In these respects MK-801 offers benefits not seen with another glutamate blocker, 2-amino-7-phosphonoheptanoic acid (APH). Brian Meldrum of the Institute of Psychiatry in London and his colleagues have shown that APH also protects rat hippocampal neurons from ischemic damage, but only if it is injected directly into the brain before ischemia is induced—a distinct drawback if the drug were to be used clinically in humans.

One way the Merck researchers measure the therapeutic effects of MK-801 is by determining how many neurons the drug rescues from death. But according to Bruce Volpe, also of Cornell, "you need to do more than count the number of cells. Cell sparing is very important, but it is also critical to assess neuronal function." Volpe finds that of the 15 to 20% of heart attack victims who survive a subsequent 6 hours of coma, fewer than 10% can function well enough to return to their jobs. So a critical test for any protective drug would be to preserve neuronal function, particularly of the ischemia-sensitive hippocampal neurons that are essential for cognitive activities.

MK-801 "probably works on the sodium channel that is controlled by NMDA [*N*-methyl-D-aspartate] receptors," Iversen says, and its activity requires the presence of glutamate. "In the jargon of the trade, MK-801 is called an open channel blocker because it requires the ion channel [that is activated by glutamate] to be in the open position before it can act."

Because MK-801 is somewhat similar in its action to the psychostimulant phencyclidine (PCP), Iversen cautions that "we don't know how widely a compound like MK-801 can be used because of its similarities to PCP." He proposes that PCP may act by binding at two different receptor sites, one of which is the same class of NMDA receptors affected by MK-801. Jaffe indicates that it is still too early to tell whether injected doses of the drug cause PCP-like effects in the volunteers now being tested.

The Food and Drug Administration (FDA) approved MK-801 for initial clinical testing in the United States, and Merck is now conducting studies in volunteers for their tolerance to injected doses of the drug. According to Jaffe, if MK-801 shows no unexpected side effects at doses comparable to therapeutic levels in animals, then Merck will apply to the FDA to test it as a neuroprotective agent. ■ **DEBORAH M. BARNES**

ADDITIONAL READING

E. H. F. Wong *et al.*, "The anticonvulsant MK-801 is a potent *N*-methyl-D-aspartate antagonist," *Proc. Natl. Acad. Sci. U.S.A.* **83**, 7104 (1986).

R. P. Simon *et al.*, "Blockade of *N*-methyl-D-aspartate receptors may protect against ischemic damage in the brain," *Science* **226**, 850 (1984).

Values of Fundamental Constants Adjusted

Since many of the fundamental physical constants are related, when new measurements of improved accuracy accumulate, it is necessary to adjust the values of all to make them consistent

After a 5-year study, the Committee on Data for Science and Technology (CODATA) of the International Council of Scientific Unions has released its new recommended values of the fundamental physical constants.* As compared to those in the previous 1973 CODATA recommendations, the uncertainties in the new values are smaller by about a factor of 10, reflecting significantly improved accuracy in measurements, sometimes by altogether new techniques.

Although there are no earth-shaking changes in any of the constants, some of their values have changed by more than three times the uncertainties listed in the 1973 adjustment (see table). The statistical probability for this is only 1%, but statistics can be distorted by "bad data" in the literature that are not recognized. "Once you get rid of the bad data, everything hangs together well," says E. Richard Cohen of the Rockwell International Science Center in Thousand Oaks, California, who coauthored the CODATA report with Barry N. Taylor of the National Bureau of Standards (NBS) in Gaithersburg, Maryland. "No more big changes are expected in the future," adds Cohen.

Fundamental constants are different from international standards, such as the length of the meter and the duration of the second, and fall into several categories. Some are constants of proportionality in the equations of fundamental physical theories, such as Planck's constant (h), which relates the energy of a photon to its frequency, and the speed of light (c), which relates the energy of a body to its mass. Other constants, such as the mass (m_e) and charge (e) of the electron, characterize the elementary constituents of matter.

Still other constants are not fundamental in the usual sense, but nonetheless play a similar role. Some of these constants are conversion factors that relate the values of "as maintained" electrical standards to their-

Recommended values of selected fundamental constants from the 1986 least-squares adjustment.

