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Review

Magnetotactic bacteria, magnetosomes and their application

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ABSTRACT

Magnetotactic bacteria (MTB) are a diverse group of microorganisms with the ability to orient and migrate along geomagnetic field lines. This unique feat is based on specific intracellular organelles, the magnetosomes, which, in most MTB, comprise nanometer-sized, membrane bound crystals of magnetic iron minerals and organized into chains *via* a dedicated cytoskeleton. Because of the special properties of the magnetosomes, MTB are of great interest for paleomagnetism, environmental magnetism, biomarkers in rocks, magnetic materials and biomineralization in organisms, and bacterial magnetites have been exploited for a variety of applications in modern biological and medical sciences. In this paper, we describe general characteristics of MTB and their magnetic mineral inclusions, but focus mainly on the magnetosome formation and the magnetisms of MTB and bacterial magnetosomes, as well as on the significances and applications of MTB and their intracellular magnetic mineral crystals.

Contents

1. Introduction

MTB are a group of Gram-negative prokaryotes that passively align and actively swim along the geomagnetic field and other fields (Bazylinski and Williams 2007). This ability is based on specific intracellular structures, the magnetosomes, which, in most MTB, are nanometer-sized, membrane-bound crystals of the magnetic iron minerals magnetite (Fe_3O_4) or greigite (Fe_3S_4) (Lefèvre et al. 2011). These intriguing microorganisms were first documented by Salvatore Bellini as early as 1963 (Jogler and Schüler 2009). He microscopically observed a certain group of bacteria swam toward the Earth's North Pole and hence named them "magnetosensitive bacteria". Eleven years later, Blakemore (1975) independently described these microorganisms and coined the terms magnetotaxis for the phenomena and MTB for the bacteria. The discovery of MTB proved to have a serious impact in a number of diverse research fields including microbiology, geology, mineralogy and biomineralization, crystallography, chemistry, biochemistry, physics, limnology and oceanography, and even astrobiology (Bazylinski and Schübbe 2007).

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Despite the ubiquitous occurrence of MTB and their high abundance in the sediments of many freshwater and marine habitats, the isolation and cultivation of MTB are difficult due to their fastidious lifestyle (Postec et al. 2012). Because of this, the research in this area has been slow at times. However, with the development in biotechnology and magneto-technology, some progress has been made in laboratory MTB culture, biomineralization, ecology of MTB, magnetisms of MTB and magnetosomes, and identification of fossil magnetosomes in sediments.

The goal of this review is to give a broad overview over the current knowledge of the physiology, ecology, phylogeny, and molecular biology of MTB. Further, we will summarize new insights into the general feature and formation mechanism of magnetosomes. And what is more, the magnetism, significance, and application of MTB and magnetosomes will be presented. Finally, we will briefly discuss some related perspectives and possible directions for future studies.

2. Magnetotactic bacteria

2.1. Physiology, ecology, and phylogeny of MTB

MTB are commonly distributed in water columns or sediments with vertical chemical stratification (Bazylinski and Williams 2007). They can propel themselves through the water by rotating their helical flagella. One interesting microbiological aspect of MTB is that they can swim at speeds nearly twice that of *Escherichia coli* cells in spite of being larger in size and in spite of having less flagellar proteins (Sharma et al. 2008). Further, in presence of magnetic fields, different strains of MTB show different morphological properties and adjustments as swimmers, presumably due to intracellular magnetosome arrangements (Sharma et al. 2007). These observations highlight the interesting diversity of microbiological species. Generally, they swim to the magnetic north in the northern hemisphere, to the magnetic south in the southern hemisphere, and both ways on the geomagnetic equator (Lefèvre et al. 2011). Almost all the MTB are microaerophiles or anaerobes or facultatively anaerobic microaerophiles. Therefore, they are generally found in relatively high cell numbers at the oxic–anoxic interface (OAI) and the anoxic regions of the habitat or both (Bazylinski and Williams 2007). MTB have been shown to be the dominant species of the bacterial population in some environments, implying a remarkable ecological significance (Spring et al. 1993). The sulfate concentration in freshwater systems is very low and the OAI is located on the water-sediment interface or several millimeters below it (Bazylinski and Schübbe 2007).

The MTB of various morphological types have been found from the freshwater sediments (Thornhill et al. 1994; Amann et al. 2006), including bacillus, vibrios, spirilla, cocci, and multicellular forms (Fig. 1). MTB are known to produce two types of minerals, *i.e.*, iron oxides and iron sulfides (Bazylinski and Frankel 2004). Those that produce iron oxides only biomineralize magnetite (Fe_3O_4) (Frankel et al. 1979), those that only produce iron sulfides biomineralize greigite (Fe_3S_4) (Heywood et al. 1990), and those that both produce iron oxide magnetite (Fe_3O_4) and iron sulfide greigite (Fe_3S_4) (Bazylinski et al. 1995). In freshwater systems, only iron oxide-producing MTB have been found (Faivre and Schüler 2008). Recently, MTB were found in freshwater in Lake Miyun, northern China (Lin et al. 2009). Moreover, MTB were also detected in extreme environments. Mono Lake, located in California in the United States, is an alkaline and saline lake which is iron limited due to the low solubility of the metal at high pH. Nevertheless, MTB were still found in this environment (Faivre and Schüler 2008). In addition, various magnetic cocci were discovered in mud sediments which have a high content of organic matter (Flies et al. 2005). The distribution of OAI in marine and freshwater is similar, but in many mostly undisturbed marine coastal habitats, the situation is markedly different (Bazylinski and Williams 2007). MTB which can produce both iron oxide and iron sulfide are present in marine and lake environments (Faivre and Schüler 2008). A wide variety of MTB were found in salt marshes, particularly in the surface layers of sulfidic sediments where they co-occur with sulfide oxidizing bacteria (Simmons and Edwards 2007). Large quantities of marine magnetotactic cocci were found in a seawater pond within an intertidal zone at Huiquan Bay in the China Sea (Pan et al. 2008). A marine magnetotactic spirillum was isolated and characterized from an intertidal zone of the China Sea (Zhu et al. 2010). It is reported that in some harbor with chemical stratification, various chemicals can create vertical concentration gradient with depth in the water, MTB were also found in the aqueous layer in microaerobic zone of this environment (Bazylinski et al. 1995).

Only a limited number of MTB have been isolated in pure culture so far (Arakaki et al. 2008). Among them, *Magnetospirillum gryphiswaldense* MSR-1, *Magnetospirillum magneticum* AMB-1, *Magnetospirillum magneticum* MGT-1, *Magnetovibrio* MV-1, *Magnetococcus* sp. MC-1, Marine magnetic spirillum QH-2, *Magnetospirillum* sp. WM-1 and *Magnetospirillum magnetotacticum* MS-1 are all affiliated to the α-*Proteobacteria*; *Desulfovibrio magneticus* RS-1 is affiliated to the δ-*Proteobacteria* (Fig. 2). Additionally, the 16S rDNA analysis of uncultured MTB was also reported. Previous studies (Keim et al. 2004; Simmons et al. 2004) suggested that different sources of multicellular magnetotactic prokaryotes are affiliated to the δ-*Proteobacteria*. It has been reported that the *Corynebacterium* tentatively named *Magnetobacterium bavaricum* is affiliated to *Nitrospira* (Fig. 2). 16S rDNA analysis of MTB MHB-1 was carried out by Flies et al. (2005) and the results showed that the sequence homology of MHB-1 with *M. bavaricum* was 91.0%.

2.2. Molecular biology of MTB

M. magnetotacticum MS-1 was first used for molecular genetic study (Schüler and Frankel 1999). It was suggested that some genes of this bacterium can be expressed in *E. coli*, the transcription and translation elements of the two microorganisms are compatible, which is necessary for molecular genetic manipulation (Waleh 1988). The *rec*A gene of this organism was cloned and expressed in *E. coli* by Berson et al. (2006). They cloned a 2 kb DNA fragment from *M. magnetotacticum* MS-1 that complemented iron-uptake deficiencies in *E. coli* and *Salmonella typhimurium* mutants lacking a functional *aro*D gene. These indicate that this 2 kb DNA may regulate the uptake of iron (Berson et al. 2006).

