Caspar and Klug – Physical Principles in the Construction of Regular Viruses

§The Functional Organization of Virus Particles

1. infective agent is high molecular weight RNA or DNA
2. nucleic acid molecule is contained in a protective protein package

Since nucleic acid element is what synthesizes the proteins, the smaller the nucleic acid, the less proteins. Some should only be able to code 2 or 3 protiens

“The infectivity of a virus must persist in a latent state outside the host cell” 1C2P1 – thus nucleic acid must be contained in a protective shell

There are only a limited number of efficient designs possible for a biological container which can be constructed from a large number of identical protein molecules. – Helical tubes or Icosahedral shells

§Simple or Minimal Viruses

Based on Crick and Watson – “Small viruses are built up of identical protein subunits packed together in a regular manner to provide a protective shell for the nucleic acid.” – 2C1P1 idea is the nucleic acid is limited, so use less of it to make a small repeated protein. Confirmed by X-Ray diffraction and electron microscopy

C&W mistake, not all small. 2C1P2 C&K instead use term “simple” for “those viruses which have a regular particles structure and have as their main chemical components only nucleic acid and protein.

2 types – Rod – isometric “sphere” or icosahedral virus

§Grades of Structural Organization in Viruses

talks about grading viruses, from nucleic acid only, to simple, to complex. NO RELEVANCE

§Sub-Assembly and Self-Assembly

Last sections purpose is to say large structures are built out of small ones.

“The components of a virus … can be synthesized separately by a sub-assembly process and then associated … to form a complete system.” – allows control. Mistake means throw out sub-unit not the whole

self-assembly: coded into the sub-units is the structure for the whole. “The protein subunits and the nucleic acid chain spontaneously come together to form a simple virus particle because this is their lowest energy state.” This state is identical since the subunits are identical. “Arragning identical units in identical environments necessarily produces a symmetrical structure, and there are only a geometrically limited number of kinds of symmetry” – 3C2P1

“identical” environments, not really only need that the lowest energy structure has the maximum number of stable bonds.

Again, unique (misformed) subunits would require unique environments not provided by the molecule on whole and thus would not be incorporated. 4C1P1

§Structural Studies

Studied Xray of TMV (helical) to get idea of self assembly. Applied to spherical.

§§HELICAL VIRUSES

§Tobacco Mosaic Virus

Proteins (all indistinguishable) organized in helix with RNA attached interior in very specific way.

Protien plus RNA is structurally stronger than separate.

Protein bonds strongest – hydrophobic bonds important, studied polymerization-depolymerization reaction

Salt links between RNA and protein

RNA in protein is protected against ribonuclease and temperature changes 5C1P3 – *this is actually cool and can be used to explain why capsids matter*

§Helical Symmetry

packing subunits in identical environments – identical bonds – necessarily results in symmetrical structure. – BACKWARDS – a symmetrical structure can be divided into identical geometric units (the asymmetric units) which are all equivalent – so consider the symmetries possible to build a structure, necessarily will get equivalent subunits – 5C2P1/2

TMV – each subunit has 3 bonds, fix the distance and angle of the bonds and it determines the structure completely.

Roll up plane lattice (as described above) into a cylindrical surface, does not disturb bonding geometrically.

§Physical Considerations

RNA determines length

§Flexible Rods

viruses with helical symmetry but are flexible, bendy. The local bonds does not change much as the helix axis bends, so the bonds hold is **quasi-equivalent** environments – 7C2P1 *First mention of quasi-equivalence*

X-ray studies by Caspar and Holmes of dahlemense strain of TMV show that perterbations can occur in subunit interactions with no failure of shell. – 7C2P2

§§ICOSAHEDRAL VIRUSES

§Cubic Symmetry

Crick and Watson – out of all of the types of symmetry possible for a structure of limited extent, only the cubic point groups were likely to lead to an isometric particle.

Importance of cubic symmetry – The three coordinate directions in space are not independent, but instead equivalent. 7C2P5

3 types of cubic symmetry – tetrahedral (12), octahedral(24), and icosahedral(60). Icosahedral has largest number of subunits, which means units could be smallest.

§Icosahedral Symmetry

Crick and Watson did not assess merits of symmetry types. Biological evidence that icosahedral symmetry is preferred in nature

-X-ray diffraction of Caspar (1956) on tomato bushy stunt virus

-Klug, Finch, Franklin (1957) turnip yellow mosaic virus

Both showed they have cubic symmetry and are icosahedral

Regular Icosahedron

-electron microscope observation of William and Smith (1958) Tipula iridescent virus

-X-ray diffraction by Finch and Klug (1959) poliovirus

At this point thought was icosahedral allowed for largest number of subunits

“if one desired to ‘enclose’ a space around a central point by a set of domains on a closed surface, the ratio of the number of domains to the surface area covered is smallest if icosahedral symmetry is employed” – 8C2P3 – efficiency

§Experimental Background

1. X-Ray diffraction results: (turnip yellow mosaic virus, Klug and Finch 1960 and tomato bushy stunt virus, Caspar, Finch, and Klug) show that icosahedral symmetry is present down to the molecular level in most of particle. But if protein shell has strict icosahedral symmetry then it must be made up of 60 or a multiple of 60 subunits (they called structure unies).
2. Chemical evidence: Subunits have all been found to be identical within a given virus and molecular weights are limited.
3. Electron microscope observations: adenovirus (Horne et al 1959) turnip yellow mosaic virus (Huxley and Zubay 1960, Nixon and Gibbs 1960). The number of morphological units observed is never 60 or a multiple of 60. In most cases is greater than 60.

§§THE GEOMETRY OF ICOSAHEDRAL VIRUSES

§The Problem

Using observed molecular weight, approximating shape, shell of 60 units is only as large as the smallest virus.

Established for turnip yellow mosaic and wild cucumber mosaic virus that number of subunits is above 60

Problem, strict equivalence would allow for only multiples of 12,24,60 subunits to cover a sphere.

§Quasi-Equivalence

Solution inspired by geometric principle applied by Buckminster Fuller in construction of geodesic domes

Only one way in which iso-dimensional shells may be constructed from a large number of identical protein subunits and this necessarily leads to icosahedral symmetry.

Shell has same bonds throughout but in slightly different environments (biology fits rules of minimum energy, not mathematical concepts) - 10C2P2

Allow for bending of 5 degree either way from standard per Pauling 1953 – 10C2P3

§Folding of Plane Nets

Triangulate sphere into as equal subdivision as possible – generates multiple quasi equivalent packings.

Consider the triangulations of the sphere as derived from the folding up of a plane equi-triangulated net onto a polyhedron with icosahedral symmetry. – why is in Caspar and Klug 1963 which I cant find.

Shown by Pawley 1962 that there are only two types of plane nets (w/o mirror symmetry) which can be folded onto the surface of convex polyhedral and maintain nearest neighbor contact. Lattices with 4-fold and 6-fold rotational symmetry (so based on square and equilat tri) – 13C1P1

Square can only make cube – strain is great if real units are 3D

Triangular net can make tetrahedron, cube, or icosahedron.