

The main methods of medical imaging

Medical imaging is a unique, non-invasive set of techniques that make it possible to visualise biological processes actually within living organisms themselves. It is a key means for providing insight into physiology and pathology, and ultimately for disease diagnosis, prognosis and therapy. Imaging is therefore the first-choice investigative tool in several branches of medicine and biology.

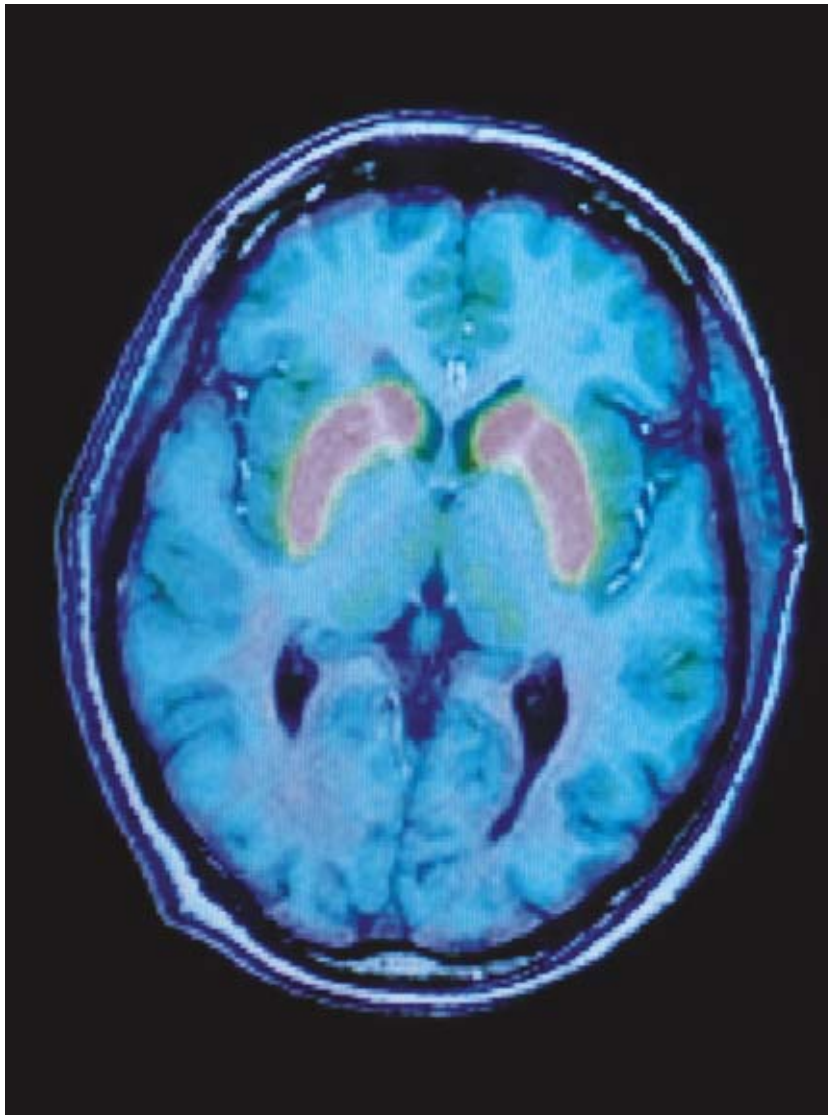
Medical imaging started with X-ray radiation and then developed further with the discovery of artificial **radioactivity** and the allied screening techniques. The next leaps forward, first to **Nuclear Magnetic**

Resonance (NMR) and then to **superconducting** magnets, led to technological breakthroughs in **Magnetic Resonance Imaging (MRI)**.

One of the key dynamic human brain imaging methods is **Electroencephalography (EEG)** which uses **electrodes** fitted on the scalp to measure the electrical activity produced by the brain through synaptic currents generated in **neurons**. EEG gives information on the time-locked neurophysiological activity of the brain, and in particular the cerebral **cortex**. This information is used in neurology for diagnostics, or in **cognitive** neuroscience for research.

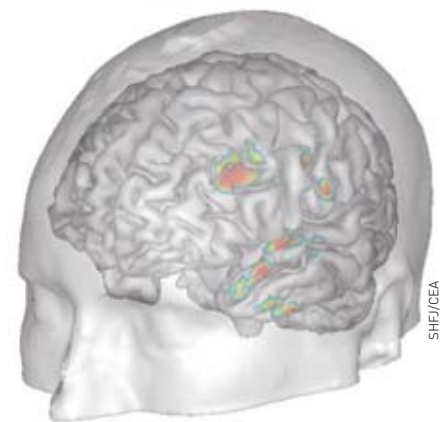
Magnetoencephalography (MEG) records the **magnetic fields** produced by the currents generated by neurons in the brain, using sensors fitted close to the head. MEG is employed in clinical settings by neurologists, especially when the focus is on epilepsy, and for cognitive neuroscience research. MEG can also be used to study developmental disorders like dyslexia, psychiatric disorders like schizophrenia and neurodegenerative disorders like Parkinson's and Alzheimer's.

