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CALIFORNIA INSTITUTE OF TECHNOLOGY

Pasadena, California

August 30, 1956

An Application to the National Science Foundation

For a Grant to Support

Research in Theoretical and Quantitative Biology

Institutions:

The California Institute of Technology
The University of Chicago
University of Colorado School of Medicine
New York University College of Medicine
The Rockefeller Institute for Medical Research

Administrative Direction:

Division of Biology
California Institute of Technology, Pasadena, California

Total Budget and Duration:

$105,857 for five years or $211,710 for ten years

Starting date:

July 1, 1957

Administrative officer to whom payments should be mailed:

George W. Green, Vice President for Business Affairs
California Institute of Technology
Pasadena, California

Approved for the California Institute of Technology:

/s/ G. W. Beadle
G. W. Beadle, Chairman, Division of Biology

/s/ G. W. Green
G. W. Green, Vice President for Business Affairs

/s/ L. A. DuBridge
L. A. DuBridge, President

Approved for the University of Chicago:

Approved for the University of Colorado School of Medicine:

Approved for New York University College of Medicine:

Approved for The Rockefeller Institute for Medical Research:

Research in Theoretical Biology

Background:

In 1946, after a distinguished career in physics, Professor Leo Szilard became an active research worker in biology. As such, he has had great influence, not only because of his own research efforts, which were to a large extent made in collaboration with Professor Aaron Novick of the University of Chicago, but also because of his catalytic influence on workers in other laboratories. The evidence submitted with this application makes it abundantly clear that in this respect Szilard is a unique person. The persons primarily responsible for suggesting that this proposal to the National Science Foundation be made,* together with others who support it, are convinced that science will profit greatly if he is given research support with freedom to move about among the five participating institutions.

Theoretical biology needs to be strengthened and it is believed that the proposed plan will be a significant factor in accomplishing this.

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* Theodore Puck, University of Colorado School of Medicine
Max Delbrück, California Institute of Technology
Bernard D. Davis, New York University College of Medicine
Rollin D. Hotchkiss, The Rockefeller Institute for Medical Research

The Proposal:

It is proposed that the National Science Foundation make a five- (or ten-) year grant for the salary and travel of Leo Szilard with the understanding that he will spend time at each of the five institutions making this proposal, working in collaboration with the persons indicated in his memorandum, with others or alone. He would be given an appropriate appointment and title at each of these institutions.

It is requested that the grant be made to the California Institute of Technology.

Supporting Evidence:

The following attached documents are offered in support of this proposal:

1. Memorandum by Leo Szilard indicating his interest in the proposal and stating his understanding of how the plan would work.

2. Curriculum Vitae of Leo Szilard.

3. A partial bibliography of Leo Szilard listing some of his papers in physics and his publications in biology.

4. Supporting letters from the participating institutions.

Budget:

Annual salary	$ 14,800
Travel and subsistence per year*	2,500
Contribution to TIAA retirement fund, 7-1/2 % of salary	1,110
Total annual direct cost	18,410
Indirect cost 15 %	2,761
Total annual cost	$ 21,171
Total for five years	$ 105,855
Total for ten years	$ 211,710

* This item is based on the assumption that the equivalent of three cross country trips will be made per year and that two-thirds to three-fourths of Dr. Szilard's time will be spent away from home base.

Aug 30 1946

Memorandum by Leo Szilard

At present I am a member (Professor of Biophysics) at the Enrico Fermi Institute for Nuclear Studies at the University of Chicago. This position, while it may be regarded as very desirable in many respects, does not represent the proper setting for the pursuit of my biological interests.

I take the liberty to submit herewith a memorandum in which I propose to serve as a Senior Research Scientist-At-Large either for five or for ten years.

I understand that under the terms of such a position I would be free to pursue my scientific interests anywhere in affiliation with universities or research institutes. Initially, however, I would be affiliated with the California Institute of Technology, Pasadena, California; the Rockefeller Institute for Medical Research in New York; the Department of Pharmacology of the Medical College of New York University in New York; the Department of Biophysics, Medical School, University of Colorado, in Denver; and the Enrico Fermi Institute for Nuclear Studies at the University of Chicago, Chicago.

In general my research will be in the field of quantitative biology. More particularly, I expect to be concerned with the formation of adaptive enzymes in microorganisms, and the formation of antibodies in spleen cells in vitro, problems connected with the growth of microorganisms and tissue cells in vitro, the growth of viruses in microorganisms, as well as in tissue cells in vitro, and the transformation as well as the transduction of genetic characters in microorganisms.

