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From Schizomycetes to Bacterial Sexuality
A case study of discontinuity in science

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I. Introduction

This case study in scientific biography is intended to examine the process of scientific growth and discovery by joining the assets and skills of a participant-reminiscer with those of a more detached behavioral scientist. The particular arena of interest is the convergence of genetics with bacteriology that attended the work of Lederberg and Tatum in 1946. At the time we began in 1973 there were few precedents for such a self-conscious collaboration. A similar collaboration which examines the development of radio astronomy in Britain after World War II has recently culminated in "Astronomy Transformed" by David O. Edge and Michael J. Mulkay (New York: Wiley, 1976).

For the past 30 years bacteria have been favored objects for research on DNA. Together with their parasitic viruses, the bacteriophages, these simple organisms continue to offer indispensable advantages for seeking deeper insight into the chemical basis of heredity, and for bringing such knowledge to practical application. The importance of bacteria as agents of infectious disease, clearly established by 1876, might also be thought to have accelerated inquiries into their basic biology. Paradoxically, the opposite may have been true, as will be discussed further in section III.

But before bacteria could be routinely accepted as paradigms of research in terrestrial biology, the question of whether "bacteria have genes, like all other organisms" had to be clarified. The crucial experiment was conducted at Yale University in 1946 by Joshua Lederberg (1925-   ), and E.L. Tatum (1909-1975).{ 1 }

Their approach was to demonstrate genetic recombination - the exchange of genes between different cells - in a typical bacterial species like Escherichia coli. Existing dogma in microbiology held that bacteria could not be crossed. They reasoned that if a sexual mode of reproduction occurred in bacteria at all, it might be quite a rare event. Therefore, particular attention was paid to an efficient selective design, the genetic characteristics of the input strains being arranged so as to make it easy to detect even the very rare occurrence of new recombinant types. In these experiments, biochemically defective mutants, whose ability to grow could be manipulated by altering the composition of the growth medium, proved to be especially suitable research material. Tatum's recent work with Beadle had established the feasibility of preparing such mutants and their advantages for a wide variety of investigations, in a fungus, Neurospora, whose genetics was already well established. The production of similar mutants in bacteria, which Tatum had pioneered, was now to be the Ariadne's thread to lead them back to an understanding of the genetic structure of these organisms.

Their basic design was to establish two different, complementary mutant strains requiring different nutritional factors. Neither of them would be able to grow alone, in a selective synthetic medium. Thus genetic recombinants, no matter how rare, can be detected by plating large numbers of bacteria grown together into this medium. Typically, one may plant a billion organisms in a single Petri dish, and recover a hundred recombinant colonies. These methods, and the target strain E. coli K-12 have become standard for contemporary research in bacterial genetics, as recited in several hundred new publications a year.

Our elaboration of this 1946 discovery traverses Lederberg's autobiography of his entree into research; the history-of-ideas of the problem (which was more difficult to perceive than to solve); and some sociological observations on a series of issues raised by these accounts. Recognizing the difficulty of systematically communicating a tangled web of facts, commentary and criticism, we hope this pattern of ever-widening perspective may be helpful to readers of diverse persuasions.

The following sections are in fact the fruit of a collaboration in which the conventionalized roles of the participant in the historical event and of the interviewer-scholar were repeatedly redefined as each of us tried his hand at the tasks of the other. In nearly all oral histories of science,{ 2 } the scientist participant responds to questions by the interviewer who has reviewed the relevant documents. Our procedure differs in several important respects: first, our effort was iterative -- new possibilities suggested in the course of discussion led to renewed search for apposite material; and second, these searches (made by the participant as well as by the interviewer) consulted archival materials both personal and public, and other individuals knowledgeable about our problem. In the process, both authors learned a good deal about the other's perspectives.

This iterative procedure evolved gradually; but one constant element in our inquiry was the conviction that personal reminiscence, though indispensable, had to be corroborated by contemporary documents or other testimony.{ 3 } As professional historians know, documents (especially multiple documents) can confuse as well as illuminate events. Moreover, it now is clear that accounts of the same discovery by different participants do not square very well with one another owing to their unique perspectives on the event.{ 4 } Autobiography is especially prone to what Kurt Stern calls "retrospective memory" {5} and particularly deserves the constraints imposed by documentation.

II. Personal history - an inside story

This section is presented in the first person by Joshua Lederberg, to help convey impressions and information which are asseverated by personal recollection. However the narrative is so profoundly informed by critical dialogue with my co-author that it is scarcely pure autobiography.

The pivot of my account is September 1941, when I enrolled as an entering undergraduate at Columbia College in New York City. My earlier education was framed by the New York City public school system: especially by the cadre of devoted and sympathetic teachers who went far beyond their duty in encouraging a precocious youngster whose demands they could not always meet from their own knowledge, and the "elitist" high school system as represented by Stuyvesant High School - open by competitive examination to students with a bent for science and technology. Even more important perhaps was the local Washington Heights branch of the Carnegie-New York public library system. These institutions symbolized and embodied the melting pot ideology. My father was an orthodox rabbi, born and educated in Israel, and thus had more prestige, possibly higher aspirations for his children, and less income than most of our neighbors. Like many other first-generation Jewish youths in New York City at that time, I was recruited into an efficient and calculated system of Americanization, fostered by the rich opportunities and incentives of the educational system.

My earliest recollections aver an unswerving interest in science, as the means by which man could strive for an understanding of his origin, setting and purpose, and for power to forestall his natural fate of hunger, disease and death. This may have been the most acceptable deviation from the religious{ 6 } calling of my family tradition. It was reinforced by the role of Albert Einstein and Chaim Weizmann as culture heroes - heroes whose secular achievements my parents and I could understand and appreciate regardless of the intergenerational conflicts evoked by my callow agnosticism and ostentatious rejection of the orthodox Jewish ritual. The Jewish faith is remarkably tolerant of skepticism, and the set of mind thus encouraged may have carried over into my reflex responses to other sources of authoritative knowledge.

The library was my university as I went through grade school and junior high school. My most prized Bar-Mitzvah present was a copy of Bodansky's "Introduction of Physiological Chemistry".{ 7 } I had already devoured Bodansky at the local library along with hundreds of other works in the sciences, mathematics, history, philosophy and fiction. Books by Jeans, Eddington and especially Wells, Huxley and Wells' encyclopedic 'The Science of Life' were the most influential sources of my perspective on biology and man's place in the cosmos, seen as evolutionary drama.

Stuyvesant High School offered unusual opportunities for practical work in machine shops and analytical laboratories as well as straight classroom teaching.

Having begged for and been granted access to the Cooper Union Library (near Stuyvesant), I had also read many research papers - but neither these, nor my teachers could really say much of the life of the scientist at work.

Playing at research in high school and then for some months at the American Institute's Science Laboratory (a predecessor of the Westinghouse Science Search) did focus my interests in chemical cytology; and I entered Columbia with the idea of learning the chemistry of cellular components so as "to bring the power of chemical analysis to the secrets of life". I looked forward to a career in medical research where such advances could be applied to problems like cancer and the malfunctions of the brain.

My curriculum at Columbia was somewhat unconventional. As soon as a dubious bureaucracy would permit, I registered in a number of graduate courses in the Department of Zoology. Not until my last term had I matured enough to seek and profit from a rounding of my humanistic education at the hands of teachers like Lionel Trilling and James Gutman.

Professor H.B. Steinbach, who taught the introductory Zoology 1 course, helped arrange a laboratory desk in the histology lab where I could pursue some small research of my own. I became interested in the cyto-chemistry of the nucleolus in plant cells, hoping to develop new staining methods that could reveal its composition. The then recent publication of McClintock and Rhoades on the genic control of nucleolar synthesis in maize also introduced me to the power of genetic analysis in cell biology.

Professor Franz Schrader's course in cytology introduced me to some of the problems of mitosis. I became curious about how the drug colchicine interferes with the mitotic spindle. Herein was my first (trivial) "discovery": an apparent gradient of susceptibility to colchicine down the onion root meristem; but there was no way to determine whether this was an intrinsic difference in the cells, or a transport problem.

This work led to two other starts: (1) an effort to induce chromosome aneuploidy in mice by the application of limiting levels of colchicine during spermatogenesis, and (2) a broader inquiry into the effects of narcotics and other specific inhibitors on the mitotic process. It was easy to disrupt spermatogenesis with colchicine; I saw giant (presumably polyploid) spermatids, but I was unable to verify the successful maturation of these peculiar cells. The matter has never been satisfactorily investigated and may still be of some importance as a prototype of teratogenesis from environmental causes.

The problem of the cytophysiology of mitosis led me to specialize in courses in cell physiology.However, at that time this was preoccupied primarily with energy metabolism. I learned little that appeared to be useful for the problems of protein synthesis and fiber assembly in mitosis.

I first met Francis Ryan in September 1942, when he returned from his postdoctoral fellowship at Stanford University with E.L. Tatum to become an instructor in Zoology. He brought back the new science of Neurospora biochemical genetics and a gift of inspired teaching that was to be a decisive turning point in my own career. I had little or no contact with him in formal courses, but by January 1943 I was working in his laboratory assisting in the preparation of media and handling of Neurospora cultures. For the first time I was able to observe significant research as it was unfolding and to engage in recurrent discussions with Francis - and with an ever widening group of graduate students in the department - about Neurospora, life, and science.

Hitler achieved power in Germany when I was eight years old - just old enough to have no doubt about the eventual outcome of his march across Europe. Eight years of fascinated horror at the unfolding of history followed -- the persecution of the German Jews, the flight of intellectuals like Albert Einstein, the occupation of Austria, Munich, the Nazi-Soviet pact and partition of Poland, the fall of France, the victory of the RAF over Britain,... Pearl Harbor. We knew that the War would dominate our lives until a painful victory was won. The actual disposition of our efforts was in the hands of a slowly evolving bureaucracy. Awaiting the final call to military service, most of us simply continued our daily pursuits speculating when we would be called upon in our particular fashion.

My own response was to enlist in the Navy V-12 college training programs upon reaching my 17th birthday, well before I was eligible for the draft. This opened the door to further training for commissioned rank. Fortunately, Columbia College contracted with the Navy among the services, and when V-12 was called to active status on July 1, 1943, I could continue my studies at the same institution! {8} The V-12 curriculum was designed to compress pre-medical training to about 18 months of instruction, and the 4-year M.D. curriculum into 3 calendar years. We also got a modicum of Naval officer-candidate preparation and physical education, leaving little time for extra-curricular research.

My further months at Columbia College were alternated with spells of duty at the U.S. Naval Hospital, St. Albans, L.I. Here I was assigned to the clinical parasitology laboratory. The practical use of my previous training in cytology was the examination of stool specimens for parasite ova, and the routine examination of blood smears for malaria among the Guadalcanal veterans of the First Marine Division. This gave an opportunity to look for the chromosomes of Plasmodium vivax. The "chromosomes" were so tiny and the Feulgen staining so faint that it is difficult to insist on the reality of those observations. However, this experience informed me of the sexual stages of the malaria parasite, and this undoubtedly sensitized me to the possibility of cryptic sexual stages in other microbes (perhaps even bacteria.)