Positron Emission Tomography (PET) consists in intravenously administering a tracer **molecule** labelled with a radioactive **isotope** and using external detection techniques to track how a normal or diseased organ functions. Radioactive **tracers** present the same physico-chemical properties as their non-radioactive counterparts, with the exception that they are able to emit radiation. This means that they act as a marker that is followed, using appropriate detection methods, to track the previously-labelled molecule's kinetics through the body. The data gathered is then analysed and transformed using a mathematical model to generate a screen image showing where the radio-tracer settles in the body. PET is a widespread technique in physiological or pathophysiological studies on **cognition** and behaviour and is commonly used to study central nervous system disorders



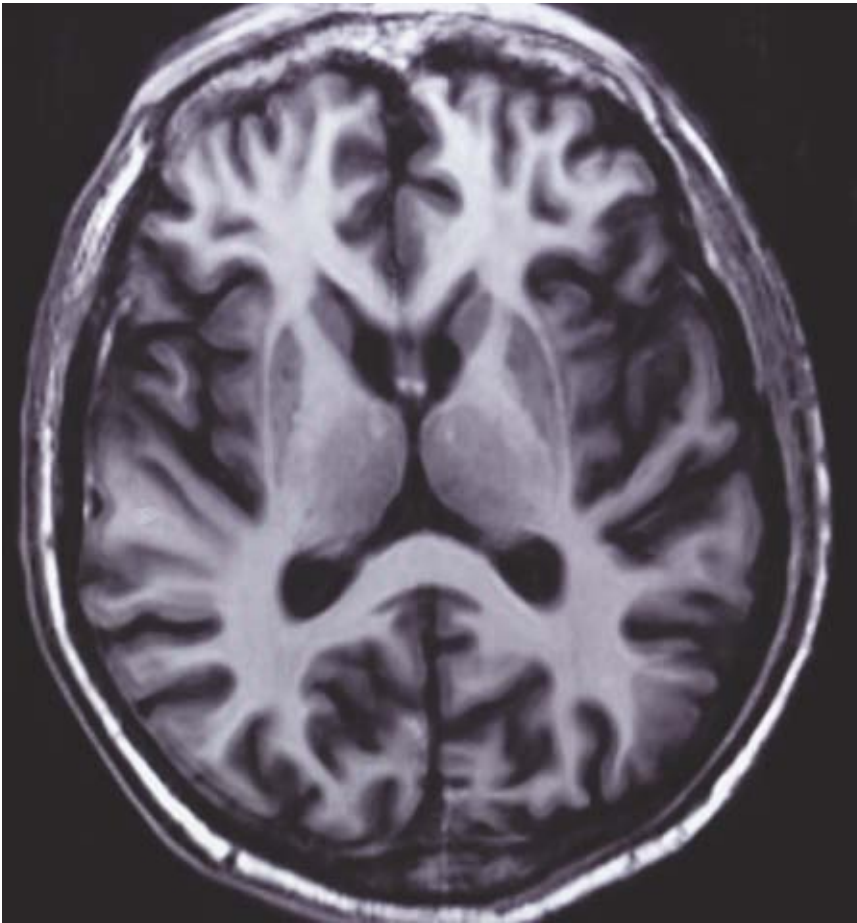
P. Stroppa/CEA

A PET image. The PET camera detects the positrons emitted by radioactive tracers previously injected into the living subject, and 3D images of the target organ are reconstructed by computer analysis.



SHF/CEA

Melancholic depression. PET images measuring regional energy activities merged with the aMRI image of the patient's brain. Areas of hypoactivation are individually detected.



P. Stropas/CEA

Image acquired through the SHFJ's 3-T MRI system at Orsay (Essonne). This technique provides extremely high-precision analysis of infectious or inflammatory lesions, brain vessel damage, and tumours.

such as epilepsy, cerebral ischaemia, stroke, and neurodegenerative disorders (Parkinson's disease, Huntington's disease).

