Home with the harvest. Young girl carrying rice in eastern Bhutan.

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carotenoid. The production of various carotenoids other than β-carotene could provide additional health benefits as carotenoids have been implicated in reducing the risk of certain types of cancers, cardiovascular disease, and age-related macular degeneration. Fortunately, excess dietary β-carotene, in contrast to excess vitamin A, has no harmful effects, so plants with enhanced β-carotene content should be a safe and effective means of vitamin delivery.

Field-testing will tell us whether production of carotenoids in rice endosperm will entail any metabolic trade-offs. Shunting more of the common precursor GGPP into carotenoid production might result in a decrease in other compounds whose synthesis is dependent on GGPP. For example, tomatoes engineered to produce more phytoene exhibit signs of dwarfism, attributed to a 30-fold reduction in the plant hormone gibberellic acid, which shares the precursor GGPP with phytoene (*7*). However, unlike tomato plants that express phytoene synthase in all their tissues, the rice plants engineered by Ye *et al.* express the introduced phytoene synthase only in the endosperm, which reduces the potential for metabolic disruption throughout the plant.

Presumably, it should be possible to engineer the pathways for many of the 13 essential vitamins into plants, once the pathways are known and the corresponding genes have been cloned (*8*). Indeed, the model plant *Arabidopsis* has already been successfully engineered to synthesize vitamin E (*9*). Improving the mineral content of plants so that they can serve as sources of the 14 minerals required in the human diet presents researchers with a different set of challenges (*8*). Unlike vitamins, which are synthesized by the plants themselves, plants must take up essential minerals from the soil. Iron deficiency is the leading nutritional disorder in the world today, affecting over 2 billion people. As with vitamins, many of the world's staple foods are not good sources of iron. Current efforts are centered on understanding how plants take up and store iron (*10*, *11*). Rice has been engineered to have higher levels of the iron storage protein ferritin in the grain (*12*), but the question remains as to whether these engineered rice plants will be a good source of dietary iron.

The road to better nutrition is not paved with gold and, hence, agribusiness has not centered its efforts on the nutritional value of food. The work that culminated in the production of golden rice was funded by grants from the Rockefeller Foundation, the Swiss Federal Institute of Technology and the European Community Biotech Program. Like the plant varieties that made the green revolution so successful, the rice engineered to produce provitamin A will be freely available to the farmers who need it most. One can only hope that this application of plant genetic engineering to ameliorate human misery without regard to short-term profit will restore this technology to political acceptability.

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PERSPECTIVES: PLUTONIUM CHEMISTRY

Toward the End of PuO_2's Supremacy?

Charles Madic

Owing to the ubiquitous presence of oxygen in the terrestrial environment, oxides occupy a central position in the chemistry of many elements. This is true not only for natural elements but also for artificial elements, particularly for the most famous one: plutonium. On page 285 of this issue, Haschke *et al.* (*1*) demonstrate convincingly that the supremacy of plutonium dioxide (PuO_2), long thought to be the most stable plutonium oxide under oxidizing conditions, is over. The results have implications for both military and civilian applications and for the long-term storage of plutonium.

The element plutonium was first created in December 1940 at the University of Berkeley, California, by a team of American scientists headed by Glenn T. Seaborg (*2*). During the summer of 1942, Cunningham and Werner (*3*) prepared a weighable amount of a solid plutonium compound, PuO_2 (2.77 μg). Thus, for the first time in human history, an artificial element was made visible to human eyes. This historical sample of PuO_2 is still kept at the Lawrence Hall of Science in Berkeley, California (*4*). Humanity became inescapably aware of the implications of these discoveries at the end of World War II: The atomic bomb that destroyed Nagasaki, Japan, on 9 August 1945 was made of plutonium prepared as part of the Manhattan Project.

It was soon recognized that plutonium chemistry is dominated by the existence of numerous oxidation states, from +III to +VI. In 1967, Russian scientists discovered that Pu(VII) can also exist (*5*). Despite the fact that plutonium thus possesses five oxidation states (III to VII), its oxide chemistry is far simpler. According to most textbooks (*4*, *6–8*), the plutonium-oxygen phase diagram contains the following crystalline solid oxides: $PuO_{1.50}$, $PuO_{1.52}$, $PuO_{1.61}$, PuO_{2-x}, and $PuO_{2.00}$, all of which involve only plutonium oxidation states III and IV. No plutonium oxide with an O/Pu stoichiometry higher than 2 was observed, despite numerous attempts to prepare PuO_3, the oxide corresponding to Pu(VI) (*4*).

