Magneto-Aerotaxis

Richard B. Frankel[1] · Timothy J. Williams[2] · Dennis A. Bazylinski[3]

[1]Department of Physics, California Polytechnic State University, 1 Grand Avenue, San Luis Obispo, CA 93407, USA

[2]Department of Biochemistry, Biophysics and Molecular Biology, Iowa State University, Ames, IA 50011, USA

[3]School of Life Sciences, University of Nevada, Las Vegas, 4505 Maryland Parkway, Las Vegas, NV 89154-4004, USA

Abstract Magnetotactic bacteria orient and migrate along geomagnetic field lines. Magneto-aerotaxis increases the efficiency of respiring cells to efficiently find and maintain position at a preferred microaerobic oxygen concentration. Magneto-aerotaxis could also facilitate access to regions of higher nutrient and electron acceptor concentration via periodic excursions above and below the preferred oxygen concentration level.

Introduction

History

The terms "magnetotaxis" and "magnetotactic bacteria" were first used by Richard P. Blakemore in his landmark 1975 paper (Blakemore 1975) announcing the discovery of aquatic bacteria from Woods Hole, Massachusetts that migrated northward in water drops along magnetic field lines. Using transmission electron microscopy he found that the cells were roughly coccoid with two bundles of seven flagella each on one side of the cell. He also found the cells contained chains of elongated, electron-dense, iron-rich crystals, later shown to consist of magnetite (Fe_3O_4) (Frankel et al. 1979). The crystals were contained in intracytoplasmic vesicles arranged adjacent to the cytoplasmic membrane in the cell. He noted the probable relationship of the chains of crystals and magnetotaxis in the cocci and other magnetotactic bacteria recovered from aquatic sediments in Woods Hole. Blakemore (1975) postulated "Perhaps the iron-rich cell inclusions serve as magnetic dipoles which convey a magnetic moment on the cells, thus orienting the cells in magnetic fields. Magnetotaxis would result if, within each cell, a fixed spatial relationship existed between the orienting mechanism and cell propulsion". In a sense, all subsequent research on magnetotactic bacteria follows from these and other original observations in that paper. In this review, we describe and discuss recent work on magnetotaxis.

General Features of Magnetotactic Bacteria

Magnetotactic bacteria inhabit water columns or sediments with vertical chemical concentration stratification, where they occur predominantly at the oxic–anoxic interface (OAI) and the anoxic regions of the habitat or both (Bazylinski et al. 1995; Bazylinski and Moskowitz 1997; Simmons et al. 2004). All known magnetotactic bacteria phylogenetically belong to the domain Bacteria and are associated with different subgroups of the Proteobacteria and the Nitrospira phylum (Spring and Bazylinski 2000; Simmons et al. 2004). They represent a diverse group of microorganisms with respect to morphology and physiology (Bazylinski and Frankel 2004).

The magnetotactic bacteria are difficult to isolate and cultivate (Bazylinski and Frankel 2004) and thus there are relatively few axenic cultures of these organisms. Most cultured strains belong to the genus *Magnetospirillum*. Currently recognized species include *M. magnetotacticum* strain MS-1 (Blakemore et al. 1979; Maratea and Blakemore 1981; Schleifer et al. 1991), *M. gryphiswaldense* (Schleifer et al. 1991) and *M. magneticum* strain AMB-1

(Matsunaga et al. 1991). Several other freshwater magnetotactic spirilla in pure culture have not yet been completely described (Schüler et al. 1999). Other species of cultured magnetotactic bacteria include a variety of as yet incompletely characterized organisms: the marine vibrios, strains MV-1 (Bazylinski et al. 1988) and MV-2; a marine coccus, strain MC-1 (DeLong et al. 1993; Meldrum et al. 1993a); and a marine spirillum, strain MMS-1 (formerly MV-4) (Bazylinski and Frankel 2000; Meldrum et al. 1993b). There is also an anaerobic, sulfate-reducing, rod-shaped magnetotactic bacterium named *Desulfovibrio magneticus* strain RS-1 (Sakaguchi et al. 1993, 2002). These cultured organisms, except *D. magneticus*, are facultatively anaerobic or obligate microaerophiles. All are chemoorganoheterotrophic although the marine strains can also grow chemolithoautotrophically (Bazylinski et al. 2004; Williams et al. 2006). The genomes of several strains, including *M. magnetotacticum* strain MS-1 and strain MC-1, have been partially sequenced while that of *M. magneticum* strain AMB-1 (Matsunaga et al. 2005) has been recently completed.

Several uncultured, morphologically conspicuous, magnetotactic bacteria have also been examined in some detail. A very large, rod-shaped bacterium, *Candidatus* Magnetobacterium bavaricum, has been found to inhabit the OAI in the sediments of calcareous freshwater lakes in Bavaria (Spring et al. 1993; Spring and Bazylinski 2000). Cells of this organism biomineralize multiple chains of tooth-shaped crystals of magnetite. A multicellular bacterium, referred to as the many-celled magnetotactic prokaryote (MMP) (Rogers et al. 1990), biomineralizes crystals of iron sulfides (Mann et al. 1990; Farina et al. 1990; Pósfai et al. 1998) and is comprised of about 20–30 cells in a roughly spherical arrangement that moves as an entire unit. There is evidence that suggests that the MMP is a sulfate-reducing bacterium (DeLong et al. 1993) and organisms like it have been found in marine and brackish aquatic habitats around the world.

All studied magnetotactic bacteria are motile by means of flagella and have a cell wall structure characteristic of Gram-negative bacteria (Bazylinski and Frankel 2004). The arrangement of flagella varies between species/strains and can be either polarly monotrichous, bipolar, or in tufts (lophotrichous). The MMP is peritrichously flagellated as a unit but not as individual cells, which are multi-flagellated on only one side (Rogers et al. 1990). It is the only magnetotactic bacterium whose external surface is covered with flagella. Like other flagellated bacteria, magnetotactic bacteria propel themselves through the water by rotating their helical flagella. Because of their magnetosomes, magnetotactic bacteria passively orient and actively migrate along the local magnetic field **B**, which in natural environments is the geomagnetic field. Reported swimming speeds (Table 1) vary between species/strains, from ca. 40 to 1000 μm/s. In general, the magnetotactic spirilla are at the slower end ($<$100 μm/s) (Maratea and Blakemore 1981) and the magnetotactic cocci are at the faster end of the range at $>$100 μm/s (Blakemore 1975; Moench 1988; Cox et al. 2002).

