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Figure Legend: A photograph of a 1% agarose gel stained with ethidium bromide representing reaction products from PCR amplifications using the GeneAmp™ Kit from Perkin-Elmer Cetus according to manufacturer's instructions. The reactions were conducted with (lanes 1 and 3) and without (lanes 2 and 4) the inclusion of 1 unit of Perfect Match polymerase enhancer. Lanes 1 and 2 represent 100 ng of human genomic DNA amplified with two 26-mer primers separated by 1400 nucleotides. Lanes 3 and 4 represent 100 ng of mouse genomic DNA amplified with two 23-mer primers separated by 550 nucleotides.

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*Patents Pending
†GeneAmp is a trademark of Perkin-Elmer Cetus
COVER  Inspired by Leonardo da Vinci’s “Proportions of the Human Figure According to Vitruvius,” the cover image symbolizes that the creativity of scientists is at the center of technological advances. Scientists’ curiosity about biological processes has often led to discoveries that proved useful for biotechnology. One-half of the figure’s appendages are robot-like, showing that technology is an extension of its creator. The figure holds a flask of microorganisms, an antibody, and oligonucleotide primers, representing some of the tools of biotechnology discussed in this issue; the fistful of dollars signifies the entrepreneurial aspect of biotechnology. See pages 1643 to 1681. [Illustration by Julie Cherry]

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Frontiers in Biotechnology

The line between pure research and practical application has always been difficult to draw. Some like to claim they are doing pure research with no practical purpose in mind. There is an implication that "pure" is not only nobler but also more difficult intellectually than "applied" research. Equally vociferous are those on the applied side who suggest that they labor for the good of mankind, whereas the ivory tower types are simply enjoying themselves. Those demarcations are gone forever, or should be. It is a wise person who can state with certainty what basic research result will never be practical, or what applied research will not lead to new basic insights, or which is intellectually more demanding.

This issue of Science, assembled under the fine editorial supervision of Kelly LaMarco, is devoted to frontiers in biotechnology, and anyone reading through the issue will be fascinated both by the practical ramifications of theoretical studies and the theoretical ramifications of practical studies.

The article by Adams et al. contributes a short cut of immediate practicality and great interest to the understanding of the human genome. By providing expressed sequence tags of complementary DNA, a large number of new genes are being uncovered (particularly in the brain). At the same time, lighthouses are being provided along the chromosomes to guide the way for weary sequencers struggling with foggy restriction maps. In the DNA area, Erlich et al. discuss the polymerase chain reaction, a tool that has become so powerful that focus is being directed at making it more accurate (10⁻⁸ nucleotide mistakes per cycle). This, together with methods to warn on the multiplication of contaminating sequences, has increased the power of the PCR for forensic analyses and research applications.

Intermediary metabolism was declared a dead subject by the conventional wise men some years ago, but modern metabolic engineering has brought it back to life. The metabolic pathways of bacterial factories now operating around the globe can be improved by enhancing copies of a gene at a rate controlling point, adding a gene to remove a poisonous product, or adding several genes to introduce a new pathway into an organism that stops short of the desired product. Bailey points out that this metabolic engineering has already had many practical results and is developing new theory. Stephanopoulos and Fellino are applying recombinant DNA technology to metabolic pathways, concentrating on the problem of branch point control. Among the clever ideas is to insert into the derived organism a similar enzyme, but from a different species, so that it has a different control architecture. This introduces new flexibility and better metabolic characteristics into the old organism.