Development of MTB culture technology on agar plate provides the possibility of screening nonmagnetic mutants which have no magnetosomes. Non-magnetic mutant of *M. magneticum* AMB-1 in which Tn5 was shown to be integrated into the chromosome were obtained on agar plate (Matsunaga et al. 1992). Using transposon mutagenesis, Nakamura et al. (1995) identified a gene, designated *mag*A, that encodes for a protein with significant sequence homology to the cation efflux proteins, KefC, a potassium-ion-translocating protein in *E. coli*. The gene of *mag*A was expressed in *E. coli* and inverted membrane vesicles prepared from *E. coli* cells indicated that energy was required for iron transport (Nakamura et al. 1995). The expression of *mag*A was higher when wild-type *M. magneticum* AMB-1 cells were grown under iron-limited conditions rather than iron-sufficient conditions in which they would produce more magnetosomes (Nakamura et al. 1995). Therefore, the role of the *mag*A gene in magnetosome formation is uncertain. However, recent reports suggested that *mag*A could serve as a candidate for a genetically encoded contrast agent for magnetic resonance imaging (MRI) (Goldhawk et al. 2009). Wahyudi et al. (2003) identified a gene, designated as *aor*, that encodes

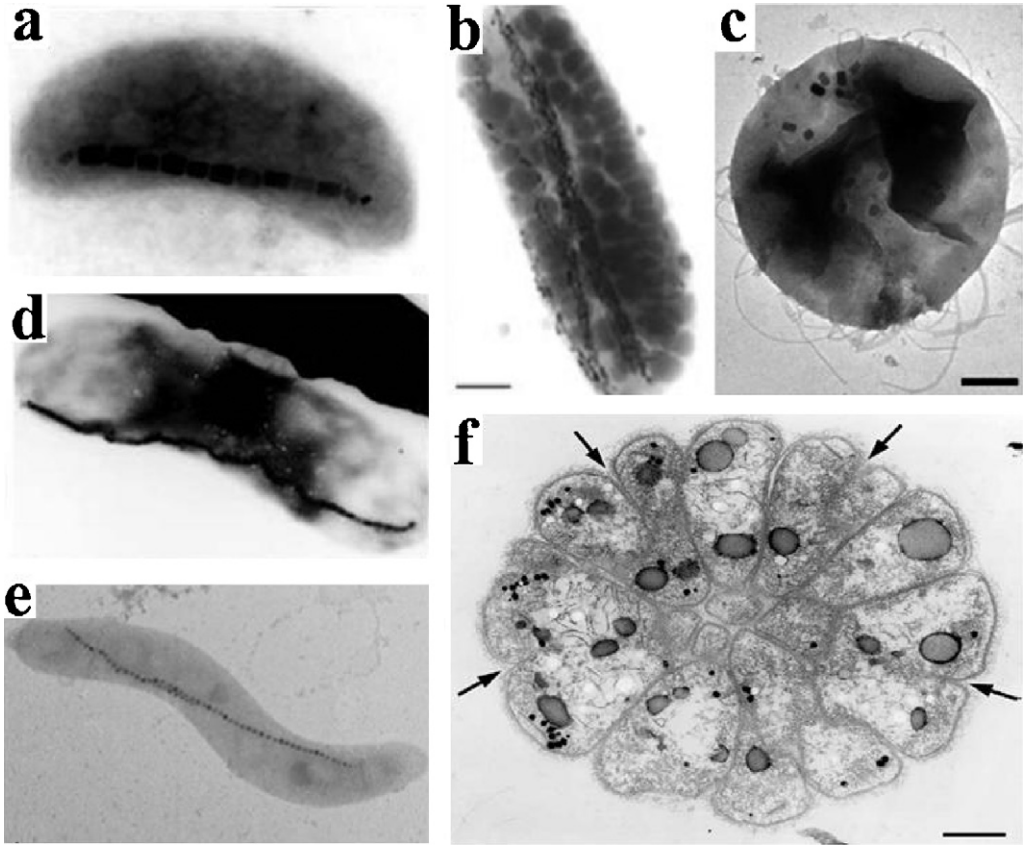

Fig. 1. Various morphology of MTB, vibrios: a; rods: b (Bar = 1.0 μm) and d; coccoid: c (Bar = 200 nm); spirilla: e; multicellular organism: f (Bar = 1.0 μm). Figure a and d reproduced from Scheffel and Schüler (2006), figure b reproduced from Baumgartner and Faivre (2011), figure c reproduced from Lefèvre et al. (2011), with permission from Springer. Figure e and f reproduced from Schüler (2008) and Keim et al. (2004), respectively, with permission from John Wiley and Sons.

for a protein with homology to the tungsten-containing aldehyde ferredoxin oxidoreductase (AOR) from *Pyrococcus furiosus*, which functions for aldehyde oxidation. The gene of *aor* was found to be expressed under microaerobic conditions and localized in the cytoplasm of *M. magneticum* AMB-1 (Wahyudi et al. 2003). Additionally, iron uptake and growth of non-magnetic mutant of *M. magneticum* AMB-1 were lower than wild type. These indicated that *aor* gene may contribute to ferric iron reduction during magnetosome formation in *M. magneticum* AMB-1 under microaerobic respiration. Calugay et al. (2004) inserted Tn5 transposon into an open reading frame (ORF) coding for a periplasmic transport binding protein kinase gene homolog. The growth inhibition imposed by the exogenous non-assimilable iron chelator nitrilotriacetate was relieved in wild type but not in non-magnetic mutant of *M. magneticum* AMB-1, by the addition of the isolated wild type siderophore (Calugay et al. 2004). These implied that the interruption of periplasmic transport binding protein kinase gene homologue is required for siderophore transport into *M. magneticum* AMB-1.

Using reverse genetics, the *mam*22 gene was cloned in *M. magnetotacticum* MS-1 (Okuda et al. 1996) and a gene encoding for a homologous protein, *mam*A, was found in *M. gryphiswaldense* MSR-1, *M. magneticum* AMB-1, and *Magnetococcus* sp. MC-1 (Grunberg et al. 2001; Komeili et al. 2004; Amemiya et al. 2005). Okuda et al. (1996) used the N-terminal amino acid sequence from a 22 kDa protein specifically associated with the magnetosome membrane to clone and sequence its gene. On the basis of the amino acid sequence, the protein shows high homology to protein of the tetratricopeptide repeat (TPR) protein family (Okuda et al. 1996). However, the function of the protein in magnetosome formation is still unclear. A deletion of *mam*A in *M. magneticum* AMB-1 resulted in shorter magnetosome chains and it was concluded that *mam*A is required for functional magnetosome vesicle formation (Komeili et al. 2004). Recent study showed that the loss of *mam*A resulted in the change of the number of crystals produced per cell, while the formation of the magnetosome membrane was not affected (Murat et al. 2010). The majority of the genes essentially participating in magnetosome formation are grouped in four conserved gene clusters present within a large unstable genomic region called the magnetosome island (MAI) (Murat et al. 2010). Although the size and gene content of the MAI vary significantly between species, this region shares common characteristics in all MTB analyzed thus far: it is well conserved; it has a low GC content; it is located between two repetitive sequences; and an integrase is present in the flanking region of the first repetitive sequence (Matsunaga et al. 2007; Lefèvre et al. 2011). Dynamic analysis of MAI in *M. magneticum* AMB-1 revealed that this region as undergone a lateral gene transfer (Fukuda et al. 2006). Similar genomic regions have been found in the genomes of other MTB (Schübbe et al. 2003; Ullrich et al. 2005; Richter et al. 2007).

