Magnetic properties of materials

• Ferromagnetic: material with a permanent magnetic dipole

• Paramagnetic: material attracted by a magnetic field

• Diamagnetic: material repulsed by a magnetic field

• Non-magnetic: material insensitive to a magnetic field
Magnetic properties of nanoparticles

- Each spin is a small magnet
- Interaction between neighboring spins is dominated by the spin exchange interaction.
- In most materials $J < 0$ and the material is non-magnetic (paramagnetic or diamagnetic)
Superparamagnetic nanoparticles

- In a ferromagnetic material, spins tend to align with each other due to $J > 0$ exchange interaction.
- Magnetic domains are formed that tend to cancel each other to decrease the magnetostatic energy of the system.
- In the presence of an external magnetic field, the domains tend to align to it generating an attractive interaction.
- Once the external magnetic field is removed, domains remain aligned and the material became magnetic (unless $T$ is raised).
Superparamagnetic nanoparticles

- In a paramagnetic material, spins are not subjected to exchange interactions.
- Their magnetic field mediated to zero by thermal agitation and magnetic dipole tendency to cancel each other.
- In the presence of an external magnetic field, the spins tend to align to it generating a weak attractive interaction.
- Once the external magnetic field is removed, thermal agitation cancel residual magnetization.
Superparamagnetic nanoparticles

- In a superparamagnetic material, spins are substituted by small ferromagnetic domains.
- In the presence of an external magnetic field, the domains tend to align to it generating a strong attractive interaction.
- Once the external magnetic field is removed, thermal agitation cancel residual magnetization.
- Loss of magnetization prevents aggregation!
Superparamagnetic nanoparticles

TABLE 1. Functional Properties of Magnetic Nanoparticles

<table>
<thead>
<tr>
<th>Equation(^a)</th>
<th>Relationship with Nanoparticle Properties</th>
</tr>
</thead>
<tbody>
<tr>
<td>( R2 = \frac{1}{T2} = \frac{2.56\pi^2\gamma^2}{405} M_s V \cdot \frac{r^3}{D(1+L/r)} ) (1)</td>
<td><img src="image1" alt="Graph" /></td>
</tr>
<tr>
<td>( \frac{1}{\tau} = \frac{1}{\tau_0 e^{\alpha V/nV}} + \frac{kT}{3nV} ) (3)</td>
<td><img src="image2" alt="Graph" /></td>
</tr>
<tr>
<td>( F_m = V(M_s \cdot \nabla) B ) (4)</td>
<td><img src="image3" alt="Graph" /></td>
</tr>
</tbody>
</table>

\(^a\)\(T2\), transverse relaxation time; \(\gamma\), proton gyromagnetic ratio; \(M_s\), saturation magnetization; \(V\), nanoparticle volume fraction; \(r\), nanoparticle core radius; \(D\), diffusivity of water molecule; \(L\), thickness of surface coating; \(SLP\), specific loss power; \(\mu_0\), vacuum permeability; \(H\), magnetic field strength; \(\rho\), density of particle; \(L(\xi)\), Langevin function; \(\omega\), angular frequency; \(\tau\), relaxation time; \(K\), magnetic anisotropy constant; \(k\), Boltzmann constant; \(V\), particle volume; \(\eta\), viscosity of solution; \(F_m\), force experienced by a particle; \(B\), magnetic field intensity.
Superparamagnetic nanoparticles

MRI contrast agent
Superparamagnetic nanoparticles

Synthesis

Coprecipitation

Precursor salts (FeCl2, FeCl3) are dissolved in water and precipitated in basic conditions

\[ \text{Fe}^{3+} + 2 \text{Fe}^{2+} + 8 \text{OH}^- \rightarrow \text{Fe}_3\text{O}_4 + 4 \text{H}_2\text{O} \]

Nanoparticles are poorly monodisperse and have not exceptional magnetic properties due to crystal defects but the procedure is cheap and suitable for large scale production.

