Fundamentals of Magnetic Biotransport

Lucia Del Bianco
Dip.to di Fisica e Scienze della Terra
Università di Ferrara
lucia.delbianco@unife.it

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Outline

- Brief introduction on magnetic biotransport
  - *Magnetophoresis*

- Some concepts of magnetism and fluid dynamics

- Newtonian particle transport: the magnetic force term

- Magnetophoresis of ferromagnetic, dia- and para-magnetic particles

- Some examples

BIOTRANSPORT

Biotransport is concerned with understanding the movement of mass, momentum, energy, and electrical charge in living systems and devices with biological or medical applications.

Why magnetic particles in biotransport?

- They can be manipulated/stimulated/monitored by an external magnetic field (***action at a distance***).

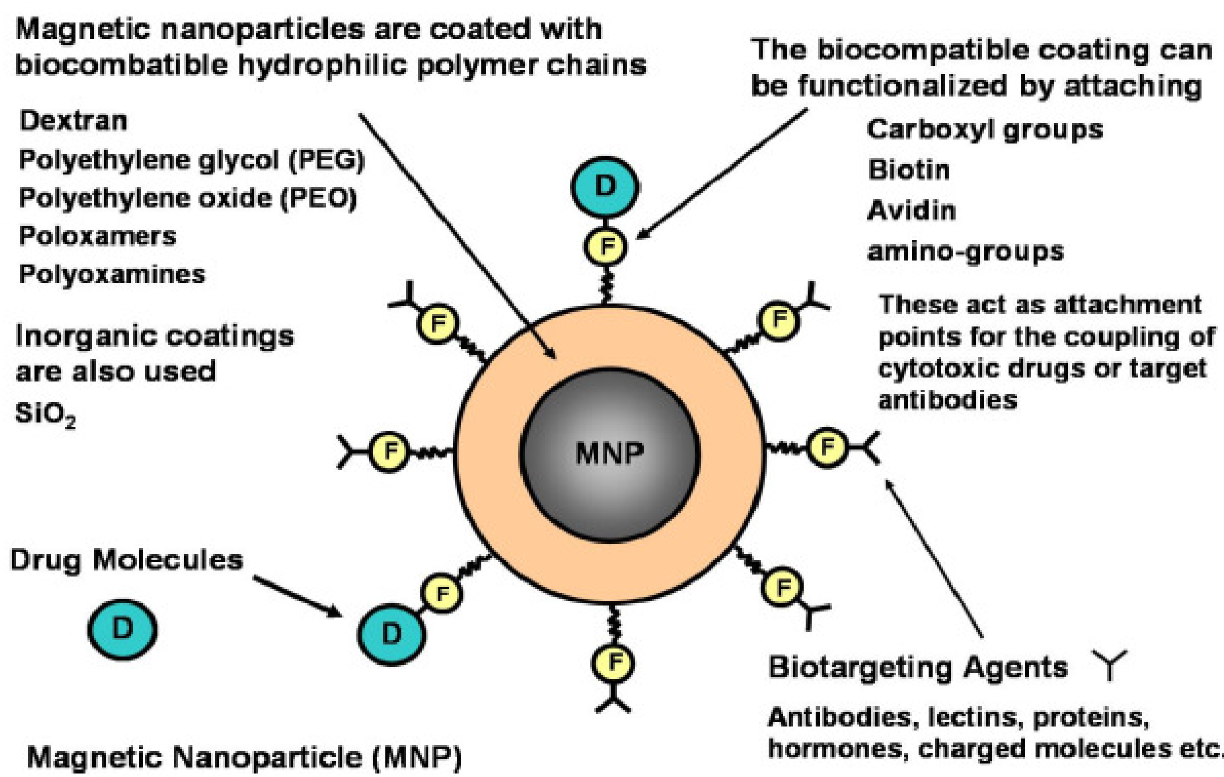
- They have controllable size $\Rightarrow$ Ideal for probing and manipulating bioparticles and biosystems (proteins, viruses, genes, cells). ***They can get close to a biological entity of interest***

- They can be coated with biocompatible molecules **to make them interact with or bind to a biological entity**, thereby providing a controllable means of tagging or addressing it.

- They are ***non toxic and well-tolerated*** by living organisms when properly prepared and functionalized.

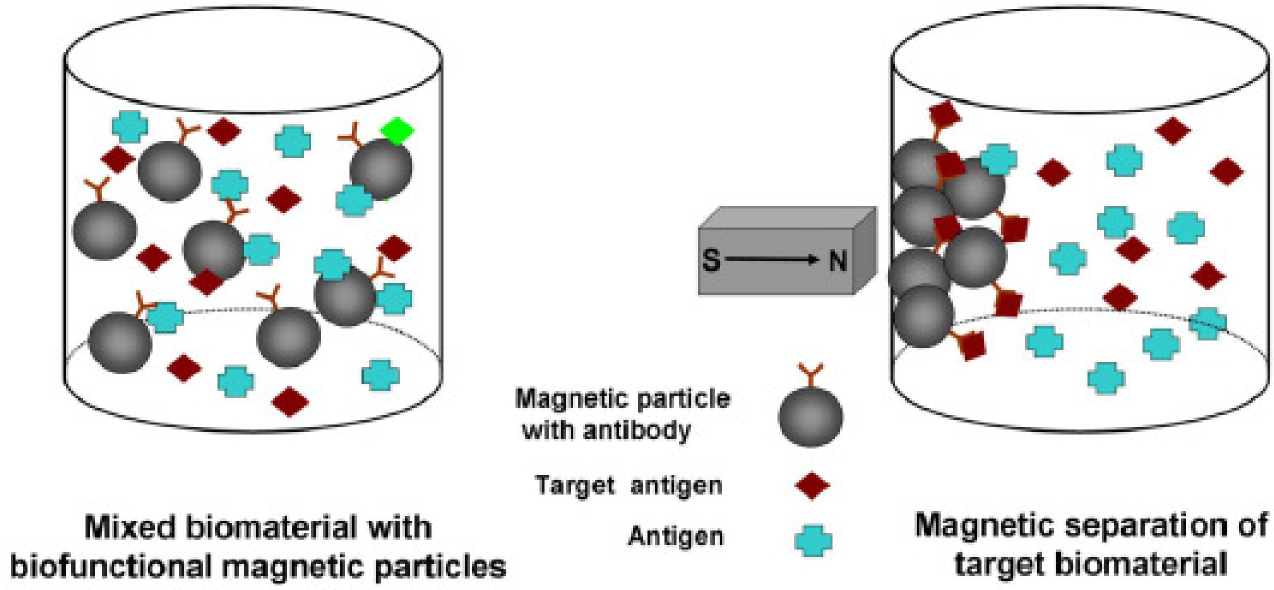
Particle functionalization

- To avoid the formation of aggregates
- To enhance biocompatibility
- To promote selective binding
- To shield the magnetic particles from the surrounding enviroment
- To prevent the leaching of potentially toxic components



from: E.P. Furlani, Materials 3, 2412 (2010)

Magnetic labelling and separation
(in vitro application)



