Mathematical Virology

Using Mathematics to solve Real World Problems

08.11.2021

Benedikt Schmidt

Mathematical virology: a novel approach to the structure and assembly of viruses

- a paper by Reidun Twarock, Departments of Mathematics and Biology, University of York
- 2006
- goal: understand the structure and life cycle of viruses
- benefit: crucial impact on public health sector
    - design of antiviral therapeutics
- mathematical tools from the area of quasicrystals

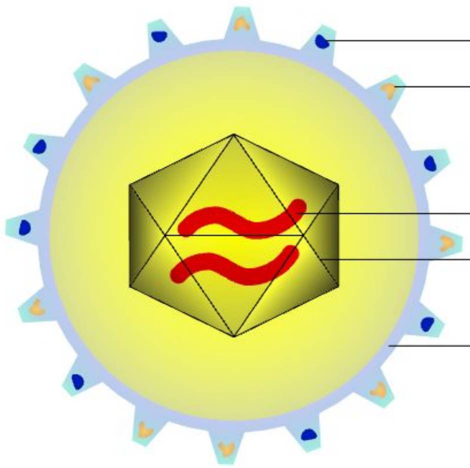
Source: Twarock R. Mathematical virology: a novel approach to the structure and assembly of viruses. Philos Trans A Math Phys Eng Sci. 2006 Dec 15;364(1849):3357-73.

Outline

- What is a virus?
  - Icosahedrons and rotational axes
- Caspar-Klug Theory
- Viral Tiling Theory

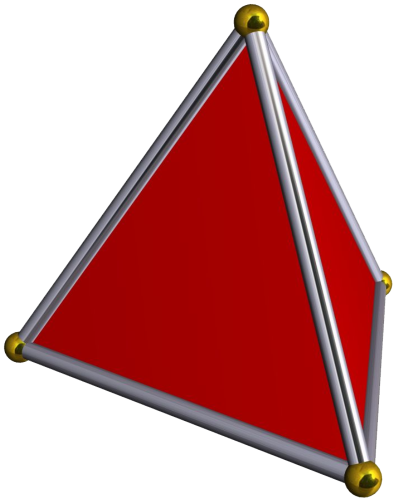
A virus is a submicroscopic infectious agent that replicates only inside the living cells of an organism

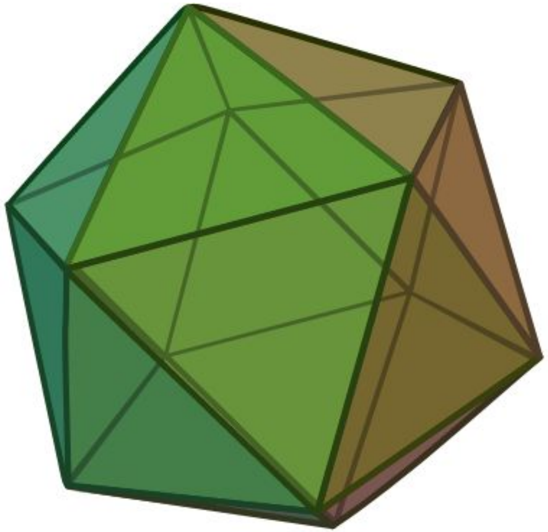
- Capsid: protein shell of a virus, enclosing its genetic material



Source: https://en.wikipedia.org/wiki/Capsid (13.10.2021)

a polyhedron is a three-dimensional shape with flat polygonal faces, straight edges and sharp vertices

