March 16, 1938

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 serological reactions and their specificity. On going through the literature 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 polysaccharide 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. 523. I remember that you in Octobe
offered this one to me for loan. I looked it up
in Cold Spring Harbor but did not study it sufficient.
y careful, so I would like to see it again. We
will of course send it back when we have it suf-
Ficiently assimilated.

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

$$A + B \rightarrow AB$$

in a vessel containing $N_A$ particle, $A$ and $N_B$ par-
ticle, $B$. The rate of formation should be

$$\frac{dN_{AB}}{dt} = N_A \cdot N_B \cdot (D_A + D_B)(a_1 + a_2)$$

where $D_A, D_B$ are the diffusion coefficients and $a_1$ and $a_2$ the diameters of $A$ and $B$ respectively.
The formula is derived by assuming that every 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 an 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 concentration, so they should also be bimolecular reaction. In that case their temperature dependence should be only the result of the temperature dependence 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 precipitation 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 rate is 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 irreversibly fast. Therefore the physico-chemical literature does not give a good theory of collision rates.

Yours very sincerely,

K. Delbrück