

**Images displaying a number of structures and techniques on biophysics studies into macromolecules referenced as 'Dr Fuller'.**

**Contributors**

Fuller, Watson, b.1935

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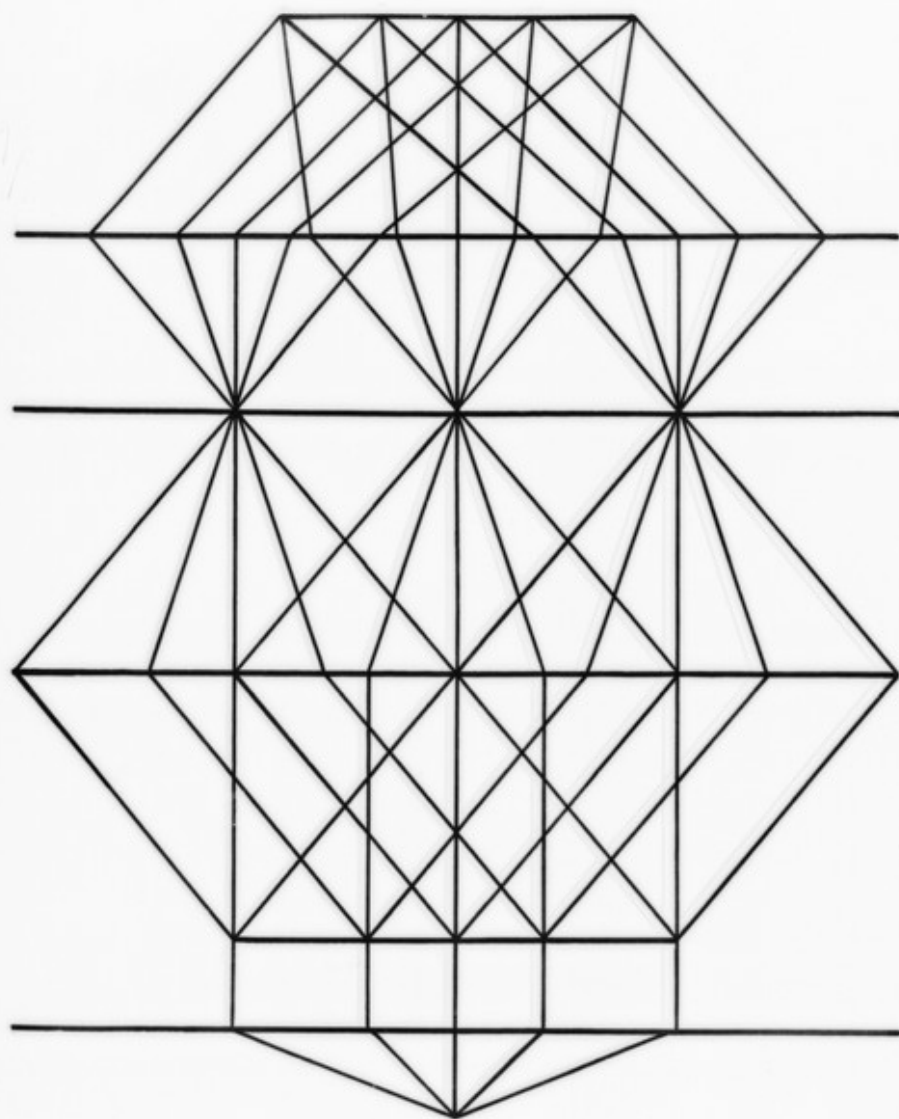
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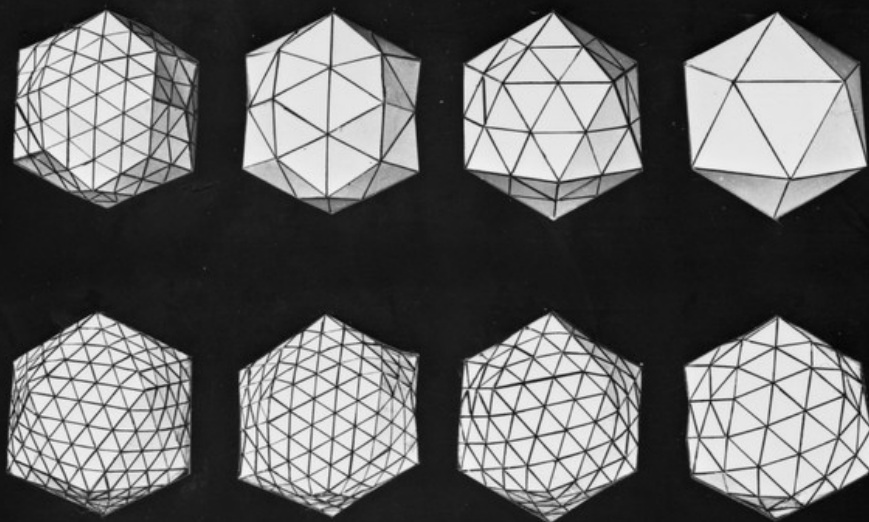
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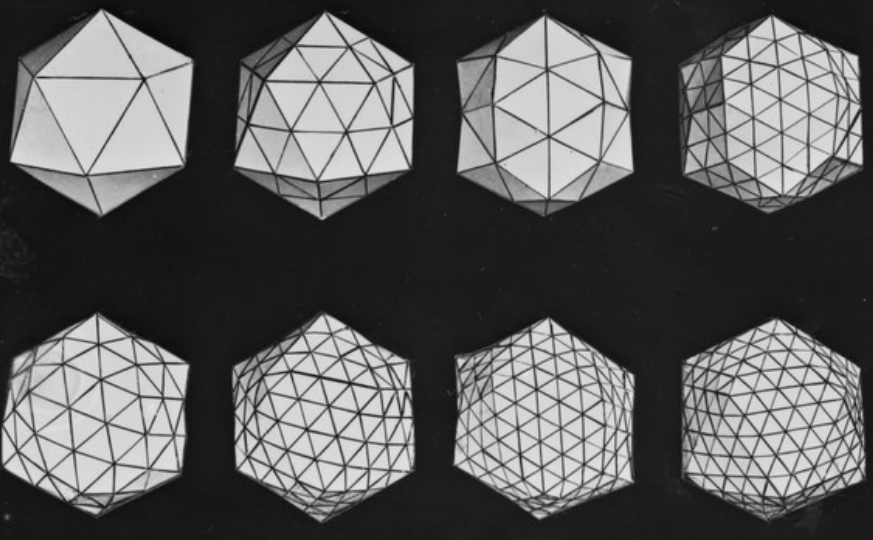
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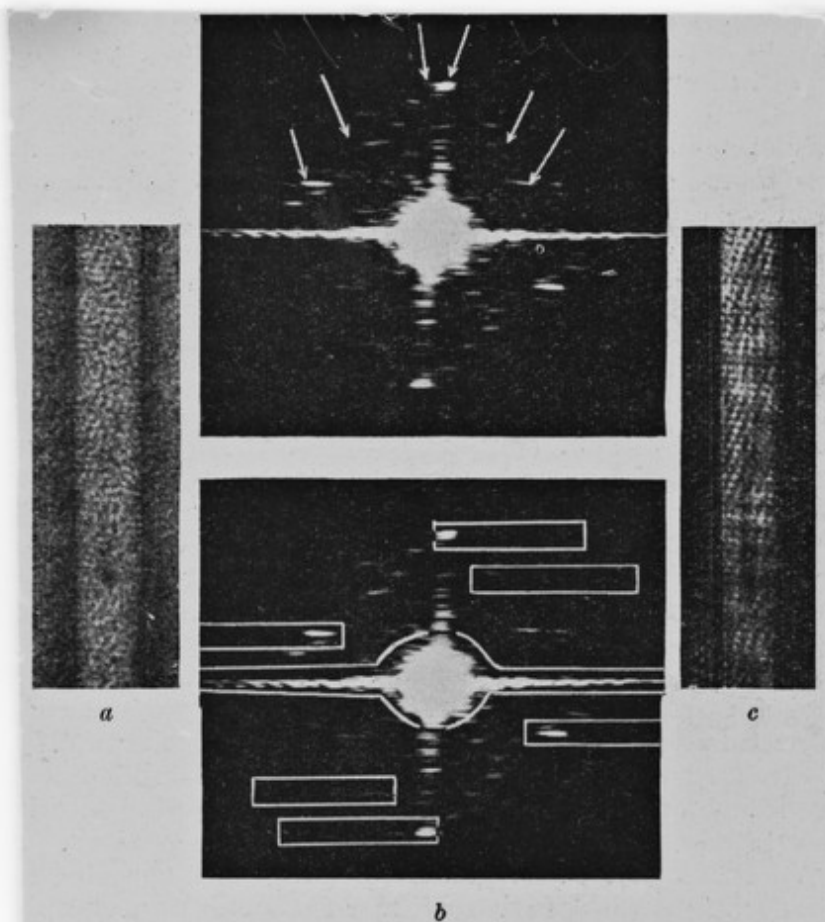


