

## Power from the deep

### Microbially powered fuel cells tap into an abundant ecosystem energy circuit.

Edward F. DeLong and Paul Chandler

Enormous amounts of potential energy lie buried in marine sediments in the form of reduced carbon compounds. The most familiar form of this vast energy reserve is petroleum, which drives the lion's share of today's energy economy. The next most obvious submarine energy reserve, even more abundant than petroleum, is methane. At deep-sea conditions of low temperature and high pressure, large amounts of this natural gas are found in sub-seafloor reservoirs of frozen methane hydrates<sup>1</sup>. Yet there is another abundant, but less obvious, marine energy reserve: sediment-associated organic carbon, which represents about 2% of the dry weight of marine sediments along continental margins. Is it possible to tap into this vast, dispersed form of submarine energy? If so, how? The answer, in part, is that microbes already have tapped into this large energy reserve. Now, in two papers, one in this issue<sup>2</sup> and the other in a previous issue of *Science*<sup>3</sup>, researchers harness microbially generated power by constructing a fuel cell that can exploit the naturally occurring voltage gradient created by microbial activity in marine sediments.

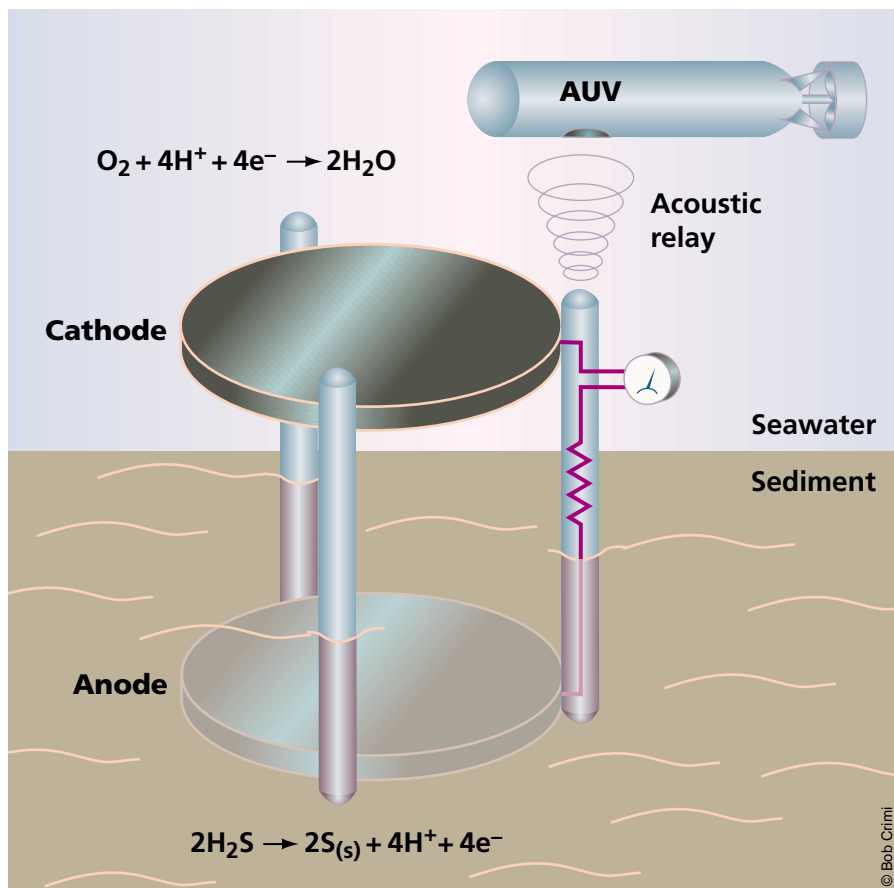
Microbial oxidation of sub-seafloor organic carbon produces electron-rich reductants (such as  $\text{Fe}^{2+}$  or  $\text{HS}^-$ ) that create a voltage gradient between ocean sediments and the surrounding oxygen-rich seawater. Researchers first harvested electrical energy from marine sediments in laboratory-based aquariums, demonstrating that it is possible to tap into the sediment-water voltage gradient<sup>3,4</sup>. This is achieved by placing a graphite anode in anaerobic sediments and connecting it, through an external load, to a cathode placed in the overlying seawater. In the sediments, bacterial respiration of organic carbon either directly or indirectly donates electrons to the anode. At the cathode, the sediment-derived electric potential drives the reduction of oxygen to water ( $\text{O}_2 + 4\text{H}^+ + 4\text{e}^- \rightarrow 2\text{H}_2\text{O}$ ). Electrical energy is harvested by placing a load in the circuit that connects the anode and cathode in this very simple, natu-

