

(Very thin program)

Dear Gus:

I hasten to reply with comments on the ms. On the whole it looks quite all right, and I imagine you should not wait too long to round out the details left out of the Nature preliminary.

Most of my comments are reproduced on the enclosed marginal notes. To save weight, I have cut out text on which I had no comment.

My main criticism is that you should expand the discussion somewhat, both from the standpoint of theoretical implications (N.B. my marginal comment there) and more important, to anticipate reasonable objections in somewhat more detail. E.G. the experiments are somewhat thin from a statistical point of view, and while the null hypothesis of complete independence of reaction is perhaps nearly excluded, this is some distance from the proposition of complete exclusion. I would also be worried about the possibility of incomplete exclusion in terms of quantity. Suppose that only about 20% of cells can make any antibody, and that among these one predominates. Your incidence/count relation mainly tests the idea that the other 80% are each making subliminal levels of antibody. These may not be serious objections (especially if Lennox and Cohn have an agreeable conclusion) but it would be better for you to display the largest measure of circumspection, rather than your critics, and then still to reach a reasonable conclusion.

Is there any possibility of making a suitable reference to Coons? I have his permission (at your option) to cite 'Coons, A.H. and Tanaka, N.' (unpubl.) and cited in his paper for the Gatlinburg meeting. The abstract is enclosed, and it could be cited simply as the Biology Research Conference on 'Genetic Approaches to Somatic Cell Variation', Gatlinburg, Tenn., April 2-5, 1958. This will be published as a supplement to J Cell Comp Physiol (like last year's) I wish I could suggest as much for Lennox and Coons— you might leave it to Mac to work that out.

During a flight to California last month, I met a chap from Copenhagen named Sorkin, and it turned out he has been interested in propagating antibody-forming success with results so far ambiguous but promising. Anyhow he mentioned a paper I haven't been able to find, by Moeschlin, on the adherence of bacteria to antibody forming cells. He promised eventually to find the reference and send it, but I haven't received it yet. Do you know it?

A statistical treatment of table 2 is warranted. You have two incomplete 2x2 contingencies, and this poses something of a problem. One possible approach is to deal with each of them separately, and assume a binomial distribution. E.G. You have 27:0 T⁻:T⁺ among the A⁺. If T and A are independent, the expectation that any single A⁺ will be T⁺ is 20/154. The probability that none of 27 will be

$$p_0 = .023 = \left(\frac{154-20}{154}\right)^{27}$$

$\left(\frac{172-27}{172}\right)^{20}$ *probably best to present these p's separately unless a complete solution is worked out.*

Similarly, for the second half of the table, $p_0 = .033$. ~~It is not clear whether when can simply combine these probabilities; you may want some more sophisticated advice. The combined probability is $\frac{1}{172} \left[\left(\frac{154-20}{154}\right)^{27} + \left(\frac{172-27}{172}\right)^{20} \right]$ see P.S. over~~

I will have to talk further with Hilary Koprowski about the tumor angle. But I had a letter last week from a ~~max~~ student of Haurowitz's who suggested a post-doctoral fellowship on the same problem, and I have to interview her later this week. As to your own visit, 6 mos. would be fine. I'll talk to Mac in Stockholm to get his point of view. That won't be till August. We'll be in Madison till about July 24.

Yours,

Iskua

PTO

P.S: One suggestion is to calculate the χ^2 for each of three p_0 's, sum and recalculate p_{00} for the sum with double degrees of freedom. This gives $p_{00} \sim .007$.

A maximum-likelihood solution can also be worked out and will send you result if it is any different.