Programme of Research, 1954

1. X-ray diffraction studies of viruses

Since the classical studies of Bernal and Fankuchen on the X-ray diffraction of tobacco mosaic virus (TMV), much progress has been made in the techniques of interpreting complicated diffraction patterns, and the ideas of micro-biologists concerning the structure of the simpler viruses have developed considerably. It therefore seems that the time has come to undertake a new investigation, by X-ray diffraction, of those viruses such as TMV which can be obtained in a well-orientated form.

A suitable X-ray camera for this purpose has been constructed, and work on TMV specimens associated with varying amounts of water has already been started.

When water is added to dry TMV, the greater part of the high-angle diffraction pattern remains unchanged. There are, however, important changes in that part of the diagram corresponding to spacings of about 20 Å. It is hoped that a quantitative study of these differences will give some idea of the location, in the virus particle, of that part of the water most closely associated with it, and will thus define the boundaries of some of the structural components of the virus.

With the aid of a special low-angle camera (which has been designed and made in this laboratory) measurements will be made of the positions and intensities of equatorial reflections. These are related to the inter-particle distances, and their positions can therefore be varied by varying the water content. In this way it should be possible to measure a large number of equatorial reflections, and to measure their structure-amplitudes and signs in a manner similar to that used by Perutz in his studies of haemoglobin. A Fourier transform would then give a circularly averaged projection of the rod density, and thus should allow a decision to be made as to whether or not the ribonucleic acid lies at the core of the rod-like particle (as has been suggested by several authors).

Preliminary qualitative observations indicate that the rod-like particles do have a heavy core - that is, that the RNA lies near the centre. Similarly, preliminary observations on TMV of varying water content suggest that the particle contain a structural component having at least one dimension of about 20 Å. Following a more precise study of these two points, it should be possible to proceed to a more general interpretation of the X-ray diagram as a whole. This diagramme shows several hundred reflections, and is characteristic of the type of diagramme produced by molecules of helical symmetry.

A further aid to the interpretation of the X-ray diffraction diagrammes may also be provided by the possibility of staining the virus particles with phospho-tungstic acid.

Later we hope to be able to study other rod- shaped viruses, and, also, the smaller RNA-free fragments which are always found associated with preparations of TMV.

2. **PROPOSED X-RAY DIFFRACTION STUDY OF SOLUTIONS OF POLY-ELECTRO--LYTES.**

The high charge density of synthetic polyelectrolytes causes strong electrostatic interactions in solutions of these substances, and brings into prominence many of the phenomena which are observed, to a lesser degree, in solutions of proteins and other naturally occurring large molecules. In particular, it is believed that long-chain polyelectrolyte molecules form spontaneously a partially ordered system even in relatively dilute solution - an effect similar to that observed by Bernal and others for tobacco mosaic virus.

The behaviour of polyacrylic acid in solution has been extensively studied by Kachalsky and his co-workers, and it is now proposed to study derivatives of this substance by means of X-ray diffraction. Both the caesium salt of poly-acrylic acid and the sodium salt of poly- -bromo-acrylic acid will be prepared in Prof. Kachalsky's laboratory for this work. We shall thus be provided with solutions of polyacrylic derivatives containing <u>either</u> a heavy cation <u>or</u> a heavy anion, and it will therefore be possible to study separately, by X-ray diffraction, both the ordering of the actions and the ordering of the anions in solution.

For this purpose it is proposed to use a Guinier-type X-ray camera (with bent quartz monochromator) specially designed for use with liquids. The camera design is such that the liquid can be examined either in the static state or in flow,

and at any accurately controlled temperature between 0° and 100°C. The body of the camera can be evacuated or filled with hydrogen to eliminate scattering of X-rays by air.

It is hoped that a study of the structure of solutions of synthetic polyelectrolytes will lead to a better understanding of the behaviour of the more complicated, biologically important, polymer solutions.