Interaction among Virus, Cell, and Organism

Lysogeny, a concept once out of favor, is the basis of our understanding of relations between cell and virus.

André Lwoff

An organism is an integrated system of interdependent structures and functions. An organism is constituted of cells, and a cell consists of molecules which must work in harmony. Each molecule must know what the others are doing. Each one must be capable of receiving messages and must be sufficiently disciplined to obey. You are familiar with the laws which control regulation. You know how our ideas have developed and how the most harmonious and sound of them have been fused into a conceptual whole which is the very foundation of biology and confers on it its unity.

For the philosopher, order is the entirety of repetitions manifested, in the form of types or of laws, by perceived objects. Order is an intelligible relation. For the biologist, order is a sequence in space and time. However, according to Plato, all things arise out of their opposites. Order was born of the original disorder, and the long evolution responsible for the present biological order necessarily had to engender disorder.

An organism is a molecular society, and biological order is a kind of social order. Social order is opposed to revolution, which is an abrupt change of order, and to anarchy, which is the absence of order.

I am presenting here today both revolution and anarchy, for which I am fortunately not the only one responsible. However, anarchy cannot survive and prosper except in an ordered society, and revolution becomes sooner or later the new order. Viruses have not failed to follow the general law. They are strict parasites which, born of disorder, have created a very remarkable new order to ensure their own perpetuation.

For very many years, a group of eminent researchers have devoted their activity to the study of viral order. My own work simply prolongs a long chain of discoveries and ideas. I intend to discuss certain aspects of the relations between virus and cell and between virus and organism, and specifically the interaction between viral and cellular metabolism. I shall attempt to trace the development and evolution of the concepts, their ontogeny and phylogeny.

In this development one man has played a decisive role. By the logic of his thinking, by the rigor of his method, and in the selection of his followers, Max Delbrück has profoundly influenced the evolution of contemporary virology and of molecular biology. One of his followers, Hershey, in 1952, was responsible for a fundamental discovery: bacteriophages reproduce themselves from their sole genetic material. This strange property, which seemed to be a singularity of the bacteriophage, quickly became a general property of the viruses and even more than a property, a characteristic. Actually, any organized particle reproducing itself only from its own genetic material is and can only be a virus. Thus, thanks to Hershey, the category "virus" could be separated from the category "microbe," so that it became possible to distinguish the viruses by their essential difference, that is, to define them. This was also the discovery which has governed all interpretation of data with regard to the various aspects of viral development and all of the evolution of fundamental virology.

A molecule of nucleic acid can reproduce itself, express its potentialities, and give rise to virions, only within a cell. Here it finds whatever it lacks: enzymes, building blocks, a source of energy, and ribosomes. The virus is necessarily an intracellular parasite.

The genetic material of a virus has thus entered the cell. The cellular and viral molecules will confront each other, and the fate of the two partners will be decided. Two extreme cases may present themselves. Either the virus will multiply in the cell or else the cell will enslave the virus. Quite naturally, investigation was first directed toward the total war, which offers greater attraction for the combative intellect than peaceful coexistence.

When the genetic material of a highly virulent bacteriophage penetrates a bacterium, the bacterial chromosome is disintegrated and the bacterium consequently becomes incapable of producing messengers and bacterial proteins. The DNA of the bacteriophage synthesizes its own messengers with the aid of ribonucleotides synthesized by its host and of the enzymes of its host. The messengers of the bacteriophage will establish themselves on the bacterial ribosomes. With the aid of the activated transfer RNA and of the bacterial enzymes, the proteins of the bacteriophage are synthesized. Some of these proteins are enzymes necessary, for example, for the manufacture of specific constituents of the phages such as 5-hydroxymethylcytosine. Others are enzymes necessary for the replication of the bacteriophage DNA. Still others are structural proteins of the virion. One of the last to be formed is endolysine, which destroys the wall of the bacterium, provokes its rupture, and ensures the liberation of the virions. When we examine the kinetics of production of the various proteins, we find that each is formed in a given period of the evolutionary cycle. Everything takes place as if a system of sequential repression and derepression were acting.

