Reflections on Scientific Lives

A microbiologist/biochemist surveys the changing scene

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Historical Events in Microbiology(Biochemistry);
current textbook style

Leading textbooks of microbiology are now heavy encyclopedic tomes of ca. 1,000 pages; in an early chapter, only about 25 pages deal with the history of the subject. Typically, some of pioneering researches of several 19th century "giants" (e.g., Pasteur and Koch) are described and later events are summarized in a long table of one-line entries, telegraphic style.

I have compiled part of an "example table" by combining entries from several recent texts (see below). They are given verbatim, except for minor editing to improve the English. In tables of this kind, the name of the investigator is sometimes not included. The first historical observation and depiction of microorganisms is almost always given erroneously. In 1665, Robert Hooke described the microfungus *Mucor*; about eleven years later, Antoni van Leeuwenhoek observed bacteria (see Gest 2004 and 2009: The discovery of microorganisms by Robert Hooke and Antoni van Leeuwenhoek, Fellows of the Royal Society, Notes and Records of the Royal Society vol. 58, pp. 187-201, 2004; Homage to Robert Hooke (1635-1703): New Insights from the Recently Discovered "Hooke Folio." Perspectives in Biology and Medicine 52(3): 392-399, 2009.

A typical textbook table of notable events in microbiological (biochemical) research

1835 A. Bassi discovers that a silkworm disease is caused by a fungus

1881 L. Pasteur developed the first artificial vaccine (vs anthrax)

1885 T. Escherich discovers *Bacterium coli*, a cause of infant diarrhea (later renamed *Escherichia coli*)

1899 M. Beijerinck The concept of a virus is proposed to explain tobacco mosaic disease

1929 A. Fleming discovers penicillin

1937 H. Krebs discovers the tricarboxylic acid cycle

H. Wood working with propionic acid bacteria is the first to discover that heterotrophs utilize CO_2 in metabolism

1944 O. Avery, C. Macleod and M. McCarty DNA is genetic material

1945 Max Delbruck and S. Luria Bacteriophage replication mechanism is elucidated

1946 E. Tatum and J. Lederberg Bacteria transfer DNA by conjugation

1952 J. Lederberg and N. Zinder Bacterial transduction

A. Hershey and M. Chase show that bacteriophages inject DNA into host cells

1953 J. Watson and F. Crick propose the double helix structure for DNA

1964 C. Yanofsky and colleagues demonstrate linear correspondence between a gene segment and a protein sequence

1966 M. Nirenberg, H. G. Khorana and others decipher the DNA genetic code

1969 T. Brock and H. Freeze Isolation of *Thermus aquaticus*, source of Taq DNA polymerase

1973 S. Cohen, A Chang, R. Helling, and H. Boyer Recombinant DNA

1982 S. Prusiner Prions, infectious agents consisting solely of proteins, are discovered

How would a new generation of young scientists learn how these discoveries were made? Who were these investigators? Where did they work? How long did it take for the discovery to be made – one month? one year? ten years?

Two Snapshots in the History of Microbiology

1665

The bubonic plague is raging in London -- more than 7,000 deaths each week. Pharmacist William Boghurst, a heroic helper, explained the disease as follows:

> "Plague or pestilence is a most subtle, peculiar, insinuating, venomous, deleterious exhalation arising from the maturation of the faeces of the earth extracted in the aire by the heat of the sun and difflated from place to place by the winds and most tymes

gradually but sometymes immediately aggressing apt bodyes."

In the same year, Robert Hooke, Fellow of the Royal Society of London, published his great classic *Micrographia,* which contained the first description and drawing of a microorganism, the microfungus *Mucor.* Hooke, a prolific inventor, described *Mucor's* very thin cylindrical and transparent stalks which had "a white knob that grew on the top of each of them." His observations were made with a microscope of his own construction.

1894

Dr. Alexandre Yersin, an officer in the French Medical Colonial Corps, is sent to Hong Kong at the suggestion of Louis Pasteur. A plague epidemic had developed in the city; people were dying by the hundreds. Yersin is instructed to study the outbreak and try to isolate the causative agent. With help from an English priest, he manages to build a small shack to live in, outside, but adjoining, a hospital. The shack contains a small folding bed and a very small makeshift laboratory. Yersin gave a few dollars to two English sailors who were helping to take care of the hospital morgue. With their connivance he got into the morgue for a few minutes and had access to the corpse of a patient who had just died of plague. Yersin punctured the patient's swollen inguinal lymph node (i.e., bubo) with a sterile pipette, ran to his small laboratory and went to work. He wrote in his notebook: June 20, 1894 "The specimen is full of microbes, all looking alike, with rounded ends, staining very poorly (gram negative); this is without question the microbe of plague."

