

June 14, 1957

Dr. F. H. C. Crick  
Cavendish Laboratory  
Cambridge, England

Dear Crick:

Enclosed is a manuscript and a copy of a letter I wrote to Alex Rich. As you will see from it, I did not get the May issue of the Proceedings until just now and so I added a note <sup>and an</sup> ~~in the~~ appendix to my paper referring to your work. If you see anything basically wrong with my views, please drop me a line or send me a cable. For another ten days I can still withdraw this paper without causing anyone any appreciable inconvenience.

If Brenner has a manuscript or if his suggestions have been published in the meantime, I would greatly appreciate receiving a copy.

Please give my kind regards to Brenner and tell him I would like to hear what he thinks about my manuscript.

Incidentally, when does your group assemble in Cambridge in September? I am suppose to give a talk in Berlin at the annual meeting of the German Chemical Society early in October, and I shall probably knock around in Europe during September and would like to spend some time with your group in September, particularly if the group is fully assembled (I mean Benzer, Dulbecco, Streisinger, as well as Brenner).

With kind personal regards,

Yours sincerely,

Leo Szilard

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Encl.



UNIVERSITY OF CAMBRIDGE

DEPARTMENT OF PHYSICS

TELEPHONE  
CAMBRIDGE 54481

Medical Research Council Unit  
CAVENDISH LABORATORY  
FREE SCHOOL LANE  
CAMBRIDGE

20th June, 1957

Dr. L. Szilard,  
Enrico Fermi Institute for  
Nuclear Studies,  
University of Chicago,  
Chicago 37,  
Illinois,  
U.S.A.

*Paper*

Dear Szilard,

It was very nice of you to send us your manuscript. We were also delighted to know that you hope to come in September - we shall all be in Cambridge then (though I'm not sure about Dulbecco). Do come for as long as you care to stay.

We have only had time to digest the part of your paper dealing with coding, and I had better say straight away that we don't like it. The type of code you suggest is extremely restrictive. There are theoretically 8000 possible tripeptides, and your code only allows 20 of them. To fix ideas consider a version of your code with 10 3-letter words and 10 4-letter words. Then if you code for sequences having more than  $30 + 40 = 70$  amino acids you are certain to get at least one sequence of three letters occurring twice. Moreover, on statistical grounds you would expect more than this. Now, whereas the same pairs have occurred more than once (as one would expect from random sequences) no triple of amino acids has so far occurred twice. I am sending under separate cover a paper by Brenner to appear in PNAS, in which all the known sequence data is collected together. As you can see quite a modest selection from this will disprove all possible versions of your code.

There is a minor technical slip in page 5. The repeat of a fully extended polypeptide chain is indeed about 7.2 A, but this repeat contains two amino acids, so that the average distance between amino acids is about 3.6 A. There also appears to be a typing error in this paragraph (polypeptide for polynucleotide).

I have shown your paper to Brenner and Orgel, and the above criticisms are the joint work of the three of us.

P.T.O.

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The idea that molecules based on di-, tri- or tetra-nucleotides and one amino acid might be involved in protein synthesis has been briefly mentioned in my contribution to the discussion of a meeting which took place in February, 1956 in London, and published early this year in The Biochemical Society Symposia, No. 14 "The Structure of Nucleic Acids and their role in Protein Synthesis", Cambridge University Press.

There are a number of points on the second part of your paper which we should like to discuss, but it seems easiest to leave them until September.

With best wishes,

Yours sincerely,

*Francis Crick*

F. H. C. Crick

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BY AIR MAIL

PAR AVION  
AIR LETTER  
AEROGRAMME



Dr. L. Szilard,

Enrico Fermi Institute for  
Nuclear Studies,  
University of Chicago,

Chicago 37,

Illinois

U.S.A.

← Second fold here →

Sender's name and address:

Dr. Crick,

MRC Unit,

Cavendish Lab.,

Cambridge England.

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OR SENT BY ORDINARY MAIL.

