Magnetic Bacteria:
A Future in Industry and Medicine
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When Salvatore Bellini, an early microbiologist, looked through a microscope at a simple drop of pond water, he probably saw a multitude of bacteria behaving in different ways. The miniscule squiggles swarming across a microscope slide are indistinguishable to the naked eye, and identifying these organisms can be dubious even under today's power of magnification. The unique behavior of a subset of these bacteria, however, allowed for the serendipitous discovery of a group of these organisms now referred to as magnetotactic bacteria. The magnetic properties of these bacteria, explored below, may one day hold future applications in industry and medicine.

A History of the Discovery of Magnetotactic Bacteria

Salvatore Bellini was the first to characterize these magnetic microorganisms at the University of Pavia in 1963 (Bellini, 2009). Bellini was investigating water and sediments from potholes and shallow lakes when he noticed that in many of his samples, a peculiar group of bacteria always swam in one direction, accumulating on one side of the microscope slide. In addition, he observed that some of these microorganisms, when suspended in a droplet of collected water, swam towards the arm of his microscope (Bellini, 2009). Wondering if the composition of the microscope influenced this behavior, he sequentially replaced the microscope arm, lenses, and stage with metals, followed by wood and then cardboard, to see if the organisms would behave differently. However, the organisms' behaviors did not alter regardless of the changes Bellini made to either the parts or the materials of the microscope. Suspicious that the bacteria were being guided by an external stimulus, he attempted to manipulate them with a magnet, discovering that they immediately followed the magnet. Further experiments with both live and dead cells exhibited the same ability to follow a magnet, leading Bellini to surmise that these "magnetosensitive bacteria," as he called them, contained an internal compass that oriented them to a magnetic field (Bellini, 2009).

Bellini's findings remained largely hidden until Richard Blakemore rediscovered these magnetic bacteria in 1982 (Blakemore, 1982). Blakemore had spent some time investigating microorganisms living in mud, and he too noticed the accumulation of particular microorganisms to one side of the slide. He observed that, regardless of how the slides were turned or the direction of light that fell upon the slide, the organisms always swam in the same direction. Aware that other species of organisms exhibited magnetic behavior, Blakemore realized that these cells also could be repelled or attracted to a magnet, depending on the pole that faced the cells (Blakemore, 1982). This time, a publication documenting this strange behavior attracted a great deal of interest from other scientists, bringing magnetic bacteria into laboratories as a research specimen.

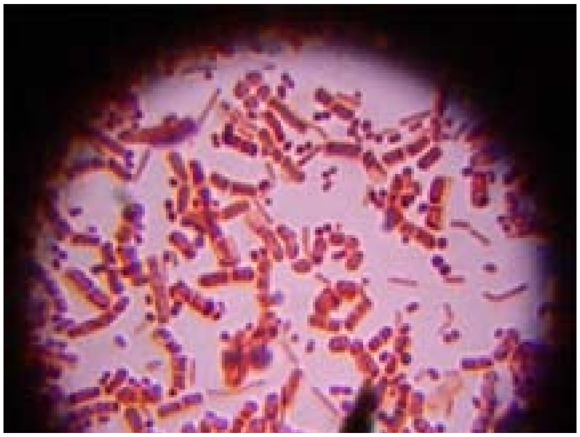

Figure 1. The multitudes of bacteria that Bellini came across in his studies of microscopic organisms were similar to the ones shown here.

Now referred to as magnetotactic bacteria, these microorganisms are defined based on a particular group of characteristics. Many are microaerophilic, meaning that they prefer low oxygen levels for growth. They also exhibit motility, directed by the earth's geomagnetic field to swim either up or down in water, presumably to reach regions where oxygen levels are optimal (Blakemore, 1982). In order to detect this magnetic field, these bacteria contain chains of iron oxide particles or crystals called magnetosomes that function like miniature compass needles inside of them. The bacteria themselves are diverse in shape and size, as are the magnetosomes inside of them (Blakemore, 1982). Despite the diversity in these crystals, however, the magnetosomes' ability to interact with magnetic fields and their miniscule size makes them nanoparticles with many potential applications.

