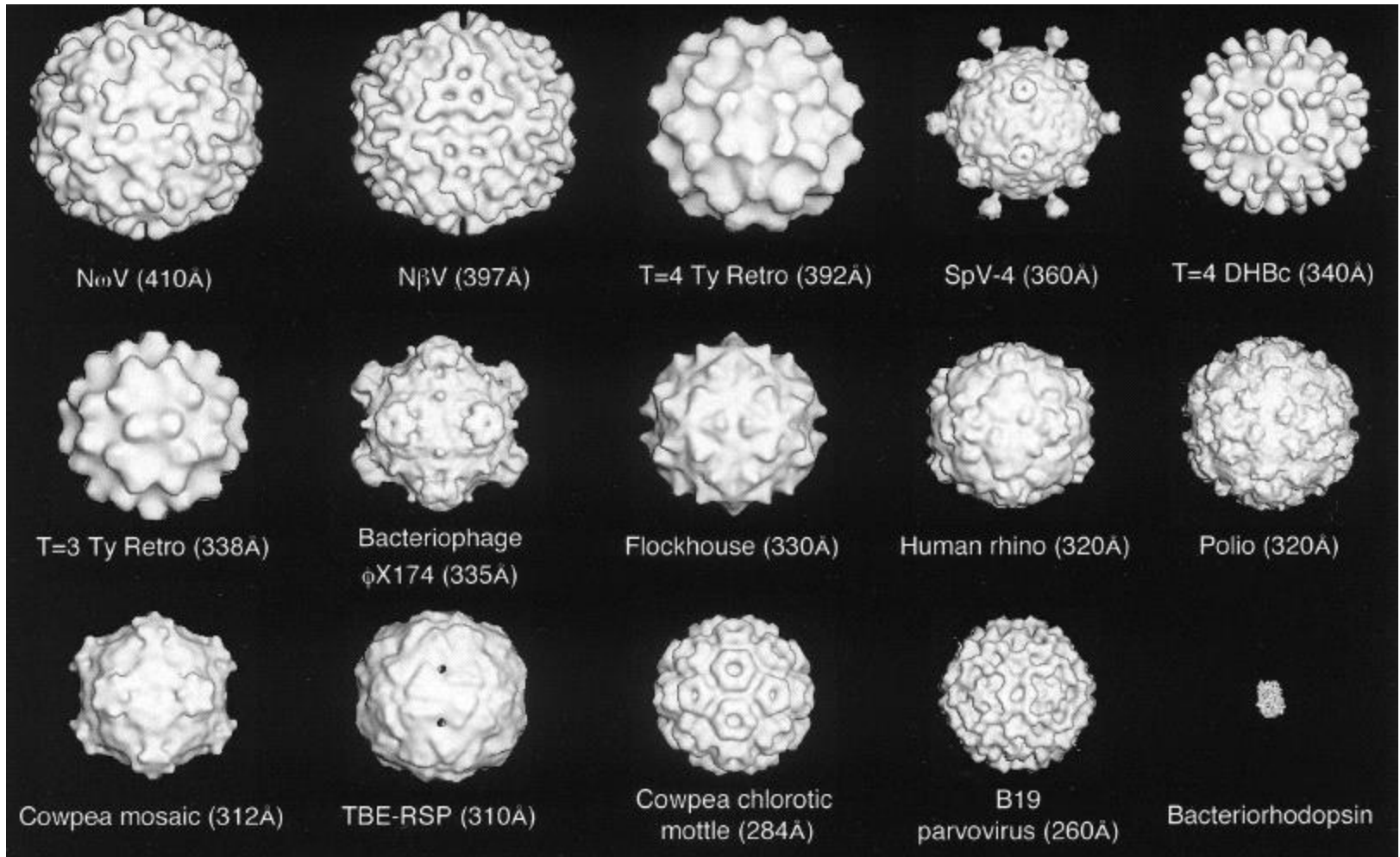
Detailed Structural Data

Ex.: **Dengue Virus**
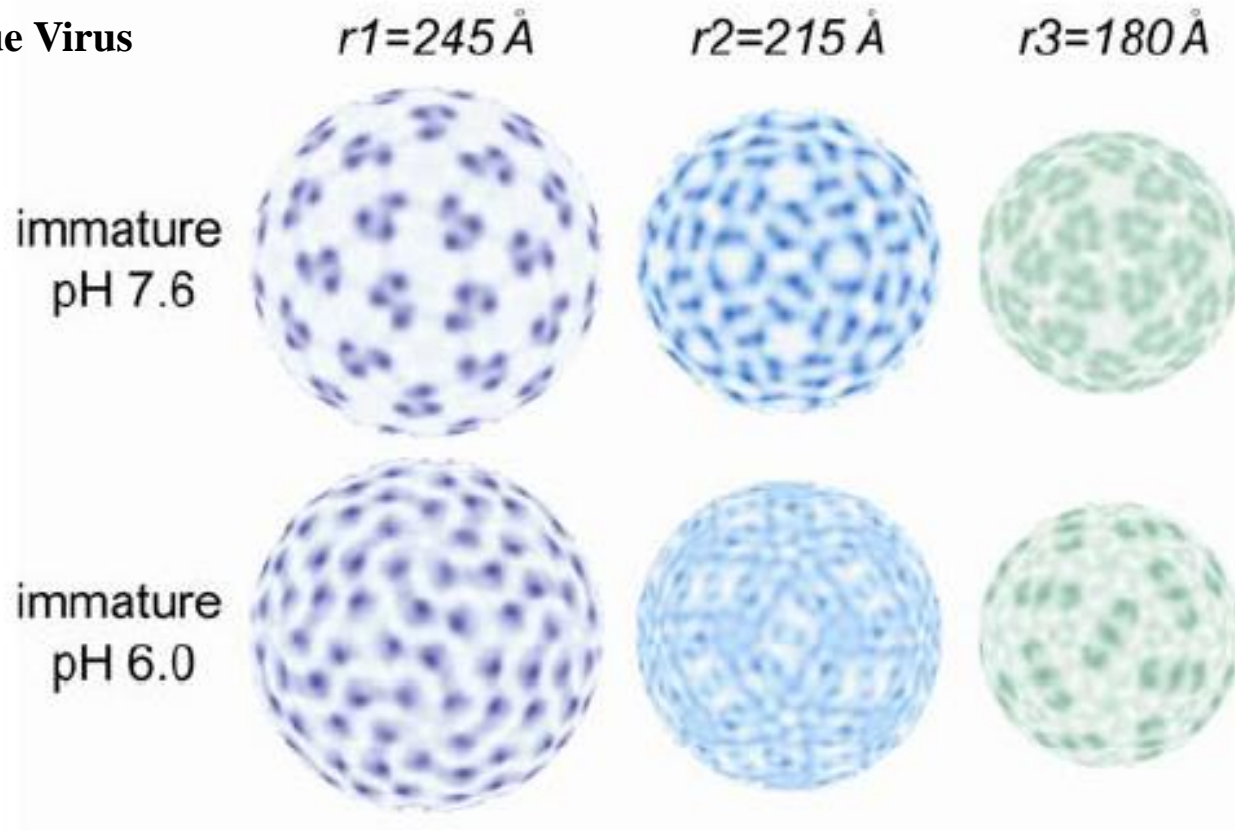
Radial sections of virion density cryo-reconstructions and projection of the density on the sphere of maximal density

Available from cryoEM community

Detailed Structural Data
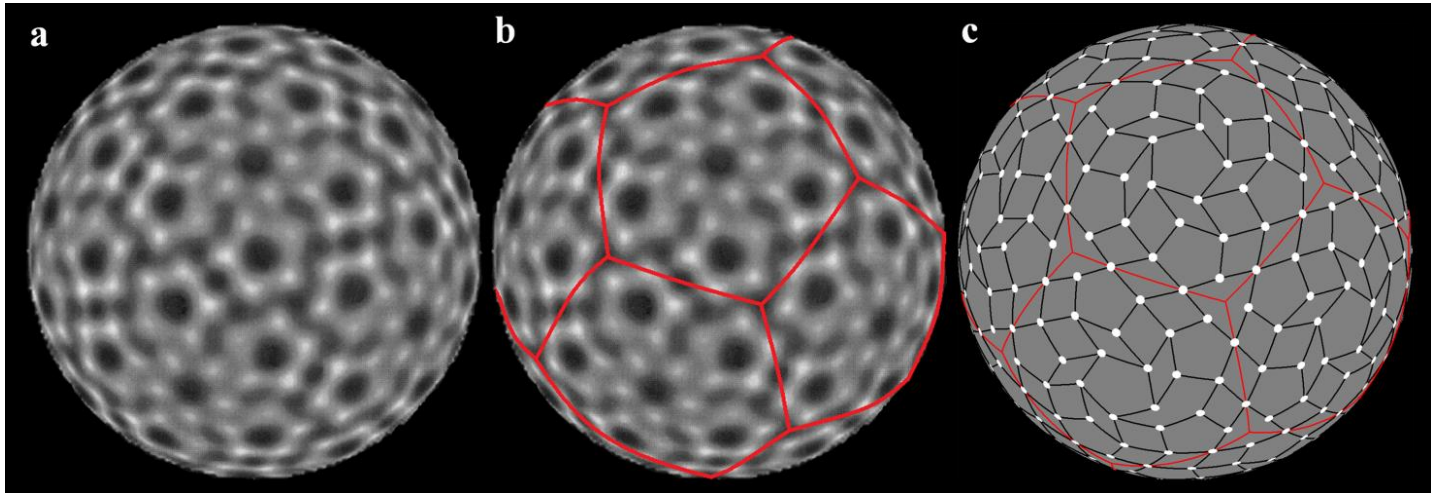
Ex.: **Bovine Papilloma Virus**

O.V. Konevtsova et al.
Phys. Rev. Lett. 2012
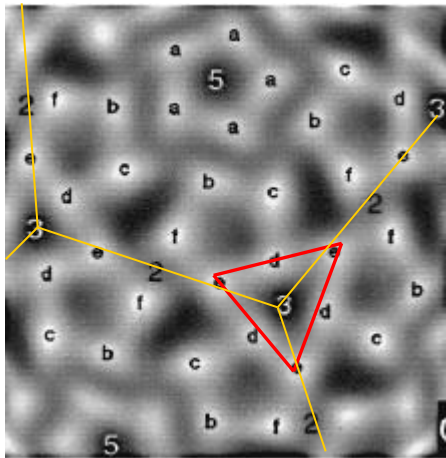
→ ***Quantitative*** structure analysis

→ ***Physical models***

→ Direct ***comparison*** with the data and predictions

Basics : How it started

F.H.C. Crick & J.D. Watson (1956), D.L.D. Caspar & A. Klug (1962) :
Basic principles of virus structure

Key insight :   Limited volume   =>   Limited genome size
=> only few sorts of proteins of limited size
typically one protein for capsid formation

Proteins are *"identical"* subunits in *"identical"* environments

=> First: irreducible 3D symmetry, then: *icosahedral* symmetry

Thermodynamics :