Table 1 Lengths, swimming speeds, and magnetic dipole moments of selected motile microorganisms. Magnetotactic bacterial species are designated with an * in front of their name

Organism	Average cell length μm	Observed swimming speed μm/s	Magnetic moment Am^2	Refs.
* *Magnetospirillum magnetotacticum* strain MS-1	3	44	5.0×10^{-16}	Dunin-Borkowski et al. 1998
* *Candidatus* Magnetobacterium bavaricum	9	40	3.2×10^{-14}	Spring et al. 1993
* Many-celled Magnetotactic Prokaryote (MMP)	8	170/100		Greenberg et al. 2005
* *Candidatus* Bilophococcus magneticus	1	69		Moench 1988
* Unidentified Woods Hole Coccus	1	159	7.0×10^{-16}	Kalmijn 1980
* Coccus "ARB-1"	1	1000		Cox et al. 2002
* Strain MV-1	2		7.0×10^{-16}	Dunin-Borkowski et al. 1998
* Morro Bay greigite-containing Rod	3.6		9.0×10^{-16}	Kasama et al. 2006
Anisonema platysomum (protist)	20		7.0×10^{-13}	Torres de Araujo et al. 1986
Escherichia coli	2	20		Berg 1999
Psuedomonas aeruginosa	1.5	55		Garcia-Pichel 1989
Vibrio comma	4	200		Garcia-Pichel 1989
Thiovulum majus	15	600		Garcia-Pichel 1989

Detection of Magnetotactic Bacteria

Magnetotactic bacteria can be detected and roughly enumerated in environmental samples using phase contrast or differential interference contrast microscopy and a bar magnet or Helmholtz coil pair. In this method, a drop of water and sediment from an environmental sample is placed directly on a microscope slide or on a cover slip which is placed on a rubber o-ring with the drop on the underside (called a hanging drop). The bar magnet is placed on the microscope stage near the drop so the axis of the magnet is parallel to the plane of the slide or cover slip and oriented radial to the drop. The magnetic field (**B**) at the drop should be at least a few gauss. Magnetotactic bacteria in the drop will swim persistently toward or away from the bar magnet and accumulate along the edge of the drop, close to the near pole of the bar magnet or on the other side of the drop farthest away from the near pole. If the magnet is rotated 180°, the bacteria will rotate and swim away from their position toward the opposite side of the drop, i.e., they swim in the same direction relative to **B**. Another 180° rotation of the bar magnet will cause the bacteria to return to the original position at the edge of the drop. Bacteria that swim toward the "south" magnetic pole of the bar magnet, i.e., swim parallel to **B**, are said to have North-seeking (NS) polarity because they would swim northward in the geomagnetic field; bacteria that swim away from the "south" magnetic pole or toward the "north" magnetic pole, i.e., swim antiparallel to **B**, are said to have South-seeking (SS) polarity (Fig. 1). Using this assay, it has been found that magnetotactic bacteria from Northern hemisphere habitats are predominantly NS whereas those from Southern hemisphere habitats are predominantly SS (Blakemore 1975; Blakemore et al. 1980; Kirschvink 1980; Nogueira and Lins de Barros 1995). It should be noted that because of the rapid diffusion of oxygen from the air into the drop, this assay is carried out under oxic conditions. A device, known as a bacteriodrome, in which the magnetic field rotates in the horizontal plane at constant angular velocity, is also useful for detecting bacteria in environmental samples and for measuring some of their magnetic properties (Hanzlik et al. 2002).

Magnetotaxis involves passive orientation and active swimming along the field by bacteria. Cells are not appreciably pulled or pushed by the field which is demonstrated by the fact that killed cells in suspension also orient but do not move along the field. While many magnetotactic bacteria swim persistently in one direction relative to the field under oxic conditions, they are able to reverse direction without turning around under anoxic conditions (Frankel et al. 1997). Other bacteria, particularly magnetotactic spirilla, migrate in both directions along the field with occasional spontaneous reversals of the swimming direction without turning around under both oxic and anoxic conditions (Blakemore 1982; Spormann and Wolfe 1984; Frankel et al. 1997). It

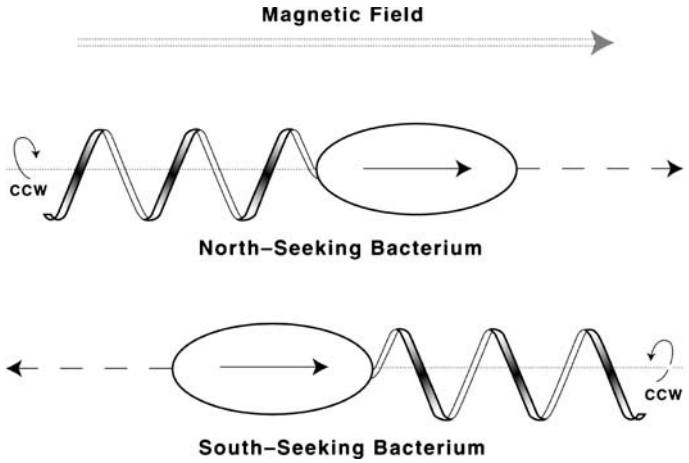

Fig. 1 Transmission electron micrograph of *Magnetospirillum magnetotacticum* showing the chain of magnetosomes. The magnetite crystals incorporated in the magnetosomes have a cuboctahedral morphology and are about 42 nm in diameter. The magnetosome chain is fixed in the cell and the interaction between the magnetic dipole moment associated with the chain and the local magnetic field causes the cell to be oriented along the magnetic field lines. Rotation of the cellular flagella (not shown) causes the cell to migrate along the field lines

should be noted that magnetotaxis is a misnomer, i.e., cells do not swim towards or away from the stimulus (the magnetic field) unlike in other forms of taxis known in bacteria (e.g. phototaxis).