As far as we know, the bacteriophage itself controls its own regulation. The bacterium infected by a virulent bacteriophage has become a virus factory which cannot be stopped except by its

The author is head of the Department of Microbial Physiology, Pasteur Institute, Paris, France. This article is the lecture he delivered in Stockholm, Sweden, 11 December 1965, when he received the Nobel Prize in Physiology or Medicine, which he shared with Jacques Monod and François Jacob. It is published here with the permission of the Nobel Foundation and will also be included in the complete volumes of Nobel lectures in English, published by the Elsevier Publishing Company, Amsterdam and New York.

own disintegration. A bacterium has no control over the development of a virulent bacteriophage. But this is an extreme case. The relations between virus and bacterium do not always have this dramatic character.

As a matter of fact bacteriophages exist which do not kill all the bacteria which they infect. Some infected bacteria survive and perpetuate the ability to produce bacteriophages. These are lysogenic bacteria. Their investigation has profoundly modified our ideas on the relations between cell and virus. As so often happens, the hypotheses and theoretical concepts preceded the facts. Let us therefore begin with the theory.

In 1923, Duggar and Armstrong proposed the bold idea that viruses are not small bacteria but rebellious genes that have escaped from the chains of coordination. In 1925 and again in 1928 this idea was taken up and developed by Eugène Wollman. To him the transmission of properties from one bacterium to another was the result of the transmission by the external environment of certain genes endowed with a relative stability, and the viruses were compared to lethal genes. Today we know that the viruses and the chromosomes of their host cell may have important nucleotide sequences in common. It would be difficult to assume that such common structural characteristics could be the result of chance. Many virologists believe that viruses originated by mutation from cellular elements, that is, from normal structures. The virus, this element of disorder, arose from cellular order. Plato is justified, and the ideas of Duggar and Armstrong and those of Eugène Wollman now seem prophetic visions.

These ideas were bitterly opposed for a long time. In papers published between 1925 and 1940, very often a passion shows through whose violence astonishes us. The scientific discussions frequently recall the invectives of the heroes of Homer. It is my impression that the scientific mind today is much better prepared for the acceptance of new ideas, and we must also say that new ideas are in general firmly grounded in experimental data.

Let us return to the past and attempt to determine how our knowledge and our ideas on viruses and lysogeny, as well as our concepts of the relations between cell and virus, have evolved.

Since 1915, Twort had thought that the bacteriophagy might be due to a virus. This was also the opinion of d'Hérelle: bacteriophages are viruses which kill the bacteria. Lysogeny came to confuse the bacteriologists. D'Hérelle at first denied the lysogeny. Later, he became convinced that he had discovered it. None of this is important, but the bacteria producing bacteriophages posed a curious problem.

Jules Bordet wrote in 1925: "The faculty for producing bacteriophages is incorporated in the heredity of the lysogenic bacteria. It is inherent in the normal physiology of the bacterium." Nevertheless, it is of interest to note that the great immunologist did not conceive that heredity might be linked to a structure. For Bordet, heredity was the perpetuation of an individual physiology. The bacteriophage is not a materialized hereditary property, and Bordet affirmed in 1931: "The invisible virus of d'Hérelle does not exist. The intense lytic activity represents a pathological exaggeration of a normal function of the bacterium." It seems strange to us today that such an eminent mind could have conceived of specific functions independent of any specific structure.

In 1929 lysogeny underwent a revival. Sir MacFarlane Burnet and his collaborator Margot MacKie began to investigate lysogenic salmonellas. These Australian authors noted that only 0.1 percent of the bacteria contain bacteriophages. However, since all possess the property of producing bacteriophages, they must contain a specific *Anlage* coordinated in the hereditary constitution of the bacterium. The bacteriophage is "liberated" only if the bacterium is "activated." In the thinking of Burnet, this liberation probably corresponds to an unmasking, for he wrote in 1934: "We are forced to admit that each lysogenic bacterium encloses one or several particles of a bacteriophage which multiply by binary division with the bacterium."

Everybody at that time believed that viruses were small microbes. A small microbe would necessarily have to reproduce itself by division. What, then, was the significance of this noninfectious phase? It might not represent anything important. We know of many organisms, specifically the protozoa, which go through a noninfectious stage during their cycle of evolution. Burnet had discovered the noninfectious phase of the bacteriophage in the lysogenic bacterium. In 1937 Eugène and Elizabeth Wollman noted that immediately after infection the bacteriophage passes through a noninfectious stage. This was confirmed in 1948 by Doermann, a follower of Max Delbrück, who for the first time methodically investigated the complete cycle of a bacteriophage.