rally powered fuel cell (Fig. 1). In both of the laboratory-based preliminary investigations<sup>3,4</sup> at least a  $0.01 \text{ W/m}^2$  electrode footprint area was produced by the fuel cells over experimental periods of weeks to months.

Laboratory experiments are fine and good, but do these microbial fuel cells work in the real world? In this issue, Tender *et al.*<sup>2</sup> demonstrate the *in situ* use of these simple microbial fuel cells to exploit the naturally occurring voltage gradient in marine sediments. The authors deployed and monitored their fuel cells for eight months to a year at two different sites, one in a shallow harbor in Tuckerton, New Jersey, and one off the coast of Oregon. Both fuel cells were remarkably stable in these natural marine environments,

producing a constant power output greater than  $0.025 \text{ W/m}^2$ . The electron-donating reactions at the anode also seem rechargeable, as demonstrated by a rapid rise in voltage when the current was reduced. Part of the current appears to be generated by the oxidation of sulfide (a waste product of bacterial anaerobic respiration) to sulfur on the anode surface. But that's not the whole story. Interestingly, power generation seems also to promote the natural selection on the electrode of microbes, including members of the *Geobacteraceae* family<sup>3,5</sup>, that can oxidize organic matter and couple this to the direct transfer of electrons on the anode. Yet another suite of microbes that oxidizes sulfur to sulfate, again transferring electrons directly to the anode, also seems to play a role<sup>2</sup>.

What are some of the potential applications of the fuel cells described by Tender *et al.*? Sensor systems developed for oceanography, environmental monitoring, or military applications immediately come to mind. These sensors for monitoring physical, chemical, and biological parameters in the environment need to operate at remote and widely distributed locations, using self-



**Figure 1.** Fuel cell-powered distributed sensor networks. Model for the potential use of an *in situ* fuel cell, outfitted with associated environmental sensors. In this configuration, the fuel cell-powered sensors (generic dial) acoustically download data to an automated underwater vehicle (AUV) as it passes by the water column.

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contained energy sources. Energy reserves for such sensor systems can be resupplied by delivering fresh batteries or additional fuel and oxidizers, but this is often too difficult, time consuming, or costly to consider. As a consequence, sensor systems must often be deployed with all the energy they will require during their planned operational life, or they must exploit energy sources available in the local environment. This need is well met by the sediment–seawater microbial fuel cells described by the authors. This new technology, as its efficiency improves, could very conceivably meet the energy requirements of low-power sensors deployed at the water–sediment interface, to depths as great as 1,000 meters<sup>4</sup>.

A central aspect of these microbial fuel cells is that they rely on natural voltage gradients and a supply of organic fuel provided by the natural environment. The voltages and power densities they generate must be sufficient, however, to power the majority of currently available sensors and instrumentation. There are several ways to step up voltages (with little energy consumption) and improve the efficiency of the microbial fuel cells. Optimizing the electrode materials and surface area to enhance power density should be possible. Additionally, it may be possible to supply exogenous fuel and reductant, although the cost-benefit ratio of this type of modification, as compared with using conventional battery technologies, would have to be evaluated carefully. As the specific microbial–electrode interactions become better characterized, it may even be possible to enhance the essential biological mechanisms of electron transfer. In this scenario, electrodes might be seeded with a genetically optimized microbial catalyst before deployment. Such improvements, combined with ultra-low-power micro-sensors and low duty cycles, might allow sensors to be deployed in the environment indefinitely. The simplicity and low cost of such systems could enable the distribution of multiple sensor suites for environmental monitoring over very wide geographic areas.