Magnetic Resonance Imaging (MRI) is a non-invasive *in vivo* imaging method. MRI is capable of studying 'soft' tissue such as the brain, bone marrow, or muscle, for example. It can be used to map anatomic structure (**anatomical MRI**, or **aMRI**), monitor organ function (**functional MRI**, **fMRI**) and track various processes of **metabolism** (**Magnetic Resonance Spectroscopy**, **MRS**). After its first developments in 1946, MRI uses the physical phenomenon of **NMR** that exploits the magnetic properties of **atomic nuclei**. Certain nuclei, such as the **hydrogen** nuclei for example, have a weak **magnetic moment**, or **spin**. NMR works by detecting variations in the **magnetisation** of atomic nuclei in response to an extremely powerful magnetic field and **electromagnetic wave**-driven excitation. When an electromagnetic wave is applied at the right frequency, i.e. the **resonance frequency**,

these nuclei change alignment and emit signals as they return to their initial position. Technological advances in computing and magnetic fields have taken NMR from condensed matter physics on to chemical analysis and then structural biology, and more recently into medical imaging.

Anatomical MRI. MRI makes it possible to visually display all body organs. The resonance, under a very-high magnetic field, of water molecules, which are naturally abundant in most biological tissues, is used to generate cross-sectional images detailing brain structures (**grey matter**, **white matter**) down to the millimetre and even less. Radiologists use 'anatomical' imaging to detect and localize brain lesions.

Functional MRI. The recent acceleration in data acquisition and processing has led to the advent of 'functional' MRI, which is able to show neural activity in different brain regions. Indeed, speaking, reading, moving or thinking all activate certain areas in the brain. This neuronal activation triggers a local increase in blood flow in the brain regions concerned. Although it cannot directly detect neuronal activity, fMRI is able to detect the local, transient increase in blood flow that neuronal activity causes, which it does by gauging the magnetization of the **haemoglobin** contained in red blood cells.

Diffusion MRI (dMRI). Diffusion MRI is a powerful tool for measuring the movements of water molecules at the microscopic scale, thereby providing a precise architecture of the neuronal tissue and its variations. It offers a more direct method of measuring than other conventionally used imaging techniques. Diffusion MRI makes it possible to investigate tissue structure at a much finer scale than the millimetre scale offered by MRI image **resolution**, with the added advantage of being much faster.

This array of medical imaging technologies is rounded off by **nuclear magnetic resonance spectroscopy (MRS)**, a non-invasive method of gaining biochemical and metabolic information on the central nervous system. MRS, which is based on the same principles as MRI, can be used to provide precise quantitative data on dozens of different molecules.



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dMRI can diagnose certain pathologies very early on and provide images of the connective fiber clusters (white matter) that network the various brain regions together.

Superconductivity and superconductors



One of the main fields of application of superconductivity is medical imaging. This is the 3-tesla magnetic resonance imager at the SHFJ hospital in Orsay (Essonne).

Some historical background

Trains “flying” above the track using magnetic levitation, electricity storage finally resolved using giant magnetic coils, electrotechnical instruments and electric power transmission cables with no joule losses, magnetic fields that can be used to explore the human body and deliver even higher resolution images. People have been marvelling at the potential uses of superconductivity since 1911 when Dutch physicist Heike Kammerlingh-Onnes first discovered the extraordinary property exhibited by superconducting materials; their electrical resistance drops to zero below a certain critical temperature (which varies with their isotopic mass). This discovery won him the Nobel Prize in Physics in 1913.

Apart from zero electrical resistance and optimal electrical conductivity, the superconductors discovered by Kammerlingh-Onnes (later named type I superconductors) possess another remarkable property manifested by the Meissner effect, discovered in 1933 by German physicists Walter Meissner and

Robert Ochsenfeld. If we ignore the London penetration depth⁽¹⁾, superconductors can be said to exhibit perfect diamagnetism, i.e. the superconducting material fully expulses its internal magnetic field up to a certain critical field value whereas, in theory, the magnetic field of a material with perfect conduction of electricity should equal that of the externally applied field. Herein lies the second obstacle that continues to hamper superconductor applications: superconductivity is lost at above a critical magnetic field strength. For many years physicists thought there was only one type of superconductivity and that the magnetic anomalies observed in some samples were due solely to the presence of impurities. In the 1950s, however, Russian physicists Vitaly L. Ginzburg and Lev Davidovitch Landau came up with the theory that

(1) In 1935, Fritz and Heinz London proposed another explanation for the Meissner effect by claiming that the magnetic field decreases with depth from the surface of a superconducting material over a characteristic length λ_L , known as the penetration depth.

there were actually two types of superconductors.

