Single domain magnetic nanoparticles as a magneto-mechanical actuators for remote drug release from polyelectrolyte microcapsules

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Drug delivery

Process of drug delivery can be divide for 3 steps:

1. Encapsulating drug into carriers
2. Localization of carriers in the target area
3. Controlled release drug from carriers

For release drug from carriers can be used different physical methods.

Ultrasound destruction of microcapsules

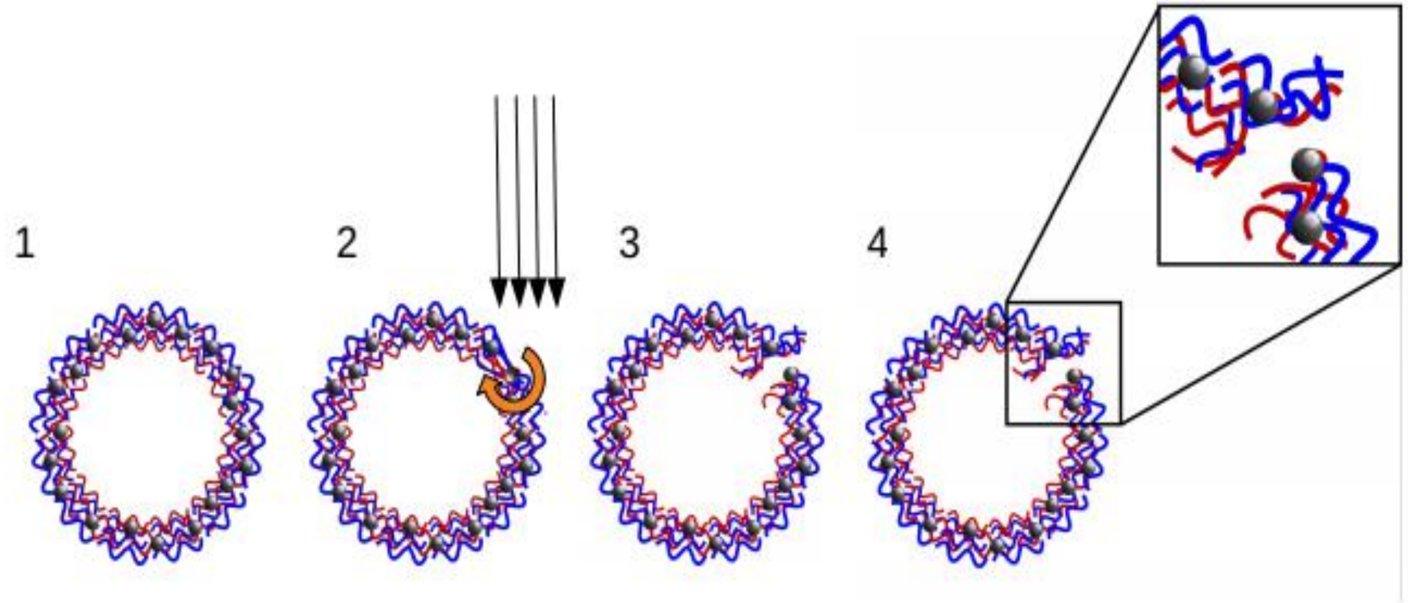
Laser heating of microcapsules

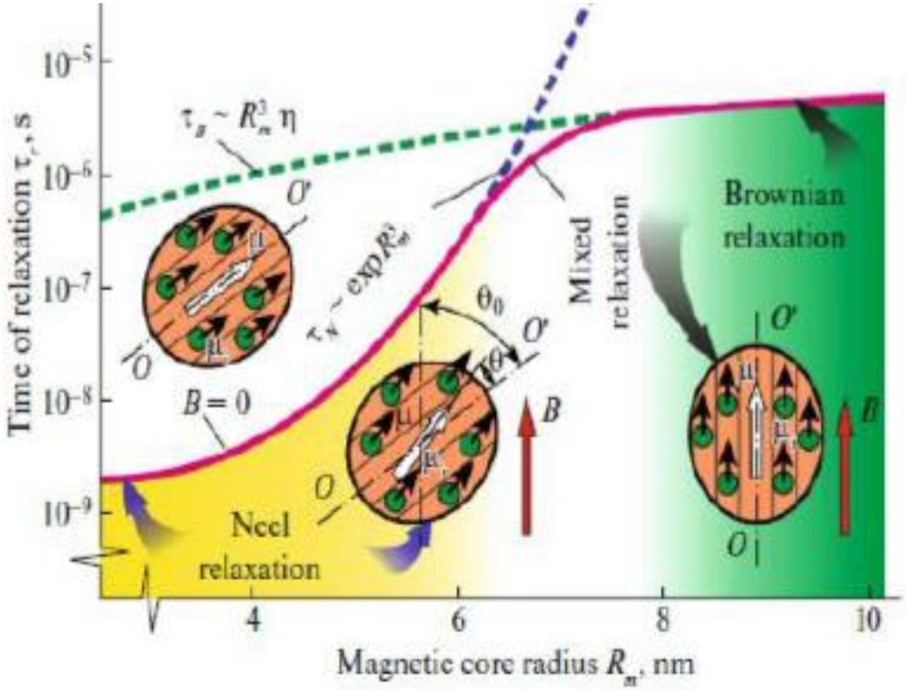
High frequency magnetic field destruction (magnetic heating)

