these transporters in this process. The possible regulation of *ABCG5* and *ABCG8* (and other known target genes) by LXR suggests that LXR may be an excellent target for developing drugs to decrease serum cholesterol.

Although a full understanding of the regulation of cholesterol absorption in the intestine will require more work, the identification of genes mutated in sitosterolemia provides important insights into this process. Four ABC proteins have now been implicated in the regulation of cholesterol homeostasis. Future studies will need to determine the structural and functional properties of these proteins and whether they act in concert or in separate pathways of cholesterol metabolism.

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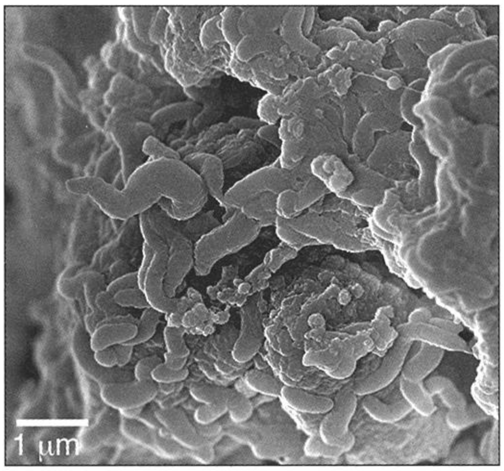
PERSPECTIVES: BIOGEOCHEMISTRY

Sulfate Reducers—Dominant Players in a Low-Oxygen World?

Crisogono Vasconcelos and Judith A. McKenzie

Sulfate-reducing bacteria may be one of the oldest forms of life on Earth. They can be traced back billions of years in the geologic rock record to the Early Archean (3900 to 2900 million years ago), when oxygen concentrations in Earth's atmosphere were low. Ancient sulfate-reducing bacteria left their first mark on their environment in pyrite minerals (FeS_2) as old as 3400 million years (*1*). Today, these microorganisms are widespread in marine and terrestrial aquatic environments. Their ability to adapt to extreme physical and chemical conditions enables them to play an important role in global geochemical cycles (*2*), but their role in the formation of ore deposits has remained controversial. Strong support for such a role is now provided by Labrenz *et al.* on page 1744 of this issue (*3*), who have discovered sulfate-reducing bacteria that can tolerate low levels of oxygen and can precipitate zinc sulfide minerals.



The role of microbes in ore deposit formation. Scanning electron microscopy image of vibrio-shaped sulfate-reducing bacteria that are intimately associated with dolomite crystals produced in a culture experiment conducted at room temperature (*9*). The bacteria are 3 to 5 µm in length. The sample was prepared by chemical fixation and critical-point drying.

Throughout geologic history, the sulfur cycle was strongly correlated with the carbon cycle because the two cycles are intrinsically connected through microbial metabolism. The sulfur cycle thus constitutes one of the best examples of the impact exerted by living organisms on geochemical cycles (*4*). Dissimilatory sulfate-reducing bacteria use sulfate mainly as an electron acceptor (without assimilating sulfur) in the anaerobic oxidation of inorganic or organic substrates such as $H_2 + CO_2$, lactate, acetate, and propionate. As a consequence of their metabolism, large amounts of reduced sulfide ions are produced and accumulated in their natural habitats. The sulfide ions combine with available metal ions to form insoluble products, most commonly FeS_2, leading to the production and transformation of natural mineral deposits (*5*).

The importance of this major biogeochemical process is evident in the fluctuations in the sulfur isotope content of marine sulfate during the Phanerozoic, that is, during the past 570 million years. Bacterial sulfate reduction controls the isotopic composition of marine sulfate, driving the $^{34}S/^{32}S$ isotopic ratio, expressed as $\delta^{34}S$, to more positive values during periods with increased deposition of carbonaceous sediments. For example, in the early Phanerozoic, the $\delta^{34}S$ value of marine sulfate (as recorded in marine deposits) increases by about 15 per mil, indicating a period with increased microbial sulfate reduction within anoxic (oxygen-deficient) sediments called black shales (*6*). Intervals with increased activity of sulfate-reducing bacteria, and associated increased impact on geochemical cycles, can thus be deciphered from the geologic record.

The role played by sulfate-reducing bacteria in natural processes is undoubtedly very important under anoxic or oxygen-free conditions. Anyone who has ever stepped into black stinky mud and smelled the H_2S released has experienced firsthand the activity of sulfate-reducing bacteria. These microbes undoubtedly play an important role in the early diagenetic alteration of sediments rich in organic matter. Their importance, however, for other geologic phenomena, such as the formation of sulfide ore deposits, remains controversial, not least because of their air intolerance. But this is not the case for the bacteria discovered by Labrenz *et al.* (*3*), which can tolerate low levels of oxygen (they are aerotolerant). These bacteria may be important players in geochemical cycling and in the concentration of metals into sediment-hosted sulfide ore deposits.

Using scuba divers to gain access to a flooded mine tunneled into a Pb-Zn ore deposit, Labrenz *et al.* were able to retrieve samples containing microbial biofilms. Applying microscale techniques, they demonstrate that the collected aerotolerant sulfate-reducing bacteria assemblage has the ability to form a pure precipitate of sphalerite (ZnS). The bacteria can scavenge zinc from waters with very low zinc concentrations (less than 1 part per million), essentially stripping the water of the metal. This observation has interesting implications for understanding how economic ZnS deposits may have formed. And it has even more exciting implications for possible biotechnological applications. Imagine if these aerotolerant sulfate-reducing bacteria could be used to remove trace metals, such as Zn, As, or Se, from contaminated drinking water! Because

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they can tolerate low levels of oxygen, these bacteria may provide a means to control metal concentrations biologically in groundwater and wetland-based remediation systems.