In October 1944 I was reassigned to begin my medical course at Columbia College of Physicians and Surgeons. As a medical student, I attempted to continue research studies on the control of mitosis: namely a search for a hypothetical humoral factor that regulated the size of the regenerating liver after partial surgical excision. With a fellow student, Anthony Iannone, I performed some encouraging parabiosis experiments. However, neither the available assay methods nor our surgical skills and facilities approached what was needed for the task. First year medical students at P&S were not, in any case, encouraged to do research and my intellectual and social environment continued to center on the Morningside Heights campus.

The important biological discovery of 1944 was the identification by Avery, McCarty and MacLeod of the substance responsible for the pneumococcus transformation.{ 9 } This phenomenon appeared to be the transmission of a gene from one bacterial cell to another; but this interpretation was inevitably dimmed by the level of general understanding of bacterial genetics at that time. Avery's findings were promptly communicated to Columbia by Dobzhansky (who visited Rockefeller) and by Alfred Mirsky (of the Rockefeller faculty) who was a close collaborator of Arthur Pollister in the department . The Rockefeller work was the focus of widespread and critical discussion among the faculty and students there. Mirsky was a vocal critic of the chemical identification of the transforming agent. I believe he was essentially persuaded that this was an instance of gene transfer, but he was not yet prepared to concede that the evidence to date settled so important a question as the chemical identity of the gene as pure

DNA (versus a complex nucleoprotein).

My information about Avery's work was second-hand until I actually read the paper on January 20, 1945 at Harriett Taylor's urging. At that time she had already arranged to pursue her postdoctoral studies with Avery at the Rockefeller Institute after she completed her Ph.D. that spring. My immediate response is recorded as " ... unlimited in its implications... Direct demonstration of the multiplication of transforming factor... Viruses are gene-type compounds [sic] ... excruciating pleasure of reading."

What could be done to incorporate this dramatic finding into the main stream of biological research; how could one further advance these new hints about the chemistry of the gene? One answer to this urgent question that occurred to me would be to attempt a similar transformation by DNA in Neurospora. Not only did this organism have a well understood life-cycle and genetic structure. It also had the advantage of being amenable to selection for rare nutritionally self-sufficient (prototrophic forms) which would facilitate the assay for the transformed cells.

Sometime between January and May, 1945, I brought this suggestion to Francis Ryan who replied that he had been speculating along somewhat similar lines, and that he would be glad to have me work with him on the question. As a brief vacation was looming (to follow rigorous examinations in Anatomy) we agreed that we might begin in June, and so we did. However, we soon discovered that the Neurospora mutant would spontaneously revert to prototrophy. We did not therefore have a reliable assay for the effect of DNA in Neurospora. However, the details of the reverse mutation phenomenon resulted in my first scientific publication {50}.

Questions about the biology of bacteria would then continue to fester so long as bacteria remained inaccessible to a conventional genetic analysis for lack of a sexual stage. But was it true that bacteria were asexual? Some of the more sophisticated textbooks and especially Dubos' monograph, 'The Bacterial Cell'{ 10 } , indeed had footnotes indicating the inconclusive status of claims for the morphological exhibition of sexual union between bacterial cells. Little genetic testing of this hypothesis had been done. Another important input to this intellectual confrontation was an appreciation of sexuality in yeast, via the graduate research work of Sol Spiegelman and Harriett Taylor. Yeast is at least superficially a closer analogue to bacteria. It had long been known that yeasts produced spores through a sexual process, but the occurrence of clear-cut mating types in yeast had not been demonstrated until 1935 by Winge{ 11 } and then further exploited for genetic analysis by Lindegren and Spiegelman. These successes only dramatized the importance of finding a sexual stage if it existed, in a variety of microbes.

Some of my notes dated July 8, 1945 articulate - on neighboring pages - hypothetical experiments involving (a) a search for mating between the medically important yeast-like fungi, the monilia and then (b) the design of experiments to seek genetic recombination in bacteria (by the protocol that later proved to be successful). These notes also coincide within a few days, with the beginning of my course in medical bacteriology at medical school. They may have been provoked by the repeatedly asserted common wisdom that bacteria were "Schizomycetes", asexual primitive plants.

Dubos's monograph cites a host of muddled, and two clear-cut, studies (Gowen and Lincoln, Sherman and Wing) intended to look for genetic exchange in bacteria by the methodology of genetic exchange. But even these two instances lacked the advantage of any selective method for the detection of recombinants. Therefore they would have overlooked such a process if it occurred less often than perhaps one per thousand cells.

Within a few days I set out on my own experiments along these lines -using in the first instance a set of biochemical mutants in bacteria which I began to accumulate in Ryan's laboratory.

Meanwhile at Stanford Ed Tatum, whose doctoral training at Wisconsin had been in the biochemistry of bacteria, was returning to bacteria as experimental objects,having published two papers on the production of biochemical mutants in E. coli.{ 12 } During that summer of 1945 Francis learned that Ed was about to move from Stanford University to set up a new program in microbiology at Yale. He suggested that rather than ask Tatum merely to share his newly founded collection of bacterial mutants, I should ask to work directly with him and get the benefit of his detailed experience and general wisdom. The war was nearing a victorious conclusion; civilian life and academic schedules might soon be renormalized and make such a visit possible. With this encouragement, I then wrote Tatum of my research plan (Fig. 1) and applied for such an accommodation. Dean Aura E. Sevringhaus of P&S also approved such a visit as qualifying for an elective quarter offered to medical students during their third year of study.

Tatum congenially agreed and suggested that I arrive in New Haven in late March, to give him time to set up his laboratory. I had some hint that he may have been formulating similar experimental plans, but these were never pressed upon me. This arrangement suited him by leaving him free to complete his current work in the biochemistry of Neurospora, and still follow up the long shot gamble in looking for bacterial sex.

It took about six weeks from the time the first serious efforts at crossing were set up in mid-April 1946 to establish well-controlled, positive results and by mid-June Tatum and I felt that the time was ripe to announce them. A remarkable opportunity was forthcoming at the international Cold Spring Harbor Symposium. This year, it was to be dedicated to genetics of microorganisms, signalling the postwar resumption of major research in a field that had been invigorated by the new discoveries with Neurospora, phage, and the role of DNA in the pneumococcus transformation. Tatum was already scheduled to talk about his work on Neurospora. Happily, we were also granted a last minute insertion into the program (ca. July 11) to permit a brief discussion of our new results.

The discussion was lively! The most contentious criticism was Andre Lwoff's concern that the results might be explained by cross-feeding of nutrients between the two strains without their having in fact exchanged genetic information. Having taken great pains to control this possibility, I felt that the indirect evidence we had gathered should be accepted as conclusive, and there was more time spent than necessary in argument whether more direct proofs should be furnished that the purported recombinants were indeed pure strains. Fortunately, Dr. Max Zelle took me aside after the meeting and most generously offered to advise and assist me in the direct isolation of single cells under the microscope. These subsequent observations did quiet remaining concerns of the group at the Pasteur Institute that

Lwoff had assembled ,e.g. Jacques Monod, Francois Jacob, Elie Wollman, which was to make the most extraordinary contributions to the further development of the field. These single cell methods were also most useful in later investigations in several directions.

The most gratifying evidence of the acceptance of these claims by my scientific colleagues was the trickle (later a torrent) of requests for the cultures of E. coli K-12 to enable others to repeat the experiments. The first significant publications of this kind came from Dr. Luca Cavalli-Sforza, originally from R.A. Fisher's laboratory at Cambridge and later from Milan and Pavia. This prompted the beginning of an extended transatlantic (and now collegial) collaboration which was most gratifying from both the scientific and personal standpoint.

The tribute that is owing to Francis Ryan and Ed Tatum needs a larger frame than this article to be justly recorded. At a time when the public image of scientific fraternity is so problematical, it is important to record the survival of norms{ 13 } and behavior exemplifying mutual respect, helpfulness, consideration, and above all a regard for the advance of knowledge, even in a system that inevitably puts a high premium on competition and self-assertion. I have never encountered the extremities that Jim Watson painted in his self-caricature of ruthless competition (The Double Helix), which is hardly to argue that they do not take place. However, even by the most optimistic normative standards, the generosity and selflessness of my own teachers stand out as examples to be emulated, and to pass on to those whom I might in turn have the privilege to influence. Perhaps the greatest tribute to their skill as teachers is that they have made it impossible, to this day, for me to dissect my own innovation and creativity from the ideas that they may have planted and certainly nourished in the course of my learning and collaboration with them.

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Since 1946, E. coli K-12 has been the subject of innumerable investigations, some of which have substantially revised and enlarged our first simple models of the sexual behavior of E. coli {19} . The detailed story of the ripening of the initial discovery is an example of international cooperation and competition that deserves a richer and better informed treatment than is possible here.

The main burden of the present article is not only to examine how the discovery was attained in 1946, but also to ask more sharply: "Why then?" --or perhaps even more pointedly, "Why not many years earlier?". From a purely technical standpoint, equally decisive experiments might have been conducted say in 1906, at a time when the rediscovery of Mendelism had swept the imaginations of every other biological discipline. Could we say that the 1946 discovery was postmature?

These are not questions that can be answered with the precision of research on mechanisms of cell biology, but we believe they demand examination for reasons that go far beyond idle curiosity. They are vitally important to the self-criticism of science with respect to the efficiency with which its avowed aims are pursued. For some groping towards a better understanding, we will now turn to a review of the historical context of the understanding of bacterial life cycles prior to 1946.

III. Intellectual History of the idea of Bacterial Asexuality

This 'history of scientific thought', prior to 1946, emphasizes factors that may have discouraged inquiries into sexual processes in bacteria.

Bacteria were first noticed as objects of scientific microscopy by van Leeuwenhoek on May 26,1676. However, the limitations of the microscope and of cultivation technique hindered the delineation of their life histories for two centuries. Bacteria assumed the image of a crucial link in the "Chain of Being", the bridge between inanimate and animate forms of matter. This image was highlighted in the "spontaneous generation controversy": what could be better substantiation of the reduction of biology to mechanistic laws than the demonstration of the spontaneous (re-)generation of living forms from inanimate matter?

By 1861 the experiments of Louis Pasteur had displaced the commonsense observation of "spontaneous" putrefaction with the now prevalent view that the atmosphere and other natural media are almost universally contaminated, so that special precautions are needed to demonstrate the continuity of microbial life from pre-existing spores and cells. Together with the persistence of the Chain of Being image, the phobia of contamination was to play an important role in the further development of bacteriology.

In 1875, Ferdinand Cohn published a definitive taxonomic system of bacteria and coined the epithet Schizomycetes to categorize the entire group. This label, "fission-fungi", reinforced Cohn's categorization of the place of bacteria in the living world. These were not parabiological apparitions; they were simply primitive plants which "only reproduce by asexual means", a view that was hardly challenged for 70 years. This doctrine was no mere arbitrary whim; it was a reaction both to the doctrine of spontaneous generation and to the equally fantastic claims of interconvertibility of bacterial forms and of complex life cycles. To Cohn's mind, such claims resulted from contamination and faulty technique that would dangerously confound the newly clarified taxonomy of bacteria based on stable pure lines.{ 14 }

Medical microbiology could not have emerged as a science without the doctrinal base laid down by Cohn and the pure culture methods of Robert Koch. The identification of specific bacterial species as the causes of specific infectious diseases made it a matter of the highest practical as well as theoretical urgency to reject preparations, ideologies or results that might be subject to contamination.

