FELLOWSHIP APPLICATION FORM

CONFIDENTIAL

JOHN SIMON GUGGENHEIM MEMORIAL FOUNDATION

551 FIFTH AVENUE • NEW YORK 17 • N • Y •

APPLICATIONS and accompanying documents should reach the Secretary of the Foundation not later than October 15 of each year.

In what field of learning, or of art, does your project lie? Biology

Concise statement of project Mutation in microorganisms; an attempt to understand the mechanism by which genetic changes are brought about in those biochemical characteristics that influence the growth of bacteria.

PERSONAL HISTORY:

Name in full Francis Joseph Ryan

Present address 501 W. 113th St, New York 25, N.Y.

Telephone University 4-6670

A permanent address 501 W. 113th St., New York 25, N.Y.

Present occupation Associate Professor of Zoology

Place of birth Brooklyn, N.Y. Date of birth February 1, 1916

If not a native-born American citizen, date and place of naturalization

Single, Married, Widowed, Divorced Married

Name and address of wife or husband Elizabeth J. Ryan, 501 W. 113, New York 25

Name and address of nearest kin, if unmarried

Ages of children, if any

Have you any constitutional disorder or physical disability? No

With this application please submit a small recent photograph. Please see attached sheet.

EDUCATION:

1. Give a summary of your education in the following form:

	Name of Institution	Period of Study (*give dates*)	Degrees, Diplomas, Certificates (*give dates*)
Academic: College	Fordham	1933-1934	
	Columbia	1934-1937	A.B. 1937
University	Columbia	1937-1941	A.M. 1939
			Ph.D. 1941
Technical			
Professional			
Musical			
Artistic			
Special Study			

2. Give a list of the scholarships or fellowships you have previously held or now hold, stating in each case the places and periods of tenure, the studies pursued during your incumbency, and amounts of the stipends: National Research Council Fellowship in Zoology, Stanford University, 1941-42; worked on the development of frogs eggs and on the genetics and growth of Neurospora; $2200.

3. State what foreign languages you have studied, and whether you are able to consult works on your subject in these languages. Estimate your proficiency in reading, writing and speaking each of them: German: read easily, speak and write with some difficulty.
French: read, am at present learning to speak and write.
Spanish: read, speak and write with difficulty.

2. Of what learned, scientific or artistic societies are you a member?

Phi Beta Kappa
Sigma Xi
American Society of Zoologists
American Society of Bacteriologists
Botanical Society of America
Genetics Society of America
Society of Vertebrate Paleontology
Marine Biological Laboratory Corporation, Woods Hole
New York Academy of Sciences
American Society of Naturalists
Harvey Society

ACCOMPLISHMENTS:

1. Positions held (professional, teaching, scientific, administrative, business):

Name of Institution or Organization	Title of Position	Years of Tenure (*give dates*)	Compensation
Columbia University	Instructor	1942-1944	$2,800
" "	Assistant Professor	1944-1946	4,000
" "	" "	1946-1948	5,500
" "	Associate Professor	1948-	6,600

2. Of what learned, scientific or artistic societies are you a member? Please see attached sheet.

3. Submit a full account of the advanced work, research, or creative work you have already done, giving dates, subjects, and names of your principal teachers in these subjects. What are your present attainments in your proposed field of study?

4. Submit a *list* of your publications with exact titles, names of publishers, and dates and places of publication.
(Please submit two copies of each statement requested under items 3 and 4, above. Please do not submit copies of publications or manuscripts.)

PLANS FOR WORK:
Submit a statement giving detailed plans for the work you would pursue during your tenure of a Fellowship. This statement should include, *inter alia:* a description of the project, including its character and scope, and the significance of its presumable contribution to knowledge, or to art; the present state of the project, time of commencement, progress to date, and expectation as to completion; the place or places where the work would be carried on, and the authorities, if any, with whom it would be done; your expectation as to publication of the results of your work; and your ultimate purpose as a scholar or artist. *This statement should be complete and carefully prepared.* (Please submit one more copy of PLANS FOR WORK than the number of your references.)

