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NOTE ON THE FUTURE OF THE A.R.C. RESEARCH GROUP IN BIRKBECK  
COLLEGE CRYSTALLOGRAPHY LABORATORY

Rosalind E. Franklin

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NATURE OF THE PROBLEM

The work is concerned with what is probably the most fundamental of all questions concerning the mechanism of living processes, namely the relationship between protein and nucleic acid in the living cell. It is known that the nucleic acids carry genetic information, and that they are intimately connected with the synthesis of proteins. While a considerable amount is known about the molecular structure both of the nucleic acids and of proteins, almost nothing is known of the in vivo relationship between the two types of molecule. The plant viruses consist of ribonucleic acid and protein, and provide the ideal system for the study of the in vivo structure of both ribonucleic acid and protein and of the structural relationship of the one to the other. Such a study is being undertaken in this laboratory, using the methods of X-ray crystallography.

Although the work is at present being done exclusively on plant viruses, there is no doubt that a large part of the results obtained will also be relevant to the problems of animal viruses - the smaller animal viruses have recently been shown to be of similar composition to the plant viruses, and to be crystallisable.

NATURE OF THE RESEARCH

The highly regular and ordered structure of viruses makes it

possible to use the method of X-ray diffraction for their study. On the other hand the size of the virus molecules and the nature of the structural problems involved are such that the standard methods of X-ray crystallography are quite inapplicable. A substantial part of our effort must therefore be devoted to the developing of new methods and of new apparatus. The methods must be (and are being) developed as the research proceeds.

### RESULTS ACHIEVED

The results so far obtained give every reason to believe that the major problems of the structure of the simpler viruses can be solved by the methods of X-ray diffraction.

New information has been obtained concerning the morphology of the tobacco mosaic virus particle, the location of the ribonucleic acid in the particle, and the structural arrangement of the virus protein. Some preliminary results have also been obtained concerning the sub-structure of turnip yellow mosaic virus.

None of these results could have been obtained by any other technique available at the present time. Moreover in no other laboratory, either in this country or elsewhere, is any comparable work on virus structure being undertaken.

The results so far achieved have exceeded our most optimistic estimates of what we should be able to do at this early stage, and give us confidence that, provided the necessary means are available, our X-ray diffraction studies will lead to very substantial advances in this fundamental field of biological science in the future. This

is, however, essentially a long-term research problem, and a substantial research group will probably require from 5 to 10 years to achieve the principal results which we seek.

#### RELATION TO WORK IN OTHER LABORATORIES

Our work on the structure of viruses has been made possible by the generous collaboration of biologists and chemists in virus laboratories elsewhere. In particular, at Berkeley (U.S.A.) and Tübingen (Germany) chemical and electron microscope studies of viruses have made very rapid progress in the last few years. Neither of these laboratories (nor, indeed, any other virus laboratory) is equipped to carry out structural studies by means of X-ray diffraction, and each has therefore sent us a number of important new virus derivatives for study. Our results are thus intimately connected with the work of these two great virus laboratories. This collaboration is proving most fruitful.

At present we are the only group anywhere in the world carrying out this type of study in virus structure. One other laboratory, in the U.S.A., is most lavishly equipped for the purpose, and is about to start a similar programme. The extensive measurements which we have been making over the past two years put us in an advantageous position for the immediate future. If this work is to be kept going in this country, however, it is essential that we should be well enough equipped to enable us to keep pace with this American laboratory.

## FUTURE REQUIREMENTS

### (a) General

The type of work which we have undertaken is of fundamental importance in biological science. It is also, inevitably, expensive. To proceed efficiently in such work it is necessary to be able to plan ahead for a period of about 5 years. While it is not, of course, possible to foresee detailed requirements over such a period, a very approximate general estimate can be given.

In making this approximate general estimate it should be emphasized that this does not take into account the very substantial amount of special equipment which is already in the possession of the Birkbeck College Crystallography Laboratory, and which we are able to use. If our research programme were to be carried out in any other laboratory not already equipped in this way the estimated cost would be many times higher.

### (b) Personnel

The research team should consist of:

- R.E. Franklin
- A. Klug
- 2 research assistants (at present J.T. Finch and K.C. Holmes)
- 1 technician
- 1 computing assistant.

The mean annual amount to be spent on salaries over a period of five years would be of the order of £6,000.

### (c) Laboratory expenses

An annual charge of the order of £1,000 would be made by the laboratory for technical and administrative services, consumables,

small apparatus, etc.

(d) Special equipment

As the research develops new specialized equipment will be continually required. This item is the most difficult to estimate. The mean annual expenditure might be £1,500-£2,000.

(e) Miscellaneous

Money will be required for special purposes from time to time. For example some large-scale computing work will have to be done on an electronic computer such as ACE at the N.P.L. This may require up to £500 p.a.

(f) Biochemical work

As stated in previous reports, it is important that arrangements should be made for a biochemist to be engaged to work with the Birkbeck group, to prepare the special virus derivatives required for structural studies. A separate budget should be made for this. Costs might be of the order of £3,000 p.a.

CONCLUSION

Making some allowance for steadily rising costs, and excluding the requirement of a biochemist, the annual cost of maintaining in Birkbeck College a research group which could efficiently apply itself to the study of the fundamental problems of virus structure would be of the order of £10,000 p.a.