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modular designed particles

Publications and Reviews

Technological Applications

Implementation in Life Sciences

magnetic micro- and nanoparticles

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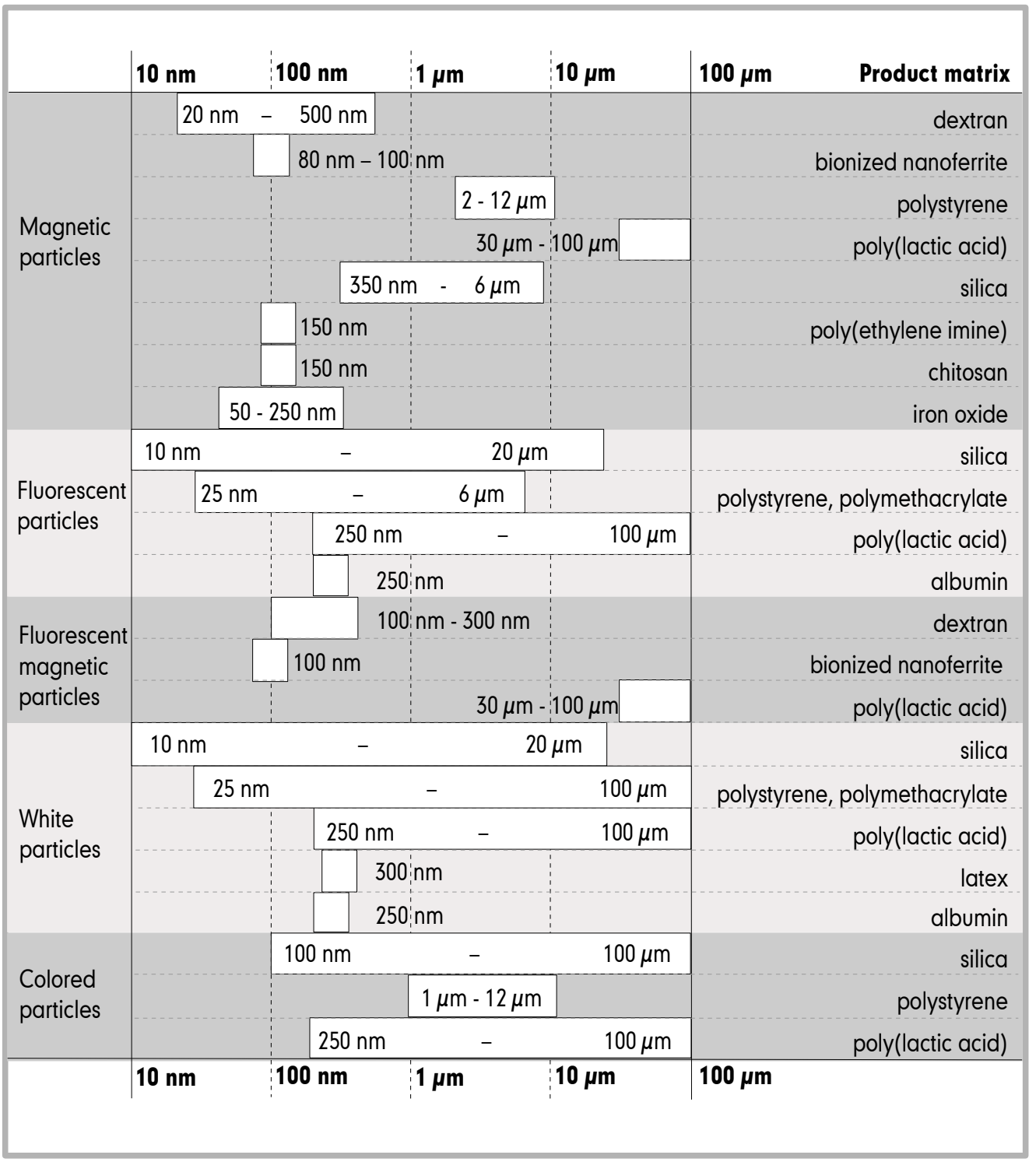
Product overview



micromod Partikeltechnologie GmbH
Friedrich-Barnewitz-Straße 4, D-18119 Rostock
Tel.:+49 381/54 34 56 10, Fax: +49 381/54 34 56 20
Technical Support Tel.: +49 381/54 34 56 14
E-mail: info@micromod.de, Internet: www.micromod.de

