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Noninvasive Detection Magnetic Particles in Biological Objects

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Background

- Numerous modern nanomaterials contain magnetic particles of micron, submicron and nano sizes. In this regard, a special place is occupied by carbon nanotubes (CNTs) and nanomaterials based on them. In particular, CNTs can include catalytic iron particles, as well as other magnetic particles encapsulated therein. For example, 3-D composite BSA/CNT nanomaterials containing bovine serum albumin (BSA, matrix) and CNT (filler) or their aqueous suspensions are promising as various bioresorbable bone implants, or as bioavail for laser welding of biological tissues [1].

[1] Gerasimenko A.Yu., Ichkitidze L.P., Podgaetsky V.M., Selishchev S.V. / Biomedical applications of promising nanomaterials with carbon nanotubes // Biomedical Engineering, 2015. Vol.48. No6, March. PP. 310-314. DOI: 10.1007/s10527-015-9476-z

Application of magnetic particles in molecular biological studies: example 1

Some magnetic particles:

•MP-SiO2 (for the isolation of nucleic acids)
• MP-NH2 (for sewing proteins or spacers with the corresponding functional group)
•MP-streptavidin (for the capture of biotinylated products)
• MP-COOH (for sewing proteins, nucleotide probes or spacers with the corresponding functional group)
• MP-oligo (d) T (for isolation of poly (A) mRNA)
•MP-protein A and MP-protein G (for isolation of antibodies, immune complexes, cells

Description and properties of magnetic particles SileksMagX-Glyoxal

Basis: Iron oxide encapsulated in an inert envelope

Type of magnetization: Superparamagnet (no residual magnetization)

Particle shape: Sphere

Size: 400-600 nm

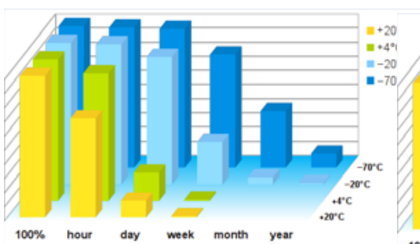
Concentration: 5 mg/ml

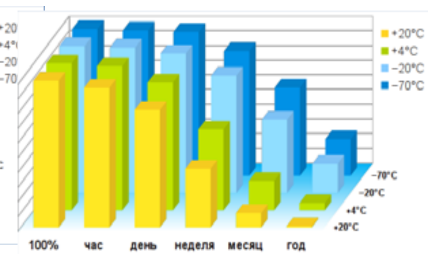
Particle capacity: 500 μg BSA per 1 ml particles - high activation rate

