Chapter 17
Magnetic Particles for Biomedical Applications

Raju V. Ramanujan

17.1 Introduction

This chapter discusses applications of magnetic materials in bioengineering and medicine [1–8]. Magnetism and magnetic materials have been used for many decades in many modern medical applications, and several new applications are being developed in part because of the availability of superior electromagnets, superconducting magnets and permanent magnets [9–12]. Advances in the synthesis and characterization of magnetic particles, especially nanomagnetic particles, have also aided in the use of magnetic biomaterials [6–12]. We begin with an introduction to magnetism and magnetic materials, followed by a discussion of the characterization, synthesis techniques and applications of magnetic biomaterials [8, 9]. Magnetic materials can be applied to cell separation, immunoassay, magnetic resonance imaging (MRI), drug and gene delivery, minimally invasive surgery, radionuclide therapy, hyperthermia and artificial muscle applications [1–5, 7]. Physical properties which make magnetic materials attractive for biomedical applications are, first, that they can be manipulated by an external magnetic field – this feature is useful for separation, immunoassay and drug targeting, and second, hysteresis and other losses occur in alternating magnetic fields – this is useful in hyperthermia applications.

In biology, there has been much interest in the possible use by bees and pigeons of magnetic materials as biological compasses for navigation. Some magnetotactic bacteria are known to respond to a magnetic field, they contain chains of small magnetite particles and they can navigate to the surface or bottom of the pools that they live in using these particles. These particles can be obtained by disruption of the cell wall followed by magnetic separation; the presence of the lipid layer makes these particles biocompatible and they can be readily functionalized for a variety of biomedical applications.

The earliest known biomedical use of naturally occurring magnetic materials involves magnetite (Fe_3O_4) or lodestone which was used by the Indian surgeon Sucruta around 2,600 years ago. He wrote in the book Ayurveda that magnetite can be used to extract an iron arrow tip. Current areas in medicine to which magnetic biomaterials can be applied include molecular and cell biology, cardiology, neurosurgery, oncology and radiology.

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In the human body, there is a constant movement of ions within and outside the cells as well as across cellular membranes. This electrical activity is responsible for magnetic fields, called biomagnetic fields, which we can measure using sensitive instruments placed outside the body. The study of such fields, called biomagnetism, is a fascinating area related to magnetism which is not covered in this chapter due to lack of space. Of course, the effect of magnetic fields on humans and animals is also the focus of many studies, examples being the effect of the electromagnetic field produced by power lines and cell phones on humans. Of course, we are all immersed in the earth's magnetic field of about 0.5×10^{-5} T while the magnetic field of a neutron star is of the order of 10^8 T!

Here we focus on the origin of magnetism in materials, the types of magnetic materials used in medicine, and contemporary and future applications of magnetic biomaterials.

17.2 Magnetism and Magnetic Materials

Magnetism is known to all of us from childhood as the phenomenon by which some materials attract or repel other materials from a distance; examples of such materials include iron, lodestone and some steels. Broadly, magnetic forces are generated by moving charged particles, leading to magnetic fields. There are a number of excellent references to magnetism and magnetic materials, and an introduction is provided in Callister, from which the following discussion is derived [10].

Consider a material placed in an external magnetic field. The atoms in this material possess an atomic moment which responds to this external field. It is useful to think of magnetic dipoles existing in magnetic materials; these dipoles can be considered to be small bar magnets with north and south poles. The dipoles possess a magnetic dipole moment which can respond to the external magnetic field. Some field vectors are needed to understand this response: the external magnetic field strength is denoted by H (units A/m), the magnetic induction in the material is denoted by B (units tesla) and the magnetization by M (units A/m). B, H and M are related by

$$\mathrm{B} = \mu_0 (\mathrm{H} + \mathrm{M}) \tag{17.1}$$

where μ_0 is the permeability of free space (its magnitude is 1.257×10^{-6} H/m) and M is the magnetic moment m per unit volume of the material. The value of M depends on the type of material and the temperature and can be related to the field H through the volumetric magnetic susceptibility χ by the relation

$$M = \chi H \tag{17.2}$$

17.2.1 Categories of Magnetic Materials

We now discuss the magnetic response of bulk material. In simple cases we can understand in a straightforward fashion this response in terms of the behavior of individual atoms. In other cases, interactions between individual atoms makes the picture more complicated. The magnetic response results in materials being classified as either diamagnetic, paramagnetic or ferromagnetic. Antiferromagnetism and ferrimagnetism fall within the broad category of ferromagnetism.

