nent of emissions from steel mills and vehicle exhaust, primary sources of air pollution in the contaminated Hamilton Harbor location, and they cause germ cell mutations in mammals. PAHs such as benzo(a)pyrene and dimethylbenzanthracene induce dominant lethal mutations in female mice when given by intraperitoneal injection (*8*), an exposure route of uncertain relevance to inhalation.

New evidence shows that PAHs associated with inhaled particles also may cause changes in humans during development. Pregnant women exposed to elevated levels of particulate matter and carcinogenic PAHs in ambient air have an increased risk of delivering a low–birth weight child compared to women with lower exposures (*9*). This risk is doubled if the exposure occurs during the first month of pregnancy (*10*). A link also exists between somatic mutation in newborns and transplacental exposure to common air pollutants, including polycyclic organics (*11*). Studies in humans indicate that elevated air pollution also may cause DNA damage in male germ cells (*12*). Evidence on cigarette smoking, another source of exposure to PAHs, suggests the possibility of smoking-associated germ cell mutations (*13*).

Despite the study's elegant experimental design, the findings by Somers *et al.* (*2*) should be interpreted with caution. First, their tandem-repeat assay has been validated with only three chemical mutagens, and the transmission of these chemically induced changes to the second-generation offspring has not yet been examined (*7*). Second, the mutational mechanisms by which these tandem-repeat changes are induced are unclear. The mechanisms operating at some tandem-repeat sequences in mice are fundamentally different from those in humans (*7*). Nonetheless, the doubling dose for ionizing radiation–induced DNA changes in this assay is similar to that for coding genes in the definitive mouse specific-locus assay for germ cell mutations, despite differences in the absolute mutation frequencies in these two assays.

Although air pollution has dropped substantially in recent decades in the United States and many other developed countries, epidemiological studies continue to show adverse health effects at current levels of particulate matter and ozone (*1*). Regulations to protect public health have been strengthened because of this and other evidence. The new work now adds another area of potential concern. Confirmation of the Somers *et al.* findings (*2*) would extend the adverse health effects of air pollution beyond effects on somatic cells in the exposed generation to germ cells—with the attendant implications for health risks to future generations.


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14. We thank R. J. Preston, R. D. Owen, L. D. Claxton, C. L. Yauk, S. D. Perreault, J. B. Bishop, and M. D. Shelby for helpful comments. This article was reviewed at the National Health and Environmental Effects Research Laboratory of the U.S. Environmental Protection Agency and approved for publication.

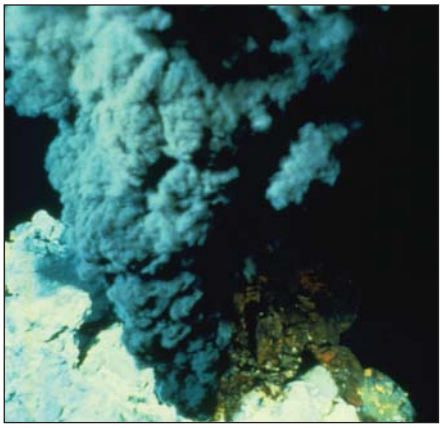

GEOCHEMISTRY

# Life's Chemical Kitchen


**Barbara Sherwood Lollar**


The first photographs from the submersible *Alvin* in 1979 stunned us all. An expedition to the tectonic spreading centers of the East Pacific Rise was staffed by oceanographers and geologists, but few biologists. After all this was an exploration of the deep-sea floor far from the Sun's life-sustaining rays. However, like a scene through Captain Nemo's portals, tube worms, mussels, and clams the size of dinner plates formed part of the macrofauna that testified to a complex biological ecosystem not dependent on photosynthesis (*1*). What are the recipes for sustaining life in this kind of chemical kitchen? Chemolithotrophic (literally chemical- and rock-consuming) microbes use the reactants provided by cooling basalt flows as substrates to drive a variety of chemical reactions, including methanogenesis, and $SO_4^-$ and $S^0$ reduction at the high-temperature vents, and oxidation of $H_2S$, $CH_4$, $Fe^{2+}$, and $Mn^{2+}$ under lower temperature regimes (*2*). But are there substrates for chemolithotrophic microbes away from the hydrothermal vents? On page 1002 in this issue, Foustoukos and Seyfried (*3*) provide experimental evidence for another possible source of substrates that may serve as key ingredients in the chemolithotrophic deep biosphere.

