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Evolution of Scientific Research

History tells us that the frontiers of science will change. A review of the past hundred years of physics provides partial guidance as to future research in other natural sciences. Instrumentation and knowledge pioneered by physicists have improved capabilities in other sciences and medicine. A useful indication of the role of physics is provided by the October 1993 issue of Physics Today devoted to a centenary of the Physical Review. From 1893 to about 1960 this journal published most of America's important physics papers. A sudden blossoming of American physics occurred about 1930. Physics Today provides information about names and activities of key scientists of that exciting decade. In the period 1946 to 1960 knowledge underlying much of today's instrumentation and high technology was created.

The centenary articles in Physics Today were prepared by distinguished authors, some of them Nobelists. The topics (briefly treated) include lasers, fiber optics, nuclear magnetic resonance (NMR), semiconductors, superconductors, nanostructures, and medical cyclotrons. Today most of them are of technological and economic consequence while having impact on other sciences. For example, according to Nicolaas Bloembergen:

...The widespread commercial applications of lasers include their use in fiber optic communication systems, surgery and medicine, printing, bar-code readers, recording and playback of compact disks, surveying and alignment instruments, and many techniques for processing materials. Laser processing runs the gamut from sculpting corneas by means of excimer laser pulses to the heat treatment, drilling, cutting and welding of heavy metal parts in the automotive and shipbuilding industries by CO2 lasers with continuous-wave outputs exceeding 10 kilowatts.

...Lasers have revolutionized spectroscopy, and they have given birth to the new field of nonlinear optics. They are used extensively in many scientific disciplines, including chemistry, biology, astrophysics, geophysics and environmental sciences.

...[T]he physicists who did the early work were ...intrigued by basic questions of the interaction of molecules and magnetic spins with microwave and millimeter-wave radiation. Could atoms or molecules be used to generate such radiation, they asked themselves, and would this lead to better spectroscopic resolution?

NMR techniques were originally developed to investigate nuclear properties. But soon it was discovered that the technique was a powerful tool for structural chemistry, biochemistry, and later for medical imaging. A series of improvements in the technology now lead to the belief that nuclear magnetic imaging (NMI) will surpass x-rays for medical diagnostics. George Pake has evaluated the motivation leading to the discovery of NMI:

Magnetic resonance imaging could arise only out of the nondirected research, not focused upon ultimate applications, that gave rise to what we know today as NMR. The key was the series of basic quests to understand the magnetic moments of nuclear spins; to understand how these magnetic moments interact in liquids, crystals and molecules; and to elucidate the structures of molecules of chemical interest. Out of these basic quests came the knowledge that enabled a vision of an imaging technique. Without the basic research, magnetic resonance imaging was unimaginable.

Magnetic resonance imaging is an irrefutable testimonial to the enormous value of basic research.

Initial motivation for research on semiconductors was the possibility of developing a solid-state substitute for the vacuum tube. Encouraging experimental results were obtained in 1947. Achieving practical applications and reliability required tremendous efforts, much of which occurred in the Bell Laboratories. In the development of semiconductor devices, including computers, thousands of solid-state physicists were involved. They worked with engineers, and some became engineers. A residue from the efforts is an electronics industry with annual revenues of hundreds of billions of dollars. Another result is that most scientific instrumentation today includes computers. An enormous reservoir of knowledge of solid-state physics has been accumulated. But the future looks less rosy than the past. The number of corporations supporting semiconductor research has declined steeply, and operations in the remainder have been curtailed. Alan D. Fowler comments that a slowdown in the pace of technological development will inevitably erode the military advantages of the United States. A decrease in the federal support of condensed-matter physicists will have a like effect and in addition slow the ultimate progress of science, technology, and medicine.

