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RESEARCH ARTICLE

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EDIToRIAL

Degrees of Uncertainty

According to the dictionary, a doctor of philosophy is a person skilled in, and therefore entitled to speak authoritatively on, any branch of knowledge; an eminently learned person. Also, it is the highest degree conferred on successful scholars in any of the fields of natural science by a university. And the Latin root of "doctor" implies the role of a teacher. But there is nothing in any of these statements to place the Ph.D. awardee in the real world of employers and career paths. A recent report (see Science, 21 April, page 358) from the National Academy of Science's Committee on Science, Engineering, and Public Policy (COSEPUP) entitled "Reshaping the Graduate Education of Scientists and Engineers" focuses on concerns about the ultimate employability of our Ph.D.'s, and what COSEPUP recommends may well provoke debate in the scientific community.

The report observes that the three main sites of employment for Ph.D. scientists and engineers (academia, industry, and government) are all experiencing constraints on growth and an increased need to respond rapidly to new competitive challenges. COSEPUP acknowledges that the principal role of graduate training in the United States is to produce the academic and research leaders of the future. However, in light of current political realities and perceived pending economic transitions, COSEPUP states that the graduate training enterprise should sustain the "creativity and intellectual vigor needed to address a growing range of social and economic concerns" such as the environment, health, energy, and the provision of products and services for industrial competitiveness. As regards the latter goal, COSEPUP concludes that present-day graduate programs are too narrowly focused and produce scholars with highly specialized (and perhaps unneeded) skills, and that inadequate attention has been devoted to the role of scientific expertise in serving these broader societal needs.

It will scarcely come as a surprise that there are exciting opportunities for scientists to contribute to the solution of current everyday problems. Congress apparently agrees and, despite budget balancing, has protected basic research for now. That advanced training should be a career requirement for preparation to make such contributions is also not a surprise. What is remarkable, at least to this observer, is COSEPUP's implicit acceptance of what seems to be a call for graduate programs that sound like graduate technical colleges and for recruitment of students who have formulated more realistic career expectations. The report admonishes graduate mentors that they have an obligation to inform their students "accurately and explicitly of their career options" and proposes that prospective graduate students be informed by an electronic database of their employment options in specific fields, including access to financial aid, time to degree granting, and job placement rates. Certainly, knowing these characteristics of training programs and job opportunities will be useful to students and faculties, but are these the most important bases for career decisions?

An electronic job exchange listing fluctuations in slots in graduate program Y or consumer demand for posts in field X is an unnerving departure from today's idealized approach to attracting new students to scientific careers. Is this practical reality likely to be well received by graduate trainees, their students, or prospective employers? Is a hard-nosed economic assessment of career paths the way to go? Will the student so recruited be entitled to claims of liability if mentors fail to predict the emergence of an exciting new field? When successful scientists give reasons for their career selections, they cite curiosity, fascination with natural phenomena, Inspiring professors, the zeal for discovery, or chance life experiences, but rarely "earning a living." Will the provision of more facts about the economic realities of even large categories of science and technology make those fields more or less attractive? Do we want our next generation of colleagues to be defined on the basis of what they may be able to earn or on the basis of what they think they can contribute to the solution of the world’s problems, regardless of what the economic predictors were when they opted for more education?

The highest objective of graduate training should be the continuous development of a cadre of well-trained creative scientists who will grow to compete successfully for the funds that allow them to survive and contribute. The idea that they can help solve societal problems in ways other than through independent, investigator-initiated research projects must certainly be a part of their education. However, should we now strive to train generic "flexible" scientists who can move productively across fields as employment demands rise and fall—and what will we lose if we do?
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Letters

Impetus for NSF Policy

In his article about academic facilities Jeffrey Mervis (News & Comment, 17 Mar., p. 1590) writes:

NSF [the National Science Foundation] decreed in 1983 that universities should not use federally funded equipment to become testing labs for private industry, reflecting a fear among academics that tight research budgets might tempt universities to sell their souls to industry.