The genomic DNA of four strains of MTB, including two facultatively anaerobic vibrios, *Magnetovibrio* MV-1 and *Magnetovibrio* MV-2, a microaerophilic cocci, *Magnetococcus* sp. MC-1, and an obligate microaerophilic spirillum, *M. magnetotacticum* MS-1 was analyzed by pulsed-field gel electrophoresis (PFGE) (Dean and Bazylinski 1999; Bertani et al. 2001). Results revealed that genome sizes of strains MV-1, MV-2, MC-1, and MS-1were estimated to be 3.7 Mb, 3.6 Mb, 4.5 Mb, and 4.3 Mb, respectively. The high similarity observed between the restriction fragments of MV-1 and MV-2 indicated that the strains were closely related (Dean and Bazylinski 1999). Genomic DNA of these strains exhibits

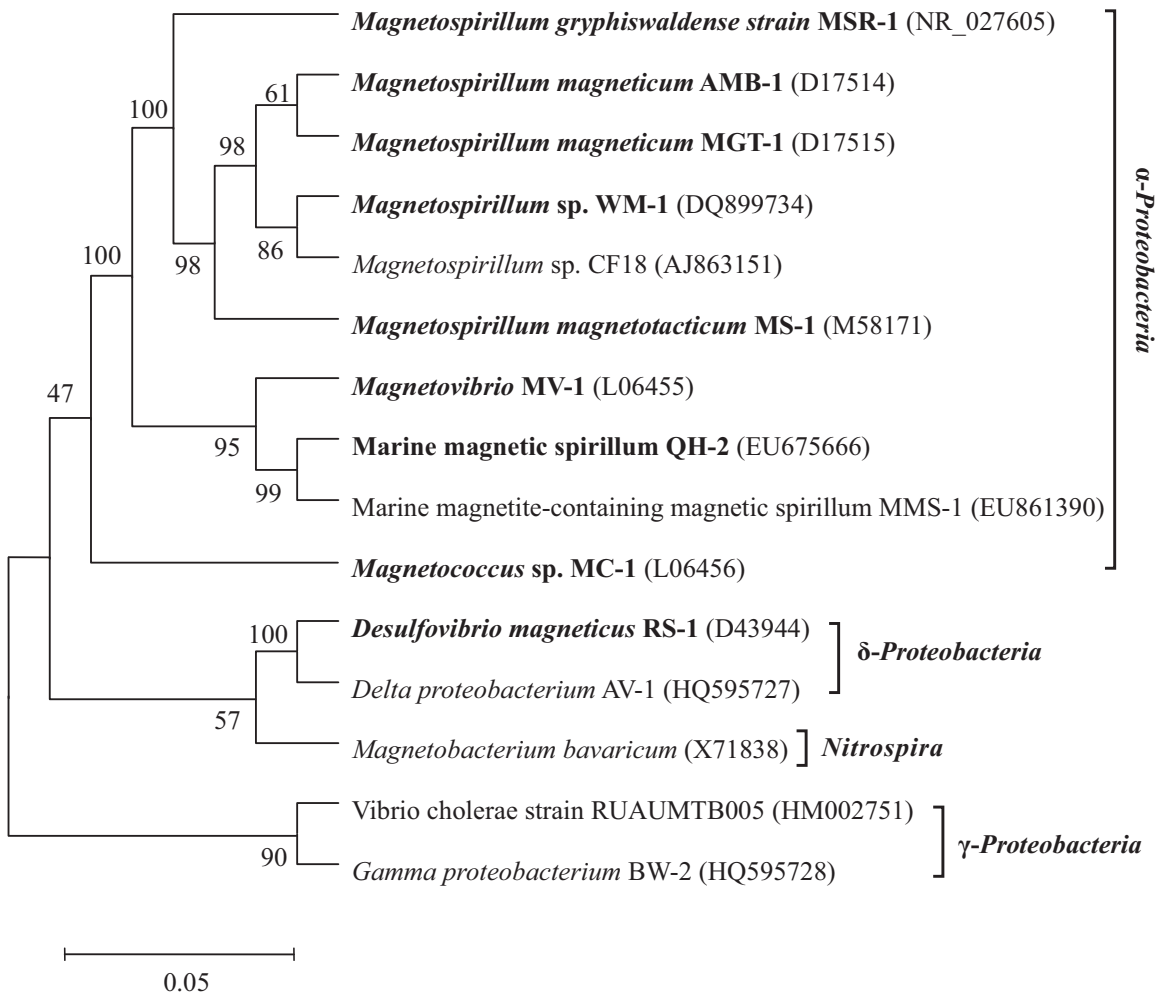

Fig. 2. Phylogenetic relationships of MTB. Pure culture MTB are indicated in bold characters.

a GC content of 52–64% (Jogler and Schüler 2006). The genome sequence of strain MC-1 has been recently completed (http://www.ncbi.nlm.nih.gov/genome?term=Magnetococcus%20sp.%20MC-1) and annotation is in progress. The genome of strain MS-1 is partially sequenced and annotated and is available for study at the NCBI website (http://www.ncbi.nlm.nih.gov/genome?term=Magnetospirillum%20magnetotacticum%20MS-1). The genome draft sequence of *M. gryphiswaldense* strain MSR-1 comprises 4.3 Mb of chromosomal sequence and a 0.04 Mb plasmid sequence. Genetic information of strain MSR-1 can be found at http://www.ncbi.nlm.nih.gov/nuccore/CU459003. The 5.0 Mb-sized genome of *M. magneticum* AMB-1 has been completed and can be found at the NCBI website (http://www.ncbi.nlm.nih.gov/genome?term=Magnetospirillum%20magneticum%20AMB-1). The genes were annotated, with an *E* value 0.1 (Matsunaga et al. 2007). Genome sequencing of the magnetic sulfate-reducing bacterium *D. magneticus* RS-1 has been recently completed (http://www.ncbi.nlm.nih.gov/genome?term=NC_012796). The genomes of these strains consist of a single, circular chromosome and there was no evidence for the presence of plasmids in strains MV-1, MV-2, MC-1, and MS-1. However, native plasmids were detected in strains MSR-1, AMB-1, RS-1 and MGT-1.

As more genomic sequence of various MTB became available, genes thought to be involved in the magnetosome formation were identified. Up till now, the genes related to the synthesis of magnetosomes are mainly as follows: *mag*A, *mam*A, *mam*B, *mam*C, *mam*D, *mam*E, *mam*F, *mam*G, *mam*H, *mam*I, *mam*J, *mam*K, *mam*L, *mam*M, *mam*N, *mam*O, *mam*P, *mam*Q, *mam*R, *mam*S, *mam*T, *mam*U, *mam*W, *mam*X, *mam*Y, *mgl*462, *mam*12 (*mam*C), *mam*22 (*mam*A), *mm*22, *mms*5, *mms*6 (*mam*D), *mms*7 (*mam*D), *mms*13 (*mam*C), *mms*16, *mms*24 (*mam*A), *mms*F, *mps*A, *thy*, *bfr*1, and *bfr*2 (Jogler and Schüler 2006; Bazylinski and Schübbe 2007; Baumgartner and Faivre 2011).

It has been reported that *mam*B and *mam*M are putative iron transporter genes, a deletion of *mam*B resulted in loss of magnetosome membrane vesicles. MamB stability depended on the presence of MamM by formation of a heterodimer complex (Uebe et al. 2011). The *mms*13 (*mam*C), *mms*7 (*mam*D), *mms*5 (*mam*G), and *mms*6 genes, which often appear as a coherent gene cluster in MTB, used to encode Mms (for magnetic particle membrane specific) protein (Komeili 2012). Recent report indicated that *mms*13 (*mam*C) and *mms*16 are putative membrane anchors genes (Rodríguez-Carmona and Villaverde 2010). However, a deletion of *mam*C or the entire *mam*GFDC cluster only resulted in the mild effects on biomineralization of magnetosomes (Scheffel et al. 2008). Several studies have confirmed that Mms6 is capable of controlling the morphology of magnetite crystals *in vitro*, and a recent genetic analysis has provided compelling evidence for a similar *in vivo* function for this protein (Arakaki et al. 2010; Tanaka et al. 2011). It has been reported that a deletion of *mms*6 resulted in the reduction of the size of magnetite crystals and the level of the Mms proteins that are normally tightly associated with the magnetite crystal (Komeili 2012).

Murat et al. (2010) suggested that *mam*I and *mam*L are putative transmembrane segment genes. The individual deletions of *mam*I,

*mam*L and *mam*Q resulted in a loss of the magnetosome membrane from AMB-1 (Murat et al. 2010). The *mam*XY gene cluster of the MAI used to encode a MamY protein. A deletion of *mam*Y resulted in the generation of slightly smaller magnetosome membranes (Komeili 2012). When the individual genes of *mam*E, *mam*O, *mam*M, and *mam*N were deleted, the mutants only formed chains of empty magnetosome membranes (Murat et al. 2010).