Self-Assembly is a *process akin to crystallization*
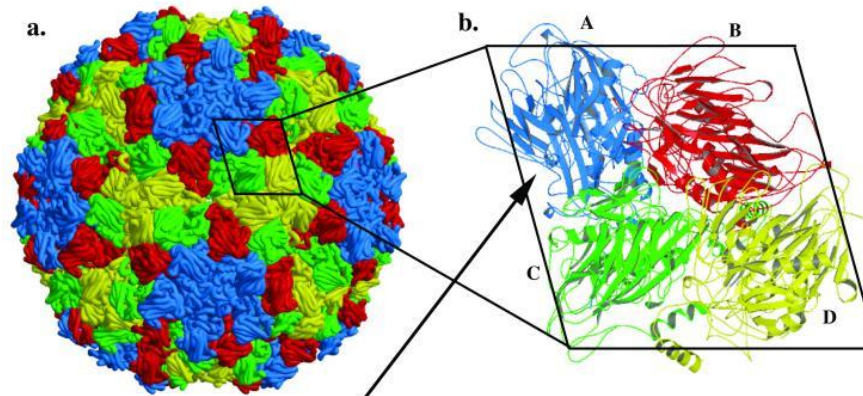
Energy of a Phase Transition
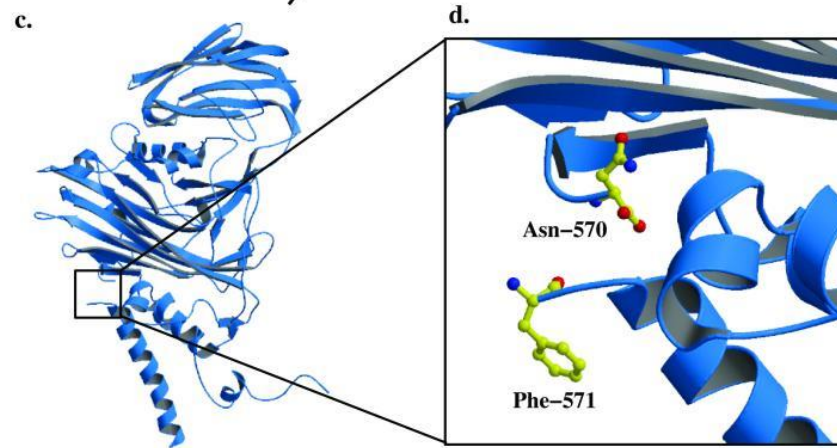
Energy of a Protein Conformation

Energy of a Covalent Bond

Different levels of Matter Organization and Energy Scale Separation Principle

Transition : isotropic solution of individual proteins → unconventional 2D "crystal" with non-trivial spherical topology

I. Selection Rules for Positions of Protein Centers of Mass
based on :

- Spherical Topology

- Asymmetry of individual proteins

- Global icosahedral symmetry of the Assembly

II. Relation Structure – Assembly Thermodynamics

Role of protein asymmetry

Moments of mass distribution. Simplest asymmetry property - chirality
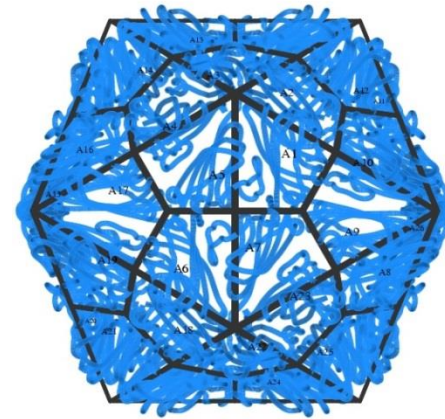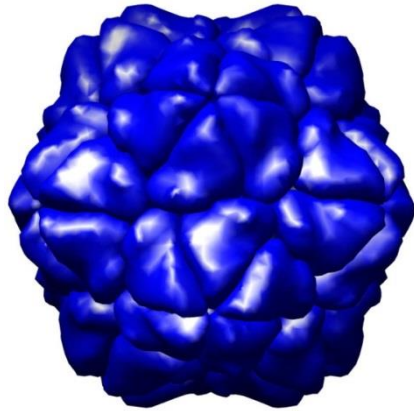
Asymmetric Protein $\longrightarrow$
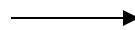
Non-zero chirality of fixed sign ε_i ;
$\sum_i \varepsilon_i \neq 0$:
$\rightarrow$ any distribution is also chiral

Rotational symmetry of an icosahedron ***I*** : *no inversion nor mirror planes*

Icosahedral Rotational Group *I*
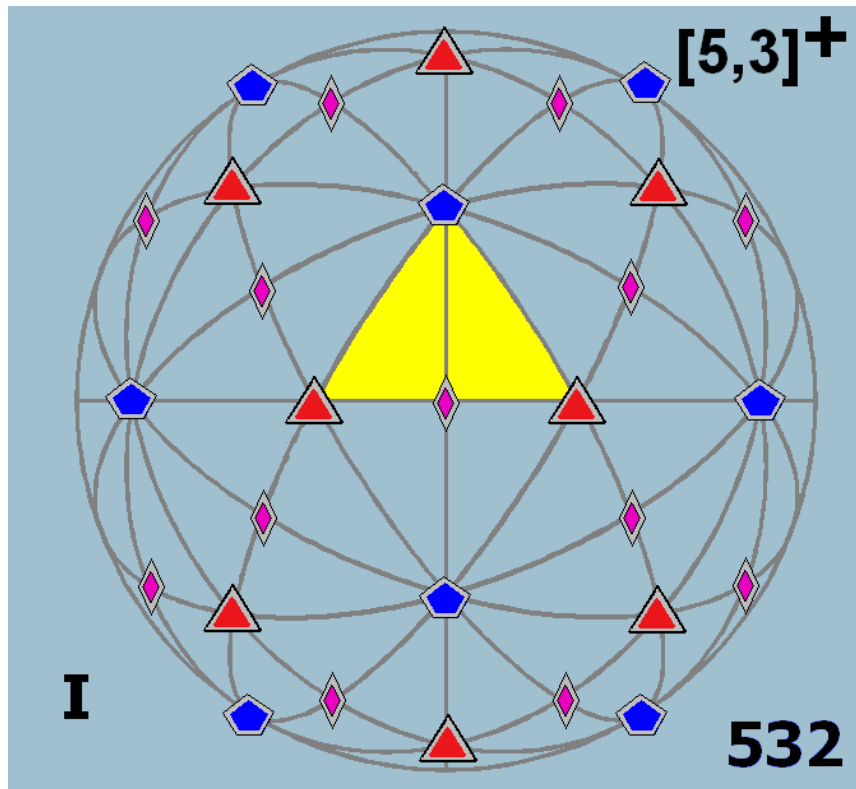
Möbius Tessellation of a sphere by the action of
Icosahedral Symmetry Elements
with the fundamental domain of the Group *I*
(called in Virology – "Asymmetric Protein Unit")

Group G = *I* consists of 60 elements
|G| = 60

Dimension of its regular orbit of the
group action on point coordinates is
also dim [Orb$_G$] = 60

Maximal dimension for Irreducible
3D rotational group

To compare with
dim [Orb$_G$] = 24 for G = *O*
octahedral rotational group
and
dim [Orb$_G$] = 12 for G = *T*
tetrahedral rotational group

Icosahedral Symmetry

- 12 vertices

- 20 faces
  (equilateral triangles)

- 5-3-2 symmetry axes

- 60 identical* subunits
  in identical environments
  can form icosahedral shell
  * asymmetric
  and not 120 as it could be for
  symmetric subunits

5-fold axis

3-fold axis

2-fold axis
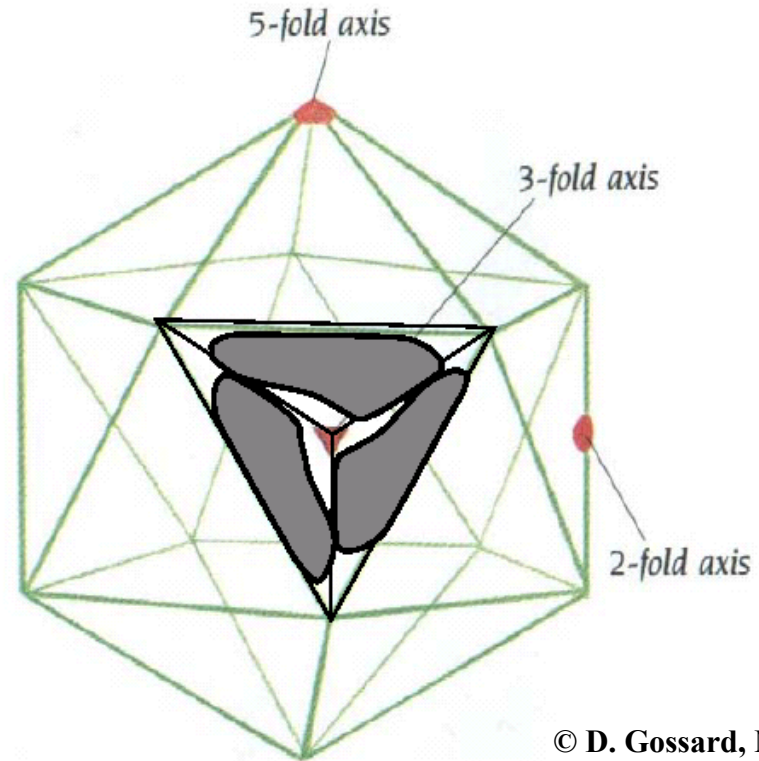
© D. Gossard, MIT

Maximal number of identical asymmetric proteins in a shell

To compare with 24 subunits in the octahedral shell, and 12 subunits in the tetrahedral shell cases, respectively.

Bigger Capsid shells

- Evolutionary pressure pushes to increase the genome size
$\Rightarrow$ to make larger capsid $\Rightarrow$ to use *more protein subunits*

- *Not possible* to form icosahedral shell of identical subunits *in identical environments* with more than 60 subunits

- Viruses with more than 60 subunits were observed

- *Questions* :

  - How can more than 60 subunits form an icosahedral shell ?

  - Will any number of subunits work ?

  - If so, how would they be organized ?