For most bulk materials, the response to an external magnetic field is weak, e.g., in diamagnetic and paramagnetic materials. Diamagnetism is very weak and not permanent; it persists only as long as the external field is present. It occurs due to a change in the orbital motion of electrons due to the external field, the direction of the induced magnetic moment is opposite to the field. In an inhomogenous field, such materials are attracted towards regions where the field is weak (Fig. 17.1). In paramagnetism, each atom has a permanent dipole moment because of incomplete cancellation of its electron magnetic moments. When a field is applied these atomic dipoles *individually* tend to align with the field, much as a compass needle aligns with the earth's magnetic field.

Diamagnetic and paramagnetic materials exhibit magnetization only in the presence of an external field; the low values of susceptibility χ imply that the magnetic induction in such materials is very weak. Typical values of susceptibility, at room temperature, for diamagnetic copper is -0.96×10^{-5}, for paramagnetic aluminum is 2.07×10^{-5} and paramagnetic manganese sulfate is 3.7×10^{-3} [10].

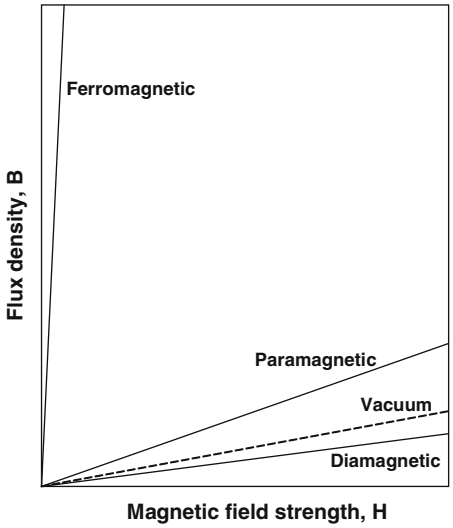

Fig. 17.1 Schematic of the flux density B as a function of H for various materials [10]

Feromagnetism is the most familiar type of magnetism. It occurs, for example, in body centred cubic (b.c.c.) iron, cobalt, nickel, and in many alloy compositions based on Fe, Co and Ni. Ferromagnetic materials, unlike dia- and para- magnetic materials, show permanent magnetic moments even in the absence of an external field. The susceptibility values are very high compared to those of para- and diamagnetic materials, reaching up to 10^6. The magnetic moments in such materials arise mainly from atomic spin magnetic moments. More importantly, interactions between atoms cause spin magnetic moments to align with one another in a *cooperative* fashion. Thus, large regions in a crystal can have atoms with their spins aligned with one another. When all the magnetic dipoles are aligned the magnetization reaches its saturation value (M_s), e.g., the magnitude of M_s for nickel is 5.1×10^5 A/m.

As mentioned earlier, ferromagnetism results from a cooperative *parallel* alignment of spins. In other materials, e.g., MnO. The magnetic moment coupling between atoms (or ions) results in the spin moments of neighboring atoms being aligned in *opposite* directions. Such materials are antiferromagnetic. In the case of MnO, the moments of adjacent Mn^{2+} ions are antiparallel, thus the material has no net magnetic moment (Fig. 17.2).

Some materials, including the magnetic biomaterial magnetite (Fe_3O_4) mentioned in the introduction, exhibit ferrimagnetic behavior [10]. Hexagonal ferrites and garnets are other ceramic materials that fall in this category. Cubic ferrites, such as magnetite, can be represented as MFe_2O_4, where M is a metal. In the case of Fe_3O_4, Fe ions exist in both the +2 and +3 valence states. The magnetic moments of the two types of Fe ions differs; in this case, there is a net magnetic moment because for the solid as a whole the spin moments are not completely cancelled; although the spin moments of the Fe^{3+} ions cancel one another, the magnetization arises from the parallel alignment of the moments of the Fe^{2+} ions (Fig. 17.3). By adding other ions such as Ni^{2+} and Co^{2+} to Fe_3O_4, ferrites having a range of magnetic properties can be produced. This flexibility can be used to tune the magnetic properties for hyperthermia applications by creating cubic mixed-ferrite material.