2 Magnetic nano- and microparticles

Cordula Grüttner

micromod Partikeltechnologie GmbH, Friedrich-Barnewitz-Str. 4, 18119 Rostock, Germany

2.1 Overview

In the recent years, **micromod** has developed a large variety of magnetic nano- and microparticle types. The development of each particle type was with emphasis on a specific application in theranostics. The particle sizes range from only a few nanometers up to several micrometers. Most of the particles are available with different surface coatings and can be specifically linked to biomolecules like proteins or antibodies.

	Product matrix	10 nm	100 nm	1 µm	10 µm	100 µm	Product type
magnetic particles	dextran		20 nm – 100 nm				nanomag®-D-spio, -CLD-spio
	dextran			130 nm – 500 nm			nanomag®-D, -CLD, -silica
	dextran		130 nm				perimag®
	bionized nanoferrite		80 nm – 100 nm				BNF particles
	polystyrene			2 - 12 µm			micromer®-M
	poly(lactic acid)					30 µm-100 µm	PLA-M particles
	silica			350 nm - 6 µm			sicastar®-M, sicastar®-M-CT
	poly(ethylene imine)		150 nm				PEI-M particles
	chitosan		150 nm				nanomag®-C
	iron oxide		50 - 250 nm				Iron oxide particles
fluorescent magnetic particles	dextran			100 nm - 300 nm			nanomag®-CLD-F
	bionized nanoferrite		100 nm				BNF-F particles
	poly(lactic acid)					30 µm-100 µm	PLA-M-F particles
		10 nm	100 nm	1 µm	10 µm	100 µm	

2.2 Types of magnetic nano- and microparticles

2.2.1 nanomag®-D

nanomag®-D are available with particle diameters of 130 nm, 250 nm and 500 nm and can be separated with a permanent magnet. The particles are prepared via the core-shell method with a core of magnetite and a dextran shell consisting of 75-80% (w/w) magnetite in a matrix of dextran (40.000 Da). Due to the irregular shape of the iron oxide multicore the nanoparticles are partially thermally blocked at room temperature. Also due to the relatively fast separation of the nanomag®-D, the particles are very interesting for several substrate based biosensor schemes. Exemplary separation processes of 500 nm nanomag®-D particles are shown in Fig. 1.

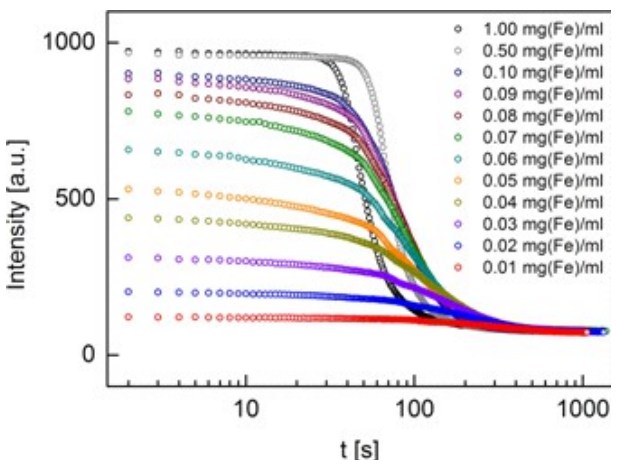


Fig. 1: Separation process of nanomag®-D for different iron concentrations.

The nanomag®-D are designed with the surface functionalities OH (plain), NH2 and COOH for the covalent binding of proteins, antibodies or other molecules. They are also available with covalently bound proteins (avidin, streptavidin, protein A, albumin) or other biomolecules (biotin, glutathion), and can be provided with covalently bound antibodies on request. They are offered with nickel(II) chelator nitrilotriacetic acid (NTA) or ready to use with the corresponding nickel complex (Ni-NTA) for the binding of histidine labeled proteins. These particles are also available with various hydrophilic surfaces (PEG 300, PEG-NH2 or PEG-COOH) and with negative surface potentials (e.g. COOH, SO3H).

