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REFERENCES


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EDITORIAL

A Multipurpose National Laboratory

At a time of turbulence in science policy, it may be useful to consider the activities of some of the major federal organizations conducting research and development (R&D). One of these is the Oak Ridge National Laboratory (ORNL). Many of its programs relate to the development of technologies for efficient production and use of energy. Other projects relate to global competitiveness, climate change, and environmental cleanup.* The ORNL is oriented toward applications. Often projects are carried out by multidisciplinary teams. Basic research is conducted, much of it motivated by efforts to reach practical goals.

The total budget of the ORNL is about $500 million. Funds to support the laboratory come mainly from various divisions of the Department of Energy (DOE). Other federal agencies contribute, especially the Department of Defense. There is a growing involvement by industry. Some individual investigators obtain funds from wherever they can be obtained, including the National Science Foundation and the National Institutes of Health.

Employees of the ORNL number about 5000, of whom 30% have technical degrees, including 900 with the Ph.D. The laboratory is host each year to 30,000 visitors, 4400 of whom spend 2 weeks or more there. These guest scientists and engineers, one-third from industry, constitute a reinforcement of staff by a total of 1500 full-time equivalents and are key elements in technology transfer.

At the ORNL are 10 major user facilities that include a High Temperature Materials Laboratory, a Surface Modification and Characterization Collaborative Research Center, and a Bioprocessing Research Facility. Access to the facilities is possible for qualified investigators from universities, industry, and other laboratories. Permission is granted on the basis of scientific merit, technical feasibility, and the compatibility of the proposed research with the facility’s equipment. Most of the research results are published in the open literature. However, proprietary research can be conducted, and the ORNL now participates in more than 50 cooperative R&D agreements, or CRADAs, which allow industry to work closely with ORNL experts and equipment. Major companies are involved.

The visitors come to obtain knowledge. They are also attracted to the special facilities. For example, research on and development of high-temperature materials have been notably successful, leading to discovery of useful aluminides and tough ceramics. These have good potential for improving the efficiencies of heat engines. Equipment for research is much superior in quantity and quality to that of most universities and companies.

Another example of resources of the ORNL is competence in creating specialized equipment. Capabilities in computation, engineering design, machining, and electronics have enabled it to produce complicated robotic devices. This capability was attractive to the Department of the Army. The ORNL produced for it prototypes of a robotic munitions transferring machine and a robot for detection and disposal of land mines. Robots for discovery and cleanup of hazardous wastes have also been produced.

Diverse R&D projects number in the hundreds. They include high-efficiency heat pumps; insulation research; renewable energy from improved yields of biomass; bioprocessing of waste paper; changing the properties of surfaces by ion bombardment; crystallography using slow neutron beams; portable, highly sensitive analytical devices for contaminant volatile organic chemicals; bioremediation in the rhizosphere; cryopreservation of Drosophila embryos; and mutations in mice induced by radiation and chemicals.

The Oak Ridge reservation on which the ORNL is located was the site of intense uranium-related activities during and after World War II. Production has stopped, but contamination associated with it remains. Cleanup efforts are being conducted at annual costs in the many hundreds of millions of dollars. The ORNL is participating in monitoring and furnishing new technology for the effort.

At the ORNL one encounters a can-do spirit—confidence in ability to make important contributions to the future of this country. There is an undercurrent of apprehension regarding the future of the laboratory. However, one source of optimism is the belief that Secretary O’Leary will foster use of DOE facilities to aid our nation’s economic competitiveness.

Philip H. Abelson

*Detailed information about ORNL can be obtained from Dr. Alvin Trivelpiece, Director, Oak Ridge National Laboratory. Telephone: 615-576-2900.
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B Factory Proposals

I write in response to the article by Faye Flam, "Cornell leads battle of the B factories" (News, 27 Aug., p. 1111).

There are five principal concerns about the proposal by Cornell University. First, synchrotron radiation heating of the vacuum chamber is far beyond anything that has been allowed before in any storage ring anywhere in the world. Second, the superconducting cavities proposed by Cornell are specified to operate at twice the accelerating gradient of any superconducting cavity that has ever been used in an accelerator. Third, the so-called “crab-crossing” technique, which was proposed by Brookhaven and the Stanford Linear Accelerator (SLAC) physicists for use in future linear colliders, has never been tried. Fourth, the manpower resources of Cornell are marginal for the task. Fifth, there is concern about the schedule.