Fig. 4. *a*, Electron micrograph of a negatively stained particle of tobacco mosaic virus (ref. 7). Patches of stain are visible in the central hole. *b*, Diffraction pattern of *a* ( $\times 1.6$ ). The arrows indicate the position of the spots which are constant features of the diffraction patterns of TMV images (ref. 4). The other spots do not recur in all patterns and are attributed to irregularities in the staining and non-systematic perturbations in the particle structure. The asymmetry between the left and right sides of the 69Å and 23Å layer lines shows that in this particle the contrast is unequally developed on the two sides. That is to say, the image is largely one-sided. *c*, Filtered image of *a*, admitting only the diffracted rays shown boxed in the lower photograph in *b* ( $\times 330,000$ ).

by the stain determines the position and hence the allocation of the diffracted rays. Thus before any filtering can be carried out, the geometry of the particle lattice must be solved. But the point is that the information carried by a diffracted ray is contained not only in its

array, it is also in the phase of this unit.

Second, the length shortens up the intensity of the filtered image. The images are fifty times as bright as in Figs. 4*b* and *c*.

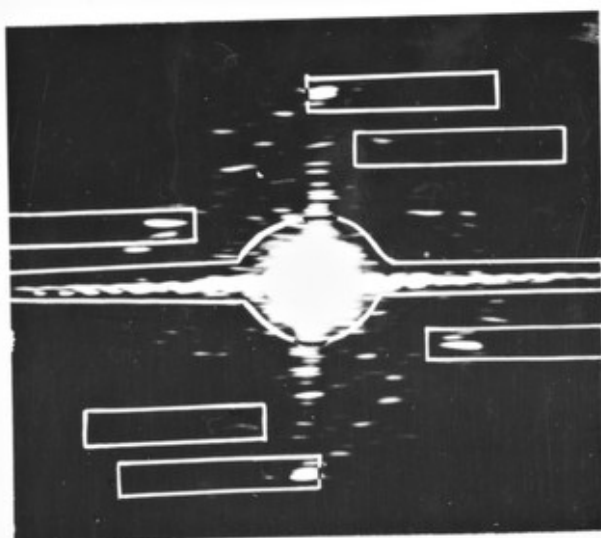
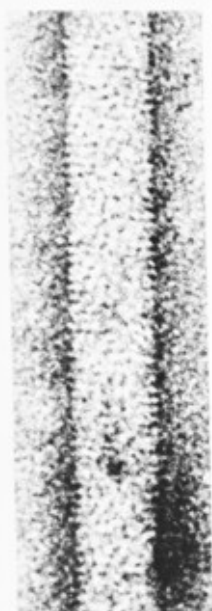
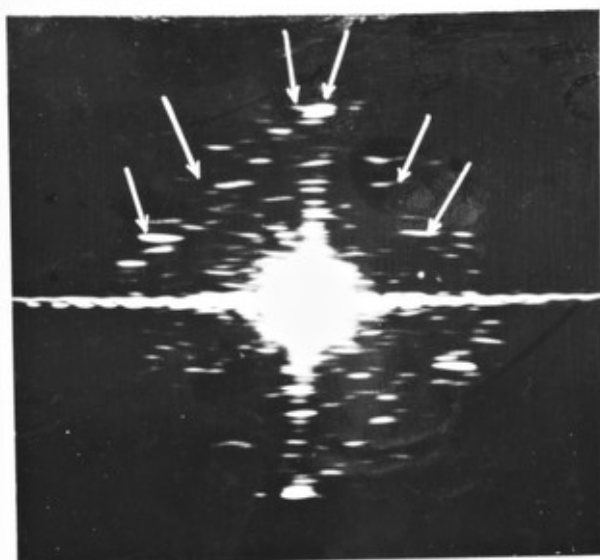
Two approaches to one of the filtering problems known from X-ray data are shown in Figs. 4*b* and *c*.

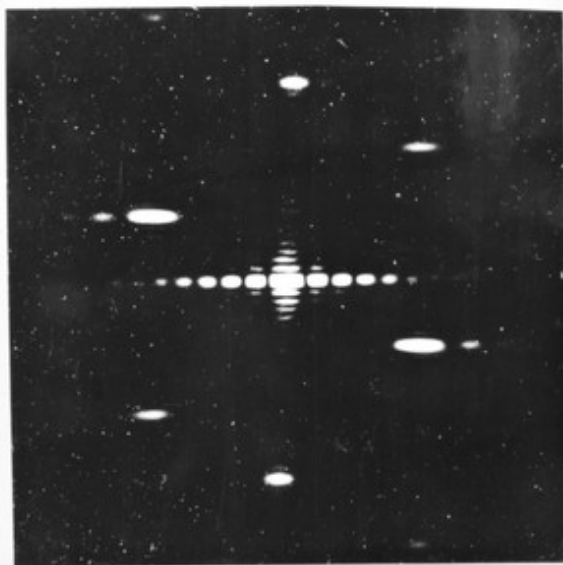
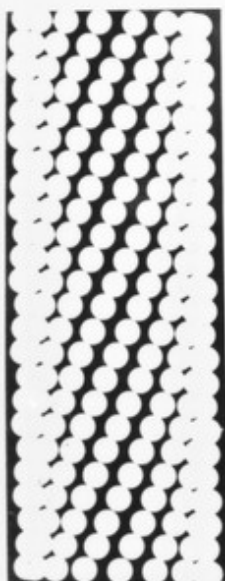
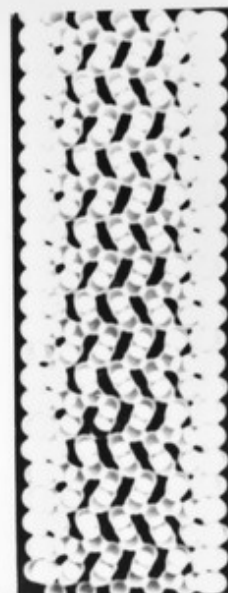
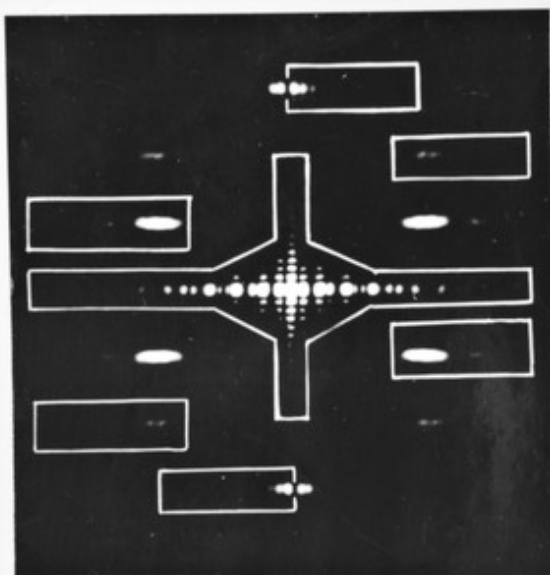
The subunit is reproduced. Its diffraction pattern can be seen in the two side-by-side images. The dominant features are the two side-by-side images.

The diffraction filter are shown in only one whether or not they were reduced to the same size as shown in Figs. 4*b* and *c*.

The filtered particle structure shows the grooves and sub-units. The protein is shown and what is from the bottom of the sub-unit. The sub-unit is shown in the filtered image.

The helical structure is prepared in the filtered image.