2.2.2 nanomag®-D-spio

The superparamagnetic nanomag®-D-spio are available with particle diameters of 20 nm, 50 nm and 100 nm and cannot be separated with a conventional permanent magnet but in a high gradient magnetic field (magnetic column). The particles are prepared by precipitation of iron oxide in the presence of dextran. The functionalized nanomag®-D-spio consist of about 55-85% (w/w) iron oxide in a matrix of dextran (40.000 Da) in dependence on the diameter and surface modification. The particles show differences in the size of the iron oxide domains for different particle diameters. These particles are preferably applied for detection purposes in magnetic resonance imaging (MRI) or in magneto-immuno assays and show good specific power absorption rates for hyperthermia applications for a particle diameter of 100 nm.

The particles are designed with the surface functionalities OH (plain), NH2 and COOH for the covalent binding of proteins, antibodies or other molecules and are available with covalently bound proteins (avidin, streptavidin, protein A, albumin) or other biomolecules (e.g. biotin) as well as with various hydrophilic surfaces (PEG 300, PEG-NH2 or PEG-COOH).

2.2.3 perimag®

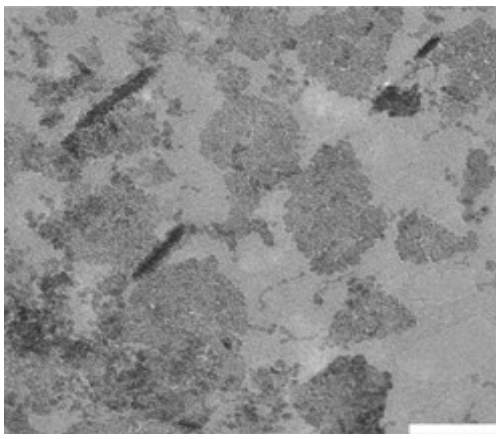


Fig. 2: Exemplary TEM image of perimag® nanoparticles [1]. The bar indicates 50 nm

perimag® exhibit excellent properties as contrast agents for Magnetic Resonance Imaging (MRI) and Magnetic Particle Imaging (MPI) [1, 3, 4]. The particles are suitable for homing and tracking of stem cells in regenerative medicine as well as for hyperthermia applications [5]. They are prepared by precipitation of iron oxide in the presence of dextran and are available with a particle diameter of 130 nm. The iron oxide crystals have sizes between 3 nm and 8 nm clustered to multi-core particles that are mostly superparamagnetic (Fig. 2) [1]. The particles cannot be separated with a conventional permanent magnet but in a high gradient magnetic field.

The perimag® are designed with the surface functionalities OH (plain), NH2 and COOH for the covalent binding of proteins, antibodies or other molecules [6] and are available with covalently bound streptavidin for the binding of biotinylated molecules. Furthermore, the particles can be manufactured under clean room conditions upon request.

2.2.4 nanomag®-CLD

nanomag®-CLD are prepared via the core-shell method with a core of magnetite and a dextran shell. The particles are available with particle diameters of 300 nm and 500 nm for separation with a permanent magnet.

They are designed with NH2, COOH and PEG-COOH for the covalent binding of proteins, antibodies or other molecules and are available with covalently bound streptavidin or other protein surfaces on request.

2.2.5 nanomag®-CLD-spio

Superparamagnetic nanomag®-CLD-spio are prepared by precipitation of iron oxide in the presence of dextran and are available with particle diameters of 20 nm and 100 nm. They cannot be separated with a conventional permanent magnet but in a high gradient magnetic field. The particles consist of about 70-90% (w/w) iron oxide in a matrix of cross-linked dextran (40.000 Da) in dependence on the diameter and surface modification. The particles show differences in the size of the iron oxide domains for different particle diameters. nanomag®-D-spio are preferably applied for detection purposes in magnetic resonance imaging or in magneto-immuno assays and show good specific power absorption rates for hyperthermia applications for a particle diameter of 100 nm.

The particles are designed with amino groups on the surface for the covalent binding of proteins, antibodies or other molecules and can be provided with covalently bound antibodies on request.