This new view rapidly solidified as the "Cohn-Koch Dogma" of Monomorphism: "Each species of microbe is unchangeable in form and in properties and cannot transform into another species". (Henrici 1934, p. 19). It dominated both the German and the French schools of bacteriology and, by the 1890's, the notions that bacteria could reproduce sexually and that variability(if it occurred at all) might result from sexual mating were unthinkable for most bacteriologists. The problem of bacterial variation thus acquired an unsavory reputation or image. (See Lohnis 1921, pp. 1-30 for a review of evidence for monomorphism and polymorphism).

This attitude toward studies of variation may be described as a reaction formation that for many years averted bacteriologists from the systematic study of bacterial variation. In the practical sphere, genetic variation served mainly to thwart utilitarian objectives-the reliability of a vaccine, or the proof of the etiology of a newly studied disease. Variation would tend to be dismissed as a nuisance -- even today industrial microbiologists bewail the "degeneration" of their stock cultures -- rather than be confronted as a challenge to scientific insight. The preeminence of utilitarian motives in bacteriological work (be it medical, foods, agricultural or industrial) probably gave more weight to this attitude than would apply in more theoretically motivated disciplines.

A simple recapitulation of the history of resistance of microbiologists to the methodology and the cognitive framework of genetic biology is that monomorphist doctrine, when strictly construed, threw out the baby of bacterial genetics along with the dirty bathwater of contamination.

The critical early years of modern bacteriology 1860-1880 coincided with one of the most notorious of allegedly 'premature discoveries': Mendel's seminal work on the delineation of genes as the units of heredity. Undoubtedly, the new discipline of bacteriology would inevitably have been profoundly affected if mendelism had become established doctrine and part of the conceptual framework shared by Pasteur, Cohn and Koch. With the notorious exception of Naegeli{ 15 } and the problematical one of Beijerinck in the 1890's, there is hardly any evidence of mutual influence between Mendel's neglected work and the 19th century microbiologists.

A more challenging problem in this intellectual history, not to our knowledge investigated, is the mutual influence of Darwin and Pasteur. Darwin was aware that speciation in imperfect (asexual) fungi would have to be analyzed separately from evolution in higher organisms and could have contributed as a theorist to the debate over polymorphism in bacteria. Darwin was also deeply interested in the controversy over spontaneous generation { 16 }, and he and Pasteur were surely aware of one another's principal findings and claims, if only from the popular press. While Pasteur, for his part, made some vague use of evolutionary ideas , the main recorded intersection of their ideas in print concerns the role of earthworms as agents of soil turnover.

By the time Mendel's laws were rediscovered in 1900 microbiology was firmly established as a medical science of superordinate importance. It was a specialized discipline already separated in the educational schema from the studies of higher plants and animals. Its mystique, connected with its concerns for infectious disease, imposed particular experimental and cognitive approaches to these organisms, one that, as we have seen, relegated genetic variation of bacteria to the category of nuisance to be avoided and ignored. Not until the early 1940's did bacterial variation again become an arena of critical investigative inquiry in its own right - particularly with the work of Luria and Delbruck on the spontaneity of mutations for resistance to bacteriophage. But even the discussions of these years were marked by a vicious cycle of intensified self-discouragement that went like this: "Bacteria may have no genes, or at least they have no sexual processes by which we could do the crosses to determine the laws of heredity along Mendelian lines. Hence it is hardly profitable to study bacterial mutations when we will be unable to draw clear analogies between the phenomena of heritable change in bacteria and those of other organisms." But these mutational phenomena were the only tools by which one could hope to examine the initial questions of genes in these organisms!

The doctrinal rigidity of Cohn's taxonomy notwithstanding, there remained good reasons to assign bacteria a special status in the hierarchy of living organisms. They were very small; they appeared to comprise structures far simpler than those of other cells; they were characteristically unpigmented and motile like animals; but like plants they lived in solutions without eating solid particles. And at one time one might even have believed that they were amenable to spontaneous generation. Once such a cluster of attributes becomes established in scientists' imagery, it requires special provocation to try to splinter away some of its elements.

Particularly troublesome was the evident lack, until about 1935, of an organized nucleus in bacteria, so far as the cytological methods could tell. Even then, the claims for the demonstration of "nuclear bodies" with special stains -- including the DNA-specific Feulgen reaction -- were unpersuasive until the development of electron microscopy in the 1950's. At that, these new methods showed that the visions of mitosis asserted by some imaginative cytologists after 1946 were illusory. The DNA of the bacterial cell is typically organized into a single tightly wound filament that obviates the later evolved differentiation of separate chromosomes and a mitotic process that would keep them in order. Consequently, the few geneticists who made any effort to incorporate bacteria into a comparative system (like Huxley and Darlington) reinforced the image of bacteria as 'missing links', organisms so primitive that they had not yet evolved 'differentiated genes'. This ideology gave strong support to workers like Hinshelwood (v. infra) who then sought to use bacteria as exemplars of pre-genic levels of organization for physico-chemical analysis. Accordingly, bacteria might also be more immediately responsive to their environment than higher organisms, whose genes had been evolved (in part) to preserve the genetic autonomy of the organism. Until the complexity of microbial biochemistry, its homology to the metabolism of higher organisms, and the universal role of DNA in genetic systems were better understood, these speculations were at least philosophically attractive.

The biochemical analysis of microbial nutrition{ 17 } was a major impetus in the 1930's to the reexamination of the relationship of bacteria to other forms of life. The discovery of the similarity in chemical composition of bacteria to other forms; the idea that differences in nutritional requirements were secondary to losses of biosynthetic capability (that is, in some respects a bacterium is biochemically more competent than a man!) was coupled with the discovery of many specific enzymes that could be found both in bacteria and in higher organisms. These homologies also inspired Beadle and Tatum's work on Neurospora (1941), which showed the utility of a microorganism, in this case a fungus, as research material for studies in the genetics of metabolism. These studies made it possible to show how genes influenced the development of the organism through the encoding of specific enzymes, work that culminated in the deciphering of the genetic code in the 1960's.

This was also the time of renewed speculative interest in a biochemical theory for the "Origin of Life: Oparin's book of this title become widely available in English translation in 1944; and Schrodinger's ("What is Life") likewise focussed attention on fundamental questions that demanded an integration of the biology of viruses and microbes with the more traditional biology of plants and animals.

The mechanism of genetic variation, or mutation, was a fundamental issue in all of these speculations; and here again mutation in bacteria promised to be particularly important as an experimental measure, but still blurred by manifest uncertainties whether, truly, "bacteria had genes."

Another movement of biological thought during this period was the unification of Mendelism, quantitative population theory, and Darwinism into a reformulation of the theory of biological evolution. Darlington, around 1930, and later Ernst Mayr and Dobzhansky systematically developed the idea of genetic systems of varying complexity, and particularly the notion of species as mendelian breeding populations or isolated gene pools. The idea that sexuality itself was an evolved genetic system was particularly provocative, with fascinating illustrations in the life cycles of various orders of simple and more complex plant life, from fungi and algae, through the mosses, ferns and flowering plants. The concept of genetic isolation as the essential condition for the differentiation of species, -- the observable product of biological evolution -- certainly put renewed critical emphasis on the biological significance of sexuality. Indeed, according to neo-Darwinian theory every colony of an asexual biological form would have to be regarded as a distinct species, since by definition its genetic content would represent a gene pool totally isolated from that of every other. Dobzhansky's monograph, "Genetics and the Origin of Species" was widely read as the definitive reinterpretation of Darwinian theory of evolution and reinspired intense interest in the details of breeding systems as the key to the understanding of the details of evolutionary development.

The late 1930's and 1940's were then a time of renewed deep interest in the evolutionary significance of sexuality. This sharpened concerns about how to understand the evolution of organisms like bacteria which were believed to be devoid of sexual mechanisms.
The neo-Darwinian model of random variation subjected to the creative filter of natural selection was by now preeminent in the biology of higher plants and animals.
However, as Luria remarked in his 1947 review, bacteriology remained the last stronghold of the Lamarckist doctrine, e.g. in widely held beliefs that the development of drug resistance among bacteria was a hereditary change induced by the environment.{ 18 }

The scientific discussion of this issue was complicated by its Lysenkoist implications, at a time when the USSR had adopted an official (and repressive) faith in the role of environment in changing the hereditary character of crop plants and of Socialist man.
The side-effect of these political externalities in American biology (we do not speak here of the social sciences) was as much to provoke some intolerance of unconventional (i.e. unMendelian) views as to bias the judgment on scientific matters of those who were politically sympathetic to the Soviet view. So, on the one hand, informed geneticists like JBS Haldane broke with the Party on this issue, at the same time as innumerable left-inclined spectators from other fields strained hard to find support for Lysenkoism in any vaguely understood observation that looked like an environment-induced adaptation in bacteria. Whatever other effects this sorry episode of a

national-official science had, it was one more source of focussed interest on the mechanisms of genetic change in bacteria.

The most carefully worked-out theoretical model for direct genetic adaptation in bacteria was presented by Cyril Hinshelwood (a well known physical chemist, and later Nobel Prize winner in that field) who in 1946 published "The chemical Kinetics of the Bacterial Cell". This was an intellectual tour de force in describing the bacterial cell as a network of coupled chemical reactions but devoid of any specifically differentiated genetic material. It mobilized a vast amount of data in defense of this model and in opposition to the idea of discrete mutational changes in bacteria. As we now know it was existentially totally inaccurate, owing to an insufficient regard for the subtleties of population dynamics of mixed bacterial cultures subjected to natural selection (a subject that became the principal theme of F.J.Ryan's research after 1946).

Progressively deeper understanding of the life-cycles of other unicellular organisms was certainly among the provocative stimuli for a reexamination of bacteria. A 1941 symposium on the 'Genetics of Pathogenic Microorganisms' exhibits an extraordinary contrast, within a single volume, of the advanced status of genetic studies of fungi of great economic importance, like rusts and smuts, and the mumbo-jumbo that surrounded the discussions of bacterial variation. That such a conjunction could occur at all was new. It may have helped direct Lederberg's interest to those mycological precedents for microbial life cycles. More immediately he recalls the paper by Beadle and Coonradt, 1944, on heterokaryons in Neurospora, and the emphasis that Beadle put on them in his Harvey Lecture (Feb. 1945) as evolutionary precursors of sex. (Heterokaryons are associations of different nuclei within a common cytoplasm. The branched hyphae of fungi, often not completely septated, lend them to such associations, which fall short of sexuality by not going on to NUCLEAR fusion or fertilization.) Beadle's remark that one could identify such heterokaryons by their nutritional competence was also a forerunner of the selective method later applied to the discovery of bacterial sex.

The turning point: DNA, Avery, the pneumococcus transformation.

The turning point of the story, however, was the discovery in 1944 by Avery, MacLeod and McCarty that identified DNA as the transformation principle which had been shown to change rough non-pathogenic pneumococci into smooth virulent ones. The phenomenon of transformation had been discovered by Griffith in 1928. Avery's skepticism was surmounted by the work of Alloway, Dawson and Siu done in his laboratory (according to Olby {20}, almost surreptitiously in the face of Avery's hostility.) Subsequently, Avery organized the team effort that culminated in the 1944 report.