I would expect initially to cooperate in the Rockefeller Institute with R. Hotchkiss, M. Fox, N. Zinder and Paul Weiss; at New York University with Bernard Davis and Werner Maas; at the University of Colorado with Leonard Lerman and T. T. Puck; at the California Institute of Technology with Max Delbrück and R. Dulbecco; and at the University of Chicago with A. Novick and H. Anker.

In the following I wish to present two points of view that might be relevant in judging the usefulness of my serving as a Research Scientist-At-Large.

(a) At present certain branches of biology in which I am interested are in rapid progress. The problems of protein synthesis, the role of RNA and DNA, and the general problems of self-reproduction, differentiation and aging are rapidly becoming open to attack by means of new techniques. In part, this is due to progress in the field of microbiology and, in part, it is due to progress in the techniques of animal cell cultures,

for me

as well as other fields. This appears to be a situation where it would be of great advantage for anyone interested in general biological laws to be able to shift from one biological material to another, as the problem demands, and to be free from the limitations of using just the few techniques which any one person can master. This ideal is not fully attainable for anyone short of being made head of a research laboratory of some size created de novo, and thus being enabled to assemble, so to speak, from scratch a sufficiently large and varied team, and at the same time being given an administrative setup which leaves the head of the laboratory free of administrative duties in order to enable him to effectively work with such a team. However, as a Research Scientist-At-Large, it might be possible to approximate somewhat this ideal situation (which is probably not fully attainable in the United States). As a Research Scientist-At-Large, it should be possible for me to establish collaboration with a sufficiently large and varied group of scientists scattered across the country in different laboratories, and at the same time I would remain free of administrative duties.

(b) As a Research Scientist-At-Large, it should be possible for me to acquire intimate knowledge of experiments conducted with a great variety of biological material and diverse techniques, and thereby to be in a position to try to function as a "theoretical biologist." This statement requires a qualification:

Biology has not quite reached the stage which was attained by physics half a century ago when enough facts were established to permit a theoretical physicist to come up with significant insights on the basis of the established facts. Yet in biology we might be very well on the verge of a similar situation, and a few scientists who are so inclined may attempt to act, for a period of time at least, as theoretical biologists. This means that it might be well at present for a few scientists to put less emphasis on their own experiments and spend more time trying to keep in close touch with the experiments of others in the hope of being able to recognize new patterns and to gain insight into some general biological laws that have so far not clearly emerged. It may be that the main difference between theoretical physicists of the past and the would-be theoretical biologist of the present is quantitative rather than qualitative. The would-be theoretical biologist would probably not be able to keep on studying the results of others and thinking about them for a very long stretch of time. Much sooner than a theoretical physicist, he will feel impelled to do further experiments (or to induce someone else to do them) because he will feel the need to cut down the number of possible avenues along which his further thinking may be tempted to wander.

With respect to the issue of whether support should be given for five or for ten years, I wish to present the following point of view:

If the support is given for ten years, it would take me to the age of 68 years, which is the present retirement age at most universities. On the other hand, if the support is given for five years, I would have to contemplate returning to the University of Chicago when the support lapses. While I understand that the University of Chicago would be agreeable to my returning to it at any time I desire to do so, prior to reaching retirement age, yet should I return to Chicago after a lapse of five years there would arise the question of how to spend the remaining time in a productive manner.

Curriculum Vitae of Leo Szilard

I was born in Budapest, Hungary in 1898. I went through officers' school there during the first World War and studied engineering there.

In 1920 I left Hungary to continue my engineering studies in Berlin. However, the attraction of physics proved to be too great. Einstein, Planck, Von Laue, Schroedinger, Nernst, Haber, and Franck were at that time all assembled in Berlin and attended a journal club in physics which was also open to students. I switched to physics and obtained a Doctor's degree in physics at the University of Berlin under Von Laue in 1922. My thesis (1 - see attached list of publications) showed that the Second Law of Thermodynamics covers not only the mean values, as was up to then believed, but also determines the general form of the law that governs the fluctuations of the values.

Subsequently, I was a research worker in one of the Kaiser Wilhelm Institutes in Berlin and later joined the teaching staff of the University of Berlin (as Privatdozent) where I remained until 1933. Of the papers (1 - 4) published during this period, some are experimental, and some are theoretical. The last one (4) established the connection between entropy and information which forms part of present day information theory.