Cornell has estimated that it can construct a B factory for significantly less than can SLAC. However, this estimate may not accurately reflect the true costs associated with the program. In comparing costs, government officials should take into account the total cost of each proposal, including the commissioning and ongoing operational costs associated with bringing the machine up to the performance standards necessary to conduct the scientific work for which it is designed. In determining the site for the B factory, officials should also take into account the long-term interests of the U.S. high energy program. SLAC represents a billion-dollar federal investment that plays, and can continue to play, a central role in development of high energy accelerators. It seems to me unwise to create a new national lab, financed by the Department of Energy, that would require duplicating facilities already in place at SLAC, while simultaneously phasing down the nation’s premiere electron physics lab.

Finally, I disagree with the remark that SLAC “has been teetering near extinction since its last big project, the Stanford Linear Collider, proved a disappointment. . . .” The linear collider has surpassed all the performance goals set for it by this year; the data taken up to now on the linear collider will produce, among other things, a measurement of the Weinberg angle that can be surpassed only by combining 24 separate measurements from CERN; the fixed-target program in 2 months of operation has produced the best measurement of the neutron spin-structure function that exists in the world; and recent proposals for use of our facilities were sufficient in number to commit all of our available running time through 1999, if I had allowed the program committee to commit us so far in advance. This is hardly a program “teetering near extinction.”

Burton Richter
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Stanford, CA 94309

Biology at Caltech


In [the] context of the industrialization and eugenic “cleaning” of the western seaboard Caltech [the California Institute of Technology] became the spearhead of the movement in the West for progress by technology and science.

How fashionable. How politically correct. And what a skewed view of the locus of some of the major scientific advances of our century. Kay’s book is a distortion, and Olby’s review an echo thereof. According to Olby, Kay comes to the conclusion that the existence of these long-term goals [to further the “fundamental aim of social control”] in the Rockefeller Foundation’s program did not amount to a Machiavellian subversion and co-optation of academia. Rather, cultural hegemony was achieved “through the explicit and tacit constitutive processes of consensus formation.”

That is, co-optation was not necessary. They all shared the same goals. How neat.

The essential fallacy of the book and the review is purporting to divine what was in the minds and psyches of Caltech scientists and what motivations underlay their research and guided their choices at three to six decades’ remove. This is social pseudoscience.

To illuminate this fallacy, let us apply the same technique to the minds of Kay and Olby in 1993. What motivates their choice of subject matter and perspective? Might we suppose that these authors live in a dark fear that the social and cultural processes they study minutely are in fact but marginal factors in the human drama—that the (so far) hidden internal processes, the (dare we say it?) genetic factors innate within each human being are much more determinative of their
intelligence, personality, even character than the external circumstances which are social psychology's raison d'être?

Their apprehension is perhaps akin to that of the astronomers who are now startled by the concept that the universe they study may be but a quite minor part of an unobserved whole.

It has long been clear that obvious human physical characteristics such as height or eye color are genetically determined. But as long as the evidence for the genetic basis of the more subtle and distinctive human traits has been limited to nebulous correlations and twin studies, it has never been definitive and convincing. But now with the spectacular progress in our understanding of genetic processes and, in particular, with the promise inherent in the Human Genome Project, of eventual possible elucidation of direct causal linkages between genetic variations and behavioral traits, the antireductionists foresee their universe fading in significance.

How better to slow down or even halt this development of biological understanding than to impugn the motives of those whose research launched the "molecular vision of life" and thus revive the fear of genetic control, of "Brave New World" scenarios?

Could this be? No, we don't really believe these are the motivations of Kay and Olby. But by the same token we do not accept their presumption to divine the motives of the great biologists and chemists of Caltech who, in their elegant pursuit of basic scientific knowledge, established the framework for the extraordinary developments in biology today.