In 1957, the Russian-American physicist Alexei A. Abrikosov finally confirmed type II superconductivity. Type II superconductors exhibit a completely different type of magnetisation characterised by a mixed state that allows them to retain their superconducting state even in intense magnetic fields. This means they are not subject to the Meissner effect. In 2003, Abrikosov, Ginzburg and the Anglo-American physicist Anthony J. Leggett were awarded the Nobel Prize in Physics for their research into superconductors.

It was also in 1957 that American physicists John Bardeen, Leon N. Cooper and John R. Schrieffer published their theory of superconductivity, which won them the 1972 Nobel Prize in Physics. This BCS theory (named after the first letter of their surnames) postulates that electrons move through a conductor as Cooper pairs (two electrons with opposite spin). These pairs act like spin-zero bosons and condense into a single quantum state via a phonon interaction, which

is also a quantized mode of vibration. It is this electron-phonon interaction that underpins **resistivity** and superconductivity. **Ions** move in response to the ultra-fast passage of an electron (10^6 m/s), thereby creating an area of positive electrical charge which is held after the passage of the electron. This attracts another electron that pairs up with the first electron thereby resisting the **Coulomb repulsion** but not **thermal agitation**, which explains why temperature has such an adverse effect on superconductivity. The BCS theory, which applies to 'conventional' superconductors, did not however provide for the appearance of superconductivity at fairly high temperatures, i.e. higher than the temperature of liquid nitrogen (77 K, i.e. -196 °C), and *a fortiori* at ambient temperature. This 77 K threshold was reached by using compounds such as Y-Ba-Cu-O (current records stand at around 165 K, at high pressure, and 138 K, i.e. -135 °C, at standard pressure). German physicist Johannes Georg Bednorz and Swiss physicist Karl Alexander Müller were awarded the Nobel Prize in Physics in 1987 for their work on **unconventional superconductors**. They discovered a lanthanum-based copper oxide **perovskite** material that exhibited superconducting properties at a temperature of 35 K (-238 °C). By replacing lanthanum with yttrium, particularly in $\text{YBa}_2\text{Cu}_3\text{O}_7$, they were able to significantly raise the critical temperature thus developing the cuprate family of superconductors. Although these are highly effective superconductors, the fact that they are ceramics makes them difficult to use in electrotechnical applications. All **high-critical-temperature superconductors** are type II superconductors.

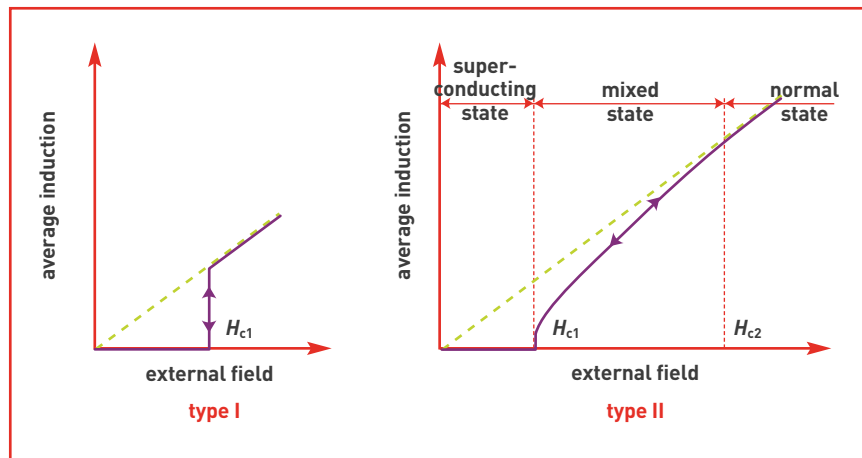


Figure 1. Average induction in type I and type II superconductors under an externally applied magnetic field.

The strange magnetic properties of type II superconductors

In the presence of a magnetic field, type II superconductors exhibit perfect diamagnetism up to certain field H_{c1} just like type I superconductors. Beyond H_{c1} , however, type II superconductors enter a mixed state that allows partial field penetration up to H_{c2} (Figure 1), thereby permitting a material to be superconducting under a high magnetic field.

This mixed state resembles an array of normal-state cores that start to fill the superconducting material at H_{c1} and over. Each region contains a flux quantum ($2.07 \cdot 10^{-15}$ weber) and is surrounded by a vortex of superconducting currents (Figure 2). When the magnetic field increases, the network densifies until it completely fills the superconducting material at H_{c2} .