It has therefore been assumed for

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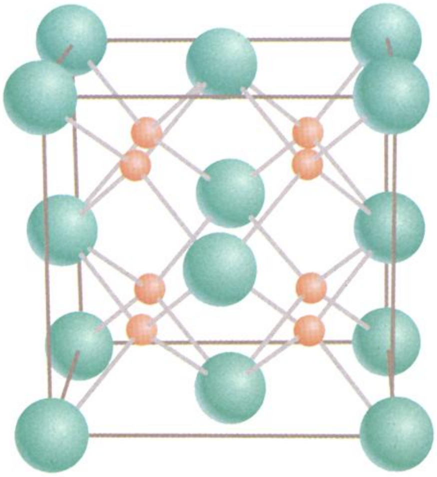

Face-centered-cubic (fcc) crystal structure of PuO_2 (Pu atoms in green, O atoms in red). The lattice constant is 4.3975 Å. PuO_{2+x} has the same structure, with a very similar lattice constant. This is one of the reasons why this compound was not identified prior to the study by Haschke *et al.* (*1*).

more than 50 years that PuO_2 is the highest plutonium oxide that can be prepared. This oxide, which crystallizes in the face-centered-cubic structure (fcc) (see the figure), was believed to be stable over a wide temperature range (from ambient to more than 2000°C). PuO_2 was therefore considered suitable as a component of nuclear reactor fuels, running either with fast or slow neutrons, for electricity production. To prepare these plutonium fuels, PuO_2 is mixed with depleted uranium dioxide, UO_2. The resulting solid solution $(U,Pu)O_2$ is then used to prepare mixed oxide (MOx) fuels. This plutonium recycling strategy has been an industrial reality in Western Europe and in Russia for many years and will also soon be implemented in Japan, where the first water-cooled nuclear reactor will be loaded with MOx fuel. Recycling of plutonium into MOx fuels requires reprocessing of uranium oxide–spent fuels. This is done industrially, for example, at Cogéma's La Hague plants (France) and British Nuclear Fuel Limited's Sellafield THORP plant (UK). Plutonium recovered from these spent fuels is converted into the semifinal product PuO_2. Plutonium recycling is not used in the United States, but PuO_2 is considered a very important compound for the long-term storage of plutonium from dismantled nuclear weapons.

For both civilian and military applications, the stability of PuO_2 was a key factor underlying the industrial strategy. The discovery by Haschke *et al.* that water and humid oxygen can slowly oxidize PuO_2 to PuO_{2+x}, accompanied by generation of hydrogen gas, calls for new evaluations of different aspects of the industrial operations involving PuO_2. Haschke *et al.* show that PuO_2 is metastable under oxidizing conditions and that it can be converted into PuO_{2+x} with x as high as 0.27, in which more than one-fourth of the plutonium atoms are oxidized from their initial oxidation state +IV into the oxidation state +VI. Surprisingly, water vapor was found to be a more efficient oxidizing agent than oxygen itself for the conversion of PuO_2 into PuO_{2+x}.

Future safety evaluations must take into account the temperature range of PuO_{2+x} stability (ambient to 350°C) and also the increased mobility of its Pu(VI) content in various transfer mechanisms. The new results will also have great consequences for the underground disposal of nuclear wastes. Until now, it was assumed that plutonium would not be very mobile in the underground geological environment because of the insolubility of Pu(IV) compounds. But Haschke *et al.* demonstrate that water can oxidize PuO_2 into PuO_{2+x}, in which more than 25% of the plutonium ions exist as Pu(VI), an ion that is far more water soluble, and thus mobile, than Pu(IV). This new property will have important implications for the long-term storage of plutonium.

The report by Haschke *et al.* will stimulate numerous future studies addressing fundamental questions related, for example, to the structure of the new PuO_{2+x} oxide, its thermodynamics properties, and the fascinating oxidizing property of water toward PuO_2.

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PERSPECTIVES: NEUROBIOLOGY

Diversity in Inhibition

Richard Miles

Yin and yang—inhibition and excitation. In the harmonious brain, excitatory and inhibitory synaptic signals coexist in a purposeful balance. But, whereas the neurons that the brain uses to transmit excitatory signals often have rather stereotyped properties, the cells that signal inhibition in the cortex and hippocampus are highly diverse and strikingly different from their excitable cousins. Inhibitory cells (also called interneurons because their effects are often short-range) signal to other neurons by liberating an inhibitory neurotransmitter from synaptic sites. Two articles in this week's issue add to a flood of new data on interneurons and their importance in brain function. In the first, Martina *et al.* (*1*) show on page 295 how the expression of Na^+ channels in neuronal dendritic branches endows one group of inhibitory neurons with an enhanced excitability and an increased speed of electrical signal transmission. In the second, Gupta *et al.* (*2*) present on page 273 an elegant attempt to classify cortical inhibitory cells by their synaptic effects on target neurons.

Cortical inhibitory neurons differ in many ways from their excitatory pyramidal cell partners. They have an entirely different calcium economy (*3*) and, perhaps consequently, it is difficult to induce long-term potentiation at the synapses that excite them (*4*). More importantly, inhibitory cells and circuits are built for speed. Interneuron action potentials are traditionally faster than those of pyramidal cells. This speed may result from the selective expression of specific K^+ channels that repolarize neurons after each action potential (*5*). Furthermore, the kinetics of synaptic events that excite inhibitory cells are faster than those that excite pyramidal cells (*6*). Rapid excitation probably depends on a distinct form of the postsynaptic AMPA receptor that mediates signaling at excitatory junctions with interneurons (*7*). The functional result is that pyramidal cell action potentials can induce interneuron firing with remarkably

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