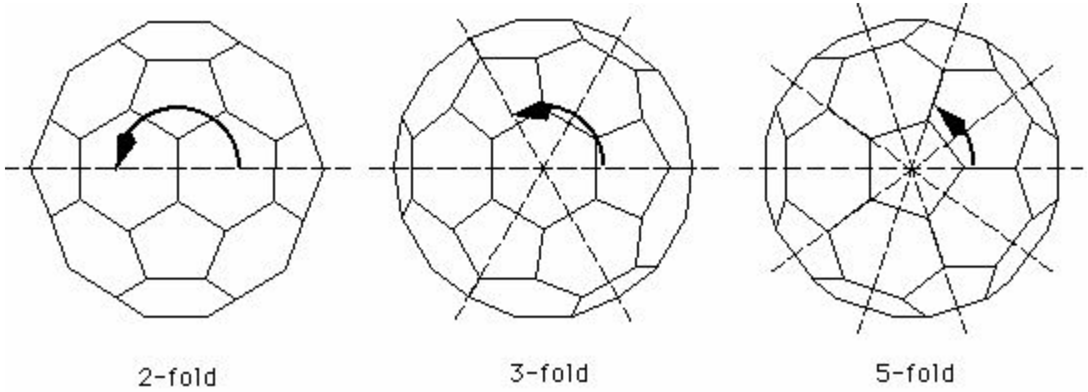




Source: https://en.wikipedia.org/wiki/Icosahedron (13.10.2021)

x-fold rotation axis

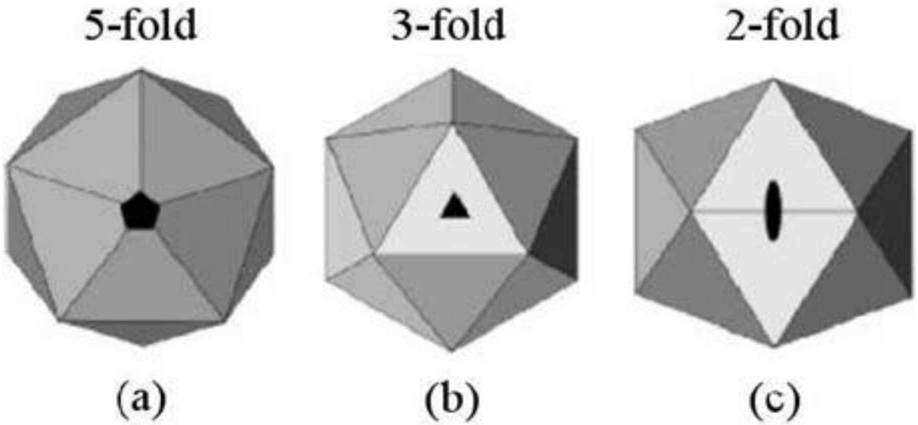
If an object appears identical x-times in a 360° rotation, then it has an x-fold rotation axis



Source: *https://www2.fkf.mpg.de/andersen/fullerene/symmetry.html (13.10.2921)*

Icosahedron: rotational symmetry axes

- 6 fivefold
- 10 threefold
- 15 twofold



Source: Luque, Reguera, Theoretical Studies on Assembly, Physical Stability and Dynamics of Viruses, Sub-cellular Biochemistry 68:553-95, 2013