The distinction between the two types of superconductivity is coupled to the concepts of coherence length ξ and pene-

tration depth λ_L , which characterise the interface between a normal region and a superconducting region. ξ represents the spatial variation of the superconducting state (i.e. the density of the superconducting electrons) and λ_L the London penetration depth of the magnetic field. It is the ratio of these two characteristic lengths, known as the *Ginzburg-Landau parameter* and written as κ ($\kappa = \lambda_L/\xi$), that determines which type of superconductivity is involved. If $\kappa < \sqrt{2}/2$, the superconductor is type I, and if $\kappa > \sqrt{2}/2$, the superconductor is type II.

At the interface, the penetration of the magnetic field, as defined by λ_L , corresponds to an increase in free energy in the superconducting material, while the formation of the superconducting state, characterised by the coherence length, is related to a decline in free energy. The interface's energy balance varies with the ratio κ . In type II superconductors, the

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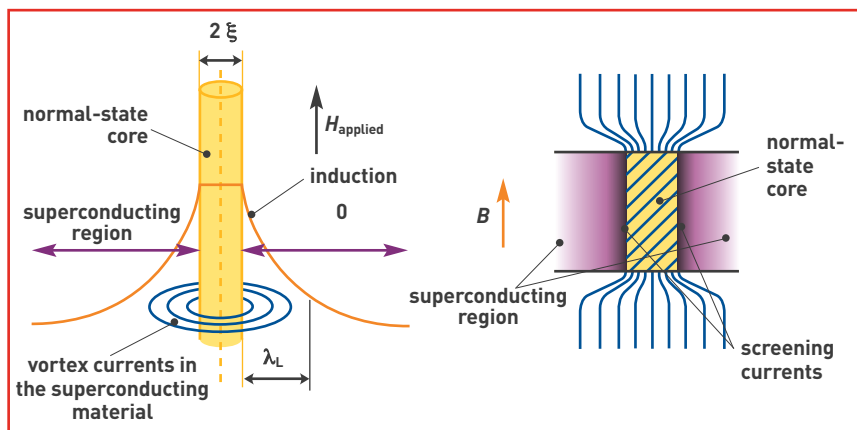
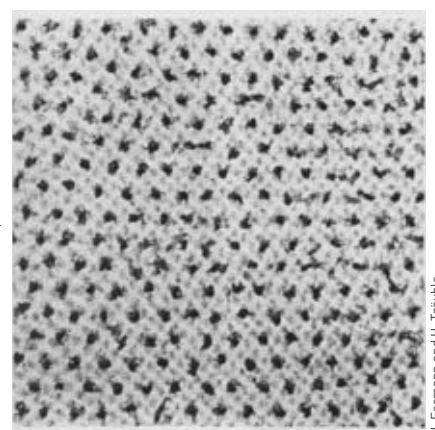


Figure 2. Diagram of a vortex illustrating penetration depth and coherence length.



Magnetic pattern on the surface of a superconductor in mixed state.

(taken from Lavoisier, "Matériaux supraconducteurs")

(taken from Lavoisier, "Matériaux supraconducteurs")

U. Essemann and H. Träuble

material		ξ (μm) 0 K	λ_L (μm) 0 K	κ	T_c (K)	$\mu_0 \cdot H_{c1}$ (teslas) 0 K	$\mu_0 \cdot H_{c2}$ (teslas) 0 K
type I	Al	1.36	0.05	0.04	1.18	0.010 5	
	Pb	0.083	0.037	0.5	7.18	0.080 3	
type II	NbTi	0.005	0.3	60	9.25	0.01	14
	Nb ₃ Sn	0.003 6	0.065	18	18	0.017	25.5
	YBaCuO	plane	0.003	plane 0.8	≈ 300	93	
axis c		0.000 6	axis c 0.2				

Table. Characteristics of some type I and type II superconductors. $\mu_0 \cdot H_{c1}$ and $\mu_0 \cdot H_{c2}$ represent **magnetic inductions**, where μ_0 is the **magnetic permeability** of a vacuum (and of the material in this particular case).

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mixed state therefore results from the creation of a large number of interfaces, with each interface corresponding to a negative energy balance conducive to superconductivity above the H_{c1} field (Table).

Potential avenues for application

Type I superconductivity does not present any great potential for new areas of application. Unfortunately, the critical temperature that limits superconductivity applications is very low in the two superconducting materials that currently offer real-world applications i.e. **niobium-titanium, NbTi** (9.2 K) - the first superconducting cables in niobium-titanium alloy were developed in the early 1960s - and **niobium-tin, Nb₃Sn** (18 K). These materials have to be cooled to the temperature of liquid **helium** (4.2 K)⁽²⁾ in order to activate

their superconducting properties. This temperature was the first important milestone towards achieving superconductivity at ambient temperature, which is the ultimate goal.

