NATIONAL ACADEMY OF SCIENCES

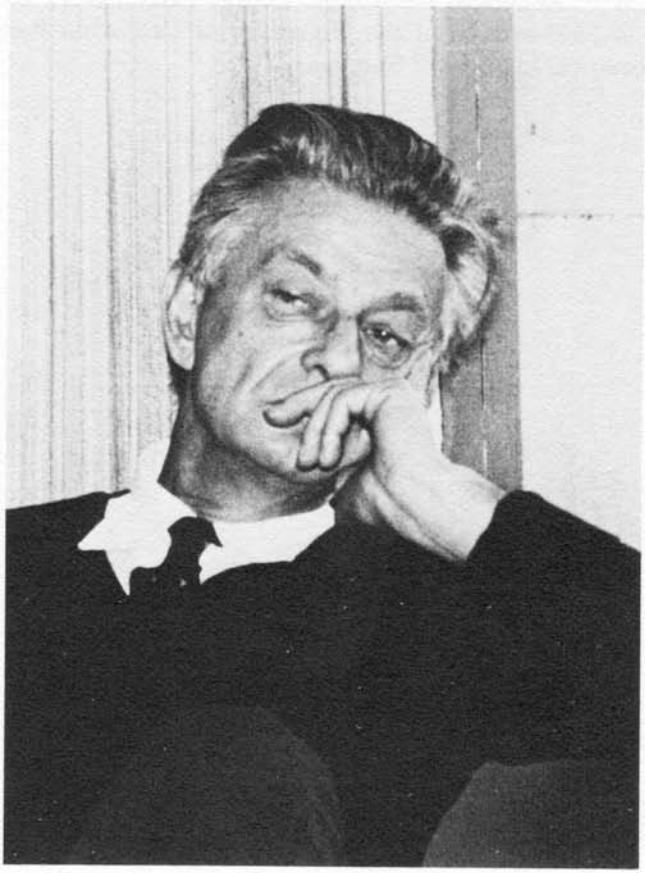
LUIGI GORINI

1903—1976

A Biographical Memoir by

JONATHAN BECKWITH AND DAN FRAENKEL

Biographical Memoir



Luigi Pirandello

LUIGI GORINI

November 13, 1903–August 13, 1976

BY JONATHAN BECKWITH
AND
DAN FRAENKEL

LUIGI GORINI, professor in the Department of Microbiology and Molecular Genetics at Harvard Medical School and a member of the National Academy of Sciences, died August 13, 1976. He was born on November 13, 1903 in Milan, Italy. His father was a microbiologist. Luigi obtained his first degree from the University of Pavia in 1925; his thesis (1925) was in organic chemistry, but his interest was in biology. He continued his studies in organic chemistry, but he was to publish only four papers in the next twenty years.

In 1931 the Italian government moved to control the universities by requiring a Fascist oath. Luigi described this period in a speech at Montana State University on February 10, 1970.

> The first uproar was *no* unanimously—we will never do that. But then came second thoughts, the rationalization: we scientists should not be involved in politics, we should not permit that others, worse than us, would take our responsibilities, etc. At the end, we were about one hundred *no's* out of about 10,000 university people. And so we quit. It was not an easy thing to do, not only materially but especially for the spirit. We, the one percent, started a double life, political underground for our soul and professional marginal for our belly. I discovered very quickly that the ability to convey opinions, to convince others, was not a gift that I had, so I did my underground work which may look romantically wonderful in retrospect, but seen from inside was a day by day realization of inefficiency.

The next ten years were spent in Turin in a succession of small pharmaceutical houses where his politics, which were Socialist, were tolerated. The work was research, development, and quality control. In these years he was married and had two children. His son from this marriage, Jan, is now following a career of research in immunology in the Laboratory of Radiation Pathology, Casaccia-Rome, and his daughter, Isa, is now a biochemist in Milan. The external circumstances of his life were relatively comfortable.