 Might we consider the concept that the officers of the Rockefeller Foundation could have favored the Caltech scientists simply because their proposals were the more insightful and ingenious, their approach the more solid, their vision of biology the more far-reaching? And how right they were! A banal explanation to be sure. But it is nice to know that sometimes philanthropy and insight succeed.

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Response: Sinsheimer and Horowitz describe my review as an "echo" of Kay's distorted view of "some of the major advances of our century." I do not accept that such is the case. The chief aim of my review was to express clearly and succinctly the thesis developed in the book, which I consider sufficiently important to deserve being widely read and discussed. Its deficiencies, which I alluded to, concerned Kay's comparative institutional analysis and the absence of any discussion of the relevance of her interpretation to the international dimensions of molecular biology. The history, in its global extent, shows the important role that social and economic relevance has played in the development of molecular biology, from polymer science and plant virology to chronic lobar pneumonia and blood chemistry. That some of this research has been supported on the grounds of its promise to aid us to "control" or deal with human problems is no surprise. How close such aims lay to "eugenics" in the popular meaning of that term is more difficult to determine.

There are grounds for querying Kay's statements about the continuity of the eugenic goals of the Caltech program, but I believe these stem more from her use of words like "intervene," "social control," and of course "eugenics" in different contexts and with different shades of meaning. There is a world of difference between the old eugenics and "reform eugenics." Nevertheless, I accept her conclusion that the Rockefeller Foundation asked for projects that had relevance to social needs and that it was not prepared to go on supporting science simply for its own sake. The Foundation officers accepted this remit, and scientists were aware of it. I see nothing morally reprehensible in this (1).

Sinsheimer and Horowitz stress the power of the new molecular genetics to conquer aspects of human nature hitherto the preserve of the "antireductionists." Leaving aside their simplistic representation of genetic and environmental determinism, and granted this newfound power, I doubt that within the scientific community, geneticists included, there is a consensus as to what effect molecular genetics will have on our understanding of the determination of human personality traits. However, we may hope that the quality of research on human behavioral genetics will improve (2).

Robert Olby
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References and Notes


2. J. Horgan, Sci. Am. 268, 122 (June 1993)


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2. J. Horgan, Sci. Am. 268, 122 (June 1993)
Genetic Variation in Africa

The demic expansion models outlined by Luigi L. Cavalli-Sforza et al. (Articles, 29 Jan., p. 639) provide a welcome empirical expansion of our understanding of the forms of genic exchange that linked human populations in the past. We originally used theoretical models of genic exchange, balanced against local selection and drift, as the basis for understanding the processes unifying Homo populations over long periods (1), and those of Cavalli-Sforza et al. confirm and extend such concepts. Genic exchange is fundamental to the multiregional evolution hypothesis, and we are not aware of any living workers who see the "parallel" emergence of modern forms that Cavalli-Sforza et al. describe. Far from parallelism, we see human evolution happening everywhere because every area has always been part of the whole.

Cavalli-Sforza et al. assert, however, as have others, that there is greater genetic diversity in Africa, both nuclear and mitochondrial, which they see as evidence for recent modern human origins on that continent. Such assertions may be misleading, as it is our expectation that Africa should have greater genetic diversity, whatever the source of human modernity. We see five reasons for this.

1) Size. Africa is huge, 35 times the size of New Guinea, where it is argued that a third of all human mitochondrial DNA variability is to be found.

2) Environmental diversity. Africa is the only Old World landmass that straddles the Equator, producing two dynamic latitudinal environmental clines. Cavalli-Sforza et al. compare its genetic variation with that of New Guinea without compensating for the fact that Africa spans more than seven times that island's single latitudinal range. Moreover, Africa encompasses an exceptional variety of environments and geographic barriers conducive to genetic drift and relative isolation. Thus its potential for both adaptive and nonadaptive genetic variation is enormous.

3) Time depth. In both currently competing views of our origins, Africa has been occupied longer than any other region. Other things being equal it should have developed greater diversity in its nuclear and mitochondrial genomes.