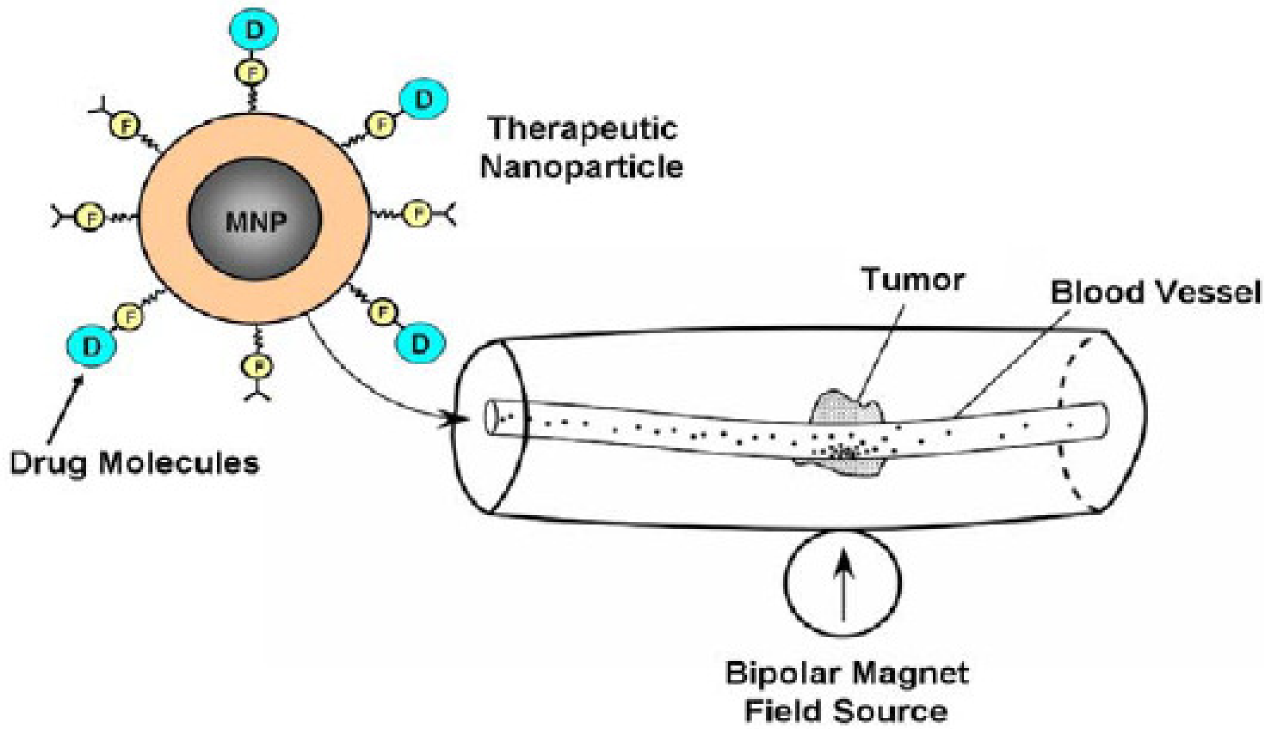
<u>Two-step process</u>:

Tagging or labelling of the desired biological entity with magnetic particles.

Separation of the tagged entities using an external field.

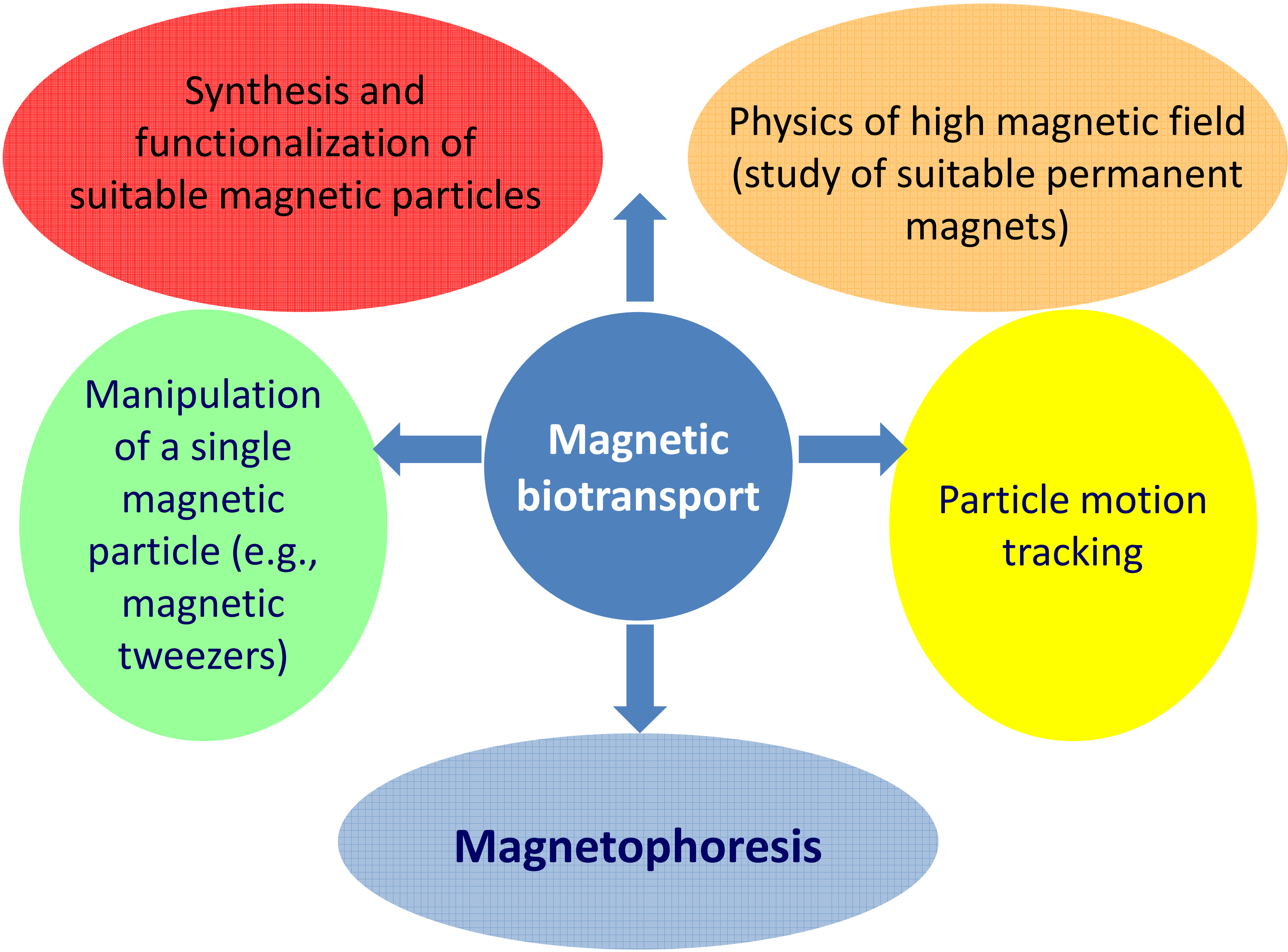
from: E.P. Furlani, Materials 3, 2412 (2010)

Drug delivery



Magnetic (nano)-particles with bound drug molecules reach the tumor site through the vascular system using a local magnetic field gradient.

from: E.P. Furlani, Materials 3, 2412 (2010)


Synthesis and functionalization of suitable magnetic particles
Physics of high magnetic field (study of suitable permanent magnets)
Manipulation of a single magnetic particle (e.g., magnetic tweezers)
Magnetic biotransport
Particle motion tracking
Magnetophoresis

Magnetophoresis

The term **magnetophoresis** concerns the behavior of a magnetic particle moving through a viscous medium under the influence of an external magnetic field.