As NSF's deputy director, I oversaw the development of that “decree.” While it may reflect the suggested fear among academics, that fear did not provide the impetus for the policy. Rather, the impetus was strong concern in the commercial testing laboratory community about what it perceived as unfair competition from federally funded scientists in tax-exempt university laboratories. While the policy did temporarily allay that community's concerns, they still persist and can be expected to emerge again as a serious issue sooner or later. In the present federal environment, it may be sooner rather than later.

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Who Survived the Cretaceous?

Alan Feduccia's concise review of the explosive evolution of birds and mammals from a tiny starting point at the beginning of the Tertiary (Perspective, 3 Feb., p. 637) provokes an ecological question. What animals are most likely to survive a serious nuclear winter? Those whose food in some form does not directly depend on immediate photosynthesis. That is to say, those that eat dormant seeds and insects, those that eat decaying organic matter (especially nongreen plant parts), and those that eat waterfowl. And especially those that are very good at finding small particulate bits of these resources, scattered and dwindling until sunlight again can penetrate the clouds in amounts sufficient for serious vegetation growth.

That is to say, seed- and detritus-eating invertebrates and the invertebrates and small vertebrates that eat them and each other. In the context of Feduccia's scenario, the transitional shorebirds at the bases of the bird radiations are precisely among these morphs, along with insectivores, little marsupials, small rodents, snakes, small lizards, frogs, granivorous birds, small raptors, and lots of arthropods.

Was there an explosive radiation of these birds, as well as other vertebrates, after the upper Cretaceous cleaning of the slate? It would be hard to avoid in the absence of virtually all large terrestrial vertebrates. Just imagine the possibilities of rebuilding the food pyramid with the world reduced to a large number of diverse little beasts.

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Authorship Criteria

The News article “Multiauthor papers on the rise” by Antonio Regalado (7 Apr., p. 25) states that the New England Journal of Medicine recently published an article with 280 authors (1). However, according to our criteria for authorship, the only persons who can legitimately lay claim to authorship on the paper he cited are the seven listed on the title page, not the hundreds of trial participants listed in the appendix. Our policy on authorship is clear. Only those who make substantial contributions to conception and design, or analysis and interpretation of data, who draft the article or revise it critically for important intellectual content, and who give final approval of the version to be published should be considered authors (2). When multi-institutional
studies are submitted to us with more than a dozen names on the title page, we insist that all persons listed there sign a statement that they fulfill all of these criteria. We believe that in every paper, each listed author must be able to take public responsibility for its content.

Jerome P. Kassirer
Editor-in-Chief,
New England Journal of Medicine,
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References

■

EPA and Biotechnology Regulation

The Policy Forum “A need to reinvent biotechnology regulation at the EPA” by Henry I. Miller (16 Dec., p. 1815) gravely misportrays an approach to reviewing biotechnology products of which I am proud.

The contention on which the Policy Forum is based, that the Environmental Protection Agency (EPA) regulates or singles out for special treatment products because they are created using recombinant DNA, is wrong. EPA has had a functioning program addressing biotechnology products under the Federal Insecticide, Fungicide and Rodenticide Act and the Toxic Substances Control Act since 1986 (1). That regulatory program focuses on identifying and minimizing risks to public health and the environment. Early indications are that many biotechnology products provide lower-risk agricultural and industrial approaches. For example, biological pesticides may present lower risks than do older chemical pesticides. In general, EPA wishes to promote development of environmentally safer products and technology. EPA’s accomplishments in the biotechnology area show that it is achieving this goal.

EPA has an established record of bringing a range of biotechnology products through field testing to commercialization while safeguarding public health and the environment. At the same time, EPA’s activities reassure the public concerning biotechnology products.

Readers who would like additional information are referred to documents in the public domain (2) that describe the EPA program.