Quasi-equivalence

D.L.D. Caspar & A. Klug, *Cold Spring Harbor Symp.* **27 (1962)**

- Not all protein subunits are equivalent

  - *"Nearly-identical subunits" in "slightly different environments"*

- How to relate different environments ?
  $\Rightarrow$ Simple geometrical scheme $\Rightarrow$
    - pentamers at vertices
    - hexamers elsewhere

- Only certain number of subunits can form an icosahedral shell
  $\Rightarrow$ Selection rules :
  - only N = 60 T, with $\mathbf{T = h^2 + hk + k^2}$
  with **h, k = 1, 2, 3, …** can work
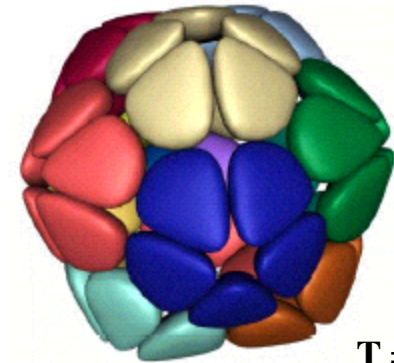
T = 1
(h,k) = (1,0)
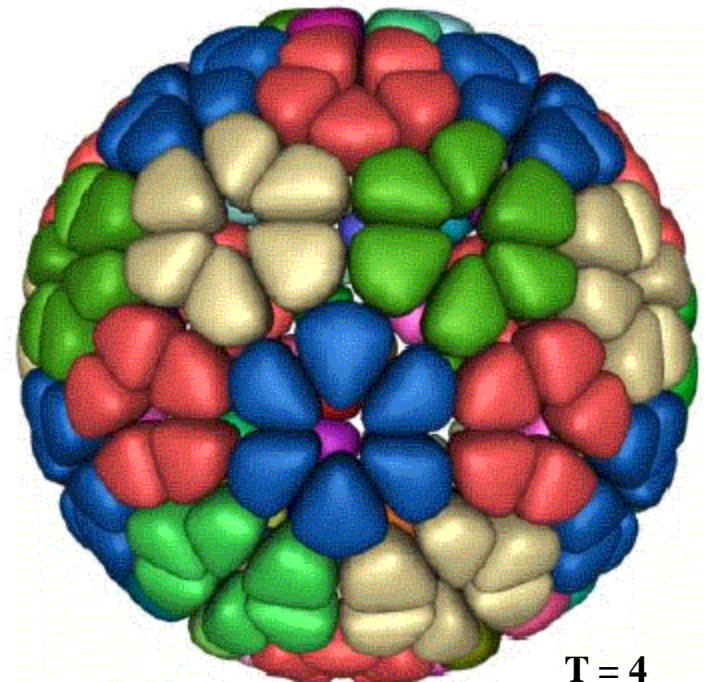
T = 4
(h,k) = (2,0)

Geometrical model of Quasi-equivalence

D.L.D. Caspar & A. Klug, *Cold Spring Harbor Symp*. **27 (1962)**
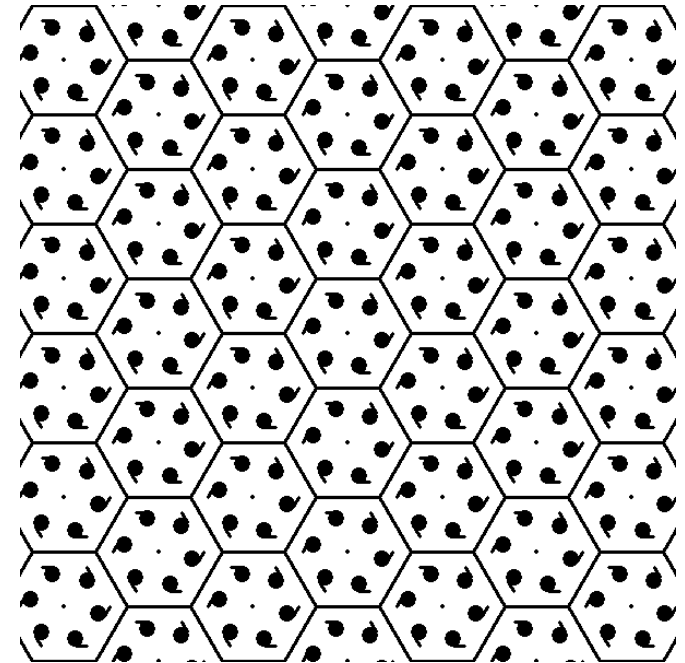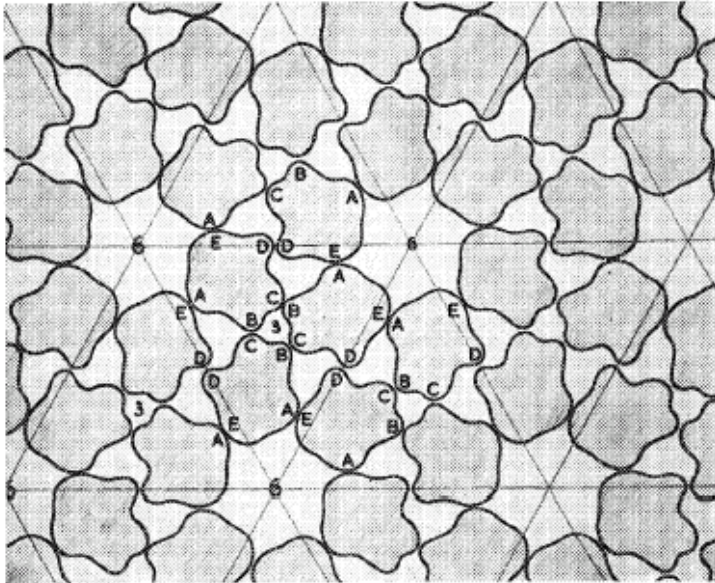
FIGURE 6. Asymmetric units arrayed in an equilateral-triangular plane net. Besides having translations, here *a* and *a*, the lattice has 6-fold rotational axes of symmetry. Although the asymmetric units are in 6 different orientations in space, they are all exactly equivalently related.
Each unit here 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. (Note that only two of these bonds are absolutely essential for coherence of the array.)

Asymmetric proteins in general positions in the hexagonal unit cell (regular orbit of the 2D space group)

Protein environments are equivalent due to the lattice translation

Geometrical model of Quasi-equivalence
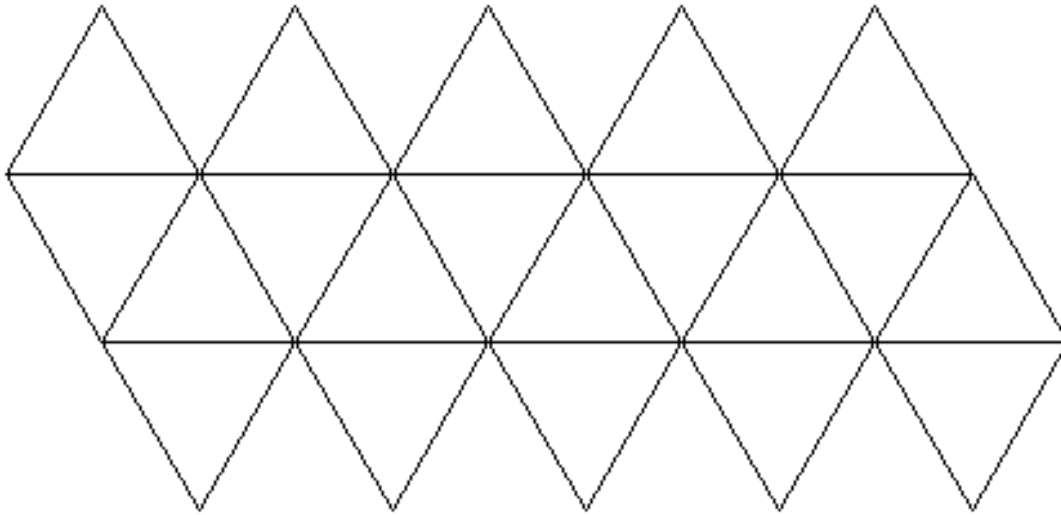
Net of an Icosahedron is **commensurate** with the hexagonal lattice
Local order is hexagonal
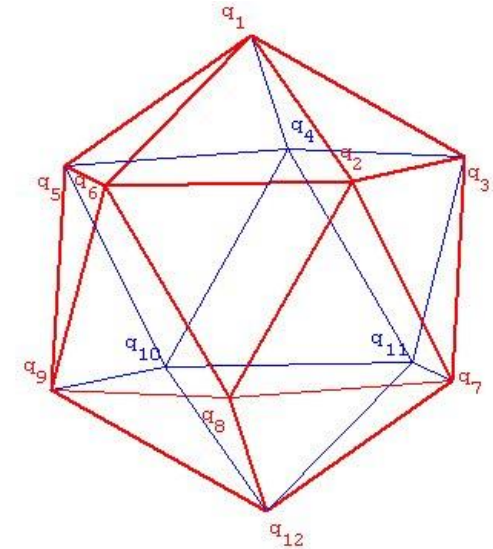
Folded Icosahedron

Mapping of the Hexagonal Lattice to the Surface of an Icosahedron
(**"slitting the net and folding"**)

Geometrical model of Quasi-equivalence

Selection rules :

Number T of different environments = Triangulation Number

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

But

Not unique
+
No relation with assembly thermodynamics

A
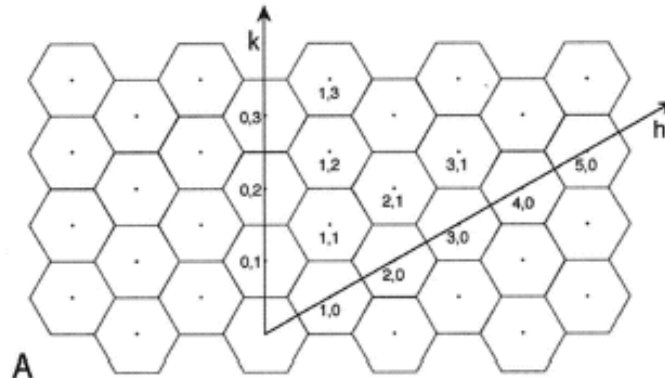
h k	T	Example
1 0	1	bacteriophage φX174
1 1	3	tomato bushy stunt virus
2 0	4	Sindbis virus
1 2	7d	polyoma virus
3 1	13l	reovirus
1 3	13d	infectious bursal disease virus
4 0	16	herpesvirus
5 0	25	adenovirus

Notations: d = *dextro* (right handed)
l = *laevo* (left handed)

F

B $T=3$ (h,k=1,1)

C $T=4$ (h,k=2,0)
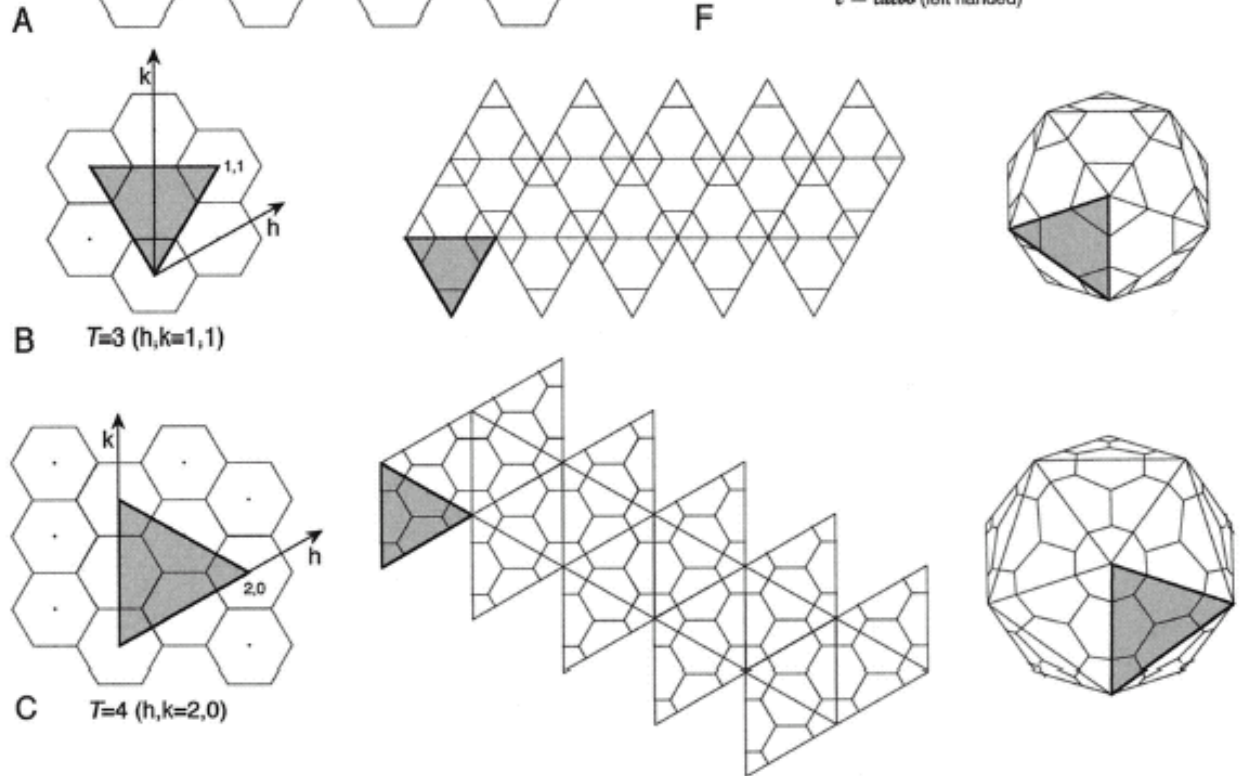
Conventional and Unconventional Capsid Structures

