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Introduction of Magnetotactic Bacteria and their uses in Medicine

[1] **Dr. Rohit Paliwal,** [2] **Mrs. Shweta Paliwal**
[1]Professor, Department of Physics, Shreejee Institute of Technology and Management, Khargone, India
[2] Dept. Head, Department of Chemistry, Aaditya International School, Khargone, India
Email – [1]rohitpaliwalsjitm@gmail.com, [2]paliwalshweta44@gmail.com

Abstract: *It's a known fact how the magnetic field of the Earth is veritably important for life. Relation between living system and the earth magnetic field has been delved for numerous times. catcalls and their migration routes are the first one of the effects that comes to mind when we state living effects. The Earth's magnetic field is still accepted to be the main factor for catcalls and other flying living beings to complete their peregrination rightly. The changes in migration routes, which are observed from time to time, are occasionally said to be due to the changes in the magnetic field. Still, no light has been exfoliating to this matter yet. The Earth's magnetic field has not been sufficiently studied, and its part on small living models similar as bacteria has not been adequately bandied. One of the stylish exemplifications in this field is relation between the Earth's magnetic field and "magnetostatic bacteria (MTB)", which were discovered by Salvatore Bellini in 1963. presently, it's claimed that magnetostatic bacteria have a wide use in microbiology, mineralogy, limnology, drugs, biophysics, chemistry, biochemistry, geology, crystallography, and astrobiology. Although the significance of this issue magnetic bacteria is still limitedly used in medical area. Thus, more performance is necessary to explore world of this bacterium that is seeker for new remedy strategies in the medical field. Because of the reason stated then and to attract the attention of scientists to this content this short review has been prepared.*

Key Words: *Magnetotactic bacteria; Medicine, The Earth's magnetic field; Bacteria; Magnetotactic bacteria; Medicine.*

1. INTRODUCTION:

Magnetic bacteria, which is known as magnetostatic bacteria (MTB) can produce nanosized and membrane-bound magnetite patches with regular morphology and size within the single- sphere region under mild conditions at normal temperature and pressure. In other words, magnetic bacteria synthesize nano bacterial magnetic patches (BMPs), which offer high technological eventuality as they can be accessibly manipulated with magnetic force. BMPs are ultrafine magnetite dishes (50- 100 nm compasses) of regular morphology produced by Magnetospirillum magneticum AMB- 1. magnetic structures aligned in chains are allowed to serve as natural compass needles allowing the bacterium to resettle along redox slants through the Earth's geomagnetic field lines. Despite the discovery of this unique group of microorganisms several decades ago, the mechanisms of magnetic China clear memoir mineralization have not been completely illustrated yet (1). Magnetotactic bacteria (MTB) are a morphologically, metabolically, and phylogenetically different group of prokaryotes. Magnetotactic bacteria (MTB) are a gram-negative prokaryote bacteria group that moves according to the Earth's magnetic field lines and can acquaint, resettle along geomagnetic field lines because of their intracellular single- sphere magnetic nano- demitasse patches with bio membrane bounded, which are appertained as magnetosomes (2- 4). Biologically, MTB are prokaryotic microorganisms living in water. They move by the propulsion of their helix- shaped flagella. Another microbiological fact that makes them intriguing is, although they are bigger and have lower protein in their flagella, they can move about doubly as presto as Escherichia coli (5). MTB's different strains show different morphological parcels and directions, conceivably due to magnetosome order (6).

Colourful morphologies of MTB, similar as rods, vibrio, helical, cocco bacteria and multicellular bacteria were set up in brackish remainders 7,8). It's known that MTB produce two minerals similar as iron oxide and iron sulfide (9). Some produce Fe_3O_4 (magnetite) others produce Fe_3S_4(Greigite) (10,11), some produce both (12). MTBs in freshwaters produce only Fe_3O_4. MTBs in lake and saltwater ecosystems produce both magnetite and Greigite (13). Development of new and fast ways in biology and electron microscopy have revealed the presence of colourful microorganisms able of producing inorganic fine chargers in the intracellular grounds or as the extracellular frames.

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Calcium carbonate and Calcium phosphate essential selenium, iron oxides (magnetite) and so on can be synthesized through natural processes. Some of these chargers are formed with regular morphologies at specific locales in a largely controlled manner. As its stated above, one of these chargers is magnetite and it's one of the fine patches produced by natural processes. still, it has been using in practical operations similar as a magnetic carrier in bioassay, magnetic controlling device in perfection machine and memory or marker device in colourful electronic appliances.