When the war came, Luigi refused induction and went partially underground with the assumed name Carlo Cattaneo. Cattaneo was a nineteenth century Italian patriot and opponent of the monarchy who edited a journal of science and politics. Luigi avoided arrest when the police came for him in 1942 and escaped to Milan, where he found work in a very small research institute (Istituto Giuliana Ronzoni) owned by an anti-Fascist industrialist. There he met Annamaria Torriani, who had just finished her studies. She was to be his colleague in the laboratory and in the resistance, and later his wife. They had one son, Daniel, who is now eighteen and a student at Rhode Island School of Design.

In the resistance, Luigi was involved in the collection and distribution of news among several cities. He also carried food, medicines, and documents to the partisans in the mountains above Milan. Although a pacifist and nominally unarmed, one of his occasional duties was to collect money. This meant going to the prospective contributor, taking out a gun, and explaining the advantages of supporting the cause.

When Milan was liberated (April 25, 1945), the Socialist party gave Luigi the task of taking over a property in the mountains at Selvino which had been a summer camp for children of Fascists. The most needy at the time were Jewish children from the liberated concentration camps who had

begun to appear in Milan. Luigi and Annamaria decided to use Selvino for them. In the next three years it served as a rehabilitation center for about a thousand children. They were from several countries of origin, and ranged from three-year-olds to teenagers. Selvino was to help rebuild their confidence prior to their emigration to Palestine. Luigi was nominally the administrator, but mainly a friend and counsellor. At the same time he was doing scientific work at the Institute in Milan. In 1976 Luigi and Annamaria were honored by the government of Israel for their work at Selvino, and an account of these activities was placed in the Martyrs and Heroes Archives at Yad-Vashem, Israel.

The last group of children left for Israel in 1948. Meanwhile, Luigi's academic title had been restored, but only at its former level as beginning assistant. Annamaria went to the Pasteur Institute in Paris. Her work there together with Melvin Cohn and Jacques Monod is well known (she is now a professor of biology at Massachusetts Institute of Technology). Luigi joined the laboratory of Claude Fromageot at the Sorbonne as a member of the CNRS (Centre National Recherche Scientifique), and he soon was independent.

Over the next seven years there were seventeen papers published dealing with aspects of bacterial proteolysis and the biochemistry of extracellular enzymes. Much of this work was on the mechanism of protection of various bacterial proteases by ions such as calcium and manganese. He and his coworkers were able to show that the metal ions protected these enzymes against autodigestion by stabilizing particular protein conformations. This work had wide impact in that it provided a strong suggestion that proteins do not have unique folding patterns, but can exist in several different stable states. This work was a continuation of his earlier interests in microbiology, and its quality was recognized early by the award of the Kronauer Prize (1949, University of Paris).

The work on physiology of proteolysis led to the discovery in 1954 of an unusual bacterial growth factor, catechol. Bernard Davis, who was then interested in aromatic biosynthesis, invited Luigi to his Department of Pharmacology at New York University. In 1957, Luigi joined the Department of Bacteriology and Immunology at Harvard Medical School, of which Dr. Davis had become head.

Soon after arriving in New York, Luigi, working together with Werner Maas, made a fundamental discovery in bacterial regulation. It was known at the time that some bacterial enzymes in sugar degradative pathways were inducible. There were also indications of regulation of enzyme synthesis in biosynthetic pathways, since the level of such enzymes was somewhat lower when the end-product was available than when it had to be made. Gorini and Maas showed that if partial starvation of the end-product of the pathway was arranged—they used an arginine-limited chemostat—the rate of synthesis of an enzyme in the arginine pathway became high (derepression). This phenomenon, "bacteria in overdrive," showed that enzyme synthesis in biosynthetic pathways was variable over a wide range, somehow responding to the endogenous level of end-product. This finding had a profound impact on thinking about regulation of gene expression and played a major role in the development of the concept of the repressor. Kenneth Schaffner, who has reviewed the early history of this field, puts it this way:

> Arthur Pardee recalls that the short paper by Gorini and Maas particularly "attracted attention" because it was "simply presented." . . . The demonstration, particularly striking in the case of Gorini's and Maas' experiment, that elimination of the repressing metabolite could result in a rapid and continued rate of constitutive enzyme synthesis, suggested . . . that inducible systems might perhaps be analyzed by a similar mechanism of negative control. . . .*

*K. Schaffner, "Logic of Discovery and Justification in Regulatory Genetics," *Studies in the History and Philosophy of Science*, 4 (4) (1974):349–85.