Conventional « spherical » viral capsids exhibit spatial organization consistent with the Caspar & Klug selection rules
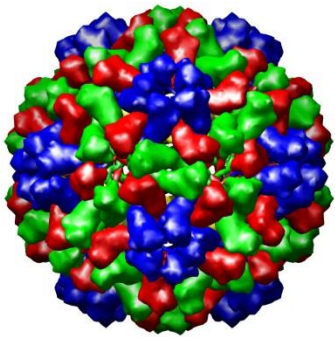
Cowpea Chlorotic
Mottle Virus (CCMV)
T = 3
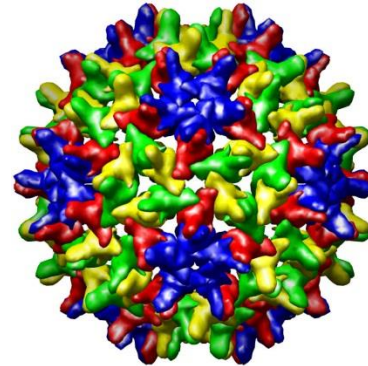
Hepatitis B Virus
(HBV)
T = 4

However, unconventional capsid structures don't
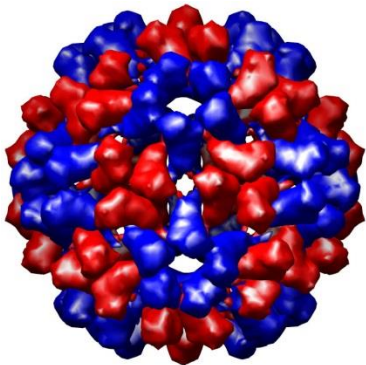
L-A Virus
T = 2
forbidden by
Caspar-Klug
selection rules
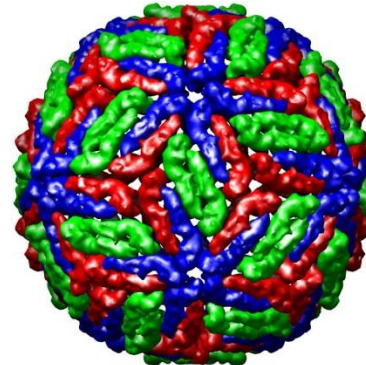
Dengue Virus
T = 3
but *without*
Caspar-Klug
hexamers

Looking for other ideas :   Is it possible to propose common selection rules ?

Basic Ideas from Statistical Condensed Matter Physics

One type of proteins → One statistical ***density distribution function***

Physical equivalence → Proteins located in a system of maxima
of a ***single irreducible*** density function

Assembly thermodynamics → Free energy invariant wrt the density function

Simple analogs : Atomic solids

Physical equivalence   → Atoms in atomic crystals (lattice nodes)
in a simple system

Physical equivalence   → Atoms in atomic quasicrystals
in a more comlex system

Thermodynamics   → Crystallization theory : Density waves

Landau Theory of Crystallization : Static Density Waves

$\rho = \rho_0 + \Delta\rho$
Density in the
crystal state

Classical crystal case: $\Delta\rho = \sum_{\mathbf{k}} \rho_{\mathbf{k}} \exp(i\mathbf{kr})$

***Density* deviation from its value ρ_0 in the isotropic state =**

= *System of Plane Waves with the fixed length of wave vectors |k|*

Critical System of Density Waves $\Delta\rho = \sum_{\mathbf{ki}} \rho_{\mathbf{ki}} \exp(i\mathbf{k_i r})$
where $\rho_{\mathbf{ki}}$ are Order Parameter Components

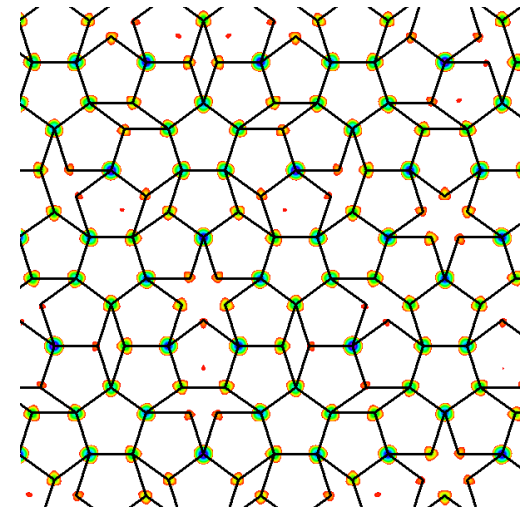***For crystals formed by one type of atoms the atomic positions are associated with the maxima of the Critical System of Density Waves (CSDW)***

Quasicrystals:

Small finite number of different environments generated by a single irreducible density function

Per Bak, Phys. Rev. Lett. **54**, 1517 (1985)

S.B. Rochal et al. , Phys. Rev. B. **72**, 024210 (2005)

Landau Theory of Crystallization : Static Density Waves

Free energy expansion near the isotropic-to-crystal phase transition : $F_0 + F_2 + F_3 + F_4 + \ldots$

$$F_2 = \int d^2k\, A_{\mathbf{k}}\, \rho_{\mathbf{k}}\, \rho_{-\mathbf{k}} = A(T, c)\, |\rho_{\mathbf{k}}|^2 \,; \quad F_3 = B(T, c) \sum_{\mathbf{k1, k2, k3}} \rho_{\mathbf{k1}}\, \rho_{\mathbf{k2}}\, \rho_{\mathbf{k3}}\, \delta(\mathbf{k_1 + k_2 + k_3})$$

$$F_4 = C(T, c) \sum_{\mathbf{k1, k2, k3, k4}} \rho_{\mathbf{k1}}\, \rho_{\mathbf{k2}}\, \rho_{\mathbf{k3}}\, \rho_{\mathbf{k4}}\, \delta(\mathbf{k_1 + k_2 + k_3 + k_4})$$
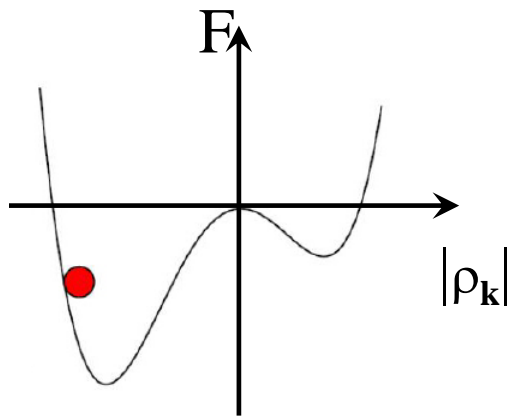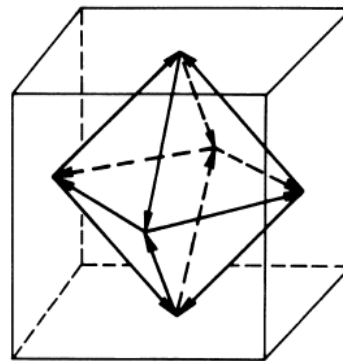
B.C.C. Lattice *2D Hexagonal Lattice*
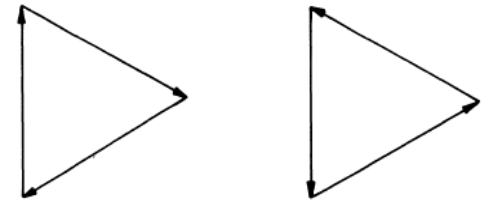
S. Alexander & J. McTague,
Phys. Rev. Lett. **41**, 702 (1978)

Currently :
In P. Chaikin & T. Lubensky Textbook
« Principles of Condensed Matter Physics »

Contributions to the Cubic Term in the Free Energy – Choice of the thermodynamically favorable state

Assembly of protein shells : Spherical Density Waves

$\rho = \rho_0 + \Delta\rho$
Density in the self-assembled state

2D spherical distribution of finite asymmetric units in 3D space:
$\Delta\rho = \sum_{l \in N} \sum_{|m| \le l} \rho_{lm} Y^l_m (\Theta, \phi)$
Density deviation from its value ρ_0 in the isotropic state =
= ***System of Waves on a Sphere with the fixed wave number l***

Asymmetric Proteins have no Proper Symmetry. Because of the Asymmetry the final structure has ***neither spatial inversion nor symmetry plane*** elements => ***only odd spherical harmonics*** in $\Delta\rho$

Restrictions on the free energy form:

Free energy density expansion near the assembly transition : $F_0 + F_2 + F_3 + F_4 + \dots$

$F_2 = A(T, c) \sum_m a_m \rho_{lm} \rho_{l(-m)}$

$F_3 = B(T, c) \sum_{m1, m2, m3} a_{m1, m2, m3} \rho_{lm1} \rho_{lm2} \rho_{lm3} \delta(m_1 + m_2 + m_3) \qquad \equiv 0 \qquad$ **(!!!)**

$F_4 = \sum_k C_k(T, c) \sum_{m1, m2, m3, m4} a_{m1, m2, m3, m4} \rho_{lm1} \rho_{lm2} \rho_{lm3} \rho_{lm4} \delta(m_1 + m_2 + m_3 + m_4)$

Possibility of 2nd order transition → specific kinetics

Assembly of protein shells : Spherical Density Waves
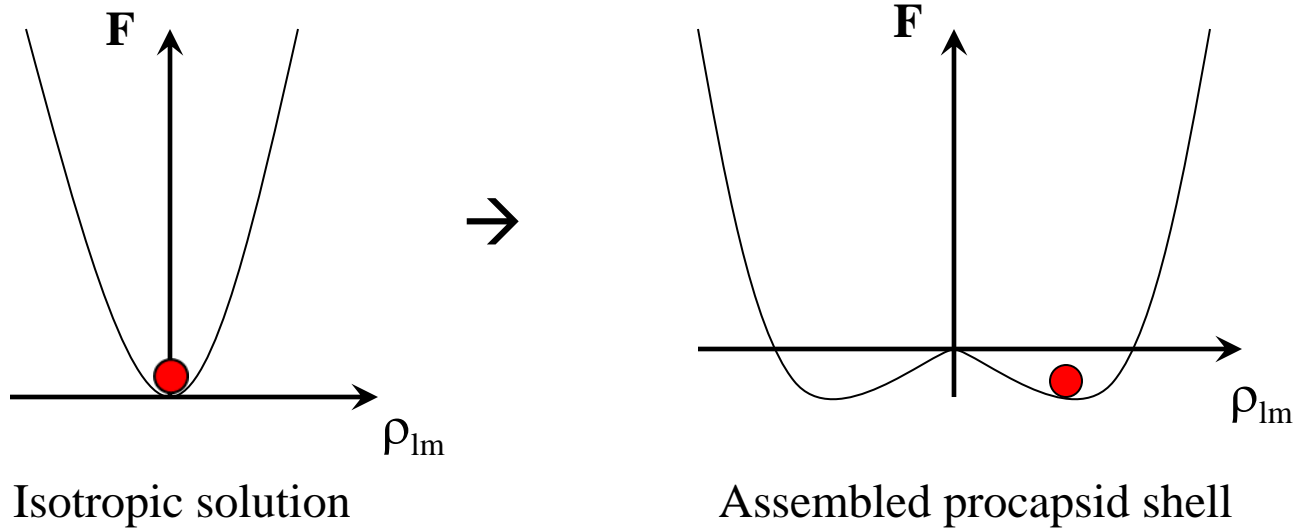
No coexistence of two states → **Rare intermediate products of assembly**
→ **Slow dynamics**

→ No one-by-one steps → **No polymerization-like assembly process**

Experiment:
- **no incomplete capsids**, either isolated proteins in solution,
or fully assembled shell;
- very slow dynamics called **"protein sitting"**

"Structural" selection rules

What is proposed instead of Caspar-Klug selection rules for T number ?