THE 'APSELEY' AIR LETTER

Form approved by Postmaster General No.—71995/IW



June 24, 1957

Dr. F.H.C. Crick  
Medical Research Council Unit  
Cavendish Laboratory  
Cambridge University  
Cambridge, England

Dear Crick:

Since I wrote you about a week ago, I looked at known amino acid sequences in polypeptides in the hope that they would throw light on the mechanism of polypeptide synthesis. The attached memorandum gives the conclusion to which they lead. Since my manuscript was to be held until further notice, I can now withdraw it without any trouble, which I shall do without delay.

I am pursuing further the considerations relating to the rate of protein synthesis, and shall probably incorporate parts of the manuscript which relate to this problem into another paper that is in preparation.

With kindest regards,

Sincerely,

Leo Szilard

m

P.T.O.



P.S. I just received your letter of June 20th. Since I wrote you I spent a week in Denver and looked at the amino acid sequences given by Brenner in his manuscript which he had sent to Joe Gamow. As you see from the attached memorandum, my conclusions are identical with yours.

I am particularly grateful for your having pointed out a rather fatal slip relating to the distance between amino acids.

Since I felt from the start that I was on insecure grounds, I had asked that the manuscript be held until I could check it with others, and therefore no inconvenience will arise if I now withdraw it.

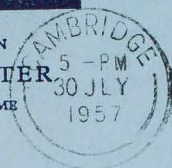
I shall continue with the considerations relating to the expected maximal rate of protein synthesis.

The scant hint, which you make in your paper and which Brenner makes in his manuscript (that Gamow showed me) concerning Brenner's idea on polypeptide synthesis, has whetted my curiosity. Please tell Brenner if he has anything on paper (and he ought to spell out his ideas in writing as soon as convenient) I should appreciate receiving a copy of the manuscript.



BY AIR MAIL

PAR AVION  
AIR LETTER  
AEROGRAMME



Dr. L. Szilard,

Enrico Fermi Institute for Nuclear Studies,

The University of Chicago,

Chicago 37,

Illinois,

U.S.A.

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Second fold here

Sender's name and address: Dr. Crick,

M.R.C. Unit,

Cavendish Laboratory,

Cambridge, England.

AN AIR LETTER SHOULD NOT CONTAIN ANY  
ENCLOSURES; IF IT DOES IT WILL BE SURCHARGED  
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THE 'APSLEY' AIR LETTER

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To open cut }



UNIVERSITY OF CAMBRIDGE

DEPARTMENT OF PHYSICS

Medical Research Council Unit  
CAVENDISH LABORATORY  
FREE SCHOOL LANE  
CAMBRIDGE

TELEPHONE  
CAMBRIDGE 54481

30th July, 1957

Dr. L. Szilard,  
Enrico Fermi Institute for Nuclear Studies,  
The University of Chicago,  
Chicago 37,  
Illinois,  
U.S.A.

Dear Szilard,

Please forgive me not replying earlier to your letter of 24th June, but Alex Rich has been here and I haven't had a moment.

Brenner has nothing on paper about his idea, but we're looking forward to discussing the whole problem with you in September, especially as we've recently thought of a second possibility. Both Seymour Benzer and Mahlon Hoagland will have arrived by September 12th, so I suggest you arrive any time after that. If you would like me to fix up accommodation for you do let me know. I would suggest you stay with us but conditions are rather primitive and the house is full of girls and children. If you could give me some idea of what you like - do you prefer a college to a hotel, for example - and when you expect to arrive I'll try to find something.

With best wishes,

Yours sincerely,

*Francis Crick*

F. H. C. Crick



August 9, 1957

Dr. F.H.C.Crick  
University of Cambridge  
Medical Research Council Unit  
Cavendish Laboratory  
Free School Lane  
Cambridge, England

Dear Crick,

Many thanks for your letter of July 30th, suggesting that I come at some time after September 12th. I shall send you a wire when my travel plans are definitely fixed, giving both the date of my arrival in Cambridge and the date of my scheduled departure.

The Garden House Hotel used to be a nice place to stay in Cambridge. If you think that Trinity, King's, or St. John's would be preferable, and if you can arrange for my staying there on short notice without any inconvenience to anyone, that would be nice also, but there is no reason whatever for exerting yourself unduly in this direction.

With kind regards,

Sincerely,

Leo Szilard