At Harvard the arginine pathway was Luigi's main research for some years. His group was concerned early with sorting out the physiological role of the derepression phenomenon from the other mechanism controlling flow in the pathway, end-product inhibition of the first enzyme. Luigi was interested in whether the system might really function by a combination of induction and repression and eventually established that apparent strain differences in regulation reflected differences in repressor protein only. Luigi and his co-workers continued to publish work on the regulation of the arginine biosynthetic genes until his death.

In 1964 Luigi and his colleagues published the first of a long series of papers on bacterial ribosomes that were to dramatically change the thinking of biologists about the function of the ribosomes. Up until that time, it was thought that all the specificity of translation of the genetic code lay in the interaction between transfer RNA and messenger RNA. Ribosomes were seen as passive templates upon which this process took place. In 1961 Gorini, Gundersen, and Berger noticed the peculiarity that an arginine auxotroph in the presence of a streptomycin-resistant mutation could be restored to prototrophy by the addition of streptomycin to the growth medium. Rather than ignoring this finding as one often does with peculiar observations, Luigi followed it up, and in 1964 he and Eva Kataja presented evidence that streptomycin was altering the specificity of translation via an interaction with the ribosome. (There already existed evidence that streptomycin acted on the ribosome.) From this they suggested that "the ribosomal structure could include the accuracy of the reading of the code during translation."* There quickly followed work in collaboration with Drs. Julian Davies and Walter Gilbert providing direct *in vitro* confirmation of this proposal.

*Luigi Gorini and E. Kataja, "Phenotypic Repair by Streptomycin of Defective Genotypes in *E. coli*, *Proceedings of the National Academy of Sciences* (USA), 51:487–93.

Luigi proceeded over the next twelve years to develop a new field: the study of factors influencing the fidelity of translation of the genetic code. The influence of ribosomal mutations was extensively studied. Certain mutations to drug resistance, which affected a ribosomal protein, were found to decrease drug-dependent misreading. Other mutations in the same protein caused total dependence on streptomycin for growth in any medium. It appeared that the ribosome was then so distorted as to function usefully only in the presence of an agent causing translational ambiguity. A new type of ribosome mutation, "ram" (ribosomal ambiguity), was discovered which increased misreading even in the absence of antibiotics.

Much work followed on the types of mutations corrected by misreading. While initially it appeared that chain-terminating (nonsense) mutations were the only ones affected, work from Luigi's laboratory subsequently showed that the translation of missense and even frame-shift mutations could be changed by alteration of the ribosome. Further, altered transfer RNA molecules appeared particularly sensitive to ribosomal mutations.

Luigi also had characteristically original ideas about other aspects of antibiotic action, such as the possibility that streptomycin might bind to RNA directly and affect ribosome assembly. In some of his last work, evidence was obtained for a link between mutations affecting the ribosome and mutations in RNA polymerase, suggesting that there may be unexplored levels of interaction between transcription and translation.

All this work, of course, was done with a long succession of collaborators—graduate and medical students, postdoctoral fellows, and other visitors. But Luigi always worked in the laboratory himself. He arrived first in the morning and was not above looking at his colleagues' experiments before

they came in themselves. He was blessed with a remarkable vitality. The whole story of ribosomal suppression was discovered when he was in his sixties, and even after his formal retirement at seventy the work continued with fifteen papers. Luigi's science was well recognized. He became an American Cancer Society Professor (1964), received Harvard's Ledlie Prize (1965), and was elected to membership in the National Academy of Sciences (1971).

But it was not only science that he discussed with his colleagues; it was more often politics or literature. He slept little and was extraordinarily well organized. He read the local papers and the *New York Times, The New York Review, The Guardian, Le Monde,* and *Jerusalem Post* weeklies as well as books they mentioned, and that is what he talked about, often indignantly, passionately, always interestingly.