Magnetosomes

All magnetotactic bacteria contain magnetosomes, which are intracellular structures comprising magnetic iron mineral crystals enveloped by a phospholipid bilayer membrane (Gorby et al. 1988). The magnetosome membrane is presumably a structural entity that is anchored to the mineral particles at particular locations in the cell, as well as the locus of biological control over the nucleation and growth of the mineral crystal (Scheffel et al. 2005; Komeili et al. 2004, 2005). The magnetosome magnetic mineral phase consists of magnetite, Fe_3O_4, or greigite, Fe_3S_4. The magnetosome crystals are typically of order 35 to 120 nm in length, which is within the permanent single-magnetic-domain (SD) size range for both minerals, although magnetite crystals with lengths up to 250 nm are known (Spring et al. 1998; McCartney et al. 2001; Lins et al. 2005). In the majority of magnetotactic bacteria, the magnetosomes are organized in one or more straight chains of various lengths parallel to the

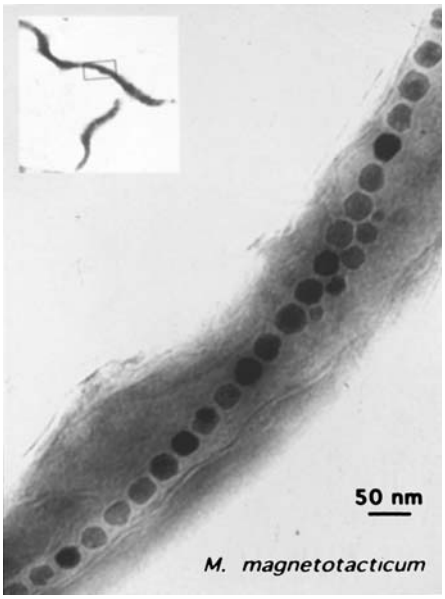

Fig. 2 Schematic representation of magnetotactic NS and SS polarity showing the two possible orientations of the cell's magnetic dipole with respect to the cellular poles (i.e., the flagellum). In both polarities, the magnetic dipole orients parallel to the magnetic field. If both NS and SS cells rotate their flagella ccw under oxic conditions, the cell with NS polarity will migrate parallel to the magnetic field, whereas the cell with SS polarity will migrate antiparallel to the magnetic field. Migration directions under oxic conditions are indicated by *dashed lines*. Under anoxic conditions, the cells switch their flagellar rotation to the opposite sense, and the cells migrate opposite to the direction shown without turning around. The flagellum is a left-handed helix. Just as a left-handed screw advances when turned ccw and retracts when turned cw, ccw and cw flagellar rotation pushes and pulls the cell, respectively

axis of motility of the cell (Fig. 2). Clusters of separate magnetosomes occur in some species, usually at the side of the cell where the flagella are inserted. The narrow size range and consistent morphologies of the magnetosome crystals in each species or strain are clear indications that the magnetotactic bacteria exert a high degree of control over the processes of magnetosome formation. Recent progress in elucidating the biomineralization process and the construction of the magnetosome chain in magnetotactic bacteria will be presented elsewhere in this volume.

All known freshwater magnetotactic bacteria and some marine, estuarine and salt marsh strains have magnetite magnetosomes. Other strains in the latter habitats have greigite magnetosomes. While none of the latter are available in pure culture, recognized greigite-bearing magnetotactic bacteria include the MMP (Mann et al. 1990) and a variety of relatively large, rod-

shaped bacteria (Heywood et al. 1991). The magnetosome greigite crystals are thought to form from non-magnetic precursors including mackinawite (tetragonal FeS) and possibly a sphalerite-type cubic FeS (Pósfai et al. 1998). Some greigite-bearing magnetotactic bacteria contain magnetite and greigite magnetosomes, co-organized within the same magnetosome chains but with distinct morphologies for each mineral (Bazylinski et al. 1993b, 1995).

Cellular Magnetic Dipole

Magnetosomes within the permanent SD size range are uniformly magnetized with the maximum magnetic dipole moment per unit volume. Magnetic crystals larger than SD size are non-uniformly magnetized because of the formation of domain walls or so-called vortex or flower configurations (McCartney et al. 2001). Non-uniform magnetization has the effect of significantly reducing the magnetic moments of the crystals. Crystals with lengths below about 35 nm are superparamagnetic (SPM). Although SPM particles are SD, thermally induced reversals of their magnetic moments result in a time-averaged moment of zero. Thus, by controlling particle size, magnetotactic bacteria optimize the magnetic dipole moment per magnetosome. For magnetosomes arranged in a chain, as in *M. magnetotacticum*, magnetostatic interactions between the SD crystals cause the magnetic moments to spontaneously orient parallel to each other along the chain direction (Frankel 1984; Frankel and Blakemore 1980). This results in a permanent magnetic dipole for the entire chain with a magnetization approaching its saturation value (0.6 T). Since the chain of magnetosomes is fixed within the cell, the entire cell is oriented in the magnetic field by the torque exerted on the magnetic dipole, causing the cell to migrate along the magnetic field as it swims. The permanent magnetic structure of magnetosome chains has been demonstrated by electron holography (Dunin-Borkowski et al. 1998), and by pulsed magnetic field remanence measurements on individual cells (Penninga et al. 1995; Hanzlik et al. 2002).

Reported and estimated magnetic moments of several organisms are shown in Table 1. For the smaller organisms the moments are ca. 1.0×10^{-15} Am^2, and the corresponding magnetic energy in the geomagnetic field of 50 μ Tesla is 5.0×10^{-20} J. This value is greater than thermal energy at room temperature, 4.1×10^{-21} J. The average orientation of a cell along the magnetic field as it swims is determined by the ratio of magnetic to thermal energy (Frankel 1984). For a ratio of 10, the average projection of the magnetic dipole on the magnetic field, $< \cos\Theta > = 0.9$, which means the cell can migrate along the field at 90% of its forward speed. Thus, a magnetotactic bacterium is, in effect, a self-propelled magnetic compass needle.

