SCIENCE

Published by the **American Association for the Advancement of Science (AAAS),** *Science* serves its readers as a forum for the presentation and discussion of important issues related to the advancement of science, including the presentation of minority or conflicting points of view, rather than by publishing only material on which a consensus has been reached. Accordingly, all articles published in *Science*—including editorials, news and comment, and book reviews—are signed and reflect the individual views of the authors and not official points of view adopted by the AAAS or the institutions with which the authors are affiliated.

Membership/Circulation

Director: Michael Spinella
Fulfillment: Marlene Zendell, *Manager*, Gwen Huddle, *Assistant Manager*; Mary Curry, *Member Service Supervisor*; Pat Butler, Helen Williams, Laurie Baker, *Member Service Representatives*
Promotions: Dee Valencia, *Manager*; Hilary Baar, Angela Mumeka, *Coordinators*
Research: Kathleen Markey, *Manager*; Robert Smariga, *Assistant*
Financial Analyst: Jacquelyn Roberts
Administrative Assistant: Nina Araujo de Kobes
***Science* Member Services**
Marion, Ohio: 800-347-6969;
Washington, D.C.: 202-326-6417

Advertising and Finance

Associate Publisher: Beth Rosner
Advertising Sales Manager: Susan A. Meredith
Recruitment Advertising Manager: Janis Crowley
Advertising Business Manager: Deborah Rivera-Wienhold,
Financial: Julie Eastland, *Manager*; Andrew Joyce, *Analyst*
Marketing Manager: Laurie Hallowell
Traffic Manager: Tina Turano
Recruitment: Michele Pearl, *Operations Manager*; Dan Moran, *Traffic Manager*; Debbie Cummings, Millie Muñoz-Cumming, Angela Wheeler, *Sales*
Reprints Manager: Corrine Harris
Permissions Manager: Arlene Ennis
Marketing Associate: Allison Pritchard
Sales Associate: Carol Maddox
Send materials to *Science* Advertising, 1333 H Street, NW, Washington, DC 20005, or FAX 202-682-0816.

ADVERTISING SALES: East Coast/E. Canada: Richard Teeling, 201-904-9774, FAX 201-904-9701 • **Southeast:** Mark Anderson, 305-856-8567, FAX 305-856-1056 • **Midwest:** Donald Holbrook, 708-386-6921, FAX 708-386-6950 • **West Coast/W. Canada:** Neil Boylan, 415-673-9265, FAX 415-673-9267 • **Germany/Switzerland/Austria:** Ric Bessford, World Media Services, Germany; +49-089-39-00-55, FAX +49-089-39-00-15 • **Japan and Far East:** Mashy Yoshikawa, Orient Echo, Inc., Japan; +3 3235-5961, FAX +3 3235-5852 • **UK, Scandinavia, France, Italy, Belgium, The Netherlands:** Andrew Davies, Great Britain; +44-457-838-519, FAX +44-457-838-898
European Recruitment: AnneMarie Vis; +44-223-424-695, FAX +44-223-424-695 • **Other:** For recruitment advertising inquiries contact *Science* Advertising: 202-326-6555; For product advertising inquiries contact 202-326-6544, FAX 202-682-0816.

■

Information for Contributors appears on pages 600-602 of the 31 July 1992 issue. Editorial correspondence, including requests for permission to reprint and reprint orders, should be sent to 1333 H Street, NW, Washington, DC 20005. **Science Telephone:** 202-326-6500, TDD 202-408-7770. London office: 071-435-4291. **Other AAAS Programs:** 202-326-6400.

LETTERS

Tenure for Foreigners in Japan

Alun Anderson's article "Japanese academics bemoan the cost of years of neglect" in the special issue devoted to Science in Japan (23 Oct., p. 564) mentions the small number of foreign faculty members at Japanese national universities (p. 569) but could be somewhat misleading. As I have discussed elsewhere (*1*), the reason Japanese universities have hired only an infinitesimal number of foreign faculty, and in most cases have given them only term appointments (whereas all Japanese citizens, at any level, have tenure), is not "[g]overnment regulations" that "are not exactly welcoming," but rather discriminatory internal regulations adopted by the individual universities. Also the new law was adopted in 1982, not 1987, as the article states.