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References and Notes
2. ibid. 59, 45600 (1 September 1994); ibid., p. 45524 (23 November 1994); ibid., p. 60495; ibid., p. 60519; ibid., p. 60535; ibid., p. 60542; ibid., p. 60545; most of these documents may be accessed through the Internet at gopher.epa.gov, under the rules and regulations (Toxics Program) entries for 1 September 1994 and (Pesticide Program) 23 November 1994. Readers may also contact my office at 202-260-6900 for further information.

■

Reading Disability, Attention-Deficit Hyperactivity Disorder, and the Immune System

The article “Quantitative trait locus for reading disability on chromosome 6” by Lon R. Cardon et al. (14 Oct., p. 276) describes a possible gene for a reading disability, dyslexia, localized to 6p21.3, a region within the human major histocompatibility complex (MHC). This finding accords closely with our observation (1) that

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the quantity of the product of the C4B gene, located in the same general area on chromosome 6, was decreased in the plasma of subjects with attention-deficit hyperactivity disorder (ADHD) or their mothers, or both. This gene codes for one of the complement components that are important in protection against pathogens such as viruses and bacteria.

The relation between reading disability and ADHD is controversial, and great effort has been made to distinguish between the two disorders and their cognitive consequences (2). However, it is possible that the disorders are slightly different manifestations of the same underlying pathophysiological process. The C4B protein also appears to be deficient in some subjects with autism (3), and this deficiency results from the inheritance of a null (no protein produced) allele of the C4B gene (4).

Most of the genes located within the MHC are associated with the immune system and play important roles in regulating normal and autoimmune processes. We and others have found that autism is associated with a number of immune anomalies (5) or autoimmune processes (6), or both. Circumstantial evidence that there is an association of autoimmune diseases with reading disability has also been found (7), but to date few, if any, studies have explored autoimmune processes in ADHD. Some cases of reading disability, ADHD, and autism may share a common susceptibility gene on chromosome 6 that may be related to the immune system. Obviously, other specific genes or environmental processes, or both, are also involved in the development of these disorders.

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References

Response: The possibility of the same gene contributing to reading disability and ADHD is plausible and is consistent with recent results suggesting a common genetic etiology for these two traits. We agree with Warren et al. that some cases of reading disability and ADHD may "share a common susceptibility gene ... that may be related to the immune system."

Although we have not evaluated the specific role of the C4B protein in subjects with reading disorder, several twin studies, including our own, have yielded evidence for a genetic overlap between reading disorder and ADHD (1). At present, it is unknown whether or not the MHC region on chromosome 6 is involved in this overlap.
Amorphous Stability and Trehalose

The feature Frontiers in Materials Science (31 Mar., pp. 1918–1953) focusing on glasses and amorphous materials was informative. The News article by Karen Celia Fox, “Putting proteins under glass” (p. 1922), however, does not specify that the glassy state in Sea Monkeys or brine shrimps and many other such organisms is formed by a particular sugar, the simple disaccharide trehalose (α-D-glucopyranosyl α-D-glucopyranoside) (1). Consistent with this observation, trehalose shows properties superior to those of other sugars in the stabilization of proteins and, in particular, during the long-term or high-temperature storage of dried formulations (2, 3). For example, restriction enzymes dried in trehalose can be stored for months at 70°C with no detectable loss of activity (3). Finally, the efficacy of trehalose probably results from a combination of three properties, namely, the nature of glass formed (the glass transition temperature, T_g, for trehalose is 110°C), water replacement (greater flexibility because of the lack of direct hydrogen bonds between the two rings), and its chemical stability and inertness (4). The latter is a particularly important consideration in the use of glasses for stabilizing protein, as the poorly appreciated reactivity of reducing sugars with proteins, also known as the Maillard reaction, is accelerated both by the removal of water and at low water activities (4, 5).

