Essays of an Information Scientist, Vol:8, p.151-159, 1985
Current Contents, #16, p.3-11, April 22, 1985

Current Comments®

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The 1985 NAS Award for Excellence in Scientific Reviewing Goes to Ira Herskowitz for His Reviews of Phage Biology

Number 16 April 22, 1985

Ira Herskowitz, molecular biologist, has been awarded the 1985 National Academy of Sciences (NAS) Award for Excellence in Scientific Reviewing. Editor of the *Journal of Molecular Biology*, and professor in the Department of Biochemistry and Biophysics, University of California, San Francisco, Herskowitz will receive the award at the academy's 122nd annual meeting in Washington, DC, on April 22.

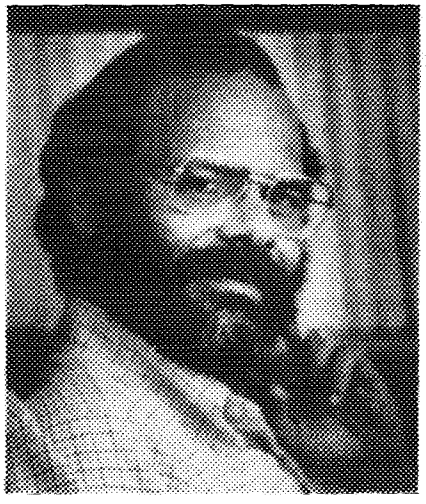
He is the seventh scientist so honored, and, at the age of 39, is the youngest among this group of outstanding authors of scientific reviews. I hope this will encourage other young scientists to write reviews.

ISI® and Annual Reviews Inc. have cosponsored this award and its $5,000 honorarium since its establishment in 1979. The award honors James Murray Luck, who founded *Annual Reviews* and served as its editor-in-chief until his retirement in 1969. Luck remains on the editorial committee of the *Annual Review of Biochemistry*, which he started in 1932, and on the board of directors of Annual Reviews Inc.

The NAS Award recipient is selected by an independent committee appointed by the NAS. Neither ISI nor Annual Reviews is involved in the nomination of candidates or in the selection of the recipient. The discipline from which reviewers are chosen rotates annually among the biological sciences, the physical sciences, including mathematics and engineering, and the social and behavioral sciences. This year, Herskowitz was selected from among a number of outstanding candidates in the biological sciences. The last recipient of the NAS Award for reviews in the biological sciences was Victor McKusick, Johns Hopkins University School of Medicine. He was recognized in 1982 for his reviews of basic and clinical aspects of human genetics.[1]

The NAS cited Herskowitz for his "incisive reviews of phage biology," particularly for his 1973 and 1980 reviews[2,3] of bacteriophage lambda. His most-recent review on lambda has just been published.[4] Bacteriophage lambda is a bacterial virus that has been used extensively by geneticists to study how certain genes are turned on and off in the microorganism *Escherichia coli* (*E. coli*). Unlike most viruses, which invariably replicate themselves within cells and destroy the infected host cell, the bacteriophage lambda does not always kill the *E. coli* cells that it has entered. In fact, under some environmental conditions, infection of *E. coli* with bacteriophage lambda results in a "lysogenic response," in which the host cell survives and stably acquires the genetic material of the bacteriophage.

Herskowitz was cited by the NAS for, among other things, his discussions of gene regulation and cell physiology that govern whether infection with bacteriophage lambda either kills the host cell (the lytic response) or becomes incorporated in the cell's genetic material (the



Ira Herskowitz

lysogenic response). His own research has contributed to the understanding of this lysis-lysogeny decision.