Yersin then examined blood, lymph nodes and other organs of dead rats lying on the streets and found they were full of the same bacilli that he had observed in the people dying of the plague. He named the organism *Bacterium pestis.* It was later renamed *Yersina pestis.*

The historical record shows that explanations of complex biological phenomena usually required the efforts of many scientists over long periods of time. In a number of instances, there were sudden surges of clarification when a lone investigator or a small group performed a crucial experiment, perhaps using a new technique, or reinterpreted known facts in a new way.

What factors predispose to creativity in scientific research? This question is discussed in the philosophical writings of Max Perutz who was awarded a Nobel Prize in Chemistry (1962) for solving the crystal structure of hemoglobin. His pioneering work paved the way for many later researches of proteins important in the metabolism of microorganisms and other forms of life. Perutz's success was based on persistent and very hard work, inspirations, and a web of interactions with other scientists at just the "right times." In his 2003 book (see Further Reading, at end):

"There is little benefit in following scientists' daily grind but much in tracing the unique combinations of theoretical knowledge and manual skills, the web of personal encounters and accidental observations, the experience, temperament, moods and clashes that go into the making of discoveries, even though the crucial leap of the

mind is often impenetrable. There is also something to be said for finding out why others, seemingly just as able, were too blind to grasp what Nature tried to tell them."

Basic vs applied research

Much has been written comparing basic ("pure") research and applied ("industrial") research. Applications of knowledge from microbiology, biochemistry and molecular biology are now especially prominent in biotechnology (i.e., "biotech"). A very large number of biotech companies have been established, ranging from "start-ups" with less than 10 employees to organizations with thousands of scientific personnel. Many graduate students and post-doctoral fellows are now faced with making a career choice—academic science vs biotech. The choice dictates the kind of life style that ensues, and it is a fundamental decision.

According to a recent book by Steven Shapin, the march of modern events has led to an entity he calls "The Scientific Life" (University of Chicago Press, 2008). This refers to a blend of "relative" freedom to do basic research coupled with working on money-making projects. Shapin states that his book deals "very substantially with American industrial scientists, entrepreneurs, venture capitalists, and Organization Men: research managers at electrical and photographic firms, team-playing organic chemists, Southern California investors in high-tech companies, engineering professors, trying to develop and sell intellectual property and to get ahead in their academic careers." He discusses biotech at some length, but apparently forgot to include it in

his list. Shapin's last chapter is an Epilogue titled "The way we live now."

It begins with a photo of a reception at the University of California San Diego on a beautiful April day in 2004. The reception is essentially an outdoor "networking" cocktail party on a deck attached to an architect-designed building. Who is there?

"They are scientists, engineers, and research physicians; high-tech and biotech entrepreneurs; CEO, CSOs, and CTOs of start-up companies; venture capitalists and angel investors; intellectual property lawyers and service providers to the high-tech community; and academic administrators basking in pleasure—both at the perfection of the day, of course, and, especially, at the sight of all of these people assembled on the premises of a major pubic research university. It is a visible sign that the university is fulfilling one of its major acknowledged functions in a late modern economy, building bridges between knowledge making and wealth making, doing the sort of things that make political and business leaders happy."

That says it all, in a nutshell.

A review of Shapin's book by William Deresiewicz appeared in *The Nation*, March 16, 2009 ("Lab Test," pp. 23-28). Following are some excerpts:

> Shapin's narrative begins with the shift from science as a calling to science as a job. . . .Does the profit motive distort and degrade the unpredictable path of scientific discovery? Through the early decades of the twentieth century, the old notions came

under still greater pressure. The allegiance to knowledge for the sake of knowledge and consequent elevation of "pure" over applied research, the principled disdain for self-enrichment and corollary belief in the scientist's moral superiority, the commitment to investigative autonomy and free exploration as essential to the scientific project—all these were challenged by the explosive growth of industrial science. . . .