Magnetism concepts
(magnetic moment, magnetization, magnetic susceptibility, H field gradient)

Fluid dynamics concepts
(Stokes law, Archimedes law)

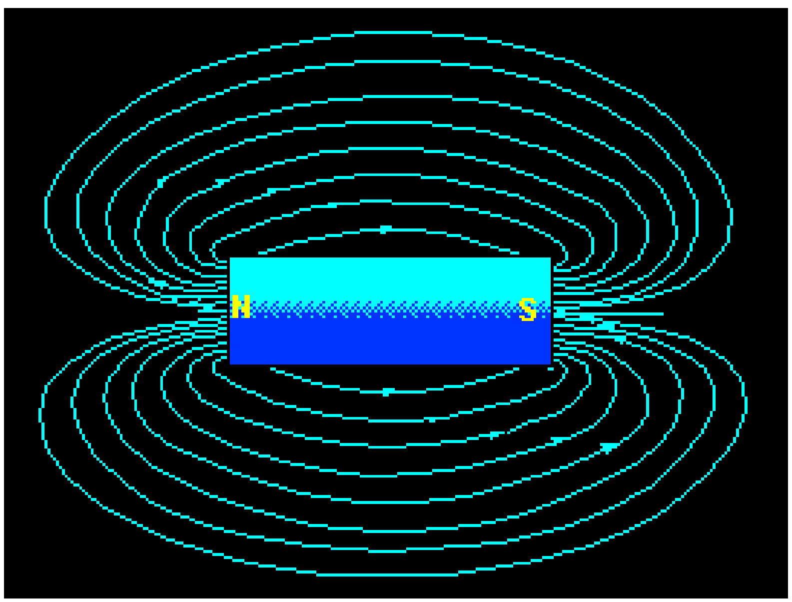
The magnetic field **H**

$\vec{H}$ is the field, created by a unit magnetic pole p, that has an intensity of 1 Oe at a distance of 1 cm from the pole (cgs system).

Lines of force: The field strenght is given by the number of lines passing through a unit area perpendicular to the field.

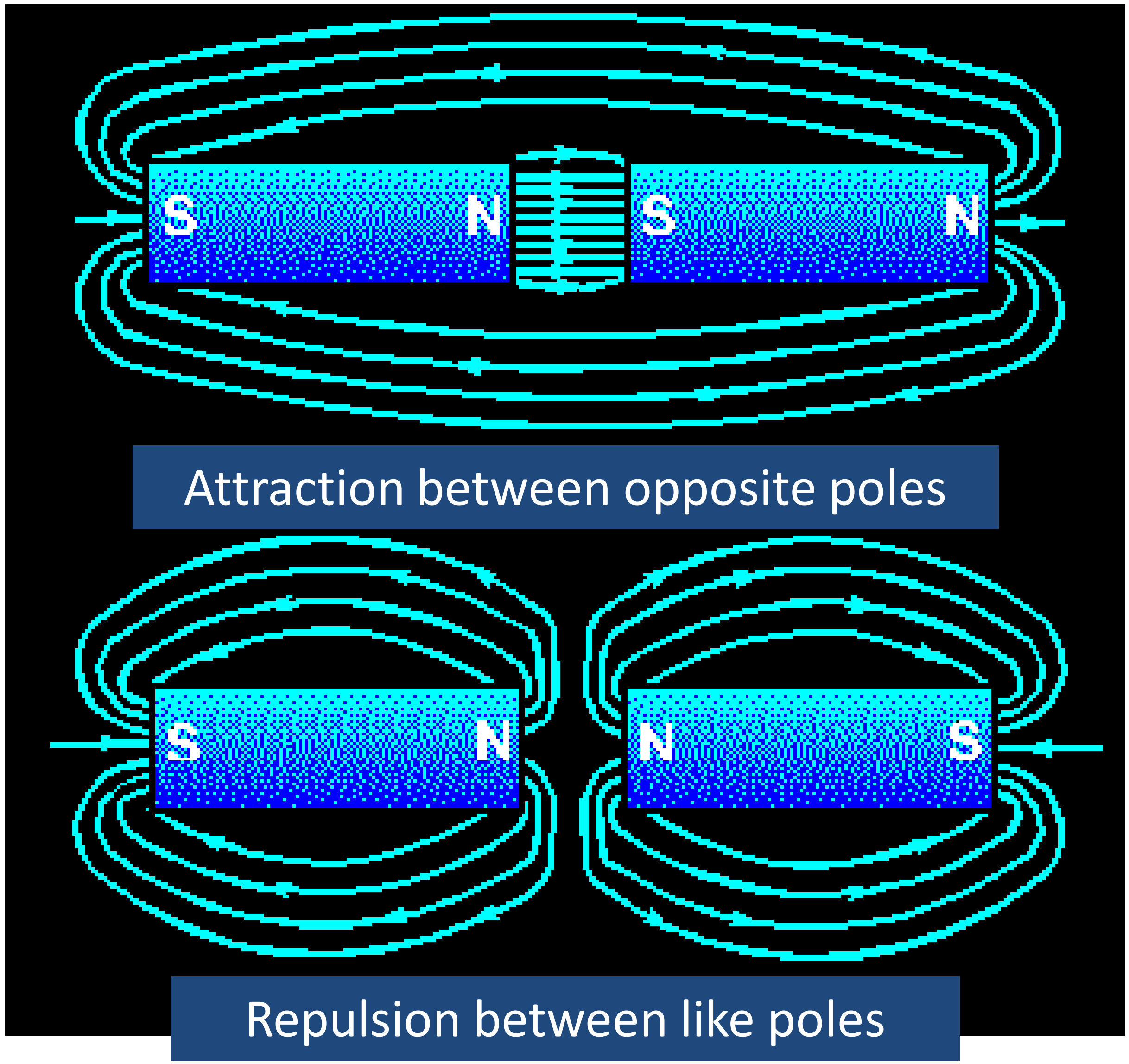
A magnetic field produces a force on a second pole: $\vec{F} = p\vec{H}$

However, a single magnetic pole does not exist. **Only magnetic dipoles do exist.**

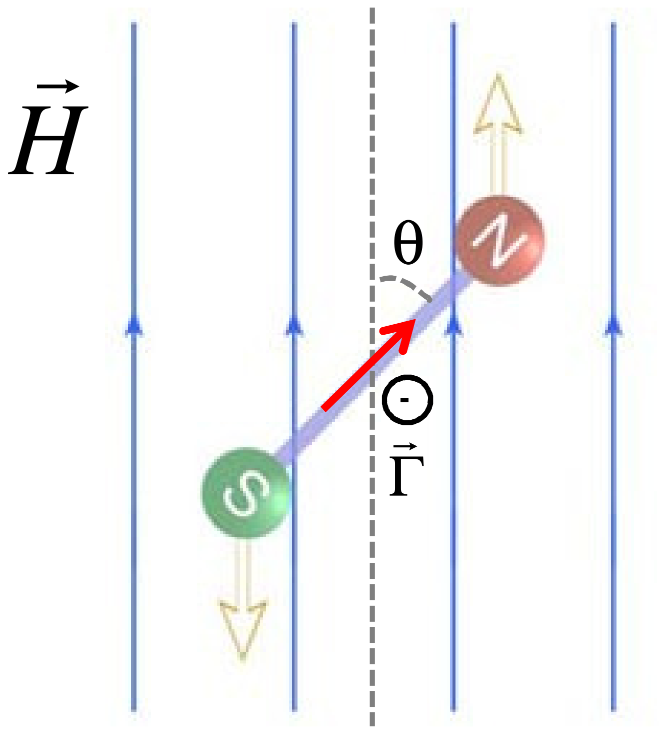


A dipole consists of two magnetic poles (North and South). The lines of the field $\vec{H}$ are directed from N to S.