However, Wollman understood that the bacteriophage particle, the virion, is not the direct descendant of the infecting particle. An infectious and a noninfectious phase necessarily would have to alternate. In a nonlysogenic bacterium, this alternation should take place in each bacterial cycle. In each division, each lysogenic bacterium *should* liberate *one* bacteriophage.

In 1938, Northrop started with the idea that bacteriophages are proteins and decided on a parallel investigation of the kinetics of the production of enzymes and that of the production of bacteriophages in a lysogenic bacterium. He concluded from his experiments that the bacteriophage, like the enzymes, is produced during the normal growth of the bacterium. At this point an important remark is necessary. Whether, in a bacterial population, one bacterium in a hundred produces one hundred bacteriophages or whether each of the bacteria produces one, the overall kinetics will remain the same. In 1949, the new school of American virologists, to which virology owes so much, condemned lysogeny. In nature, no problems exist but only solutions. The solution, the lysogenic bacterium, is enslaved as a typing tool for the identification of the bacterial families. Like those wisps of cloud that a breath of wind dispels, the problem is blown away from the temple of science and a smell of sulfur is left floating in the air. Lysogeny has become a heresy.

However, a few heretics survive—and among them Jacques Monod, who played a decisive role in my decision to return to the problem of lysogeny. I decided to operate with individual bacteria.

Here I must make a confession. I was led to this decision because I do not like either mathematics or statistics. I began my career as a protozoologist. I like to see things, not calculate probabilities.

Consequently, I took a lysogenic bacterium and immersed it in a drop of culture medium. The bacterium divided, the daughters were separated, and at each division a specimen was taken from the medium. One bacterium thus

divided 19 times without liberating bacteriophages, and the daughter bacteria were still lysogenic.

When we subject lysogenic bacteria to lysis, we note that they do not enclose any bacteriophage. Lysogeny is consequently perpetuated in a noninfectious form. We were then in 1950—and Hershey's discovery dates from 1952. However, I did not like the idea that noninfectious virions might exist. The noninfectious phase should be something different from a virion. The term "prophage" was therefore proposed, and it seemed that the world eagerly awaited its coming. In spite of its French origin, the Greek word was rapidly and unanimously adopted.

By giving a name to an unknown particle, we confer on it the dignity of a problem. The problem of the prophage had been posed, and now the history of lysogeny began again.

The prophage and the bacteria live in equilibrium. However, in a large population of lysogenic bacteria, we always find bacteriophages. How and why? Should we consider the problem as statisticians? Should we calculate the probability that a bacterium will produce bacteriophages within a given time? Should we content ourselves with a formula which would have expressed the state of health of the population in terms of Greek symbols? I have already said that I do not have a statistical soul, that my mind tends to the concrete, and that I like to observe because I like to see. Accordingly, I again observed isolated bacteria. Some of them multiplied normally. Others multiplied for a time and then the descendants underwent lysis. And each of the bacteria which were lysed liberated bacteriophages. All this happened as if, in some drops of the medium, the development of the bacteriophage had been induced. This was my conclusion and I published it, to my regret. I now had to show that induction was not a fanciful hypothesis but a reality.

With Louis Siminovitch and Niels Kjeldgaard we went to work on an enterprise that was hard and discouraging because it seemed fruitless for a long time. After a year of effort, our faith was finally vindicated. Bacteria were irradiated by ultraviolet radiation. For an interval of 45 minutes, they continued to grow, but then they began to undergo lysis. In the process, each of them liberated some hundred bacteriophages. Induction had been discovered. And since induction affected 99.9 percent of the population, any statistical analysis was obviated. I was saved.

It thus appeared that the development of the prophage into bacteriophage is a mortal disease. The prophage is a potentially lethal factor. Irradiation forces it to express its potentialities.

For a long time, it was believed that such lethal agents as ultraviolet radiation or x-rays kill the cell because they destroy an essential structure. This concept seemed perfectly natural. It was in harmony with concepts in regard to death. After all, it is simple to consider death as the result of the suppression of some indispensable function. However, because every theory is a generalization, the risk in a theoretical concept increases with the fraction of truth it contains. Biological theories explain the various phenomena of life either in terms of disappearance of structure or of function, or in terms of the development of new structures. Our minds are tuned to a mode that we might call positive or negative. It is apparently difficult to make the transition from one to the other or to realize that the two modes are not necessarily incompatible. Radiations sometimes kill by provoking alterations in or disappearance of structures. Sometimes, too, it permits a potentially lethal gene to express or to effect new syntheses, whether this concerns a bacterial protein or a virus, and thus to engender disease and death. Radiation may trigger lethal syntheses.