Biographical Information

Born in 1946 in Brooklyn, New York, Herskowitz was raised in the Midwest. His decision to enter the field of genetics is fitting, since he is an identical twin (his brother, Joel, is a pediatric neurologist in Boston) and his father, Irwin H., is a *Drosophila* geneticist and author of a widely used textbook on genetics.[5]

Herskowitz was introduced to bacteriophage genetics at the California Institute of Technology, Pasadena, where he received his BS degree in 1967. He did his doctoral work on bacteriophage lambda with Ethan R. Signer, in the Department of Biology, Massachusetts Institute of Technology (MIT), Cambridge. The 1970 paper[6] based on this research was cited in at least 100 subsequent publications. Herskowitz remained at MIT for postdoctoral work with David Botstein, in the Department of Biology, during which time he also served as an instructor in the same department. During this period, he began to do research on yeast gene expression. Herskowitz explains that his interest in yeast and lambda genes stems from the same "ultimate question.... How do you turn genes on and off? Put another way, what molecular mechanisms are responsible for an undifferentiated cell deciding to become, for example, a liver or brain cell?"[7]

In 1972, Herskowitz joined the Department of Biology and Institute of Molecular Biology at the University of Oregon, Eugene, where he eventually became a full professor. In 1981, he moved to the Department of Biochemistry and Biophysics, University of California, San Francisco, where he is professor and head of the Division of Genetics. In addition to teaching and continuing his research, Herskowitz became vice chairman of his department in 1982.

In 1983, the American Society for Microbiology, the American Association of Immunologists, and the American Society for Experimental Pathology recognized Herskowitz's contributions to lambda and yeast biology by awarding him the 1983 Eli Lilly Award in Microbiology and Immunology. The award, which is accompanied by a $2,000 honorarium, is given annually to a researcher under 35 in the US or Canada for fundamental research in microbiology or immunology.

Herskowitz is currently president of the Genetics Society of America, editor of the *Journal of Molecular Biology*, and associate editor of both the *Annual Review of Genetics* and *Genetics*. He also is on the editorial board of *Molecular and Cellular Biology*. He has also served as associate editor for *Virology*, and has lectured extensively throughout the US, including special lectures at Notre Dame, Wisconsin, Harvard, and Princeton.

Why Write Reviews?

Why does this obviously busy person take on the demanding task of writing scientific reviews? The primary reason is a desire to make bacteriophage lambda understandable to as wide an audience as possible. He explains: "I know that

the areas in which I've written reviews are considered arcane and incomprehensible. So much is known about lambda that unless you're working in it, it's inaccessible. That's where I hope I've been successful—in making it accessible to people."[7]

Like several other winners of the NAS Award, Herskowitz perceives the significance of the relationship between review writing and teaching. In both, he tries to communicate the link between information and ideas. He explains: "A nucleotide sequence or a mutant is just raw data. The important step is to take this information and make logical and critical deductions based on it. I try to stress that in teaching, in individual research projects, and in review articles."[7]

In addition to emphasizing the link between ideas and information, Herskowitz tries, in his reviews, to create what he terms "documents of record...a picture of the state-of-the-field at a given time." He cites as examples of this perspective the "fabulous amount of progress" made and recorded in his reviews between 1973 and 1980. He notes, "There is an obvious progression from one review to the next. The first review said that we know a lot but we still don't know what we want to know about lambda. The second one said that we know a lot more, and now we have a pretty clear idea of what we want to know."[7] Apparently, these reviews have been more than "historical records." The 1973 paper has been his most-cited and perhaps most-influential publication.[2] His 1980 paper[3] has already been cited at least 70 times.