If Edward Jenner were alive today, he would undoubtedly be delighted at the incredible development of the vaccina virus. Moss traces its history down to its modern reconstructions, in which it serves as a magnificent molecular tour bus designed to carry foreign genes into unsuspecting organisms. These passenger genes can in some cases be important tools for scientific research, and in other cases the proteins they generate will provide immunity against infection. As a vehicle for research, the recombinant vaccina vector has already established itself, and as a vehicle for producing live vaccine, it needs improvement, but is rapidly approaching practicality for such dread diseases as rabies, rinderpest in cattle, and AIDS. Immunity can be approached as Waldmann does in discussing the use of monoclonal antibodies in diagnosis and therapy. At one extreme is the monoclonal antibody OKT3, which has been approved by the Food and Drug Administration for treatment of acute renal allograft rejection. It is far from a perfect application, but is the only example so far of a monoclonal antibody licensed for clinical use. Monoclonal antibodies can also be used to kill bad tissue, such as cancer tissue. The antibody power is enhanced by attachment of a biological poison such as ricin or a physical agent such as an alpha emitter, which can be used to damage tissue adjacent to that with which the antibody interacts.

This selection of a few examples illustrates the enormous power of a combination of basic research and practical application. The increasing power and benefit of these tools makes one wonder how anyone could possibly suggest that all biotechnology be stopped in its tracks, but the power of the methods does raise the legitimate question that caution should be exercised in its application. The authors in this issue are illustrative of the workers in this area, not simply by the power of the methods and alert to minimize their side effects.—Daniel E. Koshland, Jr.
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jected to a governmental risk assessment.

However, agricultural research even with plants or microbes that have been powerfully modified by a variety of traditional genetic techniques, has not been routinely subject to governmental “case by case” evaluation, except for certain plant pests, noxious weeds, or organisms considered to be veterinary vaccines. And when one considers that an individual plant breeder “may introduce into the field 50,000 genotypes per year on average or 2,000,000 in a career” (2, p. 66), and that many of these are transgenic, it is clear that the logic of the ESA’s position is flawed (4).

Simon cites what he considers to be another contradiction between the NAS-NRC reports and the ESA paper, noting the NAS-NRC conclusion that intergeneric organisms present no unique hazards per se and that most engineered organisms are expected to be less fit than their parental organisms. He continues, “Conversely, [the ESA report] predicts that ‘organisms with novel combinations of traits are more likely to play novel ecological roles.’” These statements are not necessarily incompatible. An intergeneric organism may not represent a “novel combination of traits” with respect to ecological, genetic, or even phenotypic factors. Conversely, intragenic genetic changes can confer changes that exert drastic effects. As we emphasized one must consider carefully the function of coding or regulatory elements that have been transferred; less important is the technique used to confer the genetic change or the presumed evolutionary distance between the nucleic acids being recombined.

Simon characterizes our proposal as “too little” and derides it as “self-regulation.” Actually, it provides an algorithm that has unlimited flexibility. Depending on what is judged to be an acceptable regulatory burden on researchers and the government, an appropriate level of scrutiny for certain organisms, and other factors, the mechanism can vary widely—from an extremely stringent scheme with a high proportion of required case-by-case governmental risk assessments to a more laissez-faire one in which there is complete exemption or a requirement only for notification for the majority of experiments. Whatever the choice, the cardinal principles of sound regulation would be met.

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REFERENCES AND NOTES
4. The recent U.S. Kiawah Island International Symposium (November 1990), “Biosafety Results of Field Tests of Genetically Modified Plants and Microorganisms,” at which the results of nearly 150 field trials were described, affirmed at least the short-term predictability of the safety of recombinant DNA-manipulated organisms.

The Trabi: Not a Problem

I would like to make a few comments regarding Michael Balter’s article “Microbes and ‘the Trabi problem’” (News & Comment, 12 Apr., p. 205). I am originally from Poland and have been in the United States for 10 years. While living in Poland I owned a Trabant. I bought it in 1971 for 65,000
zloty, or 1 year's salary for a medical school faculty member. I had to prepay and wait 10 months before it finally was delivered. For ten long years I drove my beloved Trabant around Poland and Eastern Europe. In 1980, I drove it to Norway, where I worked for 3 months as a biochemist in Bergen. I never had the feeling that I was driving a "running gag." Some people in Norway had never seen a Trabant before, but no one invited me to an auto graveyard. I did not think it was the best car in the world, but, given the conditions of life in Poland and other Eastern European countries, it was very economic and convenient.