In a recent characterization of the Rockefeller work as premature, and thus comparing it to Mendel's long-neglected discovery, Stent { 19 } has confused legitimate skepticism about the proper interpretation of pneumococcus transformation with a lack of appreciation for its significance for biological theory. Lacking other means of categorizing genes in bacteria, one could not be sure of the homology of transformation in pneumococcus with genetic change in higher organisms. Furthermore, although the identification of the active substance as DNA was a plausible, and in retrospect, the correct chemical interpretation, this issue deserved the kind of skeptical challenge it elicited from Mirsky precisely because of its overarching importance.

As noted in Section II the Avery group report was the subject of lively debate at Columbia, in view of its portent for the chemistry of the gene, and was the immediate provocation for Lederberg's entry in 1945 into the field of microbial genetics. It was also highlighted in by Dubos { 10 }, as the avenue by which the chemistry of heredity might be solved. These developments were the immediate context in which the problem of bacterial sex was confronted in 1945. In a sharply focussed critique of the status of this problem, Dubos { 10 } wrote:

> If bacteria do really reproduce by sexual methods, it should be possible to cross closely related species and strains and to determine something of their genetical behavior. Although there have been isolated reports of successful crossing, most workers who have attempted to cross related strains have reported only failure. (Gowen and Lincoln 1942) ["Most" here refers to two papers: the one cited, and Sherman and Wing, 1937.]
>
> In effect, the evidence presented to establish sexual reproduction in bacteria is not convincing. (p. 181)

Some sense of how things seemed earlier in the 30's is conveyed by Sherman's perception of his own work. As Editor of the Journal of Bacteriology, on receiving a manuscript from Tatum and Lederberg in 1947, he wrote: "At the time [our 1937] work was done, variability in bacteria was scarcely a respectable subject -- let alone ideas on sex! However I have always thought that the approach used was a good one...

He was, it seems, one of the few occupied with the problem. C.F. Niven, one of Sherman's students at Cornell, recalled how little interested others were:

> Sherman's interest in bacterial sexuality dates back to his earlier days as a USDA bacteriologist,...During my eleven years stay at Cornell, Sherman's keen and intense desire to either prove or to disprove the existence of bacterial sexuality was evident almost on a daily basis. He repeatedly attempted to encourage his graduate students, myself included, to pursue further some of his earlier work, much of which was never published because of its inconclusive nature.Many of us did have a go at some of his ideas, but I'm afraid that our interests naively resided elsewhere...We youngsters could not become believers, and when Sherman expressed denial [of] bacterial sexuality, we generally viewed his negativity in the sense of a denial from an eager bride."
> (Niven to Lederberg, 7 March 1974)

Although Sherman was on the right track in the general design of his crossing experiment, which looked for recombination of markers for sugar-fermentation, that design can be (retrospectively) faulted on two grounds. It did not use a powerful method of selecting for recombinants -- hence it would overlook any process that involved less than a few per thousand cells. Furthermore, the markers themselves were rather unstable, so that their variation was too easily confused with the outcome of possible recombination.

The major textbooks in microbiology and bacteriology continued to assert the asexuality of bacteria. Moreover, microscopists had found no persuasive morphological evidence of sexual reproduction in any representatives of bacteria or in blue green algae. This was so even though a rich variety of sexual processes had been observed in "higher" microorganisms: fungi and protozoa, starting with Leeuwenhoek's original descriptions of copulating protozoa. These studies of sexual process in non-bacterial microorganisms (eukaryotes) shaped researchers' images of what such processes were like. Roger Stanier has observed "[This] led to the establishment of a certain idea of the nature of sexuality which....made it very difficult to entertain the possibility that bacteria might handle things differently.....Once natural laws of wide validity are established, there's a natural tendency [sic] to treat them as universal". (Stanier to Lederberg, 2 February 1974).

The adoption of E. coli strain B as the 'standard research organism' by the phage group in the earlier 1940s did a great deal to strengthen the rigor and access to mutual criticism of work in that field. But it also encouraged the universalist fallacy, and delayed the recognition of important phenomena like bacterial sexuality and lysogenicity for which, by unpredictable chance, that strain happened to be ill-suited.

IV. The growth of science: cognitive and social factors

Continuity and Discontinuity in the Growth of Science

Historians of science have often noted that the various sciences are not equally well developed at a given time. The more we already know about a subject, the more new questions are raised, and more further research is stimulated. Sectors of science, like the reputations of individual scientists thus appear to be subject to cumulative and self-augmenting processes.{21}

All of this makes for considerable turbulence{22} in the advance of different sectors of scientific knowledge, which may be functional; but it is difficult to see the mechanism by which the larger scale aspects of the scientific process are necessarily adjusted to optimize the cognitive goals of a system which has evolved in response to many social, historical and accidental factors.

Besides unevenness in the growth of divers fields, scientific growth is also subject to temporal discontinuity: to prematurity and what we have called post-maturity. Premature contributions are neglected or overlooked at the time of discovery by the contemporary community of scientists: in retrospect they are viewed as having been "ahead of their time". Mendel's discovery of particulate inheritance in 1865, lost to view for thirty-five years, is perhaps the most famous episode of prematurity. Since premature discoveries are, by definition, not incorporated into the body of knowledge at the time, they do not form bridges to immediate future knowledge. They are often insufficiently or unclearly connected to the immediate scientific past or, as Gunther Stent has put it, to "canonical knowledge". {23} Still another formulation, this time in the Kuhnian framework, is that such discoveries are not consonant with the prevailing paradigm -- with dominant views about the central challenges and methods of attack prevailing in the field. These are not of course the only sources of prematurity in science. The organization of scientific knowledge and activity into specialties makes its own contribution. As both origin and outcome of the extension of scientific knowledge, specialization is in large measure functional for the scientific enterprise. But it is also dysfunctional insofar as knowledge may become encapsulated within disciplines and fragmented in specialties. {24} Thus the cognitive elements necessary for understanding new contributions may be present in science at a given time but be "misplaced": that is, they may not be available in the domain in which the contribution first appears. That contribution, premature in its own domain, is apt to be relegated to the archives or lost to view altogether unless it is perceived and communicated across specialty boundaries by researchers who have the perceptual set required to understand it. It has also been noted that obscurity, either of the discoverer or his place of publication, and incompatibility with prevailing religious or political doctrine have been social structural barriers to the incorporation of scientific ideas into ongoing scientific work and thus have contributed to their neglect.

That premature discoveries and resistance to what later proved to have been authentic and significant contributions have social as well as epistemological sources has been suggested by Barber, Merton and Cole {25}. Postmature discoveries by contrast have been noted now and again but neither the pattern of postmaturity nor its problematics has been systematically discussed. In self-exemplifying style, focus on the problem of post-maturity is itself postmature.

The postmature contribution is a mirror image of the premature one. Whereas the premature was made at an early time, but was not (or could not be) understood by contemporaries, the postmature discovery -- by retrospective judgment -- failed to be made at a time when it was both technically achievable and could be understood and its importance appreciated. Characteristically, important discoveries generate a wake of new questions and techniques, sometimes a large infrastructure of information and further challenges to falsification, which lead in turn to new discoveries. Why the first pebble was not dropped may be the puzzle that raises the question of "postmaturity", especially when far-reaching waves are eventually generated.

This judgment of course implies a norm of homogeneous, successive, and consistent development of scientific knowledge across a broad front, perhaps constrained by the limitations of the current paradigm.

Thus Linus Pauling reports that "there was no reason why" he should not have discovered the alpha helix eleven years before he and R.B. Corey actually did so. {26} And C.N. Yang remarks that it is "startling that parity conservation [one of the space-time symmetry laws] was believed for so long without experimental evidence". {27} Experimental cues that parity was not conserved were observed as early as 1928 {28} but the avowed law was not considered problematical until 1955. Yang and T.D. Lee's discovery and theoretical elaboration of parity nonconservation brought them the Nobel Prize in physics just two years later.

The two kinds of discontinuity in scientific development differ in the kind of evidence used to ascertain them. Premature discoveries are located in the domain of factual history; postmature discoveries in the domain of counterfactual history. We identify premature discoveries through the fact that they were rediscovered {29} later --- postmature discoveries through the counterfact that they could have been discovered earlier. {30} Premature discoveries are often described as having been "neglected" and postmature ones can be described as having been "delayed". Such formulations smack of Whig reinterpretation of history {31} but they serve quite the contrary theoretical purpose. They provide convenient handles for grasping and analyzing discontinuities in the growth of scientific knowledge and help alert us to the difficulties of a model of undeviating progress of scientific knowledge.

The occurrence of postmature discoveries calls attention to the fact that there is always a population of problems competing for the attention of subsets of scientists {32}. But, given limitations on their time, attention and resources, they can actually deal with only a limited fraction of the problems that may be apparent at a given "stage of scientific development".

Most of the time scientists continue work along lines similar to those they had been working on earlier. Systematic evidence has yet to be gathered on inertia in problem choice over the course of scientific careers. However, scientists are apt to develop increasingly great investments in expertise and knowledge in a given area (equivalent to what the economists refer to sunk cost) and the social system reinforces that inertia by imposing selective demands and opportunities for remaining in that area. Thus, scientists are hired into slots to teach certain specialties while others in their departments are not as qualified to do so as they are; they receive information which will be selectively pertinent to their continuing research interests and they are called upon to write or speak on subjects others define as their areas of expertise. Taken together, the individual motivation to remain in a specialty area owing to prior investment and the social reinforcement to do so probably combine to produce something like "cumulative inertia" with respect to problem choice. {33}

Such limitations require choices among mutually exclusive allocations of intellectual capital. Many discoveries will be postmature for the good reason that alternative challenges were deemed important, achievable and exciting at the time.

Preemption seems to account for the delayed discovery of Pauling's alpha helix. In 1937, there was no great pressure to explain x-ray diffraction photographs of alpha keratin and so, after part of a summer's work and no success, Pauling found other problems more engaging. Presumably the attention of other scientists at work on neighboring problems also got diverted from the structure of substances like alpha keratin. It turns out, in this case, that the same scientist responsible for the postmature discovery could also have made it earlier and testifies to knowing much earlier what needed to be known to have done so. In most cases of such near misses, however, the postmature discovery is made by others.

Preemption of attention is only one of two broad generic processes that appear to be involved in the occurrence of postmature discoveries. In cases of preemption, scientists have identified the problem but elect not to pursue it. In the second type, such decisions are foreclosed because scientists do not perceive that a problem exists. It is one thing to put a problem aside and another not to know one was there in the first place. The fixity of assumptions, beliefs and images most scientists must hold for the organization of knowledge may serve as cognitive obstacles to their perceiving what otherwise would have been clear lines of inquiry. In the case we are about to examine, convictions about the very definition of bacteria were basic to the discovery's having been delayed by some 45 years. Nomenclature and definitions, as we shall see, affect the scope of scientific inquiry, what is taken as germane and what is taken as trivial, and are perhaps the most profound and consequential of assumption structures. Assumptions when taken as fact, markedly decrease the chance that a matter will become problematic and ultimately subject to falsification.{34} How this as well as other cognitive and social elements delayed the discovery of sexual recombination in bacteria is the next matter for examination.

Cognitive and Social Processes in Problem Identification and Selection

Parity conservation and asexuality of bacteria are two examples of scientific "truths" unquestioned by most scientists for a long time. How is it that such convictions are perpetuated and then later transformed into questions worth investigating? Can we identify the difficulties in and processes by which entrenched ideas are transformed into problematic ones?