Intriguingly, *mam*K, one of the genes within the MAI, encodes a member of the bacterial actin-like family of proteins (Komeili 2012). The deletion of *mam*K in AMB-1 produced no major defects in magnetosome formation, but affected the arrangement of magnetosomes (Komeili et al. 2006). The *mam*J gene, directly upstream of *mam*K, used to encode an acidic protein with an important function in magnetosome chain formation (Komeili 2012). When *mam*J was deleted, the magnetosome-associated filaments were not seen attached to magnetosomes, and the magnetosomes were aggregated within the cell (Scheffel and Schüler 2007).

Despite some progress has been made in molecular biology of magnetosome formation and biomineralization. The possible roles and contribution to magnetosome formation of genes will need further study systematically.

3. Bacterial magnetosome

3.1. Features of magnetosome

Magnetosome, the key component of MTB, is defined as an intracellular, membrane-bounded magnetic iron-bearing inorganic crystal (Lefèvre et al. 2011). It has been realized that bacterial magnetosome represents true prokaryotic organelle, displaying a comparable degree of complexity as its eukaryotic counterpart (Schüler 2008). The morphology, composition, size and arrangement of the magnetic mineral crystal are subject to a species-specific chemical, biochemical and genetic control (Komeili et al. 2004). The size range of bacterial magnetosomes has physical significance which is reflected in their magnetisms (Lefèvre et al. 2011). Mature magnetite crystals typically fall within a narrow size range of about 35–120 nm (Schüler 2008), except the very large magnetite crystals with lengths up to 250 nm produced by an uncultured coccus (Ulysses et al. 2006). Bacterial magnetosomes in this range are stable single-magnetic domains (SD) and are permanently magnetic at ambient temperature (Bazylinski and Frankel 2004). The crystals within the SD size range are uniformly magnetized and have the maximum magnetic dipole moment. Magnetic crystals smaller than the SD size range are superparamagnetic (SP) at ambient temperature, which means they do not have persistent remanent magnetizations (Bazylinski and Schübbe 2007). On the contrary, particles with lengths above about 120 nm are nonuniformly magnetized because of the formation of domain walls (McCartney et al. 2001). The domain walls will tend to form multiple magnetic domains of opposite magnetic orientation, thereby reducing the total magnetic remanence of the crystals (Bazylinski and Schübbe 2007). Therefore, by controlling particle size, MTB have optimized the magnetic dipole moment per magnetosome.

It has been reported that different morphologies of magnetosome crystals were observed in MTB by various forms of electron microscopy (Lefèvre et al. 2011). These shapes include cubo-octahedral, bullet-shaped, elongated prismatic, and rectangular morphologies (Fig. 3). Generally, crystal shape is consistent within cells of a single bacterial species or strain, even though minor variations have been found in crystals of some species grown under different conditions (Bazylinski and Schübbe 2007). In the majority of MTB, magnetosomes are arranged in one, two or multiple chains (Fig. 3), which are usually fixed to the cell, parallel to each other along the length of the chain by minimizing the magnetostatic energy (Lefèvre et al. 2011). Dispersed aggregates clusters of magnetosomes occur in some MTB usually at one end of the cell (Schüler 1999; Cox et al. 2002). Although these organisms clearly possess a net magnetic dipole moment, in a magnetic field, they also behave like MTB that have chains of magnetosomes (Lefèvre et al. 2011). Recently, a consensus is emerging that newly formed magnetic crystals are at the end of magnetosome chains inside the bacterial cells, especially with the evidence that the crystals toward the peripheral ends of magnetosome chains are smaller than those in the center of the chains (Faivre and Schüler 2008; Naresh et al. 2009).

The primary mineral in the magnetosomes was identified as magnetite or greigite (Lefèvre et al. 2011). Several other iron sulfide minerals have also been identified in iron sulfide-containing magnetosomes, including mackinawite (tetragonal FeS) and a cubic FeS that are thought to be a precursor to greigite (Bazylinski and Frankel 2004). In addition, it has been reported that magnetic monoclinic pyrrhotite (Fe_7S_8) and nonmagnetic iron pyrite (FeS_2) were identified in a many-celled magnetotactic prokaryote that produces iron-sulfide magnetosomes but probably represent misinterpretations of electron diffraction patterns (Farina et al. 1990; Mann et al. 1990). The magnetosome membrane which encloses magnetite crystals, is thought to control the size and shape of the magnetosome crystal, and appears to originate as an invagination of the cytoplasmic membrane (Tanaka et al. 2006). The membrane may act as potential gate for compositional, pH and redox differentiation between the vesicle and the cellular environment (Schüler 1999). Lipid analysis of purified magnetosomes indicated that the magnetosome membrane consists of proteins, fatty acids, glycolipids, sulfolipids, and phospholipids (Lefèvre et al. 2011). The proteins that are unique to the magnetosome membrane have been designated the Mam (for magnetosome membrane) or Mms (for magnetic particle membrane specific) proteins (Bazylinski and Schübbe 2007). Although numerous magnetosome membrane proteins have been discovered, the exact role of the magnetosome-specific proteins has not been elucidated. The functional groups in the magnetosome surface have been identified as carboxyl, hydroxyl and amino (Han et al. 2007). It has been reported that the bacterial magnetosomes have good biocompatibility (Xiang et al. 2007; Han et al. 2008).

3.2. Mechanism of magnetosome formation

Our knowledge of the magnetosome formation mechanism mostly comes from studies involving several strains of different *Magnetospirillum* species. This is mainly due to the fact that these organisms can be cultivated more readily than most other MTB, which have facilitated their physiological and biochemical analysis (Schüler 2002). The mechanism of magnetosome formation is hypothesized to be a complex process that involves several discrete steps, including magnetosome vesicle formation, extracellular iron uptake by the cell, iron transport into the magnetosome vesicle and biologically controlled magnetite or greigite mineralization within the magnetosome vesicle (Bazylinski and Schübbe 2007). It is well known that the iron uptake, transport and crystal biomineralization steps are temporally ordered. However, it is ambiguous whether magnetosome vesicle formation precedes or follows crystal biomineralization, or if both steps occur simultaneously. An early electron microscopy study showed that the iron-starved cells of *M. magnetotacticum* and *M. gryphiswaldense* contained empty and partially filled magnetosome vesicles (Bazylinski and Frankel 2004; Scheffel et al. 2005). These indicated that the magnetosome vesicles apparently exist prior to the biomineralization of the mineral phase.

Although magnetosome formation is still not fully understood in detail, various hypothetical models on the formation mechanism