If awarded a Fellowship—

When would you wish to commence the study proposed? September, 1950.

What is your estimate of its probable duration? 12 months during which time I shall be on sabbatical leave with a salary of $3,000.

REFERENCES:

Submit a list of names of persons from whom confidential information may be obtained concerning your abilities, especially in relation to the work you propose, and from whom expert opinion may be obtained as to the value and practicability of your proposed work. (All statements by references to the Foundation are held strictly confidential.)

Name of Reference	Position	Address
G.W. Beadle	Professor of Biology Executive Office of the Department	Biological Laboratories California Institute of Technology, Pasadena, Calif.
E.L. Tatum	Professor of Biology	Department of Biology Stanford University, Cal.
K.W. Cooper	Associate Professor of Biology	Department of Biology Princeton University Princeton, N.J.
Franz Schrader	Professor of Zoology	Department of Zoology Columbia Univ., New York, 27
~~Theodosius Dobzhansky~~	~~Prof. of Zoology~~	~~Department of Zoology~~ Columbia Univ., New York, 27

If you have applied or expect to apply elsewhere for any fellowship or scholarship for the same period, state the facts regarding such applications: I intend to apply to the Conference Board of Associated Research Councils and to the Rockefeller Foundation as alternate possibilities.

If you apply elsewhere for any fellowship or scholarship after presenting this application, please notify the Foundation immediately.

SIGNATURE _____

PLACE AND DATE OF MAILING _____

SUGGESTIONS CONCERNING APPLICATIONS

1. If convenient, please type application and additional material.
2. Use paper the size of this sheet, 8½" x 11", if possible, for writing all documents submitted.
3. Every page or document submitted must bear the applicant's name plainly written.
4. Whenever the space provided in this form is not suitable for an applicant to present fully the facts of his or her case, it is requested that they be stated in a separate document.
5. Only one copy of the application form should be submitted to the Foundation by the applicant; the other may be retained by him for his own files.
6. It is suggested that applications and accompanying documents be sent by registered mail, addressed to the John Simon Guggenheim Memorial Foundation, 551 Fifth Avenue, New York 17, N. Y.
7. If you do not get a receipt for your application within a reasonable time, please notify the Foundation.

Francis J. Ryan

LIST OF PUBLICATIONS

1940 Francis J. Ryan and Ronald Grant. The stimulus for maturation and for ovulation of the frog's egg. Phys. Zool. 13:383-389.

1941 Francis J. Ryan. The time-temperature relation of different stages of development. Biol. Bull. 81:432-440.

1941 Francis J. Ryan. Temperature change and the subsequent rate of development. J. Exp. Zool. 88:25-54.

1943 Francis J. Ryan. Crossing-over and second division segregation in fungi. Bull. Torrey Bot. Club. 70:605-611.

1943 Francis J. Ryan, F.W. Beadle and E.L. Tatum. The tube method of measuring the growth rate of Neurospora. Am. J. Bot. 30:784-799.

1944 Francis J. Ryan, E.L. Tatum and A.C. Giese. The four-carbon respiratory system and growth of the mold Neurospora. J. Cell and Comp. Physiol. 23:83-94.

1944 Francis J. Ryan and Erwin Brand. A method for the determination of leucine in protein hydrolysates and in foodstuffs by the use of a Neurospora mutant. Jour. Biol. Chem. 154:161-175.

1944 Robert Ballentine, Gwendolynn M. Tuck, Lillian K. Schneider and Francis J. Ryan. An unidentified growth factor for a gas gangrene Clostridium. Jour. Am. Chem. Soc. 66:1990.

1945 Francis J. Ryan, Robert Ballentine, Lillian K. Schneider and Gwendolynn M. Tuck. Certain sulfonamide drugs and certain derivatives of ascorbic acid in experimental gas gangrene in wounded mice. Surgery 17:47-53.

1945 Erwin Brand, Leo J. Saidel, William H. Goldwater, Beatrice Kassel and Francis J. Ryan. The empirical formula of beta-lactoglobulin. Jour. Am. Chem. Soc. 67:1524-1532.