Philip H. Abelson
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Mind and Brain

It is ironic in an issue focused on Frontiers in Neuroscience that the editorial introduction by Daniel E. Koshland Jr. (29 Oct., p. 635) does not reflect our current understanding of the relationship between mind and brain. Koshland appears to equate bad parenting and the effects of a poor environment with those of "evil spirits" and suggests that only nonscientists might put these forth as causes in situations of brain malfunction. Is it really possible to be unaware of the rather large literature demonstrating environmental and rearing influences on gene expression and neural development? The false dichotomy that is put forth is perpetuated in the subsequent statement that manic-depressive illness "cannot be successfully treated by counseling or psychiatry," but is responsive to the chemical lithium. Aside from erroneously limiting the profession of psychiatry to the practice of psychotherapy (one wonders who actually prescribes the lithium), the statement discounts the enormous psychological and social costs associated with manic-depressive illness that are not adequately addressed by medication alone. The criticism of social interventions continues in other observations, such as the statement that retraining programs are not likely to help homeless individuals who are mentally ill. It would be interesting to know from what scientific data base this point of view is extracted, as even individuals with profound and documented organic deficits (for example, stroke) may benefit from retraining programs.

Furthermore, what is the evidence for brain disease in the criminal who stabbed the tennis star? Is a world in which individuals are deprived of individual rights as a result of vague diagnoses of brain malfunction really a societal advance? Koshland might review 300 years of English common law before asserting that forensic evaluations of mental status simply involve brain-damaged criminals being designated as cured by their being "nice to a psychiatrist."

The scientific method requires both an informed knowledge of the data base and openness to the possibility that one is incorrect in one's assumption; Koshland's editorial consists more of dogma and dialectic than of science.

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Response: I have never said, nor do I believe, that counseling or psychiatry are valueless or that environment and bad parenting are without effect on the mind and behavior. I do believe that modern neurobiology has shown that some brain malfunction can be present at birth and that some illnesses, such as manic depression, are far more susceptible to drug therapy than to counseling therapy. There are many psychiatrists who welcome the new knowledge, use it in their practice, and understand its implications and limitations. There are others who resent the new advances and misquote those who see the complexity of nature and nurture. I do not lump all psychiatrists in a single group any more than I lump all homeless in a single group or attribute all brain influences to either nature or nurture.—Daniel E. Koshland Jr.
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science, many are ineducable or irresponsible. I am aware of no support for this proposition.

If the problem of mavericks and quacks could somehow be addressed by a consensus process (2), as Foster et al. suggest, resources might be better directed elsewhere. We ought to ponder, for example, whether the efforts of professional societies might be better focused on developing and testing materials useful for helping judges and juries, or most lawyers for that matter (3), distinguish science from pseudoscience (4, pp. 438 and 441). Indeed, if scientists, physicians, and engineers invested more time and energy in pursuit of deeper scientific literacy in the general population, potential benefits could vastly exceed those contemplated by Foster et al.

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References

3. T. G. Field, ibid., p. 95.

In their Policy Forum about the Supreme Court’s Daubert decision, Foster et al. appear to advocate the use of tests of statistical significance where p < 0.05. They argue that, were a less restrictive criterion to be used, even more spurious positive findings would result. What the authors do not say is that the trade-off for avoiding false-positive error is increased false-negative error. Biostatisticians have recognized that this choice is one that must be made in light of the circumstances and consequences under which a decision is made (1). In the context of toxic substances lawsuits, there are good grounds to attempt to balance the chances of false-positive and false-negative error (2).

Foster et al. correctly observe that epidemiology is far more salient evidence of causation than animal toxicology studies. But their argument that animal studies should not be admitted as evidence ignores the reality that epidemiologic studies exist for only a tiny fraction of the synthetic agents in common use today (3). Extrapolating from animal studies may not be easy, but the case for barring them in court is a weak one (4).

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References

Foster et al. suggest an intuitively appealing method for dealing with scientific evidence. Because scientists are comfortable with the truth-finding mechanism of their own community and agnostic (or skeptical) about the truth-finding capacity of the adversarial system, it follows that they would want courts to rely on peer review, court-appointed experts, professional organizations, and the reports of scientific consensus groups. But it is worth thinking about whether such a reliance of scientists is good for the nation or for science.

Daniel E. Koslidian Jr.'s notes in his editorial of 10 September (p. 1371) that early environmentalists alerted us to pollution problems without the benefit of expert opinion and peer review. If professional consensus had been necessary, the inherent conservatism of science would have delayed action within the legal system at significant social cost. To be effective, law must be structured to deal with problems as they arise, sometimes before full data are available.