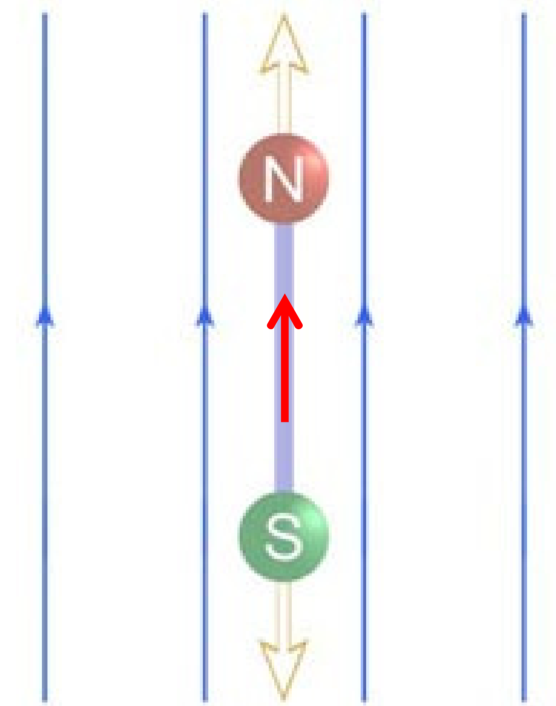
Two dipoles interact according to the well-known rule



A dipole in a uniform field



A couple acts on the dipole



$\vec{\mu}$

$$\vec{\Gamma} = \vec{\mu} \times \vec{H}$$

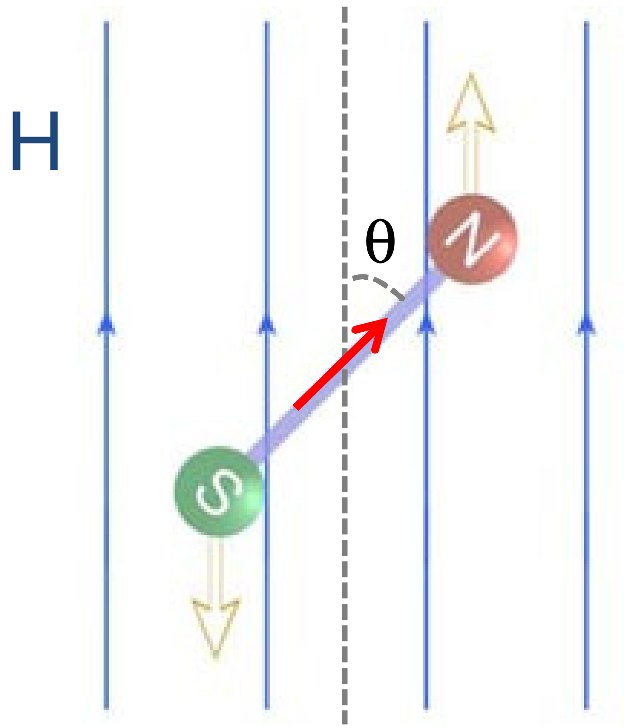
Torque → turning effect

$$\Gamma = \mu H \sin \vartheta$$

Magnetic moment

Moment of the couple exerted on the dipole when it is at θ = 90° to a uniform unitary field H (directed from S to N)

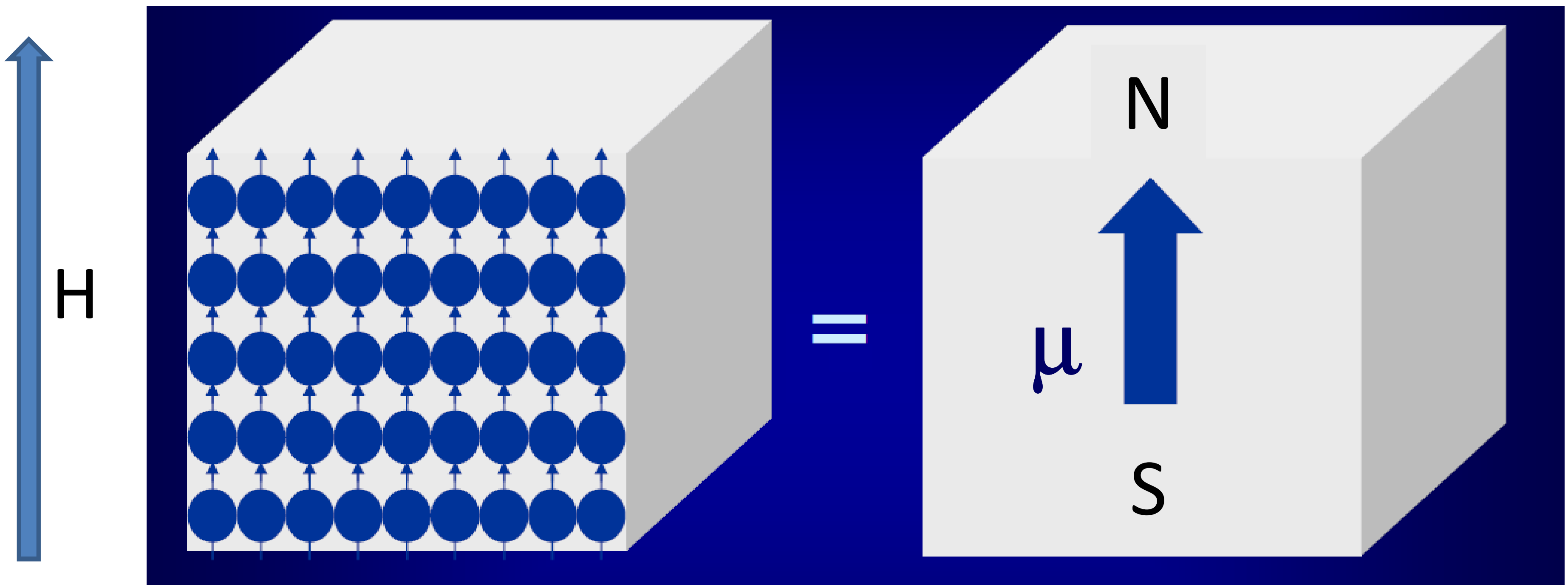
Magnetic energy



A magnet whose moment is not parallel to the field must have a certain potential energy U relative to the parallel position.

