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CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA

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Dear Dr. Heidelberger,

Dr. L. Pauling and I are planning to run a research-seminar on Protein structure here next term, in which we want to discuss in particular the inferences one can draw from ~~the~~ the serological reactions and from their specificity. On going through the litteratur on the subject we find that we will be rather handicapped by the fact, that most of the immunological Journals are not available here in Pasadena. We would appreciate it therefore very much if we could have reprints of your papers on the poly-saccharide reactions. When I called on you in October last you were kind enough to let me have reprints of four of your papers from the J. of Exper. Med. (Vol. 65 p. 647 and p. 885, and Vol 66 p. 229 and p. 251). I wonder whether we could have some more, in particular the theoretical

one from Vol 61 p. 583. I remember that you in October offered this one to me for loan. I looked it up in Cold Spring Harbor but did not study it sufficiently careful, so I would like to see it again. We will of course send it back when we have it sufficiently assimilated.

I have been speculating a little on the theory of the absolute value of the reaction rate of serological reactions and have arrived at the following formula. Consider the rate of formation of a compound AB from the antigen A and antibody B

$$A + B \longrightarrow AB$$

in a vessel containing N_A particles A and N_B particles B per cc. The rate of formation should be

$$\frac{d\,N_{AB}}{dt} = N_A \cdot N_B \cdot (D_A + D_B)(a_A + a_B)$$

where D_A, D_B are the diffusion coefficients and a and b the diameters of A and B respectively.

This formula is derived by assuming that <u>every</u> collision between A and B leads to a union. If there is an activation energy, the reaction will be slower, also if the collision must be one between specifically oriented particles. So far as I could test the formula it fits at least the order of magnitude of the observed reaction rates. In your experiments you do not observe this primary reaction but the later stages of formation of the precipitate. One can of course not easily make a theory of the absolute rate of these collisions, but as you have found they seem to be proportional to the concentrations, so they should also be bimolecular reactions. In that case their temperature dependance should be only the result of the temperature dependance of the diffusion coefficients, and this in turn is predominantly determined by the change in viscosity of the solvent, and therefore equal for all

steps in the precipitine reaction. I should be very thankful if you could let me know whether these considerations have been worked out long ago by other people (as I suspect) and where I could find their papers. Ordinary physical chemistry is little concerned with collision numbers in liquids, because the reaction rates are either predominantly determined by activation energy, and any uncertainty in this makes a closer analysis of the collision rates futile, or, if the collision rate determines the reaction rate, the reaction goes immeasurably fast. Therefore the physico-chemical literature does not give a good theory of collision rates.

Yours very sincerely

M. Delbrück