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Noncoding DNA, Zipf's Law, and Language

Faye Flam (Research News, 25 Nov. 1994, p. 1320) reports that Eugene Stanley and his colleagues (1) have found that Zipf's law (2) applies somewhat better to noncoding than to protein-coding DNA sequences. The article implies that the statistical difference between protein-coding and noncoding DNA sequences is a surprising new discovery and that noncoding DNA resembles some sort of language.

The fact that nucleotide sequences of protein-coding regions have a different statistical structure than those of various kinds of noncoding regions (such as introns or intergenic spacers) has been well known since at least 1981 (3). In fact, many routine methods for discriminating between coding and noncoding DNA regions are based on such differences (4). It is therefore difficult to appreciate the alleged novelty of the findings of Stanley and his colleagues.

Zipf's distribution is not specific to language. Zipf himself said that it is far more general. Diverse examples of log-rank distributions that fit Zipf's law include relative sizes of cities (2, p. 416), income (2, p. 484; 5), number of species per genus (2, p. 231), and number of papers per scientist in a given field of research (2, p. 514; 6). There is no reason to conclude that a general population is a language even if a sample drawn from this population is characterized by Zipf's distribution.

The oligonucleotide frequency distribution in noncoding DNA does not appear to fit Zipf's law any better than does the distribution in coding regions. As may be seen clearly in the figure accompanying Flam's article, both log-rank distributions are similar and both display a nonlinear, rather than a linear, trend. In both cases, only a portion of the range can be approximated by a linear function when the data are plotted on log-log coordinates. A reasonable conclusion is that both coding and noncoding regions fit Zipf's law rather poorly, if at all.

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References

Corrections and Clarifications
In the report "Continent-ocean chemical heterogeneity in the mantle based on seismic tomography" by Alessandro M. Forte et al. (21 Apr., p. 386), note 14 (p. 388) should have included the following sentence at the end: "We note, however, that this classical measure of significance does not take into account the red spectrum of the observed nonhydrostatic geoid, whose harmonic coefficients cannot be properly regarded as a random distribution; therefore, the statistical significance of the measured correlation coefficient is possibly less than 99%."
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43. The Xenopus cDNA clone was restricted at the position corresponding to the 11th amino acid and fused in-frame to the Myc epitope of the pC52 MT vector described in (20). In vitro RNA synthesis was as described (20, 42).

44. Immunohistochemistry was as described in (20).


49. AC explants were dissected at around stage 9 and maintained in 0.5 × MB5 [H. B. Peng, Methods Cell Biol. 36, 659 (1991)]. AC explants showed ectopic N-CAM staining after 36 hours post fertilization.


52. Xhwi coding sequence was obtained with primers based on the published sequence (53). The Xhwi insert was subcloned into pC52 vector (20, 53).


54. E. A. Jones and H. R. Woodland, Cell 44, 345 (1986); Development 107, 785 (1989); J. Lee and H. Weintraub, unpublished data.

55. We performed immunostaining on neuroD injected embryos with an antibody to GFAP (G-A-5, Boehringer Mannheim, No. 814369). Staining (in both wild-type and injected embryos) was only observed in embryos fixed in Dent's solution (47). The staining pattern indicated that no ectopic GFAP-expressing cells were observed on the neuroD injected side and that the staining in the CNS may even be reduced (unpublished data). Since GFAP stains only astrocytes, we cannot rule out the possibility that ectopically expressed neuroD may generate other glial cell types.


57. Although we have seldom noticed ectopic neuron formation in tissues derived from other germ layers, we frequently observed that the numbers of embryos injected with neuroD were poorly formed and deficient in immunostaining against the muscle marker myosin heavy chain protein. It is difficult to interpret these results because neuroD may be titrating endogenous E proteins or id proteins, leading to a non-specific effect. We also performed injections into the vegetal pole of two-cell stage embryos and into the 844 bottom tier of 32-cell stage embryos. Although we observed reproducible morphological effects that is, a bulging mass protruding from the abdomen, we did not see any ectopic N-CAM staining in these embryos except for one case. One embryo showed severely disturbed internal organ development and dispersed but strong N-CAM staining in the abdominal cavity.