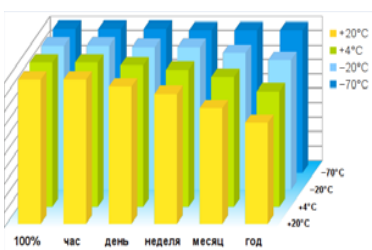
Storage buffer: water

Storage conditions: +4 °C, do not freeze

Long-term storage of nucleic acids in the *FinalWash buffer*

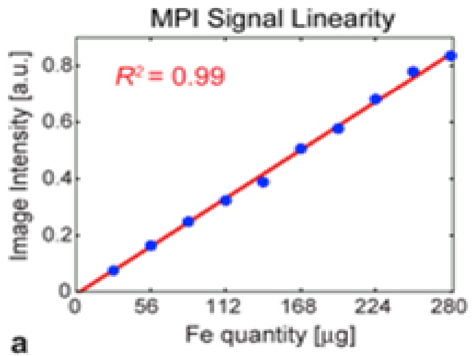


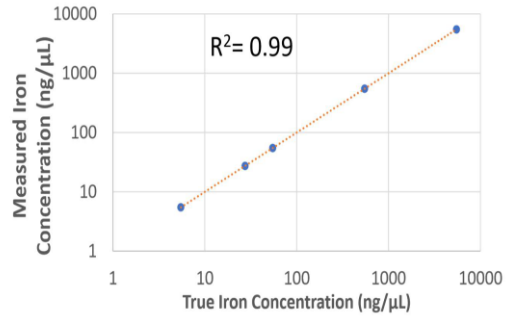


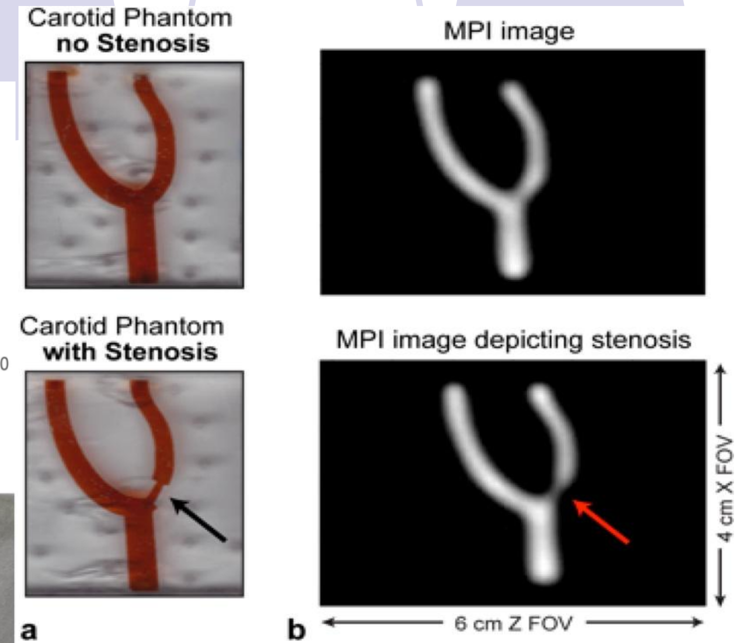


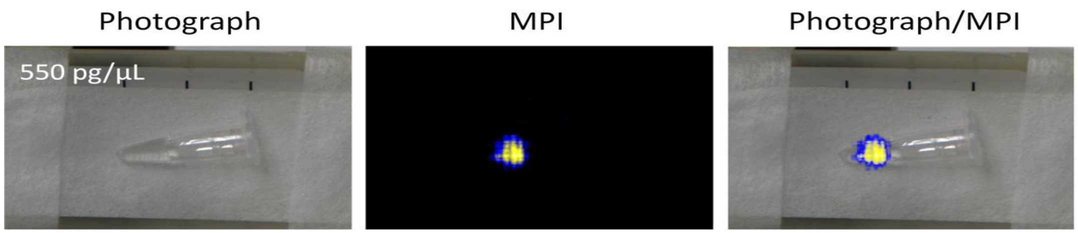
Water MilliQ	Water with addition *RNasin*	In a coupled form on magnetic particles in the buffer *FinalWash*