"By mid-century [20th], the typical scientist was no longer an independent investigator toiling in splendid isolation or an unworldly academic ensconced in an upper floor of the ivory tower but an increasingly well-paid company man working project to project on tasks selected by superiors with the goal of enhancing the bottom line. . . .

"Some scientists, including those with experience in the private sector, deplore what they see as the conformity, hierarchy and materialism of the corporate environment. Others though, are equally disillusioned by academia—not only the burden of teaching duties and the constant scrabble for grant money but the paradoxical fact that universities, having absorbed a great deal of managerial philosophy of late, have created environments that are often more hierarchical, tightly controlled and inimical to intellectual autonomy, especially for the young scientist, than corporations. Still others welcome the integration of the two spheres. . . .

"Does injection of the profit motive into scientific research

distort the kind of questions that get investigated and degrade the quality of the results that get produced? There are strong reasons to believe that it does."

Shapin's book was also reviewed by H. Allen Orr in *The New York Review of Books*, March 26, 2009 (p. 34, "Which Scientist Can You Trust?"). From his review, the essence of the book emerges quite clearly. Much is devoted to the question of whether or not scientists are "priests of nature, endowed with exceptional moral competence, or ordinary people who have acquired esoteric technical knowledge. . . . And to what extent do personal virtues matter in the practice of science."

Another topic: Is, or was, research in industrial companies "more regimented than in academia"? Again, the answer is obvious despite the few examples Shapin gives of companies where a few exceptional senior scientists had free time to pursue their own research interests. To be sure, the present difficulties of young scientists in obtaining research grant funds is a serious problem --"the game of grants" -- but stringent review is certainly a mechanism for filtering out research plans that are not of basic significance or well designed. Some of the examples Shapin cites for *entrepreneurial science* (as contrasted with academia) are almost entirely based on previous basic research in universities, the National Institutes of Health, or independent non-profit institutes. Orr notes: "There can be little doubt that, at least in some areas of science, particularly biology and information technology, entrepreneurial science will grow in size and, possibly, significance."

It is abundantly clear that in contrast to Shapin's perception, research by individuals or small groups in academia in the decades between 1940 and 1990 gave us a Golden Age of Basic Discovery in the biological and medical sciences. . . .general biology, biochemistry, general and medical microbiology, virology, genetics, molecular biology, etc. This led to important advances in medicine, agriculture and public health, and biotechnology, now exploited by commercial companies. To cite only one of numerous examples, the discovery and development of the first antibiotic, penicillin, came from a handful of scientists; one in a hospital research laboratory in London and a small group of investigators at the University of Oxford. But the *basic* advances did not come from industry to a significant extent.

The correct time frame of great strides in understanding major aspects of biology was given by Susan Hockfield, President of the Massachusetts Institute of Technology (*Science*, 27 April, 2009; p. 1147). She refers to "the convergence of the life sciences with the physical sciences and engineering" as follows:

> "The next convergence follows from the elucidation of the structure of DNA in the 1950s and from subsequent fundamental discoveries in molecular and cellular biology. These discoveries created a revolution in the life sciences and drove the development of recombinant DNA technology and the launch of the biotechnology industry. By the mid-1980s, the explosion of data from genomics and proteomics brought about a second revolution, further accelerating life science innovation."

There is no doubt that the contributions of the basic ideas and experimental studies contributed by industry to these revolutions were minor.

Further comments by Orr:

> "Though generally sound, Shapin's discussion is in some ways unsatisfying, For one thing, he draws his main evidence for the role of the personal from the interaction of venture capitalists with entrepreneurs, an interaction that has more to do with investing than with science. . . . Also, Shapin's discussion of industrial science mostly breaks off around the middle of the twentieth century. . . . Is research at Pfizer really shaped by the personal virtues of it scientists?"….While there can be no doubt that the figure of the independent academic scientist has been overly romanticized, when it comes to truly transformational science, it is at least possible that the lone wolf mythology isn't entirely mythological."

<u>What history tells us</u>

Modern biotech originated almost entirely from basic research in academia and nonprofit institutes, from research aimed at explaining the mechanisms of cell (organism) growth and development. A very large number of investigators contributed to the solution of complex questions, using diverse experimental systems. Two outstanding academic scientists merit particular attention in connection with the emergence of biotech, Ernst B. Chain and Joshua Lederberg.