Nevertheless, induction was only a stage in our knowledge of the lysogenic bacteria. Induction, like the prophage, raised a whole series of new problems. Their investigation quickly surpasses the specific cases of the bacteriophage and of lysogeny and merged with the fundamental problems of molecular biology.

First of all, what is the nature of prophage? The use of radioactive molecules showed that the prophage is a deoxyribonucleic acid. It is the genetic material of the bacteriophage, a conclusion in harmony with the discoveries of Hershey.

Next, where is the prophage located? The discovery of sexuality in *Escherichia coli* and the investigation of the bacteriophage lambda made it possible to answer this question, and in a general way. The prophage is attached to the bacterial chromosome. It is localized on the chromosome at a well-defined point, the receptor, which is unique and specific for each type of bacteriophage.

A temperate bacteriophage infects a nonlysogenic bacterium under conditions in which the bacterium will survive. The genetic material of the bacteriophage then penetrates the cytoplasm, explores the bacterial chromosome, recognizes the receptor, and pairs with it. Recognition and pairing can only be the consequence of structural homology—that is, of common nucleotide sequences. The DNA of the temperate bacteriophage is a circular—that is, closed—structure. The sector of the bacteriophage that is homologous with the bacterial chromosome opens, the bacterial chromosome also opens, and thus the genetic material of the bacteriophage is inserted, like a bacterial gene, into the bacterial chromosome. It becomes an integral part of the chromosome and behaves as if it were a bacterial gene. It will be reproduced by the system of enzymes which reproduces the chromosome of the bacteria. It happens sometimes that the prophage, when it detaches, wins out by taking with it some bacterial genes. These bacterial genes will be reproduced by the enzymes which provide for the autonomous multiplication of the bacteriophage.

Several years ago, in 1953, it occurred to me that the properties and activity of a molecule or of a particle might not be dependent only on its structure but also on its geographic situation, and I wrote: "The position is the fourth dimension of the prophage." My friends chided me for this formula by saying that it was devoid of meaning, and at the time they were perhaps right. I still believe that, under its somewhat esoteric and fanciful aspect, it has a profound significance.

In a bacterium, the DNA-RNA polymerase synthesizes RNA on a DNA matrix and not on an RNA matrix. However, in vitro, the same enzyme is able to utilize RNA as matrix. It is likely that, in a bacterium, the DNA-RNA polymerase is at the locus of its activity and not where it would have an opportunity to engage in actions reproved by molecular morals. In a normal cell, each molecule is at the place where it should be and not elsewhere, and that is why each of them does what it should do and not something else. We must then ask whether certain diseases of cellular metabolism are not provoked by molecular incursion into foreign ter-

ritory. Molecular societies obey the same laws as more complex societies.

Let us go back to the lysogenic bacteria. Now then, the prophage is reproduced by bacterial enzymes. Why does the lysogenic bacterium not produce bacteriophages? We believe today that at least one of the genes of the prophage expresses itself and produces a repressor. This repressor attaches itself to an operator gene and blocks the expression of the structural gene that determines the formation of the enzymes necessary for autonomous reproduction of the bacteriophage. A lysogenic bacterium produces virions if it is derepressed, and here we are again entangled in the problem of induction.

In addition to such physical agents as ultraviolet and various other kinds of radiation, we know of many chemical inducers, such as the organic peroxides, ethylene-imines, and mitomycin. All inducers have in common the property of disturbing the metabolism of nucleic acids. According to Goldthwait and Jacob, the final product of the change might be a derivative of adenine. The product will attach itself to the active repressor and thus bring about an allosteric modification. The active repressor will become an inactive aporepressor. An operon being derepressed, a structural gene can express itself, and a new enzyme is produced which assures the autonomous multiplication of the viral genetic material and permits the expression of all of the genes that regulate viral structures.

The vegetative phase takes its course, virions are formed, and the bacterium explodes and dies.

Thus the inducing agents act by inactivating the repressor. Now, then, the repressor is responsible for immunity. This is why, under the action of inducers, the immunity of the lysogenic bacteria to the superinfective homologous phage is lost.

When a nonlysogenic bacterium is infected by a temperate phage, it will either undergo lysis or become lysogenic. The conditions of the environment here decide the evolution of the genetic substance of the bacteriophage; that is, they decide the fate of the bacterium. In order to be effective, these conditions must begin to operate within 7 minutes after infection. The fate of the bacterium-virus system manifestly depends on whether a repressor or the key enzyme responsible for autonomous multiplication is formed first.