Type II superconductors can withstand very strong magnetic fields, and are also able to carry extraordinarily high current densities, up to another critical value that varies with the magnetic field (Figure 3). This fact heralded the development of the first superconducting **magnets**. The current densities that can be generated under these conditions are huge in comparison with what can be achieved with domestic or industrial electrotechnical applications (around 10 A/mm²).

Since the 1970s, the CEA has been focusing its research on the production of large-scale intense **permanent magnetic fields (magnetic confinement of fusion plasmas**, particle physics, medical imaging). In fact, these are the pre-



The discovery of high-critical-temperature superconductivity made it possible to see how superconductivity manifests in the open air in the form of a magnet floating above a pellet of liquid-nitrogen cooled YBaCuO, which is now a famous example of the effect.

dominant applications of type II superconductors, mainly NbTi⁽³⁾, where superconductivity significantly cuts down on electric power consumption despite the **cryogenic** efficiency of the facilities - in fact, one watt dissipated at 4.2 K requires a minimum consumption of 300 W at ambient temperature in the largest industrial power plants. While researchers the world over still dream of developing superconducting materials that function at room temperature, it would seem that applied superconductivity will still have to rely on the use of very low temperature cooling for the foreseeable future.

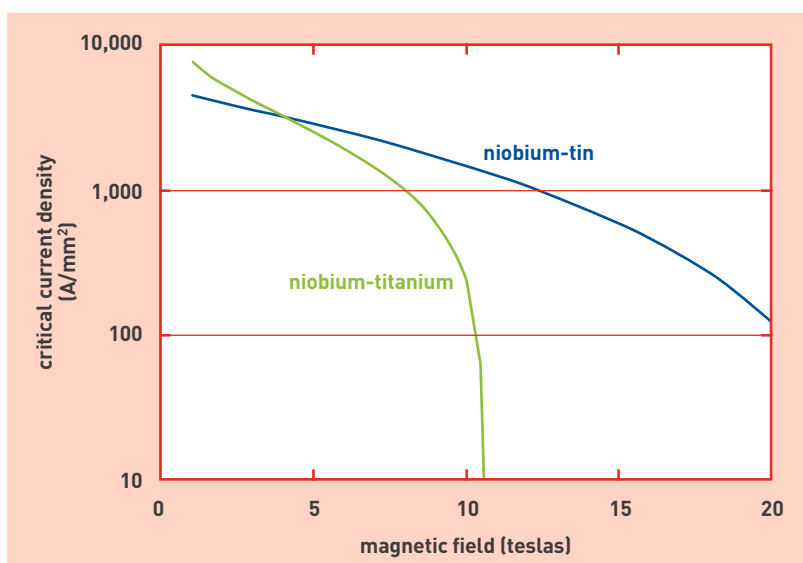


Figure 3. Characteristic critical current densities in relation to a 4.2-K magnetic field for the two superconducting materials most widely used, particularly in the manufacture of superconducting magnets.

(2) The history of superconductivity actually goes as far back as William Ramsay who, in 1895, was the first person to isolate helium. Indeed, where would the science of superconductivity be today if it wasn't for helium which is the key component of the ultra-low cooling process? Note also that Kammerlingh-Onnes finally succeeded in producing liquid helium in 1908 following unsuccessful attempts by James Dewar in the late 19th century, thus paving the way to the discovery of superconductivity.

(3) Produced in quantities of around 1,500 to 2,000 tons per year.

LEG Grenoble

The different types of magnetism

The origins of **magnetism** lie in the properties of **electrons** as explained by the laws of **quantum physics**. Part of an electron's magnetic properties (*spin magnetism*) results from its quantum-mechanical **spin** state, while another part results from the orbital motion of electrons around an **atom's** nucleus (*orbital magnetism*) and from the magnetism of the **nucleus** itself (nuclear magnetism). This is put to use, in particular, for **nuclear magnetic resonance** imaging in the medical field. Magnetism is therefore produced by electric charges in motion. The force acting on these charges, called the **Lorentz force**, demonstrates the presence of a **magnetic field**.

Electrons have an intrinsic **magnetic dipole moment** (the magnetic quantum state being the Bohr *magneton*), which can be pictured as an electron's rotational motion of **spin** around itself in one direction or another, oriented either upwards or downwards. The *spin quantum number* (one of the four numbers that 'quantifies' the properties of an electron) equals $1/2$ (+ $1/2$ or - $1/2$). A pair of electrons can only occupy the same *orbital* if they have opposite magnetic dipole moments.