→ Symmetry **restriction on the choice of density functions** :

Density function invariant with respect to the rotational icosahedral symmetry group *I* can be constructed   ***not for all odd l***
but only for $l = \textbf{15 + 6i + 10j}$;   i, j = 0, 1, 2, 3, …

Protein distribution in capsids of small viruses   →   icosahedral density waves with
$l = \textbf{15}, l = \textbf{21}, l = \textbf{25}, l = \textbf{27}, l = \textbf{31}$, etc.

→ **Restriction on possible protein positions**
However , **no limitation of the Caspar-Klug type** : all integer T are possible

Number of different types of maxima = Number T of protein environments

→ for a **small viruses** (with $l < \textbf{44}$):   Icosahedral density functions
$\Delta \rho_l(\Theta, \phi) = \sum_{|m| \leq l} \rho_{lm} Y^l_m (\Theta, \phi) = B f_l(\Theta, \phi)$

are ***unique functions without fitting parameters***

Selection rules

Critical System of Density Waves (CSDW) in the considered case :

$$\Delta \rho_{cr} = B f_l(\Theta, \phi) = \sum_{|m| \leq l} \rho_{lm} Y^l_m(\Theta, \phi)$$

where ρ_{lm} span active irreducible representation (IR) of the symmetry group G_0 of the parent state. « Active IR drives the transition ».

Active IR of G_0 must subduce the identity representation of the symmetry group G of the ordered state ($G \subset G_0$).

$B f_l(\Theta, \phi) = \sum_{|m| \leq l} \rho_{lm} Y^l_m(\Theta, \phi)$ must span the identity representation of G.

The representation subduced from G_0 to G must contain the identity representation of G.

Frequency of subduction: $n_l = (1/|G|) \sum_G \chi(g)$

$\chi(g)$ is the character of the $G_0 = SO(3)$ group element g;
the sum runs over the elements $g \in G$ of the icosahedron rotation group I ;
$|G| = 60$ is the I group order

Subduction Criterion: $n_l \neq 0$ or $n_l = 0$ →   selection rules for l:

Selection rules

Constructive form

Frequency of subduction: $n_l = (1//G/) \sum_G \chi(g)$

$\chi(g)$ is the character of the element $g \in SO(3)$: $\qquad \chi(l, \alpha) = \dfrac{\sin[(l + 1/2)\alpha]}{\sin(\alpha/2)}$

Conjugacy classes of the *I* group:

- Identity E
- 15 rotations C_2, order 2
- 20 rotations C_3, order 3
- 12 rotations C_5, order 5
- 12 rotations $(C_5)^2$, order 5

$$n(l) = (1/60) \left[2l + 1 + 15\chi(l, \pi) + 20\,\chi(l, 2\pi/3) + 12\,\chi(l, 2\pi/5) + 12\,\chi(l, 4\pi/5) \right]$$

$n_l \neq 0$ for $\quad$ **$l = 15 + 6i + 10j$** ; $\qquad$ i, j $= 0, 1, 2, 3, \ldots$

Selection rules and groups not generated by reflections

CSDW   B $f_l(\Theta, \phi)$ are homogeneous functions of degree l

Any scalar function invariant wrt I group : $F(g\,\vec{r}) = F(\vec{r})$ $g \in I$, $\vec{r} = (x,y,z)$
can be expanded in formal series $F(J_0, J_1, J_2, J_3)$
$\{J_i\}$ is the integrity basis –
full set of generators of the ring of polynomials invariant wrt I group:

$J_0 = x^2 + y^2 + z^2$ $J_1 = \prod_{i=1}^{6} \vec{n}_i\,\vec{r}$ $J_2 = \prod_{i=1}^{10} \vec{p}_i\,\vec{r}$ $J_3 = \prod_{i=1}^{15} \vec{q}_i\,\vec{r}$

I group is not generated by reflections $\rightarrow$ (J_0, J_1, J_2, J_3) form syzygy -
an algebraic relation of the form $(J_3)^2 = P(J_0, J_1, J_2)$ in 30th degree

$\rightarrow$ Invariant homogeneous functions of degree l

$$G_l(x,y,z) = J_3[\; \sum_{15 + 2k + 6i + 10j\,=\,l} A_{k,i,j} (J_0)^k (J_1)^i (J_2)^j \;]$$

on a sphere $J_0 = Const$ $\rightarrow$

$$B\,f_l(\Theta, \phi) = J_3[\, A_{0,0} + A_{1,0}J_1 + A_{0,1}J_2 + A_{2,0}(J_1)^2 + A_{1,1}J_1J_2 + \ldots + \sum_{15 + 6i + 10j\,=\,l} A_{i,j}(J_1)^i (J_2)^j \,]$$
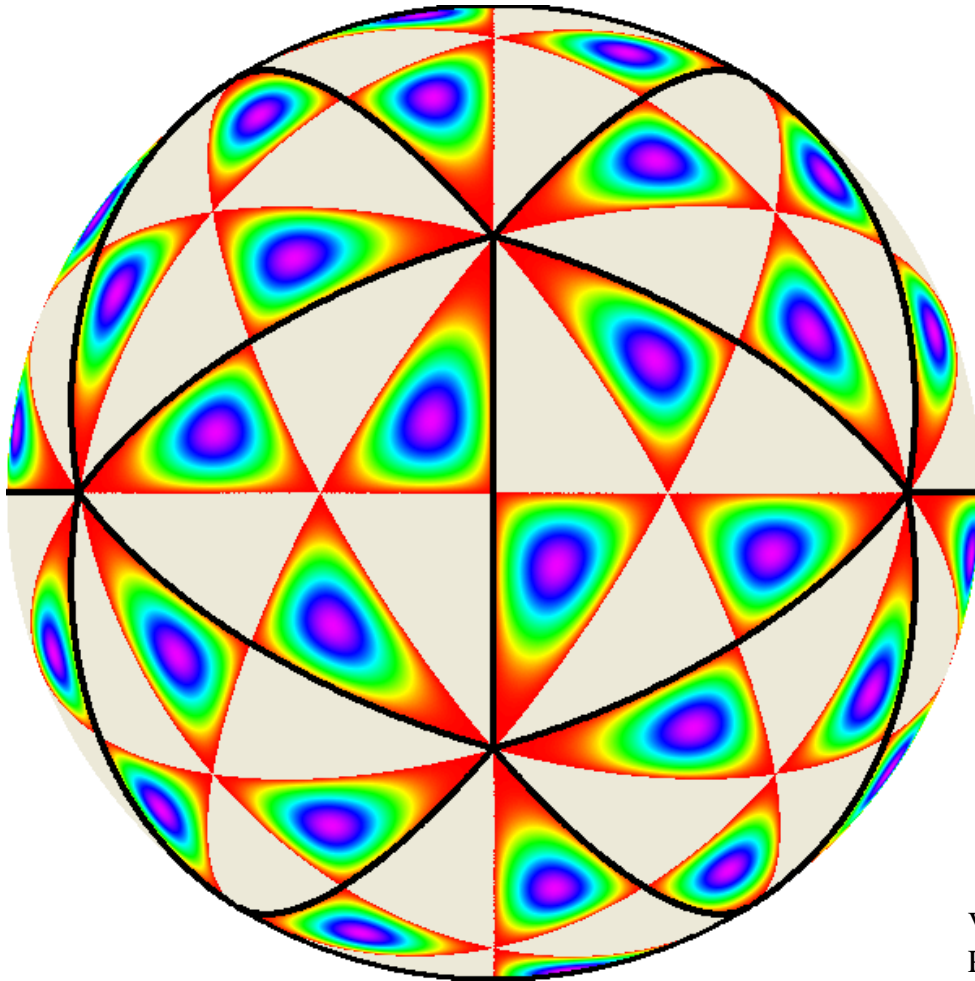
$\rightarrow$ $l = 15 + 6i + 10j$; $i, j = 0, 1, 2, 3, \ldots$

V.L.Lorman & S.B. Rochal,
Springer Lect. Notes, **11** (2015)
Group theory methods in virology

Irreducible icosahedral density functions

The explicit form is obtained by averaging of $Y^l_m(\Theta, \phi)$ over the I symmetry group

$$\Delta \rho_l(\Theta, \phi) \propto f_l(\Theta, \phi) = (1/60) \sum_G Y^l_m(\Theta, \phi)$$

Protein density distribution with the minimal possible wave number :
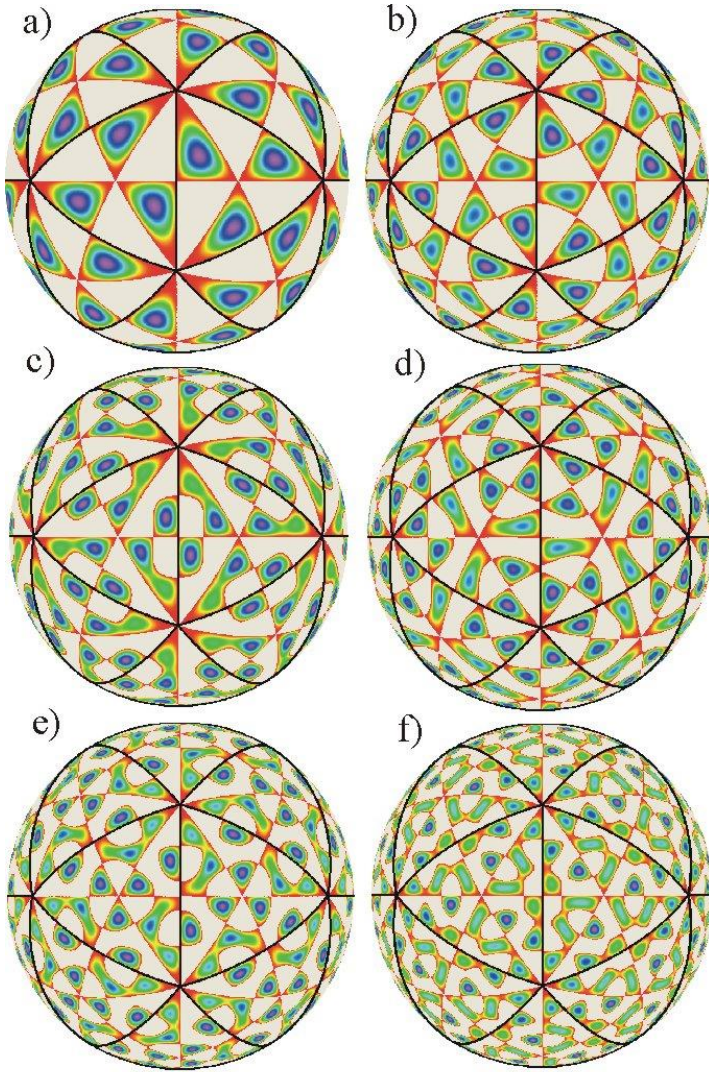**$l = 15$**