The historical framework of the emergence of bacterial sexuality as a scientific issue was summarized in section < >. Here we may reexamine some broader questions relating to the delay or postmaturity of scientific discovery.

Technical difficulty leading to research failure is not sufficient to explain the present example. Some investigative failures, particularly those that are inexplicable, may stimulate new research into the relevant methodology. (Perhaps this can be said of whole sciences!) But failure which is readily attributable to "mere" sloppiness is more likely to dampen new efforts and divert research attention elsewhere. Few bacteriologists could have been motivated to take up a problem which seemed to have little intellectual merit and substantial procedural difficulty. Scientists manifestly distinguish between reputable and disreputable error. Error of all kinds is to be avoided, but it is one thing to be wrong in spite of having taken all appropriate precautions; another to be misguided and inept. There are, as a consequence, strong incentives to avoid problems which are "error prone", problems which in the past have acquired a reputation for producing results which turned out to be irreproducible. All this is reinforced by norms which prescribe caution when making claims which undermine prevailing views. These norms, rarely articulated by scientists, protect active researchers from time-wasting diversions and minimize the number of false reports enshrined in the archive.

After repeated episodes of failure attributable to contamination of samples, something like the process of reaction formation made the further study of bacterial variation {35} aversive. This apparently psychological explanation of the foci of attention of individual scientists has a social counterpart. Scientists in the aggregate, after all, share similar opinions about scientific problems; some are considered promising, others are not; some are likely to yield solutions easily, others with difficulty. The collective focus of attention in each science represents the sum of individual decisions about what not to study (decisions affected by shared opinions), and these decisions in their turn affect the subsequent reputation of problems, unless of course new solutions are found which alter collective scientific opinion. So much for why microbiologists might have avoided the problem of bacterial variation.

The fact was that many did not even see it as problematic. As we have noted, bacteria were, by definition, asexual for the practical purposes that evoked the characterization. According to the great classifier Ferdinand Cohn, they were fission fungi or schizomycetes. As such, they did not reproduce by means other than fission. Since sexual recombination could not occur in bacteria and since the same organism did not change its form during its lifetime, monomorphism became the rule of the day. It thus becomes clear that the labelling of scientific phenomena has consequences for the way that scientists think about phenomena much as social labels are said to be socially consequential definitions of those who are labelled. {36}

By reorienting the scientist's perception, labels influence the choice of problems, and may delay the reexamination of fallacious traditions of misplaced concreteness or precision. They come to be self-fulfilling prophecies {37}. Consider the impact of the terms atom, ether and noble gas on scientists' conceptions of matter. For centuries, atoms were indivisible; and ether was the substance which filled space. Noble gases were inert or unable to form compounds. By reinforcing the security of current theory and encouraging further exploration, labels tend to outlive the rational arguments on which they were based. They are one of the principle mediators of rigidity in collective memory and intelligence. This is not to deny the constructive function of labels for scientific development (obviously they are required for abstract thinking) or even that labels always dampen scientists' skepticism about the traditional images. Explicitly dogmatic labels may have quite the opposite effect in stimulating scientists to challenge the received word, as it seems to have for Neil Bartlett who demonstrated that noble gases were not inert and could indeed form compounds. Labels carrying less explicit dogmatic freight than, say, "noble gas" may restrict scientists' thinking most of all. Systematic analysis of the effects of labels on scientific development should enhance what we know about the classical sociological problem of the social effects of definitions of the situation in science.

Disciplinary structure and the investigation of bacterial sexuality.

Disciplinary structure also exerted its own effects on bacteriologists who might have examined the problem of bacterial sexuality. By the later part of the nineteenth century, bacteriologists were principally concerned with bacteria as pathogenic organisms and the means of eradicating them. Members of the French, German and Austrian schools were oriented to the (enormous) practical medical implications of their work. The notion that bacteria deserved equal attention as strategic targets of fundamental science was for some time the special province of a small group of Dutch scientists known as the Delft School.

Proudly evoking their descent from Leeuwenhoek, the Delft School of bacteriology clearly separated themselves from the medical bacteriologists who maligned bacteria. Martinus Beijerinck, who independently discovered the tobacco mosaic virus and was the principal figure in this group was at odds with prevailing dogma about the invariability of bacteria. He was prompt to cite the importance of DeVries new findings on mutation in plants, and offered some of the first and most coherent challenges to strict monomorphism. {39} He also relied on "enrichment culture" methods, which were an early forerunner of the selective techniques successfully applied later in the discovery of bacterial recombination. He was personally involved in the rediscovery of Mendel's work {40}. He thus was far better informed than most of his contemporary microbiologists about the new work on plant hybridization and mutation that would have been instrumental in planning an investigation of sex in bacteria and understanding the observations. Lederberg finds it surprising that Beijerinck did not discover bacterial recombination in the first decade or so of this century.But in fact he strongly reechoed the Cohnian dogma of Schizomycetes.

Nevertheless, Beijerinck, A.J. Kluyver, and C.B. vanNiel had an important indirect influence through their espousal of comparative biochemistry as an approach to the understanding of evolution and of fundamental cellular processes.

Although Beijerinck and other members of the Delft school were likely candidates for making the discovery of bacterial sex, students of genetics were not. Geneticists were occupied with larger organisms in which the products of crossing (the bases for studies of heredity) were easier to observe. Bacteria are very small and were then almost impossible to work with cytologically -- and besides, following Cohn and the bacteriologists, they were believed, even defined not to have sex. Thus the problem of sexual recombination fell between disciplinary stools, finding a place neither in bacteriology nor in genetics. As long as the monomorphic view prevailed in bacteriology and as long as there appeared to be no urgent motive for bacteriologists or geneticists to want to know whether bacteria reproduced sexually, the subject would remain an unacknowledged and long-gestating bastard.

Although the Delft school was the major deviant from the strictly medical orientation of bacteriological study in 1900, by 1925 a considerable fraction of the published research was conducted by Ph.D.'s, many of whom had been trained originally as chemists or biologists. In a crude effort to assess the disciplinary rigidity of bacteriology, we examined the biographies of American authors of papers published in two leading journals. In 1925, less than a fourth of the 49 identifiable authors of papers in the Journal of Infectious Diseases and only half of the 44 in the Journal of Bacteriology were MD's. Contrary to a more naive view of the frame of the discipline that we had previously entertained, plainly MDs did not dominate the literature at that time nor were strictly medical issues of paramount concern.

The gap between genetics and medical bacteriology might better be characterized as a barrier between fundamental and applied science. This gap appears to be endemic -- turning up as it does in many areas of physics and engineering as well as in the biological sciences and medicine and seems a likely source of lost opportunities for systematization of knowledge. {41} While there is no inherent conflict between theory and practice, examples of their convergence -- as for example Wiener's cybernetics or Claude Shannon's work in communications -- are remarkably few. The sporadic communication between scientists and practitioners is reflected in the tenuous linkages of their published writings, which has led Derek Price to proclaim that science and technology develop essentially independently of one another. {42} Be that as it may, the hindered interaction of science and relevant applications is apt to create discontinuities in knowledge on both sides.

So far, our discussion of the discovery of bacterial recombination has focussed on discontinuities in scientific development and some of its sources. Now we turn to a separate but not altogether unrelated question. What can be learned about the impact of the social contexts of science by examining the present case, the scientists's social origins, the educational system in which he was trained, the institutional contexts in which his specific research interests developed and some specific features of the discovery of bacterial recombination?

Lederberg was, as he noted, the son of a Rabbi, raised and educated in New York City in the 1930's. The best data on hand on the religious origins of American scientists show that Jews are statistically over-represented in the professoriate, especially in recent decades. They now comprise about 10 percent of all professors in the physical and biological sciences as compared to the general population figure of about 3-5 percent.

Even in the light of this predisposition, the differentiation of Lederberg's scientific interests occurred at a very early age, as can be documented, e.g., by a letter from one of his teachers. She writes of the twelve-year old Lederberg:

> Early in 1937 ... I had a most unusual
> pupil whom I still remember vividly. I can still remember how
> he prepared a paper on the classification of Protozoa.... using

> a graduate text for a reference.....It is more than just possible that I am guilty of being the first one to teach you that bacteria divide only by simple fission. (Mrs. Fanny S. Rippere 2/24/59; 3/10/59)

In addition to its conventional academic and commercial high schools, New York had several elite schools which were open only by competitive examination. Stuyvesant High School and later Bronx High School of Science, unlike Boston's Latin School, emphasized science and mathematics and brought substantial numbers of bright boys together with able teachers in a comparatively demanding and advanced science curriculum. Bright girls could attend Hunter High School which put a premium on preparing its students for the liberal arts colleges but not for the sciences per se. Lederberg's scientific indoctrination was augmented by attending the American Institute Science Laboratory. In the 1930's, New York's cosmopolitan atmosphere offered great opportunities of all kinds to motivated youngsters.

Data on men and women in Who's Who (1976-77) are consistent with this assertion (25). About 13 percent are native-born New Yorkers while the City has had slightly more than 5 percent of the nation's population since the turn of the century (26). But an even greater share of American scientists come from New York City. Twenty percent of the physical and biological scientists in American Men and Women of Science who were American-born, list their birthplace as New York City (27).However, until detailed information is available on the religious and geographical origins of American scientists, it will not be clear whether New Yorkers are overrepresented among Jewish scientists generally or particularly among those of Nobel prize caliber.

Lederberg was 16 years old when he graduated from high school. Columbia University and the towers of its Medical Center (near his home) symbolized the wide world of learning and first class-science for him. But it seemed then that he had little choice but to go on to the City College of New York in the light of the Lederberg household's finances. {48} Even though it seemed out of reach, Lederberg applied to Columbia nonetheless. He was awarded a tuition scholarship just large enough to allow him to attend that fall.

He sized up the opportunities then available on Morningside Heights, decided that he was unenthusiastic about classical Mendel-Morgan genetics and elected to spend most of his time on cytochemistry and physiological embryology. If these seem highly specific interests for a 16-year-old, they were nonetheless consistent with his self-defined research program of "understanding the chemical nature of life".

Dobzhansky had just arrived from Cal. Tech. He and others at Columbia, such as Alfred Pollister were well integrated into the New York scientific communication network which kept them in close touch with work at the nearby Rockefeller Institute where Avery, Dubos and Rous worked. Pollister's collaborator, Mirsky, in fact shuttled between the two institutions.

When Lederberg was a sophomore, he met Francis Ryan, as he recounted earlier. Ryan, "adopted" Lederberg and found work for him as a laboratory assistant. It was from Ryan that Lederberg first heard about the new biochemical genetics of Neurospora. And it was Ryan who persuaded Lederberg that chemistry and genetics need not be so far removed from one another as Lederberg had thought.

In short, Columbia provided as much informal access to the research front in biology as any other American university at the time.

Quantitative studies of the impact of college environments on the production of future scientists show weak "school effects" in comparison to the much stronger effects of "inputs" or student abilities. These studies understandably have not focussed on detecting effects of particular collegiate environments and particular teachers nor on differential outcomes in specialized disciplines; whether, for example, the University of Chicago in the postWorld War II period was especially productive of nuclear physicists or Cal Tech of the 1950's, of molecular biologists.{49}

These general findings aside, Columbia College did offer a number of specific opportunities to Lederberg. He was strategically located in an information network which encompassed the various strands of biology described earlier. It offered the opportunity to be adopted by a Ryan who would nurture his interest in research. It was also fortunate for Lederberg that Ryan was not yet so well established as to be already preoccupied with training many graduate students who would have prior claims on his time. On the other side, Lederberg's precocity facilitated his use of an advantageous social structural location in ways that other students with more conventional assets could not.