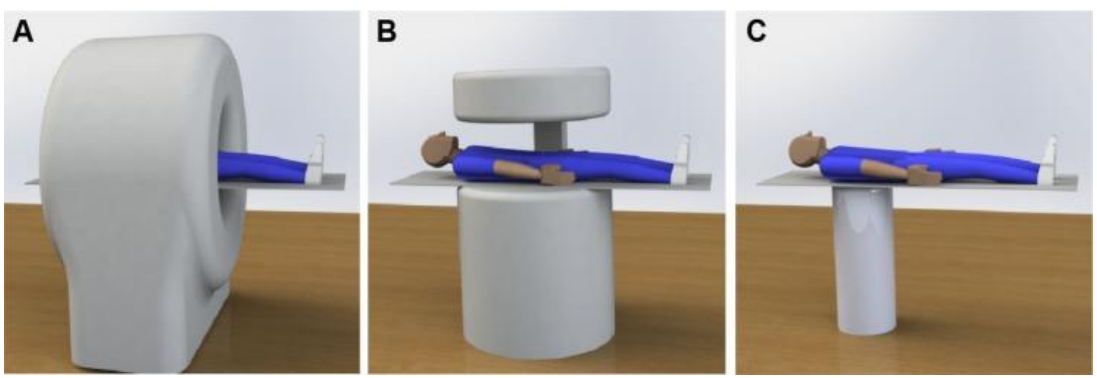
Magnetic Particle Imaging









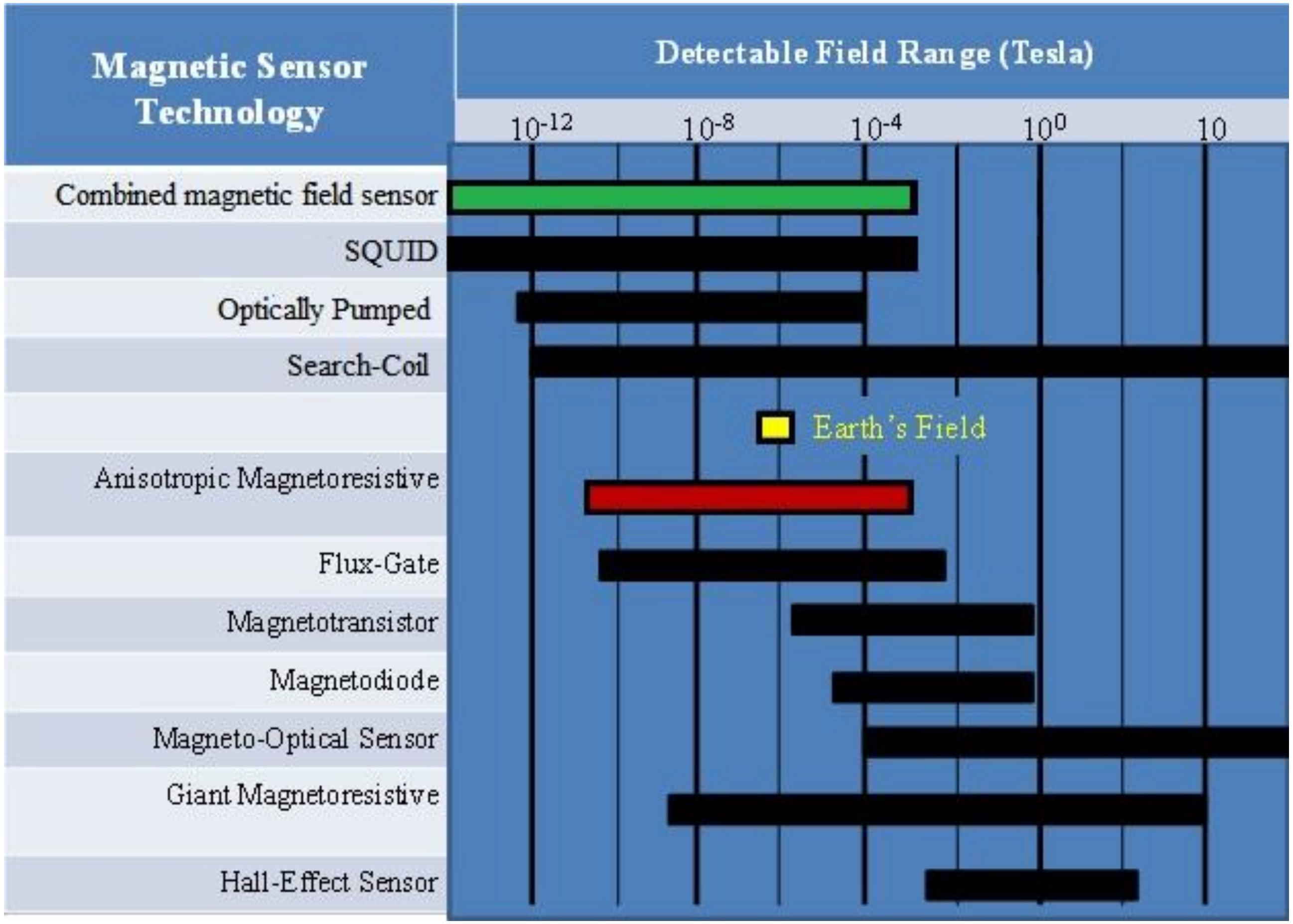


Concept of the three main scanner geometries

The magnetization signal in the 600 mT field with MPI is more than ten million greater than the magnetization signal in the 7 T field with MRI.