4) Central place. For much of the Pleistocene, phenotypic skeletal variability in polypopulc Homo was greater at its African center of origin (1, 3). This corresponds to the expectations of central and peripheral population concepts, and we assume the phenotypic variation observed in fossil samples reflects these geographic patterns of genetic variation.
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References

Response: Thorne et al. discuss genetic diversity in Africa and the reasons for it, a subject we only touched upon in our article. We do expect greater diversity in Africa than in the rest of the world because this continent has been occupied by modern humans and their immediate ancestors for a longer time. Thorne et al. give time depth of human occupation as the third of five reasons for this expectation, but give four other reasons, of which the first (size), second (environmental diversity), and fifth (genetic exchange) are unconvincing: Asia tends to come before, or to be comparable with, Africa for these three reasons; comparison with New Guinea is not taken from our article. Reason four (central place) is really another facet of reason three (time depth). The real issue, however, is the relevance of our observations to the multiregional evolution hypothesis, which these authors espouse.

This hypothesis was inspired by claims of regional continuity of cranial morphology, which are, however, far from being accepted unanimously by paleoanthropologists. Several articles in (1) have reexamined them independently, and there is a roughly one-to-one split among “pro” and “con” discussants. A recent, thorough reanalysis (2) uses a new morphological approach, reaching conclusions that disagree with the multiregional hypothesis.

What is the relevance of our observations to this hypothesis? Can one, should one, integrate it with that of demic expansions? This would involve Homo sapiens sapiens expanding from Africa and admixing with descendants of H. erectus or archaic H. sapiens in other parts of the world. The gene frequency data we have presented do not indicate a need to postulate such admixtures; but at the same time, they do not exclude them, as we mentioned in our article and explain in more detail (3). Because of the absence of recombination, mitochondrial DNA data are more informative on this issue and have so far not given evidence in favor of the participation of older local inhabitants in the European, East-Asian, or Oceanian gene pools. One cannot, however, say that this did not happen infrequently (4).

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Corrections and Clarifications
Reference 4 in the article “Demic expansions and human evolution” by L. L. Cavalli-Sforza et al. (29 Jan., p. 639) was incorrect. It should have read as follows: “F. Weidenreich, Evolution 1, 221 (1947); C. Coon, The Living Races of Man (Knopf, New York, 1965); M. H. Wolpoff, in (2), pp. 62–108.”
There Are Places You Expect To Find Water Hazards. Your Lab Shouldn't Be One Of Them.

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19. The percentage of row 4 and row 6 NBs present in \( \text{wgr}^{114} \) homozygous embryos is as follows: NB 4-1, 0% (\( n = 34 \)); NB 4-2, 20% (\( n = 318 \)); NB 4-3, 0% (\( n = 34 \)); NB 4-4, 3% (\( n = 34 \)); NB 6-1, 4% (\( n = 78 \)); NB 6-2, 0% (\( n = 298 \)); and NB 6-4, 0% (\( n = 78 \)). The percentage of row 6 NBs present in \( \text{wgr}^{114} \) homozygous embryos is as follows: NB 6-1, 9% (\( n = 66 \)); NB 6-2, 0% (\( n = 66 \)); and NB 6-4, 1.5% (\( n = 66 \)).
23. Cuticles from homozygous mutant embryos in (E) and (I) were picked by their non-wild-type cuticle phenotype; cuticles from mutant and wild-type embryos from the experiment shown in line 2 of (A) were indistinguishable, and one is represented in (G). Homozygous \( \text{wgr}^{114} \) embryos scored for the eve+ RP2 were identified by the loss of eve+ dorsal mesoderm cells near the amnioserosa.

24. For each experiment shown in Fig. 3A, the staged embryos were divided into three groups: one-third were fixed at time shift began and one-third were fixed at the time shift concluded (to score the NB pattern); the remaining third were fixed at 14 hours of development (to score for the eve+ RP2 neuron and epidermal segmentation).
25. Supported by the NIH, an NSF Presidential Young Investigator Award, and the Searle Scholars Program. We thank N. Patel and R. Holmgren for comments on the manuscript. Antibodies and fly stocks were provided by R. Holmgren, P. Gergen, R. Nusse, A. Bejsovec, and Y. Hiromi.