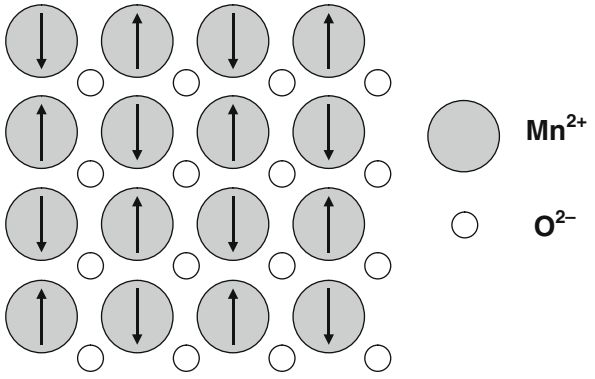

Fig. 17.2 Schematic of antiparallel alignment of spin magnetic moments in antiferromagnetic MnO

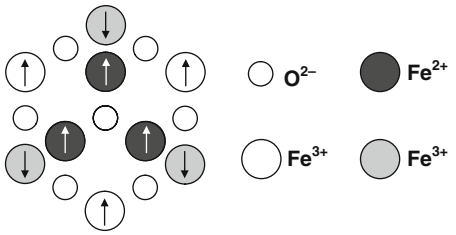

Fig. 17.3 Schematic depicting the spin magnetic moments for Fe^{3+} and Fe^{2+}in Fe_3O_4

17.2.2 The Influence of Temperature

It can be expected that temperature will play an important role in determining magnetic properties, since entropy effects will be more dominant at high temperatures. The magnetic properties of both ferri- and ferro-magnets depend on the coupling forces between neighboring atoms; at higher temperatures, entropy effects favor a random arrangement of spins, resulting in a reduction in saturation magnetization. The saturation magnetization decreases with increasing temperature; at the Curie temperature T_c it becomes zero and the material becomes paramagnetic above this temperature. The Curie temperature, e.g., of cobalt is 1,120 °C and that of magnetite is 585 °C. Thus a given material can change its magnetic behavior depending on the temperature; its use as a magnetic biomaterial will consequently depend on the relative values of the service temperature and the Curie temperature. The ferromagnetic to paramagnetic phase transformation described above has been used to act as an on-off switch in hyperthermia applications; the magnetic material is designed to have a Curie temperature equal to the temperature required for hyperthermia.

17.2.3 Magnetization Processes in Ferromagnetic and Ferrimagnetic Materials

The B-H loop enables us to classify magnetic materials into different categories, the simplest division being that of soft and hard magnetic materials. In a hard magnetic material, the area within the B-H loop is much larger than that in a soft magnetic material, and the coercivity is large, giving rise to a "fat" B-H loop; this implies a greater amount of hysteresis in a hard magnet. On the other hand, soft magnets have skinny B-H loops; as a result, soft magnets are be easily magnetized and demagnetized.

Examples of magnetically soft materials are commercial iron ingot, oriented silicon-iron and Ferroxcube A (48% $MnFe_2O_4$ –52% $ZnFe_2O_4$) with saturation magnetic induction of 2.14, 2.01 and 0.33 T, respectively. Hard magnets are difficult to demagnetize, hence they are referred to as permanent magnets. The energy product, $(BH)_{max}$ is one of the useful parameters to classify hard magnets; it is the area of the largest B-H rectangle we can construct in the second quadrant of the B-H loop. Two types of hard magnets are commercially useful: conventional and high

energy. Examples of conventional hard magnets are Cunife (60% Cu-20% Ni-20% Fe) with a remanence of 0.54 T and an energy product of 12 kJ/m^3 and sintered ferrite 3 (BaO-6 Fe_2O_3) with a remanence of 0.32 T and an energy product of 20 kJ/m^3. The usual range of energy product of conventional hard magnets is between 2 and 80 kJ/m^3, while that of high energy magnets is greater than 80 kJ/m^3. Examples of the latter are samarium–cobalt magnets ($SmCo_5$) and neodymium–iron–boron ($Nd_2Fe_{14}B$) magnets with typical remanence values of 0.92 and 1.16 T respectively and energy product values of 170 and 255 kJ/m^3 respectively [10].

17.2.4 Factors Affecting Magnetic Properties

From a materials standpoint it is useful to distinguish those properties that are structure sensitive from those that are relatively structure-insensitive; susceptibility and coercivity fall in the first category while saturation magnetization is an example of the second. Manipulation of the properties can be performed by altering the composition, crystal structure, stress state and size of the material. Since size plays an important part in many magnetic biomaterials applications, we now consider the effect of particle size on magnetic properties (Fig. 17.4).