He had an unusually genuine and strong sense of outrage over injustice and inequality. He was particularly concerned about the plight of minority groups in this country and of third world peoples in general. Luigi accepted many invitations to speak at black southern colleges, taking these opportunities to actively oppose the pseudoscientific theories that were used to support racism. For instance, in a talk at Southern University on February 21, 1974, referring to genetic theories of inequality:

> All this nonsense could be disregarded as no more than science fiction in bad taste if it were not the fact that in this way science is dangerously and irresponsibly misused to justify the right to power and wealth for the benefit of only a few racial groups, or families, or individuals, no matter what were the means these groups or their ancestors used to acquire their present dominant position in society.

Luigi was heavily involved in anti-Vietnam War activities, and when Henry Kissinger was awarded the Nobel Prize for Peace in 1973, Luigi organized a petition protesting the

award. The petition was sent to the Nobel Committee and received publicity in this country.

His attitudes toward science and the role of scientists in society influenced many around him. This influence is exemplified by a paragraph from the Ph.D. thesis acknowledgement of one of his students, Dirk Elseviers.

> Luigi Gorini directed my work in Boston. His creativity, enthusiasm and energy are a constant stimulus for everybody around him. He has taught me that the satisfaction in doing science lies in doing it and in nothing else. [But] above all that it is of capital importance to keep in touch with reality; our lives are in the hands of politicians and not of Science. I really like him.

And in Luigi's own words, again from his speech at Montana State University:

> My job here tonight is to make you realize that for me, like for hundreds of us scientists, my own scientific interest means a lot intellectually but, morally speaking, science alone does not satisfy entirely my conscience. I will try to be the most unequivocal radical possible and at the same time constructive, so that when I quit, your opinion about me should not be similar to that expressed a long time ago by the fascist Italian police about someone whom I know after his first confrontation with them. He was very happy to be released, for a time at least, but a few years later he discovered by chance the written motivation for letting him out and he was really not satisfied. The police file sounds like the following: "Lonely anarchist; he is not dangerous."

When he "quit," Luigi left behind him a spirit of rigorous scientific curiosity and social conscience which has affected many of those who were close to him.

HONORS AND DISTINCTIONS

ACADEMIC POSITIONS

1946–1949	In charge of Department of Biochemistry, Instituto Scientifico di Chimica e Biochimica Giuliana Ronzoni, Milan, Italy
1949–1951	Attaché de Recherches, Centre National Recherche Scientifique, Laboratoire de Chimie Biologique, Sorbonne, Paris, France
1951–1954	Chargé de Recherches, Centre National Recherche Scientifique, Laboratoire de Chimie Biologique, Sorbonne, Paris, France
1954–1955	Maître de Recherches, Centre National Recherche Scientifique, Laboratoire de Chimie Biologique, Sorbonne, Paris, France
1955–1957	Visiting Researcher, Department of Pharmacology, College of Medicine, New York University, New York
1957–1962	Lecturer, Department of Bacteriology and Immunology, Harvard Medical School, Boston, Massachusetts
1962–1964	American Cancer Society Associate Professor, Department of Bacteriology and Immunology, Harvard Medical School
1964– June 30, 1974	American Cancer Society Professor, Department of Microbiology and Molecular Genetics, Harvard Medical School
July 1, 1974	Professor Emeritus, Department of Microbiology and Molecular Genetics, Harvard Medical School

HONORS

1925	Highest *cum laude* honors awarded by the University of Pavia
1927	Prize for Advancement in Organic Chemistry awarded by the Politecnico of Milan
1949	Prize Kronauer awarded by Faculté des Sciences, Sorbonne, Paris
1963	Elected to the American Academy of Arts and Sciences

1965	Ledlie Prize awarded by Harvard University
1971	Elected to the National Academy of Sciences

PROFESSIONAL AND HONORARY SOCIETIES

American Society for Microbiology
Federation of American Societies for Experimental Biology
Society of General Physiologists
American Society of Biological Chemists
American Association for the Advancement of Science

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1925

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1933

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1935

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1938

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1946

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1947

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1948

With A. Torriani. Action de la penicilline sur l'activité protéolytique des bactéries acido-protéolytiques. Biochim. Biophys. Acta, 2:226–38.

1949

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1950

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Le rôle du calcium dans l'activité et la stabilité de quelques protéinases bactériennes. Biochim. Biophys. Acta, 6:237–55.

1951

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1952

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