Magnetotaxis

Adaptiveness of Magnetotaxis

The original model of magnetotaxis was based on the assumption that all magnetotactic bacteria have a polar preference to their swimming direction and are microaerophiles indigenous in sediments (Blakemore 1975; Blakemore and Frankel 1981). The geomagnetic field is inclined downward from horizontal in the Northern Hemisphere and upward in the Southern hemisphere, with the magnitude of inclination increasing from the equator to the poles. NS cells swimming northward in the Northern hemisphere and SS cells swimming southward in the Southern hemisphere would migrate downward towards the sediments along the inclined geomagnetic field lines. Thus, polar magnetotaxis appeared to guide cells in each hemisphere downward to less oxygenated regions of aquatic habitats. Once cells have reached their preferred microhabitat they would presumably stop swimming and adhere to sediment particles until conditions changed, as for example, when additional oxygen was introduced, or when disturbance of the sediments caused them to be displaced into the water column. This theory is supported by the predominant occurrence of NS polar magnetotactic bacteria in the Northern hemisphere and SS polar magnetotactic bacteria in the Southern hemisphere, as determined by the magnetotaxis assay under oxic conditions (Blakemore 1975; Blakemore et al. 1980; Nogueira and Lins de Barros 1995). Because of the negative and positive sign of the geomagnetic field inclination in the Northern and Southern hemispheres, respectively, polar magnetotactic bacteria in both hemispheres therefore swim downward toward the sediments under oxic conditions.

Magneto-Aerotaxis

The discovery of large populations of magnetotactic bacteria at the OAI in the water columns of certain chemically stratified aquatic habitats, and the isolation of obligately microaerophilic, coccoid, magnetotactic bacteria strains in pure culture, has led to a revised view of magnetotaxis (Frankel et al. 1997). The original model did not completely explain how bacteria in the anoxic zone of a water column benefit from magnetotaxis, nor did it explain how the polar magnetotactic cocci such as strain MC-1 form horizontal microaerophilic bands in semi-solid oxygen gradient media instead of accumulating and growing at the bottom of the tube. Bands of strain MC-1 and *M. magnetotacticum* were studied in oxygen concentration gradients in thin, flattened capillaries. When the head space gas was switched from air to pure

N_2, the bands moved up the capillary, eventually to the meniscus. When the N_2 was replaced with air, the bands moved back to their original position. Pure O_2 caused the bands to move further down the capillary. This shows that magnetotaxis and aerotaxis work together in these magnetotactic bacteria. The behavior observed in strain MC-1 and *M. magnetotacticum* has been denoted "magneto-aerotaxis" (Frankel et al. 1997).

Two different magneto-aerotactic mechanisms, polar and axial, have been proposed for strain MC-1 and *M. magnetotacticum*, respectively (Frankel et al. 1997). The magnetotactic bacteria, including magnetotactic cocci in addition to strain MC-1, which swim persistently in one direction along the magnetic field **B** in the hanging drop assay, are polar magneto-aerotactic (NS or SS). Those, including the magnetotactic spirilla in addition to *M. magnetotacticum*, which do not show a polar preference in their swimming direction and swim in either direction along **B** with frequent, spontaneous reversals of swimming direction, are axial magneto-aerotactic. The distinction between NS and SS does not apply to axial magneto-aerotactic bacteria.

Polar Magneto-Aerotaxis

The large majority of naturally occurring magnetotactic bacteria, including many magnetotactic marine and freshwater spirilla, display polar magnetotaxis. Although NS cells swim persistently parallel to **B** under oxic conditions it was demonstrated that under reducing conditions they swim antiparallel to **B** without turning around (Frankel et al. 1997). This suggests that the sense of flagellar rotation (presumably ccw) is unchanged as long as the cells remain under oxic conditions, and furthermore, that the opposite sense of flagellar rotation (cw) occurs under reducing conditions and likewise remains unchanged as long as the cells remain under reducing conditions. Thus, instead of a temporal sensory mechanism, polar magneto-aerotactic cells have a two-state sensory mechanism that determines the sense of flagellar rotation and consequently swimming direction relative to **B** (Fig. 3). Under higher than optimal oxygen tensions, the cell is presumably in an "oxidized state" and cw flagellar rotation causes the cell to migrate persistently parallel to **B**, i.e., downward in the Northern hemisphere. Under reducing conditions, or suboptimal oxygen concentrations, the cell switches to a "reduced state" in which cw flagellar rotation causes the cell to migrate antiparallel to **B** (upward in the Northern hemisphere). The two-state sensing mechanism results in an efficient aerotactic response, provided that the oxygen-gradient is oriented vertically so that it is more or less antiparallel to **B**, guiding the cell back toward the optimal oxygen concentration from either reducing or oxidizing conditions. This is especially important because adaptation, which would lead to spontaneous reversals of the swimming direction, is never observed in controlled experiments with the cocci. This model accounts for the fact that cells

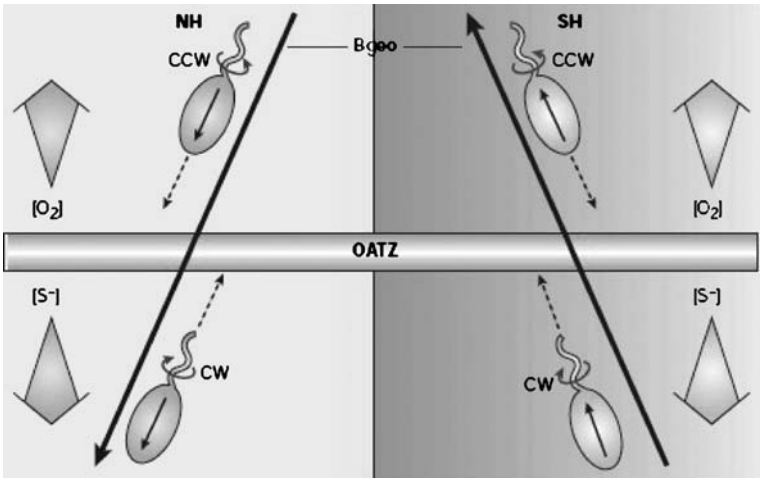

Fig. 3 Schematic showing how polar magneto-aerotaxis keeps cells at the preferred oxygen concentration at the oxic–anoxic interface (OATZ) in chemically stratified water columns and sediments (NH, Northern hemisphere; SH, Southern hemisphere; Bgeo, geomagnetic field). In both hemispheres, cells at higher than optimal oxygen concentration ('oxidized state') swim forward by rotating their flagella counter clockwise (ccw: see Fig. 1), until they reach a lower than optimal oxygen concentration ('reduced state') that switches the sense of flagellar rotation to clockwise (cw), causing the cell to back up without turning around. Note that the geomagnetic field selects for cells with polarity such that ccw flagellar rotation causes cells to swim downward along the magnetic field lines in both hemispheres