Bioremediation is not the only way we can apply these versatile organisms. Given the wide spatial and temporal distribution of sulfate-reducing bacteria and their distinct preference for low-oxygen to oxygen-free conditions, they can also provide clues to processes that may have been more widespread in the geologic past. Modern laboratory and field studies of sulfate-reducing bacteria and their metabolic products, both inorganic minerals and organic compounds, can provide valuable information for evaluating the role these microbes may have played in the geologic past. There is a general consensus that the low-oxygen conditions dominating Earth's surface during the first ~2000 million years of our planet's history favored the proliferation of sulfate-reducing organisms and that they, in turn, controlled their environment. This implies that a single process—bacterial sulfate reduction—has been in operation from the Early Archean until today. This process is widespread in different oxygen-poor environments at variable temperatures and pressures and results in mineralization of organic matter and direct and indirect mineral precipitation. It may be possible to roughly estimate the magnitude of the environmental impact exerted by these microorganisms during the evolution of our planet, directly or indirectly through their metabolic activity.

For example, the unequal distribution of dolomite [$CaMg(CO_3)_2$] in geologic time relative to limestone ($CaCO_3$), both of which are common sedimentary rocks, has remained an enigma. Dolomite is found in far greater abundance than limestone during Earth's early history and during periods when atmospheric oxygen levels may have been low compared with modern values (*7*). In laboratory experiments at low temperatures, sulfate-reducing bacteria mediate dolomite precipitation (see the figure), implying a link between this specific microbial process and dolomite formation (*8*, *9*). Apparently, the microbes can overcome kinetic factors inhibiting dolomite precipitation during their metabolic activity. It is probably not a coincidence that dolomite is often the host rock of many Pb-Zn sulfide ore bodies. Sulfate-reducing bacterial assemblages can accumulate metals to form a valuable ore deposit while simultaneously promoting the dolomitization of the host rock.

The comprehensive study of microbial controls on geochemical cycles is a relatively new direction in the geosciences. Linking the microbial biosphere to the study of the geosphere can produce exciting new discoveries, such as that reported by Labrenz *et al.*, and lead to a better understanding of many heretofore unexplained geologic phenomena. New discoveries can be expected as geomicrobiologists probe deeper into the low-oxygen realms dominated by sulfate-reducing bacteria. A particularly challenging new microbial frontier lies beneath the sea floor, deeply buried in sediments and within the hydrothermal systems plumbing the oceanic crust.

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10. We thank Y. van Lith for providing the figure.

PERSPECTIVES: ECOLOGY

The Lion and the Lamb Find Closure

Alan Hastings

Interactions between victims and enemies—between prey and predator, plant and herbivore, host and parasite, even between host and pathogen—are a central feature of all ecological communities. Even in the earliest ecological studies of interactions between victims and their enemies, a fundamental problem emerged: As these interactions appear to be inherently unstable, how is coexistence achieved? Gause's early experiments with different species of microorganisms illustrated the coexistence problem (*1*). The enemy species would either cause the extinction of the victim species and then starve, or would reduce the numbers of the victim species to such low levels that the enemy species would starve before the victim was eliminated. Yet the world is full of enemies and victims that coexist. What is the answer to this apparent paradox? The initial mathematical models of the 1920s and 1930s developed by Lotka (*2*), Volterra (*3*), and Nicholson and Bailey (*4*) did not provide easy solutions. Not surprisingly, many seemingly quite different answers were proposed. These answers incorporated to varying degrees the parts played by interactions within and between both enemy and victim species, as well as spatial heterogeneity (the uneven distribution of species in a given area). The contribution made by Keeling *et al.* (*5*) on page 1758 of this issue demonstrates that many of these explanations arose out of a single framework based on stochastic (random) models that emphasized spatial heterogeneity.

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The question of what stabilizes the interactions between enemies and their victims arises even in the simplest models. Lotka (*2*) and Volterra (*3*) developed predator-prey models describing continuous interactions between enemies and their victims. They made the following assumptions: that the victim species grows exponentially in the absence of the enemy species; that the interaction between the enemy and victim species is the result of random encounters; and that the birth rate of the exploiter (enemy) depends on the frequency of encounters whereas the exploiter death rate is a constant. This model is neutrally stable, that is, at the boundary between stability and instability. Thus, a way to find stabilizing influences is to make modifications and see whether they produce stability or instability (*6*).

Nicholson and Bailey (*4*) studied the simplest interaction—that between a host insect and a parasitoid insect where both species complete their life cycles within a single year. The parasitoid lays its eggs in the developing host, and then the young develop inside the host, usually killing the host while producing the next generation of parasitoids. This interaction has been intensively investigated by population ecologists because: it is much more common than might appear (estimates are that 15% or more of insect species are parasitoids); the specialized nature of the interaction means that often the parasitoids attack only one species; and hosts are often insects of economic importance. The simplest model in this case is unstable rather than neutrally stable as a result of the time delay introduced by the discrete generations (see the