$$U = -\vec{\mu} \cdot \vec{H}$$

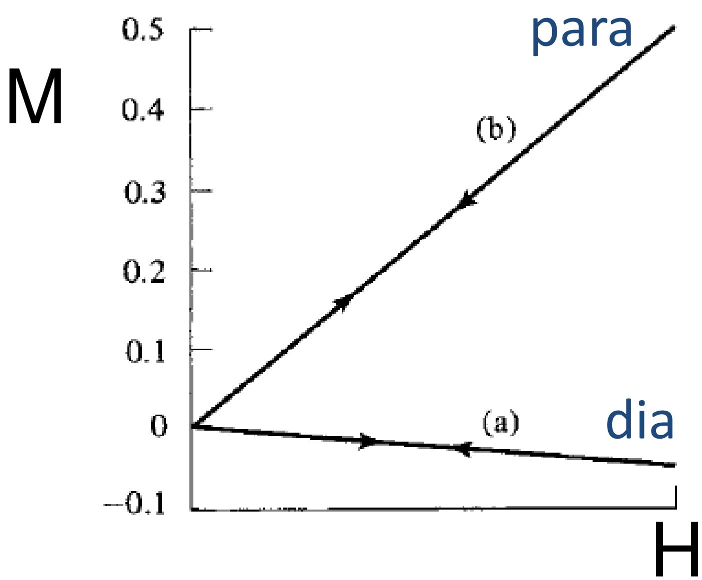
$$U = -\mu H \cos\vartheta$$

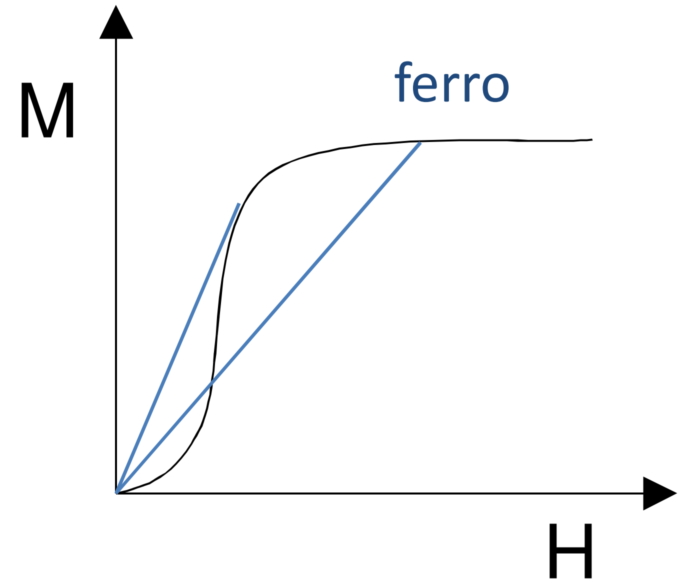


$$\vec{M} = \frac{\vec{\mu}}{V}$$

Magnetization

Magnetic susceptibility





$$\chi = \frac{M}{H}$$

χ Small and negative ($-10^{-7} \div -10^{-5}$) $\longrightarrow$ DIAMAGNETISM

χ Small and positive ($10^{-3} \div 10^{-7}$) $\longrightarrow$ PARAMAGNETISM

χ Large and positive (up to 10^{6}) $\longrightarrow$ FERROMAGNETISM (it depends on H)

A dipole in a non-uniform field

$$U(\vec{r}) = -\vec{\mu}\cdot\vec{H}(\vec{r})$$

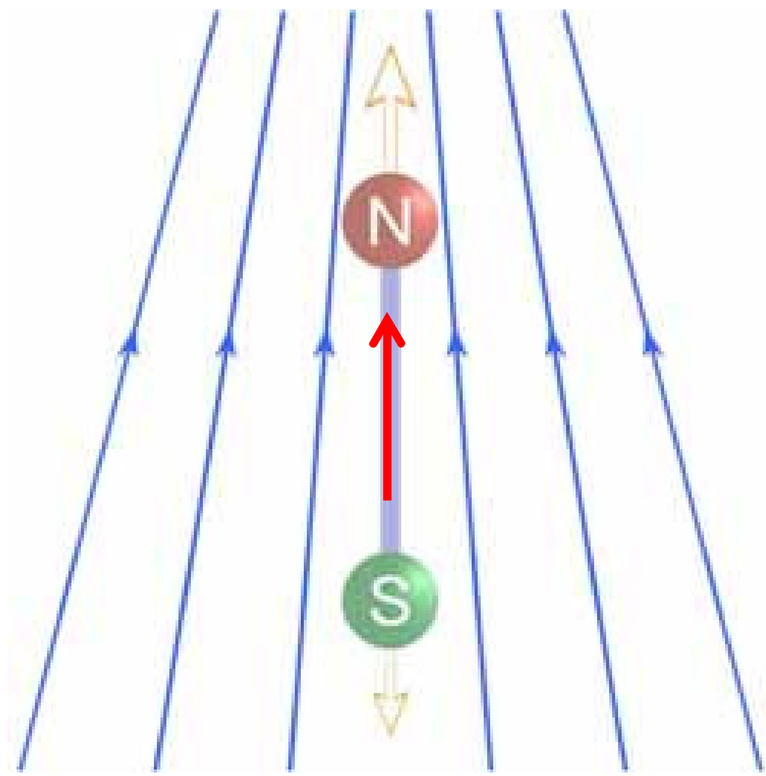
The energy of the dipole depends on its position in space

For a freely suspended dipole
(θ = 0)

$$U(\vec{r}) = -\mu H(\vec{r})$$

$$\vec{F}(\vec{r}) = -\frac{dU}{d\vec{r}} = \frac{d(\mu H)}{d\vec{r}}$$

There is a force acting on the dipole, directed along the gradient of the local field magnitude H



Since: $\vec{\mu}(H) = \vec{M}(H)V = \chi V\vec{H}(\vec{r})$

$$\vec{F}(\vec{r}) = \mu(H)\frac{dH}{d\vec{r}} = VM(H)\frac{dH}{d\vec{r}} = \chi VH(\vec{r})\frac{dH}{d\vec{r}}$$

or equivalently: $\vec{F}(\vec{r}) = \frac{\chi V}{2} \cdot \frac{dH^2}{d\vec{r}}$

Using the magnetic field **B** *(S.I. system)*

$\vec{B} = \mu_0\vec{H}$ μ_0 = permeability of free space

$$\vec{F}(\vec{r}) = \mu(H)\frac{dB}{d\vec{r}} = VM(H)\frac{dB}{d\vec{r}} = \chi VH(\vec{r})\frac{dB}{d\vec{r}}$$

$$\vec{F}(\vec{r}) = \frac{\chi V}{2\mu_0} \cdot \frac{dB^2}{d\vec{r}}$$

Magnetophoresis

The term magnetophoresis concerns the behavior of a magnetic particle moving through a viscous medium under the influence of an external magnetic field.

The presence of the continuous medium is crucial:

- Frictional force exerted on the particle
- Influence of the magnetic properties of the medium itself

Newtonian dynamics frame

$$m_p \frac{d\vec{v}_p}{dt} = \vec{F}_f + \vec{F}_m + \vec{F}_g$$

inertial force

fluidic force

magnetic force

gravitational force

The inertial force is negligible compared to frictional force for a particle with small m_p

$$0 = \vec{F}_f + \vec{F}_m + \vec{F}_g$$

Stokes law

dynamic viscosity of the fluid

$$\vec{F}_f = 6\pi\eta R_p(\vec{v}_f - \vec{v}_p)$$

hydrodynamic radius

fluid velocity

particle velocity

Frictional force exerted on a spherical object in laminar motion in a viscous fluid.

NOTE:
R_p can be larger than the physical radius of the object because of surface bound materials

Let's suppose that only the fluidic force exists (*in one dimension*)

$$m_p \frac{dv_p}{dt} = 6\pi\eta R_p (v_f - v_p)$$

Solution for $v_p(0) = 0$ $$v_p(t) = v_f (1 - e^{-t/\tau})$$

$$\tau = \frac{m_p}{6\pi\eta R_p} = \frac{2\rho_p R_p^2}{9\eta} = \frac{\rho_p D_p^2}{18\eta}$$

Time for the particle to obtain its terminal velocity, namely the velocity of the fluid

ρ_p = particle density
D_p = particle diameter

Example

For a Fe_3O_4 particle

$R_p = 1 \div 100$ nm $\Rightarrow \tau = 1.11 \div 11.1$ ns

The time during which the particle inertia plays a role is much shorter than the overall transport time in many applications.