swim away from an aerotactic band when the magnetic field is reversed. In this situation, cells do not encounter the redox condition that switches them into the other state and hence do not reverse their swimming direction. It also accounts for the fact that in a capillary with both ends open NS polar bacteria only form a stable band at the end for which the oxygen gradient and B are antiparallel. Unlike the axial cells, polar cells have been observed to stop swimming and remain stationary by attachment to a solid surface or other cells at the optimum oxygen concentration, resuming swimming when the oxygen concentration changes. Finally, in some polar strains exposure to light of short wavelengths (< 500 nm) can switch the cell into the "oxidized state" even in reducing conditions for which the oxygen concentration is suboptimal (Frankel et al. 1997).

The polar magneto-aerotaxis model would also apply to SS polar magneto-aerotactic bacteria if it is assumed that their flagellar rotation is also ccw in the "oxidized" state, and cw in the "reduced" state. In flat capillaries with both ends open, SS bacteria would also form only a single band but at the end of the capillary for which the magnetic field is parallel to the oxygen concentration gradient, i.e., at the other end from that at which the NS band forms.

When a natural sample of sediment and water containing polar magneto-aerotactic bacteria from a Northern hemisphere habitat was incubated in a magnetic field coil which inverts the vertical component of the local magnetic field, it was found that the ratio of SS cells to NS cells increased with time over several weeks until SS cells predominated. This can be understood in terms of a model in which daughter cells in each generation inherit genes for making magnetosomes, but their polarity (NS or SS) is determined by the magnetosomes inherited from the parent cell during cell division. If the parental magnetosomes are divided between the daughter cells, both cells could inherit the parental polarity. But if some cells did not inherit any parental magnetosomes, they would have a 50% probability of acquiring the opposite polarity as they start making magnetosomes. So in each generation, a minority of SS cells might be expected in a predominantly NS population. Since NS cells are favored in the Northern hemisphere, the average fraction of SS cells in the population remains low. However, when the vertical component of the magnetic field is inverted, the SS cells are favored and they eventually become the majority polarity in the population. This process might also occur in a given location during reversals or excursions of the geomagnetic field. A further indication that cell polarity is not determined genetically comes from the fact that SS cells can result when NS cells are pulsed with magnetic fields greater than the coercive force of the magnetosome chain (ca. 300 gauss), with the magnetic pulse oriented opposite to the local background magnetic field.

Axial Magneto-Aerotaxis

The aerotactic, axial magnetotactic spirilla appear to locate and remain at a preferred or optimal oxygen concentration, at which the proton motive force generated by the cell is maximal (Zhulin et al. 1996; Taylor et al. 1999), by means of a temporal sensory mechanism that occurs in many non-magnetotactic, chemotactic bacteria (Berg 1983, 1999). Cells sample the oxygen concentration as they swim and compare the present concentration with that in the recent past. The change in oxygen concentration with time is connected to the probability of switching the sense of flagellar rotation (cw or ccw) and hence the direction of migration. Axial magneto-aerotactic cells moving away from the optimal oxygen concentration toward higher or lower oxygen concentration have an increased probability of reversing the sense of flagellar rotation and hence the direction of migration along **B** which causes them to return to the band. Cells moving toward the optimum oxygen concentration have a decreased probability of reversing the sense of flagellar rotation. At constant oxygen concentration band formation does not occur and the cells revert to an intermediate probability of reversal; this is known as adaptation. In the axial magneto-aerotactic model, the bacteria must be

actively motile in order to quickly measure and respond to local concentration gradients. Since the cells use the magnetic field to provide an axis but not a direction of motility, the relative orientation of **B** and the concentration gradient is unimportant to aerotactic band formation. The combination of a passive alignment along inclined geomagnetic field lines with an active, temporal, aerotactic response provides axial magneto-aerotactic organisms with an efficient mechanism to find the OAI in habitats with vertical, chemical gradient stratification.

Redoxtaxis

It has been suggested that the polar magneto-aerotaxis model could be extended to a more complex redoxtaxis in habitats in which rapid chemical oxidation of reduced chemical species such as sulfur near the OAI results in separated pools of reductants and oxidants (Spring and Bazylinski 2000). For some magnetotactic bacteria, it might be necessary to perform excursions to anoxic zones of their habitat in order to accumulate reduced sulfur compounds. In this situation, polar magnetotaxis could efficiently guide bacteria, either downward to accumulate reduced sulfur species or upward to oxidize stored sulfur with oxygen. The "oxidized state" would result from the almost complete consumption of stored sulfur or another electron donor, and the cells would swim parallel to **B** toward deeper anoxic layers where they could replenish the depleted stock of electron donor using nitrate or other compounds as an alternative electron acceptor. Finally, they would reach a "reduced state" in which the electron acceptor is depleted. In this state the cells would swim antiparallel to **B** to return to the microoxic zone where oxygen is available to them as an electron acceptor. The advantage of polar magnetotaxis is that an oxygen concentration gradient is not necessary for efficient orientation in the anoxic zone, thereby enabling a rapid return of the cell along relatively large distances to the preferred microoxic conditions. A further benefit would be that cells avoid the waste of energy by constant movement along gradients, but instead can attach to particles in preferred microniches until they reach an unfavorable internal redox state that triggers a magnetotactic response either parallel or antiparallel to the geomagnetic field lines. In any case, greater than optimal concentrations of oxygen would switch cells immediately to the "oxidized state" provoking the typical down-seeking response of magnetotactic bacteria under oxic conditions.

Cells of MC-1, like other uncultivated magnetotactic cocci, are small (ca. 1 μm diameter) with twin, multiflagellar bundles on one side of the cell. Magnetotactic cocci have been reported to swim at speeds in excess of 100 μm/s (about 100 body lengths per second) (e.g., Moench 1988; Cox et al. 2002). In $[O_2]$ gradients in flat, thin capillaries, cells of MC-1 form microaerophilic bands of cells (Frankel et al. 1997). Some cells within the band make long,

straight traverses through the band whereas others stop swimming and attach to the walls of the capillary or to each other at the OAI. Cells thus appear to alternate between active swimming and sessile behavior.