Although he was an assiduous bibliographer, covering and digesting vast sectors of the biological and chemical literature on his own, had he gone to City College, he would not have been privy to first-hand reports of the Beadle and Tatum work, would not have learned the details of selective bacterial nutrition, would not have had the opportunity to work with Ryan and might not have heard of the Avery work until some time after in fact he did.

Six months later, in July 1945, he had written in his laboratory notebook that sexual recombination in bacteria was a meritorious problem that could be attacked with the methods related to the Neurospora work. He and Ryan had just completed a paper {50} -- Lederberg's first publication -- on reverse mutation in Neurospora which used the technique of marking mutants by their nutritional requirements. First hand experience with this technique of nutritional selection led directly to insight how to detect sexual recombination in bacteria.

The opportunity to study at Columbia thus offered access to a communication network, a research milieu, and the tutorship of an energetic but generous and considerate Ryan, which facilitated both his perception of an important problem and the technical skills to attack it. Ryan's place in the invisible college that now connected Stanford, Columbia and Yale was also instrumental in his introducing Lederberg to Tatum, and in arranging the funding of an unusual fellowship at a time before the National Institutes of Health had invigorated biological research in this country.

Being strategically located in this environment was however not determinate. After all, there were others there who did not think the question of sex in bacteria was problematic and who spent no effort to devise a method whereby it could be decisively observed. Lederberg's own brand of skepticism (which he thinks every autodidact must acquire or be hopelessly misled) combined with his facility for devising simple and effective research techniques were idiosyncratic. But his structural situation at Columbia obviously offered many opportunities for the growth and exercise of his particular abilities that might readily have been thwarted at other times and places.

Although it was not evident at the time how Lederberg would get leave to work in Tatum's laboratory -- medical schools' schedules being generally demanding and inflexible -- the fact that Lederberg was a medical student was less of an obstacle to his doing research on bacterial sex than it might immediately seem. Since he was not a regular graduate student obligated to do research for a formal dissertation, he was not subject to the constraints that usually apply at that stage of the scientific career. And this is a crucial point: unlike others who had to work on a problem with a predictable outcome, Lederberg could better afford to take on a high risk problem without much anxiety that negative results would stall him at the very start of his career.

The search for bacterial sex belongs to a particular class of scientific investigations which made it high risk. It was a voyage of discovery more than the cultivation of known ground. Not finding bacterial recombination would not demonstrate it did not exist. (It should be remembered that two earlier studies had been unsuccessful). Thus all of the effort involved in the experiment might readily have been wasted since the reward-system of science provides few kudos for those who produce negative findings. (As it turned out, the risk of a negative finding with the chosen species of bacterium could be measured precisely. It was later found that the phenomenon could be observed in just 5% of all strains of E. coli in the way that it was demonstrated in K-12, the strain that by lucky chance had been chosen.)

The experiment was high risk in another respect. The chances of achieving contaminated and thus artifactual results were still great. They had after all been documented for decades. But if the experiment was high risk in the sense of not guaranteeing reportable results it was clearly high yield by the measure of the significance of positive findings. Tatum by comparison to Lederberg already had his own laboratory {51} and a variety of projects in process. He could afford to include a long-shot experiment among them - especially if it was not expensive. The opportunity structure for investing in high flyers is stratified and favors those with some situational capital {52} or -- as in Lederberg's case (he still intended to become an M.D.) are deviant enough to be operating in another market system altogether. Therefore advantage appears to accumulate with respect to winning on high risk problems just as it does in the social realm of science. {53} Risk-taking is apparently not only a matter of psychological daring but one of position in the social structure as well.

Further development of the notions of risk-taking in problem selection in science and of problem portfolios containing items which carry variable risk would of course benefit from intensive review of the pertinent literature in economics and decision-making. By way of example, elementary utility theory posits that risk-estimation involves the probability of success, the cost of failure, and the marginal returns and their utility of different kinds of investment. Bacterial recombination for Tatum and Lederberg was a good gamble in the sense that failure would have low marginal disutility (though for different reasons for each of them), but promised large if prospectively unlikely returns.

It was clear that if Tatum and Lederberg were to be successful, the discovery would be a very important one indeed. How is it that Lederberg seemed unconcerned about revealing the details of his research design and how is it that Tatum, who himself was contemplating a similar effort, agreed to have Lederberg come to work in his laboratory and share his almost unique collection of nutritional mutants? What can be learned about competition for priority and secrecy in science from this case?

Since publication in 1957 of Merton's study of competition in science using priority disputes as a strategic research site, competition for recognition of contribution has played a central role in sociological thinking about the behavior of scientists. Merton's analysis, extended since, focusses on the abiding concern in science with originality, its functions for the advancement of scientific knowledge and its role in producing competition, secretiveness, priority fights, and, on rare occasion, outright fraud. {54}

But secretiveness and competition, Merton holds, are contained to a degree by an institutional imperative to share one's work and, by extension, one's expert knowledge and research materials. {55} Secretiveness and competition are also contained by pragmatic considerations; isolation, after all, reduces access to information, and critical corrective feedback and , at a social level can directly interfere with gaining recognition. It also, as Hagstrom notes, takes much of the fun out of doing science. {56}

The double emphasis in science on originality and open communication can lead individual scientists to experience considerable stress in deciding whether or not to share their ideas with others before those ideas are publicly earmarked as their own. No such stress can be perceived in the Lederberg-Tatum relationship, either in Lederberg's memory or from anay available documents.

Lederberg claims that he was not naive about the existence of competition and plagiary in science. However, in the light of Tatum's reputation for scrupulous fair dealing with younger associates, communicated via his close friend Ryan, Lederberg never entertained the possibility that Tatum could plagiarize the research design communicated in the letter. In any case, the competitive world of molecular genetics described by J.D. Watson in The Double Helix {57} just a few years later does not resemble the environment in which Lederberg began his career. Besides the possible role of personal idiosyncrasy in creating differences in the tone of mutual cooperation and openness, scientific fields vary in the extent to which an idea is a purloinable quantum in itself, or needs additional theoretical insights and technical skills before it can be exploited for personal recognition.

Empirical data are sketchy on the extent of competition in the sciences. The most comprehensive are confined to scientists' reports of the frequency their research has been anticipated by others. {58} But this is just one aspect of the general process of competition in science and is less germane to this discussion than the studies of scientists' attitudes about open discussion of their work before publication. Diverse and comparatively large samples of physical and and biological scientists report little anxiety about discussing their research with others. Almost half report feeling free to discuss their work with anyone. And an additional two-fifths or so report feeling free to discuss their work with most others. Most scientists apparently are willing to communicate their ideas to almost anyone and if they feel uncomfortable about it, they do not say so.{59} Lederberg's lack of concern about describing his research plans in detail to Tatum was probably fairly typical of scientists at work at the time.

But Watson's Hobbesian perspective on science is not altogether deviant and inexplicable. Hagstrom and Sullivan confirming Merton's early hypothesis, observe that competitiveness and secretiveness are most characteristic of scientists who suffer from status insecurity. {60}.

Much more work will be required to establish the diversity of competitive behaviors exhibited in the various specialties as well as within and between scientific schools. Competition within a school may well be restrained by a founder who systematically allocates problems for investigation. The Delbruck festschrift documents several examples of his role in distributing problems among members of the "phage group". {61}.

Finally, we turn to some of the effects of organized skepticism, the institutional requirement that scientists critically scrutinize each new contribution even those they believe are correct. {62} Lederberg has already recounted his debate with Lwoff and, in passing, on the further elaboration of work on the mechanisms of bacterial sex.

Here, we want only to touch upon the Cold Spring Harbor presentation and to mention one instructive episode in the exercise of organized skepticism. The episode in point involves vigorous resistance by Mirsky against the Avery, Macleod and McCarty conclusion that DNA was the transforming substance. The claim that no protein was involved in genetic transfer countered the widely held belief that a protein was the most likely candidate for being the hereditary substance. Nucleic acid molecules, as described by organic chemists at that time, were considered far too simple to carry the complex information of heredity.

This episode is instructive for our purpose not because it involved the major reformulation of Avery's work but rather because it did not -- it was criticism that proved ultimately to be unfounded. Exhibiting behavior strictly in conformity with the norms, Mirsky was skeptical of the conclusion that Avery and his colleagues had decisively ruled out the possibility that a protein might be present in the purified transforming agent. {63}

As it turns out, Rollin Hotchkiss, working in Avery's laboratory, was also concerned that traces of active protein might account for transformation. As he put it,

> My respect for proteins owed very much to long hours of fascinating learning from Alfred Mirsky... Quite on my own, then, I felt the same doubts he did..... Mirsky spoke about these objections, but not very much to Avery's group or he would have learned as I did how eager they were to see the search for traces continued. {64} On both sides then skepticism prevailed.

Hotchkiss himself took on the job of doing the required experiments which made it increasingly implausible that the genetically active nucleoprotein was cofractionated with DNA. Avery's work was thereby solidified, as it would not have been if doubts about protein had been ignored.

Conformity to the norm of organized skepticism, irrespective of any ethical value it might have contributes to the advancement of scientific knowledge. It improves the chance that error will be uncovered, and perhaps equally important, it also strengthens valid contributions by reducing residual uncertainty about them.

The impact of organized skepticism can also be observed in the records of the Cold Spring Harbor Symposium and in response to the three papers by Lederberg and Tatum announcing the discovery. The first paper, published as a terse 497 word piece in Nature, October 1946, was not the first presentation of the work but reflected earlier discussion at Cold Spring Harbor. Even as discoveries enter the archive of science, they are not unitary events limited precisely to what the contributors first proposed. Discovery is a complex on-going process elaborated by criticism and by the contributors' response to it.

Treating discovery as a process makes it possible to identify the fine-structure of the operation of organized skepticism -- how contributors anticipate criticism, what arrangements are made for public expression of criticism, what the range is of styles of critical role performance, which kinds of scientists require which kinds of evidence to become convinced of the validity of the work, and finally, how the ultimate significance of the work is assessed. {65}

The process of discovery takes in events not only in the laboratory or in front of the blackboard but also those involving response and counterresponse afterward. What we really mean by designating this or that scientist as the discoverer is then problematical. This calls into question the current practice of sociologists of science of gauging the impact of a scientist's work by counting citations to his name alone. Citation counts to the authors of originating papers probably underestimate the actual response to the work associated with them. Such counts seem to reflect a rather atomistic conception of the development of science since they neglect altogether contributions surrounding the original papers. New procedures of co-citation analysis now being used for other purposes may be a way of reconstructing the complex of published works that comprise a given contribution. {66}

V. Some conclusions and lessons

If historical analysis is to go beyond the selection of narrative detail and display some theoretical assertiveness, it ought to be asked
"what if?": that is to make a plausible case for postdicting alternative outcomes, given different hypothetical inputs.