60 **equivalent** density maxima in **equivalent** environments

T=1 capsids

V.L. Lorman & S.B. Rochal , Phys. Rev. Lett., (2007),
Phys. Rev. B (2008), Phys. Rev. E (2009), Phys.Rev. Lett. (2012)

Research Highlights : Nature Nanotechnology

Classification of protein density functions

Figure 1

Density functions for several small icosahedral viruses

a) l = 15; T = 1 (Caspar-Klug structure)

b) l = 21; T = 2 (**non Caspar-Klug structure**)

c) l = 25; T = 3 (**non Caspar-Klug structure**)

d) l = 27; T = 3 (Caspar-Klug structure)
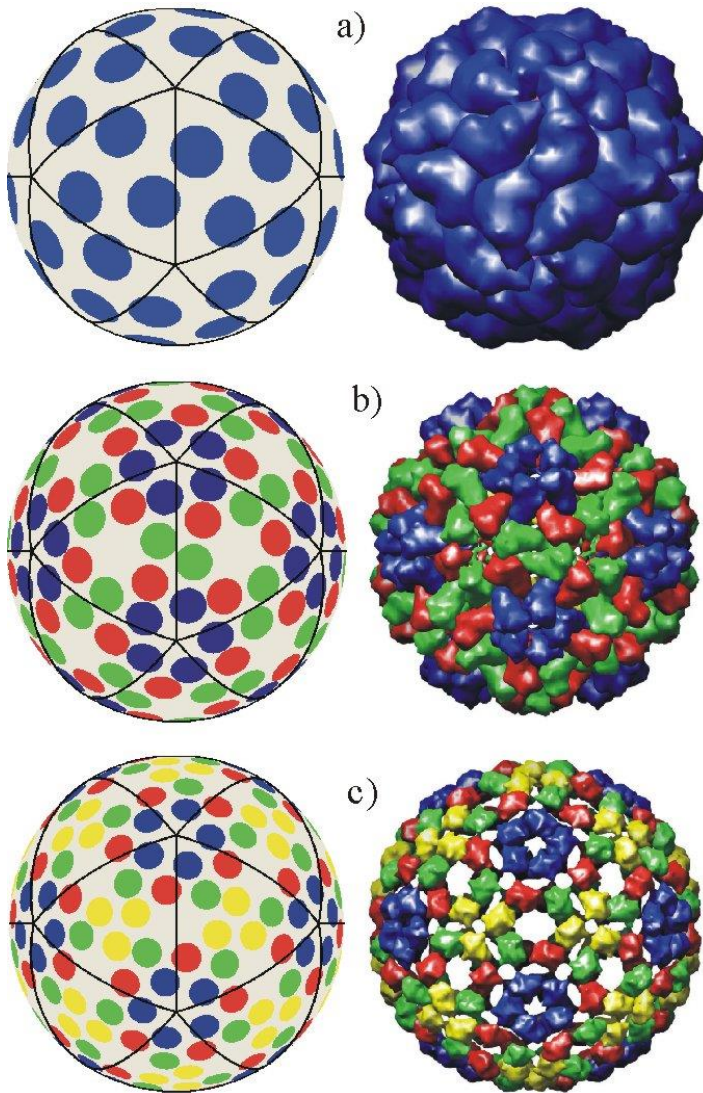
e) l = 31; T = 4 (Caspar-Klug structure)

f) l = 37; T = 6 (**non Caspar-Klug structure**)

Viruses can have the **same T** number but **qualitatively different organization** (see c and d)

Predicted protein distributions and viral structures

Examples of viruses which satisfy Caspar-Klug rules

a) $l = 15$; $T = 1$ → Satellite Tobacco Necrosis Virus
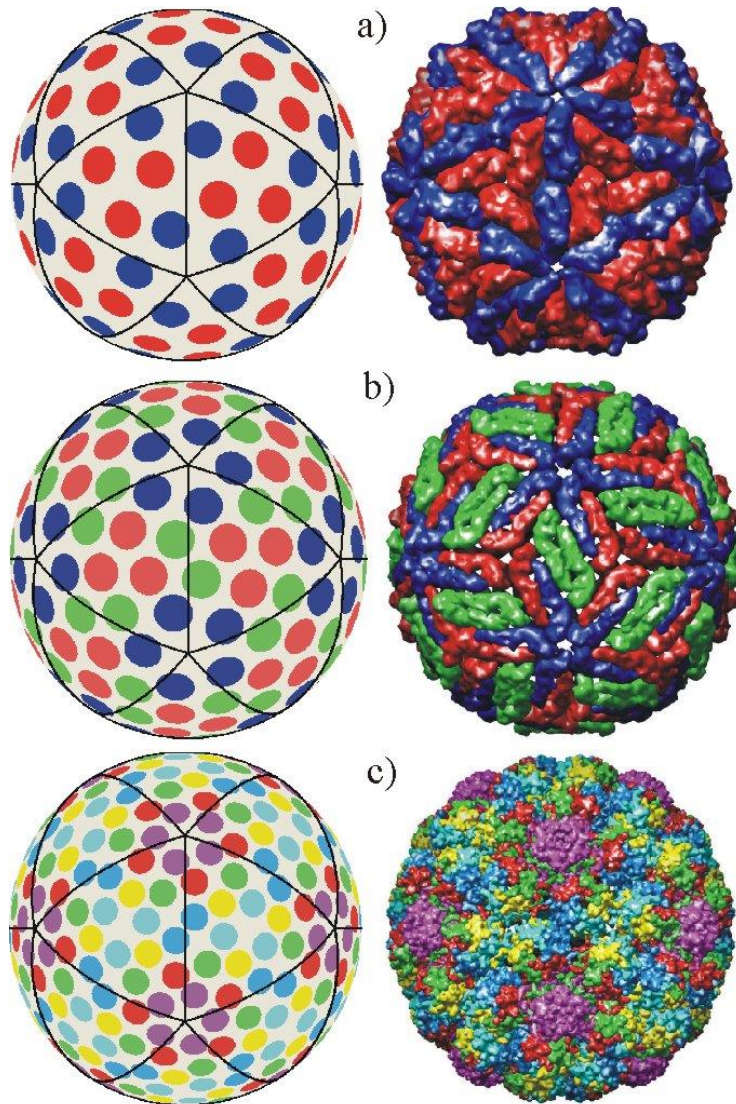
b) $l = 27$; $T = 3$ → Cowpea Chlorotic Mottle Virus

c) $l = 31$; $T = 4$ → Semliki Forest Virus

Small finite number of different environments generated by a single irreducible density function

Figure 2

Predicted protein distributions and viral structures

Examples of viruses which do not satisfy Caspar-Klug rules

a) $l = 21$; $T = 2$ $\rightarrow$ L-A Virus

$$T \neq h^2 + hk + k^2$$

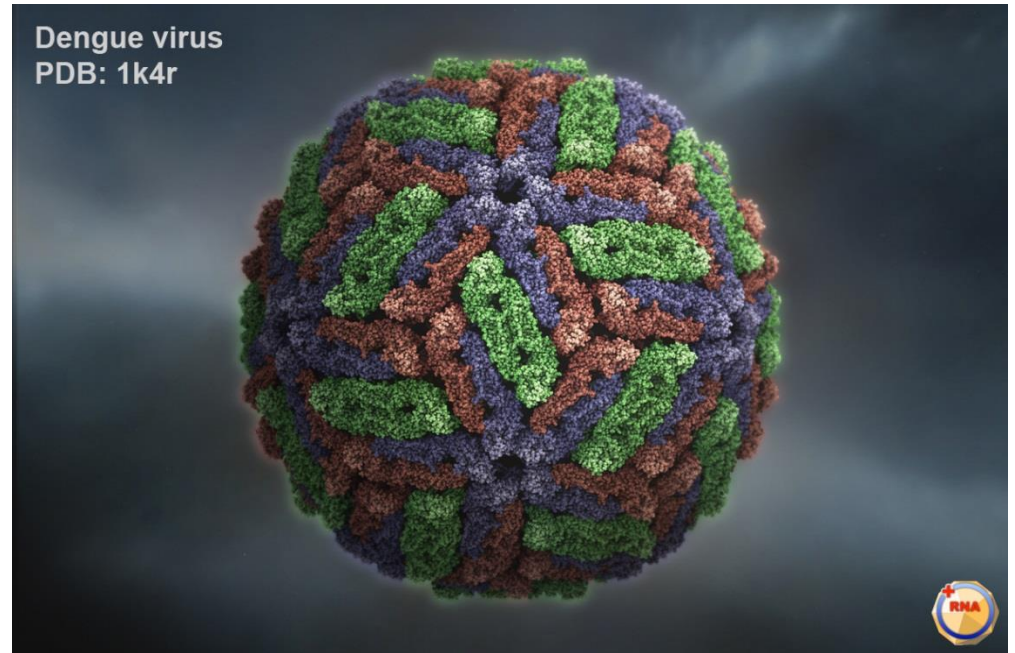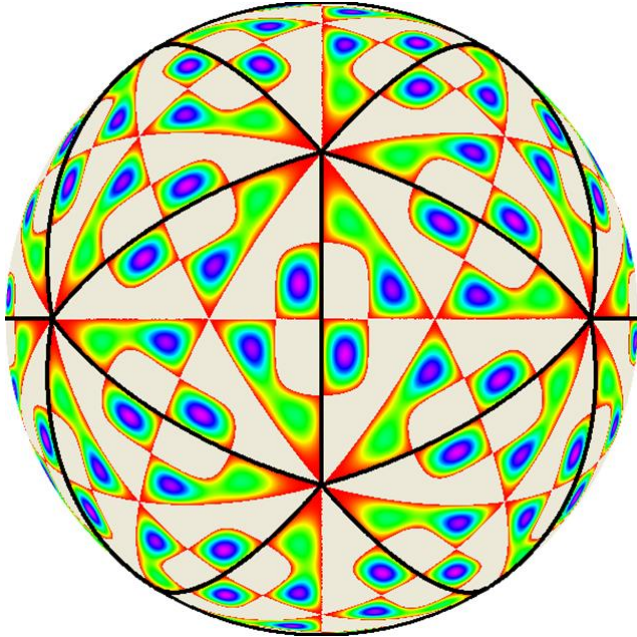b) $l = 25$; $T = 3$ $\rightarrow$ Dengue Virus