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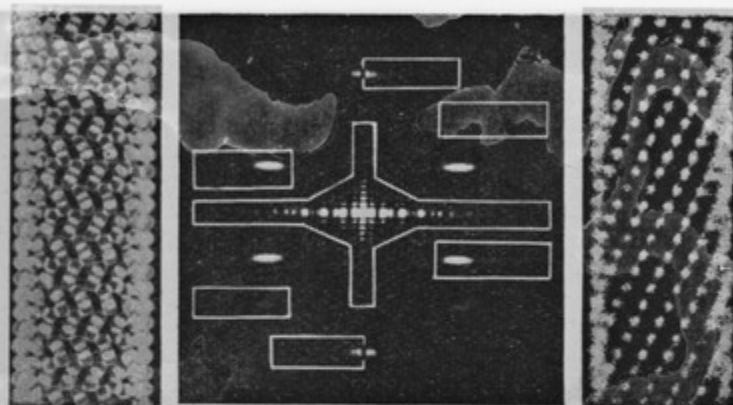
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the TMV particles  
lattices.

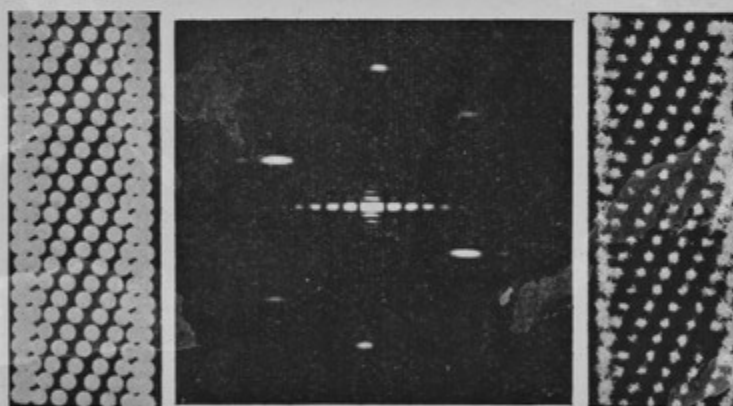
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figure are related



**a**, Positive replica of a photographic transparency representing the orthogonal projection of a helical structure on to a plane through the axis. The parameters of the structure have been chosen so that they are the same as those of tobacco mosaic virus at a radius of 100 Å. **b**, Fraunhofer diffraction pattern of **a** ( $\times 1.5$ ). **c**, Filtered image of **a**, obtained by admitting through the imaging lens only the diffracted rays indicated by the boxes in **b**.



**a**, Projection of one side only of the helical structure of Fig. 2a. **b**, Diffraction pattern of **a** ( $\times 1.5$ ). Note that the principal diffraction spots lie approximately at the vertices of a lattice. **c**, Image of **a** without any filtering. The loss of quality arises from imperfections in the optical system.

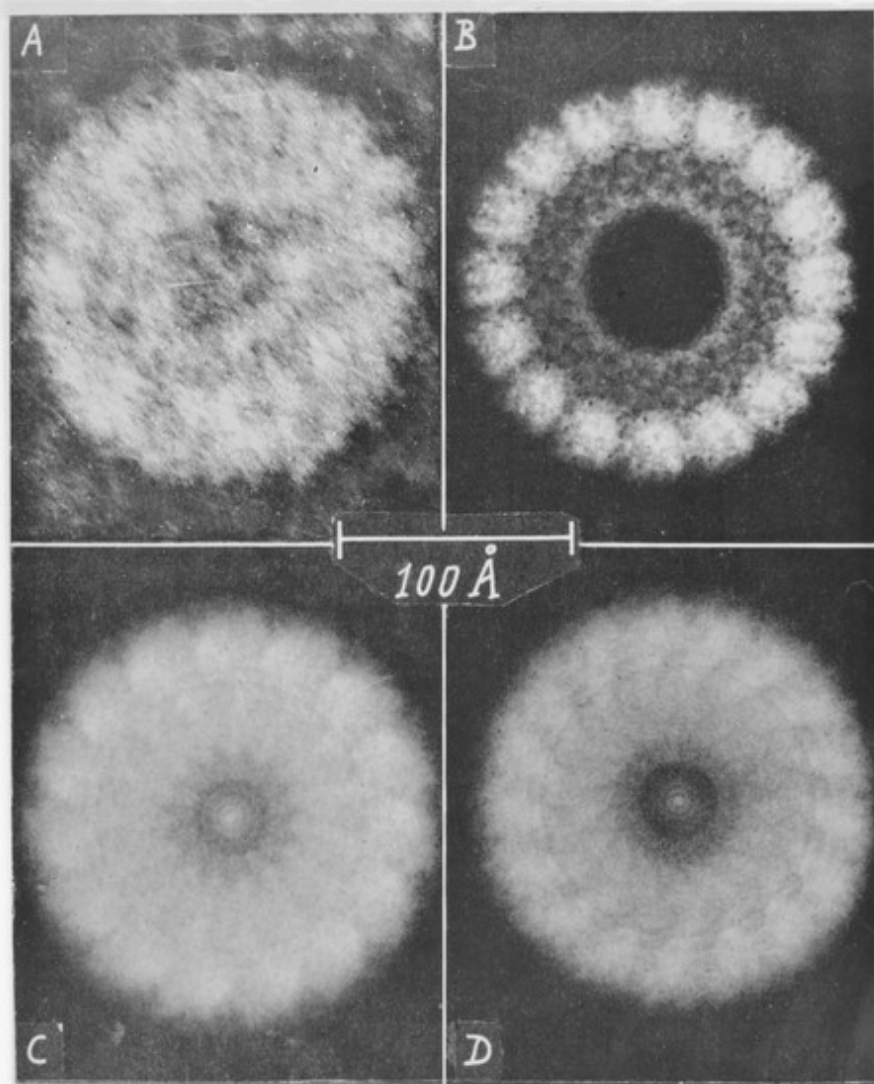
The central cross is common to both sides; thus when these rays arise from a two-sided image they have twice the amplitude they would have when formed by a one-sided image. These rays must, therefore, be reduced to half their amplitude in the filtering process. This can be accomplished by the use of a very fine copper mesh of 50 per cent transmission. The effect of this reduction is to restore the visibility  $(I_{\max} - I_{\min})/(I_{\max} + I_{\min})$  of the periodic part of the filtered image to its value in the original unfiltered image, but there is clearly room for experiment here in adjusting the contrast in the filtered image.

Fig. 4. **a**, Positive replica of a photographic transparency representing the orthogonal projection of a helical structure on to a plane through the axis. **b**, Fraunhofer diffraction pattern of **a** ( $\times 1.5$ ). **c**, Filtered image of **a**, obtained by admitting through the imaging lens only the diffracted rays indicated by the boxes in **b**.

by the allocation of space can be carried in one direction filtered in surface lattice.

In general pattern extent. spots are. In the case of introduction





Tobacco mosaic virus X-protein in the stacked disk configuration as seen "end-on." (A) Original electron micrograph. (B) Rotated  $n = 16$ . (C) Rotated  $n = 15$ . (D) Rotated  $n = 17$ .

