which suggests a predisposition toward subsequent gain or loss.

One cannot tell from these results if maintaining body fat at a constant level would prevent a decline in testosterone, but they do suggest that possibility.

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Response: Watson describes the successful use of the simultaneous replacement of DHEA and melatonin in elderly and sick mice. One should realize how dangerous and uninformative studies with mice and rats are, with regard to their meaning and interpretation for human aging research. In mice and rats, DHEA is hardly, or not at all, produced by the adrenal cortex, while melatonin plays an important role in their physiology. In humans, DHEA is an important product of adrenal cortical steroidogenesis, while a physiological role of melatonin has not yet been demonstrated. The message of our article was that one should not extrapolate too much from animal experiments. As Watson states, long-term controlled clinical trials of elderly individuals seem the only way to approach the unsolved question of whether hormone replacement therapy is efficacious and safe.

Mazur describes an interesting observation in a large group of elderly U.S. Air Force veterans. Those men demonstrating a clear decrease in total testosterone showed a considerable increase in body fat. Mazur suggests that this age-related decrease in testosterone may be the result of weight gain, and that testosterone levels might be sustained in elderly men through diet and exercise.

It should be mentioned, however, that it has not been demonstrated to my knowledge whether and how the well-known changes in body composition during aging (loss of muscle mass and increase in body fat, for example) are related to changes in testosterone bioactivity only. In parallel, decreases in levels of growth hormone insulin-like growth factor I and in DHEA also occur. I also know of no evidence that dieting and exercise might prevent the age-related decrease in testosterone. For the time being, the interesting observations by Mazur suggest that healthy, elderly males demonstrate a variable change in total testosterone levels (decrease, unchanged, and slight increase), which is accompanied by changes in body fat (increase, unchanged, and slight decrease, respectively).

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Immediate Release of Crystallographic Data: A Proposal

There has been an incredibly rapid increase in the rate of determination of three-dimensional (3D) structures of biomacromolecules. as reflected by the deposition of a new structure in the Protein Data Bank (PDB) at the Brookhaven National Laboratory (1), on average, every 5 hours. Unfortunately, in parallel, an increasing proportion of depositors take advantage of the PDB's policy of allowing structures to be kept "on hold" for up to a year after coordinate deposition. Despite a recent drop in the number of structures put"on hold," nearly half the entries deposited are not released immediately. The policy of the PDB is based on rules drawn up by the International Union of Crystallography (IUCr) in the late 1980s for papers published in IUCr journals. These rules (2) also provide the basis for the policies of most other scientific journals and of a number of government funding agencies, such as the National Institutes of Health, for work undertaken with grant support.

It is time to consider whether this policy is still appropriate. When it was debated and accepted by the community 10 years ago, the time needed to solve a macromolecular structure was often measured in years and was rarely less than 1 year. The time needed for detailed analysis of such structures was also fairly long. The 1-year hold on coordinates was therefore instituted to allow the authors to reap the fruit of their tremendous investment of time and effort. Because of recent advances in protein expression and purification, crystallization procedures, x-ray instrumentation, and computer software, the time needed to solve a structure is often shorter than the allowed hold period. In light of such developments, it is difficult to justify withholding coordinates for any period once the paper has been published.

Biomolecular structure analysis has succeeded in bringing 3D structures to the forefront of molecular biological research. This success has expanded both the interest in and utility of the information being deposited in the PDB. The molecular modeling community has grown and evolved considerably, due to the expansion of this source of experimental data. The value of the data rests in their availability to the broader community. Methods are continuously being developed to analyze new structures and their relationships to the collection of existing structures. New uses for these data, such as statistical potentials for folding and threading calculations, and interface recognition tools, are evolving rapidly. No single research group can fully exhaust this wealth of information. The value of the resource grows proportionally to the timeliness of the data and to the number of scientists who have access to them. Three-dimensional structural information is also a crucial link elucidating the role of a translated region of a DNA sequence of unknown function.

The time has come to change the rules of deposition so as to ensure that the coordinates are released concomitantly with publication of the paper (or papers) describing the structure. We are convinced that without access to the coordinates, the structures cannot be used for comparison with other proteins, for theoretical analysis or, more and more important, for drug design.

We propose that coordinates deposited at the PDB should be marked as either "for immediate release" or "to be released upon publication." We also recommend that the maximum hold for primary data (that is, xray structure factors, and nuclear magnetic resonance proton-proton distance and dihedral angle restraints) be reduced from 4 years to 1 year. The PDB is already working on a "layered approach" to deposition so that it will be possible to release entries as submitted, after the authors have checked for outliers and errors through the PDB's WEB-based AutoDep procedure, on the same day that they are deposited (with the permission of authors), or when the article related to the structure is published, if the authors request "release on publication date" rather than "hold for a year." It is clear that such a change in policy will require cooperation of both the granting agencies and the scientific journals, as well as the overwhelming support of the scientists doing the research. It should be stressed that even the current policy is not uniformly enforced. These changes would bring macromolecular crystallography into line with the requirements of other fields, such as gene sequencing, which have never allowed extended hold periods. We hope that this proposed change in the deposition policy will be publicly debated and ultimately accepted.

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Synchrotron Collaboration

The article "Dark tunnel ahead for light sources" (News & Comment, 8 Aug., p. 756) by A. Lawler discusses the funding of synchrotron radiation sources. I am concerned that the brief quote attributed to me does not accurately reflect what I was trying to convey to the interviewer. While I did remark that there has been a significant beneficial migration of experienced scientists from other laboratories (the National Synchrotron Light Source at Brookhaven, the Cornell High Energy Synchrotron Source, and Stanford Synchrotron Radiation Laboratory) to the Advanced Photon Source (APS) at Argonne National Laboratory, outside Chicago, I also stressed that those facilities continue to foster scientifically important and innovative groups that participate in extensive ongoing collaborative activities with the APS. I said that those facilities would be even more productive if they were better funded. The fact that third-generation sources open up new experimental possibilities in no way makes the second generation sources obsolete-they remain an essential part of the national scientific research infrastructure.

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Corrections and Clarifications

■ In the table of contents (p. 5) and This Week In Science (p. 9) in the issue of 2 January 1998, the Web address for the full text of the technical comments was incorrect. The full text and figures of the series "Polar wander and the Cambrian" (comment by T. H. Torsvik *et al.* and response by D. A. Evans *et al.*) can be seen at www.sciencemag.org/cgi/content/full/279/5347/9a

Letters to the Editors

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