Presence of magnetic bacteria is colonist to bring new manufacturing system for product of fine- grade magnetite and new operation areas including drug. For case, the successful insulation, civilization and colony conformation of magnetic bacteria, Magnetospiriilum sp. AMB- 1 and MGT- 1, which are tolerant to oxygen, have brought to develop the conjugative gene transfer and transposon mutagenesis systems and to promote their metabolic and phylogenetic examinations. Although pure culture of MTB had been hardly achieved little was known about how magnetic bacteria synthesize bacterial magnetic patches (BMPs) at molecular position (14).

2.MAGNETIC FIELD OF THE EARTH:

The Earth's magnetic Field the Earth can be considered as a large magnet girdled by a magnetic field. It's allowed that the Earth's magnetic field is caused by convection overflows (vertical movement caused by the temperature differences in the inner and external caste) in the liquid crust. The external core is the area between the inner core and the mantle, which is 1260 km thick and is made of iron and nickel. While the temperature in the external corridor of the external mantle is 4400^0C, the temperature goes up to 6100^0C in the corridor near to the inner core. The regular deportation of the particles in a sufficient power causes the forming of magnetic fields, allure in other words, and this causes an endless allure around the Earth. It's also allowed that the circle flows in liquid iron and nickel affects the Earth's magnetic field. The Earth's magnetic field is like a dipole magnet that has north and south poles. still, there's a 11^0 difference between the Earth's rotation axis and the dipole magnet's rotation. This means that the geographical and magnetic poles are different. It's reported that the Earth's magnetic field changes between 15- microtesla and 65 µT (microtesla) (15).

3.PROPERTIES AND HISTORY OF MAGNETOTACTIC BACTERIA:

History and parcels of Magnetotactic Bacteria These remarkable bacteria were first discovered by Salvatore Bellini in 1962 (16). Bellini noticed that a group of bacteria swam towards the direction of the North Pole and dubbed this bacteria group "magneto sensitive bacteria". In 1975, Blakemore named these bacteria "magnetotactic bacteria" by inferring from the natural term "magneto hacks" (17). The discovery of MTB caused a significant impact on exploration fields similar as microbiology, drugs, biophysics, chemistry, biochemistry, geology, limnology, crystallography, and indeed in astrobiology (18). Although they can be set up in any terrain, especially in lake and seawater territories, due to their unique life, it is not easy to insulate and cultivate MTB (19). still, the fast advances in biotechnology, magneto technology and in other fields have eased the civilization of MTB in laboratories, and sped up the inquiries (17).

Magnetotactic bacteria, described by Richard Blakemore, have long intrigued experimenters because they synthesize intracellular nanoscale (40- 100 nm) magnetic particles composed of Fe_3O_4, termed magnetosomes. It is reported patches composed of Fe_3O_4, nominated magnetosomes. It's reported that the considerably studied strains of magnetotactic bacteria include Magnetospiriilum gryphiswaldense MSR-1, M. magnetotacticum MS-1, M. Magneticum AMB-1, Magnetococcus sp. MC-1, and magneto-elliptical strain MO-1. Interestingly, a variety of advanced organisms, including notions, algae, suckers, eels, and humans, are also able of synthesizing intracellular magnetite. The conformation and physiological function of magnetic particles composed of Fe_3O_4, termed magnetosomes. It is reported chargers in these organisms are still not known sufficiently. still, thorough understanding of bacterial magnetosome conformation will serve as a model to uncover the medium of magnetosome conformation and function in other species. It's stated that current exploration focuses on the molecular mechanisms of bacterial magnetosome conformation and its practical operations in biotechnology and drug. It's also noted that functional analysis of several genes involved in magnetosome conformation, e.g., mamJ, mamK, magA have revealed the places of membrane associated proteins in transport and memoir mineralization processes needed for the installation of magnetosomes (20).