Ernst Chain (1906 – 1979)

In 1928, the microbiologist Alexander Fleming was working at St. Mary's Hospital and Medical School in London. His research centered on ways of killing pathogenic bacteria with antiseptics, and he frequently used *staphylococci* as the test organism. One day, by accident, he noted a strange phenomenon on a discarded Petri dish culture. In a circular zone around a contaminant mold colony, all colonies of *staphylococci* had been destroyed. Evidently, the mold must have secreted a lethal substance of some kind. The mold was later identified as belonging to the genus *Penicillium*, and Fleming named the mysterious secretion penicillin.

Fleming published his observations in 1929, and it is clear that he did not realize the potential value of penicillin for treatment of infectious diseases. Nine years later (1938), the scene shifts to the University of Oxford and Ernst Chain, a refugee from Hitler's Germany. He was a researcher in the Sir William Dunn School of Pathology headed by pathologist Howard Florey. Chain came across Fleming's 1929 report and convinced Florey that research on penicillin would be of interest and scientific value. Chain collected about 200 references on growth inhibitions caused by the action of bacteria, streptomycetes, fungi and yeasts on one another. It was evident that in many cases the growth inhibition was caused by specific metabolites produced by the various microorganisms. In Chain's own words: "However, next to nothing was known about the chemical or biological nature of the inhibitory substances, and it seemed an interesting and rewarding field of exploration."

Chain was determined to isolate and characterize the chemistry of penicillin and this led to an extraordinary effort under difficult conditions in wartime England. The first problem of Chain's small team was to grow *Penicillium* in substantial quantity on agar surfaces. Because limited supplies were available, they had to use an astonishing assortment of sterilized trays, pie dishes, gasoline cans, flat bottles, biscuit tins, and porcelain bedpans. Chain was successful in determining the thiazolidine-beta-lactam structure of penicillin, and was the lead author on the first paper showing the therapeutic effects of purified penicillin on infected rats and mice [E. Chain, H.W. Florey, A.D. Gardner, N.G. Heatley, M.A. Jennings, J. Orr-Ewing and A.G. Sanders: Penicillin as a Chemotherapeutic Agent, *Lancet*, Aug. 24: 226 (1940)].

Fleming, Florey and Chain shared the 1945 Nobel Prize in Physiology and Medicine. Perutz's account of the penicillin story[*Is Science Necessary?* E. Dutton, New York, 1980] notes that "only Fleming made the headlines, and mentions of Florey and Chain appeared in small print. Fleming became a world hero, while the names of Florey and Chain and their colleagues have remained unknown outside the world of science. . . . Fleming spent the remaining ten years of his life collecting twenty-five honorary degrees, twenty-six medals, eighteen prizes, thirteen decorations, the freedom of fifteen cities, and honorary membership in eighty-nine scientific academies and societies. . . . Effusive admirers soon hailed him as the greatest scientific genius of all time, and he became the subject of several "hero-worshiping biographies."

The original strain of *Pencillium notatum* studied by Fleming produced relatively small amounts of penicillin. A related organism, *P. chrysogenum*, isolated in 1951, was more useful; it produced about 60 mg of the antibiotic per liter of growth medium. However, this was still too small a yield to form the basis of an industrial isolation process. Over a number of years, several groups of scientists systematically investigated *P. chrysogenum* with the aim of isolating mutant strains that secreted more of the antibiotic. Strain E-15.1, the "final strain," produced 7000 mg of penicillin per liter, and after other improvements, the yield reached 20,000 mg per liter.

In 1948, Chain left Oxford to organize the International Centre for Chemical Microbiology at the Istituto Superiore di Sanita in Rome. There, he and his colleagues pursued research in a number of fields. A new strong interest was development of industrial-scale fermentation pilot plants as research tools. This continued when Chain moved back to England in 1964 to become head of the Department of Biochemistry at the Imperial College of Science and Technology (London); Chain's activities in Rome and at Imperial College were reviewed in a 1991 article in *Nature* [by his son, B. Chain; vol. 353; pp. 492-494]. The keynote caption of the article is "The discovery of penicillin remains one of the greatest advances in medical science. From the success of the discovery the biotechnology industry became established."