The repressor is produced by a regulator gene and acts on an operator gene. It is obvious that either gene is susceptible to mutation. A regulator gene, under the influence of mutation, will give a repressor incapable of inhibiting a given operator. An operator, as a result of mutation, may become insensitive to a given repressor. In the last analysis, the fate of a bacterium infected by a bacteriophage thus depends on the genetic constitution of the bacteriophage, on the genetic constitution of the bacterium, and on the metabolism of the bacterium which is in turn controlled by the environment. Moreover, the genetic material of the bacteriophage may confer on the bacterium not only the power of producing bacteriophages in the absence of infection but also other properties, such as the capability of synthesizing a toxin like diphtheria toxin or the synthesis of a new antigen which will modify the structure of the bacterial wall.

Be that as it may, through the infection the lysogenic bacterium has become a new organism, a cell-virus system whose fate will depend on the bacterial metabolism, which itself depends on the environment.

Any valid proposition, however singular it may appear, is necessarily the particular expression of a general law. Since generalization is one of the most productive heuristic methods, we shall attempt to express the relations between bacteriophage and bacterium in such a way that the generality on which they depend will be included in the expression. Here, then, is this general expression: the course of the viral cycle is dependent on allosteric proteins whose structure and activity are controlled by the metabolism of the host cell.

This general proposition shares at the same time both in the strictness of a law and the weakness of a hypothesis. We shall now have to abandon the heights of theoretical conception and descend into the underworld of disease.

We know that herpetic infections are frequently latent. The infected individual does not present any symptoms of disease. However, under the influence of a great number of factors, the disease erupts. The variety of the effectors is astonishing, as will be seen from the following list of those promoting the outbreak of herpes:

Local hyperpyrexia
Artificial fever
Febrile disorders (malaria, pneumonia, brucellosis, typhoid fever)
Local ultraviolet radiation
Hormone treatments
Menstruation
Unbalanced diet
Leukemia
Administration of proteins foreign to the system
Anaphylactic shock
Lesions of the Gasserian ganglion
Section of the trigeminal nerve
Emotion

During the latent infections not only are there no symptoms, but it is not possible to detect the virus. We do not know in which form it is present, and to say that the virus is masked simply masks our ignorance. When the lesions develop, the virus appears in abundance. Actually, it is the viral multiplication which is responsible for the disease. During the latent infection, the viral cycle is blocked. The agents which trigger the disease thus induce the viral development of which the disease is the consequence. We can therefore assume that all these agents, in spite of their diversity, provoke by different mechanisms the same modification of cellular chemism, and precisely that modification which will be responsible for triggering viral multiplication.

And here we become entangled in a new hypothesis, according to which the development of an animal virus is controlled in a positive or negative manner by environmental factors to the extent to which they determine the cellular metabolism.

Some experimental data will be welcome. Guanidine inhibits the development of certain viruses, and in particular that of the poliovirus. At concentrations which are inhibiting for the virus, however, guanidine does not observably influence metabolism and cellular growth. Guanidine consequently is a specific inhibitor of the poliovirus. How does it act? Does it act at the level of the nucleic acid, as some seem to think? Sensitivity to guanidine may disappear upon mutation. A structural gene is a sequence of several hundred nucleotides, and a point mutation is the substitution of one nucleotide for another. It is difficult to conceive that the presence, at some particular locus, of a nucleotide already abundantly represented along a long chain could modify

the properties of the chain so that, for example, a difference of temperature of one-tenth of one degree or the presence of 0.0002*M* guanidine would notably affect the structure and function of the molecule.

Let us therefore assume that guanidine does not act directly on the nucleic acid. The hypothesis proposed by us a few years ago is the following. Guanidine, like temperature, affects the tertiary or quaternary structure of a protein. Today we would state that it is responsible for an allosteric modification.

What is this protein?

In the presence of guanidine, viral RNA is not synthesized, and it has been believed that guanidine acts in some manner on the viral RNA-replicase. This was a logical conclusion. However, we became aware that methionine and choline neutralize the inhibiting effects of guanidine. A number of experiments have led us to believe that the guanidine must block the activity of a virus-determined transmethylase. The simplest hypothesis is that this enzyme methylates the viral RNA.