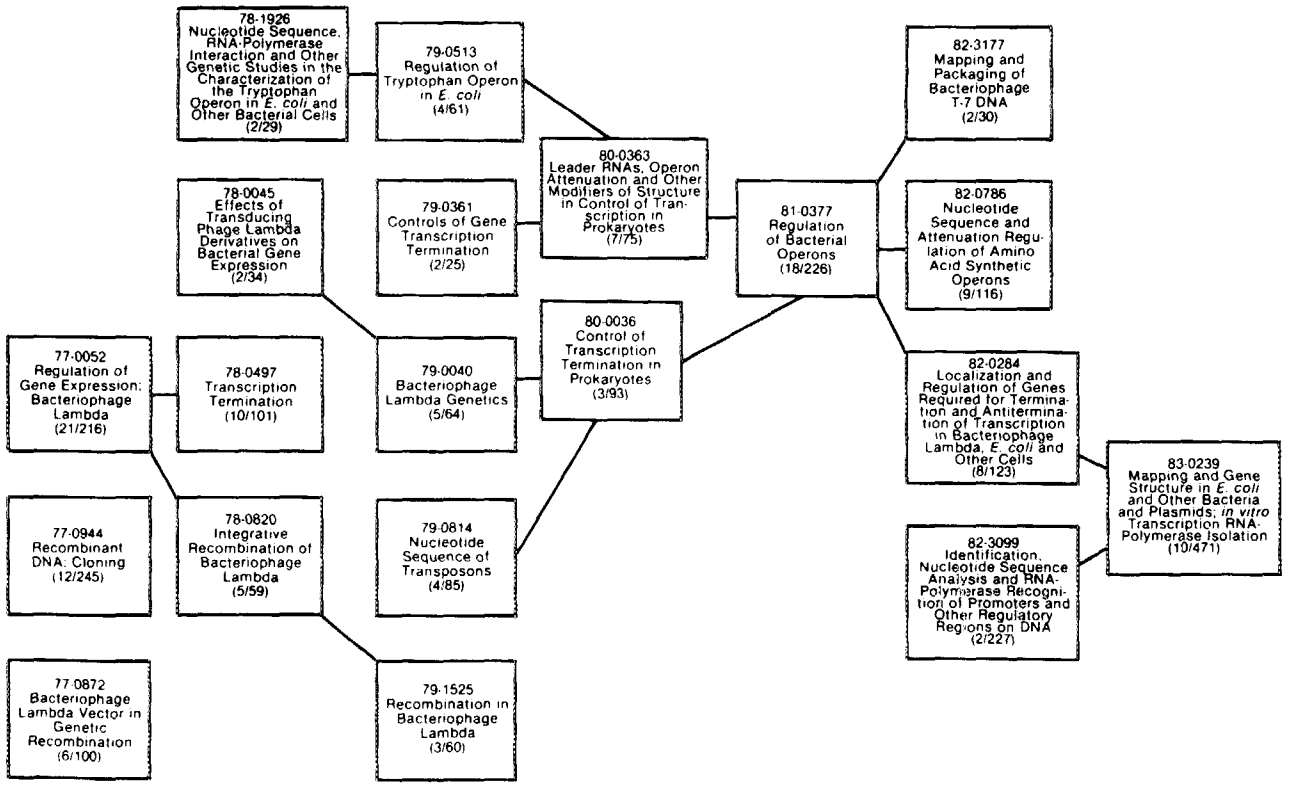
Frank Stahl, who was Herskowitz's colleague in the Department of Biology, University of Oregon, provides another perspective on Herskowitz's talent for reviewing. He describes Herskowitz as "...a walking encyclopedia in the areas in which he works." Stahl notes that "...if I need a review of anything about lambda biology or yeast biology, I have only to telephone him and I will get an authoritative review on the spot."[8] This is a special gatekeeper talent. The informal communication processes of science are often crucial elements in the advances reported formally in the literature.

Research Front Data

Herskowitz has published more than 50 papers since 1970, which together have received more than 1,400 citations. These papers are divided between publications dealing with lambda genetics and publications on yeast genetics. These latter papers deal largely with the mechanism by which yeast cell type is determined. This work centers around studying the regulatory genes coded by a master regulatory locus. Herskowitz and his colleagues have also extensively studied the process by which a cell of one sex will give rise to a cell of the opposite sex, which, in turn, will produce a cell of the same sex as the first cell. They have developed a "cassette" model for this process, which compares the activity of the mating genes in the cell to a tape recorder with interchangeable cassettes. Briefly, they compare the site on the chromosome that regulates the cell's sex with the "playback" function of a tape recorder, and the sex-determining "jumping" genes that occupy that site in alternate generations with interchangeable cassettes.[9] One of Herskowitz's papers describing this model[10] is a core document in research front #82-2456, "Regulation of yeast mating type: transposition, chromatin structure, and control of transcription."