Cells of strain MC-1 grow chemolithoautotrophically with sulfide and other reduced sulfur sources as electron donors and molecular oxygen as the terminal electron acceptor (Williams et al. 2006). In addition, these cells also fix atmospheric dinitrogen (Bazylinski, unpublished data). This is presumably true for other magnetotactic cocci that inhabit the OAI in many marine and brackish habitats (Simmons et al. 2006). However, oxidation of S^{2-} by O_2 is autocatalytic, so an inverse $[O_2]/[S^{2-}]$ double gradient (from the downward diffusion of O_2 from air at the surface and the upward diffusion of S^{2-} from the anaerobic zone through the action of sulfate-reducing bacteria) will form even without the presence of bacteria. Consumption of S^{2-} and O_2 by bacteria at the OAI makes the gradients steeper. The coexistence or overlap region (both O_2 and S^{2-} present together) is only a few hundred μm deep (Schultz and Jorgensen 2001) and has very low (< 1 μM) concentrations of both O_2 and S^{2-}. Thus, cells have to contend with relatively low nutrient concentrations, as well as diffusion-limited flux of S^{2-} from below and O_2 from above into the overlap region.

Nutrient limitation is a fact of life in many marine habitats, and results in predominantly small, fast swimming cells (Mitchell 1991). Smaller cells require lower amounts of nutrients to grow and their higher surface to volume ratio ($S/V \sim 1/R$), increases their rate of nutrient uptake relative to their nutrient requirement. This is especially advantageous in low nutrient conditions. However, consumption of nutrients results in a greater local depletion because of diffusion limitation. Cells can solve this problem by swimming and relying on chemotaxis to find areas of locally higher nutrient concentration. At minimum, cells have to swim fast and straight enough to outrun nutrient diffusion (about 30 μm/s for 1 s) (Purcell 1977). However, small cells lose their heading in times of the order of milliseconds from buffeting by Brownian motion. One solution is swimming faster so as to get farther before going off course, which is presumably the reason why small cells that swim fast are the rule in marine environments (Mitchell 1991). However, faster swimming also burns more cellular energy because the viscous drag on cells depends on their velocity, so swimming must result in increased access to nutrients.

Cells of strain MC-1 and similar marine magnetotactic cocci with bilophotrichous flagellation are fast swimmers, yet have their magnetic dipole to keep their heading. As noted above, fast swimming perhaps allows them to make traverses from one side of the overlap region to the other to sequentially access higher concentrations of S^{2-} and O_2. However, small cells such as the cocci have low carrying capacity so they have to make shorter, more frequent, traversals than larger cells. In this case, the horizontal chemical stratification could guarantee a payoff that would cover the cost of fast swimming. Then why do cells of strain MC-1 sometimes stop swimming, as seen in the bands in the flat capillaries? The answer might involve the N_2-fixing en-

zyme nitrogenase. Nitrogen fixation is energy demanding and only occurs at O_2 concentrations less than about 5 μM (Zhulin et al. 1996). As noted above, the O_2 concentration in the overlap region is less than that so cells can fix N_2 there. If a cell is fixing N_2, its energy balance might improve if it stops swimming altogether.

Cells of *M. magnetotacticum*, like all other magnetospirilla, have a single flagellum at both poles of the cell and swim at about 40 μm/s, forwards and backwards with equal facility. Cultivated cells grow heterotrophically on certain organic acids (e.g., succinic acid) as an electron source with O_2 or nitrate as the terminal electron acceptor (Bazylinski and Blakemore 1983). When O_2 is the only electron acceptor available in [O_2] gradients, cells form microaerophilic bands, seeking a preferred O_2 concentration that presumably maximizes the proton motive force generated by transfer of electrons (Zhulin et al. 1996; Taylor et al. 1999). Cells are in constant motion making straight-line excursions above and below the band. However, because there is no autocatalytic oxidation of electron donor by acceptor, access to nutrients is mostly limited by the diffusion of O_2 and electron source and consumption by the cells. In this situation, cells need only outrun diffusion in order to access increased concentrations of electron donor and acceptor below and above the preferred O_2 concentration, respectively. There is no need to incur the cost of faster swimming because the cellular magnetic dipole allows cells to maintain their heading, minimizing the straight run time for temporal chemotaxis (Berg 1983, 1999). Cells of the magnetospirilla, like those of strain MC-1, also fix N_2, but since they do not expend as much energy swimming as does MC-1, they likely do not need to stop swimming to conserve energy for N_2 fixation.

It should be noted that the situation for cells in situ in natural environments for the magnetospirilla might be more complex than that for the magnetotactic cocci. The fact that cells of magnetotactic spirilla collected from natural environments often display polar magnetotaxis in the hanging drop assay might indicate this. Many of the magnetotactic cocci collected from natural environments contain sulfur-rich globules suggesting they are actively oxidizing S^{2-} at the OAI. Many of the cultivated magnetospirilla possess genes encoding for cbbM, a type II ribulose-1,5-bisphosphate carboxylase/oxygenase, a key enzyme of the Calvin–Benson–Bassham cycle for autotrophy (Bazylinski and Williams, 2006, in this volume). Thus, the magnetospirilla might be able to grow chemolithoautotrophically like strain MC-1 and may also use inorganic electron donors as well as organic ones.

Deviations from the Magneto-Aerotaxis Models

Polar magneto-aerotaxis has been observed in some of the freshwater spirilla (D. Schüler, 2006, personal communication), bacteria that are nom-

inally axial magneto-aerotactic. Magnetic polarity was most pronounced in strains that were freshly isolated but was gradually lost upon repeated subcultivation. Polar magnetotaxis has also been observed in cells of *M. gryphiswaldense* (D. Schüler, 2006, personal communication) and *M. magnetotacticum* (D.A. Bazylinski, unpublished data) grown in semi-solid [O_2]-gradient medium and in highly reduced medium under the microscope. However, these experiments were not entirely reproducible and thus the trigger that causes axially magneto-aerotactic cells to switch into polarly magneto-aerotactic cells is not known. Since the difference between axial and polar magneto-aerotaxis at the molecular level is not known, it is possible that the two models represent the endpoints of a continuum of responses.