10 May 1993; accepted 9 July 1993

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$$\sum_{i=1}^{n} e_i^2 = \sum_{i=1}^{n} (y_i - \hat{y}_i)^2$$

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<th>Ca²⁺/Calmodulin-dependent Protein Kinase II Inhibitor</th>
<th>A Kinase Inhibitors</th>
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<td>H-85</td>
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<tr>
<td>120036</td>
<td>120035</td>
</tr>
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</table>

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<th>DPNT</th>
<th>ARC</th>
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<td>ART-355</td>
<td>Squalene, [1-3H]</td>
<td>50 µCi</td>
<td>575</td>
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</tr>
</tbody>
</table>

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<td>West Coast:</td>
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<td>4560 Horton Street,</td>
<td>172 Mine Lake Ct,</td>
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<tr>
<td>Emeryville, CA 94608</td>
<td>Suite 100,</td>
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<tr>
<td>(800) 733-7025</td>
<td>Raleigh, NC 27615</td>
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<tr>
<td>or (510) 601-3316.</td>
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¹ Anal. Biochem. 179: 37-49

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1994 McKnight Neuroscience Scholars Awards

The McKnight Endowment Fund for Neuroscience is soliciting applications in preparation for awarding McKnight Scholars Awards, which commence July 1, 1994.

The McKnight Scholars Awards were initiated in 1976 to stimulate research in neuroscience especially as it pertains to memory and, ultimately, to a clearer understanding of diseases affecting memory. Over the years this mandate has been interpreted broadly to permit support of work in many relevant areas of neuroscience. The McKnight Endowment Fund for Neuroscience administers its awards through a Board of Directors comprised of eminent scientists and representatives from the Board of Directors of The McKnight Foundation which is the source of the Endowment Fund.

Up to six 1994 McKnight Scholars will be selected from applicants who hold the M.D. and/or Ph.D. degree and have completed formal postdoctoral training. Candidates should have demonstrated meritorious research in areas pertinent to the interests of The McKnight Endowment Fund for Neuroscience and should be in the early stages of establishing their own independent laboratory and research career. Candidates must be citizens or lawful permanent residents of the United States. Award payments will be made directly to a sponsoring institution which must be located within the U.S.

Each McKnight Scholars Award provides $40,000 annually in 1994, 1995 and 1996. Funds may be used in any way that will facilitate development of the Scholar's research program. Funds may not be used for indirect costs.

Applications will be evaluated by a review committee which will recommend to the Board of Directors of the Endowment Fund candidates for appointment. Award announcements will be made on or before May 15, 1994.

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(Left) Scanning electron micrograph of two human fibrosarcoma cells (HT-1080 cells), having digested the MATRIGEL Matrix occluding the membrane pore, migrating through an 8 micron pore in the chamber membrane.

(Inset) Micrograph of cell with numerous processes on the underside of the filter following its invasion of the matrix.

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Their successful quest has helped lift the cloud of depression for millions.

Three scientists who spearheaded the search by Eli Lilly and Company for a safe and effective antidepressant drug that ultimately led to the discovery of Prozac®, have been selected to receive the 1993 Discoverers Award. The annual award honors the outstanding contributions of scientists from America's pharmaceutical research companies.

Each year, more than 12 million Americans are clinically depressed, often undergoing overwhelming feelings of melancholy, hopelessness and despair. For up to 15% of its victims, clinical depression causes them to take their own lives.

Medical researchers have long suspected depression to be caused, in part, by an imbalance of natural brain chemicals called neurotransmitters. Although there are antidepressant drugs that have effectively treated depression since the 1950's, they block the function of certain other transmitters, causing many undesirable, sometimes dangerous, side effects.

Finding an effective antidepressant drug with improved safety and without unwanted side effects became a mission at Eli Lilly and Company. The search by Drs. Molloy, Wong and Fuller led to the discovery of fluoxetine (Prozac®), a drug that selectively enhances the function of one neurotransmitter, serotonin, without blocking the others.

It was the first of a revolutionary new class of antidepressants that has helped millions of people throughout the world, and in 1990 was featured on the cover of Newsweek as a "breakthrough drug for depression." Today, Prozac® is the world's largest selling antidepressant, having been used by over 10 million people.

While these men are being recognized in a special way, their contributions are representative of the efforts of thousands of scientists who continue the search for new medicines that can bring us longer, better lives.

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