no hexamers

c) $l = 37$; $T = 6$ $\rightarrow$ Murine Polyoma Virus

$$T \neq h^2 + hk + k^2$$

Figure 3

Dengue Virus Capsid

T=3 environments; N= 180 proteins
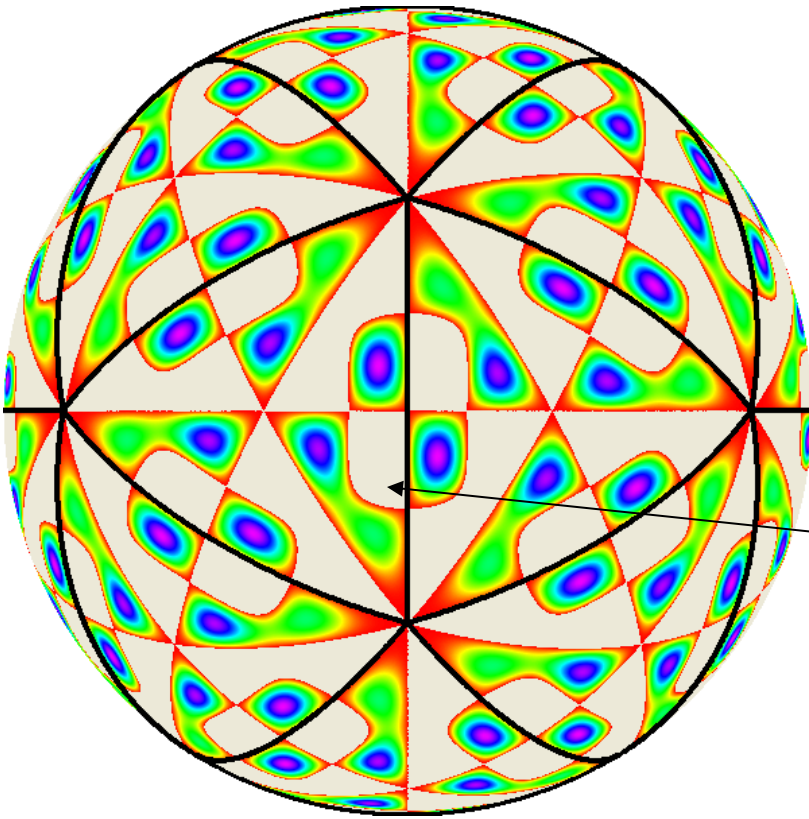**Typical rhombic motif without hexamers**

Icosahedral density distribution function with l=25

Capsid "breathing" effect

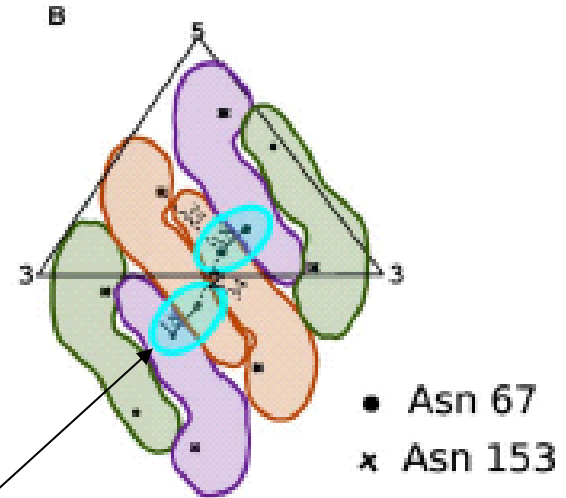K.A. Dowd, et al., J. Virol **88**, 11726 (2014), NIH & Purdue teams

Infectivity and structure

- ■ Asn 67
- ✕ Asn 153

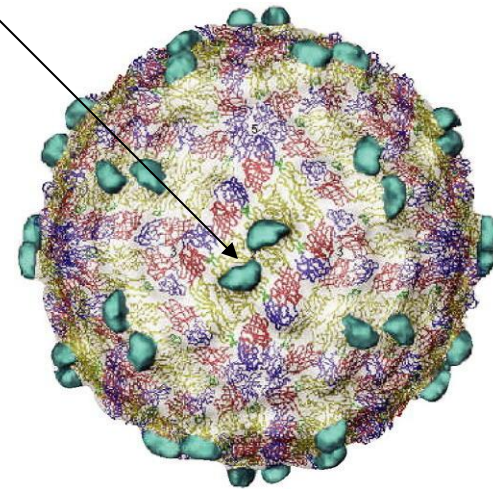Cell receptor domains bound to the **Dengue Virus** surface

Cell receptor carbohydrate recognition domains are bound to the **Dengue Virus** in the *deepest minima* of the icosahedral density distribution function with $l = 25$, *near its highest maxima*

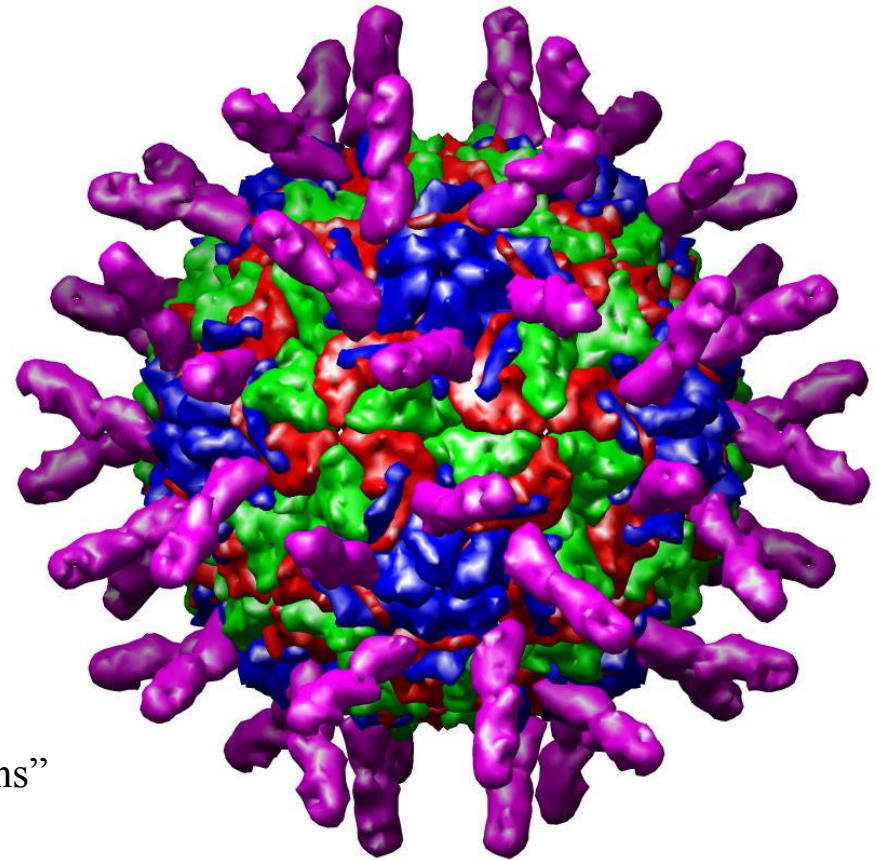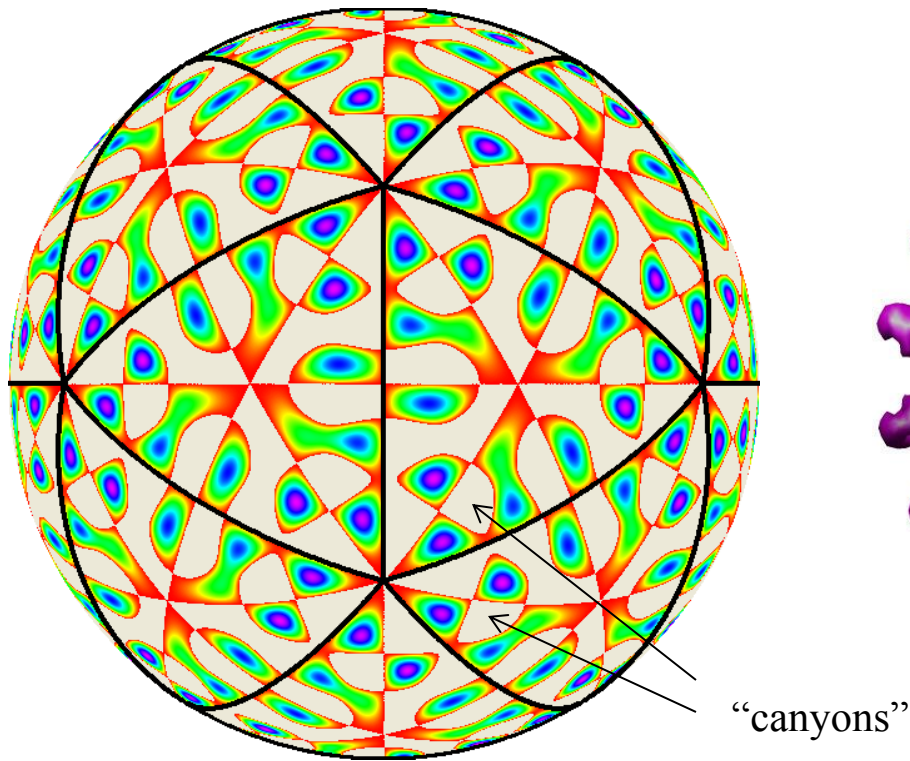$\Rightarrow$ **Relation with binding probability**

E. Pokidysheva et al. , Cell **124**, 485 (2006)
M. Rossmann's group, Purdue University
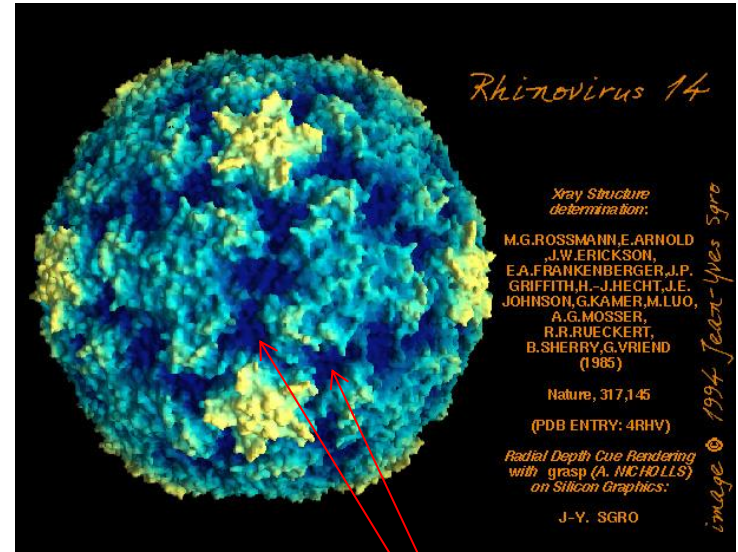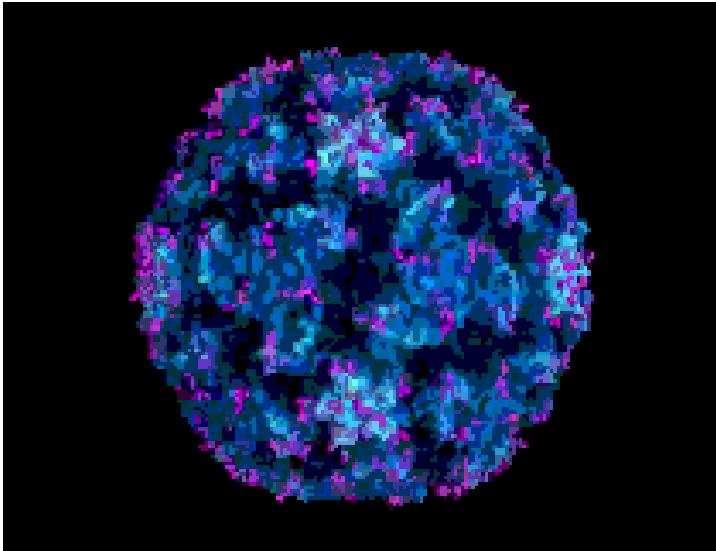
Infectivity and structure