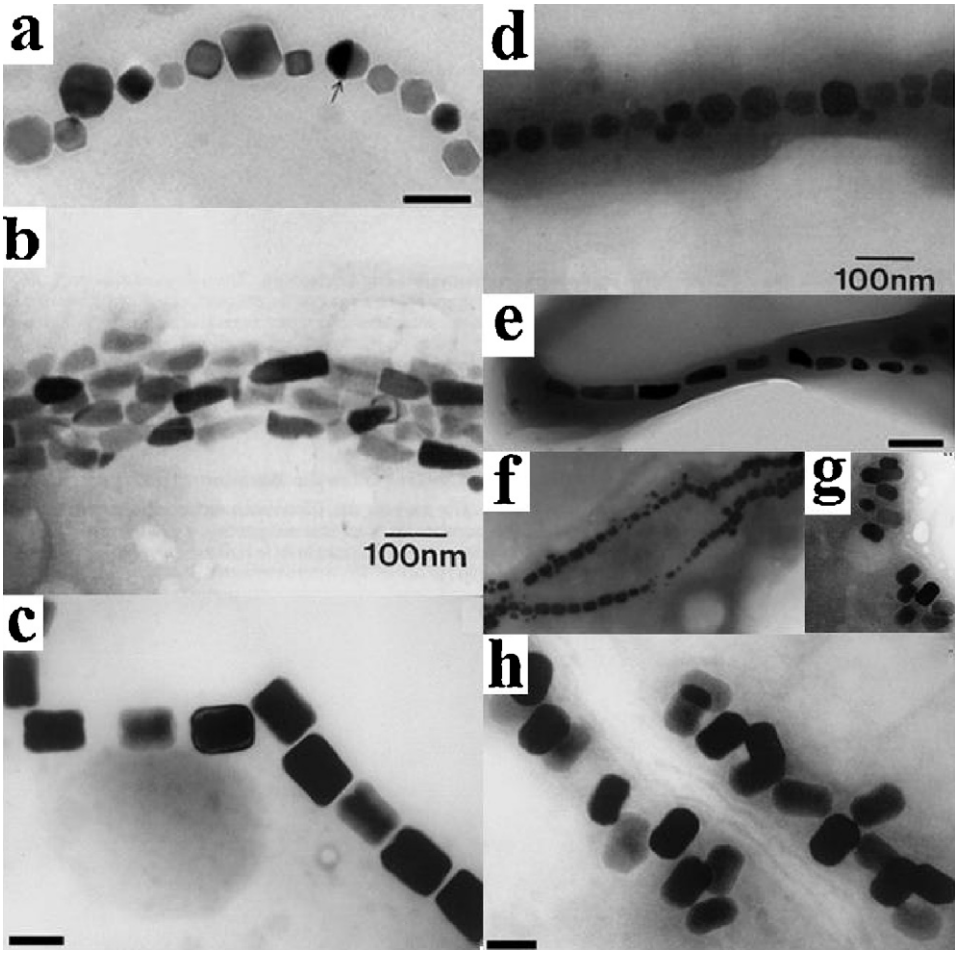

Fig. 3. Crystal morphologies and arrangement of magnetosomes, cubooctahedral: a (Bar = 200 nm) and d (Bar = 100 nm); bullet-shaped: b (Bar = 100 nm) and e (Bar = 200 nm); elongated prismatic: c (Bar = 100 nm), f and g; rectangular morphologies: h (Bar = 100 nm). a, c, d, e: arranged in one; b: arranged in multiple chains; f: arranged in two; g, h: arranged in irregularly. Figure a and e reproduced from Lefèvre et al. (2011), figure c and h reproduced from Schüler and Frankel (1999), with permission from Springer. Figure b and d reproduced from Bazylinski et al. (1994), figure f and g reproduced from Schüler (2008), with permission from John Wiley and Sons.

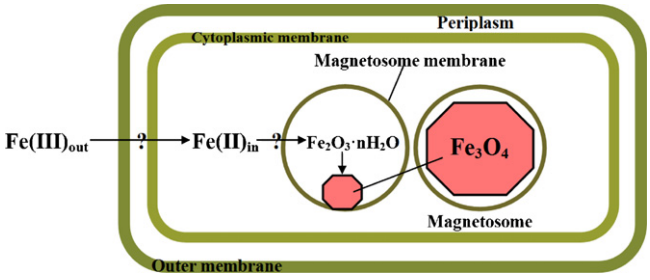

Fig. 4. Model for magnetite biomineralization in *Magnetospirillum* species.

of bacterial magnetosome have been proposed based on available information given by physiology, molecular genetics and ultrastructural cytochemistry. An early model proposed by Schüler (2002) assumes that the magnetosome formation comprises three major stages (Fig. 4). The first step in magnetosome formation is the uptake of extracellular ferric ion *via* a reductive step. Iron is then thought to be reoxidized to form a low density hydrous oxide which is dehydrated to form a high-density ferrihydrite. The final step in magnetosome formation is the biomineralization of magnetite, which encompasses all the reactions involving one-third of the ferric ions reduction and further dehydration to form magnetite.

A speculative model (Fig. 5) proposed by Jogler and Schüler (2006) also showed that magnetosome biomineralization is preceded by vesicle formation. In this model, external ferrous or ferric ion is taken up and transported into the cell by an energy-dependent process *via* an unknown uptake system. The uptake of iron is coupled to the formation of magnetite. Supersaturating ferrous ion is transported by the MamB/MamM-proteins from the cytoplasm into the magnetosome vesicles. Alternatively, iron is directly transported from the periplasmic space into the vesicles by the MamB/MamM-proteins (Fig. 5). Intravesicular iron is then thought to be partially reoxidized possibly by MamT to form a high activity ferric oxide, which may react with dissolved ferrous ions to produce magnetite. Additionally, many other proteins associated with the magnetosome membrane could play functional roles involved in nucleation and growth of magnetite crystals, redox and pH control, and connection and stabilization of the mature magnetosome vesicles (Fig. 5).

In a recent paper by Arakaki et al. (2008), the authors proposed that bacterial magnetosome biomineralization involves three major steps (Fig. 6). The first step includes the formation of magnetosome membrane invaginations from the cytoplasmic membrane primed by the GTPase, and the arrangement of the formed vesicles into a linear chain along with cytoskeletal filaments. In the second stage, external iron is internalized by transport proteins and siderophores, and accumulated into the vesicles by the transmembrane iron transporters. The internal iron must be strictly controlled by an oxidation–reduction system because of the potentially harmful effects of excess intracellular iron (Schüler and

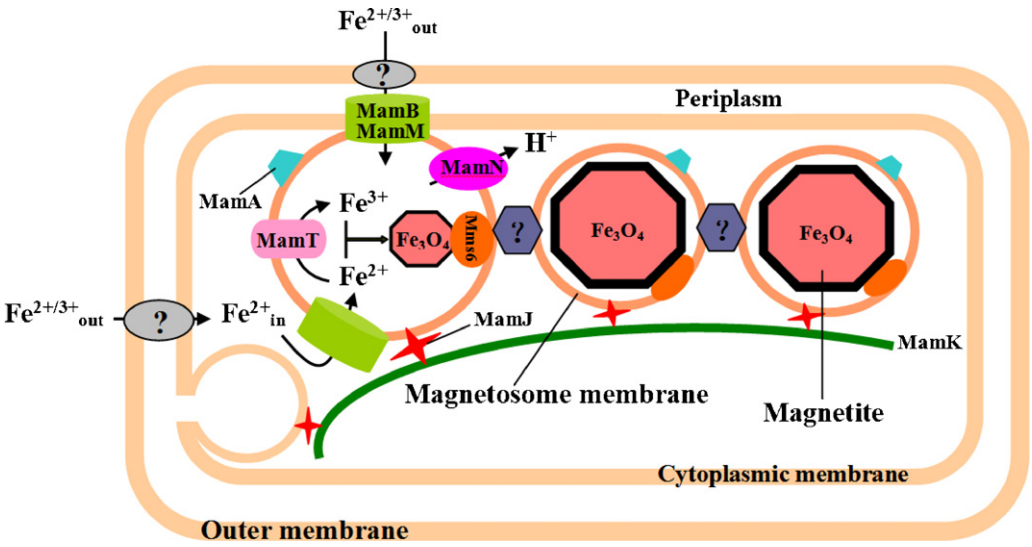

Fig. 5. Hypothetical model of magnetite biomineralization in cultured *Magnetospirillum* strains.

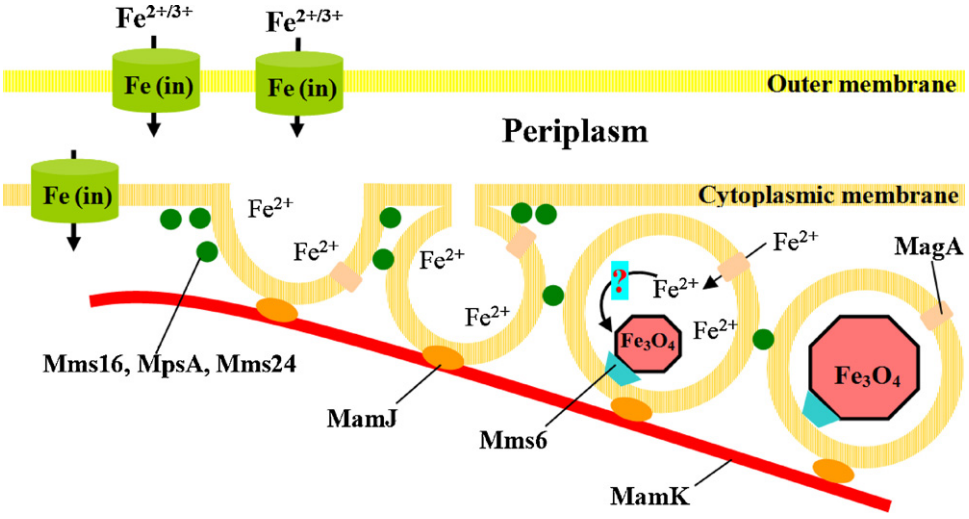

Fig. 6. Scheme of the hypothesized mechanism of magnetite biomineralization.