A list of Herskowitz's review papers is included in the references cited at the end of this essay.[2-4,11-13] As mentioned earlier, his most-influential work is the 1973 paper in *Annual Review of Genetics*. The role this review has played in phage lambda research is evidenced from the fact that it is a core paper in two of the ISI research fronts shown in Figure 1. This historiograph, or string of annual research fronts, shows the evolution of phage lambda research from 1977 to 1983. The map actually dates back to 1973, beginning with a front named

Figure 1: Historiograph (cluster string) of gene expression and mapping. Numbers in parentheses represent the number of core/citing papers.



"Bacteriophage lambda mutation." However, we have not reproduced the entire map because it would occupy an inordinate amount of space. We are able to detect the linkages from year to year by identifying the core documents that continue to be co-cited. As research in a particular field diversifies, the research fronts themselves split, merge, or disappear, and new fronts appear. For example, Herskowitz's 1973 review was frequently cited in 1977 by researchers working in an area appropriately named "Regulation of gene expression in bacteriophage lambda." Then the review emerged again as a core paper in research front #82-0284, which we named "Localization and regulation of genes required for termination and antitermination of transcription in bacteriophage lambda, *E. coli* and other cells." The eight core papers that identify this 1982 front are shown in Table 1.

Citation curves for Herskowitz's 1973 and 1980 papers are shown in Figure 2. As you can see from one of the curves, the 1973 review continues to be cited even though it may not meet the two criteria required to be included in the core for each year, that is, citation frequency and co-citation strength. For this reason, it was not included in the 1983 core. Nevertheless, the appropriate 1982 front, #82-0284, mentioned above, was linked to 1983 front #83-0239, "Mapping and gene structure in *E. coli*, other bacteria and plasmids; *in vitro* transcription and RNA-polymerase isolation." To show the relationship of that front to other areas of molecular genetics research, we've also included a higher-level map showing the more general research area "cDNA cloning, gene structure, RNA activity expression and protein structure." The multidimensional scaling map in Figure 3 was created by clustering research fronts, a process I've explained before, to illustrate the relationships between subspecialty areas. Research front #83-0239 is closely related to two other fronts on this map. Two of these, represented by the points, #2825 and #8552, concern genetic studies of DNA sequences and #3810 deals with the interaction of *E. coli* RNA-polymerase with DNA promoters in regulating transcription. For each of these, there is another group of annual core papers, many of which can be observed in the *ISI Atlas of Science: Biotechnology and Molecular Genetics*.[14] To save space on Figure 3, we have omitted four research fronts linked to #5606. They are #3219, #4002, #5673, and #8040.

One of the "reviews" of which Herskowitz is particularly proud is unusual in that it is a poster[13] that pictorially summarizes his 1980 lambda review. Described as "whimsical and informative" in his NAS citation, the poster includes more than a dozen panels describing the function of the lambda gene. Herskowitz says that he created it at the prompting of Stahl, who had originally asked him

Table 1: Core papers in *SCI*® research front #82-0284, "Localization and regulation of genes required for termination and antitermination of transcription in bacteriophage lambda, *E. coli* and other cells."

Adhya S & Gottesman M. Control of transcription termination. *Annu. Rev. Biochem.* 47:967-96, 1978.

Das A, Court D & Adhya S. Isolation and characterization of conditional lethal mutants of *E. coli* defective in transcription termination factor RHO. *Proc. Nat. Acad. Sci. US* 73:1959-63, 1976.

Herskowitz I & Hagen D. The lysis-lysogeny decision of phage λ: explicit programming and responsiveness. *Annu. Rev. Genet.* 14:399-445, 1980.

Platt T. Termination of transcription and its regulation in the tryptophan operon of *E. coli*. *Cell* 24:10-23, 1981.