"Influenced by his experiences during the first frustrating attempts at scaling-up penicillin production in the Oxford laboratories using antiquated and inappropriate technologies, Chain was convinced that progress in isolation and characterization of biologically active

substances (not only antibiotics, but vitamins, hormones, growth factors and other biological molecules active at very low concentrations) absolutely required large scale production of biological material. . . .Chain's own career also predisposed him to an interdisciplinary approach to scientific problems. He trained as an organic chemist, turned later to biochemistry, and ultimately became interested in bioengineering. . . .Both in Rome and later in London, Chain's ambitions to work on a scale unprecedented within an academic biochemistry department were fulfilled."

(Sir Ernst) Chain published a detailed history of the penicillin story, from Fleming's observations of penicillin action on the famous Petri dish, to the status of penicillin therapy in 1971 [*Thirty years of penicillin therapy*; Proc. Roy. Soc. London B 179: 293-319]. It is an outstanding paper in the annals of scientific discovery. He notes:

> "I started to work on penicillin in 1938, long before the outbreak of the war. The frequently repeated statement that the work was started as a contribution to the war effort, to find a chemo-therapeutic agent suitable for the treatment of infected war wounds, has no basis. The only reason which motivated me to start the work on penicillin was scientific interest. I very much doubt, in fact, whether I would have been allowed to study this problem at that time in one of the so-called 'mission oriented' practically minded industrial laboratories. The research on penicillin which was started as a problem of purely scientific interest, but had consequences of very great practical importance is a good example of how difficult it is to

demonstrate sharp limits between pure and applied research."

Chain discusses the problems of antibiotic-resistant pathogenic bacteria and reviews the immense efforts expended in searching for new antibiotics of clinical usefulness. There are probably lessons to be learned even today from Chain's comments on the complex relations between academia and industry.

Joshua Lederberg (1925-2008)

During the mid-1940s, Lederberg and I were in graduate school (at different universities) and we met at annual meetings of the American Society for Microbiology. He was already giving spectacular talks and clearly was destined to become an outstanding luminary. A retrospective in *ASBMB Today* (American Society of Biochemistry and Molecular Biology) gives an excellent succinct survey of his academic career (April 2008, p. 15). Part of the retrospective summarizes his famous experiments demonstrating basic features of bacterial genetics, which paved the way for making bacteria and bacteriophages model systems in the development of molecular biology and later, of applications in biotech.

"Lederberg was born in Montclair, New Jersey, in 1925 and was raised in New York City. He enrolled at Columbia University where he met Francis J. Ryan, who introduced him to the red bread mold, *Neurospora*. Lederberg received his bachelor's degree in 1944 and began working toward an M.D. at Columbia University's College of Physicians and Surgeons. Although medical students were not

encouraged to do research, Lederberg continued to do experiments under Ryan's supervision, investigating the genetics of bacteria.

"In 1946, Lederberg took a leave of absence from medical school to carry out experiments on *Escherichia coli* in collaboration with Edward L. Tatum at Yale University. He demonstrated that certain strains of bacteria undergo a sexual stage during which they mate and exchange genes. At the time, scientists believed that bacteria reproduced asexually, so Lederberg's discovery of bacterial recombination was a radical one. He and Tatum were also able to map the *E. coli* chromosome, showing the locations of several of its genes. With Tatum's support Lederberg submitted this research as his doctoral thesis and received his Ph.D. from Yale in 1947.

"Rather than go back to medical school, Lederberg decided to accept the offer of an assistant professorship in genetics at the University of Wisconsin at Madison. There, he continued to study bacterial genetics and produced a steady stream of techniques and results that became the basis of genetic engineering in the 1970s. His most important discoveries at the time were that of transduction, the transfer of genetic fragments from one cell to another by a virus, and of the extra-chromosomal genetic particles called plasmids. . . .

"In 1957, Lederberg helped found and became chairman of a new Department of Medical Genetics at the University of Wisconsin. One year later, he accepted an offer to become the first chairman of the newly established Department of Genetics at Stanford University's School of Medicine. Later that year, he was awarded the 1958 Nobel

Prize in Physiology or Medicine, along with Tatum and George W. Beadle."

A more detailed description of Lederberg's accomplishments by Gerald Weissmann can be found in *The FASEB Journal* 22:3411-3414, 2008 [Science as Oath and Testimony: Joshua Lederberg (1925-2008)].