In 1933 I went to England. I considered at that time becoming a biologist, and A. V. Hill said that he would find a position for me as a demonstrator in physiology. It occurred to me, however, just then that a nuclear chain reaction might be possible if we could find an element that would emit neutrons when bombarded by neutrons. Artificial radioactivity was discovered a few months later by Joliot and seemed to provide an important new research tool in nuclear physics. This decided me to move into nuclear physics.

In the summer of 1934 I started work as a guest in St. Bartholomew's Hospital in London and this work resulted in the establishment of the Szilard-Chalmers Reaction (5) and the discovery that slow neutrons are emitted by beryllium if the beryllium is exposed to gamma rays of radium (6). In 1939, after the discovery of the fission of uranium, the use of these slow neutrons from beryllium made it possible to see that uranium emits neutrons when bombarded by neutrons; the fast neutrons emitted by uranium could be easily distinguished from the bombarding slow neutrons.

In 1935, after a visit to New York, where I spent a few months as research associate at New York University, I accepted a position at the Clarendon Laboratory, Oxford University. During this period I worked in the field of nuclear physics (8-11). In 1938 I came to America under arrangement with Oxford University, which permitted me to spend half my time in the

United States. I was in the United States during the time the Munich Agreement was negotiated. After Munich I decided to stay in the United States on a full-time basis, and I resigned at Oxford.

In January 1939 I learned of the discovery of fission. It seemed important to find out at once if neutrons are emitted in that process, for in that case a chain reaction in uranium had to be regarded as a serious possibility. I therefore asked the permission of Columbia University to work there as a guest and perform an experiment in order to settle this question. This experiment (jointly performed with Walter Zinn) led to the discovery of the neutron emission of uranium, upon which the chain reaction is based (12, 13). The same discovery was made independently at about the same time by Fermi and his co-workers and by Joliot and his group.

In July, 1939, I recognized that a chain reaction might be set up in a system composed of graphite and uranium. Because of the serious consequences of this possibility, it seemed that this was a matter in which the government ought to take an interest. I therefore went to see Professor Einstein to enlist his help in approaching the government. After several consultations, in which E. P. Wigner and Edward Teller participated, Einstein wrote a letter to President Roosevelt; and in response to this letter, the President appointed a committee under the chairmanship of the Director of the National Bureau of Standards.

In February 1940 I described the chain-reacting uranium-graphite system in a paper I sent to the Physical Review (February, 1940). For reasons of secrecy, this paper was not published.

In November of 1940 a government contract was given to Columbia University for the development of the graphite-uranium system, and I became a member of Columbia University's National Defense Research Staff. Early in 1942 our group was moved to the University of Chicago; and on December 2, 1942, the chain reaction system was put into action.

Recently a patent was granted to the Atomic Energy Commission on the chain-reacting graphite-uranium system, jointly in the names of Enrico Fermi and myself.

In 1943 I became a naturalized citizen of the United States.

In October, 1946 I joined the staff of the University of Chicago as Professor of Biophysics in the Institute of Radiobiology and Biophysics. This institute never grew as originally intended, it had a succession of directors, and it was recently dissolved. I remained on the staff of the University of Chicago but have so far not joined any department in the biology division.

I should perhaps mention here that I have been for a number of years also Visiting Professor in the Department of Biophysics of the Medical School at the University of Colorado.

When in 1946 I was faced with the task of converting myself into a biologist, I teamed up with Dr. Aaron Novick, a physical chemist. I had known him from his work in the uranium project. We both got out training in biology through summer courses, such as Dr. Delbrück's course in Cold Spring Harbor in bacterial viruses, and Dr. Van Niel's course in bacterial biochemistry at Pacific Grove. Dr. Novick and I worked as a team until recently when the Institute of Radiobiology and Biophysics was dissolved.

A list of publications is attached, containing a short description of each paper. When we started out, we tried to understand a striking phenomenon just then discovered by A. Kelner, who showed that bacteria killed by ultraviolet light can be reactivated by shining visible light at them (B1). A detailed analysis of the phenomenon enabled us to interpret it in terms of a "poison" that is produced by ultraviolet light and is decomposed by visible light. This interpretation was at first controversial due to Dulbecco's work on light reactivation of ultraviolet killed bacterial viruses, but has in the meantime become widely accepted. My own interest in the subject waned when I could not convince myself that we were dealing with a phenomenon that serves a useful biological purpose in the life of the bacteria.

Next, we turned our attention to the study of bacterial viruses in the assumption that viruses may prove to be much simpler than bacteria. We obtained some very interesting results (2) but decided to shift after a while to the study of bacteria.

