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Closing Remarks

Sir David Phillips

I find myself in the privileged position of having the last word at this splendid meeting as the result of a happy series of accidents the last of which occurred last night at the Chinese Banquet. At a very late stage of that truly magnificent meal, when I would no doubt have agreed to almost anything, I found myself agreeing to say something at the end of the meeting. Now I must honour that undertaking and I am very glad to do so because it gives me a chance to say how much I have enjoyed and benefited from being here.

During the splendid Chinese Feast I found myself remembering a well-known Chinese curse, "may you live in interesting times", and reflecting that we have all lived under its influence and seem likely to continue to do so. Certainly we must all agree that the history of Biophysics over the last thirty years or more has been a continuous succession of interesting times and this meeting has shown that these times have by no means come to an end. Given the present state of Molecular Biology and Biophysics, it is hard to believe that nucleic acids were generally accepted as the essential constituents of the genes only thirty years ago and that the chemical constitutions of nucleic acids and proteins were still the subject of debate at that time.

You will all remember that the double-helical structure of DNA was proposed by Jim Watson and Francis Crick in 1953 and the way to the direct analysis of the three-dimensional structures of proteins was made clear by David Green, Vernon Ingram and Max Perutz in 1954 in their paper on the method of isomorphous replacement as applied to the study of haemoglobin. This year (1981) is the 21st Anniversary of the first publication describing a protein structure in three-dimensional detail, the structure of sperm whale myoglobin determined by John Kendrew and his colleagues. Already in the study of myoglobin, and in the analyses of lysozyme and many other proteins that followed in the next ten years, there was evidence in the crystallographic results that some parts of protein molecules are more mobile or conformationally variable than others. In the excitment of describing such structures, however, crystallographers very largely neglected this evidence and, as a result, the period 1965-1975 may be described as the decade of the rigid macromolecule. Brass models of double-helical DNA and a variety of protein molecules dominated the scene and much of the thinking.

There were, of course, voices crying in the wilderness. parts of enzyme molecules were seen to adopt different shapes under different circumstances and the subunits

of protein oligomers, especially haemoglobin, were seen to move with respect to one another—though perhaps in the manner of rigid jig-saw puzzle pieces in most peoples' thinking. Relying on observations of hydrogen-deuterim exchange and other phenomena, however. many scientists, Walter Englander among them, no doubt protested like Galileo "but they do move" and the message going out from this meeting is that indeed they do. We have seen how crystallography, spectroscopy and theoretical-computational studies are coming together to give us what I believe to be a much more realistic picture of macromolecules than we have had before and one that will surely lead to consequences of an importance that we can, at this stage, hardly foresee.

This meeting has certainly been for me an enormous pleasure and excitement and I am sure you would all agree that we owe Dr. Sarma and his colleagues a very great debt for having provided it for us.

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