Capsomeres

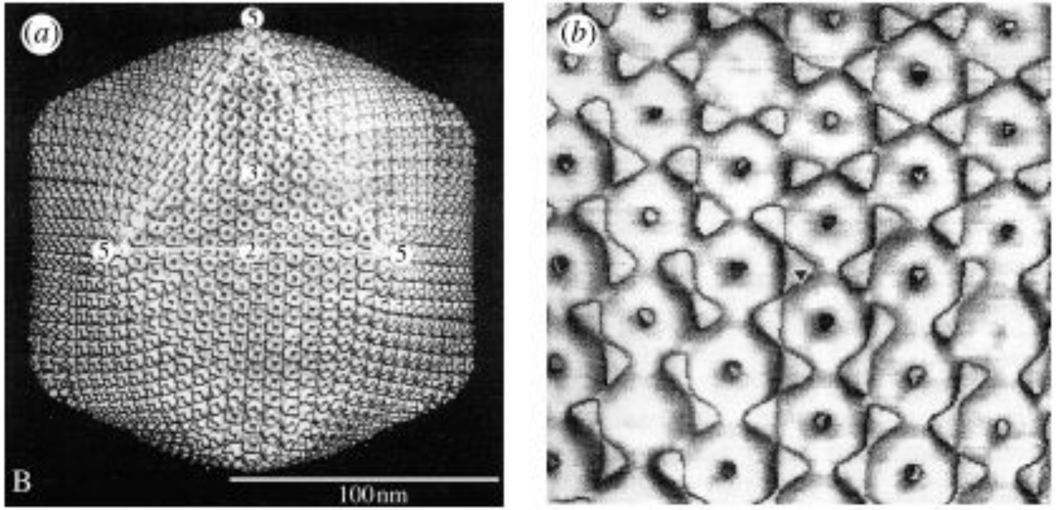


Figure 1. (*a*) Example of a viral capsid, with (*b*) capsomeres shown in magnification. Both figures are obtained from the Johnson Lab at the Scripps Research Institute.

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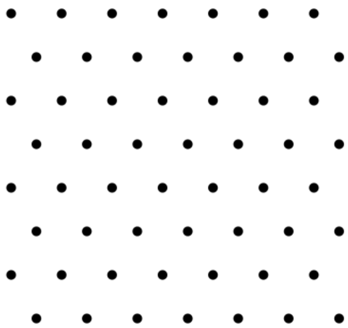
- **Caspar-Klug Theory**
- Viral Tiling Theory

Lattices

A lattice in $\mathbb{R}^n$ is a subgroup of the additive group $\mathbb{R}^n$ which:

- is isomorphic to the additive group $\mathbb{Z}^n$
- spans the real vector space $\mathbb{R}^n$



A lattice is the symmetry group of discrete translational symmetry in n directions

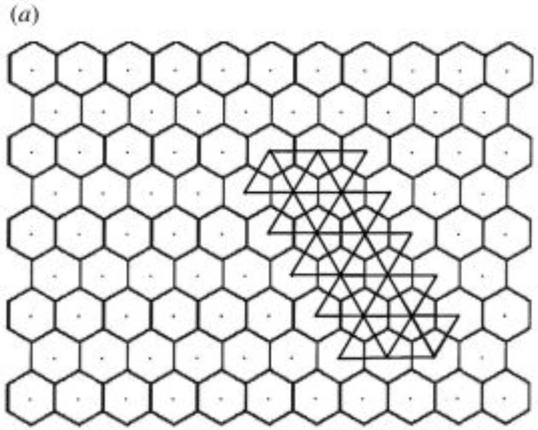
Examples:

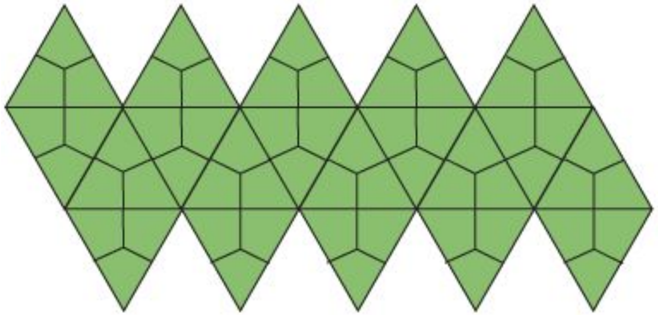
- for any basis of $\mathbb{R}^n$, the subgroup of all linear combinations with integer coefficients of the basis vectors forms a lattice
- subgroup $\mathbb{Z}^n$

Source: https://en.wikipedia.org/wiki/Lattice_(group) (27.10.2021)

Caspar–Klug theory I

- applicable to icosahedral viruses with protein subunits organized to a hexagonal surface lattice
- goal: predict locations and relative orientations of the protein clusters
- embeddings of the surface of an icosahedron into a hexagonal lattice
- blueprint for a viral capsid