Reynolds number

Ratio of the inertial force to the frictional force within a fluid.

$$R_{ep} = \frac{\rho_f v D_p}{\eta}$$

Particle Reynolds number

ρ_f = fluid density

v = velocity of the particle relative to the fluid

D_p = particle diameter

η = fluid viscosity

High R_{ep} $\rightarrow$ inertial force dominates (turbolent flow)

Small R_{ep} $\rightarrow$ frictional force dominates (laminar flow)

Purely laminar flow exists up to R_{ep} = 10 (for a rigid sphere).
In this regime the particle inertia is negligible and Stokes law holds.

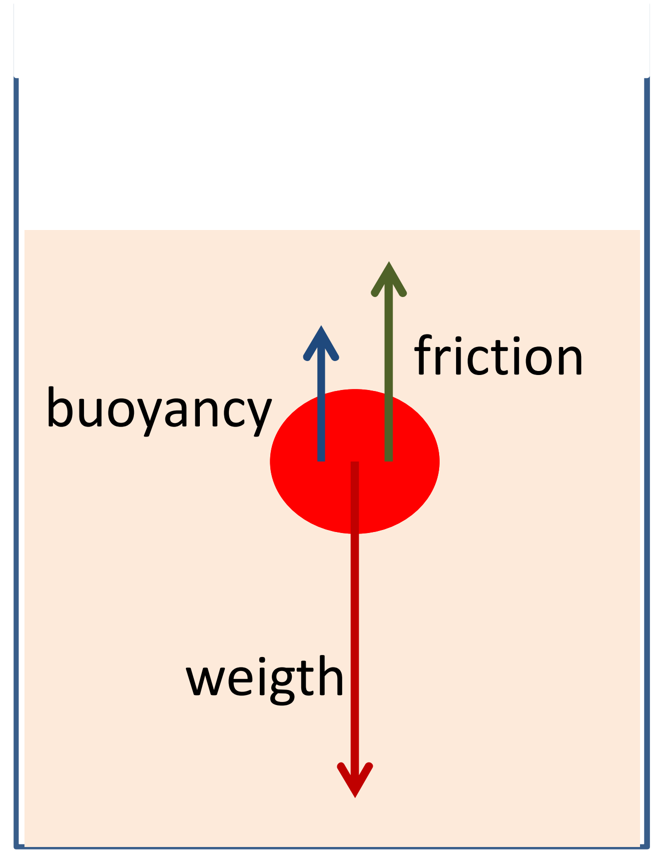
Let's suppose that only the gravitational and fluidic forces exist

$$\vec{F}_g = \frac{\pi}{6} D_p^3 (\rho_p - \rho_f)\vec{g}$$

- $\frac{\pi}{6} D_p^3$: volume of the particle
- ρ_p: particle density
- ρ_f: fluid density
- $\vec{g}$: gravitational acceleration

$$\vec{F}_f = -3\pi\eta D_p \vec{v}_p$$

$$\boxed{\vec{F}_g + \vec{F}_f = 0}$$



$$\vec{v}_p = \vec{v}_s = \frac{D_p^2}{18} \cdot \frac{(\rho_p - \rho_f)}{\eta} \vec{g}$$

or

$$\vec{v}_s = \frac{2R_p^2}{9} \cdot \frac{(\rho_p - \rho_f)}{\eta} \vec{g}$$

Sedimentation velocity

Constant velocity that the particle acquires when the two forces are balanced.

Sedimentation coefficient

It depends only on the properties of particle and medium.

$$s = \frac{v_s}{g} = \frac{D_p^2(\rho_p - \rho_f)}{18\eta}$$

The magnetic force term

$$\vec{F}_{eff} = \vec{F}_p - \vec{F}_f$$

Magnetic Archimedes law

Effective force acting on a particle in a fluid

Hence:

$$\vec{F}_{eff} = \chi_p VH \frac{dH}{d\vec{r}} - \chi_f VH \frac{dH}{d\vec{r}} = (\chi_p - \chi_f) VH \frac{dH}{d\vec{r}}$$

susceptibility of the particle

susceptibility of the fluid

volume of the particle

Similarity with:

$$\vec{F}_g = (\rho_p - \rho_f) V\vec{g}$$

$$\vec{g} \rightarrow H \frac{dH}{d\vec{r}}$$

Let's suppose that only the fluidic and magnetic forces exist

$$\vec{F}_m + \vec{F}_f = 0$$

$$\vec{v}_m = \frac{D_p^2}{18} \cdot \frac{(\chi_p - \chi_f)}{\eta} H \frac{dH}{d\vec{r}}$$

Magnetic field induced velocity
(analogous to the sedimentation velocity)

$$m = \frac{\vec{v}_m}{H \frac{dH}{d\vec{r}}} = \frac{D_p^2}{18} \cdot \frac{(\chi_p - \chi_f)}{\eta}$$

Magnetophoretic mobility of the particle
(analogous to the sedimentation coefficient)

$$\vec{v}_m = m\vec{S}_m \longrightarrow \vec{S}_m = H \frac{dH}{d\vec{r}} = \frac{1}{2} \frac{dH^2}{d\vec{r}}$$

Driving force

$$m = \frac{\vec{v}_m}{H \dfrac{dH}{d\vec{r}}} = \frac{D_p^2}{18} \cdot \frac{(\chi_p - \chi_f)}{\eta}$$

Remark:
R_p (hydrodynamic radius) and V (magnetic volume) can be unrelated
Therefore, the above relation should be re-written:

$$m(H) = \frac{(\chi_p - \chi_f)}{3\pi\eta D_p} V$$

The first relation holds if one assumes that D_p and V are the diameter and volume of a hydrodynamical sphere with $V = \pi D_p^3 / 6$

Then, χ_p = volume-averaged particle susceptibility.

Magnetophoresis of ferromagnetic particles

$$m(H) = \frac{\chi_p(H) - \chi_f}{3\pi\eta D_p} V$$

Dependence on the magnetic field

$$\chi_p(H) >> \chi_f$$

$$m(H) = \frac{\chi_p(H) V}{3\pi\eta D_p} = \frac{V M_S}{3\pi\eta D_p H}$$

$$\vec{v}_m = m(H)\vec{S}_m = \frac{V M_S}{3\pi\eta D_p}\frac{dH}{d\vec{r}}$$

M_S = saturation magnetization of the particle

H = magnetic field (larger than the saturating field)

Magnetophoresis of dia- and paramagnetic particles

$$m = \frac{\Delta\chi V}{6\pi\eta R_p}$$

$$\vec{v}_m = m(H)\vec{S}_m = \frac{\Delta\chi V}{6\pi\eta R_p} H \frac{dH}{d\vec{r}}$$

$$\Delta\chi = (\chi_p - \chi_f)$$

Two cases:

$$\Delta\chi > 0 \rightarrow m > 0$$

$$\Delta\chi \leq 0 \rightarrow m \leq 0$$

The magnetic velocity is antiparallel to the magnetic field gradient

In particular:

$$\Delta\chi = 0$$

No magnetophoretic motion

Magnetophoretic velocity of ferromagnetic particles

$$\vec{v}_m = \frac{VM_S}{6\pi\eta R_p}\frac{dH}{d\vec{r}}$$

Magnetophoretic velocity of paramagnetic particles

$$\vec{v}_m = \frac{\Delta\chi V}{6\pi\eta R_p} H \frac{dH}{d\vec{r}}$$

The velocity of a paramagnetic particle may exceed that of a ferromagnetic particle in very high fields

Magnetophoretic mobility and dipolar interactions

$$m = \frac{\vec{v}_m}{H \dfrac{dH}{d\vec{r}}} = \frac{D_p^2}{18} \cdot \frac{(\chi_p - \chi_f)}{\eta}$$