The two phenomena in which we were particularly interested were a) mutations and b) the formation of adaptive enzymes which promised to provide a tool for the study of protein synthesis.

We were dissatisfied, however, with the methods that were available for the study of these phenomena. It seemed to us necessary to study bacterial populations in the growing condition in a stationary state, i.e. we thought we ought to use a continuous flow device. We developed such a device, which we called a "Chemostat." In this particular device the rate of growth of the bacteria can be changed by changing the concentration of one of the growth factors of our choosing which we make the controlling growth factor.

We started out by using the "Chemostat" for the study of mutations and obtained quite unexpected results at the very outset. It turned out, for instance, that the rate at which certain mutations occur does not

change when we change the rate at which the bacteria divide; we could vary the rate of growth within a wide range without changing the rate at which these mutations occurred. We found one family of compounds - purines - which may cause an about tenfold increase in the mutation rate of bacteria without any appreciable killing. And we also found antimutagens, which in very small contractions will fully counteract the effect of purine-type mutagens.

In a bacterial population maintained in the "Chemostat" there occur evolutionary changes (3) and one strain of bacteria is replaced by a mutant strain, which can grow faster in the conditions prevailing in the growth tube of the "Chemostat." We observed successive evolutionary steps of this sort in each experiment of sufficiently long duration and were able to analyze the phenomenon.

Experiments on adaptive enzyme formation performed by means of the "Chemostat" are still in their infancy but it seems that the "Chemostat" will prove to be a necessary tool in that field also.

PARTIAL BIBLIOGRAPHY OF LEO SZILARD*
(with annotations)

A. Physics

(1) Zeitschrift für Physik, 1925, p. 753, 32. This paper extends the application of thermodynamics to the derivation of the laws of thermodynamical fluctuations. It was accepted as dissertation by the University of Berlin.

(2) Zeitschrift für Physik, 1925, p. 688, 33. - jointly with H. Mark. This paper reports experiments which revealed anomalous scattering of X-rays.

(3) Zeitschrift für Physik, 1926, p. 743, 35. - jointly with H. Mark. This paper reports experiments on polarizing X-rays by reflection on crystals.

(4) Zeitschrift für Physik, 1929, p. 840, 35. This paper evaluates the increase of entropy which is connected with operations of an intelligent being on a thermodynamical system if these operations are controlled by measurements of variables which are subject to thermodynamical fluctuations. This paper was accepted as Habilitationschrift by the University of Berlin.

(5) "Chemical Separation of the Radioactive Element from its Bombarded Isotope in the Fermi Effect" -- jointly with Chalmers. Nature, p. 462, 134, 1934. This paper demonstrates a generally applicable process (Szilard-Chalmers reaction) for the concentration of a radioactive element produced by neutrons if the element has to be separated from a mass of a stable element with which it is chemically isotopic.

(6) "Detecting Neutrons Liberated from Beryllium by Gamma Rays," p. 494, 134, 1934. Nature.
This paper describes the discovery of radium-beryllium photo neutrons which, being of low energy, represent a useful tool in nuclear research. They were universally used later in the discovery and investigation of neutron emission of uranium on which a chain reaction is based.

(7) "Liberation of Neutrons from Beryllium by X-Rays" -- jointly with a group of six others, p. 880, 134, 1934. Nature. Using x-rays in place of gamma rays the threshold for the emission of photo neutrons from beryllium is determined by varying the voltage of an X-ray tube and is found to be somewhat above 1.5, and well below 2 m.e.v.

(8) "Radioactivity Induced by Neutrons" -- jointly with Chalmers, p. 98, 135, 1935. Nature. In this paper a neutron induced radioactive period of about 3-1/2 hours is reported in Indium which does not fit in with the explanations found for other radioactive periods. In a later paper it is shown that it is due to an excited Indium nucleus which is isomeric with stable indium nucleus 115.

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*Some of Szilard's most important works still remain unpublishable, for reasons of national security.

(9) "Absorption of Residual Neutrons," p. , 136, 1935. Nature. This paper reports the discovery of neutron resonances at low energies, gives an estimate of their energies, and states that the energies can be measured by observing the absorption of the residual neutrons in boron or lithium.

(10) "Gamma Rays Excited by Capture of Neutrons," p. 323, 139, 1937 -- jointly with Griffiths. Nature. This paper reports on the observation of gamma rays emitted by a number of odd elements which are strong neutron absorbers. The counts observed per absorbed neutron were found to be 15 per cent identical for all these elements.