Frankel 1999). In the last step, tightly bound magnetosome proteins trigger magnetite crystal nucleation and/or regulate morphology. Various proteins associated with the magnetosome membrane are thought to have crucial functions in the accumulation of supersaturating iron, nucleation of minerals and maintenance of reductive conditions.

3.3. *Physiological conditions that favor magnetosome formation*

Actually, besides biological and genetic control, it has also been demonstrated that the formation of magnetosome is very sensitive to changes in the solution chemistry and physical conditions. Oxygen concentration, one of the most important environmental factors, not only influences the biomineralization of magnetosome of cultured MTB, but also affects the growth of these MTB. Molecular oxygen is known to be required for magnetite formation by some MTB (Bazylinski et al. 1995). It has been reported that cells of *M. magnetotacticum* MS-1 (formerly *Aquaspirillum magnetotacticum* MS-1) could grow at 0.1–21% oxygen, yet the formation of magnetite magnetosomes in this bacterium is optimal at 1% oxygen and is strongly inhibited at >5% oxygen (Blakemore et al. 1985). Magnetite formation in *M. gryphiswaldense* MSR-1 occurred only in a narrow range of low oxygen concentration (Schüler and Baeuerlein 1998). *M. gryphiswaldense* MSR-1 can biomineralize magnetite below an oxygen concentration of 20 mbar and maximum magnetite formation was found at a dissolved oxygen tension of 0.25 mbar (Heyen and Schüler 2003). It is also suggested that the decrease of oxygen concentrations can result in increased magnetite magnetosome formation in *M. magneticum* AMB-1 (Yang et al. 2001). The maximum production of magnetite magnetosomes was achieved at 2.35 μM oxygen, and the formation of magnetosomes was partly inhibited at 11.7 μM oxygen and totally inhibited at 23.52 μM oxygen (Popa et al. 2009). Among these strains mentioned above, highest productivity of magnetosomes has been reported by using *M. gryphiswaldense* MSR-1 (Heyen and Schüler 2003; Naresh et al. 2012). Heyen and Schüler (2003) have reported a cell yield of 0.4 g/L and a magnetosome productivity of ~6.0 mg/L/day. While Naresh et al. (2012) have reported even a higher cell yield of ~1.5 g/L with a magnetosome productivity of ~9.0 mg/L/day by controlling dissolved oxygen levels at 6% by devising a cyclic oxygen feeding strategy. The productivity of magnetosomes from *M. magneticum* AMB-1 (Yang et al. 2001;

Heyen and Schüler 2003) and *M. gryphiswaldense* MSR-1 (Heyen and Schüler 2003) has been reported to be quite low in comparison with that from *M. gryphiswaldense* MSR-1. Although these results indicated that magnetite formation in MTB is inhibited by high levels of oxygen and occurs only under microaerobic or anaerobic conditions, the mechanism for the low-oxygen dependence of magnetite formation is not clear.

Iron is an essential element for magnetosome formation, although it is unclear so far that the relationship between iron source and magnetosome production. In order to biomineralize magnetite, MTB require several orders of magnitude more iron than nonmagnetotactic bacteria, reaching up to 4% of their cell dry weight (Schüler and Baeuerlein 1996). It has been shown that MTB are able to take up ferric and ferrous iron (Faivre et al. 2007), and in some cases the uptake involves siderophores (Taoka et al. 2009). Siderophores are low molecular weight iron chelators that bind and solubilize ferric iron for uptake (Sandy and Butler 2009). *M. magneticum* can produce magnetite magnetosomes under various iron sources including several ferric chelates and ferrous sulfate, and the magnetosomes yield is dramatically enhanced by ferrous sulfate and ferric gallate and slightly improved by ferric quinate (Yang et al. 2001). It has been shown that in *M. gryphiswaldense* iron is mostly taken up as ferrous iron and that this is an energy-dependent and regulated process (Schüler and Baeuerlein 1996). The maximum in growth and magnetite formation occurred at an extracellular iron concentration of 100 μM, but both were found close to saturation at 15–20 μM. Iron concentrations above 20 μM iron only slightly increased cell yield and magnetosome content, while iron concentrations higher than approximately 200 μM were growth-inhibiting (Schüler and Baeuerlein 1996). Iron uptake experiments with this bacterium showed that the mean particle size of mature magnetosomes is similar to that of magnetosomes formed by constantly growing and iron-supplemented bacteria, whereas other physical properties such as crystal-size distribution, aspect ratio, and morphology are significantly different (Faivre et al. 2008). An iron shift analysis from iron-limited to iron-sufficient conditions revealed that there are no chemical intermediates in magnetite biomineralization or that they are unstable and convert to magnetite extremely quickly (Heyen and Schüler 2003).

Nitrogen source is an additional factor for growth of MTB and magnetite magnetosome biomineralization. Although both ammonium and nitrate can serve as the sole nitrogen source for growth of *M. gryphiswaldense*, the presence of nitrate significantly increased magnetite formation with an optimum concentration of 4 mM (Heyen and Schüler 2003). Increased nitrate concentrations (10–20 mM) resulted in reduced magnetite formation but did not affect cell growth. *M. magneticum* can also form magnetite under anaerobic conditions when grown with nitrate. Magnetite formation depends on the nitrate concentrations and the increase of nitrate concentrations result in reduced magnetite magnetosome formation, indicating that magnetite synthesis of *M. magneticum* is inhibited by NO_3 reduction to N_2 (Matsunaga et al. 2000). The presence of polypeptone, yeast extract and L-cysteine appeared to significantly enhance both bacterial growth and magnetosomes production (Yang et al. 2001).

Recently, some understanding of the physico-chemical importance and implications of magnetosome formation in MTB has been developed beyond the hypothesis of magneto-aerotaxis providing an evolutionary advantage to these bacterial cells (Kopp and Kirschvink 2008), thereby leading to magnetosome formation. One of the initial studies in this direction had shown that nearly no carbon was necessary for magnetite magnetosome formation (Faivre et al. 2007). This study also showed very slow magnetite production (~5 h) whereas another study showed fast magnetite production (~30 min) using carbon-rich medium (Staniland et al. 2007). Considering biochemical and microbiological aspects, these differences were resolved only very recently by experiments that led to estimation cellular energy requirements for magnetosome synthesis (Naresh et al. 2010). Further experiments by the same group have now shown conclusively that iron metabolism in MTB is more coupled with carbon and nitrogen compared to carbon and nitrogen metabolism with each other (Naresh et al. 2012). Thus, it is only very recently, an appreciation for the role of the carbon source and the amount of carbon required for microbial growth has developed toward understanding physiological conditions that favor magnetosome production.

4. Magnetism of MTB and bacterial magnetosomes

One method for measuring the total magnetic moment of MTB is based on the u-turn analysis (Esquivel and Lins De Barros 1986). In the u-turn method, the magnetic moment is determined from the width of the u-turn executed by a bacterium after an instantaneous polarity reversal of a direct field applied in the optical plane (Winklhofer et al. 2007). Another method which determines the magnetic moment from the analysis of the movement of the bacterium in rotating magnetic fields was used (Hanzlik et al. 2002). In a rotating magnetic field, a magnetotactic organism is exposed and the escape frequency is measured, giving a better estimate of magnetic moment (Steinberger et al. 1994; Cēbers and Ozols 2006). The u-turn and rotating-field methods are dependent on the motility of MTB and cannot be used to estimate the magnetic moment of inert particles or dead MTB. However, the u-turn method turns out to be less robust than the rotating-field method since the magnetotactic organism can perform trajectories not necessarily in the optical plane and the time interval is arbitrary. Another advantage of the rotating-field method over the u-turn method is that the former is insensitive to variations in swimming speed which can easily be monitored by the diameter of the circle the swimming microorganism describes in the rotating field (Winklhofer et al. 2007). To measure the total magnetic moment of inert particles, as well as magnetic particles or dead MTB, a simple method was presented, based on the application of an external oscillating magnetic field in the sites where the micro-organisms are (de Barros and Acosta-Avalos 2008).