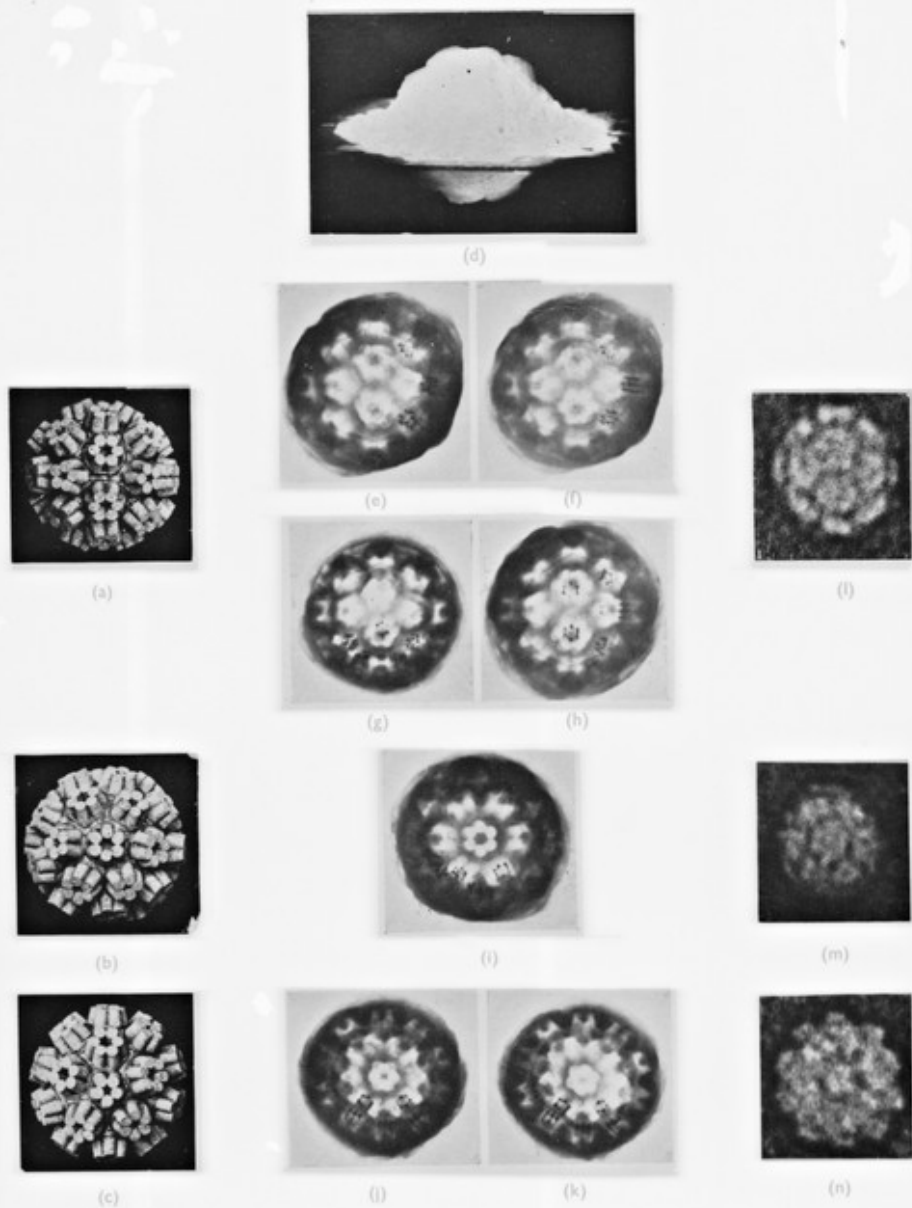


PLATE III. (a), (b) and (c) Photographs of a cork model of turnip yellow mosaic virus taken down 2-, 3- and 5-fold axes, respectively.

(d) The cork model embedded in plaster of Paris and mounted for support in a hole in fiber-board.

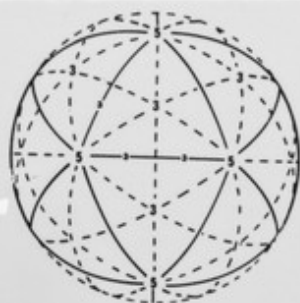
(e), (f), (g) and (h) Analogue two-sided negative stained images taken close to 2-fold directions. (e) and (f): radiographs of (d) taken in very slightly different orientations close to the same 2-fold axis. (g) and (h): radiographs of the same model (d) along two other 2-fold axes.

(i) Analogue image viewed down 3-fold axis.

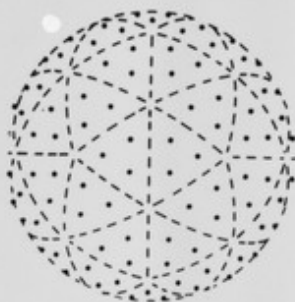
(j) and (k) Analogue images taken close to the same 5-fold axis of the model.

(l), (m) and (n) Electron micrographs of negatively stained particles of turnip yellow mosaic virus (Fisch & Klog, 1966) showing 2-, 3- and 5-fold views, respectively.

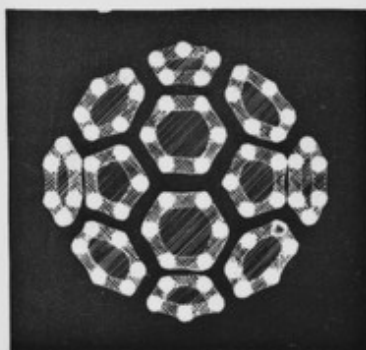
The seven analogue images are not all reproduced at exactly the same scale. The small black dots and lines correspond to patches of barium stain used to mark the orientation of the plaster-encased model.



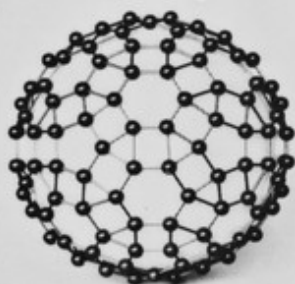
(a)



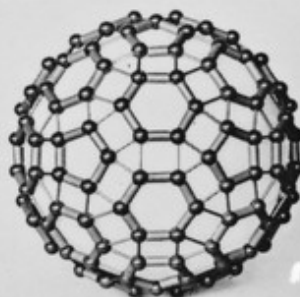
(b)



(c)



(d)



(e)

PLATE II. (a) Orthogonal projection down a 2-fold axis of the icosahedral surface lattice  $T = 3$  (dotted lines) shown in relation to the spherical icosahedron  $T = 1$  (full lines). The figures in large print indicate strict symmetry axes; those in small print the quasi- or local symmetry axes (Casper & King, 1962). The strict 3-fold axes of the shell, considered as a whole are local 3-fold axes of the surface lattice.

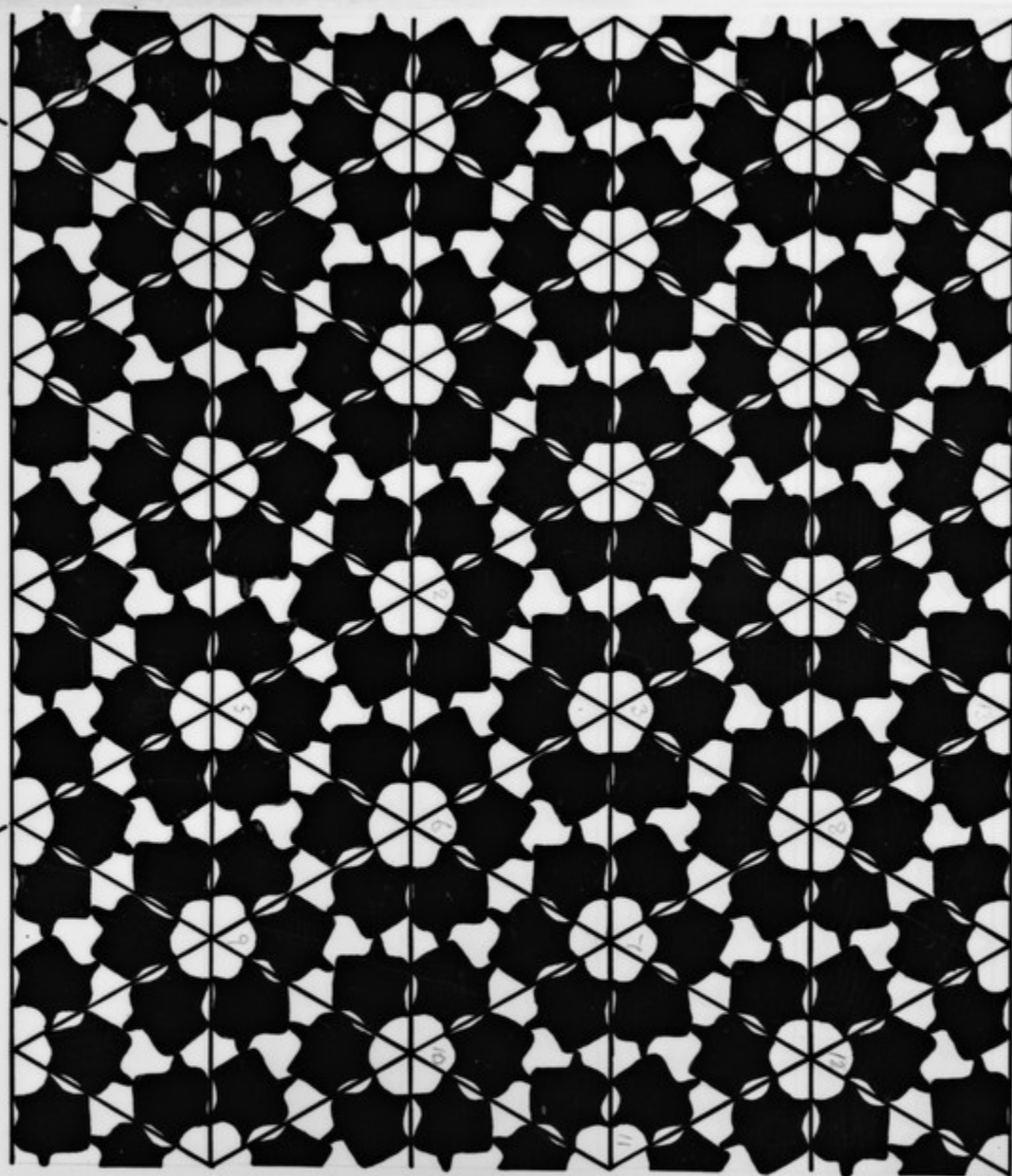
(b) The projection of the surface lattice points on the spherical icosahedron  $T = 3$  (dotted lines) shown in relation to the spherical icosahedron  $T = 1$  (full lines).