"canyons"

ICAM-1 receptor domains are bound to the Human Rhinovirus Virus in the deepest minima of the icosahedral density distribution function with $l = 33$ forming narrow "canyons"
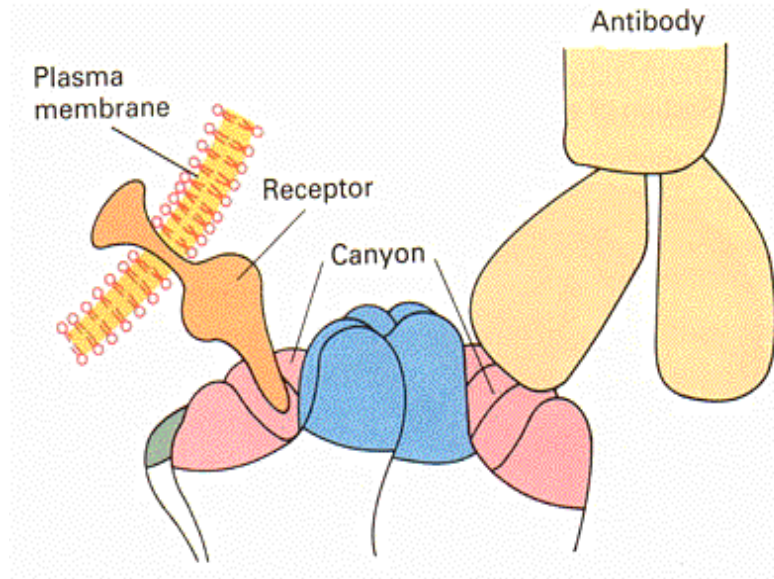
=> **Relation with binding probability**

Human Rhinovirus with the fragment of its cellular receptor ICAM-1 (intracellular adhesion molecule − 1)
ICAM-1 binds to the HRV « canyon »

Infectivity and structure

Rhinovirus 14

Xray Structure
determination:

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.RUECKERT,
B.SHERRY,G.VRIEND
(1985)

Nature, 317,145

(PDB ENTRY: 4RHV)

Radial Depth Cue Rendering
with grasp (A. NICHOLLS)
on Silicon Graphics:

J-Y. SGRO

image © 1994 Jean-Yves Sgro

"canyons"

Plasma membrane
Receptor
Canyon
Antibody

ICAM-1 binds to the HRV « canyon » too narrow for antibodies

M. Rossmann

Intermediate Summary

• Asymmetric protein assembly in capsids of small icosahedral viruses :
- Generalization of the Caspar & Klug theory of quasi-equivalence
- Generalization of the Landau theory of crystallization

• Selection rules and method for protein density distribution function construction
- Rules for protein distribution beyond the Caspar & Klug scheme
- Relation between protein density distribution and binding probability

in the same frame :

• Protein rearrangement across reversible procapsid-capsid transitions
  during maturation in certain viruses

• Capsid polymorphism in viruses, mutants and virus-like particles
- Different icosahedral shells formed by the same protein:
  Relevant density-wave parameters

• Non-icosahedral shells. Vault virus-like nanoparticles

Fundamental quantity conserved across the transition : Average wave vector of the density wave

Plane waves approximating density waves on a sphere : average wave vector $q = l/R$ related to a typical protein size
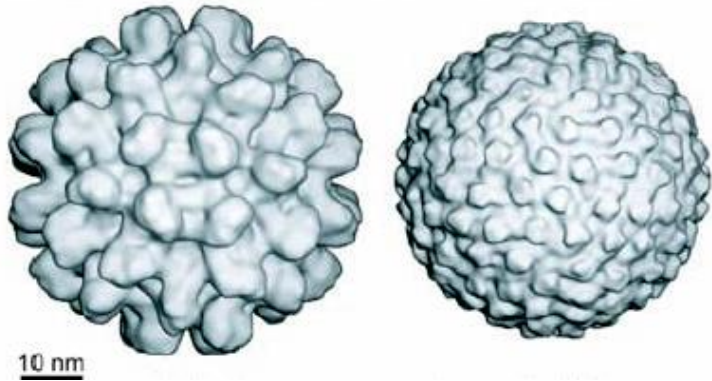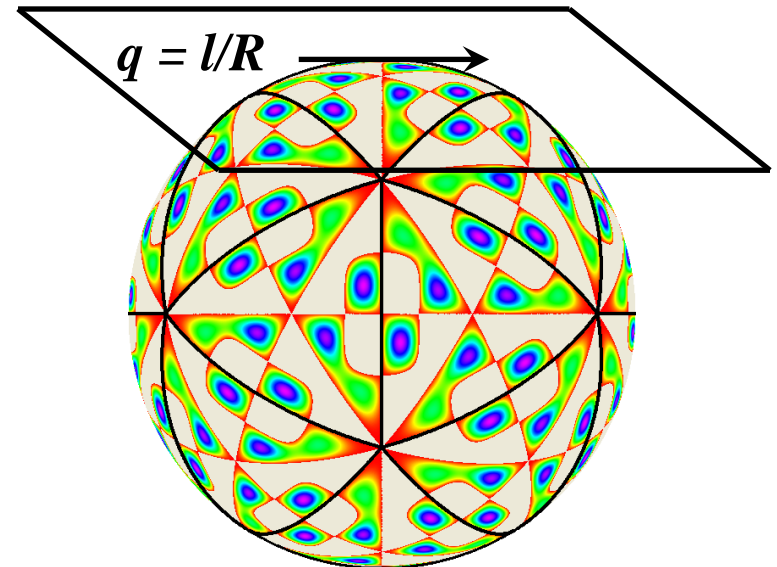

10 nm

Dengue Virus

Strong size variation : $R_{procapsid} / R_{capsid} \approx 13\%$ but $(l/R)_{procapsid} \approx (l/R)_{capsid}$

$l = 27; 2R = 59$ nm $l = 25; 2R = 53$ nm

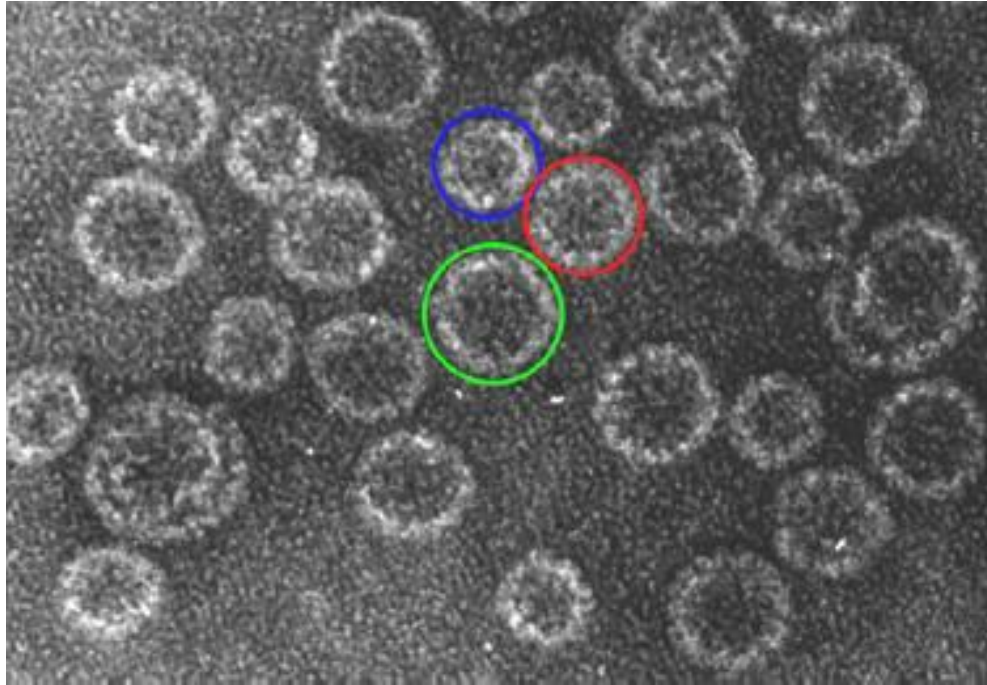Approximating plane wave : $\Delta \rho \sim \exp(i\mathbf{qr})$

To compare with the SAXS on the isotropic protein solution before the assembly. Protein "atomic factor".

$q = l/R$

Capsid polymorphism : Same proteins forming different capsids (with different number of environments) :

Example:
mutant Cowpea
Chlorotic Mottle
Virus (CCMV)

J.H. Tang et al.,
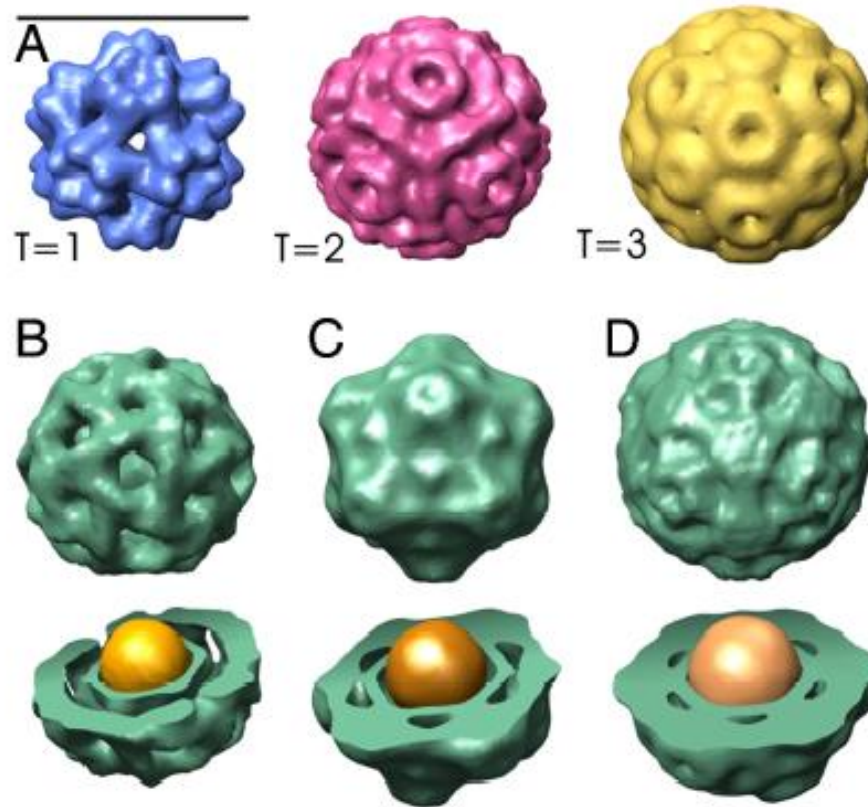J. Struct. Biol. **154**, 59 (2006)

Mutant Capsid Proteins lacking most of the N-terminal domain, ND34

Blue, red, and green circles show the three different types of particles corresponding to the $T = 1, T = 2,$ and $T = 3$ capsids, respectively.

Capsid type is "flexible" and may readily adapt to new requirements as the virus evolves

Virus-Like Particles using Capsid polymorphism

J. Sun et al., PNAS **104**, 1354 (2007)

Core = gold nanoparticle functionalized with the carboxylated PEG; Coat = BMV Capsid Proteins
Three different (but ≈ appropriate) nanoparticle sizes →
Three different VLP with coats ≈ T = 1; T = 2, and T = 3

Drug delivery optimization