Furthermore, the research agendas of scientists are necessarily selective. If courts were largely confined to consulting scientific materials previously investigated and agreed upon by science, scientists would bear a considerable responsibility to orient their research toward every potential social problem. In short, the approach of Foster et al. might require scientists to give up a great deal of the autonomy they now enjoy.

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Transportation Costs

Should the fruits of technology be served up to the inventors, the public, or the government? Vladimir Haensel's analysis of transportation costs (Letters, 8 Oct., p. 163) suggests that the government is the winner. Haensel advocates accepting the concept of total cost of transportation per mile as a guideline for deciding if and how much gasoline tax should be increased to reduce the national debt. This line of reasoning would make a Madison Avenue copy writer proud. The gist of it is that because gasoline is a small percentage (about 10%) of the total cost of automobile transportation, one could increase its cost by a large amount ($0.50 per gallon or about 50%) and only increase the cost of transportation by a small 5%. Somehow the small percentage increase of the larger category is supposed to make the large tax increase of $60 billion more palatable. The illusion is a property of arithmetic, not of transportation costs. I have mixed feelings about this suggestion. Reduction of the national debt by increased taxation may be the best use of taxes, and getting more tax may require new tricks, but increasing taxes is not the only way to reduce the debt. The main problem with the scheme is that it provides a model that can be generalized to other categories, such as housing or food or indeed anything else. Gasoline seems like a good choice now because increased engine efficiencies yield better gas mileage, which slightly mitigates the total transportation cost. But suppose science and technology produce a significant improvement in a component of building construction. One could then argue that the cost of the component improved should be increased by adding a tax. After all, housing cost, the larger category, would be increased only slightly. Now we have a model for placing government rather than the public or the inventor first in line for receiving the benefits of scientific progress.

Legislators and bureaucrats are already quite good at discovering ways to foster that end. Let's not offer a scientific imprimatur in the form of clever math.

I do not dispute Haensel's numbers, but I do question some of his assumptions. While there are drivers who are fortunate enough to have excess disposable income, many people who drive to work (and thus cannot afford to stop driving their cars) would have to give up another necessity were Haensel's proposed gasoline tax to be imposed. Also, in many parts of the United States, drivers must commute long distances, and the burden of the proposed tax would be greater on these drivers than on those who need only go short distances.

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Idolizing Wolves

Daniel E. Koslidian Jr.'s editorial "Making wolves lovable" (30 July, p. 531) leaves some misunderstandings about the wolf that I would...
like to clear up. The wolf is neither vicious nor huggable, dangerous nor lovable. It is merely one more interesting species long persecuted by humans throughout the centuries that requires a place to survive. It is true that a number of "Dr. Noitalls" have chosen the wolf to idolize, but most wolf biologists believe such idolatry is not in the long-term best interests of the species.

Koshland uses Alaska as the hypothetical state into which wolves might be reintroduced. Ironically, Alaska is the only state whose wolves are not on the Federal List of Endangered or Threatened Species. No reintroductions of wolves into Alaska are planned or necessary, and the state has even offered to supply wolves for reintroductions elsewhere. A more accurate example would have been Yellowstone National Park, where wolves were exterminated in the late 1920s and where the majority of the U.S. public favors reestablishment.

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Health Care and Life Expectancy

The observations in Daniel E. Koshland Jr.'s editorial concerning hampering basic research (8 Oct., p. 159) apply equally to the creative pharmaceutical industry. President Clinton's supposed reduction of the cost of medical care reduces a negligible part of the cost at the cost of life expectancy. The increase in life expectancy the last 50 years has been attributable to new medicines. Basic research in the pharmaceutical industry will be hampered by price reductions. The industry will be forced to reduce basic long-range research and, therefore, better medicines for our grandchildren are unlikely to be discovered.