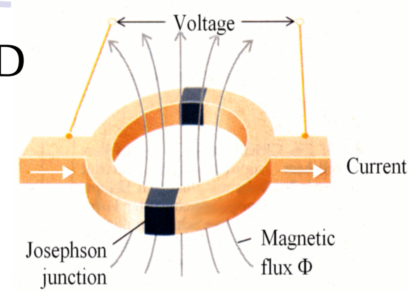
E.U. Saritas, P.W. Goodwill, L.R. Croft, et al. // *J Magn Reson*. 2013 Apr; 229: 116–126.

Methods and instruments

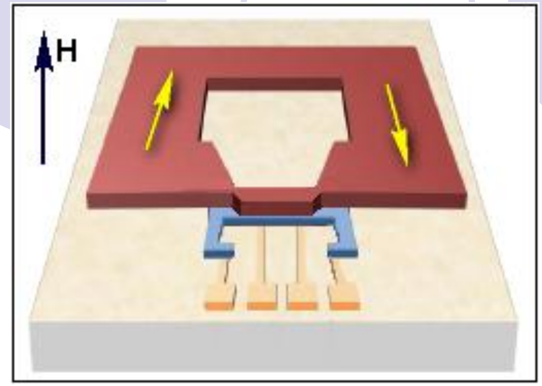


Methods and instruments: SQUIDs,CMFS and NS CMFS

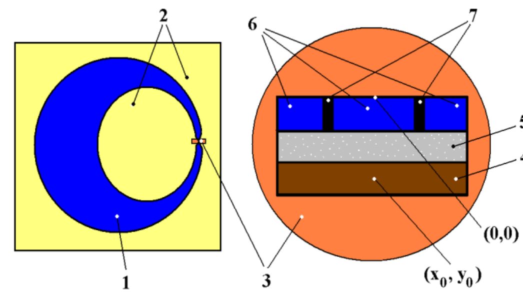
SQUID



$\Delta B \sim 3$ fT/Hz$^{1/2}$



CMFS



NS CMFS

Magma EFI HiRes

Full Capabilities

•Magma EFI HiRes Microscope addresses all static defects: shorts, leakages, and opens.

•Package shorts are a natural fit for SQUID in Magma microscopes since magnetic fields permeate all materials, e.g. power and ground planes, silicon, molding compounds, etc.

•Die shorts are located using the HiRes sensor with better than 500 nm spatial resolution. Magnetic field resolution is not limited by wavelength, but only by sensor size and scanning distance.

•Open failures are found using a space domain reflectometry (SDR) technique that applies a high frequency signal (20MHz to 200MHz) while detecting the RF magnetic field generated by the current. Using this technique on SOC packages with stacked die, TSVs and interposers, open failures in the silicon devices can be localized.