Nanoparticle can be stabilized electrostatically upon addition of acids or bases, alternatively they can be stabilized sterically upon addition of stabilizers.
Hydrotermal methods

Synthesis is performed at high temperatures and high pressures.

Fast nucleation and growth allow for the formation of very small particles and highly crystalline.

Sizes and shapes can be controlled by changing reaction conditions.

(a) 180 °C, 5 h; (b) 180 °C, 15 h; (c) 120 °C, 10 h; (d) 80 °C, 10 h; and (e) 180 °C, 10
Superparamagnetic nanoparticles
Synthesis

Other methods

• Gas-Phase Deposition
• Flow Injection Method
• Electrochemical Method
• Aerosol/Vapor-Phase Method
• Sonochemical Decomposition Method.
• Supercritical Fluid Method.
• Synthesis Using Nanoreactors (emulsions)
• Microbial Method.

Fe(III)-reducing bacteria such as Thermoanaerobacter species (i.e., Thermoanaerobacter ethanolicus strain TOR 39) and Shewanella species (e.g., Shewanella loihica strain PV-4) possess the ability of synthesizing Fe$_3$O$_4$ NPs under anaerobic conditions. The fermentation is carried out by incubation of a β-FeOOH precursor (M$_x$Fe$_{1-x}$OOH, where M is a metal) with the bacteria while maintaining the temperature at 65 °C from several days up to 3 weeks by intermittent addition of electron donors such as glucose. The microbial process is capable of producing 5–90 nm-sized particles.
Superparamagnetic nanoparticles

Stabilization

a) By surface coating using appropriate polymeric stabilizers/surfactants (carboxylates, phosphates, catechols)
b) By deposition of a layer of inorganic metals (e.g., gold), nonmetals (e.g., graphite), or oxides (e.g., SiO$_2$)
c) By generating polymeric shells that avoid cluster growth after nucleation (composite particles, nanocapsule).
d) By the formation of lipid-like coatings (e.g., liposomes/ lipid NPs) around the magnetic core.
### Superparamagnetic nanoparticles

**Approved preparations**

<table>
<thead>
<tr>
<th>Name</th>
<th>Company</th>
<th>Applications</th>
<th>Relaxometric properties $\times 1.5 \text{ T} \text{ mM}^{-1} \text{ s}^{-1}$</th>
<th>Coating agent</th>
<th>Hydrodynamic size (nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ferumoxides AMI-25</td>
<td>Guerbet, Advanced</td>
<td>liver imaging</td>
<td>$r_1 = 10.1$</td>
<td>dextran T10</td>
<td>120–180</td>
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<tr>
<td>Endorem/Feridex</td>
<td>Magnetics</td>
<td>cellular labeling</td>
<td>$r_2 = 120$</td>
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<tr>
<td>ferumoxtran-10 AMI-227</td>
<td>Guerbet, Advanced</td>
<td>metastatic lymph node imaging</td>
<td>$r_1 = 9.9$</td>
<td>dextran T10, T1</td>
<td>15–30</td>
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<td>BMS-180549 Sinerem/Combidx</td>
<td>Magnetics</td>
<td>macrophage imaging blood pool agent cellular labeling</td>
<td>$r_2 = 65$</td>
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<td>ferumoxytol Code 7228</td>
<td>Advanced Magnetics</td>
<td>macrophage imaging blood pool agent cellular labeling</td>
<td>$r_2 = 89$</td>
<td>carboxymethyl-dextran</td>
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<tr>
<td>AMI-121 Luminere/GastroMark</td>
<td>Schering</td>
<td>oral GI imaging</td>
<td>$r_2 = 189$</td>
<td>silicon</td>
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<tr>
<td>ferucarbotran SHU-555A</td>
<td>Schering</td>
<td>liver imaging</td>
<td>$r_1 = 9.7$</td>
<td>carboxyextran</td>
<td>60</td>
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<tr>
<td>Resovist SHU-555C</td>
<td>Schering</td>
<td>blood pool agent cellular labeling</td>
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<tr>
<td>Supravist feruglose</td>
<td>GE-HEALTHCARE</td>
<td>blood pool agent</td>
<td>$r_2 = 38$</td>
<td>pegylated starch</td>
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<tr>
<td>NC100150 (refs 377 and 407) Clariscan</td>
<td>GE-HEALTHCARE</td>
<td>oral GI imaging</td>
<td>na</td>
<td>sulphonated styrene-divinylbenzene copolymer citrate</td>
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<tr>
<td>ferristene Abdoscan VSOP-C184</td>
<td>Ferropharm</td>
<td>blood pool agent cellular labeling</td>
<td>$r_1 = 14$</td>
<td></td>
<td>7</td>
</tr>
</tbody>
</table>
Superparamagnetic nanoparticles