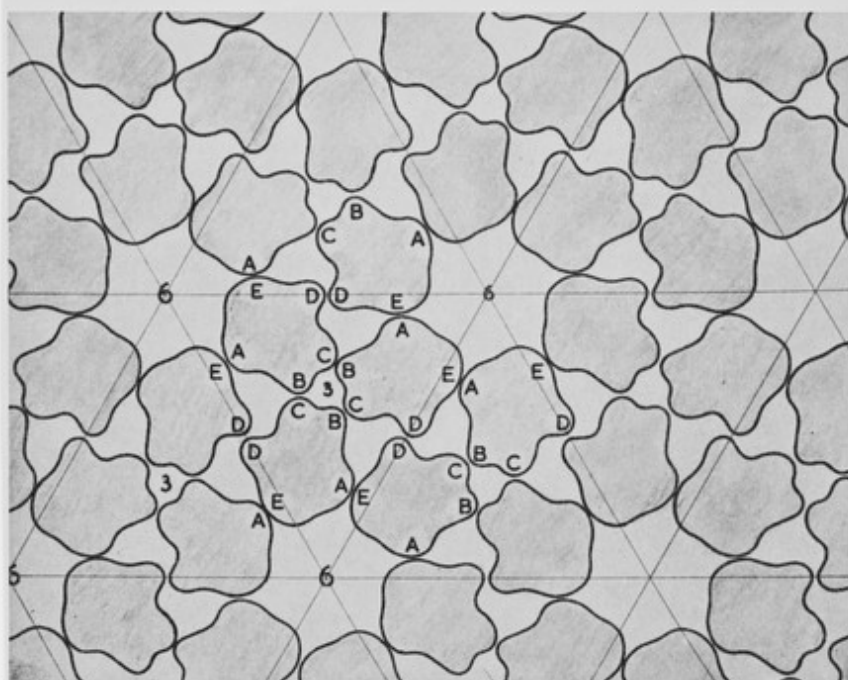
(c) A diagram of the shell of the icosahedron of the same size as the shell of the icosahedron of  $T = 3$  (dotted lines) shown in (b).

(d) A 2-fold view of a model built of 100 units (nodes) on the surface of a sphere having the angular coordinates in the  $T = 3$  icosahedral surface lattice shown in (b). The co-ordinates correspond to the positions of the smaller units comprising the 32 large morphological units in the electron micrographs of TYMY (Plate V). This model does not, and is not intended to, take into account the radial dimensions of the actual structure units.

(e) The same model as (d) with the edges of the hexamers and pentamers surrounding the 32 surface lattice points emphasized by pieces of rubber tubing. This model simulates the density of the edges of the polygons visible in the electron micrographs (compare with (c)) and was used to produce the shadowgraphs in Plate X.

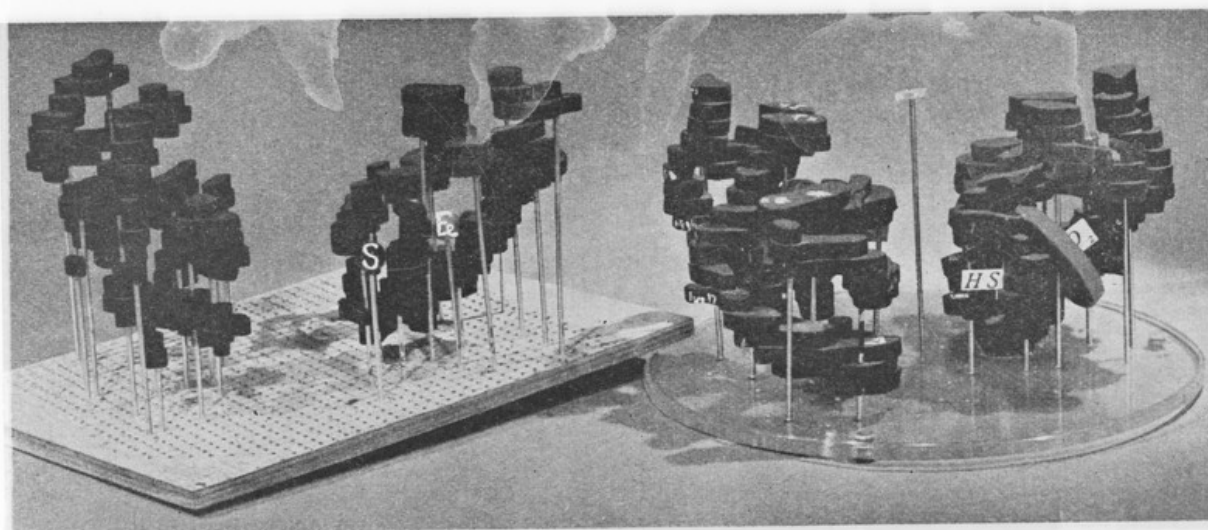
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**Figure 1.** Asymmetric units arrayed in an equilateral-triangular plane net. Besides having translations, here  $a$  and  $a$ , the lattice has 6-fold rotational axes of symmetry. Although the asymmetric units are in 6 different orientations in space, 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.)

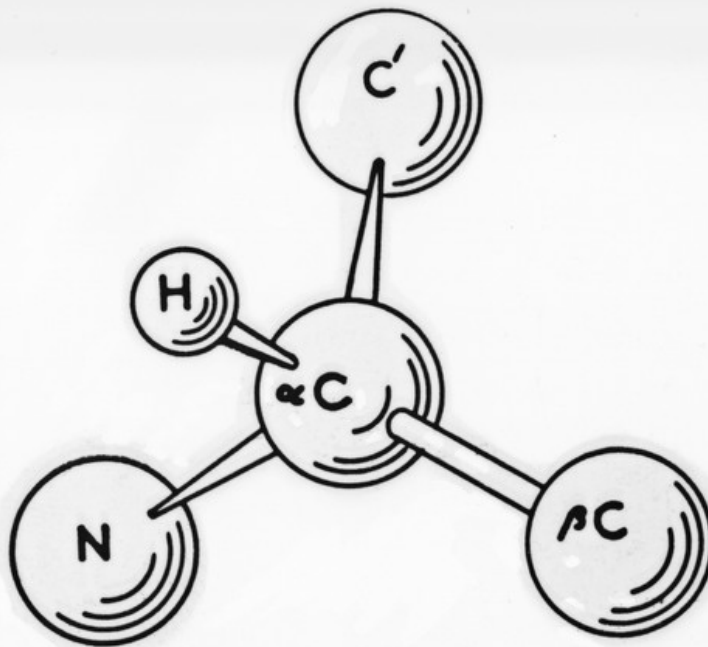


View of the two pairs of  $\beta$ -chains, showing the widening of the gap between them in the human reduced form (left), as compared with horse oxyhemoglobin (right). The heme groups in human reduced hemoglobin are indicated by balls, those in horse oxyhemoglobin by grey disks. *S* marks one of the mercury atoms of PCMB

paper on hemoglobin H (see p. 639), which shows no heme-heme interaction and appears to have the same crystal structure in the oxygenated and reduced states<sup>12</sup>. This

kinetics of inhibition suggest that these enzymes possess at least two different active sites, one for combining with the substrate and another for combining with the inhibitor. The two sites are located at different positions in the active site. There are indications of structural changes in these and other enzyme systems<sup>25</sup>.