4.MAGNETOSOME AND MAGNETITE:

Magnetosomes are a type of vesicles that's set up in the cell. This structure which is girdled by a membrane and consists of inorganic chargers containing magnetic iron is vital for MTB (4). Magnetosomes are vesicles that are in a membrane within the cytoplasm that's full of magnetite and Greigite, which help the bacteria align themselves according to the Earth's magnetic field. Magnetospirillum magneticum and Magnetospirillum gryphiswaldense, which have roughly - 20 magnetosomes along the cell's center line aligned horizontally are magnetotactic organisms that have been delved the most. This line- up along the central line creates a structure analogous to a compass needle that has the magnetic moment that's equal to the sum of each magnetosome's magnetic moment. Electron chromatographic analysis shows that there's a hair that accompanies the magnetosome chains, and that the magnetosomes are connected to this hair by acidic MamJ proteins (21) (Figure 1). In colourful electron microscopes, magnetosome chargers of colourful shapes were observed in MTB, similar as boxy octagonal, pellet- shaped, polychromatic and blockish (4).

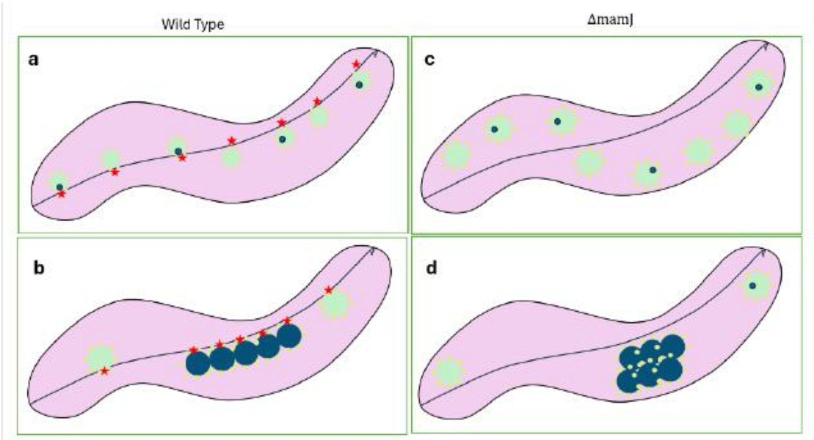

Figure 1 Magnetosomes and their alignment on the filament

Each magnetosome consists of a magnetite (Fe_3O_4) or Greigite (Fe_3S_4) demitasse enveloped by a lipid bilayer membrane deduced from the cytoplasmic membrane (9). Magnetosomes are generally organized in direct chains and acquaint the cell body along geomagnetic field lines while flagella laboriously propel the cells, performing in so- called magnetotaxis (9,22). Magnetite (Fe_3O_4) is the main chemical element of magnetosomes characterized by the high chemical chastity, fine grain size uniformity, and good biocompatibility, which can be used as a new kind of nano-magnetic accoutrements applied in numerous fields of biochemistry, magnetic accoutrements, clinical drug and wastewater treatment etc. Magnetosome conformation is the mineralization process under strict biochemical mechanisms control, including four-way iron accumulation, membrane conformation, transportation and controlled bio mineralization of Fe_3O_4 (2- 4). Magnetosomes are generally organized in direct chains and acquaint the cell body along geomagnetic field lines while flagella laboriously propel the cells, performing in so- called magnetotaxis (9, 22).

5.BEHAVIOUR OF MAGNETOSOMES IN EAST AND NORTH HEMISPHERE OF EARTH:

Magnetotactic bacteria, which are affected by the Earth's magnetic field face north in the northern semicircle, and face south in the southern semicircle (3) (Figure 2). MTB from the Southern Hemisphere swim antiparallel to the perpendicular element of the geomagnetic field toward the South and are nominated South- seeking MTB (SS- MTB). In discrepancy, MTB from the Northern Hemisphere swim resembling to the perpendicular element of the geomagnetic field lines and are pre- dominantly North- dogging (NSMTB) (23). The inclination of the geomagnetic field lines is believed to direct cells down from poisonous attention of oxygen in Face waters, thereby helping them detect and maintain an optimal position in perpendicular slants which is generally at or near the oxic- anoxic interface. Still, there are reports of SS- MTB and NS- MTB in both components (24).

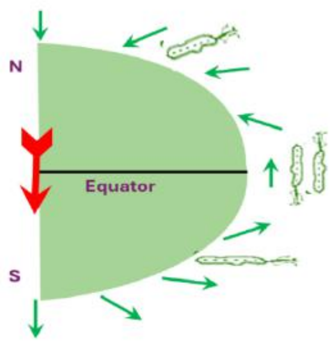

Figure 2 Inclination of the magnetotactic bacteria that move in the direction of the Earth's magnetic field.