As the ocean crust cools and ages, seawater and hydrothermal fluids hydrate ultramafic (Mg-, Fe-rich) silicates in the ocean crust to produce serpentinized rocks, Mg- and Fe-hydroxides, and abundant $H_2$ gas. Production of abiogenic short-chain hydrocarbons such as methane, ethane, and propane by serpentinization has been a subject of debate (*4*). If $H_2$ and hydrocarbons from this type of abiogenic water-rock interaction are used as microbial substrates, then chemolithotrophic life may be feasible in parts of the Earth's crust where serpentinized rocks are globally widespread, ranging from the modern seafloor (*5*) to ancient seafloor deposits in billions-of-years-old Precambrian shield rocks (*6*). A chemical recipe for life applicable to both the hydrothermal vents and to broader geological environments would have important implications not only for deep-biosphere studies, but also for understanding prebiotic organic synthesis and the emergence of life in the early Earth (*7*). In addition, such chemolithotrophic systems may be a terrestrial analog for possible subsurface microbial communities on other planets or moons (*8*).



**Black smoker vent.** View from the deep-submergence vehicle *Alvin* of black "smoke" being emitted by the *Spire* hydrothermal vent on the ocean floor. Known as a "black smoker," the *Spire* pours out a sulfurous mineral-rich fluid from its mound or chimney that is 18 m high. The volcanic fluid bubbles up due to geothermal energy in the Earth's crust, at a temperature of 365°C. Deep-sea vents provide an unusual habitat to some primitive forms of extremophile bacteria and deep-sea crabs that can survive extreme condtions. The *Spire* is located at the Broken Spur Vent Field in the Mid-Atlantic Ridge, 3080 m below sea level.

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It is here that Foustoukos and Seyfried (*3*) make their elegant contribution. The water-rock reactions responsible for producing $H_2$ during serpentinization are well known. One suggested mechanism for concurrent production of hydrocarbons involves the Fischer-Tropsch type (FTT) synthesis:

$$CO_2 + (2 + m/2n)H_2 \rightarrow (1/n)C_nH_m + 2H_2O \quad (1)$$

In metal-catalyzed reactions in the laboratory, this synthesis readily produces $CH_4$ in a gas-phase reaction. However, experiments have yielded conflicting results over (i) the feasibility of FTT synthesis in most geological environments, where synthesis would likely take place in the aqueous rather than gas phase, and (ii) whether higher hydrocarbons such as ethane and propane can be produced by this mechanism (*4*). Foustoukos and Seyfried (*3*) noted that Fe- and Mg-rich oceanic rocks are also rich in chromium. Using an Fe-Cr oxide catalyst, they demonstrated that reduction of dissolved $CO_2$ by FTT synthesis can produce not only abiogenic methane, but also ethane and propane in aqueous solutions under hydrothermal temperature and pressure conditions.

Demonstrating the production of abiogenic hydrocarbons has important implications for a wide range of issues, from the contributions of nonbiological hydrocarbons to economic deposits of petroleum hydrocarbons, to recent interest in the origin of $CH_4$ on Mars. The Foustoukos and Seyfried work (*3*) has, for the first time, demonstrated a mechanism for the production of a range of abiogenic hydrocarbons in the type of $H_2$-rich aqueous systems likely to be found both in hydrothermal vents in ultramafic rocks and in aging ocean-floor deposits undergoing serpentinization. Whether deep subsurface microbes avail themselves of the $H_2$ and hydrocarbon substrates that geology and chemistry provide must be confirmed using the burgeoning set of molecular microbiology tools and culturing techniques now available. In addition, work needs to be done to define the chemistry and substrates that support chemolithotrophic life in geological environments that are dominated by rock types other than serpentinized ultramafics, such as the recent studies in volcanic hot springs, and basalt aquifers (*9*, *10*). What is certain is that our understanding of the variety of potential recipes for chemolithotrophic life has been significantly advanced. Such progress in identifying the diverse basis for life on Earth will be essential as astrobiology missions to Mars and beyond take flight.