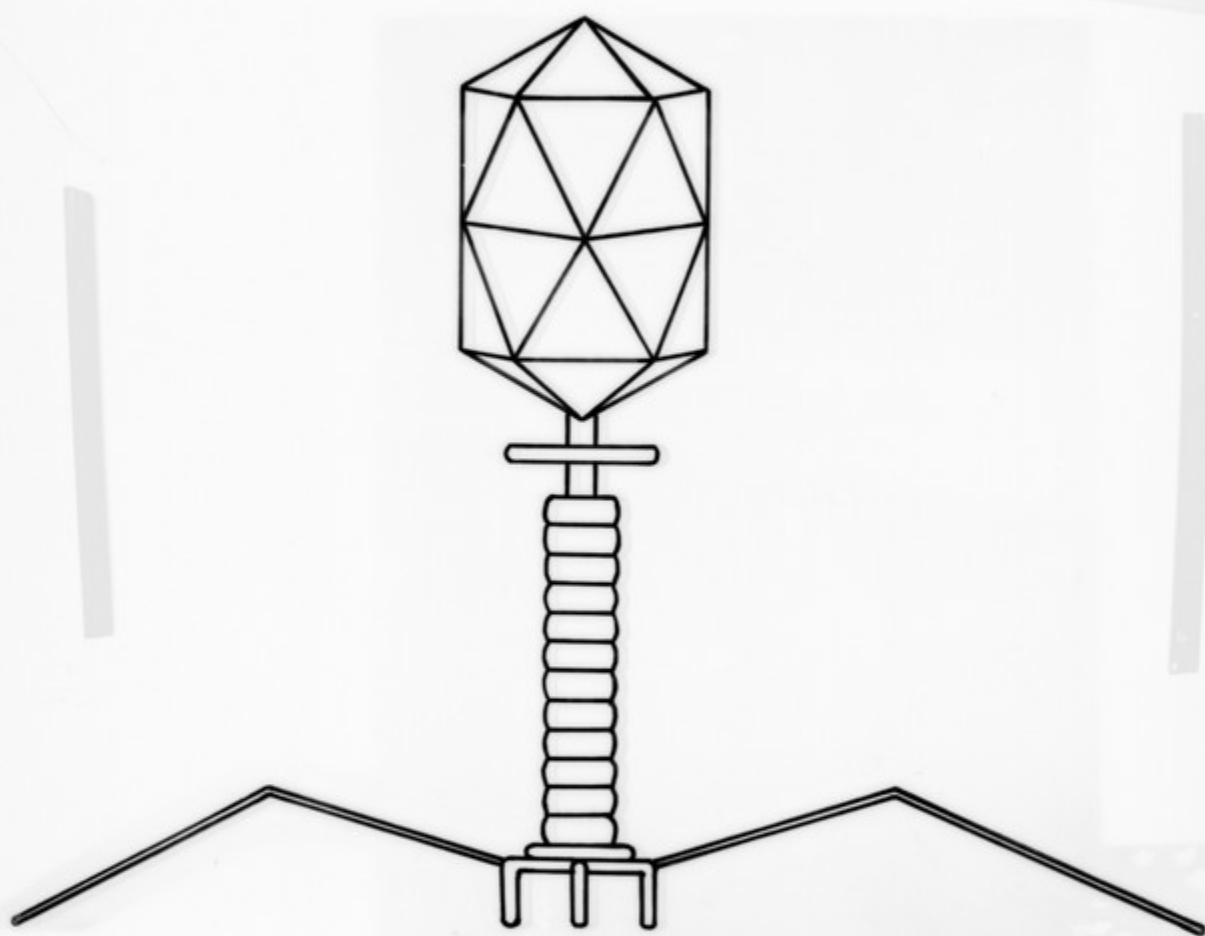
frommel and Bijvoet, 1954), and so the  
 d the  $\alpha$ -carbon atom in optically active  
 bt. Fig. 10.10 shows this arrangement in



## ROTATION OF PEPTIDES

number of peptides derived from optically  
 active amino acids. The optical rota





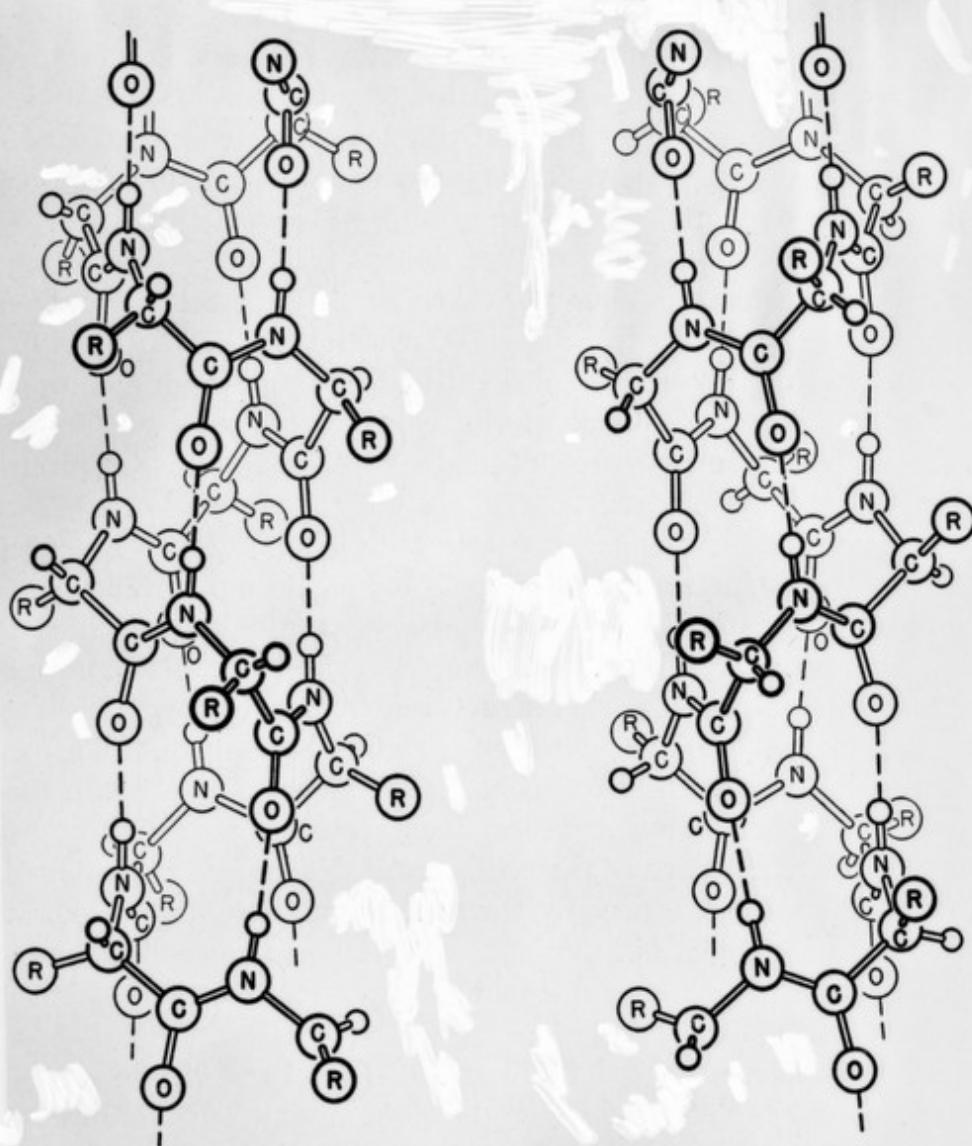
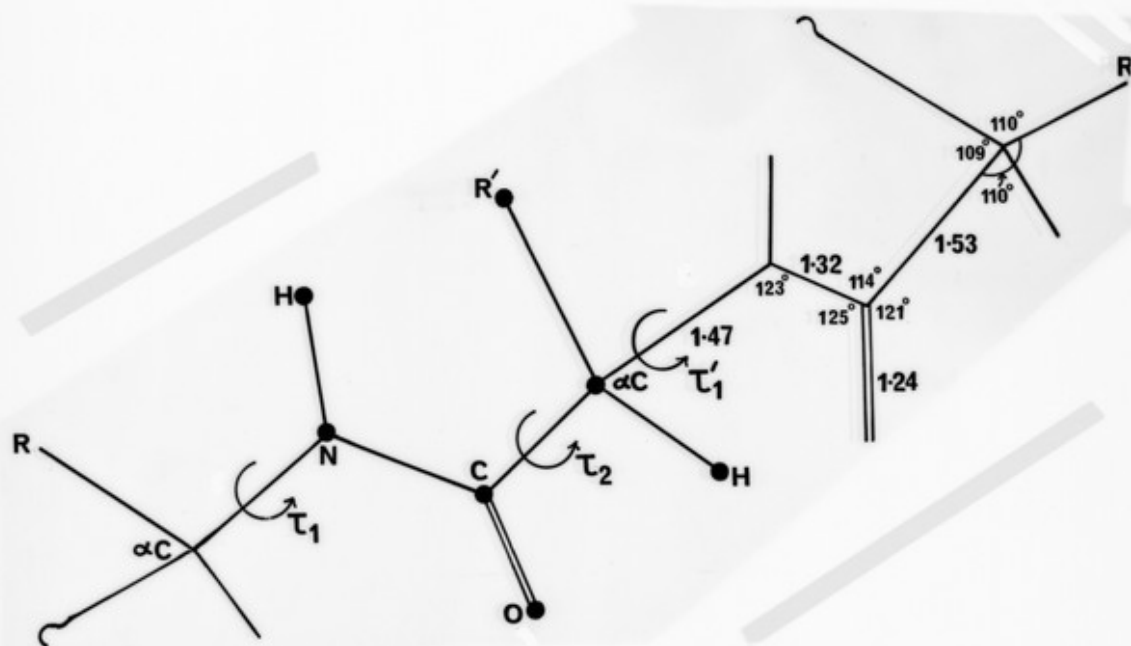