In for example drug delivery, gene delivery and hyperthermia, small magnetic particles are used [5]. In large particles (greater than about 1 μm) there are many magnetic domains; this leads to a narrow hysteresis loop. Such particles are useful in immunomagnetic separation of pathogenic microorganisms in microbiology. For smaller particle sizes (less than about 1 μm) it is energetically more favorable for only one domain to exist. The response of such particles to a magnetic field is qualitatively different, resulting in a broader hysteresis loop. If the particle size is reduced further to about 20 nm (the exact size depends on the composition of the material), the material becomes superparamagnetic, which means that the

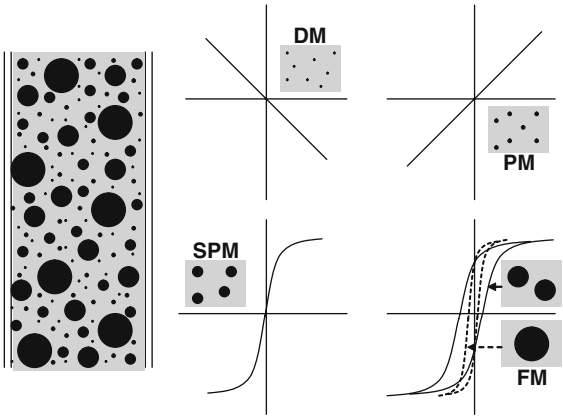

Fig. 17.4 Magnetic properties are affected by the particle size (DM = diamagnetic, PM = paramagnetic, SPM = superparamagnetic, FM = ferromagnetic) [5]

magnetic moment of the particle fluctuates because of the thermal energy (∼kT); at the atomic level the individual atomic moments continue to be ordered relative to each other. Importantly, the remanence is zero, the result is a B-H curve showing no hysteresis; this property is important for reducing the tendency of the particles to agglomerate. The physical basis for the fluctuation of the magnetic moments can be understood as a battle between ΔE, the energy barrier to moment reversal and the thermal energy (kT). In the simplest approximation the energy barrier is the product of the anisotropy energy density K and the volume V. When the particle size is small (small V), the KV term is small and comparable to the thermal energy; this leads to flipping of the magnetic moment. The "blocking" temperature T_B can be regarded as the temperature above which the material becomes superparamagnetic. Superparamagnetic particles are useful as magnetic biomaterials, some are, physiologically well tolerated; an example is dextran-magnetite. Iron oxide coated with dextran is commercially available for MRI, for cell separation and cell labeling applications.

17.3 Physical Principles

We now consider the physical principles involved in the applications of magnetic particles in bioengineering applications. In the case of targeted drug delivery we introduce drug coated magnetic particles into a blood vessel and then apply an external magnetic field. This field attracts and retains the particles at the site of the disease (Fig. 17.5). The blood vessel will exhibit a paramagnetic response to the field from entities such as the hemoglobin. It will also exhibit a diamagnetic response because

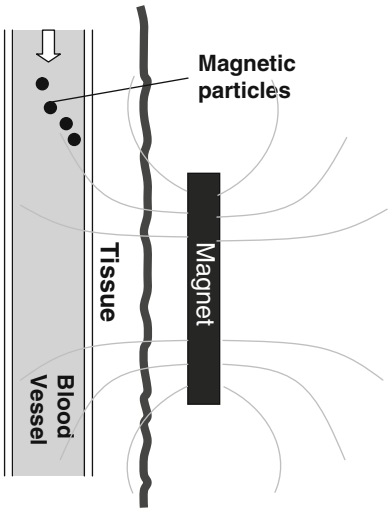

Fig. 17.5 Directed motion of magnetic particles by external magnetic field [5]

of proteins that contain carbon, hydrogen, nitrogen and oxygen atoms. These two responses are much smaller than the response by the magnetic particles. What kind of magnetic field should be applied to target the magnetic particles to the site of the disease? A magnetic field that is uniform gives rise to a torque, but usually we wish to direct the particles in a specific direction, i.e., provide translation motion; this can be accomplished by means of a field gradient. If an appropriate magnetic field gradient is present, a force acts on the particles driving them in a direction which can be chosen to so that the particles are targeted to the site of the disease (Fig. 17.6). Consider a magnetic particle in such a magnetic field gradient; for the case of magnetic nanoparticles suspended in water the magnetic force on the particle has been shown by Pankhurst to be

$$F_m = V_m(\chi_m - \chi_w)\nabla(\frac{1}{2}B.H) \tag{17.3}$$

where V_m is the volume of the particle, χ_m and χ_w are the susceptibility of the particle and water respectively, and the quantity $\frac{1}{2}B.H$ is the magnetostatic field energy density [5]. Assuming that the susceptibility of the particle is greater than that of water, this equation shows that the force is proportional to the differential in the energy density, and recalling the geometrical meaning of the ∇ operator, this magnetic force on the particle acts in the direction of steepest ascent of the energy density field.