(11) "Radioactivity Induced by Nuclear Excitation" -- jointly with Goldhaber and Hill, p. 47, 55, 1939. Phys. Rev. In this paper the previously reported period in indium is investigated and the conclusion is reached that it is due to nuclear excitation of the stable indium isotope 115.

(12) "Instantaneous Emission of Fast Neutrons in the Interaction of slow Neutrons with Uranium" -- jointly with Zinn, p. 799, 55, 1939. Phys. Rev. In this paper the discovery of the neutron emission of uranium is reported. It is estimated that two neutrons are emitted per fission. The neutrons from uranium are made visible on an oscillograph screen. As primary neutrons, radium-beryllium photo neutrons were used which, because they are slow, can be easily distinguished from the fast neutrons emitted by uranium. This discovery which was made independently by Fermi in the same year indicated the feasibility of a sustaining nuclear chain reaction.

(13) "Emission of Neutrons by Uranium" -- jointly with Zinn. p. 619, 56, 1939. Phys. Rev. Detailed report of above mentioned experiments, number of neutrons per fission measured as 2.3.

(14) "Neutron Production and Absorption in Uranium" -- jointly with Anderson and Fermi. p. 284, 56, 1939. Phys. Rev. This paper reports an investigation on the chain reaction qualities of a uranium-water system. It is estimated that 1.5 neutrons are emitted for every thermal neutron which is absorbed by uranium.

Dr. Szilard's part in bringing about of the first nuclear chain reaction; in the design of the first nuclear reactor (atomic pile) are described, insofar as these matters can be made public, in the Official Report: Atomic Energy for Military Purposes, Henry D. Smythe, 1945, Princeton University Press, pages 34, 47, etc.

B. BIOLOGY

(17) A. Novick and Leo Szilard - EXPERIMENTS ON LIGHT-REACTIVATION OF ULTRA-VIOLET INACTIVATED BACTERIA. Proceedings of the NATIONAL ACADEMY OF SCIENCES. Vol. 35, No. 10, pp. 591-600.

(18) Aaron Novick and Leo Szilard - VIRUS STRAINS OF IDENTICAL PHENOTYPE BUT DIFFERENT GENOTYPE. Science, January 12, 1951, Vol. 113, No. 2924, pp. 34-35.

(19) Aaron Novick and Leo Szilard - EXPERIMENTS WITH THE CHEMOSTAT ON SPONTANEOUS MUTATIONS OF BACTERIA. Proceedings of the NATIONAL ACADEMY OF SCIENCES. Vol. 36, No. 12, pp. 706-719, December, 1950.

(20) Aaron Novick and Leo Szilard - DESCRIPTION OF THE CHEMOSTAT. Science, December 15, 1950. Vol. 112, No. 2920, pp. 715-716.

(21) Aaron Novick and Leo Szilard - EXPERIMENTS ON SPONTANEOUS AND CHEMICALLY INDUCED MUTATIONS OF BACTERIA GROWING IN THE CHEMOSTAT. Cold Spring Harbor Symposia on Quantitative Biology. Vol. XVI, 1951.

(22) Aaron Novick and Leo Szilard - ANTI-MUTAGES. Nature, Vol. 170, p. 926, November 29, 1952.

(23) Aaron Novick and Leo Szilard - EXPERIMENTS WITH THE CHEMOSTAT ON THE RATES OF AMINO ACID SYNTHESIS IN BACTERIA. Dynamics of Growth Processes. Princeton University Press, pp. 21-32, 1954.

(24) Maurice S. Fox and Leo Szilard - A DEVICE FOR GROWING BACTERIAL POPULATIONS UNDER STEADY STATE CONDITIONS. Journal of General Physiology 39, p. 261-6, 1955.

The first of these papers (#17) investigates a phenomenon discovered by A. Kelner after the war, who showed that bacteria "killed" by ultraviolet light can be revived by shining visible light on them. Experiments designed to analyze the phenomenon are described in this paper; they lead to the conclusion that the ultraviolet light produces a "poison" which can be inactivated by light and that this "poison," if present when, subsequent to irradiation, the bacteria divide, will cause both death and mutations.

The second paper (#18) describes the discovery that, when a bacterium is infected simultaneously with two related viruses which differ from each other both in genotype and phenotype, the virus population emerging from the bacterium contains a class of viruses which have the genotype of one and the phenotype of the other.