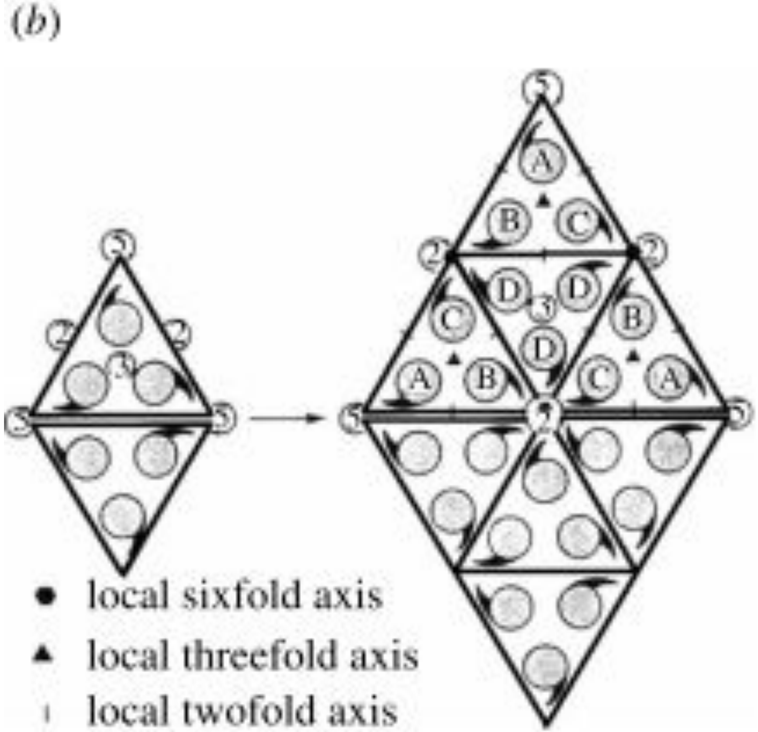


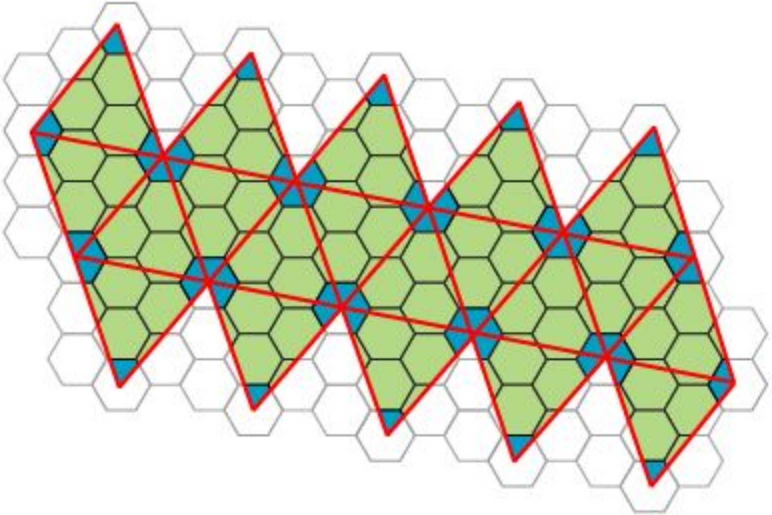


Source: https://viralzone.expasy.org/8577 (25.10.21)

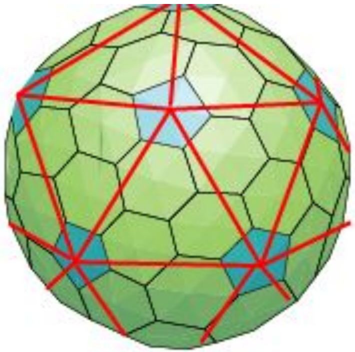
Caspar-Klug theory II

- triangulation
- 3 protein subunits per triangle
- subdivision of each triangle in 4 triangles

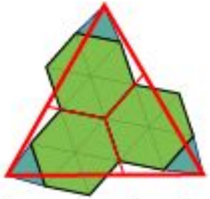




Flat view of T=7 icosahedral capsid. The blue hexagons are pentagons in the icosahedron, thereby curving the hexagon lattice into a sphere.