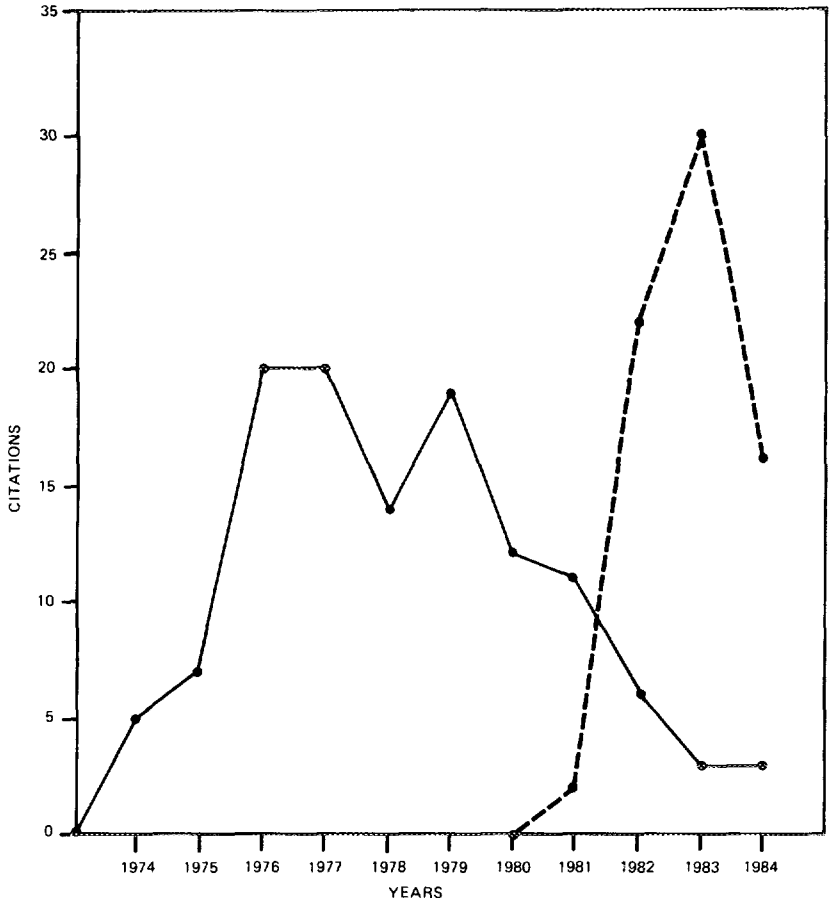
Roberts J W. Termination factor for RNA synthesis. *Nature* 224:1168-74, 1969.

Rosenberg M, Court D, Shimatake H, Brady C & Wulff D L. Relationship between function and DNA sequence in an intercistronic regulatory region in phage-λ. *Nature* 272:414-23, 1978.

Salstrom J S & Szybalski W. Coliphage λ*nut*L-: a unique class of mutants defective in the site of gene *N* product utilization for antitermination of leftward transcription. *J. Mol. Biol.* 124:195-221, 1978.

Shimatake H & Rosenberg M. Purified λ-regulatory protein cII positively activates promoters for lysogenic development. *Nature* 292:128-32, 1981.

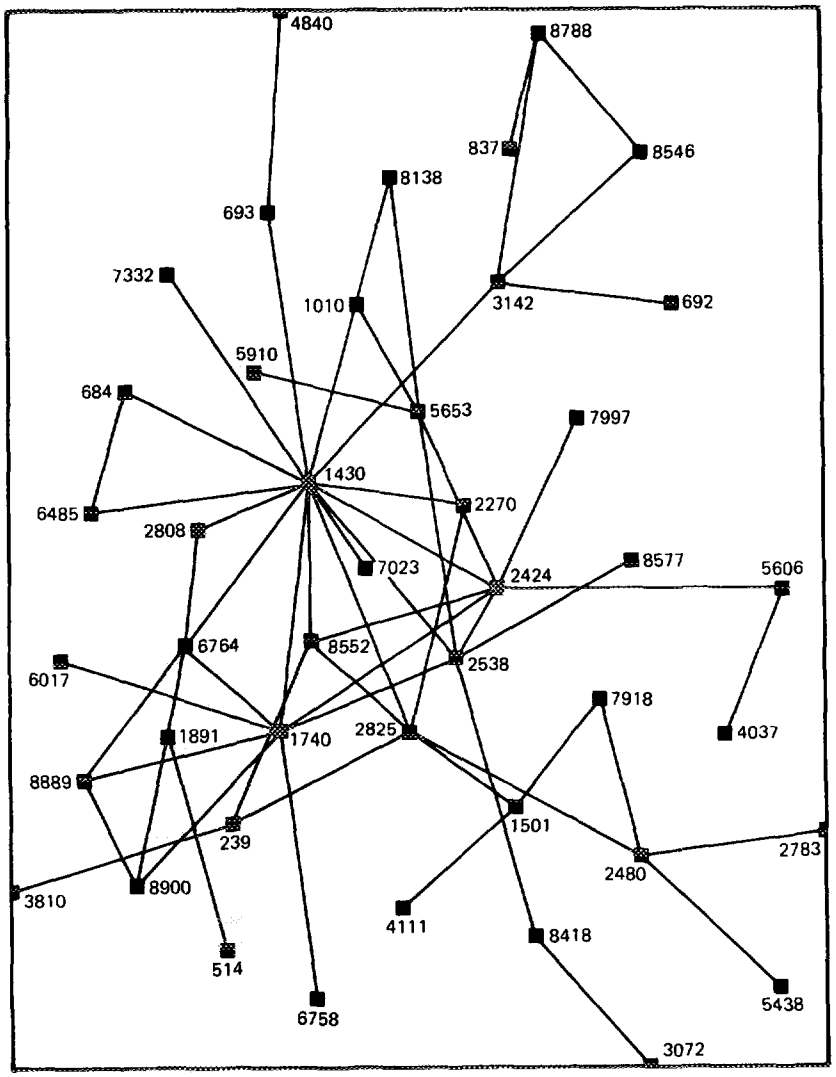
Figure 2: Chronologic distribution of citations to Herskowitz's 1973 (solid line) and 1980 (dotted line) papers in *Annual Review of Genetics*.