The DNA of the polyoma virus contains 5-methylcytosine, and so does that of bacteriophage lambda. Methionine intervenes in the modification induced by the host of this bacteriophage. However, we do not know the physiological significance of such methylation. Investigation of the poliovirus has afforded an indication that methylation in certain cases may well control the course of the viral cycle. Such methylation would be effected by a virus-determined enzyme which is sensitive to guanidine and to cellular metabolites possessing a guanyl group. Thus the evolution of viral proteins, like the evolution of proteins in general, should terminate in the development of sites capable of accepting specific effectors, inhibitors and anti-inhibitors, which are cellular metabolites. I should like to draw attention to this conclusion.

A cell becomes cancerous under the action of a virus. The virus has introduced into the normal cell its genetic material, which brings with it new functions, and these functions are the cause of the malignancy. It is reasonable to assume that a viral protein carries the phenotypical responsibility of the malign transformation.

If the functions of the oncogenic viruses, like the functions of other viruses, depend on specific effectors, we may hope some day to convert a malignant cell into a phenotypically normal one.

This leads us to remark on methodology. It would seem that we have so far been occupied in finding substances which specifically kill the malignant cell in the culture to the exclusion of normal cells or which specifically prevent the malignant cell from multiplying. The experiments are generally made in environments which may contain anti-effectors, as is the case for the couple methionine/guanidine. A change in methodology might perhaps be profitable.

There is also another obvious theoretical possibility. Instead of attempting to repress the viral functions, we might attempt to intensify them in such a manner that the virus whose cycle is blocked develops and kills the host cell.

The search for specific effectors of the viral functions and of the viral development is empirical at the moment. Such research must be developed and extended. Our ignorance of the nature of the factors which govern the relations among oncogenic virus and the cells should not incline us to pessimism but should instead be a stimulant. We should declare war on oncogenic viruses and carry it to victory.

Acknowledgments and Bibliography

The experimental data and concepts discussed here encompass a vast field. There are very many who have made important contributions to this domain. It would have been impossible to do each of them justice within a lecture of 30 minutes. I have mentioned some names, and my selection has necessarily been arbitrary. I would have liked to and I should cite, among others, T. F. Anderson, L. Astrachan and E. Volkin, L. Barksdale, G. Bertani, A. Campbell, S. S. Cohen, V. J. Freeman, N. B. Groman, L. M. Kozloff, S. Lederberg, S. E. Luria, F. W. Putnam, G. Stent, Elie Wollman, and N. D. Zinder.

The bibliography concerning bacteriophages will be found in the excellent book by G. Stent, *Molecular Biology of Bacterial Viruses* (Freeman, San Francisco, 1963) and the no less excellent treatise of W. Hayes, *The Genetics of Bacteria and Their Viruses* (Blackwell Scientific Publication, Oxford; Wiley, New York, 1964). The data concerning the effectors of the development of animal viruses are discussed in A. Lwoff, "The specific effectors of viral development" (The First Keilin Memorial Lecture), *Biochem. J.* **96**, 289–301 (1965).

NEWS AND COMMENT

The Berkeley Scene, 1966 (II): Educational Reform

One of the more provocative questions about last year's disorders at Berkeley is the extent to which they represented the uprising of an abused academic proletariat against an educational factory. Evidence on this point is inconclusive. Studies made during the crisis reported, for example, that nine-tenths of a representative sample of students agreed with the statement "Taking everything into account, Cal is a good place to go to school." But the same studies also found that 42 percent of the students said professors were more interested in research than in teaching, another 42 percent said the grading system "only slightly" reflects the student's knowledge of the subject, and one-third said classes were so large that students learned very little in them. Nearly four-fifths accepted the often-heard cliché that the university operated as a "factory."

Whatever the inconsistencies in student attitudes toward the university, one result of the Free Speech Movement was to stimulate faculty and administration introspection about the nature of the education Berkeley provides. "They felt educationally naked," commented one observer, "and they looked about for a fig leaf to help them cover up." One such fig leaf was rapid approval for a previously stalled proposal by philosophy department chairman Joseph Tussman to set up a small experimental college for lower-division students. Another was the appointment of a faculty Select Committee on Education to explore, among other things, ways of enlarging the variety of educational opportunities the university could offer. The driving force behind the proposal to reevaluate Berkeley education came from acting chancellor Martin Meyerson, but the skeleton in the closet was Mario Savio's. "If I had to name the man who has done