While oxygen is vital to humans, it's abrasive and dangerous to numerous bacteria. For this reason, magnetotactic bacteria have developed a surprising system in which the use the Earth's magnetic field like a compass to go as deep into the ground as possible. nearly all of them are anaerobic bacteria and live in conditions where the oxygen position is veritably low. For this reason, they prefer oxic- anoxic interfacial or anoxic areas. This is the most important specific of MTB

6.APPLICATIONS OF MAGNETOSOME:

Nano-technology has been identified as an area which will bring about new evolutions in material, devices and processes. New challenges of nano-biotechnology entail manufacturing more sophisticated and highly efficient biosensors and biomaterials at the nano-scale level for use in interdisciplinary fields. Matsunaga and Okamura stated that magnetic bacteria synthesize intracellular magnets which are encapsulated by lipid bilayer membranes. Sizes of bacterial magnetic particles (BMPs) vary from 50 - 100 nm in diameter, and number over 10 per cell. BMPs are composed of magnetite (Fe_3O_4) with a single magnetic domain. Easy aqueous dispersion of BMPs enables development of highly sensitive chemiluminescence enzyme immunoassays by the chemical coupling of antibodies on BMP surfaces. BMPs can likewise be used as drug delivery systems employing magnetoliposomes with high capture volumes [25]. After the discovery of MTB, it was noticed that they possess unique magnetic, physical and optical characteristics. Due to these characteristics, their use in various scientific and technological applications has been a current issue. It was claimed that by means of magnetic separation, the MTB could separate heavy metals and radionuclides [26,27]. As MTB can be retained with a magnetic recorder, the samples in water can be easily removed and the magnetically labelled cells and nanoparticles can be retained [28]. Another application field of live MTB is Nano robotics. A routing magnetic field is used to orient MTB and a torque is applied to the magnetosome chain in bacteria to propel them at a predetermined location [29].

The magnetite magnetosomes in bacteria are used to block fairly high bioactive substances. These substances can latterly be controlled by a magnetic field. Magnetite patches of MTB are used as carrier genes in determining nucleic acids (30- 33). With the help of the organized magnetosomes, nucleic acids can be insulated. In addition, it was set up that magnetosomes are helpful in determining biomolecule relations in drug and opinion (34). In recent times, magnetosomes gained significance as an implicit medicine- carrier for excrescence treatment and as discrepancy material for MRI (35, 36). The fact that MTB can swim by following the magnetic field direction and their effective exertion provides a possibility to deliver medicines to excrescences. Development of misshaped capillaries, miscellaneous blood inflow, high pressure between cells and other micro-environment parameters of excrescences affects medicine transfer to the excrescences. Microorganisms who act as micro carriers help distribute medicines unevenly while ailing the forenamed conditions (37).

Again, MTB are used in magnetic hyperthermia, which is used in excrescence remedy. Magnetic hyperthermia is a system in which magnetic nanoparticles are transferred to the excrescence and are heated by applying alternate magnetic fields. The heat generated by the nanoparticles has an anti-tumor effect. This fashion can be used in the treatment of some excrescences similar as in lung cancer. Up to now, chemically synthesized iron oxide nanoparticles display super paramagnetic or ferromagnetic characteristics in normal mortal body temperature. In a magnetic field lower than the threshold value, the chemically synthesized nanoparticles' specific immersion rate (SAR) is much lower than that of magnetosome nanoparticles. For this reason, it's claimed that it would be more profitable to use magnetosomes. Hence, the interest in the "magnetic hyperthermia" by using magnetosomes for cancer treatment has increased (38).

Practical Operations of magnetosomes are grounded on their ferrimagnetism, nano-scale size, narrow size distribution, disbandment capability, and membrane- bound structure. Bacterial magnetosomes have been used experimentally as carriers of enzymes, antibodies for largely sensitive immunoassay, and as effective sorbents for insulation and sanctification of DNA or RNA. Artificial magnetic nanoparticles have been used as carriers for cancer opinion and targeted remedy in experimental creatures. also, magnetic nanoparticles enclosed in natural membranes can be linked to genes or medicine motes and therefore could be used as carriers of medicines for targeted remedy of excrescences. Several recent reports indicate that purified, castrated magnetosomes from M. gryphiswaldense MSR- 1 are non-toxic for mouse fibroblasts in vitro, and may be useful as carriers of genes, or medicines for cancer remedy or other conditions. Still, the operations of magnetosomes have not yet been developed commercially, substantially because magnetotactic bacteria are delicate to cultivate and harmonious, high yields of magnetosomes have not yet been achieved (39).