As inflation was going on, the person to whom I sold the Trabant sold it for 250,000 zloty in 1987. It was 16 years old, plastic, and smoke-belching, but still not a "running gag." Of course, there were endless engine overhauls, new tires, batteries, and so forth, but a plastic body was eternal. I hope that someday "the Trabi problem" can be solved, but in the meantime I would like to correct the impression that no one has ever liked the Trabant. There was a time when we, the owners and the Trabant, had a lot of good times together.

Krystyna Konopka
6304 Shelter Creek Lane,
San Bruno, CA 94066

Journal of Biological Chemistry and Protein Crystallization Papers

In a recent letter (22 Mar., p. 1408), John Tainer stated that the Journal of Biological Chemistry has ceased publishing detailed protein crystallization papers. Tainer further implied that the reason for this was low citation frequency. This is not correct. The journal will be pleased to accept papers that give information on crystallization provided that they also contain sufficient additional information such that the paper, as a whole, makes a substantive contribution to biochemistry. Citation frequency is not a consideration. A summary of journal policy on this matter follows:

The editors of the Journal of Biological Chemistry encourage authors to submit manuscripts reporting new macromolecular structures by x-ray crystallographic methods. Reports of studies at all stages of structure analysis are welcome and will be considered on their own merits and on whether they are thought to further significantly our understanding of biochemistry. However, in general, manuscripts that only describe conditions for crystallization of a macromolecule or the diffraction pattern and space group of the crystals are not thought to contain sufficient information to warrant publication in the journal.

The editors of the Journal of Biological Chemistry hope that this statement corrects any misunderstanding regarding the acceptability of crystallographic manuscripts in the journal.

Herbert Tabor
Editor-In-Chief,
Journal of Biological Chemistry,
9650 Rockville Pike, Bethesda, MD 20814

Antinoise and Energy Expenditure

Every new technology has a cost that is initially overlooked. Active noise control (Research News, 26 Apr., p. 508) reduces noise by destructive interference, "leaving behind nothing but silence." But it should be obvious that the sound energy does not vanish; application of antinoise could result, in some cases, in the expenditure of twice as much energy as the original noise. Some of this energy can go into heat, so it is ironic that one of the first applications of active noise control is to quiet air conditioner ducts.

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21 JUNE 1991 ARTICLES 1681
REFERENCES AND NOTES

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Conformations and Forces in Protein Folding

Barry T. Nall and Ken A. Dill, editors

Protein folding, the self-directed transition from disorganized chains to highly ordered and functional biological structures, is of increasing practical concern for the biotechnology industry and for interpreting DNA sequences. In the biological sciences folding is of major importance in the "self-assembly" process that produces the protein catalysts that facilitate and regulate cellular chemistry. Folding plays a role in such diverse cellular processes as macromolecular transport and assembly, targeting of proteins to intracellular and extracellular locations, and in vivo stability of proteins.

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explain it all in dry scientific terms. Yet a small band of musical acousticians has found this a fascinating problem to tackle.

With the notable exception of the saxophone, most musical instruments are not the result of a single deliberate creative act. Rather, they have very complex parentage, with many (and sometimes inadvertent) inventions along the way contributing to the evolution of the trumpet or the guitar that we play today. The skilled artisans who build these magnificent devices may well look a bit askance at the physicist as a latecomer who generally provides an explanation only after the fact for why the instruments work the way they do. These explanations have so far had only a modest impact on further developments in instrument design, but their effect is likely to increase in the future.

This is because the depth of our understanding has advanced significantly over the last 30 years. Developments in electronic technology have made possible much more accurate and detailed measurements of what actually goes on inside an instrument, and fast Fourier transforms have enabled us to relate this information more effectively to our mathematical models of the vibrational motions. There is now a great deal of solid information beyond the veiled glimpse afforded by the typical textbook for a no-prerequisite course on musical acoustics of the sort that became rather popular in the 1970s.