FIG. 12-18.—A drawing showing two possible forms of the alpha helix; the one on the left is a left-handed helix, and the one on the right is a right-handed helix. The amino acid residues have the L-configuration in each case.

it is 6.5 Å for the parallel-chain pleated sheet and 7.0 Å for the anti-parallel-chain pleated sheet. Silk fibroin and synthetic poly-L-alanine have been found to have the antiparallel-chain pleated-sheet structure.<sup>115</sup> It is likely that the  $\beta$ -keratin structure (assumed by the  $\alpha$ -keratin proteins when they are stretched) is that of the parallel-chain



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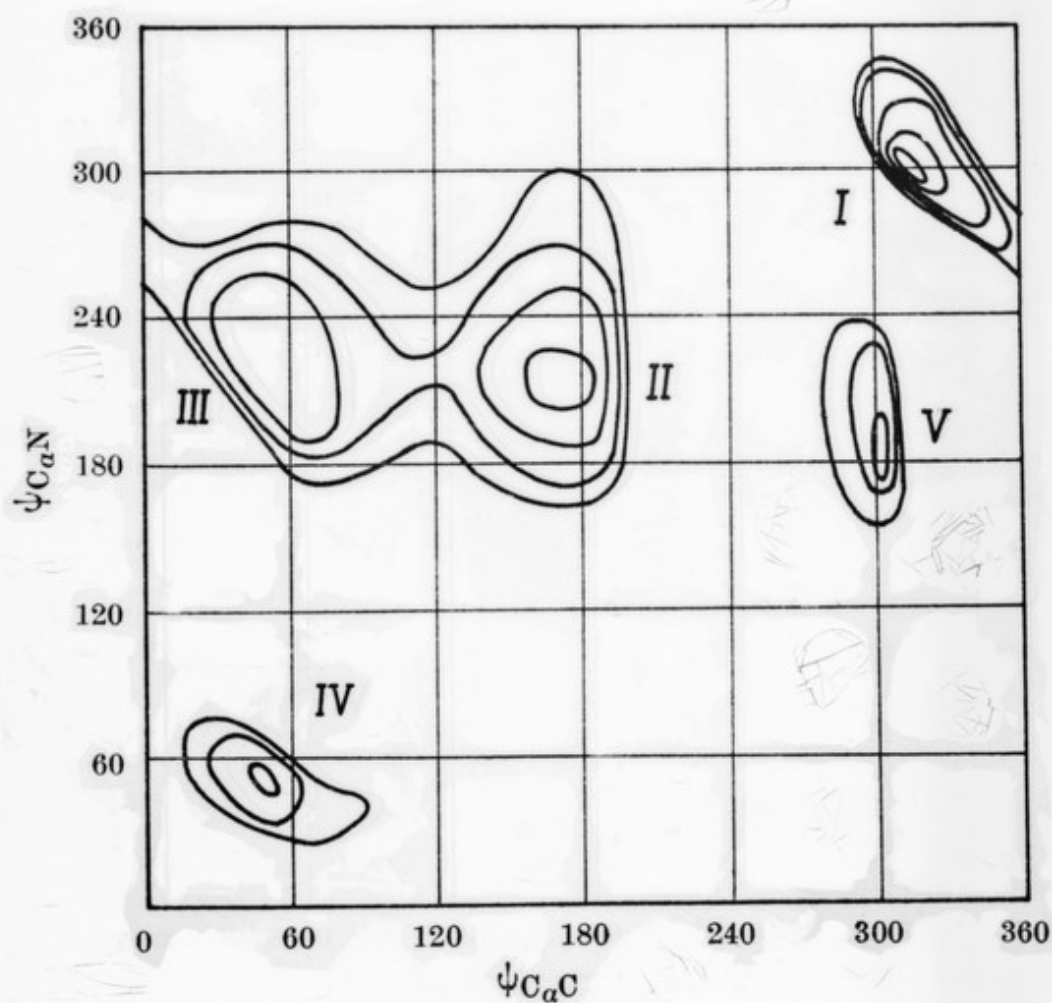


Fig. 2. Two-dimensional plot of the van der Waals conformational potential energy of a chain of poly-L- $\alpha$ -alanine as a function of the angles of rotation  $\psi_{C\alpha-C}$  and  $\psi_{C\alpha-N}$  about the non-rigid skeleton bonds of the amino-acid residue. Contour lines are drawn at intervals of 1 kcal

bounded threefold helix, similar to polyglycine II. Minimum V corresponds to a helix which has never been considered.

The steric hindrance on the N-C $\alpha$  bond by the methyl

This is the three-dimensional counterpart of using the power series  $e^{i\theta} = 1 + i\theta - \frac{\theta^2}{2} - \dots$  to achieve a rotation  $\theta$ , and the summation may be taken to any required precision.

These rotational shifts are applied sequentially starting at the free end of the probe. As each parameter is encountered, all the atoms between it and the free end of the probe (or side chain) are moved by the above process, successive parameters taking the atoms from the positions they have been left in by previous operations.

If this process is not carried out accurately, cumulative errors will arise in the building process as described earlier. Such deformations of the link involving changes of its length in excess of  $2 \times 10^{-4}$  Å have never been encountered.

### 3.1. An unguided

In this example a chain of five links was built between two regions where guide coordinates were given, there

the discussion we indicate ways in which it is thought that van der Waals and other interactions may be introduced.