7.THE FORMATION OF MAGNETOSOMES:

The conformation medium of magnetosomes is a complex process that includes the conformation of magnetosome vesicles, taking the iron mineral into the cell, carrying the iron in the magnetosome vesicles and the control of magnetite or Greigite bio-mineralisation within the vesicle 18). While the conformation of magnetosomes is not entirely understood, there are views that explain the process. In the most current abstract presented by Arakaki et al. (40), it was proposed that three major ways were present in magnetosome bio-mineralisation (17) (Figure 3). The first step involves the cytoplasm folding inwards, creating a fund to form the magnetosome membrane by GTPase, and the association of these vesicles along a line to form the magnetosomes' carrier fibre. The alternate step is involving the carrying of iron into the cell by carrier proteins and siderophores and collecting them in the vesicles by transmembrane iron carriers. The iron within the cell is rigorously controlled by oxidation and reduction mechanisms, as too important iron is largely dangerous for the cell (10, 41). The last step is concerning the conformation of magnetite in the magnetosome and the association of the morphology. It's allowed that colourful proteins of the magnetosome are affiliated to collecting oversaturated iron, the core conformation of minerals and the durability of the reducing conditions (17).

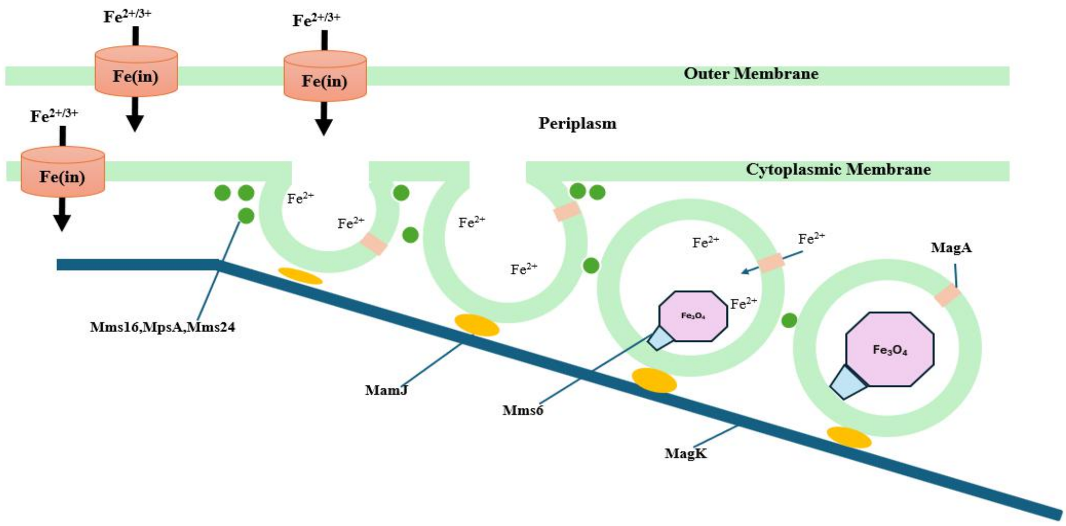

Figure 3: Magnetosomes Formation

In MTB, magnetite conformation takes place in microaerobic and anaerobic conditions, as high oxygen content has an inhibiting effect. Still, the relation between magnetite conformation and low oxygen situations are unclear (17). While the relation between magnetosome conformation and sources of iron is unclear, it's known that iron is the introductory element for magnetosome product. MTB bear further iron compared to other bacteria for the bio-mineralisation of the magnetite demitasse. This quantum can be as high as 4 of the MTB's dry cellular weight. The maximum position for growth and magnetite conformation is 100 µM, which emerges in the extra-cellular iron attention. still, the achromatism for both conditions have been observed at iron attention of 15- 20 µM. Iron attention above 20 µM slightly increase the cellular yield and magnetosome content. On the other hand, iron attention above 200 µM show an inhibiting effect on growth (42).