In the case of magnetic hyperthermia applications, a different principle is involved; we wish to raise the temperature to about 43 °C in a localized area in order to destroy cancer cells selectively [3]. This can be done by applying a magnetic field which varies with time; ferro- and ferri-magnetic material will be repeatedly cycled through the B-H loop, resulting in hysteresis and other losses which are then converted to thermal energy and result in an increase in temperature.

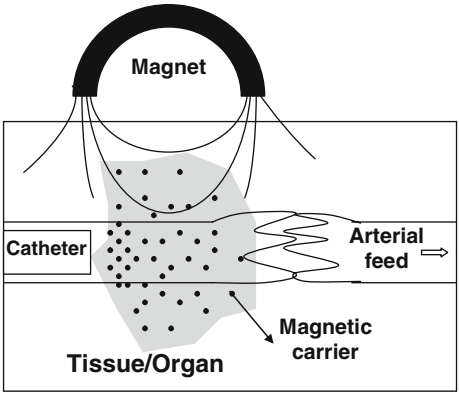

Fig. 17.6 Magnetic carrier for drug targeting and drug delivery [6]

Superparamagnetic materials can also be heated using this technique; the loss mechanisms differ from those observed in ferro- and ferri-magnetic materials.

17.4 Examples and Property Requirements of Magnetic Biomaterials

A common example of a magnetic biomaterial is magnetite. Interestingly, this is the same material used by Sucruta more than 2,000 years ago. Magnetite is found in many biological entities, from bacteria to people. It is an example of cubic ferrites which have an inverse spinel structure. It is ferrimagnetic with a Curie temperature of 578 °C and a saturation magnetization of 4.76×10^5 A/m. Another example of a magnetic biomaterial is maghemite (gamma Fe_2O_3), which is formed when magnetite is oxidized. It has a structure similar to that of magnetite, the difference being that all or most of the iron is trivalent, the saturation magnetization is 4.26×10^5 A/m. Ferritin is a protein that stores iron in humans. It contains typically 4,500 iron atoms in an approximately spherical 12 nm diameter molecule. It has a 12 subunit protein shell containing a ferrihydrite core and an antiferromagnetic core. Gadolinium(III) chelates are commonly used in MRI applications. Iron coated with activated carbon has recently been tried for magnetic drug targeting for the treatment of hepatocellular carcinomas.

The magnetic biomaterial can, in principle, also be Ni, Co, b.c.c. Fe, magnetic alloys of Fe, Co, Ni, Nd–Fe–B or samarium–cobalt materials. In all cases, however, issues of biocompatibility and toxicity limit the choice of materials; however, the use of coatings may make the use of these materials feasible. The hard magnetic materials Nd–Fe–B and samarium–cobalt have the disadvantage that large external fields are required to influence these materials. Materials with high magnetization and high susceptibility are preferred for applications such as drug targeting and magnetic separation. Most of the examples of useful magnetic biomaterials are in powder form, and usually the particles are suitably coated before use. Ideally, the magnetic material should be non-toxic and non-immunogenic. In the case of drug delivery, the particle sizes should be small enough to be injected into the bloodstream and then to pass through the required capillary systems. For in vitro applications, the requirements are more relaxed, larger particle sizes can be used, and biocompatibility and toxicity issues may be less important.

In many cases, it is required to coat the magnetic particles; this is usually done by coating with a biocompatible polymer or with other coatings such as gold, activated carbon or silica (Fig. 17.7). The coating reduces aggregation and prevents the magnetic particle from being exposed directly to the body. In addition, the polymer can be used as a matrix in which drugs, radionuclides or genetic material can be dissolved or as a site for binding of drugs; thus the magnet-coating system can act as "carrier" to deliver useful material to the targeted region. Some examples of common coatings are derivatives of dextran, polyethylene glycol (PEG) and polyethylene oxide (PEO), phospholipids and polyvinyl alcohol [2, 4].