Each atom acts like a tiny magnet carrying an intrinsic magnetic dipole moment. A nucleus (the **neutron** and **proton** individually have a half-integer spin) will have a half-integer spin if it has an odd atomic mass number; zero spin if the **atomic mass number** and charge are even, and an integer spin if the atomic mass number is even and the charge odd.

On a larger scale, several magnetic moments can together form **magnetic**

domains in which all these moments are aligned in the same direction. These spatial regions are separated by **domain walls**. When grouped together, these domains can themselves form a macroscopic-scale **magnet** (Figure E1).

The type of magnetism that comes into play is determined by how these elementary constituents are ordered, and is generally associated with three main categories of material: *ferromagnetic*, *paramagnetic* and *diamagnetic*.

Any material that is not diamagnetic is by definition paramagnetic provided that its **magnetic susceptibility** is positive.

However, ferromagnetic materials have particularly high magnetic susceptibility and therefore form a separate category.

1. Ferromagnetic materials are formed of tiny domains inside which atoms exhibiting parallel **magnetisation** tend to align themselves in the direction of an external **magnetic field** like elementary **dipoles**. In fact, the magnetic moments of each atom can align themselves spontaneously within these domains, even in the absence of an external magnetic field. Applying an external field triggers domain wall movement that tends to strengthen the applied field. If this field exceeds a certain value, the domain most closely oriented with the direction of the applied field will tend to grow at the expense of the other domains, eventually occupying the material's whole volume. If the field diminishes, the domain walls will move, but not symmetrically as the walls cannot fully reverse back to their original positions. This results in **remanent magnetisation**, which is an important feature of naturally occurring magnetite, or of magnets themselves.

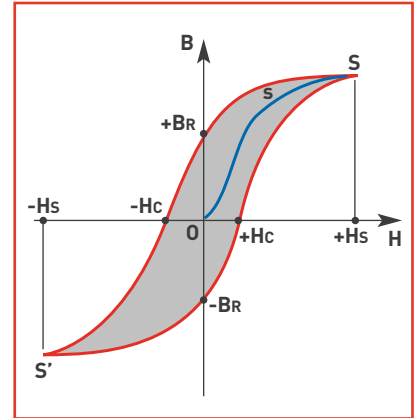


Figure E2. The induction B of a magnetic material by a coil is not proportional to its magnetic excitation (field H). While the initial magnetisation forms an OsS -type curve, shown in blue in the figure, it reaches saturation at point s . Only a partial induction is retained if the field approaches zero; this remanent induction can only be cancelled out by reversing the magnetic field to a "coercive" field value. This hysteresis loop illustrates the losses due to "friction" between the magnetic domains shown on the area bounded by the magnetisation and demagnetisation curves.

The whole process forms a **hysteresis loop**, i.e. when the induced field is plotted against the applied field it traces out a *hysteresis curve* or *loop* where the surface area represents the amount of energy lost during the irreversible part of the process (Figure E2). In order to cancel out the induced field, a **coercive field** has to be applied: the materials used to make artificial permanent magnets have a high coercivity.

Ferromagnetic materials generally have a zero total magnetic moment as the domains are all oriented in different directions. This ferromagnetism disappears above a certain temperature, which is known as the Curie Temperature or **Curie point**.

The magnetic properties of a given material stem from the way the electrons in the metallic cores of a material or of a **transition metal** complex collectively couple their spins as this results in all their spin moments being aligned in the same direction.

Materials whose atoms are widely distributed throughout their **crystal** structure tend to better align these elementary magnets via a coupling effect. This category of materials, which is characterised by a very high positive magnetic

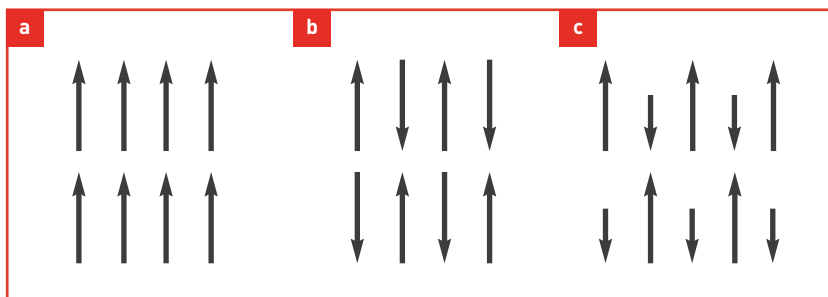


Figure E1. Intrinsic magnetic dipole moments have parallel alignment in ferromagnetic materials (a), anti-parallel alignment but zero magnetisation in antiferromagnetic materials (b), and anti-parallel alignment with unequal moments in ferrimagnetic materials (c).



