UNIVERSITY OF CAMBRIDGE DEPARTMENT OF PHYSICS

CAVENDISH LABORATORY
Free School Lane,
Cambridge.

21st January 1953.

Dr. David Harker,
Polytechnic Institute of Brooklyn,
The Protein Structure Project,
55 Johnson Street, 4th Floor,
Brooklyn 1, New York.

Dear Dr. Harker,

Thank you for your letter of 7th January. I have heard from Wyckoff who seems to think there will be little difficulty in getting our visa interview rather earlier. I shall write to the Embassy as soon as I have cleared Michael with the Divorce Court. Naturally I did not expect the travelling money before we got the visa. I will let you know later on how things can most easily be arranged.

As to the apartment, I suggest you relax first the price, and go higher, say up to $120. If there are still difficulties I think we should not worry too much about the neighbourhood. We certainly don't want to buy furniture, and we really need three bedrooms if this is at all possible. It is really very kind of you to do this for us.

I was very pleased to hear about your various forms of ribonuclease. The work in Bernal's laboratory has suffered, in my view, due to their excessive concentration on one form. Have you been able to derive any information from studying the changes due to different salt concentrations?

As to α-keratin, I think Pauling's model is on the right lines, but probably for my reasons. A tilt of about 9° is certainly indicated, not 19° as I suggested. The simple formula 5.4 sin α is correct for a tilted helix, but not for a coiled helix, as can be seen either from the exact theory which I have worked out, or from symmetry considerations. I have written more fully about this to Lang, and said he might show you the letter.

I was interested to hear about Dr. Luzzati, both from you and from Perutz. Some time ago I looked into the question of putting the haemoglobin data on an absolute scale. The question is complicated by doubts as to how many of the atoms in the crystal are ordered, and by the fact that the observed data only goes out to 2.8A°. I considered the integral $\int \rho r dv$

This can be predicted, given sufficient resolution, from the chemical formula - since one knows the radial distance of all neighbours within about 2.7A° of all the atoms irrespective of how the molecule folds up. One has to calculate the temperature factor from the data, and it is difficult to do this unambiguously unless the recorded intensities go a good way out. I came to the conclusion that one should always put the intensities on an absolute scale by direct measurement. Theory might then be able to show what fraction of the atoms is disordered.

As to the α-helix in globular proteins, I don't think anybody here now believes that haemoglobin consists mainly of long straight parallel rods, since such a model is clearly incompatable with the Patterson. The key question is whether it consists mainly of α-helices, not necessary parallel. This is plausible, since it may be made up of four non-parallel myoglobin-type units, and moreover packing considerations show that α-helices of the same sense probably prefer to close-pack at about 20° from parallel, for the reasons given in my Nature letter.

I have just drafted a paper in which I show that the total intensity in and around the 10A° region is crudely comparable with such a model. I use the relation

$$\int |\text{grad}\,\rho|^2 dV = \frac{4\pi^2}{V} \sum_{hkl} R^2 |F_{hkl}|^2 \qquad \text{where } R = \frac{2\sin\theta}{\lambda}$$

after applying a heavy artificial temperature factor to ensure convergence. This approach can be generalised by repeated differentiation, and I shall be interested to see if Luzzati is working on similar lines.

I don't think we shall be able to come to any definite conclusion here until Kendrew has the 3 dimensional Patterson of myoglobin, which we believe to be distinctly more "roddy" than haemoglobin.

With best wishes,

Yours sincerely,

Francis Crick.