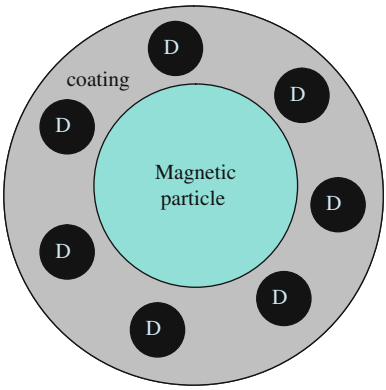

Fig. 17.7 Magnetic particle with biocompatible coating to be used for in vivo applications. D refers to functional groups

17.5 Applications

In this section we discuss present and potential future applications of magnetic biomaterials. We begin with the well studied case of magnetic separation for purification and cell labeling.

17.5.1 Magnetic Separation

Magnetic particles can be used to separate entities from their surroundings so that the surroundings can be purified or to concentrate the entities for further study [1]. This use is based on the difference in the susceptibility between a magnetically labeled entity and the surrounding medium. Examples of the use of this principle are magnetic cell sorting for cellular therapy and immunoassay (which is a process that measures and identifies a specific biological substance such as an antigen). Entities that can be labeled include cells, bacteria and some types of vesicles. The first step is to label the entities with the particles followed by the separation of the labeled entities by magnetic separation (Fig. 17.8). Usually coated particles will be used; the coating will help to bind the particles to the entities such as cells. Specific sites on the cell surfaces can be targeted for attachment by antibodies; this works as a labeling procedure since antibodies bind to their matching antigen. In order to separate out these labeled entities we can use a magnetic field gradient which can attract and "hold" the entities in specific regions, followed by removal of these entities. This method has been applied to the selection of tumor cells from blood as well as to isolate enzymes, DNA and RNA from various sources including body fluids.

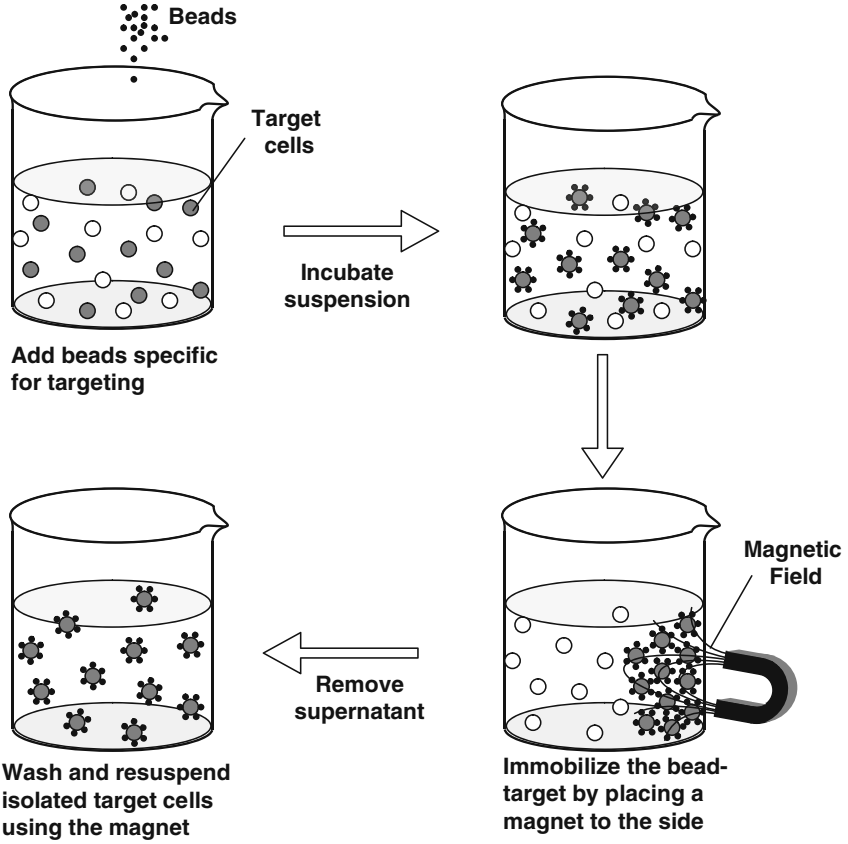

Fig. 17.8 Magnetic separation [4–6]

17.5.2 Drug Delivery

It is well known that most methods of chemotherapy are relatively non-specific. As a result, drugs are "wasted" by being distributed to areas where they are not required, and this can lead to undesirable side effects. What is required is a "magic bullet" which can be used to carry the drugs to the area where they are required. Additionally, it will be advantageous to control the release of the drug once the carrier has reached the target. Much of the work which has been performed so far relates to targeting cancerous tumors. In this case, the magnetic particle first acts as a carrier of the drug which is attached to its outer surface or, more commonly, dissolved in an outer coating. Once the drug coated particles have been introduced into the bloodstream of the patient, a magnetic field gradient, created, e.g., by a strong permanent magnet, is used to "hold" the particles at the targeted region.