http://neocera.com/products/magma-efi-hires/

Methods and instruments: Parameters SQUIDs, CMFSs and NS CMFS

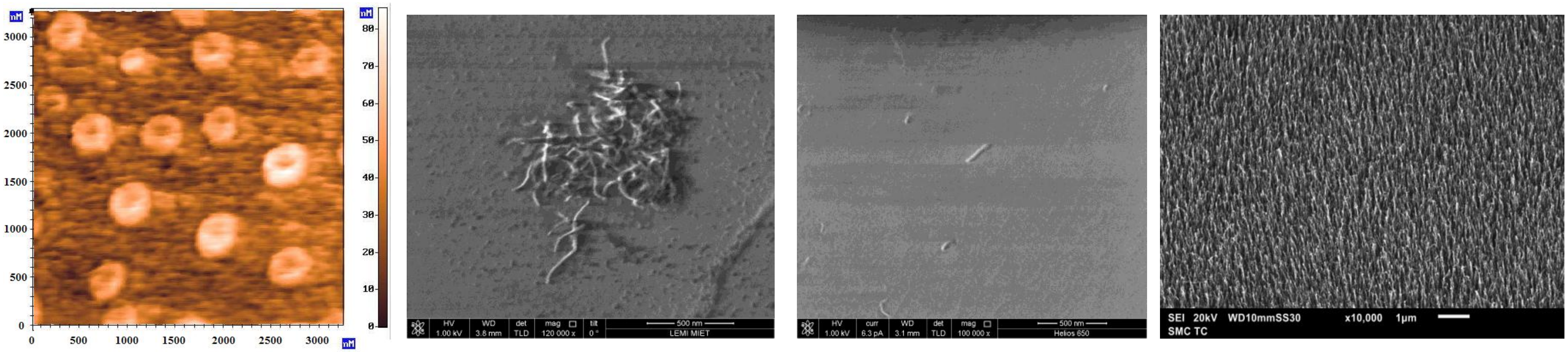
Parameter/Type	SQUID Msgreen [1]	SQUID Cryo M1000 [2]	CMFS [3] (NS CMFS [4])
Sensitivity, ft/Hz$^{1/2}$	3.5	100	3.2 (0.8)
Number of projections	1	1	1
Size, mm	7.5x7.5	8x8	10x10 (2x2)
Material	Nb-Al-AlOx-Nb	YBCO	Nb-GMR
Country	Germany	USA	France (Russia)

1. supracon.com
2. starcryo.com
3. Pannetier M., Fermon C., Le Goff G., et al. Ultra-sensitive field sensors – an alternative to SQUIDs // IEEE Trans. Appl. Supercond., **15 (2),** 892– 895 (2005
4. Ichkitidze L.P., Mironyuk A.N. Topological nanostructured film superconducting flux transformer / / Journal of Nano and Microsystem Technique, **1,** 47-50 (2012).

Aim

- We estimated the distance between a magnetic field sensor (MFS) and magnetic particles (MPs) at which the magnetic field perturbations caused by MPs can be detected at different values of other parameters.