Stoiber Productions, München

A Transrapid train using magnetic levitation arriving at the Long Yang bus station in Shanghai (China). This German-built high-speed, monorail train was commissioned in 2004 to service the rail link to Pudong international airport.

susceptibility, includes iron, cobalt and nickel and their **alloys**, steels in particular, and some of their compounds, and, to a lesser extent, some **rare earth** metals and alloys with large crystal lattices, and certain combinations of elements that do not themselves belong to this category. In **ferrimagnetic** materials, the magnetic domains group into an anti-parallel alignment but retain a non-zero magnetic moment even in the absence of an external field. Examples include magnetite, ilmenite and iron oxides. Ferrimagnetism is a feature of materials containing two types of atoms that behave as tiny magnets with magnetic moments of unequal magnitude and anti-parallel alignment. **Anti-ferromagnetism** occurs when the sum of a material's parallel and anti-parallel moments is zero (e.g. chromium or haematite). In fact, when atoms are in a close configuration, the most stable magnetic arrangement is an anti-parallel alignment as each magnet balances out its neighbour so to speak (Figure E1).

2. Paramagnetic materials behave in a similar way to ferromagnetic materials, although to a far lesser degree (they have a positive but very weak magnetic susceptibility of around 10^{-3}). Each atom in a paramagnetic material has a non-zero magnetic moment. In the presence of an external magnetic field, the magnetic moments align up, thus amplifying this field. However, this effect decreases as temperature rises since the thermal agitation disrupts the alignment of the elementary dipoles. Paramagnetic materials lose their magnetisation as soon as they are released from the magnetic field. Most metals, including alloys comprising ferromagnetic elements are paramagnetic, as

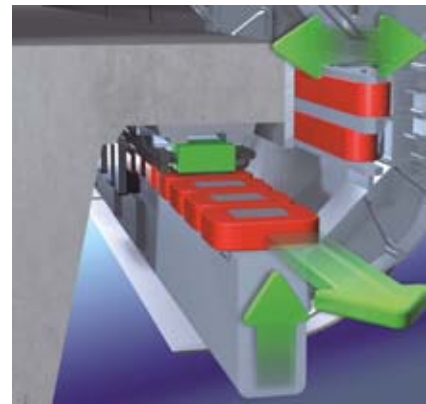
are certain minerals such as pegmatite.

3. Diamagnetic materials exhibit a negative and an extremely weak magnetic susceptibility of around 10^{-5} . The magnetisation induced by a magnetic field acts in the opposite direction to this field and tends to head away from **field lines** towards areas of lower field strengths. A perfect diamagnetic material would offer maximum resistance to an external magnetic field and exhibit zero **permeability**. Metals such as silver, gold, copper, mercury or lead, plus quartz, graphite, the noble gases and the majority of organic compounds are all diamagnetic materials.

In fact, all materials exhibit diamagnetic properties to a greater or lesser extent, resulting from changes in the orbital motion of electrons around atoms in response to an external magnetic field, an effect that disappears once the external field is removed. As Michael Faraday showed all that time ago, all substances can be "magnetised" to a greater or lesser degree provided that they are placed within a sufficiently intense magnetic field.

Electromagnetism

It was the Danish physicist Hans Christian Ørsted, professor at the University of Copenhagen, who, in 1820, was first to discover the relationship between the hitherto separate fields of **electricity** and **magnetism**. Ørsted showed that a compass needle was deflected when an electric current passed through a wire, before Faraday had formulated the physical law that carries his name: the magnetic field produced is proportional to the intensity of the current. **Magnetostatics** is the study of static magnetic fields, i.e. fields which do not vary with time.



Close-up of the magnets used to guide and power the train.

Magnetic and **electric fields** together form the two components of **electromagnetism**. **Electromagnetic waves** can move freely through space, and also through most materials at pretty much every frequency band (radio waves, microwaves, infrared, visible light, ultraviolet light, X-rays and gamma rays). **Electromagnetic fields** therefore combine electric and magnetic **force fields** that may be natural (the Earth's magnetic field) or man-made (low frequencies such as electric power transmission lines and cables, or higher frequencies such as radio waves (including cell phones) or television).

Mathematically speaking, the basic laws of electromagnetism can be summarised in the four **Maxwell equations** (or **Maxwell-Lorentz equations**) which can be used to provide a coherent description of all electromagnetic phenomena from electrostatics and magnetostatics to electromagnetic wave propagation. James Clerk Maxwell set out these laws in 1873, thirty-two years before Albert Einstein incorporated the theory of electromagnetism in his *special theory of relativity*, which explained the incompatibilities with the laws of classical physics.