Drug release can then take place by enzymatic activity or by means of a specific trigger (controlled release). Physically, the success of this method depends on

the velocity of the particles in the bloodstream, the circulation time as well as the strength of the magnetic field in the region of interest. It is easier to immobilize larger particles in the micron size range; they are less likely to "swept" away by the blood flow. On the other hand, there are many other advantages in having a reduced particle size. It appears that the optimum size may be in the 5–100 nm size range. Typically, a coated magnetite particle is used; noble metals such as gold have been used as a coating in addition to the usual polymer based coatings. Preliminary studies using metallic magnetic particles have also been undertaken. Several studies have reported success in tumor remission (the period during which the symptoms of a disease decrease) in animal models. The difficult case of targeting cytotoxic (cell killing) drugs to brain tumors has also been demonstrated in rats. Human trials using this technique for treating liver tumors have also been performed.

17.5.3 Radionuclide Delivery

Radionuclides (e.g., β–emitters, β is the symbol used to denote an electron) can also be attached to the magnetic particles and this system can then be targeted in the same way as described in the previous section on drug delivery, since the radionuclide does not have to be released in the same way as the drug; one restriction of drug delivery, i.e., control of drug release, is absent.

17.5.4 Gene Delivery

This technique has been called magnetofection, since it involves using magnetic particles to increase the efficiency of gene transfection (introduction of foreign DNA into a host cell) and expression (the process by which a gene's coded information is converted into the structures present and operating in the cell) [7]. A viral vector carrying the gene is coated on the surface of the magnetic particle; by applying a magnetic field; this particle can then be held at the target area. The virus is thus in contact with the tissue for increased duration which increases the transfection efficiency (Fig. 17.9).

17.5.5 Hyperthermia

The idea that a localized rise in temperature (typically about 43 °C) can be used to destroy malignant cells selectively is called hyperthermia; this method of treatment can be effected by magnetic particles. The basic idea is that magnetic material can be heated by an a.c. magnetic field. The mechanisms of heating for ferromagnetic materials include hysteresis losses. In the case of superparamagnetic particles heating can occur by the rotation of the particles themselves or by the rotation of the atomic magnetic moments. Other non-magnetic methods of hyperthermia are also

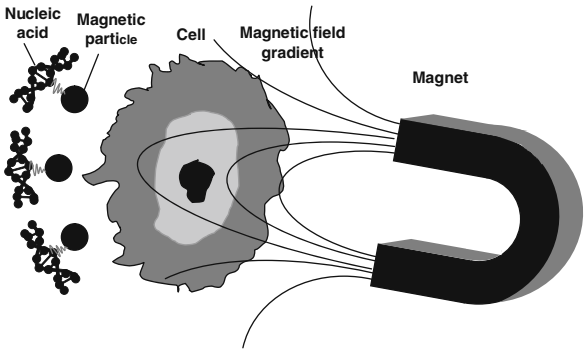

Fig. 17.9 Principle of gene delivery using magnetic particles. The cells to be transfected are positioned between the magnetic field gradient and the nucleic acids which are attached to the particles. The field causes the particles to move towards the target cells, the cell entry is accomplished, e.g., by endocytosis [7]

available. The advantage of using magnetic particles should by now be familiar, i.e., we can target the particles to the targeted region and then heat up the particles by using an external a.c. magnetic field. According to Pankhurst, typically a heat deposition rate of 100 mW/cm^3 is required, and the frequency of the field should be in the kHz range with an amplitude of a few kA/m [5]. Generally iron oxides are used for hyperthermia applications.

17.5.6 Magnetic Resonance Imaging Contrast Agent

So far, we have only considered magnetic properties associated with the electrons in the material. However, protons also have a magnetic moment, and this can be utilized in the powerful imaging technique of magnetic resonance imaging (MRI) [5]. The principle is as follows. We first apply a steady field of about 1 T to a material, causing a very small fraction of protons to line up parallel to the field. The net magnetic moment precesses like a top around the direction of this field (Fig. 17.10). In order to measure the signal produced as a result of this alignment, we now apply a transverse radio frequency magnetic field. The frequency is carefully chosen and its effect is to make the magnetic moment precess in the plane perpendicular to the steady state field. When this second field is switched off, the amplitudes of the magnetic moments relax back to their initial values. This relaxation of the response is measured by pick-up coils. Typically, the relaxation time can be reduced by means of a magnetic particle. Thus if a region is tagged using the magnetic particles, the relaxation time will be lower compared to untagged regions; thus "contrast" is provided and the particle acts as a contrast agent. Usually paramagnetic Gd based materials are used; superparamagnetic iron oxide particles, usually coated with dextran, have also been used for this purpose.