Quite possibly genetic recombination in E. coli as we know it and describe as sexuality, might have remained undiscovered until this day. Furthermore, we could ask, only partly tongue-in-cheek, how much regret that would entail. There is no question that there was already an irresistible impetus for the development of bacteria as tools for genetic investigation. Without these findings about sex in E. coli, there would nevertheless have been an enormous productivity and possibly an even sharper focus of work in the tradition of the Delbruck school. They had already discovered recombination in viruses and the discovery of sex in E. coli was not a prerequisite for the work of Hershey and Chase on the role of DNA in the virus life cycle, or that of the other virus chemists. Without the distractions of another genetic system like E. coli, even more attention might have been paid to the pneumoccocal transformation or other systems like it. There would have been a significant impediment from the lack of very detailed genetic maps of the bacterial chromosome but they might well have been built up piecemeal by other methods and partly by analogy with recombination in viruses. Perhaps even more likely there would have been less emphasis on bacterial genetics and more on the viruses with their simpler structure. It is conceivable that this would have led to even deeper and more rapid advances at the strictly molecular level, perhaps at the price of a much vaguer picture of the natural history of bacteria.

What might have been bypassed could include some aspects of phenomena like lysogenicity -- the incorporation of viruses into the bacterial chromosome -- but other branches would have inspired considerable work in that direction. So, the minimum that can be foreseen is that other parallel channels of development in the general area of molecular genetics might have been pursued even more deeply; or alternatively that some completely different one, unknown to us at the present time, would have emerged -- one that is now neglected owing to the attractiveness of the E. coli system.

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A variety of processes, social and cognitive, made the discovery of sexual recombination in bacteria a postmature contribution and thus delayed the development of the specialty of bacterial genetics:

(1) The definition of bacteria as asexual -- symbolized in their classification and denotation as schizomycetes -- diverted investigators from looking for and observing sexual recombination;

(2) Repeated experimental failure to demonstrate gene exchange in bacteria and the fact that these experiments were susceptible to contamination gave them the image of being risky and vulnerable to disreputable error;

(3) the movement in bacteriology to downgrade fundamental research on these organisms in favor of the more practical and socially rewarding studies in medical bacteriology. Thus the problem had no appropriate disciplinary home.

Using the vehicle of a detailed case study for analysis of cognitive and social processes in scientific discovery, we note that problem selection in science has at least three features deserving further analysis. First, some good problems are preempted and may eventually become postmature. Second, in calculating the returns on selecting one problem rather than another, the probability of making errors -- reputable and disreputable, is taken into account and contributes to the continuing neglect of problems that have a history of being error-prone. And third, the opportunity for taking on high risk problems in science is unevenly distributed. Such problems are typically left to the well-established who can afford to include them in their more comprehensive research programs and to the small number of others whose primary commitments are to a different system. This uneven distribution of opportunities makes for accumulation of advantage in the cognitive realm and in the social stratification of science since major advances often can be made only by assuming high risks.

Thus we suggest that problem identification and selection involves the interaction of cognitive and social elements in individual investigators' choices of what to work on and in the resulting collective foci of attention in the sciences. What is taken as problematic and worthy of investigation are the net product of these interactions.

The further study of such interactions in different fields requires information, sensitivity and expertise on both sides of a kind that is most likely to come from interdisciplinary collaborations.*

* dedicated to the memory of Francis J. Ryan, Edward L. Tatum, and Harriett Ephrussi-Taylor.

Work on this paper began at the Center for Advanced Study in Behavioral Sciences with support from the National Science Foundation. [Program on Science, Technology and Society at the Center.] Our work has benefitted greatly by repeated discussion with Robert K. Merton: his contributions should be evident throughout. Yehuda Elkana, also a fellow at the Center, helped to criticize early drafts of the paper. The junior author has been supported by the National Science Foundation's grant to the Columbia University Program in the Sociology of Science.

Footnotes 1. A longer account of Tatum's scientific biography is forthcoming in the Biographical Memoir series of the National Academy of Sciences. Memoirs on Taylor and on Ryan have appeared in Genetics, 60: 524, 1968 and ibid., 84: 1-25, 1976.

2. Saul Benison, Tom Rivers: reflections on a life in medicine and science. Cambridge: MIT Press, 1967.

Wiener, Charles ... to be furnished American Institute of Physics; project on the recent history of physics interviews

Thomas Kuhn, History of Quantum Physics. American Philosophical Society. [ref ??]

Nevins, Allan. Re Oral History ??? to be furnished

3. Space does not permit us to reproduce all relevant documentation. Where assertions are based on unsubstantiated recollections, this should be clear from the text.

4. Woolgar, S.W. 1976 Writing an intellectual history of scientific development. The use of discovery accounts. Soc.Stud.Sci. 6(Sept): 395-422.

5. David R. Zimmerman Rh: The Intimate History of a Disease and its Conquest. N.Y. MacMillan 1973, p. xv.

6. Thus we had tacitly agreed that the scientistic eschatology fulfills a Jewish interpretation of the Fall of Man.

7. In retrospect, not a bad choice for a perspective on the chemical basis of life. This work, published 1933, was unusual, for example, in its detailed treatment of Garrod's work on "Inborn Errors of Metabolism", which Beadle and others were to characterize as lost genius a decade later.

8. (For an account of the wartime officer-preparation training programs, and the contrast in Army vs. Navy administrations that made this a fortunate choice, see Herge (1948)

Herge,Henry C. Wartime College Training Programs of the Armed Services. Amer. Council Educ., Washington, 1948 See also: Medical Training in World War II, Medical Dept., U.S.Army 1974.

9. For a discussion of some reasons why this perception may have been so much more emphatic at Columbia than has been recorded by the chronicler of the invisible college of the phage group, Gunther Stent {23} see section IV.

10. It is not certain whether this work was available just before or just after these questions were raised with Ryan. In any event it was a treasure chest of critically digested data on the biology of bacteriology that put the previous history in sharp, critical perspective and furnished many ideas for new experiments.

11. more precisely by Kruis and Satava 1918, in work that had been published only in Czech, and rediscovered, independently, by Winge

12. Tatum, 1945 Proc. Nat. Acad. Sci. U.S., 31:215-219. ;
Gray,C.H. and Tatum,E.L., 1944. ib., 30:404-410.

13. Robert K. Merton, 1942 in 1973 The Sociology of Science, Chicago: University of Chicago Press, Ch. 13.
B. Barber, Science and the Social Order. N.Y.: Free Press 1952
A. Cournand and H.A.Zuckerman The Code of Science. Studium Generale 23 (Oct. 70) 941-962.

14. Many intellectual as well as political revolutions suffer in the long run from this kind of rigidification of defenses against errors that had provoked them in the first place. Thus they sow the seeds of their own obsolescence.

15. one of the most influential advocates of bacterial polymorphism: he is perhaps best known as one of Mendel's few scientific correspondents, and for having failed to understand and thereby discouraging the further dissemination of the friar's discovery.

16. According to H.E. Gruber 1974 , Darwin on Man. N.Y.: Dutton, he anticipated some arguments of Oparin that the "first primordial living things consume the complex but non-living molecules from which they evolve, so that once done, the deed becomes forever impossible". p.152

17. especially the work of B.C.J.G. Knight and Andre Lwoff, reviewed i.a., by Dubos { 10 }. These efforts at a unified system of nutrition owed a great deal to the concepts of comparative biochemistry in energy metabolism that can be attributed to Albert J. Kluyver in Delft.

18. It would be fairer to say that most bacteriologists did not admit of a distinction between hereditary potentiality and manifest phenotype that would make this a well-formed proposition.

19. See especially Francois Jacob, 1965, Genetique de la cellule bacterienne. Les Prix Nobel en 1965. E. Wollman and F. Jacob, 1959 La sexualite des bacteries. Paris:Masson. W. Hayes 1969 The genetics of bacteria and their viruses. New York:Wiley. and J. Lederberg, 1959 A view of genetics. Les Prix Nobel en 1958, for reviews and retrospections. The prehistory is well covered by Dubos { 10 } and Olby { 20 }. Current work on E. coli K-12 is reviewed periodically in Annual Review of Genetics, Annual Review of Bacteriology and Bacteriological Reviews.

20. R. Olby,1975 The Path to the Double Helix Seattle:U. Washington Press.

21. Robert K. Merton, The Sociology of Science. Chicago; University of Chicago Press, 1973. Ch. 20, originally published 1968.

22. In the hydrodynamic sense of self-sustaining vortices. This follows the usage of Millionshikov, "The Place of Value in the World of Facts," Nobel Symposium XIV. Stockholm: 1969.

23. Gunther S. Stent, "Prematurity and uniqueness in scientific discovery," Scientific American 227 (December 1972) 84-93. Stent claims that the Avery group's discovery of DNA transformation was premature but there is ample evidence that the work was widely known soon after it appeared, that it excited the imagination of many scientists, and that it was the subject of numerous inquiries between 1944 and 1953. See Robert C. Olby, "Path..."; Dubos 1976, The Professor, the Institute and DNA. New York: Rockefeller Press; J.S. Fruton 1972, Molecules and Life. New York:Wiley. J.S. Cohen and F.H. Portugal 1975, A comment on historical analysis in biochemistry. Perspec. Biol. Med. 18(2):204-207; H.V. Wyatt 1975, Knowledge and prematurity: the journey from transformation to DNA. ibid, 149-156. Be that as it may, Wyatt's and Stent's general views on the character of prematurity in science are well taken and applicable to Mendel and other more apt historical cases.

24. On communication barriers in science, see A.J. Meadows, "Diffusion of information across the sciences," Interdisciplinary Science Reviews 1 (1976) 259-267.

25. Bernard Barber, "Resistance by scientists to scientific discovery," Science 134 (September 1961) 596-602; Merton, Sociology of Science, Chaps. 16 and 17; Stephen Cole, "Professional Standing and the reception of scientific discoveries," American Journal of Sociology 76 (September 1970) 286-306. Among those who think that premature discoveries do not exist because cognitive factors cannot be separated from their intellectual context, see Yehuda Elkana, "The conservation of energy: A case of simultaneous discovery?," Archives Internationales d'Histoire des Sciences 23 (January-June 1970 31-60.

26. Linus Pauling, "The molecular basis of biological specificity," Nature 248 (26 April 1974) 769-771.

27. B. Yang, "The law of parity conservation and other symmetry laws of physics," Les Prix Nobel en 1957. Stockholm: Imprimerie Royale, P.A. Norstedt & Soner, 1958. Pp. 95-105, at p. 100.

28. After Yang and Lee had done their own work on parity nonconservation, they learned of experiments done in 1928 by R.T. Cox, C.G. McIlwraith and B. Kurrelmeyer which showed parity nonconserving effects. Jeremy Bernstein observed that "at this time the study of weak interactions was in its infancy, and there was just no theoretical context in which to put the results. In fact, it was only in 1927 that... Eugene Wigner... devised the first real mathematical formulation of parity symmetry in quantum theory. Therefore it was not as if the results had challenged an existing theory that was well understood. They were rather a kind of statement made in a void." "Profiles: A question of parity," New Yorker 38 (12 May 1962) 49ff, at p. 93.

29. Rediscovery of the phenomenon and the prior report almost always occurs in that order.

30. A given lineage may include both. Many "lost" discoveries may exist that had been premature and not yet reencountered and more late ones where new knowledge is developed in substantial lag behind the potentialities of the existing paradigm although no evidence but experience exists for either type before the fact. The surprise expressed by scientists that postmature discoveries were not made sooner seems to derive from their usually unarticulated belief that the cognitive ingredients of the discovery had been available for some time.