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Corrections and Clarifications

The four pictures of the moon accompanying the review by Ursula B. Marvin of To a Rocky Moon: A Geologist's History of Lunar Exploration by Don E. Wilhelms (9 July, p. 231) should have been in reverse order on the page.
1994 CALENDAR OF EVENTS

Endocrinology

Endocrinology Under 35
Scientific Organization: A. De Bellis (I) • E. Schipani (USA)
Rome, Italy • May 25-27

Paracrine and Autocrine Signals in the Hypothalamic Pituitary Complex
Scientific Organization: L. Martini (I) • D. de Wied (NL) • S.M. McCann (USA)
Stresa, Italy • September 9-10

Endothelins in Endocrinology
Scientific Organization: J. T. Cameron (UK) • M. J. Dunn (USA) • M. Serio (I)
Florence, Italy • October 6-8

Immunology

Differentiation Therapy
Scientific Organization: A. Kimchi (IL) • G.B. Rossi (I) • S. Waxman (USA)
Herzlia, Israel • March 7-10

Cytokines: Basic Principles and Pratical Applications
Scientific Organization: A. K. Abbas (USA) • S. Romagnani (I)
Florence, Italy • March 28-30

Primary Immunodeficiency Diseases
Scientific Organization: F. Aiuti (I) • M. D. Cooper (USA) • F. S. Rosen (USA)
Orvieto, Italy • June 18-21

New Horizons in Gynaecological Malignancies
Scientific Organization: D. Ayalon (IL)
Eilat, Israel • November 16-18

Reproduction

Puberty: Basic and Clinical Aspects
Scientific Organization: C. Bergadà (ARG)
Buenos Aires, Argentina • April 6-8

Male Factor in Human infertility
Scientific Organization: J. Tesarik (F)
Paris, France • April 21-22

Immunocoontraception
Scientific Organization: O. Nilsson (S)
Uppsala, Sweden • June 30 - July 1

Recent Advances In:
Nutritional Aspects of Osteoporosis
Scientific Organization: P. Burckhardt (CH) • R. P. Heaney (USA)
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19. For 24 buried positions that can be occupied by any one of five nonpolar residues, and 32 surface positions that can be occupied by any one of six polar residues, a total of $5^24 \times 6^{32} = 5 \times 10^{41}$ different amino acid sequences are theoretically possible. However, because only 0.1 μmol of DNA was actually synthesized, the total number of sequences in our collection cannot exceed 6 x $10^{14}$, a number 25 orders of magnitude smaller than the number of different amino acid sequences that are theoretically possible. Therefore it is unlikely that any given sequence occurs more than once in our collection.
24. The four proteins were chosen for practical reasons. Cell extracts from 10 candidates were placed in 50 mM sodium acetate buffer (pH 4.0). The proteins in four of these cases remained in solution. These four were thus promising candidates for purification at low pH over cation exchange columns. Mass spectrometry indicated that one of them was not pure after being run on such a column and therefore further characterization was done only on the remaining three. Thus the proteins were not chosen on the basis of stability per se.
27. Escherichia coli cells (strain X90 DE3) were grown in 2xYT broth in the presence of ampicillin (100 μg/ml). When the culture achieved an optical density at 600 nm of between 0.7 and 1.0, the cells were induced by the addition of isopropyl-β-D-thiogalactopyranoside to 100 μg/ml, and growth was continued for 3 hours more. Cells were harvested by centrifugation, washed in a buffer containing 50 mM Tris-HCl (pH 8.0), 200 mM NaCl, and recentrifuged. Cell pellets were then subjected to three cycles of freeze-thawing (by alternating them between a dry ice, ethanol bath for 5 min and a 10°C water bath for 10 min). The pellets were then gently resuspended in ice-cold 0.5 mM MgCl$_2$ and incubated for 1 hour. The cell debris was removed by centrifugation and discarded. The pH of the supernatant was lowered to 4.0 by the addition of sodium acetate buffer at pH 4.0 to a final concentration of 50 mM. Precipitates appeared and were removed by centrifugation and filtration (Acrodisc; pore size, 0.2 μm, Gelman Science). The cleared solution was then separated on an S-Sepharose Fast Flow ion exchange column (Pharmacia) and eluted with a gradient where buffer A was 50 mM sodium acetate, pH 4.0, 0.5 mM EDTA, and buffer B was 50 mM sodium acetate, pH 4.0, 0.5 mM EDTA, 1.0 M NaCl. Peak fractions were pooled, dialyzed into appropriate buffers, and assayed for purity by silver-stained SDS-PAGE, amino acid analysis, and mass spectrometry.
28. Laser desorption mass spectrometry and quantitative amino acid analysis were performed by T. Thannhauser and R. Sherwood at the Cornell Biotechnology Center.
33. S. Kanteke and M. H. Hecht, unpublished data.