Considerable potential exists in the exploitation of microbial activity to produce energy, in a wide variety of contexts. The oceans contain a vast amount of energy originating from sunlight and geothermal and geochemical activity which is converted into diverse energy reservoirs by biological activities. Tender *et al.* demonstrate one very simple and clean way to tap into an abundant, naturally occurring ecosystem energy circuit. Many other means of tapping into the vast array of microbial metabolic capabilities might be considered for harvesting energy from sunlight or other biological or geological processes.

Interestingly, one of the leaders of the genome revolution, Craig Venter, has begun to consider microbial energy production in creating a new institute, dubbed the Institute for Biological Energy Alternatives (IBEA; Rockville, MD)<sup>6,7</sup>. One of the IBEA's stated goals is to use microbial genomics to engineer metabolic pathways that might enhance energy production processes. In this context, The Institute for Genomic Research (Rockville, MD) in collaboration with Derek Lovley (a co-author on the Tender *et al.* report) has nearly completed analyses of the full genome sequence of an "electrode bug" relative, *Geobacter sulfurreducens*<sup>2,8</sup>. It may be

that genetically engineered superbugs, capable of ultra-efficient electrode electron transfer, could end up in a wide range of environmentally fueled and environmentally friendly fuel cells.

1. Kvenvolden, K. *Chem. Geol.* **71**, 41–51 (1988).
2. Tender, L.M. *et al. Nat. Biotechnol.* **20**, 821–825 (2002).
3. Bond, D.R., Holmes, D.E., Tender, L.M. & Lovley, D.R. *Science* **295**, 483–485 (2002).
4. Reimers, C.E., Tender, L.M., Fertig, S., & Wang, W. *Environ. Sci. Technol.* **35**, 192–195 (2001).
5. Lonergan, D.J. *et al. J. Bacteriol.* **178**, 2402–2408 (1996).
6. Marshall, E. *Science* **296**, 824–825 (2002).
7. Butler, D. *Nature* **417**, 3 (2002).
8. Pennisi, E. *Science* **296**, 1058–1060 (2002).

## A crystal clear solution for insulin delivery

**A hybrid protein cocrystal of insulin and a lipophilically modified derivative provides smoother and longer lasting control of glucose levels.**

Hans P. Merkle and Anna Jen

Formulating therapeutic proteins for delivery both at controlled rates and for prolonged periods presents many challenges. Frequently, therapeutic proteins are chemically and/or physically unstable during processing and storage, and once administered, they may undergo rapid physiological breakdown or be unable to cross biological barriers. This complexity often constrains current protein formulations to simple lyophilized injectables for rapid action. In this issue, Brader *et al.*<sup>1</sup> report a new twist in insulin delivery—the use of hybrid insulin cocrystals to better tailor the pharmacodynamic profile of the drug in diabetic patients. When they cocrystallize human insulin with a fully active, lipophilically modified insulin derivative, the authors are able to control the *in vitro* and *in vivo* release rates of insulin by varying the proportions of each subunit.

The formulation of therapeutic proteins is intrinsically difficult, demanding customized solutions and sophisticated formulation strategies. Several approaches have been designed to retain a protein and slow its absorption from the site of injection. These

include conjugation with polyethylene glycol—so-called PEGylation—to avoid rapid enzymatic cleavage and prolong the short biological half-lives of protein biopharmaceuticals<sup>2</sup>. Encapsulation in microspheres is another promising approach, allowing controlled release of the protein in a biocompatible, biodegradable matrix by hydrolytic erosion<sup>3</sup>. However, attaining stable and predictable *in vivo* therapeutic effects using these methods can be quite complex.

Interestingly, the most pioneering and successful protein formulation approach—controlled-release insulin—was developed even before television was invented. As early as the 1930s, formulations in which insulin was precipitated and crystallized with Zn(II) and protamine (an arginine-rich, basic protein) were suggested for sustained activity in the treatment of diabetes mellitus<sup>4</sup>.

Today, acceptable glycemic control in many insulin-dependent diabetics can be achieved using one of the commercially available human and nonhuman insulin formulations, consisting of amorphous or microcrystalline dispersions, which provide medium to long-term activity. Still, to overcome the clinical limitations of repetitive dose regimens and avoid the notorious long-term complications in many diabetics, the search for more efficient technologies continues.

Brader *et al.* sought to improve insulin absorption kinetics by cocrystallizing human insulin at preselected ratios with the lipophilically modified insulin derivative

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