The papers #19 to #23 describe a new way of studying bacteria by maintaining a bacterial population in a stationary (exponentially growing) state indefinitely and controlling the growth rate by controlling the rate of supply of an essential growth factor. An apparatus is described in these papers which will conveniently accomplish this and which is designated as the Chemostat.

In studying mutations in bacteria or the formation of adaptive enzymes in bacteria inaccurate, and therefore misleading, results are frequently obtained by studying bacterial cultures in flasks in which the number of bacteria increases exponentially and today the use of the Chemostat appears to be indispensable.

In the papers #19 to #22, the Chemostat is used in the study of mutations. It turns out that the rate at which mutations occur in a growing bacterial population under the conditions studied is not proportional to the rate at which cell division occurs, rather the mutation rate is constant per unit time independent of the rate at which the culture is growing. There is found one group of compounds, all purine derivatives, of which caffein is one, which greatly increases the mutation rate without having an appreciable killing effect on the bacteria.

There is another group of compounds described in these papers, all of them ribosides of purines which in small quantities will completely counteract the action of the above mentioned purine type mutagens and also reduce the rate of spontaneous mutations.

In paper #23, the Chemostat is used to study the biosynthesis of amino acids in bacteria and the regulatory mechanisms which are involved in it. The bio-synthetic apparatus of the bacteria respond to amino acid concentrations in the medium, which are exceedingly low. For instance, a bacterium which can make arginine and will do so if there is no arginine in the medium, will stop making arginine if an arginine concentration of 10^{-9} ga/ce is maintained in the medium in the Chemostat. (Novick and Szilard - unpublished.)

One way of studying such regulatory mechanisms is based on the use of a mutant which is blocked in the synthesis of an amino acid--in our case Tryptophane--and which pours out into the medium a "precursor" of that amino acid. Paper #23 utilizes such a mutant. In the absence of Tryptophane in the medium, a precursor of Tryptophane is poured out by the mutant into the medium at a rate which is independent of the growth rate of the bacteria. In the presence of Tryptophane this "precursor" is <u>not</u> poured out by the bacteria. It is conceivable that this indicates a general phenomenon of regulation through a negative feed-back of the final product at one of the <u>early</u> steps of the metabolic pathway leading to Tryptophane.

In paper #24, there is described a device called a breeder. In this device bacteria may be grown in a continuous flow of nutrient. The flow of the nutrient is controlled by the turbidity of the bacterial culture and the growth is not limited by a growth factor, as is the case in the "Chemostat."

This device was developed in order to study mutations in bacteria under conditions of growth at the maximal rate, and such a study was carried out by Maurice S. Fox.

CALIFORNIA INSTITUTE OF TECHNOLOGY

Division of Biology

August 13, 1956

Mr. William Consolazio
The National Science Foundation
Washington 25, D. C.

Dear Mr. Consolazio:

I write this in support of the proposal that the National Science Foundation grant the funds necessary to appoint Professor Leo Szilard a Roving Professor with the understanding that he will spend time at each of the five institutions named in the application, i.e., California Institute of Technology, The University of Chicago, The University of Colorado Medical School, New York University College of Medicine, and The Rockefeller Institute for Medical Research.

The idea evolved from a suggestion made by Ted Puck that we ought to explore the possibility of some kind of an inter-institutional appointment for Szilard -- that only in this way could his unique characteristics be most useful to science. Max Delbrück of this laboratory lent his enthusiastic support. The Faculty of the Division unanimously approved the plan outlined in the accompanying application. I then checked with Robert F. Bacher, Chairman of the Division of Physics, Mathematics and Astronomy, and with Linus Pauling of the Division of Chemistry and Chemical Engineering. The physicists and chemists here are equally in favor of having Szilard spend a fraction of his time at the Institute. It is therefore abundantly clear that support for the plan is widespread at the Institute.

I sincerely hope the National Science Foundation will be able to make the requested grant.

Sincerely yours,

/s/ G. W. Beadle

G. W. Beadle
Chairman

UNIVERSITY OF COLORADO
MEDICAL CENTER

4200 East Ninth Avenue
Denver 20, Colorado

July 23, 1956

Dr. G. W. Beadle
Biology Division
California Institute of Technology
Pasadena, California

Dear Doctor Beadle:

This letter for transmittal to the National Science Foundation indicates our expectations with respect to Dr. Leo Szilard's contributions and responsibilities to this department, under the proposed arrangement for his appointment as a Scholar and Visiting Professor.