Fortunately Tokyo University is a notable exception. To my knowledge, I was the first foreign faculty member to be hired with tenure by any Japanese national university (in 1984). Since then I have been running a productive research group in global seismology and have not been treated unequally in any way by the university. The most recent data available indicate that six of the eight foreign faculty members at Tokyo University are tenured. (It would be better, of course, if all were.) Our president, Akito Arima, has forcefully advocated hiring foreign faculty with fully equal terms of employment (*2*). It is regrettable that Kyoto University, Tsukuba University, Osaka University, and many others have refused to follow suit and have adopted discriminatory internal regulations that categorically forbid granting tenure to foreign faculty.

Robert J. Geller
Department of Earth and Planetary Physics, Tokyo University, Tokyo 113, Japan

REFERENCES

1. R. J. Geller, *Nature* **345**, 380 (1990).
2. A. Arima, *Kagaku Asahi* 3 (September 1990).

■

Sequencing and Computer Time

I read with interest the recent correspondence between Geoffrey J. Barton and Steven A. Benner *et al.* (Letters, 18 Sept., p. 1609) about the computer time required to compare each sequence in the current data banks with every other. My name is invoked by Benner *et al.* as an "expert in the field" who believes (or has somehow led others to believe) that exhaustive data bank comparison is "thought to be essentially impossible." In support of this view, a piece of mine in *Nature* is cited (*1*).

I would like to point out that I have never held such a view nor, more important, does my *Nature* piece give any support to the notion. Indeed, it makes no mention of the data bank alignment problem, but deals with a technique to cluster proteins in peptide hyperspace.

I would not normally raise such a matter except that much of my research over the past years has been the complete antithesis of what Benner *et al.* seem to believe. As long ago as 1987 I compared the, then quite small, National Biomedical Research Foundation data bank (4000 sequences) against itself (*2*) [repeating the exercise on a slightly larger version in 1989 (*3*)].

More recently, we aligned the SWISS-PROT data bank (*4*) in order to derive a new amino acid exhange matrix (*5*). We completed this comparison in 1 CPU (central processing unit)–day on a moderate-sized workstation using a conventional Dynamic Programming algorithm [Needleman and Wunsch (*6*) type], compared with the 400 CPU-days taken by Benner and his co-workers (*7*). We achieved this by applying a simple prefilter based on peptide composition to avoid calculating alignments for pairs of sequences that could not possibly be related within the confidence limits we had set. Clearly, a simple heuristic can save a lot of unnecessary computation.

William R. Taylor
National Institute for Medical Research, Medical Research Council, The Ridgeway, Mill Hill, London NW7 1AA, United Kingdom

REFERENCES

1. W. Taylor, *Nature* **353**, 388 (1991).
2. ———, *J Mol. Evol.* **28**, 161 (1988).
3. ———, *Methods Enzymol.* **188**, 456 (1990).
4. A. Bairoch and B. Boeckmann, *Nucleic Acids Res.* **19**, 2247 (1991).
5. D. T. Jones, W. R. Taylor, J. M. Thornton, *Comput. Appl. Biosci.* **8**, 275 (1992).
6. S B. Needleman and C. D Wunsch, *J Mol. Biol.* **48**, 443 (1970)
7. G. H. Gonnet, M. A. Cohen, S. A Benner, *Science* **256**, 1443 (1992).