2.2.6 BNF particles

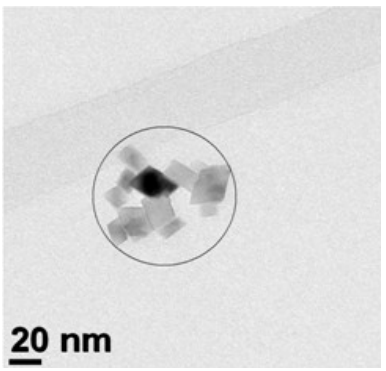


Fig. 3: Exemplary TEM image of BNF starch nanoparticles [2].

BNF particles (BNF – bionized nanoferrites) are prepared via the core-shell method with a core of 75-80% (w/w) magnetite and a shell of dextran or hydroxyethyl starch. The particles are available with particle diameters of 80 nm and 100 nm. BNF particles are magnetic multicore nanoparticles as presented in Fig. 3. They are thermally blocked at room temperature and show specific interaction with alternating magnetic fields [7-11]. 100 nm BNF particles can be separated with conventional permanent magnets, and 80 nm BNF particles have to be separated in high gradient magnetic fields or for several hours at a strong permanent magnet. Due to the their specific relaxation behaviour

in the presence of an alternating magnetic field, as presented in Fig. 4, these particles are also of special interest for substrate-free biosensors.

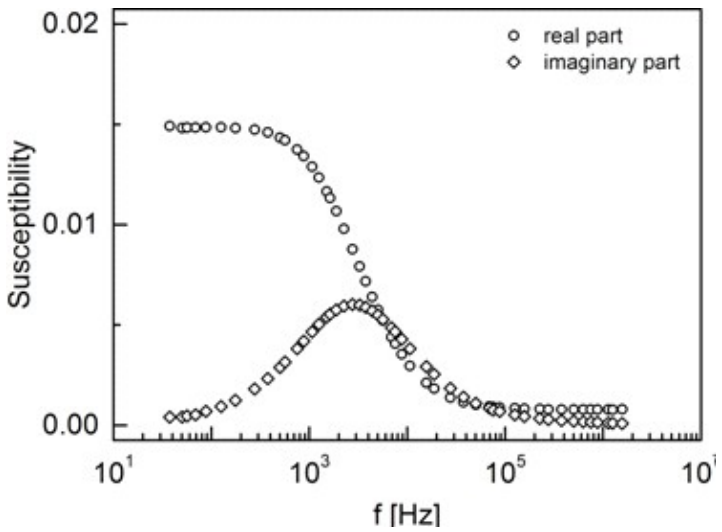


Fig. 4: AC susceptibility measurement of the BNF 80 nanoparticles

The particles are designed with the surface functionalities OH (plain), NH2, PEG-NH2, COOH and PEG-COOH for the covalent binding of proteins, antibodies or other molecules. They are available with covalently bound proteins (streptavidin, protein A) and can be provided with covalently bound antibodies on request. The particles can easily be filtered through 0.22 µm filters.

2.2.7 micromer®-M

micromer®-M are monodisperse particles which consist of magnetite around an organic matrix of a styrene-maleic acid-copolymer (Fig. 5). They are finally coated with a polymer layer for the encapsulation of magnetite and the introduction of chemical functionalities and can easily be separated with conventional permanent magnets. The particles are provided as standard products in the size range of 2 to 12 microns.

micromer®-M are designed with the surface functionalities NH2, PEG-NH2, COOH and PEG-COOH for the covalent binding of proteins, antibodies or other molecules and are available with covalently bound proteins (avidin, streptavidin, protein A, albumin) or other polymers (polyethylene imine (PEI)). Especially streptavidin coated micromer®-M particles are interesting tools for certain substrate-based biosensor schemes also with the possibility to detect single particles [12].

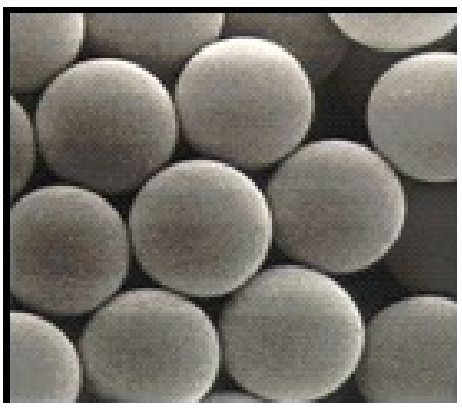


Figure 5. SEM image of 3 µm micromer®-M particles

2.2.8 sicastar®-M

sicastar®-M are available with mean diameters of 350 nm or 1.5 µm. They are produced by hydrolysis of orthosilicates in the presence of magnetite and have a hydrophilic surface with terminal Si-OH-bonds (plain). The particles have monomodal size distributions, and can easily be separated with conventional permanent magnets. sicastar®-M are extremely stable in organic solvents and at high temperatures.

