Dear Josh.

I'm sorry for the delay in answering your letter. I've been on vacation. Thanks very much for your interest in and your comments on the arabinose paper. First, to answer some of your queries.

I have completed the enzymatic analysis of all the mapped arabinose mutants. However, it takes me so long to write a presentable paper that I thought it best that the genetic and physiological experiments with intact cells be published now, while it may be of some interest. Anyway, I have so often been asked by editors to cut long papers that I decided to save them and myself the trouble of re-writing.

L-arabinose induces both isomerase and kinase.

L-ribulose cannot be used by intact cells of B/r wild type or mutants.

Group C may be permease negative. However, I have been unable to force induction of either the isomerase or kinase by growing the cells in high concentrations of arabinose.

We have not tested for epimerase activity. Group C may be deficient in the epimerase, as well as in isomerase and kinase.

As I mentioned in the footnote(5), Group B mutants, although all kinase negative, have different levels of isomerase activities, varying from 1/10 to 4 times the isomerase activity of the prototroph.

I am aware of Kalckar's and Esther's work. However, since the purpose of this paper was to describe a reliable methodology for ordering closely linked markers and to indicate the general unreliability of Demerec's and Hartman's method, I did not think it was necessary to mention the galactose work.

As far as the tables are concerned, you must remember that we are only interested in drawing attention to that data bearing on the <u>order</u> of the ara sites in the simplest possible manner, on the basis of the reciprocal crosses. I think anyone reading the paragraph entitled "Order of ara sites" on page 8 and referring to Fig. 1 and working out a few crosses with a pencil and paper should be able to grasp the method. And then by going down Table 3 he should be able to say that 13 is to the right of 2, 7 is to the right of 13, 4 is to the right of 7, etc. With your notation, the apparent deduced order that we arrive at after going over the data is given first. If one is to be more explicit, it would perhaps be better to give (in Table 1) all the orders that would possibly explain each cross, and then finally eliminate those that do not concur. By introducing the new notation, one has to first master the meaning in terms of threonine, arabinose 1,2,etc., leucine, and transfer this understanding to the notation and then back again to what they represent. Also, the dots cause confusion (as you have mentioned), being mistaken easily for decimal points. In any case, I feel that employing a new system at this time would detract from what we want to get across.

I agree with you as to the use of the \* superscript, etc. The only reason we combined data from several experiments (Table 3 and 4) is the unsightly character of the table that results if we included separate figures from each experiment.

A careful analysis of the data in Table 5, I believe, eliminates the distribution of fragments as being a major factor in the "abnormal" frequencies we cite. Julian Gross has analyzed this problem further. You will find a portion of this in the Carnegie Report, and he is in the process of writing a more detailed article for publication.

Do you know of any markers between arabinose and threonine or between arabinose and leucine? Do you know what is the enzymatic deficiency of the arabinose negative mutant in  $^{K}12$  not linked to threonine or leucine? Do you know of any such mutant in  $^{B}/r^{?}$  --- we have not been able to find one.

 $I^{t}$ m disappointed that you won't be able to participate in our seminar program. I was looking forward to the possibility of seeing you.

Best regards,

Ellis Englesberg