Constant*	Recommended value†	Uncertainty (ppm)
α^{-1}	137.0359895 (61)	0.045
e	1.60217733 (49)	0.30
h	6.6260755 (40)	0.60
m_e	9.1093897 (54)	0.59
N_A	6.0221367 (36)	0.59
m_p/m_e	1836.152701 (37)	0.020
F	96485.309 (29)	0.30
$2e/h$	483597.67 (14)	0.30

*The constants are defined in the text except m_p, the mass of the proton. †The units for e are 10^{-19} C; for h, 10^{-34} J-sec; for m_e, 10^{-31} kg; for N_A, 10^{23} mol^{-1}; for F, C mol^{-1}; and for $2e/h$, Ghz/V. The digits in parentheses are the one-standard-deviation uncertainties in the last digits of the given value.

Système International (SI) definitions. For example, the value of the volt is maintained at various national standards laboratories, such as NBS, in terms of the frequency of the alternating current in a superconducting Josephson junction. The ratio of the "as maintained" volt determined in this way to the SI definition of the volt is a constant (K_V) that differs slightly from unity.

Despite the name fundamental, the constants are not independent. The fine-structure constant (α) that is a measure of the strength of the electromagnetic interaction in quantum electrodynamics is defined in terms of other fundamental constants and is proportional to ce^2/h. Similarly, the constant relating the "as maintained" volt to its defined value is proportional to h/e. Since these "composite" constants can be measured directly and are in every sense fundamental in their own right, it is a matter of taste which constants one regards as the composites.

More important, inconsistencies may arise between the directly measured value of a constant and the value or values inferred from the separate values of the various combinations of constants in terms of which it can be expressed. The procedure for ironing out inconsistencies, which was pioneered at the University of California at Berkeley in the late 1920s by Raymond Birge, is called a least-squares adjustment. The latest and most comprehensive adjustments have been those by Taylor, William Parker, and Don-

The 1986 Adjustment of the Fundamental Physical Constants, CODATA Bulletin 63 is available in North America from Pergamon Press Inc., Elmsford, NY, 10523 for $15 and elsewhere from Pergamon Press Ltd., Headington Hill Hall, Oxford OX3 0BW, United Kingdom.

ald Langenberg in 1969 and by Cohen and Taylor in 1973.

The motivation for the new adjustment is the extraordinary amount of experimental and theoretical work published since 1973 that affects the fundamental constants. Taylor calls attention to the 1983 redefinition of the meter in terms of the distance traveled by light in a time equal to $1/c$ second as one example. This redefinition established the speed of light as an exact constant whose value is fixed.

Another important advance, made at NBS by Richard Delattes and several co-workers in the mid-1970s, permits the measurement of atomic lattice spacings (at least in silicon) in terms of optical wavelengths rather than x-rays, as was customary. The optical measurements can be directly tied to the definition of the meter, whereas x-ray measurements require an additional conversion factor similar in spirit to that tying the "as maintained" volt to its SI definition. Among other things, the lattice spacing influences the value of the Avogadro constant (N_A), which has changed in value significantly.

A completely unexpected development was the 1980 discovery of the quantum Hall effect, in which the so-called Hall resistivity (R_H) assumes only quantized values that are multiples of h/e^2. This new and still not completely understood phenomenon, whose discovery won Klaus von Klitzing of the Max Planck Institute for Solid State Research in Stüttgart, West Germany, a Nobel prize in physics, provides an accurate measurement of the fine-structure constant, as well as a method of generating an "as maintained" resistance standard. Other changes since 1973 include a highly accurate measurement of the electron anomalous magnetic moment (g-factor) by Robert VanDyck, Hans Dehmelt, and their colleagues at the University of Washington, where they trapped and stored a single electron at 4.2 K. The measurement of the electron g-factor to 1 part in 10^{11} makes it one of the most accurately known quantities in physics.