Applications of Magnetosomes and Magnetotactic Bacteria

In order to study and use these magnetosomes, scientists must be able to grow these magnetosome-containing bacteria in a reliable fashion. Extensive research has gone into the establishment of basic protocols for growth. These protocols allow for many bacteria to be cultured, or grown, on an industrial scale for the use in numerous applications. In addition, techniques have been developed that allow for magnetosomes to be isolated and separated from bacteria due to density, magnetic properties, and other characteristics (Varadan, Chen, and Xie, 2009). Therefore, the production of large amounts of these magnetic particles for various applications is feasible, making the use of these materials a possibility in the near future.

Magnets play a large role in daily activities all over the world. For example, tapes in musical cassettes and printer inks rely on magnetic principles to function. In addition, medical techniques, such as magnetic resonance imaging, are fundamentally based on magnets (Schuler and Frankel, 1999). Due to the broad range of nanomagnet applications, many scientists are focusing on understanding the formation and function of these tiny magnets in magnetotactic bacteria.

"Magnetotactic bacteria... would be useful as microscopic shovels or carpets."

There are two ways that magnetotactic bacteria might be useful. One approach takes advantage of the cells' abilities to align to a magnetic field. A second approach would be to extract the magnetosomes from the bacteria to use as small, uniformly sized magnets in devices that require such nanoscale particles. Since bacteria can reproduce rapidly under proper conditions, harvesting large scale quantities of these bacterial magnetosomes for use as nanoparticles could be cheaper and simpler than current industrial processes of preparation.

A conceivable function of these organisms as a whole is to use them in industrial preparation and clean-up. In many cases, industrial production requires the use of toxic or heavy metals, which are often difficult to handle. Since magnetotactic bacteria can be easily manipulated by the turn of a magnet, the entire cells themselves would be useful as microscopic "shovels" or "carpets" with which to move layers of substances (Schuler and Frankel, 1999). For example, when bacteria are grown in media, or food sources, containing certain metals and minerals, the metals are taken up by the bacteria. In this way, certain metals can be accumulated in the bacteria. Then the bacteria can be drawn away from the remaining mixture by applying a magnetic field (Bahaj and James, 1994). This technique would effectively remove chemicals from a mixture. In addition, bacteria can be attached to larger particles that need to be separated or isolated but cannot be taken up inside the bacteria. This technique of fixing bacteria to these particles could be useful for removing the particles, as one could then direct the bacteria and their attached cargo to swim in a certain direction along a magnetic field to a separate area. The ability to attach magnetotactic bacteria to beads and use them to push the beads along magnetic fields has been previously achieved (Martel, et al, 2006). Unfortunately, these approaches have a limited application; since the cells are so small, a large amount of them would be required to move any significant quantity of a substance. In addition, not all substances would be moveable, because viscous and heavy solutions could inhibit bacterial motility. Certain metals can also inhibit bacterial motors to prevent motility once they have been taken up into the cell (Bahaj and James, 1994).

Isolated magnetosomes are also potential candidates for additional applications. One consideration for these magnetic nanoparticles is in cancer treatments. In one type of treatment, magnetic particles are used to generate heat and kill cancerous cells in a technique known as magnetic hyperthermia. Magnetic particles can either be injected locally into the cancerous tissue or by using antibodies tagged with these magnetic particles that attach to cancerous tissues. Then, the magnets can be turned in a magnetic field to generate heat, effectively destroying the cancerous cells (Torchilin, 2006). The benefit of using biologically-derived nanomagnets made of iron oxides, like magnetosomes, is that they can be taken up by the body with minimal toxic side effects. Currently, clinical and research studies are being performed using magnetosomes of different sizes and shapes to determine the most optimal particles that will efficiently conduct magnetic hyperthermia. This research takes advantage of the wide range of shapes and sizes of magnetosomes produced in magnetic bacteria. In addition, larger particles may be useful for another technique called embolization, or clogging, of blood vessels that