■

Dividing Up the Neocortex

In a Perspective by Carla J. Shatz (9 Oct., p. 237), my view of the mechanism of cortical parcellation was not accurately represented. The protomap hypothesis suggests that post-

mitotic cells of the telencephalon have intrinsic regional properties that foreshadow prospective cytoarchitectonic areas, but does not exclude the role of extrinsic factors in cortical parcellation. In fact, the article cited by Shatz (*1*) provides the first and, so far, the most dramatic experimental evidence that the border of area 17 can be shifted significantly when the size of geniculocortical input is reduced by prenatal manipulation (*1*, p. 174 and figure 7). More recently, we confirmed this by showing that the size of thalamocortical input is directly proportional to the size of the cortex (*2*). Thus, a cortical protomap provides developmental constraints on the outcome of the interplay between cortical cells and their input from extracortical sources. The prefix "proto" in the term "protomap" was introduced to emphasize the primordial, malleable character of the developing cortex. I should not be associated with a strict determination of neural connections, as the phenomenon of initially diffuse thalamocortical projections sharpened by selective elimination was described in my laboratory, followed by experimental evidence that these competitive interactions begin prenatally (*3*). What I suggested is that the species-specific pattern and cellular characteristics of cytoarchitectonic areas cannot be determined exclusively by extrinsic sources or by neuronal activity and that there must be some intrinsic regional differences within the embryonic telencephalic wall, including possibly the transient ventricular and subplate zones (*4*). It is rewarding that the tools of molecular biology are now beginning to supply new lines of evidence for regionally restricted expression of molecules and genes within the telencephalon before or independently of thalamic input (*5*), thus supporting the basic tenet of the protomap hypothesis. I agree with Shatz that it is an important and challenging subject in developmental neurobiology and that more research needs to be done on both genetic and epigenetic regulation of cortical development.

Pasko Rakic
Section of Neurobiology,
School of Medicine, Yale University,
New Haven, CT 06510–8001

REFERENCES AND NOTES

1. P. Rakic, *Science* **241**, 170 (1988).
2. _____, I. Suñer, R. W. Williams, *Proc. Natl. Acad. Sci. U.S.A.* **88**, 2083 (1991).
3. P. Rakic, *Nature* **261**, 467 (1976); *Science* **214**, 928 (1981).
4. It seems that the results of Shatz and other investigators support this suggestion [A. Ghosh, A. Antonini, S. K. McConnell, C. J. Shatz, *Nature* **347**, 179 (1990); D. D. M. O'Leary and D. J. Bongasser, *Soc. Neurosci. Abstr.* **18**, 925 (1992); Z. Molnar and C. Blakemore, *ibid.*, p. 330].
5. Y. Arimatsu *et al.*, *Proc. Natl. Acad. Sci. U.S.A.* **89**, 8879 (1992); R. Ferri and P. Levitt, *Soc. Neurosci. Abstr.* **17**, 922 (1991); A. La Mantia *et al.*, *ibid.* **18**, 1097 (1992); S. Lu, L. D. Bogarad, M. T. Murtha, F. H. Ruddle, *Proc. Natl. Acad. Sci. U.S.A.* **89**, 8053 (1992).

■

Protection from Dementia

We wish to comment on the controversy over the role of β-amyloid deposition in Alzheimer's disease (News & Comment, 4 Sept., p. 1336) and particularly the suggestion that glutamate hyperactivity or altered energy metabolism may be a determinant of the extent to which such deposition is harmless. We have evidence (*1*) that the disease is characterized by glutamate hypoactivity with the capacity for energy metabolism maintained. Thus two abnormalities (excessive glutamate and energy depletion) that can interact with β-amyloid to destroy neurons in culture may not occur in the brain of patients with Alzheimer's. The development of neuroprotective agents will depend on a greater understanding of the function and mismetabolism of amyloid precursor proteins (APP). Processing pathways of APP appear to be affected by a muscarinic agonist (*2*) and phorbol esters (*3*) which mimic the transduction pathways of neurotransmitters that use phosphoinositide breakdown as a second messenger. Hence an additional rationale for some transmitter-based therapies is emerging. In Alzheimer's disease circum-