8.BIOPHYSICS OF MAGNETOTACTIC BACTERIA:

Each MTB has iron patches that can be seen with an electron microscope. Before knowing the chemical condition of the iron within, it was understood that every cell has a constant magnetic dipole moment. When the bacteria that were attained from a terrain rich with slush were subordinated to a magnetic palpitation of a many hundred Gaus for 1 µs anti-parallel to the swimming direction, it was seen that the cells were shortly bewitched in magnetic beats of 200- 800 Gaus palpitation bulks. It was observed that the bewitched cells made a volte-face and began to swim in the contrary direction. This result shows that each bacterium has a specific magnetic moment (43). In order to understand how the commerce between MTB and the Earth's magnetic field takes place, the cell's magnetic moment should be taken as base. The main factor that orientates the bacterium in the direction of the magnetic field is the commerce energy between the bacterium's magnetic moment and the external magnetic field. The bacterium's thermal energy is the factor that makes the bacterium syncope aimlessly, and it's directly commensurable of the terrain's temperature (Thermal energy = kT, k- Boltzmann constant, T- Temperature). In order for the MTB to acquaint themselves in the direction of the magnetic field, the commerce energy and the external magnetic field must be lesser than the thermal energy. The Langevin function can be used to compare these two powers. In the classical paramagnetic proposition, the Langevin function defines the average array of the magnetic dipole groups that do not interact with each other within a magnetic field. The Langavin function is defined with the following equation. $\cos \theta = L\,(MH/kT)$.

In the equation over, θ is the angle between the (H) direction of the terrain's magnetic field and the bacteria's magnetic moment direction (M). The average array in an external magnetic field is determined by the rate of the applied magnetic field and the bacterium's magnetic field (MH) to the thermal energy of the bacterium (kT). When the MH/kT rate exceeds 10, the magnetic moments of the patches in the bacterium come aligned with the magnetic field (43). Thus, the MTB come aligned with the magnetic field direction (Figure 4). Different approaches have been used to determine the dipole moment magnitude of MTB. The studies showed that some magnetosomes contain magnetic iron oxide, also known as attraction. In another study, the shape, size and average number of magnetosomes in a cell were studied. It was determined that each cell contains roughly 20 magnetosomes with an aligned edge length of 420 A° (23). Still, it is not fully clear how the MTB limit the magnetosome confines to a single active sphere, and why they're in a chain. In addition, it's allowed that this limitation is caused by the commerce between the membrane that encompasses the magnetic flyspeck and the cell. The magnetic disciplines that are in a single chain are aligned similar that the magnetic axes resemble to each other. Therefore, the total magnetic energy of the magnetosome is the sum of all the magnetic moments of each flyspeck. The magnetic moment of MTB is responsible of aligning according to the Earth's magnetic field. These bacteria bear as ferromagnetic bio-magnets (43).

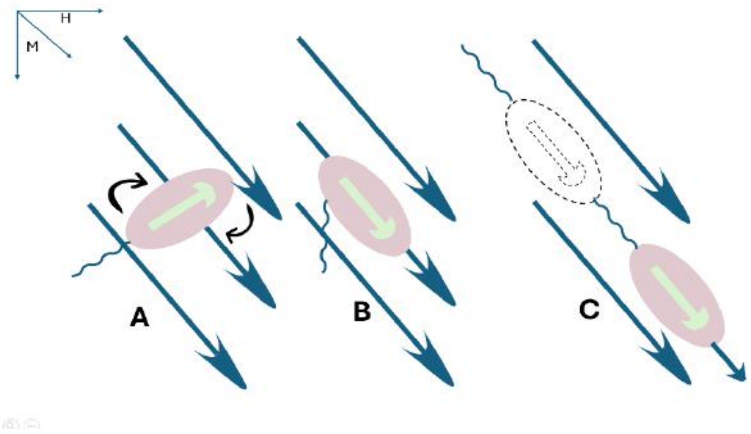

Figure 4: The alignment of magnetotactic bacteria in the direction of the outer magnetic field

9.CONCLUSION:

In the treatment of numerous conditions, especially cancer, it's veritably important that the medicines only reach the tumoral cells (as a target cell), and that a point- shot is directed at these ailing cells. In order to avoid surgery and side goods of medicines, a target subject among current experimenters in having bacteria and small-scale robots cooperate. The idea that the medicine to be carried to problematic cells by bacteria, in other words, using bacteria as little robots have been met with enthusiasm in the scientific community. Especially since they can swim in blood and have attractions within them, the use of magnetotactic bacteria by directing them to target cells with an applied magnetic field has been raised as a content. As a result, the end of this paper is to attract attention to these microorganisms that have come the limelight in exploration and their medical operations. The increase number of studies and supports in this exploration field may open up new horizons.

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