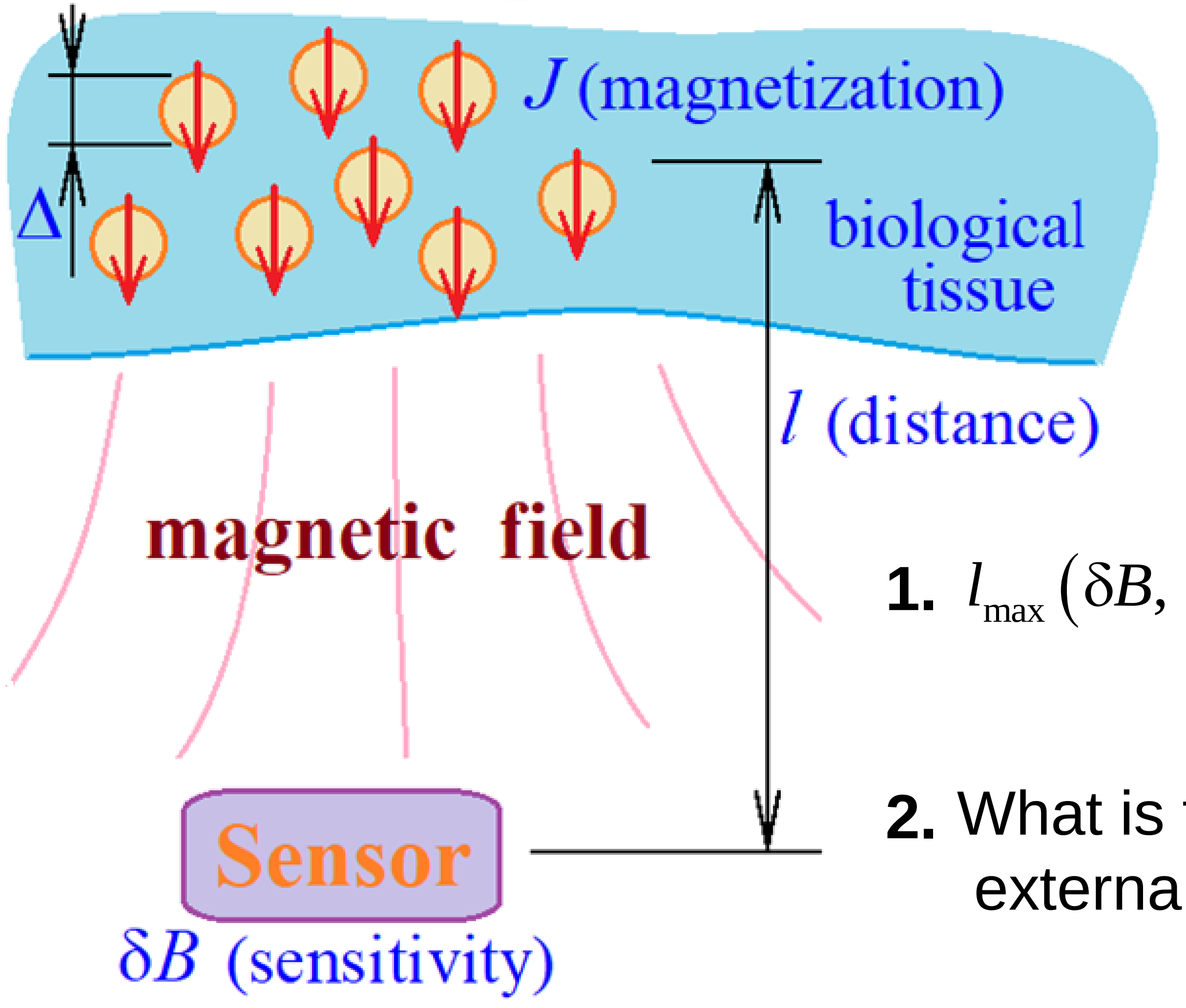
Results



a b c d

Surfaces of composite nanomaterials BSA /MWCNT: (a) - picture in tunnel force microscope; (b) - pictures in a scanning electron microscope (clusters of MWCNT). There are: (c) – MWCNT; (d) - forest of SWCNT

Detecting of magnetic particles in biological systems



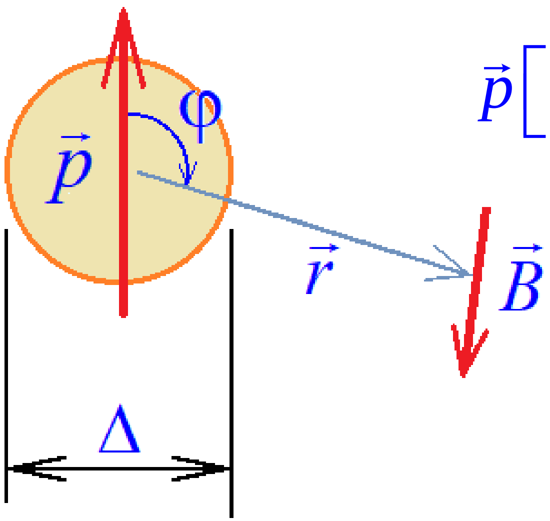
The questions to investigate:

1. $l_{max}(\delta B, J, \Delta, n) = ?$

(n – concentration)

2. What is the effect of external magnetic field?

Magnetic field of a magnetized particles



$\vec{p}\left[\mathrm{A}\times\mathrm{m}^2\right]$ – magnetic moment of a particle