The particles are designed with the surface functionalities NH2, COOH, N-hydroxysuccinimide (NHS) and epoxy for the covalent binding of proteins, antibodies or other molecules. They are available with covalently bound proteins (avidin, streptavidin, protein A, albumin) and biotin and can be offered with nickel(II) chelator nitrilotriacetic acid (NTA) or ready to use with the corresponding nickel complex (Ni-NTA) for the binding of histidine labeled proteins. Furthermore, sicastar®-M are available with a hydrophobic octadecyl (C18) surface and are deliverable with an organic polymer shell (core-shell method) on request.

2.2.9 sicastar®-M-CT

sicastar®-M-CT consist of aggregates in the size range of 3 - 30 µm with a mean diameter of 6 microns. The particles are produced by hydrolysis of orthosilicates in the presence of magnetite and show a homogeneous distribution of magnetite in the silica matrix due to the special preparation method. They have a hydrophilic surface with terminal Si-OH-bonds and can easily be separated even in highly viscous media with conventional permanent magnets. sicastar®-M-CT are extremely stable in organic solvents and at high temperatures.

The particles are designed with the surface functionalities OH (plain), NH2, COOH and epoxy for the covalent binding of proteins, antibodies or other molecules and are available with covalently bound proteins (avidin, streptavidin, protein A, albumin). sicastar®-M-CT can be offered with nickel(II) chelator nitrilotriacetic acid (NTA) or ready to use with the corresponding nickel complex (Ni-NTA) for the binding of histidine labeled proteins and are available with a hydrophobic octadecyl (C18) surface.

2.2.10 nanomag®-silica

nanomag®-silica are prepared via the core-shell method with a core of magnetite and a dextran shell with a simultaneous cross-linking of the dextran strands by silica nanostructures. The particles have a diameter of 250 nm and a magnetite content of 75-80%. These particles can easily be separated with a conventional permanent magnet.

nanomag®-silica are designed with the surface functionalities OH (plain), NH2 and COOH for the covalent binding of proteins, antibodies or other molecules and are available with the hydrophobic octadecyl (C18) surface especially for nucleic acid separation.

2.2.11 nanomag®-C

nanomag®-C are prepared via the core-shell method with a core of magnetite and a chitosan shell and have a diameter of 150 nm and a magnetite content of 75-80%. They can easily be separated with a conventional permanent magnet. The particles have already amino functionalities without any further surface modifications (surface: plain).

2.2.12 PLA-M particles

PLA-M particles consist of magnetite (40% w/w) in a matrix of poly(D,L-lactic acid) with a molecular weight of 17.000 Da. The particles are available with mean diameters of 30 µm and 100 µm. They are established in the field of magnetic drug targeting in connection with a controlled drug release. The half-life time of the beads under *in-vivo* conditions mainly depends on the molecular weight of the polymers and increases with the molecular weight of the polymer. The PLA-M particles can also be offered with carboxylic acid or amino groups on the surface and can be loaded with drugs on request.

2.2.13 PEI-M particles

PEI-M particles are prepared via the core-shell method with a core of magnetite and a poly(ethylene imine) shell. The particles have a diameter of 150 nm and a magnetite content of 75-80% and can be separated with a conventional permanent magnet.

2.2.14 Iron oxide particles

Iron oxide particles are available with hydrodynamic diameters of 50 nm and 250 nm. The surface of the 50 nm particles is colloidal stabilized with carboxylic acid groups. The 50 nm particles possess nearly no sedimentation tendency and cannot be separated with conventional permanent magnets. For magnetic separation a high gradient magnetic system is recommended. The 250 nm iron oxide particles consist of monodisperse magnetite aggregates and can be separated with permanent magnets. They possess a low tendency of sedimentation and are also available with gold labeling.