T=7 icosahedral capsid



Triangular facet

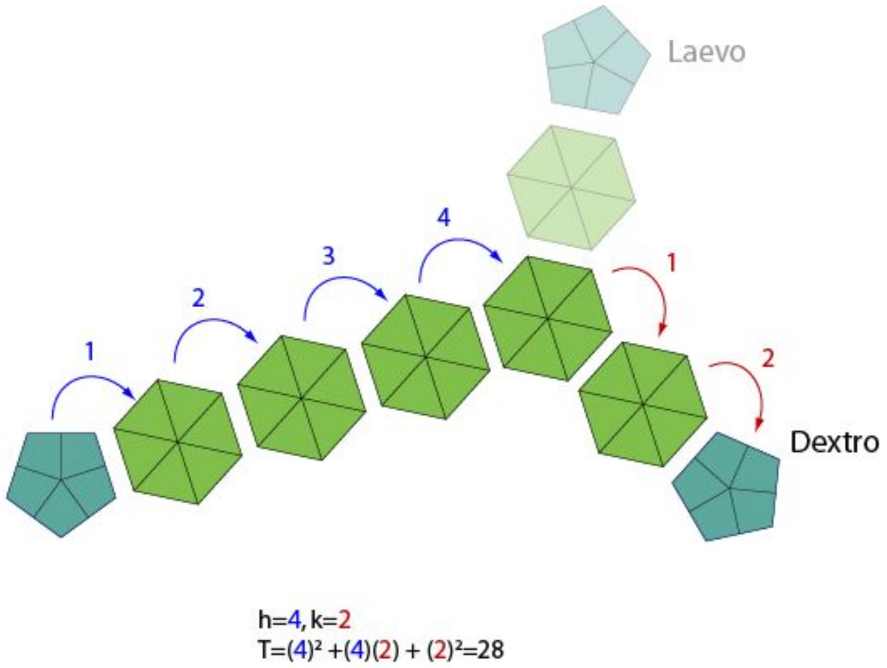
T=7 icosahedral assymetric unit

Source: https://viralzone.expasy.org/8577 (25.10.21)

Triangulation number T

- counts the number of symmetrically distinct but quasi-equivalent triangular facets in the triangulation per face of icosahedron

- $T = h^2 + hk + k^2$
  - h: number of units in straight line toward next pentagone
  - k: number of units shifted in either side to reach the next pentagon



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- **Viral Tiling Theory**

Viral tiling theory I

- differs from the Caspar–Klug theory by the introduction of more general types of surface lattices
- incorporates Caspar-Klug theory
- describes how surfaces can be tessellated in terms of a set of building blocks called tiles
- tilings inferred via projections from higher-dimensional lattices

Coxeter Group H_3

- group consisting of 120 Elements
- action of these elements can be represented as reflections and rotations in the three dimensional space
- can transform one single point of space into 120 different points
- result is a geometrical object that consists of 120 vertices
- generalized lattices can be inferred from H_3
- rotational symmetries of the icosahedral group are generated by the reflections r_j in H_3

Source: https://geometricgroups.jimdofree.com/group/coxeter-h3/ (25.10.21)