63. We thank all members of the Weintraub laboratory for encouragement and valuable discussion; Y. Zhuang who generated ES tumours with an amazing phenotype that contributed to the origin of this project; A. Chen and C. J. Lai for help with animal care; J. Spence, C. McGarner who helped with sequencing; T. Doniach, U. Rutishauser, I. Dawid, A. Ruiz I Altaba, R. Harland, B. Szaro, T. Thor, E. Lund, R. Rupp, E. Jones, A. Ribera, and D. J. Anderson for providing us with markers; R. Ruiz for providing a mouse cDNA library, G. Friedrich, for a mouse genomic library, and C. Kintner, for a xenopus cDNA library; S. Parkhurst, Y. Zhuang, J. Partridge, J. Gogos, A. Chen, M. Horowitz, S. Handel, D. Waring, A. Ruiz I Altaba, C. Kintner, and S. Tapscoft for their critical reading of this manuscript; H.W thanks N. Weintraub, M. Groudine, M. Burger, A. Spence, K. Stelzer, and S. Tapscoft for sight and insight; and J.E.L. thanks S. Parkhurst and J. Angel for constant encouragement. Supported by grants from the NIH and HH-M (H.W.); by MDA and Paul Cohen Named Fellowship (J.E.L.); by NIH fellowship (S.M.H.); by NIH and The Well Foundation Fellowship (D.L.T.).

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Vignettes: Sportstech

Such sports as mountaineering, sailing, skiing, scuba diving as well as traditional bat-and-ball games have all been subject to technological improvement. Whether these advances have added to the pleasure derived from such activities may be doubted and it is also doubtful if they have had any beneficial effects outside the individual sports in question. Sports technology does not seem to be a strategic technology.


Let me... make this modest proposal: an artificial indoor ski area in downtown Los Angeles. What would it look like? You may have seen in a sporting goods store the moving carpets that are mounted like large tilted conveyor belts and allow a skier to ski down the incline so that the skis sliding down and the carpet moving up roughly balance and, to a stationary observer, the skier stays in place. In addition to boots, skis, and poles, the skier is given a pair of goggles (skiers are used to these) where the lens is replaced by two microtelevision screens. The rest of the story tells itself. We play on those screens moving scenes of ski slopes that are coordinated with the varying speed and pitch of the conveyor belt carpet. Everything else is a matter of technological refinement: blowers to simulate the rushing of the wind, a harness to suspend the wayward or crashing skier, and more. And let me briefly extol the virtues of the new kind of skiing, the reduction of gasoline consumption and automobile pollution, the infinite variety of conditions and terrains, the instant, continuous, and wide availability of skiing, and the supreme safety of the sport.


closely identified with the moral character that entitled scientists to that professional autonomy which has allowed systems of peer review to flourish in most walks of scientific life. In the 19th century the annamer or the calculating machine could be seen to pose a threat against this still budding self-sufficiency, because these devices seemed to dislocate mastery over nature and control over the values of precision from the scientist to the manufacturer of instruments.

Why, then, has precision had such a strong impact on Western culture? At the end of the book, Wise addresses this interesting question, and he rightly points to a general tendency to pursue unity, apparent also for example in the centralization of nation states and international commerce. Wise sees scientific conventions, such as standards, as both "agents of unity and products of agreement." This is in fact how scientists at the turn of the century liked to view the matter: international commerce and international science would create unity between nations and ensure peace. But history has corrected that optimistic view. Several essays in this book do in fact emphasize that unity and agreement on standards often emerge only after acrimonious disputes. Therefore, when unity has been achieved someone has lost out; the smooth surface of standardized science also hides the ragged edges of discontent.

Seen Wadhams

Department of History and Philosophy of Science, University of Cambridge, Cambridge CB2 3RH, UK


Books Received


Drug and Alcohol Abuse Reviews, vol. 6.