Lederberg's experimental work was only one aspect of his erudition and wide knowledge of the sciences, medicine, and human affairs. I valued his judgment on controversial questions in microbiology and we maintained a relevant correspondence over many years. We exchanged reprints, and even a partial list of the papers he sent me shows his extraordinary intelligence and knowledge. He was really in a class all by himself.

Titles of some of Lederberg's papers in my file:

Forty years of genetic recombination in bacteria. *Nature* 324: 627-628, 1986

Genetic recombination in bacteria: A discovery account. *Ann. Rev. Genet.* 21: 23-46, 1987

How DENDRAL was conceived and born. In: ACM Conference on the History of Medical Informatics, pp. 5-24. Association for Computing Machinery, N.Y., 1987.

The second century of Louis Pasteur: A global agenda for biomedical research. *Molecular Biology and Infectious Diseases,* Elsevier, Paris, pp. 19-30, 1988.

Pandemic as a natural evolutionary phenomenon. *Social Research* 55: 343-359, 1988.

Ontogeny of the clonal selection theory of antibody formation. Reflections on Darwin and Ehrlich. *Molecular Basis of the Immune Response*, vol 546 of the Annals of the New York Academy of Sciences, pp. 175-187, 1988.

The Gene (H.J. Muller 1947). In: Anecdotal, Historical and Critical Commentaries on Genetics. *Genetics* 129: 313-316, 1991.

The interface of science and medicine. *Mount Sinai J. of Med.* 59: 380-383, 1992.

Bacterial variation since Pasteur / Rummaging in the attic: Antiquarian ideas of transmissible heredity, 1880-1940. *Amer. Soc. Microbiol. News* 58: 261-265, 1992.

What the double helix (1953) has meant for basic biomedical science /A personal commentary. *J. Am. Med. Assoc*. 269: 1981-1985, 1993.

Smaller fleas. . . *ad infinitum*: Therapeutic bacteriophage redux. *Proc. Natl. Acad. Sci*. 93: 3167-3168, 1996. Inscribed: *"I should have recalled your discussion on this in Perspectives 1993." JL.*

Some early stirrings (1950 ff.) of concern about environmental mutagens. *Environ. & Molec. Mutagenesis* 30: 3-10, 1997.

In the 1992 paper in *American Society for Microbiology News*, there is a box, based on an interview with Lederberg. It notes that from 1978 to 1990, he served as President of Rockefeller University. Then, as a University Professor, he continued research in the field of

transcriptional specificities in mutagenesis in bacteria. Some of his remarks are still cogent:

"Even though we've seen some dimming of unblinking support for scientific research, and molecular biology is of course much more crowded, any of my students still has a crack at revolutionary discovery if they will but seize the day," he said.

"Although public scrutiny of scientific research and standards of accountability are more stringent, perhaps more hostile than in the recent past, Lederberg doesn't see a recrudescence of scientific McCarthyism. "Yes, the screws are a little bit tighter, and people are going to look more closely at marginal research, including plagiarism as well as imputed fraud. However, anyone who exercises a modicum of common sense and integrity has no rational basis for being deterred.

"Unfortunately, social vigilance about the integrity of scientific research may create the impression that the discipline is loaded with crooks and predators," Lederberg said. *"We urgently need to dispel the idea that the that the primary motivation of researchers is to beat their competitors. I firmly believe that idealism and the excitement* ***of*** *discovery are necessary parts of science."* (Italics added)

More on history

Lederberg, like Perutz, had a strong interest in the history and sociology of scientific research. He noted that "Missing from most primary literature in science are all but the faintest clues about the social context of discovery—how the scientific community is shaped by its operating norms

and institutions, as well as by its fraternal and intergenerational networks….Biography depicts directly the personal relationships among scientists, their mutual debts, their etiquettes, sometimes their jealousies and transgressions." [see his introduction to *The Excitement and Fascination of Science: Reflections by Eminent Scientists*, Vol.3, Part 1 (Ann. Reviews, Palo Alto, CA (1990). Unusual insights into this aspect of scientific life were provided by bacteriologist Dr. Claude Dolman, who was a professor at the University of British Columbia for many years.