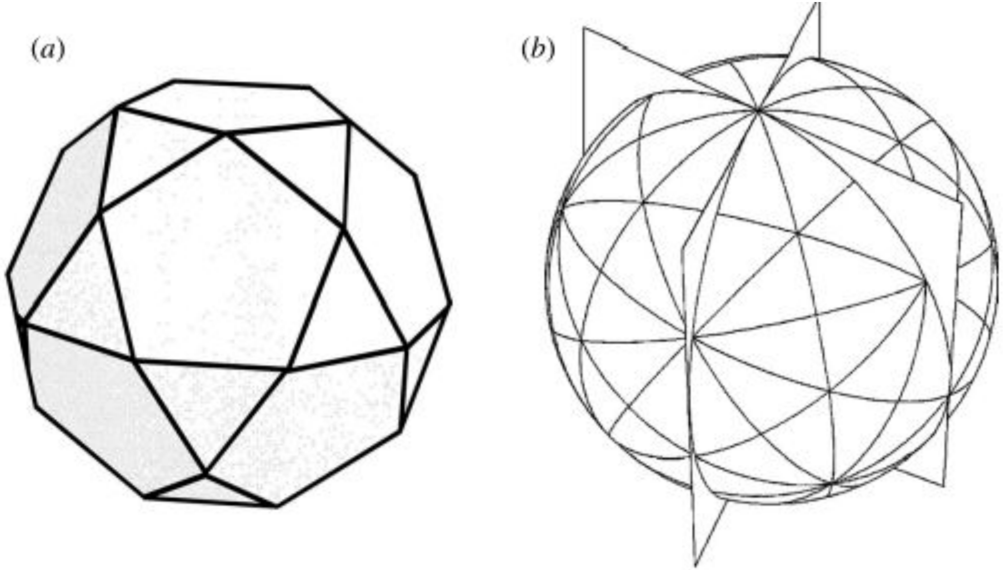


Figure 3. (*a*) The root polytope of H_3 and (*b*) examples of the reflection planes encoded by the root vectors.

Viral tiling theory II

- vectors in the root system of H_3 are related to a particular choice of basis vectors of the icosahedrally symmetric lattice D_6 via projection
- hence we can work with the root system of H_3 directly
- idea: extend the root system of H_3 by a further vector
- new operation
- iterated action leads to pint sets with icosahedral symmetry
  - starting point for the construction of generalized grids with icosahedral symmetry

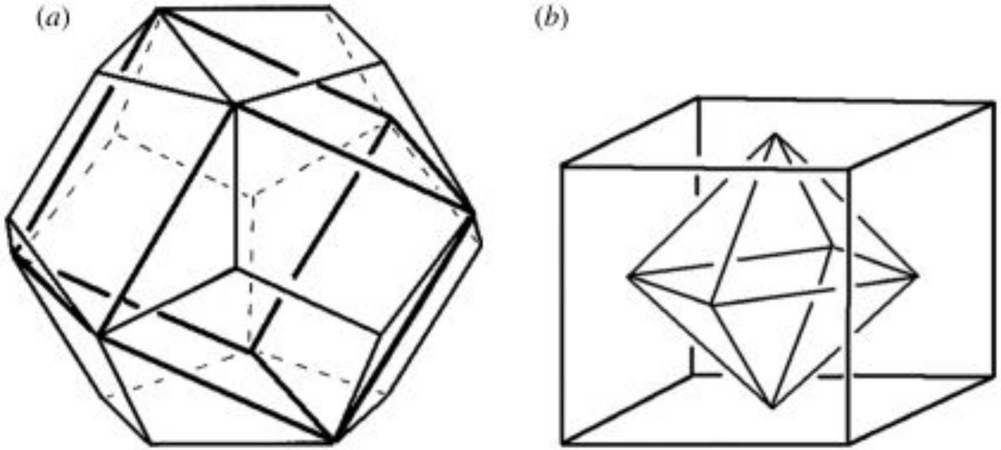


Figure 4. (*a*) A cube inscribed into a dodecahedron and (*b*) a tetrahedron inscribed into a cube.