31. Herbert Butterfield, The Whig Interpretation of History. New York: Scribner, 1951. First published 1931.

32. In 1961, Merton suggested that conflict and competition among lines of social scientific development (and presumably in the physical and biological sciences also) deserves study. Sociology of Science, p. 58. It would appear that this problem has been preempted from further attention until now.

33. Robert McGinnis, "A scholastic model of social mobility," American Sociological Review 33 (October 1968) 712-722. The axiom of cumulative inertia holds that the longer an individual resides in a particular location, the greater the probability of his remaining there. For its application in science, Thomas Gieryn, "Generational differences in scientists' research interests," Paper to be presented at the 1977 meeting of the American Sociological Association.
See Joel Yellin, "A Model for Research Problem Allocation Among Members of a Scientific Community," Journal of Mathematical Sociology 2 (1972): 1-36 for a model emphasizing relations between population growth in scientific communities, problem distribution and specialization.

34. See Robert Jervis, Perception and Misperception in International Politics. Princeton: Princeton University Press, 1976. p. 187 ff. for an insightful account of rigidity of perceptual sets in political decision-making. The same observation can be problematic and unproblematic for different investigators at the same time, see Bernard Barber and Renee C Fox, "The Case of the floppy-eared rabbits: An

instance of serendipity gained and serendipity lost," American Journal of Sociology 64 (1958) 128-136. It is surprising that so little systematic work on error in science exists. See Jean Rostand, Error and Deception in Science. Trnsd. A.J. Pomerans. New York: Basic Books, 1960.

35. Bacterial variation (the notion that bacteria were polymorphic) was assumed to be an artifact of contamination after Koch developed a usable procedure for pure cultures. But genetic variation is not the same as uncontrollable variation in experimental results. The latter is generally defined as "noise" rather than phenomena of interest and undermines the validity of observations, as Philip Teitlebaum reminded us. Noise also makes certain problems aversive but for reasons different from those noted here.

36. Labelling theory and studies of the impact of labelling on deviant behavior are now active areas of investigation in sociology. See Edwin Lemert, Human Deviance Social Problems and Social Change. Englewood Cliffs: Prentice-Hall, 1972. Along different lines, Dorwin Cartwright, in reviewing research on the "risky shift" in social psychology, observes that the inept label persists in the face of accumulating evidence that groups choose more rather than less conservative options and that it has substantially delayed reorientation to the problem. "Determinants of scientific progress: The case of research on the Risky Shift," American Psychologist. 28 (March 1[73) 222231. For a contrary view on the impact of labelling this phenomenon, see Franz Samuelson, "Paradigms, Labels, and Historical Analysis," American Psychologist 29 (December 1973) 1141-1143.

37. Merton, Sociology of Science, Ch. 13.

38. This was probably not so for Koch whose zeal to have the pure culture method accepted universally may have led him to greater dogmatism about the absence of bacterial variation than the evidence required.

39. Martinus Beijerinck 1901, Mutation bei Bakterien. Versl. Akad. Wetensch., Amsterdam, 9:310.

40. Beijerinck, Robert Olby writes, brought Mendel's work to de Vries' attention and thus forced de Vries to acknowledge that he had been anticipated by thirty-five years. Origins of Mendelism. New York: Schocken Books, 1966. Pp. 127-128.

41. Joseph Needham, "Limiting factors in the advancement of science as observed in the history of embryology", Yale Journal of Biology and Medicine 9 (1935-36) 1-18.

42. Derek J. de S. Price, "Is technology historically independent of science? A study in statistical historiography, "Technology and Culture 7 (Fall 1965) 553-568.

43. Drawn from S.M. Lipset and EC. Ladd, "Jewish Academics in the United States: Their achievements, culture and politics," American Jewish Yearbook 1971, pp. 89-128, at p. 93.

44. Harriet Zuckerman, Scientific Elite. New York: Free Press, 1977. Ch. 3. This finding no doubt reflects the fact that Jews are most often

found in mobile fields such as molecular biology and theoretical physics, precisely those which most often receive Nobel prizes.

45. Who's Who in America tends to underrepresent the business elite and to overrepresent academic and clergymen. It is not clear whether these biases would lead New Yorkers to appear more frequently in its pages or less. Given municipal crime rates, New Yorkers are also apt to be overrepresented among criminals as well. The sociology of New York and of other great cities is still to be investigated.

46. Ira Risenwaike, Population History of New York City. Syracuse: Syracuse University Press, 1972. P. 188 and U.A. Bureau of the Census, Historical Statistics of the United States. Series A6-8. P. 8, Part I, No. 93-98.

47. This finding is not consistent with data on the educational origins of American scientists which show that New York state colleges produce no more than their share of doctorates in science. R.H. Knapp and H.B. Goodrich, Origins of American Scientists. Chicago: University of Chicago Press, 1952. New York City colleges however may exhibit a different pattern. Taking the City College and Columbia College as two unrepresentative instances, we note that both have produced an excess of doctorates in science relative to the number of their male graduates. City College alumni get 2.3 times as many Ph.Ds. in science as its alumni pool would predict and Columbia College alumni, 1.4 times that number. Calculated from L. Harmon and H. Soldz, Doctorate Production in United States Universities: 1920-1962. Washington, D.C.: National Academy of Sciences-National Research Council, 1963. #1142, Appendix 5 and Knapp and Goodrich, 1952, Appendix 4.

48. In this, the Lederbergs were only slightly atypical of families producing American Nobel laureates in science. Laureates come from families headed by professionals far more often than the run of scientists but this does not mean that they were affluent. The fathers of Nobelists who were professionals were usually professors, teachers and physicians -- comparatively high in prestige and education but not necessarily well-to-do. Zuckerman, Scientific Elite, Chapter 3.

48. Alexander W. Astin, "Undergraduate achievement and institutional 'excellence'," Science 161 (16 August 1968) 661-668 and "Undergraduate institutions and the production of scientists," Science 141 (1963) 334-338. A recent study of collegiate origins of science doctorates shows that institutions active in research in certain fields do not conspicuously "overproduce" baccalaureates who go on in those fileds. But it is clear that the colleges which graduate an excess of science doctorates seem to specialize; their alumni are clumped in certain sciences. Studies of "school effects" are still insufficiently detailed to account for the observed differences. Bruce Cathey, "Science Recruitment Patterns in Baccalaureate Institutions: A Study of Differential Ph.D. productivity by Field," Unpublished Master's Essay. Department of Sociology, Columbia University. January 1977.

50. Francis Ryan and Joshua Lederberg, "Reverse-mutation and adaptation in leucineless Neurospora," Proceedings of the NAtional Academy of Sciences, U.S.A. 32 (June 1946) 163-174.

51. Tatum had weathered his own struggle for recognition at Stanford,

having been labelled a chemist dubiously appropriate for a Biology Department. He left in 1945 during a period of stagnation in the department and the university. This brief sojourn at Yale was of course another item of good fortune for Lederberg. In 1948 Tatum returned as a full professor. Cf {1}. On problems encountered in redefining departmental intellectual commitments and establishing new interdisciplinary departments, see Peter M. Blau, The Organization of Academic Work. New York: John Wiley, 1473. Pp. 189-216.

52. Recent work on social standing and risk-assumption in agriculture is consistent with this general position. J.W. Gartrell, E.A. Wilkening and H.A. Presser, "Curvilinear and linear models relating status and innovative behavior: A reassessment," Rural Sociology 38 (1973) 391-411; D.E. Morrison, "Review of Frank Cancien, 'Change and Uncertainty in a Peasant Economy'", Contemporary Sociology 2 (1973) 262-265. A number of studies now find that social status and willingness to assume risk are linearly related.

53. On the accumulation of advantage in science, see Merton, Sociology of Science, 439-459, Jonathan R. Cole and Stephen Cole, Social Stratification in Science. Chicago: University of Chicago Press, 1973 and Zuckerman, Scientific Elite, Ch. 3.

54. Merton, Sociology of Science, Chs. 14-16.

55. Merton, Sociology of Science, Ch. 13, first published 1942 and Bernard Barber, Science and the Social Order. New York: Free Press, 1952.

56. Warren O. Hagstrom, "Competition in science," American Sociological Review 39 (February 1974) 1-18, at p. 10.

57. James D. Watson, The Double Helix. New York: Atheneum, 1968.

58. Jerry Gaston, Originality and Competition in Science. Chicago: University of Chicago Press, 1973; Hagstrom, "Competition in science"; and Daniel Sullivan, "Competition in bio-medical science: Extent, structure and consequences," Sociology of Education 48 (Spring 1975) 233-241. Experience with anticipation varies across the sciences and with age and recent productivity of individual investigators.

59. Gaston, Originality and Competition, p. 118; Hagstrom, "Competition", p. 9; Sullivan, "Competition in bio-medical science", p. 238. 40. Merton, Sociology of Science, p. 308n. First published 1957. Sullivan, "Competition in bio-medical science," suggests that elite scientists may also be very competitive but his data do not permit him to draw solid conclusions on this. P. 237.

61. See J. Cairns, G. Stent, and J.D. Watson, eds. Phage and the Origins of Molecular Biology. Cold Spring Harbor, N.Y.: Cold Spring Harbor Laboratory of Quantitative Biology, 1966.

62. Merton, Sociology of Science, Chs. 12 and 13. The normative structure in science and its role in scientists' behavior is a matter of dispute and considerable skepticism among some sociologists of science. Critics of the Mertonian formulation include: Barry Barnes, "On the reception of scientific beliefs", in B. Barnes, ed., The

Sociology of Science. Harmondsworth: Penguin, 1971. Pp. 269-291; S. B. Barnes and R.G.A. Dolby, "The scientific ethos: A deviant viewpoint," European Journal of Sociology 11 (1970) 3-25; Michael Mulkay, "Norms and Ideology in Science," Social Science Information 15 (1976) 637-656; Ian Mitroff, The Subjective Side of Science. New York: Elsevier, 1974.

63. A.E. Mirsky and A.W. Pollister, Journal of General Physiology 30 (1946) 117.

64. R.D. Hotchkiss, "Gene, transforming principle and DNA," in Cairns, et al. Phage, pp. 189-200, at p. 189.

65. Studies of the applications of science also treat discovery as a process but from a somewhat different perspective. See J.H. Comroe and R.D. Dripps, "Scientific basis for the support of biomedical science," Science 192 (9 April 1976) 105-111.

66. H. Small and B. Griffith, "The structure of scientific literature: Identifying and graphing specialties," Science Studies 4 (1974) 17-40.

Some afterthoughts on references
add to {33}

See Joel Yellin, "A Model for Research Problem Allocation Among Members of a Scientific Community," Journal of Mathematical Sociology 2 (1972): 1-36 for a model emphasizing relations between population growth in scientific communities, problem distribution and specialization.

Add to {65}

Project Hindsight:

C.W. Sherwin and R.S. Isenson, "First Interim Report on Project Hindsight" Summary, 30 June 1966; revised 13 October 1966, No. AD 642-400, Clearinghouse for Federal Scientific and Technical Information, Springfield, Virginia 22151.
770428 Yellin is redundant at lines 1778-83, 1985-9