The predominance of freshwater, south-seeking, magnetotactic cocci in a pond in the Northern hemisphere was reported by Cox et al. (2002) without discussion. Simmons et al. (2006) recently observed a population of uncultured, marine magnetotactic bacterium, collected from the anoxic zone of a coastal pond in the Northern hemisphere, that were primarily SS under oxic conditions in the hanging drop assay. Other, polar magnetotactic, bacteria in the sample were generally NS as expected although on occasion the ratio of SS to NS cells was greater than 0.1. Since the SS cells were not identified, it is not clear whether they are microaerophiles, leaving open the possibility that they use the magnetic field to find a preferred position in a vertical concentration gradient of a molecule or ion other than O_2 or at a specific oxidation–reduction potential. If the organism turns out to be microaerophilic, then the SS response is difficult to understand on the basis of the magneto-aerotaxis models. However, since the cells do not migrate up to the surface of the pond, something must cause them to reverse direction and swim downward in the water column. Alternatively, they may not be actively swimming and may be attached to particles. The solution to this intriguing mystery will probably require examination of the motility of the cells in an oxygen concentration gradient.

Finally, the magneto-aerotaxis model comprises passive magnetic orientation and active swimming due to flagellar rotation with the rotation sense determined by oxygen or redox sensing. On the basis of analysis of kinematics in magnetic fields, Greenberg et al. (2005) have proposed that the MMP may have magnetoreception, i.e., a magnetic field-sensing mechanism.

Bacterial Hemerythrins, [O_2]-Sensing, and Magneto-Aerotaxis

Hemerythrins are a group of O_2-handling proteins originally identified in certain marine invertebrates including sipunculids, priapulids, annelids, and brachiopods (Dunn et al. 1977; Vergote et al. 2004). Many prokaryotes are known to have open reading frames (ORFs) that encode for putative hemerythrins including proteins with hemerythrin-like domains. On the

basis of the large number of these ORFs encoding for hemerythrin-like proteins identified in genomes, magnetotactic bacteria appear to contain the highest number of hemerythrin-like proteins among the prokaryotes. The genomes of *M. magnetotacticum*, *M. magneticum* and strain MC-1 each contain approximately 30 or more ORFs that encode for putative proteins with hemerythrin-like domains. None of these proteins have been characterized, however. Given that magnetotactic bacteria occur predominantly at the OAI and/or anoxic regions of the water column, O_2-binding proteins such as hemerythrins may serve as a sensory mechanism for O_2, and thus play a key role in magneto-aerotaxis.

Hemerythrin domains contain a sequence motif that includes five histidine residues and two carboxylate ligands that coordinate two iron atoms; reversible O_2-binding occurs at the diiron site located in a hydrophobic pocket of the protein (Stenkamp et al. 1985). Thus, these hemerythrins, both eukaryotic and prokaryotic, share certain conserved amino acid residues associated with the diiron site, in the form of the motifs H... HxxxE... HxxxH... HxxxxD (where H = histidine, E = glutamate, D = aspartate, and x_n = conserved spacer region) (Stenkamp et al. 1985; C.E. French, 2006, personal communication). These putative hemerythrins include short (≤ 200 amino acid residues) single-domain proteins, such as the hemerythrin-like protein McHr (131 amino acid residues) of the methanotrophic bacterium *Methylococcus capsulatus* (Karlsen et al. 2005), as well as longer proteins in which the hemerythrin-like domain is associated with one or more other domains (especially those involved in signal transduction), such as the multi-domain protein DcrH (959 residues) from the bacterial sulfate-reducing bacterium *Desulfovibrio vulgaris* (Xiong et al. 2000). For magnetotactic bacteria, some ORFs that encode for putative hemerythrin-like proteins are located within the magnetosome membrane protein gene islands in strain MC-1 (Mmc1DRAFT_1515 from draft genome) and *M. gryphiswaldense* (ORF12, ORF13; Schübbe et al. 2003; Ullrich et al. 2005). Two adjacent ORFs that encode putative proteins with hemerythrin-like domains have been identified in the genome of the magnetotactic vibrio strain MV-1, although it is not known if these ORFs are situated within the magnetosome island (D.A. Bazylinski, unpublished). One of these MV-1 hemerythrin-like proteins is of a single-domain kind (202 residues). The other (748 residues) contains multiple domains, including two histidine kinase-like domains (the second of these a putative histidine kinase-like ATPase) followed by a hemerythrin-like domain and a carboxy terminus signal receiver domain (Fig. 4). Other putative multi-domain proteins from other magnetotactic bacteria also include hemerythrin domains associated with signal transduction domains (e.g., histidine kinases, methyl-accepting chemotaxis proteins).

In marine invertebrates, hemerythrin is used for O_2 transport between tissues (Stenkamp et al. 1985). The function of hemerythrins in prokaryotes is unclear, and they may perform disparate functions in different or-

Fig. 4 Domain structure of a putative hemerythrin-like protein predicted from an ORF identified in the genome of the magnetotactic vibrio strain MV-1, based on translation of ORF, showing the following putative domains: HisKA (histidine kinase A), HATPase (histidine kinase-like ATPase), hemerythrin, and REC (signal receiver domain). Polypeptide is 748 amino acid residues long

ganisms. The putative chemotaxis protein DcrH from *D. vulgaris* contains a hemerythrin-like domain at the carboxy terminus, and has been suggested to have a role in O_2-sensing (Xiong et al. 2000). The hemerythrin-like McHr protein from *Meth. capsulatus*, may furnish oxygen-dependent enzymes with O_2 (Karlsen et al. 2005). It has also been suggested that hemerythrin is part of a detoxification mechanism for bacteria that have a low tolerance for O_2 (anaerobes, microaerophiles) (Xiong et al. 2000). Many motile bacteria are exposed to variable [O_2], and, like magnetotactic bacteria, may selectively migrate to anoxic and oxic conditions (such as to obtain electron donors and acceptors, respectively), so hemerythrins may serve to differentially bind and release O_2 (C.E. French, 2006, personal communication). For magnetotactic bacteria migrating within and through the OAI, hemerythrins may serve to bind O_2 when the cell is exposed to elevated O_2 concentrations, and then release the O_2 when the cell descends into anoxic conditions (C.E. French, 2006, personal communication). Multi-domain proteins with both signal transduction and hemerythrin domains suggests a role in O_2-sensing, as proposed for DcrH in *D. vulgaris* (Xiong et al. 2000). Even single-domain hemerythrins may serve a sensory function, if they are co-transcribed and/or acting with signal transduction proteins. Given the prevalence of hemerythrin-like ORFs in the known genomes of magnetotactic bacteria, including those within the magnetosome protein gene island (Ullrich et al. 2005), hemerythrins may play a role in magneto-aerotaxis (including directing flagellar rotation). However, this has yet to be determined.