Approved preparations

Treatment of iron deficiency in adult patients with chronic kidney disease

Superparamagnetic iron oxide, particle size: 17-31 nm, coated with PSC (polyglucose sorbitol carboxymethylether)

The nanoparticles enter circulation and are captured by RES macrophages in the liver. Once inside the phagosomes, the polymeric coat is degraded and iron is slowly released and enters the intracellular storage iron pool or transferred to plasma transferritin.
Superparamagnetic nanoparticles

Theranostic applications

Targeted imaging

Multimodal imaging

MRI/NIRF/PET trimodal imaging (a, NIRF; b, PET; c, MRI) with HINPs that were conjugated with both $^{64}$Cu-DOTA and Cy5.5.
Superparamagnetic nanoparticles

MRI imaging

a) SPIO affects T2
b) Gd3+ affects T1
c) Core-shell nanoparticle enable both imaging modes.
Superparamagnetic nanoparticles

MRI imaging
Superparamagnetic nanoparticles

Magnetic hypertermia
Superparamagnetic nanoparticles

Magnetic targeting

FIGURE 4. Tracking injected cells via magnetic NPs. Human lymph nodes before (A) and after (B) intranodal injection of iron oxide-labeled cells. Cells could be tracked for 2 days after injection as they traveled through lymphatic system. (C) Magnetic NPs can also be loaded with small molecule therapeutics and immobilized at the disease site via external magnetic field to increase dose. Adapted and reprinted with permission from refs 41 and 42. Copyright 2005 and 2009 Future Science Group and Nature Publishing Group.
Superparamagnetic nanoparticles
Signal activation via receptor clustering
Superparamagnetic nanoparticles
Detection via nanoparticles clustering

Nanoparticles clustering due to receptor binding cause a relative increase that can be detected by a miniaturized imaging apparatus.
Superparamagnetic nanoparticles
Other strategies for magnetic activated therapy
Superparamagnetic nanoparticles

Libraries for selective cell binding (macrophages vs epithelial cells)
Superparamagnetic nanoparticles
Molecular separation form biological samples
Iron oxide nanoparticles (15 nm) coated with amminosilanes, delivered by intratumor injection

Recurrent glioblastoma multiforme

Based on the distribution of nanoparticles as shown in a post operative CT, the NanoPlan® estimates the treatment temperatures and the necessary magnetic field strength

NanoTherm® therapy is carried out in a magnetic field applicator (NanoActivator™), which was developed specifically for the therapy. The machine's 100 kHz oscillating coil current can be continuously adjusted.

Establishment of the first NanoTherm® therapy treatment center at the Charite-Universitätsmedizin Berlin, Clinic for Radiooncology, Campus Virchow
**Superparamagnetic nanoparticles**

**MagForce**

<table>
<thead>
<tr>
<th>CLINICAL TRIALS/TUMOR TYPES</th>
<th>ADVANCEMENT</th>
<th>EU Regulatory Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glioblastoma multiforme</td>
<td>Phase I Feasibility study</td>
<td></td>
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<tr>
<td>Prostate carcinoma</td>
<td>Phase II Efficacy study</td>
<td></td>
</tr>
<tr>
<td>Pancreatic carcinoma</td>
<td></td>
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</tr>
</tbody>
</table>

Survival increase after recurrence increased to 13.6 from 6.3 months

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