1945 Erwin Brand, Francis J. Ryan and Eugene M. Diskant. Leucine content of proteins and foodstuffs. Jour. Am. Chem. Soc. 67:1532-1534.

1945 Francis J. Ryan, R. Ballentine, E. Stolovy, M.E. Corson, and L.K. Schneider. The Biosynthesis of Pantothenic Acid. Jour. Am. Chem. Soc. 67:1857-1858.

1946 Francis J. Ryan, Robert Ballentine, Lillian K. Schneider, Edith Stolovy, Mary E. Corson and Elizabeth J. Ryan. The use of antibiotics, vitamin analogues and other compounds in experimental gas gangrene. Jour. Inf. Diseases 78:223-231.

*1946 Francis J. Ryan and Joshua Lederberg. Reverse-mutation and adaptation in leucineless Neurospora. Proc. Nat. Acad. Sci. 32:163-173.

1946 Francis J. Ryan. The application of Neurospora to bioassay. Fed. Proc. 3:366-369.

*1946 Francis J. Ryan, Lillian K. Schneider and Robert Ballentine. Mutations involving the requirement of uracil in Clostridium. Proc. Nat. Acad. Sci. 32:261-271.

*1946 Francis J. Ryan. Back-mutation and adaptation of nutritional mutants. Cold Spring Harbor Symp. on Quant. Biol. 11:215-227.

1947 Francis J. Ryan, Lillian K. Schneider and Robert Ballentine. The growth of Clostridium septicum and its inhibition. Jour. Bact. 53:417-434.

1947 Francis J. Ryan and Lillian K. Schneider. The relation of the bacterial production of ammonia gas to the growth of other organisms. J. Bact. 54:209-211.

*1947 Francis J. Ryan. Genetics, biochemistry and the growth of microorganisms. Euclides. 77:297-308.

*1948 Francis J. Ryan. On the stability of nutritional mutants of bacteria. PNAS 34:425-435.

*1948 Francis J. Ryan. The germination of conidia from biochemcial mutants of Neurospora. Am. J. Bot. 35:497-503.

*1948 Francis J. Ryan and Lillian K. Schneider. Consequences of mutation during the growth of biochemical mutants of Escherichia coli. I. The pattern of adaptation in histidineless cultures. J. Bact. 56:699-708.

1948 Francis J. Ryan, Vertebrate Zoology and Evolution. A Laboratory Guide. Kings Crown Press.

1948 Francis J. Ryan, Vertebrate Zoology and Evolution. A Lecture Guide. Kings Crown Press.

*1948 T. C. Sheng and Francis J. Ryan. Mutations involving the production of conidia and the requirement for leucine in a mutant of Neurospora. Genetics 33:221-227.

*1949 Francis J. Ryan. Reverse mutation of biochemical mutants. Proc. 4th International Congress for Microbiology. Copenhagen, 1947:384.

*1949 Francis J. Ryan. Interactions during the growth of mutating populations of bacteria. Proc. 6th International Congress for Experimental Cytology. Stockholm, 1947. Acta Physiol. Scandinavica 18:220-224.

*1949 Francis J. Ryan and Lillian K. Schneider. Mutations during the growth of biochemical mutants of Escherichia coli. Genetics 34:72-91.

*1949 Francis J. Ryan and Lillian K. Schneider. The consequences of mutation during the growth of biochemical mutants of Escherichia coli. II. The inhibition of histidine-independent bacteria by histidineless bacteria in unshaken cultures. J. Bact. 58:181-189.

*1949 Francis J. Ryan and Lillian K. Schneider. The consequences of biochemical mutants of Escherichia coli. III. The inhibition of histidine-independent bacteria by histidineless bacteria in aerated cultures. J. Bact. 58:191-200.

*1949 Francis J. Ryan and Lillian K. Schneider. The consequences of mutation during the growth of biochemical mutants of Escherichia coli. IV. The mechanism of inhibition of histidine-independent bacteria by histidineless bacteria. J. Bact. 58:201-213.