Dr. Leo Szilard possesses one of the most versatile and keenly analytic minds of our generation. His ability logically to dissect problems and to consider new and unconventional approaches to their solution is a scientific asset of enormous value.

We are expecting Dr. Szilard's specific contributions to the program of the Department of Biophysics to involve the following functions:

a) One of the main interests of this department lies in the general field of bacterial genetic processes and bacterial viruses. This area represents one of the foremost opportunities for application of molecular analysis to the problem of biological replication. The models currently developing from work in this area are fundamental in their own right; in addition, they furnish a system which can guide genetic studies in mammalian cells, which now have become accessible to investigation by quantitative techniques like those hitherto confined only to microorganisms. The department has an excellent group of younger scientists at the assistant professorial level who are pursuing problems in bacterial genetics and bacteriophage. However, with the turning of my own energies to problems of mammalian cell biology, there is need for mature advice from an older person actively interested in bacterial and virus replication. These younger men possess good training, drive, and real creative ability. They and their students would profit greatly from regular access to a person with the scientific maturity and intimate acquaintance with the field, which Dr. Szilard possesses, to criticize, stimulate, and assist in guiding their efforts. While we foresee that Dr. Szilard's contribution here will be mainly in the supply of guidance, criticisms, and suggestions, we hope it will be possible to provide facilities for him to undertake some experimental work himself in this area, if the occasion should arise.

b) Dr. Szilard's participation in departmental research seminars will be of great value in our training program. His ability to stimulate, challenge, and inspire graduate students is especially effective in a program like ours that is small and, to an appreciable extent, informal. His orien-

tation toward science and its problems is one which coincides completely with the philosophy of this department; i.e., an emphasis on clearness of thinking and simplicity of operations, so as to achieve maximally definitive answers, with a minimum of manipulation and complex procedure. Both the faculty and the students can learn a great deal from Dr. Szilard, and we look forward to an arrangement that will make possible continuing opportunity for participation with him in discussions and seminars.

c) For some time it has been our hope to be able to add to the lines of this department's program a study in biological regulatory and integrative mechanisms. Such investigation would have to be of limited scope and involve new and simple approaches consistent with the scale of the department's facilities. The time at which such an activity could start would be strongly dependent on progress made in the other programs, and on the availability of additional space and scientific personnel. Dr. Szilard has always had an absorbing interest in these problems, and has made critical conceptual contributions which have anticipated development of modern Information Theory. If our plans for this particular type of expansion reach fruition, Dr. Szilard would be of enormous assistance in the formulation of such an activity.

In addition to these specific activities in the Department of Biophysics, Dr. Szilard could contribute a great deal to many areas of this University. The faculties of the Physics Department, the High-Altitude Observatory, and many of the bio-medical departments will undoubtedly take advantage of the opportunity to consult with him regularly about their programs. His influence could have widespread effects throughout this scientific community.

Dr. Francis Manlove, Director of the Medical Center, approves of these arrangements, and is so indicating in a separate covering letter.

Sincerely,

/s/ Ted Puck

Theodore T. Puck, Ph.D.
Professor and Head
Department of Biphysics

UNIVERSITY OF COLORADO

MEDICAL CENTER

4200 East Ninth Avenue
Denver 20, Colorado

Office of the Director
Dean of the Department of Medicine

July 27, 1956

Dr. G. W. Beadle
Biology Division
California Institute of Technology
Pasadena, California

Dear Dr. Beadle:

Dr. Theodore Puck has discussed with me the proposed arrangement of a Visiting Professorship for Dr. Leo Szilard.

Dr. Szilard has given valuable advice and inspiration to members of our faculty in recent years, and I am happy to lend my support to the proposed arrangement of his affiliation with this institution.

Sincerely yours,

/s/ Francis R. Manlove

Francis R. Manlove, M. D.

FRM:rw
cc: Dr. Theodore Puck

NEW YORK UNIVERSITY--BELLEVUE MEDICAL CENTER

NEW YORK UNIVERSITY COLLEGE OF MEDICINE

550 First Avenue, New York 16, N. Y.

Department of Pharmacology

August 27, 1956

Dr. George W. Beadle
California Inst. of Technology
Pasadena, Calif.

Dear Dr. Beadle,

I am writing in support of an application, to be made by the Calif. Institute of Technology, for a grant that would make it possible for Dr. Leo Szilard to carry out research, and serve as a consultant, at several different institutions.