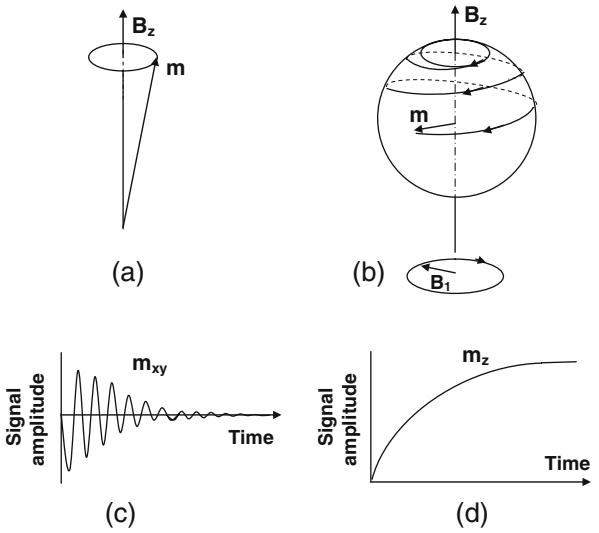

Fig. 17.10 Magnetic resonance for protons with magnetic moment **m** in a field $\mathbf{B}_z$. (**a**) The moment precesses around the field. (**b**) A second field excites the moment precession into the plane perpendicular to $\mathbf{B}_z$. (**c**, **d**) The second field is removed and the in-plane (**c**) and longitudinal (**d**) moment amplitudes relax back to their initial values [5]

17.5.7 Artificial Muscle

There have been various attempts to synthesize artificial muscles; attempts range from a robot-like metallic actuator to a more advanced soft actuator. Hydrogels, which are crosslinked polymer networks swollen with water, can be used to make soft actuators. However, most gels are relatively homogenous materials which shrink or swell uniformly, with no dramatic change in shape. Therefore there is a need to improve the response of gels. Magnetic field sensitive gels in which magnetic particles of colloidal size are dispersed and incorporated into the gels have been developed. These ferrogels combine the magnetic properties of magnetic fillers and the elastic properties of hydrogel. Shape distortion occurs very quickly and disappears abruptly when the external magnetic field is applied and removed, respectively. When these ferroqels are placed in a magnetic field gradient, forces act on the magnetic particles and as a result of strong interaction between magnetic particles and polymer chains, the ferrogel moves as a single unit. Polyvinyl alcohol (PVA) gel has been used for this application because of its mechanical properties and biocompatibility (it has been used, for example, as a synthetic vitreous body to treat retinal detachment); iron oxide particles are often used as the magnetic material.

17.6 Summary

The phenomenon of magnetism has intrigued and excited scientists for centuries. Now magnetic biomaterials can fruitfully be applied to a number of biomedical needs. Applications which are currently being investigated include magnetic cell

separation, immunoassay, hyperthermia, MRI contrast agents and drug, radionuclide and gene delivery. The greatest advantage of such materials is their ability to respond to and be manipulated by external magnetic fields. Magnetism of an atom can be thought to arise from uncompensated spins of its electrons. Magnetism associated with the proton is much weaker but is used for MRI studies. Magnetic biomaterials are usually used in particle form and can be ferro-, para-, ferri-, antiferro- or superpara-magnetic, they are often encapsulated by coatings that can be diamagnetic; this results in a wide range of magnetic responses to an applied field. The most common magnetic biomaterials are the iron oxides magnetite and maghamite, and there is considerable interest in using magnetically superior metals and alloys. Several magnetic properties are a sensitive function of size. The size can be altered by changing process parameters or synthesis techniques, and thus magnetic particles with a wide range of properties can be obtained for a given composition. It has been found that nanosized particles often possess such properties and considerable effort is now underway to create commercially attractive applications using such particles.

Since the field of magnetic biomaterials is a rapidly growing, I have relied on journal, handbook and encylopedia articles the following references are particularly useful.

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