$$\left|\vec{p}\right| = p = JV = J\,\frac{\pi\Delta^3}{3}$$

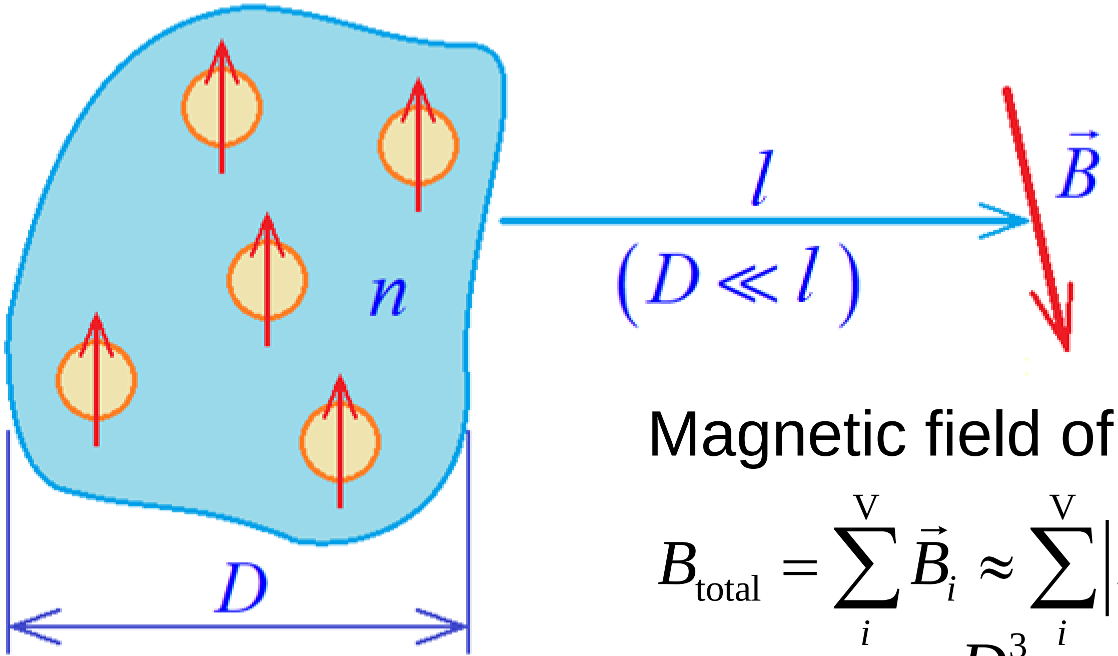
$J\left[\mathrm{A/m}\right]$ – magnetization of a particle

Magnetic field of a single particle:

$$\left|\vec{B}\right| = \frac{\mu_0}{4\pi}\times\frac{\vec{p}}{r^3}\sqrt{1+\cos^2\varphi}$$

$$\frac{\mu_0}{24}\times\frac{J\Delta^3}{r^3}\le\left|\vec{B}\right|\le\frac{\mu_0}{12}\times\frac{J\Delta^3}{r^3}$$

Magnetic field of the particles systems



n − concetration of the particles

Magnetic field of the particles system:

$$B_{\text{total}} = \sum_i^{V} \vec{B}_i \approx \sum_i^{V} \left|\vec{B}_i\right| = n\frac{\pi D^3}{6}\langle B_i \rangle \geq$$

$$\geq n\frac{\pi D^3}{6} \times \frac{\mu_0}{24} \times \frac{J\Delta^3}{l^3} = \frac{n\pi\mu_0 J}{144}\left(\frac{D\Delta}{l}\right)^3$$

$$B_{\text{total}} \approx 27.4 \times 10^{-9}\, Jn\left(\frac{D\Delta}{l}\right)^3$$

(in the units of SI)

Distance evaluation for normal condition

$$B_{total} \approx 27.4 \times 10^{-9} Jn\left(\frac{D\Delta}{l}\right)^3 \Rightarrow l_{max} \approx 0.00302 \times D\Delta \sqrt[3]{\frac{Jn}{\delta B}}$$

l_{max} – maximum sensor to object distance

δB – sensitivity of the sensor

(in the units of SI)

Estimates of the l_{max} for parameters typical values:

J = 120 000 A/m (μ of the particles = 3000, external field = 50 μT)

$n = 8 \times 10^{12}$ m^{-3} (linear density of the particles = 20 mm^{-1})

$\Delta = 10^{-6}$ m (= 1 μm)

$D = 10^{-3}$ m (= 1 mm)

$\delta B = 10^{-12}$ T (= 1 pT)

l_{max} = 3 cm

$$l_{max} \sim \sqrt[3]{J}$$

$$J \sim B_{ext}\mu$$

Results

- The measured values of the sizes of iron particles (FIG. 1) and the concentration of magnetite particles (FIG. 2) recorded by different magnetic field sensors