2.3 Types of fluorescent magnetic nano- and microparticles

Fluorescent magnetic particles allow the application of magnetic properties together with the ability of optical visualization. Selected magnetic particles of **micromod's** standard assortment are available with a green or red fluorescence. Customized magnetic particles are available with specific fluorescent dyes on request.

2.3.1 nanomag®-CLD-redF

nanomag®-CLD-redF particles show a red fluorescence (excitation: 552 nm, emission: 580 nm). The 100 nm nanomag®-CLD-redF particles are prepared by precipitation of iron oxide in the presence of dextran. They consist of about 80-90% (w/w) iron oxide in a matrix of crosslinked dextran (40.000 Da) and cannot be separated with a conventional permanent magnet but in a high gradient magnetic field. The 300 nm nanomag®-CLD-redF are prepared by the core-shell method. They consist of about 80-90% (w/w) iron oxide in a matrix of crosslinked dextran (40.000 Da) and can easily be separated with conventional permanent magnets. The nanomag®-CLD-redF particles are available with a plain surface, e.g. for stem cell labeling [13] (Fig. 8) or with amino groups on the surface for the covalent binding of proteins, antibodies or other molecules [14, 15].

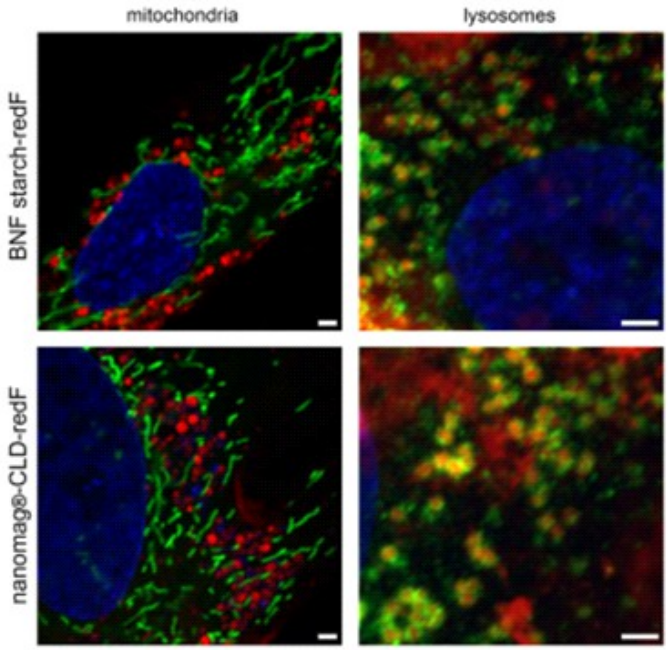


Figure 8. Intracellular localization of nanoparticles. Confocal laser scanning images of stem cells labeled with BNF-Starch-redF or nanomag®-CLD-redF and stained for mitochondria and lysosomes (both shown in green). Cell's nuclei were counterstained with Hoechst 33342 (blue).

2.3.2 BNF-F

BNF-redF particles have a red fluorescence (excitation: 552 nm, emission: 580 nm). They are thermally blocked at room temperature and show specific interaction with alternating magnetic fields. Fluorescent BNF particles are prepared via the core-shell method with a core of 75-80% (w/w) magnetite and a shell of crosslinked dextran (BNF-Dextran-redF) or crosslinked hydroxyethyl starch (BNF-Starch-redF). They are available with a particle diameter of 100 nm and can be separated with strong conventional permanent magnets. BNF-F possess a plain surface or amino groups on the surface for the covalent binding of proteins, antibodies or other molecules. They are available with covalently bound streptavidin for the binding of biotinylated biomolecules.

2.3.3 PLA-M-F

Fluorescent PLA-M particles consist of magnetite (40% w/w) in a matrix of poly(D,L-lactic acid) with a molecular weight of 17.000 Da. They are available with mean diameters of 30 µm and 100 µm (broader size distributions) and with red fluorescence (PLA-M-redF, excitation: 552 nm, emission: 580 nm) or green fluorescence (PLA-M-greenF, excitation: 502 nm, emission: 527 nm). The fluorescent PLA-M particles can be loaded with drugs on request.

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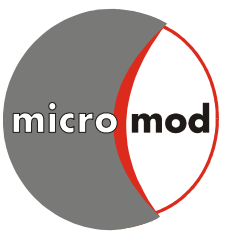

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