*1949 Francis J. Ryan. Adaptation and mutation in microorganisms. Teaching Scientist, in press.

*1949. David D. Perkins and Francis J. Ryan. Mutation in microorganisms. Ciencia y Investigacion, in press.

*1949 Francis J. Ryan. Selected methods of Neurospora genetics. Methods in Medical Research, in press.

Francis J. Ryan

PLAN FOR WORK

My project is part of an attempt to understand the factors controlling growth by use of genetic techniques. We know that genes are in ultimate control of growth, but we know little about what genes are like. We know that they control growth by enabling steps in biosynthesis, but we have only notions regarding the intimate details of this influence. We know that genes are not perfectly stable, yet we do not have adequate techniques to measure their instability. The mutation of genes results in the formation of mutant nuclei, cells or organisms. These mutants, differing from their fellows, are, during growth, thrown into a competition, the outcome of which may or may not be satisfactory. If satisfactory, the adjustment may be called an adaptation, but we do not know that all adaptations have this origin.

That microorganisms have special advantages for studies on the genetic control of growth has been adequately demonstrated in recent years. Biochemical mutants have been obtained which are unable to carry out single steps in biosynthesis due to mutations in single genes. These mutations, which we are studying in the red bread mold Neurospora and in bacteria, are frequently unstable, and we have been able to demonstrate that reverse-mutations occur. In Neurospora it has not yet been possible to measure the rate of back-mutation because of a surprising selection against the back-mutants. In Escherichia coli we have been able to satisfactorily analyze the role of selection and have, with precision, calculated mutation rates by orthodox methods. The reliability of such methods has, however, become subject to question because of an inconsistency between the assumptions involved and the behavior of mutating populations of bacteria. This inconsistency resides in the notion that mutations are random and occur with a given chance per gene per unit time. Perhaps they do, in which event a hithertofore unrecognized disadvantage is associated with a newly arisen mutant. In either event, and I trust this year's researches will allow an answer, new methods must be used for the calculation of mutation rate.

Once a reliable technique is developed, opportunities not previously available exist for the study of factors controlling mutation rate. These include external variables such as radiation and temperature, internal variables such as genetic constitution, and finally, variables peculiarly associated with the mutating gene which may allow for directed mutation. It is by indirect methods such as these that clues can be secured about the nature of the gene and the physical chemistry of mutation.

Knowledge of this character could be used directly in understanding the adaptive growth of microorganisms. The recent application of genetic techniques has shown that adaptations to drug and bacteriophage resistance have their origin in mutations. We have shown that mutations can also result in adaptations which dispense with growth factor requirements. In addition, selection for or against the mutant plays a critical role in determining whether mutation is followed by adaptation. At the present time most geneticists feel that all inherited adaptations could be explained in terms of mutation and selection. On the other hand, microbiologists have been reluctant to give up the feeling that adaptations are induced by the environment. Perhaps this is a healthy attitude, for there certainly are adaptations in Neurospora as well as in bacteria which are unorthodox either in the characteristics of the mutations which lead to them or in the nature of the selection involved. These unorthodoxies are under investigation.

Perhaps the outstanding laboratory in the world for work on the biochemical genetics of microorganisms is at the California Institute of Technology. I feel that I stem from that school through my association with its members who were with me at Stanford. For this reason I have chosen to leave the United States and to work in the laboratories of Professor Andre Lwoff at the Pasteur Institute. Lwoff is one of the world's outstanding students of microbial nutrition and has recently undertaken studies on bacterial mutation. In his laboratories are Dr. Jaques Monod, the author of "La Croissance des Cultures Bactériennes," who is active in the investigation of adaptive enzymes, and Drs. Raymond Latarajet and Elie Wollman, who are investigating the genetics and biochemistry of bacteriophage activity. In addition, closely associated with Lwoff is Professor Boris Ephrussi, who supervises a large laboratory devoted to the study of induced mutations in yeast. I furthermore believe that it would be to the advantage of my research to visit briefly other European laboratories.

Were I to spend a year with Professor Lwoff, the results of my work would be published, as usual, in scientific journals.