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From The Wheatstone Professor of Physics,

TEMPLE BAR 5651
(6 LINES).

J. T. RANDALL, F.R.S.

STRAND, W.C.2.

Dr. F.H.C. Crick,
Polytechnic Institute of Brooklyn,
The Protein Structure Project,
55 Johnson Street, 4th Floor,
Brooklyn 1, New York

17th June 1954

Dear Crick,

Thank you for your letter of June 3rd. We have been working away at the collagen structure and, like you, regret that the complete answer is so elusive. I don't wish to go into any great detail here as much of our work will be presented at the Society for Experimental Biology Symposium at Leeds in September and in my Procter Memorial lecture in the same month. This latter I expect to be published in October, some long time before the Symposium is in print I imagine.

However, I should like to summarise a few important points from our conclusions about your model:

1. We also have noted that the dichroism expected for your proposed model does not correspond with that observed.
2. Although we have not yet calculated it, we think that your structure would have negative birefringence, not positive as observed.
3. The density for hexagonal packing, assuming an average side chain, is 1.8. While you point out that your structure may contain only the smaller side chains and therefore be only part of the collagen fibre, it seems rather unlikely that alternate residues are glycine as you suggest. It is even more unlikely that it should be polyglycylproline, although this is of course not necessary.
4. Points 1 and 2 may of course also be got round if, as seems likely, the collagen system is not simple but consists of two "phases".
5. The number of close contacts might be expected to make the structure unstable.
6. The main chain radius, being rather large, one might expect packing difficulties unless only the smaller side chains are involved.
7. Enclosed are two enlargements of optical diffraction patterns: (1) contains all main-chain atoms, but no side chains, while (2) has main-chain atoms and alternate residues proline.

As you can see, there is a reasonably good general resemblance to the X-ray

diffraction diagram, particularly in case (2). There are two serious points of discrepancy: (a) The meridional 2.95A reflection is too strong; this is more obvious on the actual negative. (b) The equatorial layer does not fit at all well, maxima coming where there should be minima and vice versa.

We have calculated the equatorial form factors with and without proline and have tried the effect of adding other side chain atoms. The calculated form factors do not account for the observed relative intensity changes on swelling. The 1120 reflection expected for hexagonal packing, which is not observed, would occur at a position of larger $F^2(\text{calc.})$ than that of the observed 2020 reflection. Similarly, as stated above, the observed minimum on the equator is not given by the form factor. One reaches the general conclusion that the radius of the helix is too large.

The effects of forming super-helices of various radii were also investigated. While it is possible to choose a radius which will produce a minimum at the desired place, there does not seem to be any particularly good physical reason for assuming this radius. In any case, a definite minimum of scattered intensity is still observed for stretched fibres. Further, the most likely super-helix for your structure to assume from packing considerations would have seven residues per minor turn and the ratio of the meridional spacings $9.55/2.86$ should be 3.5 and not 3.33 (i.e. $3\frac{1}{3}$ which fits in better with a three chain model).

Yours sincerely,

J. Kendall. FRS