Two optical approaches for measuring the magnetic moment of MTB are the analysis of the birefringence arising in a pool of MTB in the presence of an external magnetic field (Rosenblatt et al. 1982b) and the analysis of the light scattered by a pool of MTB (Rosenblatt et al. 1982a). In the birefringence technique, an input-linear-polarized light beam is transformed into an output elliptically polarized light beam, and the phase shift which depends on the intensity of the external magnetic field is measured (de Barros and Acosta-Avalos 2008). The advantage of the birefringence method is that it is insensitive to the presence of nonmagnetic organisms, dust and other impurities that would contribute to light scattering. Alternatively, one could use the light scattering method (Rosenblatt et al. 1982a; Schüler et al. 1995), by which the magnetism of MTB can be determined from the change in light scattering resulting from magnetic bacteria (except the magnetotactic cocci) alignment in a magnetic field. In this case, the maximum scattering (E_{max}) occurs if the applied magnetic field is directed parallel to the light beam, whereas a perpendicular orientation with respect to the light results in minimal scattering (E_{min}). C_{mag}, the ratio of scattering intensities at different angles of magnetic field relative to the light beam, was determined as $C_{mag} = E_{max}/E_{min}$ (Schüler et al. 1995). The C_{mag} value was demonstrated to be well correlated with the average number of magnetic particles and this method has been successfully applied in the investigation of the magnetism of MTB (Schüler and Baeuerlein 1996, 1998; Wang and Liang 2009). The extended light scattering method,

developed by Zhao et al. (2007), is a simple and accurate method for quantifying the magnetism of the MTB with a common laboratory spectrophotometer. In this method, the extinction value of optical density (OD) of the cultures was recorded at the wavelength of 600 nm. The $OD_{||}$ value was measured for parallel magnetic field, the $OD_{\perp}$ value for orthogonal magnetic field and the OD value alone for normal measurements (without external magnetic field applied). A novel magnetism parameter, R_{mag}, by modifying the definition of C_{mag} to a normalized parameter with the culture absorbance obtained without application of magnetic field was expressed as $R_{mag} = (OD_{||} - OD_{\perp})/OD$. R_{mag} was found to be linearly well correlated with the percentage of magnetosome containing bacteria and this method can be used to study the bacterial magnetism for the potential utilization of magnetosomes (Zhao et al. 2007).

In order to determine cellular magnetism, simple microscopic inspection or image analysis techniques were employed to assay swimming behavior and magnetic responses of individual living cells (Bahaj and James 1993; Steinberger et al. 1994). Though simple to put into practice, it is not directly related to the magnetism of magnetosomes (Seong and Park 2001; Zhao et al. 2007). Transmission electron microscopy (TEM), especially high-resolution TEM (HRTEM) is a powerful tool to directly determine the magnetic moments of environmental samples of MTB or of isolated strains (Faivre and Schüler 2008). Based on TEM analysis, a set of six criteria for distinguishing magnetite produced by biologically controlled processes from magnetite produced by other mechanisms has been established (Thomas-Keprta et al. 2000). The criteria include single-domain size and restricted anisotropic width/length ratios, chemical purity, crystallographic perfection, crystals aligned in chains, unusual crystal morphology, and crystallographic direction of elongation of magnetite crystals (Thomas-Keprta et al. 2000). Unfortunately, TEM has some unneglectable disadvantages, for example, it requires careful and skillful sample preparation, it is quite a time-consuming work, and it delivers only qualitative information about MTB in bulk samples. These shortcomings have limited its further development.

To avoid the problems mentioned above by using light microscopy, optical technologies and TEM, techniques that can directly and nondestructively detect magnetic materials existing in MTB are needed. Vibrating sample magnetometry (VSM) can be used to characterize the magnetisms of different samples at room temperature and this method has been successfully applied in the investigation of the magnetism of MTB and bacterial magnetosomes (Moskowitz et al. 1993; Hergt et al. 2005; Fischer et al. 2008; Zhu et al. 2010; Roberts et al. 2011). Using a superconducting quantum interference device (SQUID) magnetometer (Staniland et al. 2008), comparison of temperature dependence of magnetization after zero-field cooling (ZFC) and field cooling (FC) can detect the existence of very weak magnetic moments originating from magnetic particles in a sample and give an indication of particle size (Moskowitz et al. 1993; Sakata et al. 2006). This method is called Moskowitz test and it can be used to detect the presence of biogenic SD magnetite in the form of intact magnetosome chains in sediments (Moskowitz et al. 1993). The diagnostic rock magnetic parameters are: (1) $R_{df} \approx 0.5$ (R stands for particle interaction; df is direct current demagnetization); (2) $R_{af} > 0.5$ (af represents alternating field demagnetization); (3) ARM/SIRM = 0.15–0.25 (ARM, anhysteretic remanent magnetization; SIRM, saturation isothermal remanent magnetization); (4) $\delta_{FC}/\delta_{ZFC} > 2$ ($\delta = (M_{80\,K} - M_{150\,K})/M_{80\,K}$, and $M_{80\,K}$ and $M_{150\,K}$ are the remanences measured at 80 and 150 K, respectively). Specifically speaking, magnetite transforms from cubic to monoclinic structure at the Verwey transition (T_v). The Moskowitz test is based on two facts: magnetocrystalline anisotropy of magnetite in the monoclinic phase ($T < T_v$) is much higher than in the cubic phase ($T > T_v$) and second, the magnetosomes aligned in chains generate shape anisotropy. This test appears to be a robust indicator of the presence or absence of MTB (Moskowitz et al. 1993) and also ensures the purity of magnetite in the sample (Weiss et al. 2004). A series of studies have demonstrated that the Moskowitz test is valid for both cultured and uncultured MTB cell samples where cells contain complete chains of magnetosomes (Moskowitz et al. 1993, 2008; Pan et al. 2005; Popa et al. 2009; Li et al. 2010). However, the failure of this test was also reported due to smearing or even absence of the Verwey transition as a result of magnetosome oxidation after the biomineralization of the magnetite or due to the presence of SP magnetite particles (Moskowitz et al. 1993; Weiss et al. 2004; Fischer et al. 2008).

In recent years, ferromagnetic resonance (FMR) spectroscopy, which is sensitive to magnetic anisotropy, as a means of detecting MTB has been proposed (Weiss et al. 2004; Fischer et al. 2008). FMR is in theory capable of detecting the distinctive magnetic anisotropy produced by chain arrangement and crystal elongation (Weiss et al. 2004; Kopp et al. 2006). In the case of intact MTB with uniform shape distribution, the magnetic anisotropy can be calculated exactly and be used to simulate FMR signals of randomly oriented MTB ensembles (Charilaou et al. 2011). Based on FMR parameters Kopp et al. (2006) introduced an empirical discrimination parameter α ($\alpha = 0.17A + 9.8 \times 10^{-4}\ \Delta B_{FWHM}/mT$, where $A = \Delta B_{high}/\Delta B_{low}$, $\Delta B_{high} = B_{high} - B_{eff}$, $\Delta B_{low} = B_{eff} - B_{low}$, $\Delta B_{FWHM} = B_{high} + B_{low}$, and B_{eff} is the field value of maximum absorption, B_{high} and B_{low} are the fields of half maximum absorption at low-field and high-field sides of the absorption peak, respectively) to infer MTB and magnetofossils. It has been demonstrated that cultured MTB have typically $\alpha < 0.25$ and magnetofossils $\alpha < 0.30$ (Kopp et al. 2007; Gehring et al. 2011).