The genomes of *M. magnetotacticum*, *M. magneticum*, and strain MC-1 show numerous ORFs that encode for putative proteins with PAS domains, providing many potential candidate genes for the identification of aero-, redox-, and (perhaps) phototaxis in these bacteria. In bacteria, PAS domains are responsible for sensing stimuli such as [O_2], redox potential, and light (Taylor and Zhulin 1999; Repik et al. 2000; Watts et al. 2006). For example, the aerotaxis receptor (Aer) responds to oxygen concentration in the environment, and is the first step in the intracellular pathway that governs the sense of flagellar rotation in *Escherichia coli* (Watts et al. 2006). As mentioned above, the polarly magneto-aerotactic coccus, strain MC-1, display a negative phototaxis in response to short-wavelength light, but the mechanism is unknown. It is difficult to infer the precise identity of the stimulus that the

PAS-containing protein is sensitive to based on amino acid sequence alone. This is also the case for the numerous ORFs that encode putative methyl-accepting chemotaxis proteins in *M. magnetotacticum*, *M. magneticum*, and MC-1, including putative hemerythrins.

In *Magnetospirillum* species and strain MC-1, the genes for the proteins implicated in magnetosome biosynthesis are located within a genomic island. In *M. gryphiswaldense* the magnetosome genes are located within a hypervariable 130-kb stretch of the genome within the magnetosome island (Schübbe et al. 2003; Ulrich et al. 2005). In *M. gryphiswaldense*, the genes for MamA, MamB, MamJ and MamK are located on the *mamAB* operon, and the genes for MamC and MamD are located on the *mamDC* operon (Schübbe et al. 2003; Ulrich et al. 2005). Functions for magnetosome-membrane associated proteins have been determined for MamJ and MamK. MamJ was demonstrated to be essential for the assembly of magnetosome chains in *M. gryphidwaldense*, probably through interaction with MamK (Scheffel et al. 2005); and MamK appears to be involved in the formation of a network of actin-like filaments that comprise the magnetosomal cytoskeleton and is responsible for the linear chain-like alignment of magnetosomes within the cell (Komeili et al. 2005). The presence of hemerythrin-like genes in the magnetosome islands may imply some interaction between magnetosome synthesis and O_2-handling mediated by hemerythrins, but this remains to be elucidated. In *M. gryphiswaldense*, two putative hemerythrin ORFs (ORF12, OR13) are located between the *mamAB* and *mamDC* operons (Schübbe et al. 2003).

Questions about Magnetotaxis

Magnetotactic bacteria have solved the problem of constructing an internal, permanent, magnetic dipole that is sufficiently robust so that a cell will be oriented along the geomagnetic field as it swims, yet be no longer than the length of the cell itself (ca. 1–2 μm). The solution, the magnetosome chain, is very elegant and efficient in that it makes maximum use of the minimum amount of magnetite, assuming that cells want to maximize the ratio of magnetic moment to volume of magnetite. Since magnetite is four times more magnetic than the same volume of greigite, why do some magnetotactic bacteria biomineralize greigite? This question is particularly acute for those cells that contain both magnetite and greigite magnetosomes co-organized in the same chains. Why not all magnetite? Also, SD magnetite is a clear winner over multidomain magnetite for making permanent magnets. So why are there magnetotactic bacteria that make magnetosomes up to 250 nm in length, larger than SD, hence with a lower magnetic moment per unit volume? Since arranging magnetosomes in chains is so efficient,

why do some species have dispersed clusters of magnetosomes? From the magnetism point of view, this is not as efficient as alignment in chains, because it requires the cell to align the long axes of all magnetosomes parallel to each other. Might there be other, non-magnetic roles for magnetite in cells? Possibilities include the storage and sequestration of iron as an electron acceptor/donor reserve although the iron present in magnetosomes has never been shown to be utilized by cells. Moreover, there is evidence that some species cannot utilize the iron in magnetite-containing magnetosomes and will continue to synthesize magnetosomes and limit their growth under iron-limiting conditions (Dubbels et al. 2004). Also, magnetite crystals can disproportionate H_2O_2, and probably oxygen radicals produced during aerobic respiration, suggesting magnetite magnetosomes could be an elementary catalase, or have another catalytic role. Cu, a potentially toxic element, is sometimes found in greigite magnetosomes, which suggests a possible detoxification role (Bazylinski et al. 1993a). Free iron ions within the cell are also toxic through the generation of highly reactive and toxic oxygen species such as hydroxyl radicals (Halliwell and Gutteridge 1984). The toxic effect of these ions could be eliminated by concentrating the free iron ions in a relatively inert mineral like magnetite. But this doesn't explain why the cell takes up so much iron in the first place.

There are also questions about magnetotaxis itself (Frankel and Bazylinski 2004). There are many microaerophilic organisms, including non-magnetic mutants of magnetotactic bacteria, which form aerotactic bands without the aid of magnetism. Simulations of axial magnetotactic bacteria confirm the fact that magneto-aerotaxis is more efficient than aerotaxis alone for finding the optimal $[O_2]$, meaning magnetotactic bacteria would find the optimal concentration before non-magnetic aerotactic bacteria with the same swimming speed, but only at high inclinations of the geomagnetic field. Many polar magnetotactic bacteria are fast swimmers, ca. 100 body lengths per second or more, so the efficiency argument may hold over a greater range of geomagnetic inclination for these organisms. Nevertheless, the question of whether aerotactic efficiency alone is sufficient to account for the persistence of magnetotaxis in bacteria over geologic time scales is still open.

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