to write a review of bacteriophage lambda for the Cold Spring Harbor Laboratory book[15] that now includes the poster. Herskowitz said that in creating the poster, he was trying to "conceptualize and demystify major messages learned from studies of lambda," and hopes that it is useful "for people at all different levels of familiarity with lambda."[7] He adds, "I would like people to stare at each panel of the poster and think about it. I tried to make the poster like lambda itself—further thought leads to deeper insights."[7]

In these essays on the NAS Award for Excellence in Scientific Reviewing, the award recipients have offered a variety of explanations for their decisions to write scientific reviews. John S. Chipman, professor of economics, University of Minnesota, Minneapolis, who won the award in 1981,[16] took special satisfaction in combining the synthesis of information with original thought in his reviews. The 1983 recipient, Michael Ellis Fisher, Horace White professor of chemistry, physics, and mathematics, Cornell University, Ithaca, New York, found that writing reviews contributed to his own research by helping him "rethink current understanding and insight."[17] Whatever the reason, the im-

Figure 3: Multidimensional scaling map of research fronts on "cDNA cloning, gene structure, RNA activity expression and protein structure." A=1983 research front number. B=research front title. For each named research area there is a group of two or more core documents identified in 1983.



A	B
83-0239	Mapping and gene structure in *E. coli*, other bacteria and plasmids; *in vitro* transcription and RNA-polymerase isolation
83-0514	Synthesis, chemical modification and biochemical characterization of histone variants associated with cell differentiation and changes in cell growth
83-0684	Methods of biosynthesis of DNA and cDNA cloning into *E. coli* in the production of human insulin
83-0692	Immunochemical identification of proteins after transfer blotting; characterization of DNA binding proteins
83-0693	Gene sequences and isolation of cDNA clones; characterization and transcription of *messenger* RNA