The hydrodynamic diameter of an aggregate of n particle increases as $n^{1/3.}$

Hence, m increases as $n^{2/3}$ $\longrightarrow$ flocculation

Some examples

Separation of ferromagnetic and diamagnetic particles

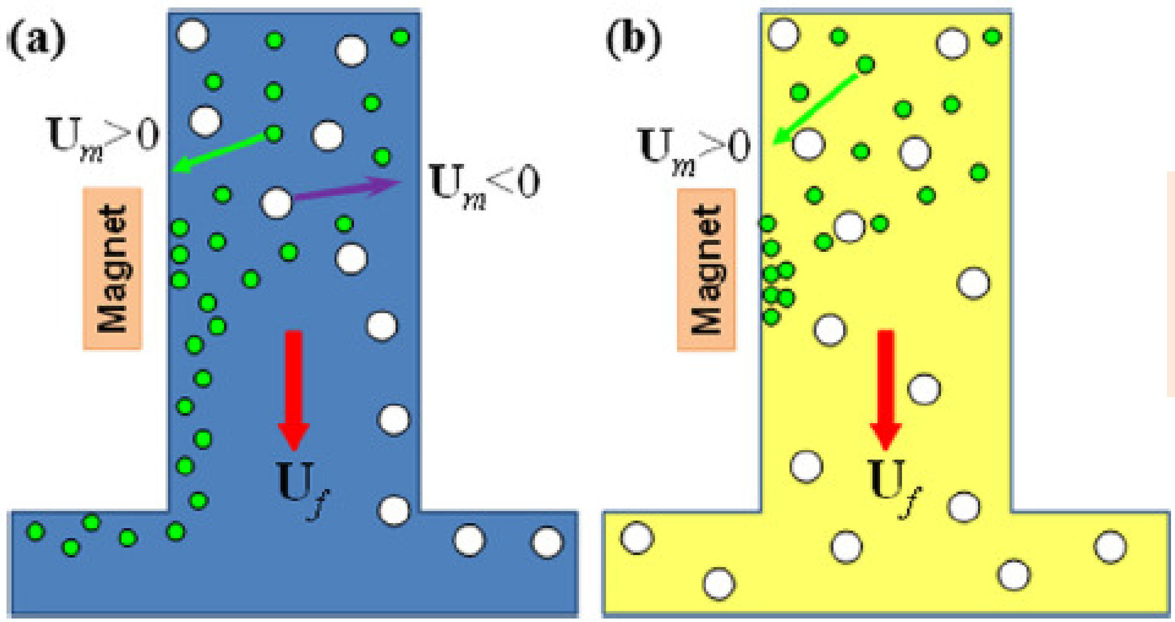
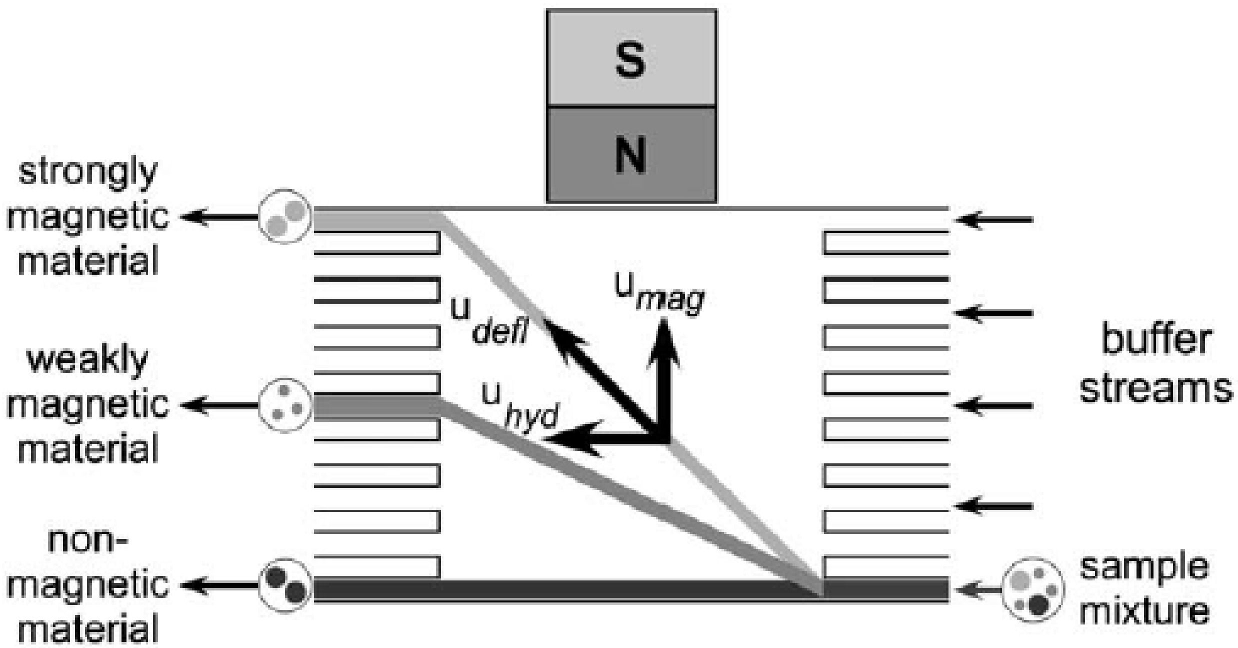


FIG. 2. Schematics illustrating and comparing the separation mechanisms of magnetic and diamagnetic particles suspended in 0.1× EMG 408 ferrofluid (a) and DI water (b), respectively. Note that $U_m > 0$ and $U_m < 0$ indicate the *positive* and *negative* magnetophoresis experienced by the magnetic and diamagnetic particles, respectively. The block arrow in each schematic indicates the direction of the suspending fluid.

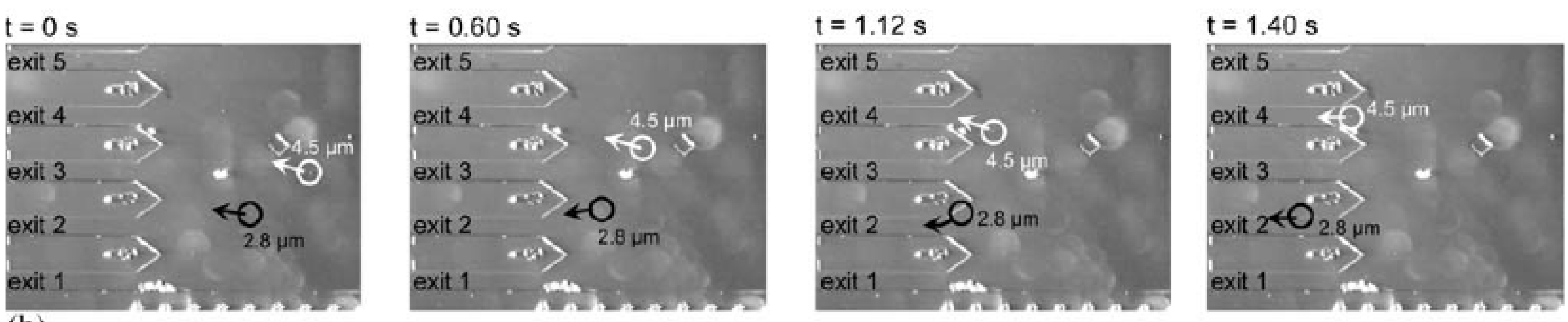
$$m = \frac{D_p^2}{18} \cdot \frac{(\chi_p - \chi_f)}{\eta}$$