Fig. 4(a)-(k) shows the initial conformation (a), which is  $\alpha$ -helical, and the conformation after each of ten cycles of the long probe. The end at the bottom of each figure is the root end (C terminal in this case) and there are two links here whose positions do not alter. The lines marked heavily are main chain bonds where rotation is allowed; these occur in pairs each side of C, except in one case where the residue is proline. The sequence in this region is HIS, PRO, GLY, ASN, PHE, and coordinates were calculated for all these side chains on every cycle as shown in the first and last diagrams. These side chains have a total of six rotatable bonds, none of which are guided, so that the derivatives  $\partial r / \partial \theta$  for these angles are all zero. This gives rise to six vanishing eigenvalues with eigenvectors involving these parameters only. The filtering process excludes any of the side

There are then ten main chain parameters so that the order of the normal matrix is 16; however, it has

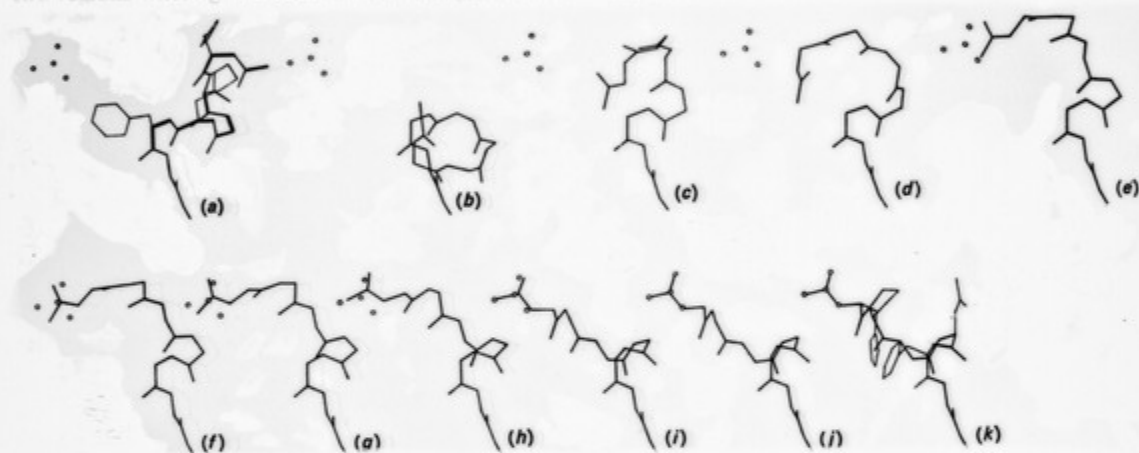


Fig. 4. Cycle by cycle record of the conformations adopted by a length of chain which is required to refold itself so that the free end of the chain comes into coincidence with the guide points shown as open circles on the left of each diagram. There are two peptides at the foot of each figure which do not move; they were guided into those positions and their positions were finalized just before this stage of the calculation was reached. The initial conformation shown in (a) is  $\alpha$ -helical. The side chains were carried throughout the calculation, but for clarity are shown in only the first and last figures.

5010

diameter of the particle is 280 Å; the tips of the molecules are about 150 Å, and the valleys between at a radius of 130 Å. These relative dimensions were used in building the cork model shown in Plate I(b), and in the drawing in Fig. 2.

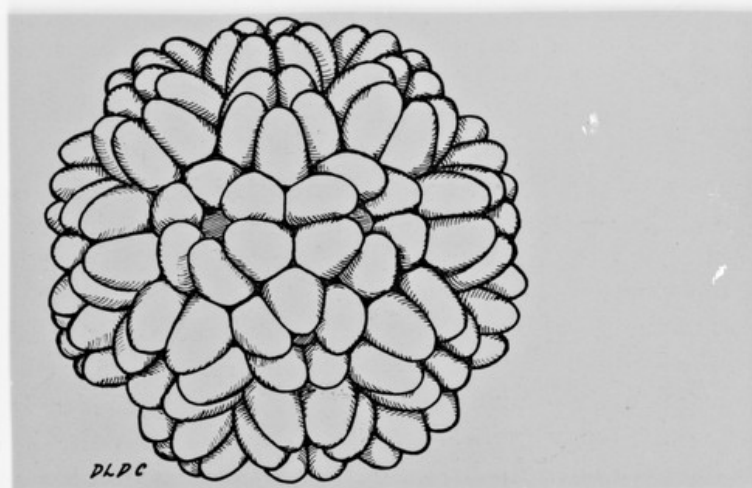


FIG. 2. A drawing of the outer surface of the TYMV particle as revealed by negative staining (approximately  $\times 2$  million).

The 180 structure units protrude about 20 Å from the main body of the particle, but their exact shape is not known. They are tilted somewhat out of the radial direction towards the directions of the 3- and 5-fold axes of the particle (although the clustering is not obvious in end-on views in negative-stain images, because the centres of contrast of the units lie below the outermost surface).

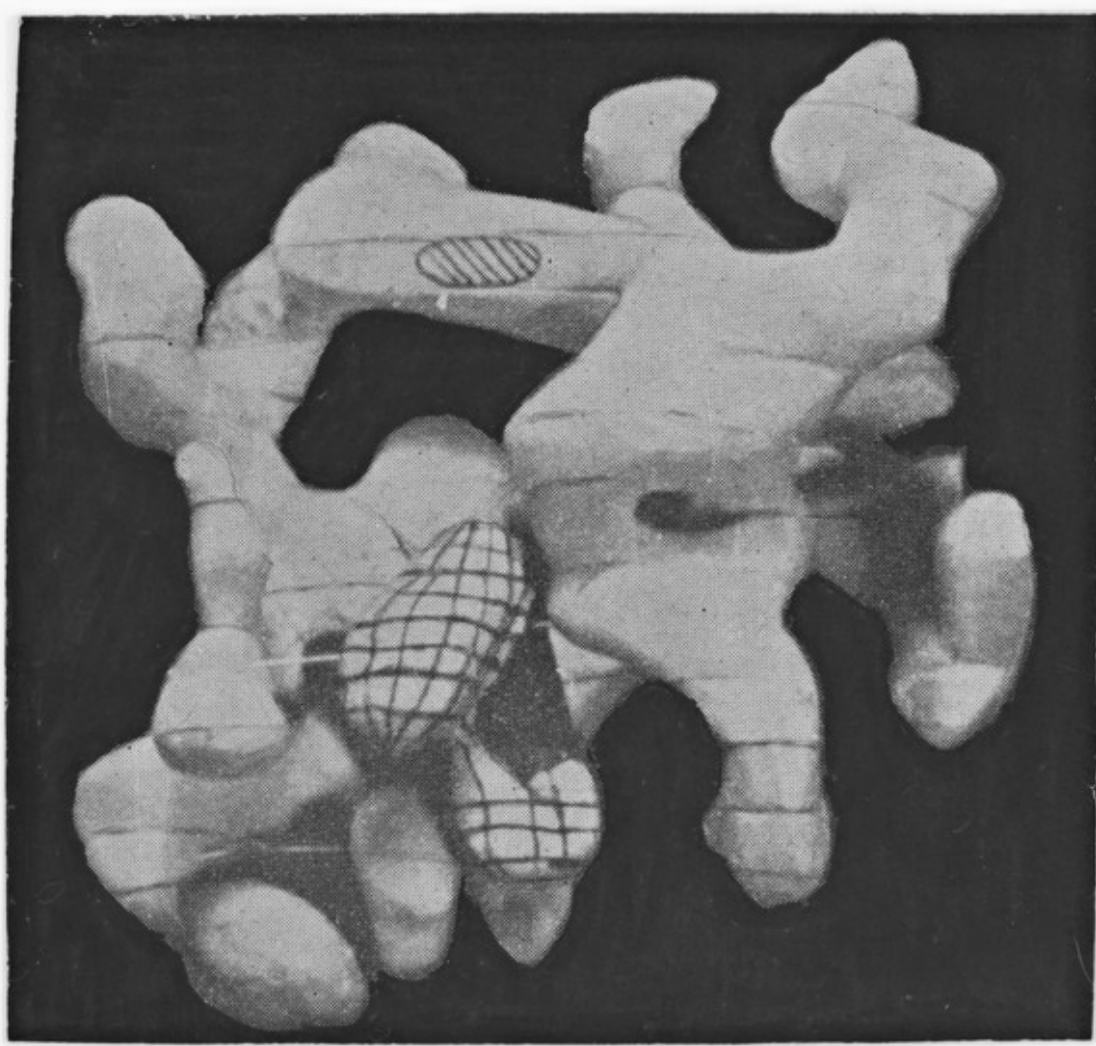
The RNA is associated closely with the hexamers and pentamers at an inner radius (see Fig. 4(b) of Part I (Klug *et al.*, 1966)).

Having proceeded so far in our mapping of the surface of the virus particle, it would be reassuring to know that the negative staining of a particle with a shape like that of our model would in fact produce the details in the images that we observe and have used in our deductions of the structure. We are indebted to Dr D. L. D. Caspar for

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the darker part of the cytophase.  
 The increase in electron density due to  $\gamma$ -acetylcholinesterase is shown as  
 density observed in the presence of di- $\gamma$ -acetylcholinesterase (watered).  
 X-ray analysis at 0.4 resolution together with the increase in electron  
 Fig. 3. Photograph of the model of a lysosomal molecule obtained by



absolutely in one place.  
 perhaps through its amino-group, but that it does not bind  
 to the enzyme with cholinesterase with bind to lysosomal