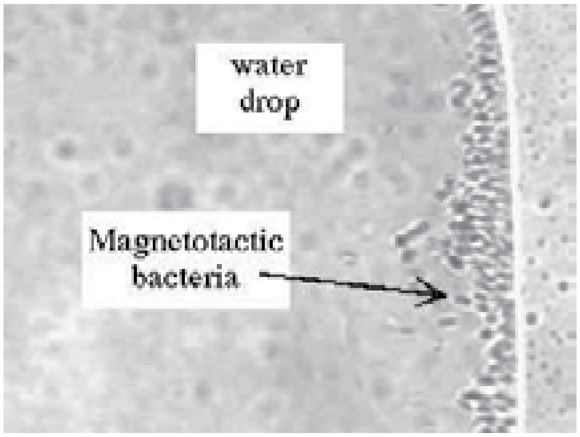

Figure 2. Microscope image of magnetotactic bacteria in a drop of water.

lead to tumors (Torchilin, 2006). This type of treatment prevents the bloodstream from accessing cancerous cells and from carrying nutrients to the tumor cells.

Another medical application of magnetosomes is to use them for drug delivery, which is the transportation of drug molecules to specific regions of the body. Due to the specific chemical composition of iron oxides in the magnetosomes, drugs can easily diffuse from the magnetosomes (Torchilin, 2006). The advantage of using magnetosomes for drug delivery in the body, rather than other methods, is the ability to control and direct their path towards particular tissues that require treatment through a magnetic field. For example, magnetosomes, or particles derived from them, carrying chemotherapy drugs could be directed towards cancerous tissues for localized release. This maneuver would minimize the impact of chemotherapy drugs on surrounding cells. This magnetic property also allows for efficient concentration of the drug at a target location, enhancing the concentration of a drug at a specific spot for more effective treatment. A similar use has been entertained in which the metal particles do not carry chemotherapy drugs, but rather radiation, which could be deposited at sites where tumors are found (Torchilin, 2006). The ability to use a magnet to concentrate the effects in one small area could greatly increase the effectiveness of chemotherapy radiation.

This particular use of magnetosomes is not just limited to cancer therapy. The same technique could be used to carry anti-inflammatory, anti-bacterial, or blood clotting drugs to localized regions (Torchilin, 2006). Once again, further research is needed to arrive at magnetic particles that are large enough to be easily directed with a magnetic field but small enough to be easily controlled through the body, so that the drugs are not released in other regions where effects may be harmful.

Another valuable application would be the use of magnetosomes as contrast agents in magnetic resonance imaging (MRI). In many cases, the difference in the magnetic field that is detected by the machine is generated by the tissue itself. However, the difference in the composition of cancerous cells versus healthy cells is not sufficient to achieve a high level of contrast, making images difficult to read. One possible solution would be to increase the magnetism of the cancer cells. In order to do this, one must use particles that have a strong magnetic dipole so that they can respond to a magnetic field; simultaneously, the particles must be small enough to be absorbed by the cells. Magnetosomes are suitable candidates as MRI contrast enhances because they meet size requirements for absorption into cells, but still have a suitably strong magnetic dipole to respond optimally to a magnetic field (Nohyun et al, 2011). In addition, since magnetosomes are biological in origin, they can be safely stored and broken down in the body. So far, experiments have demonstrated that synthetic iron oxides similar to magnetosomes are capable of enhancing magnetic resonance images, supporting the notion that magnetosomes may one day be useful for magnetic imaging techniques (Nohyun et al, 2011).

The discovery of magnetotactic bacteria occurred by accident, hardly with the intent of using these organisms in industry, technology, and medicine. However, magnetotactic bacteria have since been recognized for their potential in applications in these fields. Since their magnetosomes are small yet strongly magnetic and are naturally derived, they overcome the limitations of many biological applications of other particles that are too large or too toxic. These potential applications are some of the goals in magnetosome research. By understanding more about how these magnetosomes are made and how they function, scientists may one day be able to use these bacteria and magnetosomes on large scales for these important applications.

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