In carrying out their least-squares adjustment, Cohen and Taylor divided the fundamental constants into three groupings. The first, which they label auxiliary constants, are either fixed as is the speed of light or are so accurately known that their values would not be changed in the adjustment. In the least-squares procedure, each input datum is weighted according to the inverse square of the uncertainty in its value. Therefore, the values of the auxiliary constants, each of which may be a weighted average of the best available measurements, are held fixed.

The second grouping includes the primary stochastic data. These are values of constants whose adjusted values will be determined directly in the least-squares procedure. The 1986 adjustment involved 38 values of 12 fundamental constants. In practice, because of the relationships between the constants, any five of the twelve are independent unknowns, and the other seven are calculated from the adjusted values of these five, as are the values of most other constants of interest. Finally, there is a group of constants, such as the gravitational constant (G), that are not related by any existing theory to others, so that only direct measurements yield their values.

Weighting of the input data is actually a more complicated procedure than just using the uncertainty listed in the literature. Cohen and Taylor tested four algorithms that took varying degrees of account of the idea that the true uncertanties are not really known, but can be better estimated after iterations of an adjustment. An additional complication is that bad data (measured values of constants that differ from the "true" values by many times the nominal uncertainties listed in the literature) must be eliminated. In the end, the researchers used two so-called extended least-squares algorithms developed by Cohen, one in the early stages of the adjustment for identifying bad data and the other at the end for making the final adjustment.

One interesting conclusion of the adjustment was the recognition that two values of the Faraday constant (F) that were thrown out in the 1973 adjustment were actually quite good. Their exclusion from the 1973 adjustment was a major reason for the differences between the 1973 and 1986 recommended values. Cohen and Taylor argue that no similar situation exists in the 1986 adjustment because the data that were excluded either were of very large uncertainty (low weight) or differed greatly from other measurements of the same quantity. ■

ARTHUR L. ROBINSON

New Database for AIDS Research

New gene sequences and information about proteins of the AIDS virus are being reported so quickly that researchers are hard-pressed to keep up. To help streamline the process, scientists at Los Alamos National Laboratory in New Mexico are establishing a computerized data bank for recording and analyzing information about the molecular biology of the rapidly changing virus that causes AIDS (acquired immune deficiency syndrome). The National Institute of Allergy and Infectious Diseases (NIAID) has just awarded a 3-year grant to Gerald Myers, of the Theoretical Division at Los Alamos, who plans to have the database available by March.

Not only does the AIDS virus mutate quickly so that different isolates have different gene sequences, but in recent months researchers have also found that more than one AIDS-like virus exists—some cause disease and others apparently do not. Until now, information about the genetics of the AIDS virus has been fed into the GenBank system, which is already established at Los Alamos. The new compendium will include analytical information that GenBank is not funded to provide, will contain quarterly updates of fresh data, and will be available free to qualified investigators in both hardcopy and on floppy discs (that are IBM PC–compatible). The new resource is being established in cooperation with both GenBank and EMBL, the European Molecular Biological Laboratory in Heidelberg, West Germany, but is an independent entity.

The AIDS database will contain "DNA, RNA, and protein sequences of all the AIDS virus isolates, the sequences that recognize the T4 receptor of lymphocytes, and similar information about animal viruses that are related to the AIDS virus," according to Myers. It will identify regions of the AIDS virus genome that are most variable, and, if known, note how the altered regions affect peptide sequences and protein function. The resource will publish corrections of sequence information and will include references from the literature.

Flossie Wong-Staal and Steven Josephs, both of the National Cancer Institute, and Arnold Rabson of NIAID will act as scientific advisers for the new database project. "The next big burst of papers will probably be about the new viruses that are divergent from the AIDS virus—STLV-III (simian T cell lymphotropic virus), HTLV-IV (human T cell lymphotropic virus), LAV-2 (lymphadenopathy-associated virus), and similar isolates obtained at the Karolinska Institute in Sweden," Wong-Staal says. "I think STLV-III is probably a very recent progenitor of both HTLV-IV and LAV-2. But HTLV-IV is biologically different; it is not associated with disease."

The new database will provide information that allows researchers to draw comparisons among such related viruses, according to Myers. "This project will remove any barrier for people who want to do sequence analysis," he says. ■

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