Several new techniques including magnetic force microscopy (MFM), electron holography (EH), near-field scanning optical microscopy (NSOM) and the bacteriodrome have provided plentiful magnetic information on the bacterial magnetosomes. MFM can potentially be used to detect and localize the magnetic fields arising from nanoscopic magnetic domains, such as individual SD magnetosome (Neves et al. 2010). The MFM method has been successfully applied to investigate the magnetic properties of isolated single magnetosome and chains of magnetosomes in remanence and in the presence of external magnetic fields (Amemiya et al. 2005; Wei et al. 2011). EH, based on a TEM with a field emission source and an electron biprism, can record two-dimensional phase information about an object wave relative to a reference wave, thus making it possible to directly image. This technique has been employed to characterize the magnetic microstructure of MTB in nanometer scale, particle interactions, magnetization and coercivity force of magnetite nanocrystals (Dunin-Borkowski et al. 1998, 2001; Simpson et al. 2005). The NSOM technique has been successfully used to image magnetic moments of single intact non-fixed cell (Naresh et al. 2009). The bacteriodrome is a reflective light microscope equipped with two sets of computer-controlled field coils oriented perpendicular to each other to generate a homogeneous magnetic field rotating in the horizontal plane at adjustable intensity and rotation frequency (Pan et al. 2009b). It can be used not only for detecting MTB in environmental samples but also for measuring some of their magnetic properties (*e.g.* hysteresis loops and coercivity) (Pan et al. 2009a,b).

5. Application of MTB and magnetosomes

Soon after the discovery of MTB, the entire living cells and their magnetic inclusions have novel magnetic, physical, and perhaps optical properties that can and have been exploited in a variety of scientific, commercial, and other applications.

Using whole living MTB, the magnetic poles in meteorites and rocks containing fine-grained magnetic minerals were located (Funaki et al. 1992). It has been demonstrated that living MTB can be used for the nondestructive domain analysis of soft magnetic materials (Harasko et al. 1993, 1995). Using phagocytosis, MTB were incorporated into granulocytes and monocytes, which could be magnetically separated (Matsunaga et al. 1989). Based on the magnetotactic and microaerophilic behavior of MTB, the oxygen depletion in bottom sediments and overlying water was predicted by tracking their position and magnetic strength using a magnetic sensor (Schüler and Frankel 1999). MTB were also proposed to be used in the removal of heavy metals and radionuclides from waste water by magnetic separation (Bahaj et al. 1998; Arakaki et al. 2002). Since MTB can be trapped by a commercial magnetic recording head, cells in water samples may be quickly counted, and magnetically labeled cells and magnetic nanoparticles may be detected (Krichevsky et al. 2007). A described application of living MTB are in the area of nanorobotics. A directional magnetic field was used to manipulate MTB and force them to push 3 μm beads at an average velocity of 7.5 $\mu m\, s^{-1}$ along preplanned paths by modifying the torque on a chain of magnetosomes in the bacterium (Martel et al. 2006). Recently, cobalt doping of magnetic nanocrystals using MTB was successfully shown (Staniland et al. 2008). Additionally, biosynthesis of gold nanoparticles by biosorption on MTB was also reported (Cai et al. 2011).

Based on the special characterization of magnetosomes such as ferrimagnetism, nanoscale size, narrow size distribution, dispersal ability, and membrane-bound structure, the bacterial magnetosomes have been developed and investigated for use in various applications. Bacterial magnetite magnetosomes have been used in the immobilization of relatively large quantities of bioactive substances, which can then be governed by magnetic fields.

In initial studies, bacterial magnetosomes were used for immobilizing the enzymes glucose oxidase and uricase, which resulted in a much higher activity than when immobilized on crystals of synthetic magnetite (Matsunaga and Kamiya 1987). Specific antibodies have been devised using bacterial magnetite particles that have proven useful in various fluoroimmunoassays (Bazylinski and Schübbe 2007). Bacterial magnetite particles were also used as carriers of genes for the detection of nucleic acids and eliciting antigen-specific immunity (Ota et al. 2003; Tanaka et al. 2003; Maruyama et al. 2004; Tang et al. 2011). It was also suggested that the modified magnetosomes can be used for the isolation of nucleic acids (Sode et al. 1993; Yoza et al. 2003). Magnetosomes have been shown to be useful in detecting bimolecular interactions in medical and diagnostic analyses. Using a magnetic force microscope, biotin and other molecules attached to a monolayer-modified substrate were detected by streptavidin-immobilized magnetosomes (Amemiya et al. 2005).

Magnetosomes were incorporated into eucaryotic cells by phagocytosis and polyethylene glycol fusions, and the magnetic cells can be manipulated by magnetic fields (Matsunaga et al. 1989). It has been reported that protein displays can be designed using specific magnetosome membrane proteins as anchor molecules for the assembly of foreign proteins on the surface of magnetite magnetosomes. Many magnetosome membrane proteins were found to be used as anchor proteins, including MagA, MpsA, Mms16 and Mms13 (MamC, Mam12) (Lefèvre et al. 2011). Recently, magnetosomes have been used as potential drug carriers for antitumor treatments (Sun et al. 2008) and as a contrast agent for MRI (Vereda et al. 2009).

The most interesting uses of bacterial magnetite crystals are in geology, paleontology, and astrobiology. Because of the high abundance and the remarkable capacity for accumulating and precipitating iron and/or sulfur minerals, MTB are assumed to have great impact on the biogeochemical cycling of iron and sulfur in natural sediments (Simmons and Edwards 2007). Fossilized magnetosomes produced by MTB have been suggested as useful paleoenvironmental indicators in the sedimentary and rock records (Chang and Kirschvink 1989; Thomas-Keprta et al. 2002). Fossil magnetite from MTB appears to be well preserved in freshwater sedimentary environments (Snowball et al. 2002). Magnetite magnetofossils have also been found in rocks as old as 700 Mya (Chang and Kirschvink 1989). The fossilized bacterial magnetite has been shown to be an important carrier that can provide information about the origin of the geomagnetic field and properties of the deep Earth, history of plate motions and magnetic reversals, and even magnetic proxy records of paleoenvironmental and paleoclimate (Bazylinski and Schübbe 2007).

6. Perspectives and directions for future research

Although the tremendous progress in the study of MTB and bacterial magnetosomes has been made, there are many subtle and fascinating questions that remain to be answered. It can be hoped that there will be a breakthrough in the following aspects:

(1) Mass cultivation of MTB will be carried out in laboratories, thus providing sufficient materials for detailed studies of MTB and bacterial magnetosomes. Despite a few species can be cultured, to date none of the greigite-producing MTB has been cultivated in the laboratory. Therefore, conventional isolation and cultivation approaches should be performed with increased efforts. However, since the discovery of MTB, there are only a handful of groups that have consistently contributed toward the slowly building literature in this area. While a variety of laboratories have managed to produce isolated scientific data and literature on MTB, only a few groups have contributed consistently to the field. This is primarily due to the fastidious nature of growth of these bacteria, and thus establishment of sustained experimental systems has been a challenge. For example, even till date, there are only two reports in literature that have demonstrated the ability to culture these bacteria on solid/agar based media (Schultheiss and Schüler 2003; Naresh et al. 2010).
(2) Systematic and concerted efforts to study the function of the various magnetosome genes and proteins involved in magnetosome formation *in vivo* and *in vitro* are urgently required. Once functions of specific magnetosome genes and proteins have been determined, the application of genetic engineering techniques might possibly result in much higher yields of magnetosome particles with improved properties and a more dependable production process. The adequate MTB and magnetosomes might facilitate the development of many new commercial and scientific applications for them. Additionally, the integrative omic analysis will reveal the mechanism of magnetosome biomineralization, and generate insights into the biology and molecular processes underlying magnetotaxis.
(3) The widespread distribution of MTB in natural environments means that when they die, magnetosomes can be buried and fossilized to become magnetofossils. As single-domain particles, magnetosomes have therefore been argued to be widely responsible for paleomagnetic signals in the sedimentary record. Therefore, studies on magnetism of magnetosomes will hopefully provide useful information about the rock magnetism theory, the acquisition mechanism of the depositional remanent magnetization and environmental magnetism.

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