A	B
83-0837	Applications of high-resolution two-dimensional protein electrophoresis to protein phosphorylation and other chemical modifications
83-1010	Prenatal diagnosis of β-thalassemia by DNA polymorphism; restriction enzyme mapping and structure of globin gene
83-1430	cDNA cloning from messenger RNA in *E. coli* as probes of virus and eukaryote gene and protein structure
83-1501	Gene expression, regulation and cloning in *E. coli* K-12 and its mutants
83-1740	Oncogenes and the genetics of human cancers; viral transforming genes and their DNA structure
83-1891	Role and arrangement of nucleosomes, histones and other proteins in the organization of the nuclear matrix and the structure of the chromatin DNA
83-2270	Isolation, expression, cloning and related studies of *Saccharomyces cerevisiae* and other yeast genes and plasmids
83-2424	Nucleotide sequence of eukaryotic globin genes; characterization by messenger RNA analysis; use of viral gene expression and other *in vitro* models
83-2480	Transposable genes and TN5 insertion in *Drosophila melanogaster* and *E. coli*; evolution of transposon DNA sequences in eukaryotes
83-2538	Gene transcription, expression and sequence including protein structure and RNA activity
83-2783	Transposable gene elements and hybrid dysgenesis in *Drosophila melanogaster*; role in evolution
83-2808	DNA methylation; sequence structure and effect on gene activity
83-2825	Molecular cDNA cloning of genes in *E. coli*; nucleotide sequence and protein structure
83-3072	Transcription of class III transfer RNA genes by RNA-polymerase III in *Xenopus laevis* and other eukaryotes
83-3142	Characterization of proteins via immunochemical and biochemical methods; rapid detection and modifications related to activity
83-3810	Characterization of *E. coli* RNA-polymerase and its interaction with DNA promoters in the regulation of transcription
83-4037	Characterization of gene polymorphism in yeast, *Saccharomyces cerevisiae*; transcriptional and post-transcriptional regulation during development and differentiation in eukaryotes
83-4111	Genetic analysis of gene expression in *E. coli* and yeast by gene fusions; characterization of mutations of promoter regions
83-4840	Characterization of factors affecting messenger RNA synthesis, activity and degradation; gene expression measurement by evaluation of *in vitro* translation products
83-5438	Transposable DNA sequences and satellite DNA in *Drosophila*; role of repetitive elements in evolution
83-5606	Processing of messenger RNA of murine immunoglobulin and histocompatibility genes; cDNA probes to study B cell regulation
83-5653	Nucleotide sequence of human and mouse genes as tools to study evolution; cDNA for β-globin
83-5910	Analysis of mutagenesis and nucleotide sequence of genes of *E. coli*, yeast and other eukaryotes; mutations by frame-shifting, ultraviolet radiation, repeated sequences, hypervariable sites and slipped mispairing
83-6017	DNA sequences, properties and mutants of simian virus-40 and polyoma virus
83-6485	Molecular cloning of human genes; enzymes, fibronectin and histocompatible antigen genes
83-6758	Avian virus oncogene products; characterization of transforming proteins and induction of lymphoma in chickens
83-6764	Gene expression and relation to transformation in mammary tumor viruses, adenoviruses and mouse-human cell hybrids
83-7023	Cloning, isolation, and sequence analysis of cDNA and messenger RNA for genes from humans and other animals
83-7332	Repetitive DNA sequences in the organization of human genomic families
83-7918	Transposons of *E. coli* and *Salmonella typhimurium*; mutagenesis and construction of new gene elements
83-7997	Nucleotide sequence and gene structure of tumor and virus antigens; cap structures of messenger RNA
83-8138	Regulation of human globin genes; endonuclease and structural DNA studies in thalassemia
83-8418	RNA transcription *in vitro*; initiation and expression and characterization of RNA-polymerases
83-8546	Methods of protein purification and characterization using silver-staining and two-dimensional polyacrylamide gel electrophoresis
83-8552	Genetic studies of DNA nucleotide sequences, protein activation, messenger RNA structure and related topics

A	B
83-8577	Transcription of ribosomal RNA genes in *Xenopus laevis* mice and *E. coli*
83-8788	Two-dimensional gel electrophoresis in the characterization of protein synthesis and expression in cells
83-8889	DNA-mediated gene transfer and expression of herpes simplex virus thymidine kinase gene in mammalian cells
83-8900	Expression of genes including the thymidine kinase gene and the stability and inhibition of mammalian cell transformation

portance of critical reviews in making information accessible and meaningful should not be underestimated. It is one of our most valuable intellectual creations in helping to overcome information overload.

Next year's NAS Award will be presented for reviews in the physical sciences. Nominations should be submitted before September 16, 1985, to the Office of the Home Secretary, National Academy of Sciences, 2101 Constitution Avenue, Washington, DC 20418.

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My thanks to Joan Lipinsky Cochran and Amy Stone for their help in the preparation of this essay.

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