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<td>N-Methyl-D-Aspartate Receptor</td>
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<td>Serotonin-3</td>
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the technical processes of production—
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As systematics came to figure ever more
largely, the naturalist gave way to the zool-
ologist, the field to the laboratory. Though
the tradition of the artist-naturalist would
survive for a century and more in popular
natural history, the transition was early
viewed with alarm and some resentment.
For natural history was assumed to have an
"improving social influence" (p. 116), and,
Americans believed (and a hostile world
agreed), it was America's pristine nature
that defined them as a people.

As the professional scientist (rather fas-
tidiously) drew apart from the amateur,
the specialist from the naturalist, the magnifi-
cent plates of an earlier day, whether en-
graved or lithographed, hand-colored or
chromos, gave way to line drawings. The
natural environment, landscape, drama
(the rattlesnake charming Audubon's
mockingbird), the animal entire with a
page to itself, all had begun to disappear
by mid-century. In their place a composite
animal was depicted on a composite page,
anatomy awaiting assembly.

"What then, if anything, distinguished
American zoological illustration as Ameri-
can?" (p. 345)—or, for that matter, distin-
guished American science? (Recall that
among the pioneers of American ornitho-
graphy Wilson, Audubon, and Catesby were
none of them American-born.) Success in
winning European recognition for Ameri-
can scientific achievement rendered the
question irrelevant. Success came through
adoption of British and European styles of
illustration, and adoption of European li-
thographers as well. But how came an
equilibrant society committed to utility
possess science of a quality to win recogni-
tion from the European scientific com-
nunity? That, as this book shows, is a very
interesting question.

Picturing Nature is an impressive book,
though in research and documentation.
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William Stanton
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Books Received


The Cache Memory Book. Jim Handy. Academic, San Diego, CA, 1993. xvi, 269 pp., illus. $44.95.


Cell Surface and Extracellular Glycoconju-


Endosomes and Lyosomes. A Dynamic Rela-
tionship. Brian Storrie and Robert F. Murphy. Eds. JAI, Greenwich, CT, 1993. xiv, 453 pp., illus. $90.25. Advances in Cell and Molecular Biology of Mem-
branes, vol. 1.

Environment and Aquaculture in Developing Countries. R. S. V. Pullin, H. Rosenthal, and J. L. Maclean, Eds. Deutsche Gesellschaft fuer Technische
Zusammenarbeit, Eschborn, Germany, and Interna-
tional Center for Living Aquatic Resource Manage-
ment, Manila, Philippines, 1993. vii, 359 pp., illus.
From a conference, Bellagio, Italy, Sept. 1990.

The Logic of Discovery. A Theory of the Rational-
ity of Scientific Research. Scott A. Kline, Kluwer,
Norwell, MA, 1993. xii, 334 pp. $107 or P70 or Dfl. 175. Synthese Library, vol. 231.

The Mechanics of Brain Lateralization. Vese-


New Concepts in AIDS Pathogenesis. Luc Mont-

New Developments in Lipid-Protein Interac-

Power and Illness. The Failure and Future of Ameri-
can Health Policy. Daniel M. Fox. University of Californ-


### Vignette: A Letter from Nobel

Nowadays, when I have to associate with people, I cannot fail to notice how enormously the lack of social intercourse these last few years has damaged me. . . . I will probably never again in my life recapture my spiritual quietness.

I am not blaming you, my dear sweet little one, for things turning out this way. When all is said and done, it is my own fault, and you cannot be held responsible. Our views of life—on the need for constant mental improvement, on our duties as human beings with a higher education—are so hugely different that we should never even attempt to understand each other in these matters. It is with great pain that I draw the conclusion that my own nobility of soul has withered away and, my head bowed with shame, I am stepping out of the circle of educated persons.

Actually, it is totally senseless for me to write this to you. You will never be able to understand me on a deeper level. . . . You are not capable of grasping that for many years I have sacrificed my time, my reputation, all my associations with the educated world and finally my business—there is for a self-indulgent child who is not even capable of discerning the selflessness of those acts.

Alfred Nobel, letter to Sofie Hess, 5 December 1880, as quoted by
Kenne Fant in Alfred Nobel: A Biography (Arcade)