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NEUROSCIENCE

# Controlling the Ups and Downs of Synaptic Strength

**Tim Bliss and Ralf Schoepfer**

Both increases and decreases in synaptic efficiency can be triggered by activation of the *N*-methyl-D-aspartate (NMDA) type of glutamate receptor. How can activation of the same receptor lead to diametrically opposite changes in synaptic strength? This conundrum has long puzzled neuroscientists interested in how information is stored in the vertebrate brain. According to Liu *et al*. (*1*) on page 1021 of this issue, the answer to the puzzle appears to lie, at least in part, in the subunit composition of the NMDA receptor.

The dominant model of activity-dependent synaptic plasticity is long-term potentiation (LTP). This phenomenon, first described more than 30 years ago, occurs in the hippocampus, a cortical structure that in humans is essential for the formation of new episodic memories. In synapses displaying LTP, a brief high-frequency burst of synaptic activity leads to an immediate and enduring increase in synaptic efficiency (see the figure) (*2*). In contrast, more prolonged, lower frequency synaptic activity gives rise to long-term depression (LTD). In both cases, antagonists of the NMDA receptor block induction of the long-lasting change (*2*, *3*). The channels formed by NMDA receptors are permeable to calcium, and a rise in the concentration of calcium in the postsynaptic cell is required for both LTP and LTD. In an influential paper, Lisman proposed that long trains of low-frequency synaptic stimulation, producing a modest but prolonged rise in intracellular calcium ions ($Ca^{2+}$), led to LTD via the activation of phosphatases. In contrast, high-frequency trains, producing a greater rise in intracellular $Ca^{2+}$, led to LTP via the activation of protein kinases (*4*). Experiments in which the intracellular $Ca^{2+}$ concentration was manipulated supported the predictions of the Lisman model (*5*). The new results of Liu *et al*. (*1*) put flesh on the bones of an earlier suggestion (*6*) that the subunit composition of the NMDA receptor provides the gateway to LTP or LTD.

NMDA receptors are multimeric proteins containing, in hippocampal neurons, two obligatory NR1 subunits, usually paired with two NR2A or two NR2B subunits (see the figure) (*7*). Liu *et al*. used two NR2B-specific antagonists (ifenprodil and Ro25-6981) together with a recently developed NR2A antagonist (NVP-AAM077) to dissect subunit involvement in LTP and LTD at synapses on pyramidal cells in area CA1 of the hippocampus. Both forms of synaptic plasticity can be blocked by the NMDA receptor antagonist D-APV. The new and unexpected result is that LTP is mediated by NMDA receptors containing NR2A subunits, whereas LTD requires activation of receptors containing NR2B subunits (see the figure).

These results are satisfyingly convincing and explain the puzzling difficulty of inducing LTD in older animals: The NR2B subunit is maximally expressed in neonatal animals, and thereafter its levels decline. However, although this is the case for pyramidal cells in the hippocampus, the developmental gradient in granule cells of the hippocampal formation is much less steep, and qualitatively there is little difference in NR2B expression in neonatal and adult animals. One would therefore expect that LTD might be easier to induce in the dentate gyrus of adult animals than in area CA1. In fact, the reverse seems to be the case (*8*). As Liu *et al*. point out, the rule they have uncovered in area CA1 is not universally obeyed. In layer 2/3 of sensory cortex, for example, different rules seem to apply (*9*).

Appropriate patterns of stimulation can drive synaptic efficacy up or down at single hippocampal synapses (*10*). Given the results

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