As I visualize the scheme, it would leave Dr. Szilard free to distribute his time as he saw fit in whatever institutions might interest him from time to time. It is naturally expected that he would spend an appreciable amount of time each year at each of the institutions that are initiating the project. Since our work in the Dept. of Pharmacology at New York Univ. College of Medicine is more biochemical than biophysical in orientation, we do not expect that he would be likely to spend a large part of his time here; but if he should wish to settle for a considerable period of time here I should be delighted and I am confident that we could provide space for him.

My interest in supporting this project is based primarily on the belief that it would provide a much better chance than Szilard's present situation for the full exercise of his remarkable talents. In recent years he has engaged extensively in visiting other laboratories, where he has been most generous in giving thoughtful and deep attention to the work in progress; we have benefited considerably from such visits, and look forward to their continuation. Szilard has a unique ability to grasp instantly the most varied problems, to seize upon their significant aspects, and to apply to them unusual imaginative and critical powers. These visits have often led to valuable new experiments and have given to many young biologists a much enhanced sense of the distinction between significant and trivial problems. The position we are trying to arrange would regularize such peripatetic activities and would at the same time provide the opportunity, if his interests so directed, for an extended period of work at a single institution.

This proposal has the warm approval of our dean, Dr. Donal Sheehan.

Sincerely,

/s/ B. D. Davis

Bernard D. Davis

THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH

66th Street and York Avenue
New York 21, N. Y.

August 30, 1956

The National Science Foundation
2101 Constitution Avenue, N.W.
Washington 25, D. C.

Dear Sirs:

It seems desirable in recommending Dr. Leo Szilard's appointment as Senior Research Scientist to outline the nature of his relationship to our faculty as I picture it.

It frequently happens that biological research workers reach a point at which they possess high skills and energy for advanced investigation, and need the stimulus of serious discussion with interested scholars outside their own field. This kind of association can be of inestimable value, in providing perspective, and in obliging the research worker to recapitulate the major logical steps in his philosophy. Best of all, it helps him to perceive the significant past and future experiments which will best demonstrate or define his discoveries for intelligent scholars in another discipline. Inasmuch as biochemical and biological research rests ever more and more upon a foundation of physical understanding, a physicist who is interested in biology can be a stimulating and valuable colleague wherever this potential of energy and skill is not being optimally utilized. This kind of association happens only peripherally at the national scientific congresses as they grow in size and busyness.

Dr. Szilard is superbly suited to play this role in a number of laboratories, wherever he can be made to feel welcome. I would take it to be the function of the proposed program to give him the requisite status at each of the participating institutions so that this stimulatory function, which he already plays unofficially in a number of places, can be made available to research groups who do not have access to his quick, penetrating intelligence at present, who in fact do not know that such fruitful discussion can be had anywhere.

I believe this Institute can supply this environmental status and potential for the utilization of Dr. Szilard's talents in several of of its laboratories. It would be premature, not to say presumptuous, to attempt to suggest which of its various faculty members would enjoy contact with him and deliberately foster his participation in the uncompromisingly logical evaluation of their work. I have witnessed how his insight has already sharply altered the philosophy and design of certain experiments in muscle physiology carried out here by Dr. Czapo. Our own microbial genetics and physiology group, comprised of Dr. Maurice Fox,

Dr. Muriel Roger and myself, with a number of pre-doctoral and post-doctoral associates, will probably not see him much more than at present, five or six days, and several lunches, during a year. But I look forward fully as much to being at hand sometimes when his attention is focused on other subjects, as I am sure it will be. It is important to point out from direct experience that his advice and suggestions while theoretically oriented are always refined in mutual discussion until they result in altogether concrete and practical experimental questions.

Concerning the personal requirements, I know that Dr. Szilard's objective and analytical logicalness and his candor are effectively balanced by his perspicacity, considerateness, and sensitiveness to the interests of others. Association with him is at its most stimulating and rewarding level when not continuous, but shared with a number of institutions and colleagues, as projected.

Finally, making an appointment of this nature will be something of an opportunity for exploring new ways of furthering scientific progress. It would be in the highest interests of science if an official and nationally affiliated institution will make available funds from time to time to investigators of proven productivity without requiring the usual statement of precise work to be attempted, or institutional location. In representing this Institute, I can say that appointment of Dr. Szilard as Senior Research Scientist will, without doubt, be a fruitful step in bringing together in a number of areas the concrete material of biology and the analytical thinking of modern physical science and mathematics.

Sincerely yours,

/s/ Rollin D. Hotchkiss

Rollin D. Hotchkiss
Member

RDH:jp

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