The time is right for a monograph that can bridge the gap between those nontechnical surveys and a research literature that has grown beyond the easy grasp of any one person. So the present book is most welcome, especially because its authors are two of the leading contributors to that literature (Rossing on percussion and Fletcher on wind instruments) and both are highly regarded for the clarity of their articles. The book will be an indispensable summary (including extensive references) for anyone working in this field, particularly for aspiring researchers, who will find many clues to problems needing further attention. But it will probably find its greatest number of readers among those who specialize elsewhere and simply enjoy feeding their curiosity, especially about the workings of instruments they play themselves.

The book is not designed to be read straight through like a novel. It would recommend that the reader simply browse around in chapters 9 through 21, each of which looks carefully at a particular family of string, wind, or percussion instruments. According to the depth of interest, one may then use the first eight chapters as supplementary reference material. There the basic physics of vibrating objects and sound waves is laid out in a review that will be fully appreciated only by one who has previously studied acoustics at some length but will provide useful insight to other courageous readers as well. This organization makes it possible to concentrate the more mathematical and idealized aspects of the theory in those first chapters so that the discussion of real instruments in later chapters can remain primarily physical. Extensively studied instruments such as the violin and clarinet naturally receive the most detailed treatment. But briefer comments also offer interesting insights into everything else from the zither to the didjeridu—a little fun for everyone!

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Combustion Science


In this book Chomiak provides a remarkably broad and concise description of current knowledge regarding combustion processes. The book opens with a discussion of gas-phase combustion that does not differ greatly from that found in most general treatises on combustion. For the most part, the simplest theories that show reasonable agreement with experiment are presented. Though such results provide a good introduction to the physical phenomena involved, in some cases (the effect of stretch on laminar flamespeed, for example) recent developments that have substantially improved our ability to make quantitative predictions are left out. Turbulent combustion is the author's specialty, and the coverage of this area is both more detailed and more clearly presented than in most works on combustion. The dynamics of the transition from deflagration to detonation are also treated in considerably more detail than is usual, as are three-dimensional effects such as pulsating and spinning detonations.

The second part of the book, on the combustion of condensed-phase fuels (droplets and sprays, coal, and mass burning applications such as forest, fixed-bed, and pool fires) provides a good illustration of the critical role played by radiative heat transfer in many practical applications, a subject that is often treated superficially or ignored altogether. The treatment of combustion within the solid phase, including detonation of explosives, burning of solid propellants, and deflagration-based material synthesis methods, is another area of strength. Discussion of the environmental aspects of combustion includes a summary of the formation mechanisms of the primary flame-generated pollutants. Control strategies are discussed, but I found the treatment somewhat dated, with no mention of such recently developed methods for nitric oxide control as the suppression of NOx emissions by post-flame injection of ammonia (thermal de-NOx) or cyanuric acid (RAPRENOx).

Though most of the book is devoted to flame modeling, the last two chapters discuss the experimental methods used to characterize flame structure and some of the most widespread practical applications of combustion, such as internal combustion and turbine engines and utility boilers. The chapter on methods provides a useful introduction and guide to the literature for the nonspecialist. That on applications focuses on equipment design, featuring recent innovations that have led to improved performance, particularly in the emissions area.

This book should prove to be a popular reference work with scientists and engineers familiar with some aspect or aspects of combustion. It covers the field unusually thoroughly, summarizing and adequately referencing the most useful theoretical approaches and their results in a wide variety of subdisciplines. In those areas where substantially different approaches are available and clear distinctions cannot be made as to which is most useful (as in turbulent flame theory, for example), the alternatives are described and compared. Although numerical models (as opposed to analytical models) are not emphasized, the most useful public domain codes are usually mentioned and referenced. I found the book to be somewhat less easy to read than others on the subject, but for those who are familiar with one or more aspects of combustion and need to become familiar with another aspect, it would be a good starting point.

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Books Received

Carbon Monoxide Poisoning. K. K. Jain, Green, St. Louis, MO, 1990. x, 177 pp., illus. Paper, $37.50.