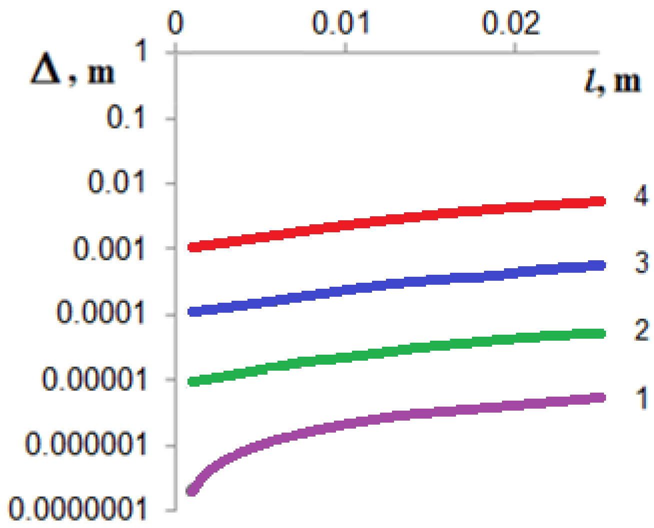


Fig.1. The dependence $D(l)$ is the minimum size of the iron particle, l is the distance from the magnetometer to the iron particle) for different sensitivity δB of the magnetometers:

1 – 1 fT, (SQUID), (NS CMFS)

2 – 1 pT, (NMR LP)

3 – 1 nT, (GMR)

4 – 1 μT (Hall)

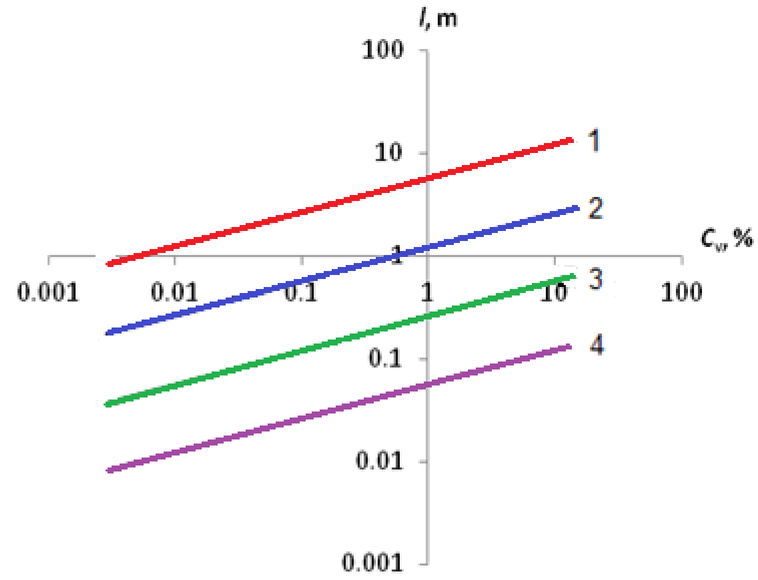


Fig. 2. dependence $l(C_v)$ at D = 50 nm, Δ= 1 mm, J^* ~ 50 A·m^2/kg, ρ ~ 5 · 10^3 kg/m^3 , and a value of δB:

1 – 10 fT ,

2 – 1 pT ,

3 – 100 pT ,

4 – 10 nT

Conclusions

- in a volume of 1 mm^3, paramagnetic particles with a size of 1 μm and a concentration of 10^{14} m^{-3} at a distance of about 3 cm from a magnetic field sensor with a resolution of less then 10 fT can be detected. It is believed that the particles are in the Earth's magnetic field;
- a single iron particle with a size of a few micrometers over a distance of 1 cm with a magnetic field sensor with a resolution of the order (or less then) 10 fT can be registered;
- magnetite nanoparticles with a volume concentration of the order of nanopercent per 1 cm distance by a magnetic field sensor having a resolution of the order of 10 fT can be identified.

Thank you for your attention!