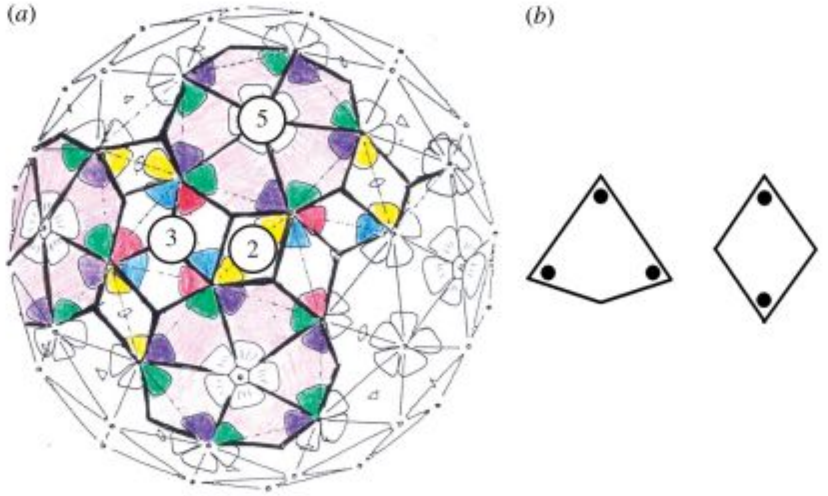
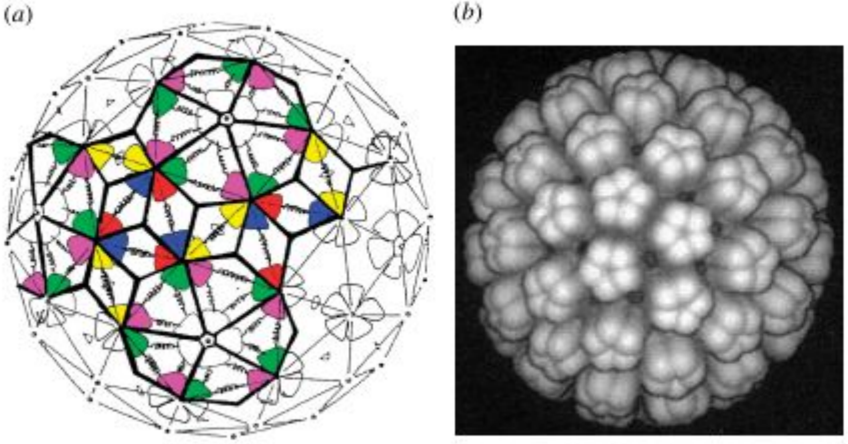


Figure 5. (*a*) The tiling representing the viral capsids of polyomavirus and simian virus 40 and (*b*) the corresponding tiles.

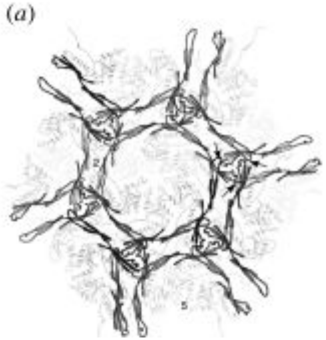
Predictions of viral tiling theory

- predicts the locations of the protein subunits
- also specifies the locations of the inter-subunit bonds between proteins in different capsomeres



Applications of viral tiling theory

- Manipulating the assembly of viral capsids
- classification of tubular malformations in viruses
- crosslinking structures



Outlook

- create more accurate assembly models for various viruses
  - anti-viral drug design
- assembly of RNA viruses
- modelling physical properties
- understanding genome packaging

Summary I

Protein containers encapsulating viral genomes are salient features of virus architecture

In most viruses, these containers are organized with icosahedral symmetry for reasons of genetic economy, and group theory can therefore be used to better understand virus geometry

Twarock has developed affine extensions of icosahedral symmetry to derive predictive information on the organization of viruses at different radial levels

Credits to Phlipp Mekler

Summary II

Since icosahedral symmetry is non-crystallographic in three dimensions, i.e. is not compatible with periodic lattices, standard techniques for affine extensions do not apply in this case

Twarock has developed a new framework for the construction of such affine extensions in the context of non-crystallographic Coxeter groups

Credits to Phlipp Mekler