L. Liang et al. , Appl. Phys. Lett. 102 (2013) 234101

Magnetic separation

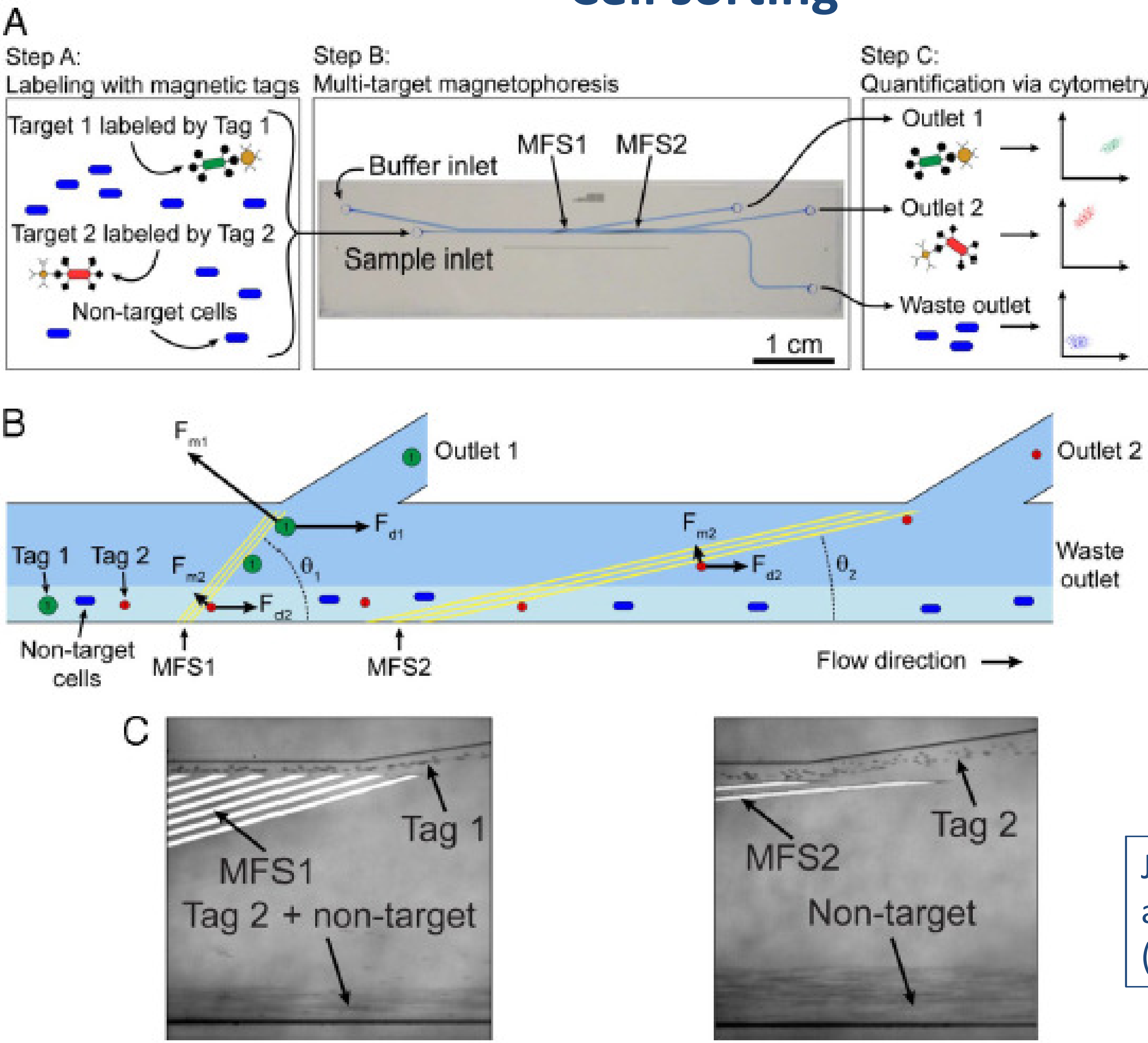


M.D. Tarn et al. , J. Magn. Magn. Mater. 321 (2009) 4115



N. Pamme et al., J. Magn. Magn. Mater. 307 (2006) 237

Cell sorting



J.D. Adams et al., PNAS 105 (2008) 18165

Manipulation of magnetic particles

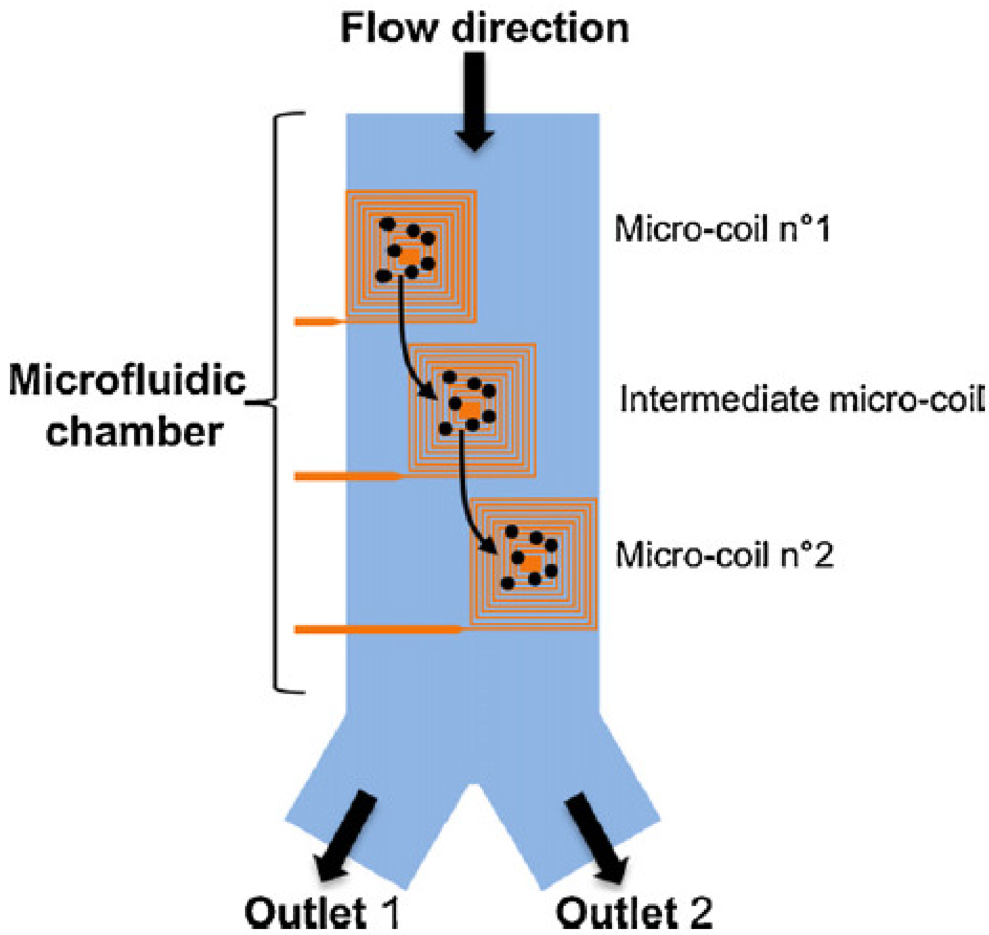


Fig. 1. Working principle of the magnetic lab-on-chip. Micro-coils (orange wires) are placed in a fluidic channel (blue stream). The successive actuation of the micro-coils allows for spatial manipulations of magnetic particles, as depicted by the two curved arrows. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

R. Fulcrand et al., Sensors and Actuators B 160 (2011) 1520

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