The Dilemma of the Fetus. Fetal Research, Medical Progress, and Moral Politics. Steven Maynard-Moody. St. Martin's, New York, 1995. xxiv, 235 pp., illus. $32.95 or £33.50.


Tokyo, and VCH, New York, 1995. xii, 284 pp., illus. $100.


Forest Ecosystems. David A. Perry, John Hopkins University, Baltimore, MD, 1995. xxi, 649 pp., illus. $80; paper, $49.95.


Myoblast Transfer. Gene Therapy for Muscular Dystrophy. Peter K. Law, Landes, Georgetown, TX, 1994 (distributor, CRC Press, Boca Raton, FL). xii, 164 pp., illus. $89.95. Medical Intelligence Unit.


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Monthly, ISSN 1355-8382 Volume 1, 1995

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Monthly, ISSN 0961-8368 Volume 4, 1995

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Quarterly, ISSN 0033-5835 Volume 28, 1995

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Monoclonal Antibodies
A new line of monoclonal antibodies (mAbs) reacts with Stat proteins 1, 2, 3, 4, 5, and 6. Stat proteins function both as cytoplasmic signal transducers and activators of transcription. The mAbs can be used in protein immunoblotting and other immunological applications. Transduction Laboratories. Circle 140.

A complete line of anti-human and antimouse Fas/APO-1 (CD95) mAbs have numerous applications in apoptosis research. Fas is a cell surface receptor that can mediate apoptosis, or programmed cell death. Two new mAbs for multidrug resistance research include anti-human LRP, clone LRP-56, which is specific for the LRP protein that is strongly overexpressed in various P-glycoprotein–negative tumor cells, and anti-human P-glycoprotein, MRK16, which is specific to a surface epitope of human P-glycoprotein. The anti-Ash/Grb-2 mAb recognizes an epitope in the N-terminal SH3 domain of human, rat, or mouse Ash/Grb-2, which is believed to play a role in signaling pathways between receptor protein tyrosine kinases and a Ras protein. Kamiya Biomedical. Circle 141.

Mutation Analysis Kit
The MisMatch Detect Point Mutation Screening Kit provides a simple, rapid method for detecting dispersed point mutations in a nonisotopic format. Target regions of at least 500 bases can be efficiently screened in a single step. The whole procedure, including data analysis, can be completed in less than a day. Ambion. Circle 142.

Magnetic Ion Exchangers
MagaCell-DEAE, MagaCell-CM, and MagaCell-PEI are magnetic ion exchangers designed for fast, easy, and efficient separation of proteins, enzymes, and nucleic acid fragments. MagaCell is used in a magnetizable batch separation technique, offering significant advantages over conventional ion exchangers. MagaCell does not require that samples be free of cellular debris or other insoluble matter because it does not incorporate conventional ion exchange columns. Washing and elution steps are easy using a simple magnet. Working gradients can be obtained quickly by changing the buffer composition in a stepwise manner. Cortex Biochem. Circle 143.

Nuclease Decontamination
RNase (ribonuclease) Inhibitor can be used to inhibit the activity of endogenous RNases in reaction mixtures used for complementary DNA synthesis, in vitro transcription, translation, and RNase-free antibody production. It can also enhance long-term stability of RNA samples in storage. Amresco RNase Inhibitor is a 50-kD protein that exhibits potent activity against RNase A-type RNases (including RNase B and C) but does not inhibit RNase T1, RNase H, or RNA polymerase and reverse transcriptase activity.

Newly offered instrumentation, apparatus, and laboratory materials of interest to researchers in all disciplines in academic, industrial, and government organizations are featured in this space. Emphasis is given to purpose, chief characteristics, and availability of products and materials. Endorsement by Science or AAAS is not implied. Additional information may be obtained from the manufacturers or suppliers named by circling the appropriate number on the Readers' Service Card and placing it in a mailbox. Postage is free.

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