Dolman received his medical education at St. Mary's Hospital Medical School (London), where Alexander Fleming was one of his teachers. During the early 1960s he renounced "the lure of the laboratory and the comforts of home" for 8 months "in order to go around the world gleaning a few bundles of historical straws." He traveled to 4 continents and 15 countries where he interviewed "many scores of distinguished persons." The journey was summarized in his interesting and informative paper "Tidbits of Bacteriological History" [Canad. J. Public Health 53: 269-278, 1962]. Dolman describes an episode of unexpected value when he paid a courtesy call to the widow of William Bulloch, who wrote the most authoritative history of bacteriology up to the 20th century (see Further Reading). She offered him a trunkful of Bulloch's papers, which contained working notes, illustrations and other material relating to his classic book.

A few of Dolman's remarks: "Too many younger scientists nowadays find it tempting to clarify an issue by doing an experiment rather than by first seeking the answer in the literature. Though I found no evidence that our predecessors were on the whole significantly more ascetic, less clay-footed, pleasanter personalities or better world-citizens than their counterparts today, yet still their achievements merit our homage. For they

were heirs to centuries of wishful thinking, of groping speculation, of controversial dogmas, of voices crying in the wilderness; and they dedicated diversities of gifts and dauntless courage to prophesying, unraveling, demonstrating and harnessing for the good of mankind those invisible agents of previously unimagined complexity, to whose mastery most of us owe our survival, and by manipulating which we as a group earn our livelihood . To deny them honour by arguing that if they had not done their work so well others soon enough would have found the way, is to make a mockery of history and a plaything of science."

Dr. Dolman (1906-1994) assembled a large and priceless collection of rare books on many aspects of microbiology and immunology, some dating back to the 16th century. The Dolman Collection is in the I.K. Barber Learning Centre of the Point Grey Campus of the University of British Columbia, Vancouver.

Summing Up

Obviously, there is no such thing as *THE* Scientific Life. We can certainly expect that an increasing variety of "9-to-5" technoscience jobs will develop in the future. Many, perhaps most, of them will not include basic research as it is usually understood. Academic science careers will continue in the usual pattern despite the chronic problems of obtaining financial support for research at the frontiers. I expect that the top universities will manage to preserve older academic traditions, while many others will gradually tailor graduate studies to train technoscientists.

Despite all its problems, academic basic research is still a long way ahead of Shapin's brave new world of technoscience/finance development. Research at the frontiers of basic knowledge is not the real subject of his book, whose title is misleading. *The Technoscience/Financial Vocation* would have been more descriptive. Essentially, it is all about making money from the scientific fruits grown mainly in academia and non-profit institutes. Nowadays, leading science magazines (*Nature, Science*) frequently include special sections about careers in biotech, biopharmaceutical corporations, etc. They discuss the ups and downs of "corporate culture." The business sections of major newspapers routinely publish relevant articles. A long report in the *New York Times* of March 10, 2009 is illustrative—key words and phrases:

Drug investors, losing patience, demand cash from companies; unsuccessful biotech company's quest for the next blockbuster; mega-mergers; second quarter dividends; controversial reverse mergers; "zombies" – companies that lurch from product to product, surviving years or even decades without ever achieving success; tender offers. One searches such reports in vain for news on fundamental research advances.

There are some attempts to modify the typical so-called "entrepreneurial model" in biotech. Genentech has 11,000 employees and about 100 billion dollars in market capitalization and boasts having 120 postdocs (trained in academia) in a "relaxed culture." According to their new executive vice president for "research and early development," Genentech plans to make sure that their scientists

"continue to have time to work on their own projects that aren't translational [i.e., *to products*], that aren't governed in any specific way, and that scientists have time to think and imagine and invent, not just do routine things." Incidentally, the laid back work environment features Friday night keg parties. [See *Science* 324: p. 583 (1 May 2009).

The oasis of academia at Genentech apparently does not include the time-consuming burden of teaching basic subjects to the next generation of scientists. We can expect that sooner or later, Genentech will have to develop a new generation of blockbuster drugs to keep up with the competition (such as from Roche, which has 80,000 employees). At the other end of the spectrum, multitudes of small start-up biotechs are teetering on the brink, praying that someone will buy them out.

Yes, many aspects of "scientific lives" involve gambles and, sometime, sacrifices. You have to decide what drives you and provides the most satisfactions; which, of course, is really not news.

Further Reading

More about the lives and research of eminent scientists can be found in the following:

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