Low frequency magnetic field destruction (magneto-mechanical effect)

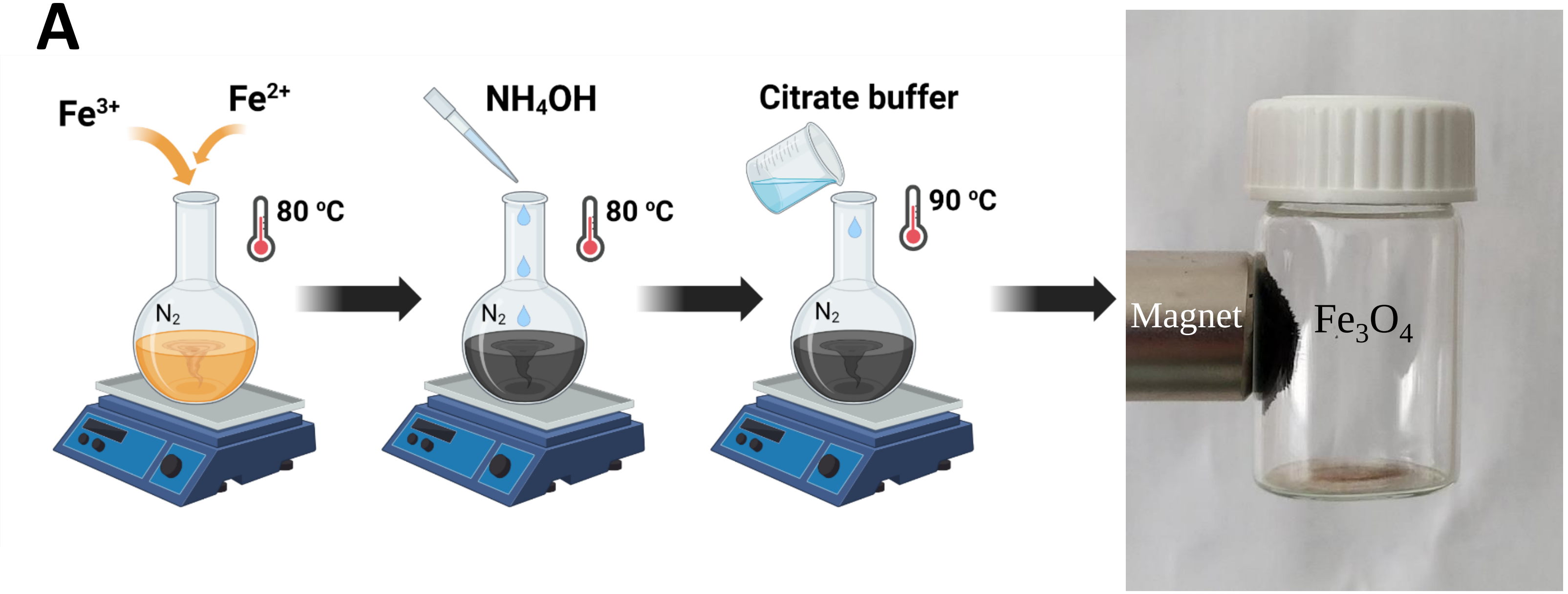
Magneto-mechanical effect

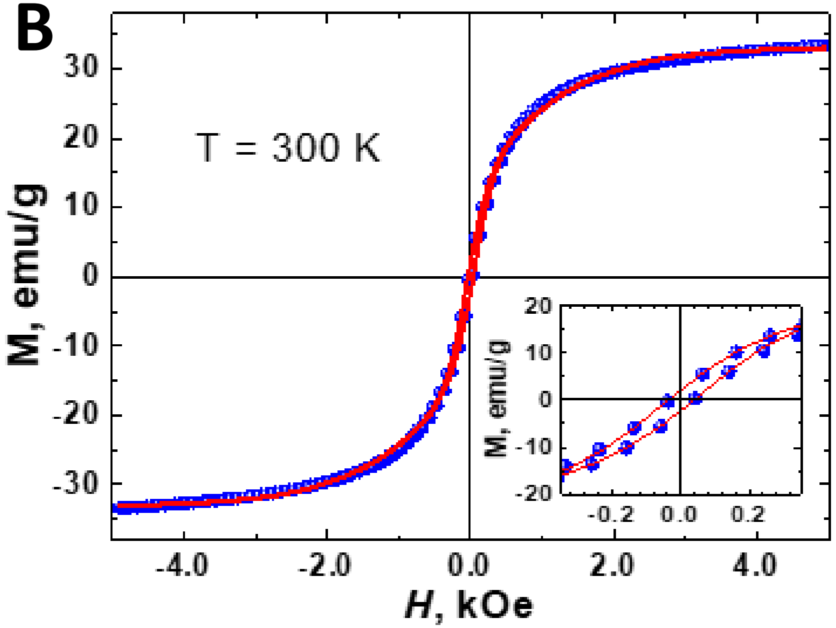
1. Microcapsules with magnetic nanoparticles (MNP) into shell
2. Magnetic field rotate MNP
3. Shell deformation by magnetic nanoparticles rotation
4. Deformed microcapsules

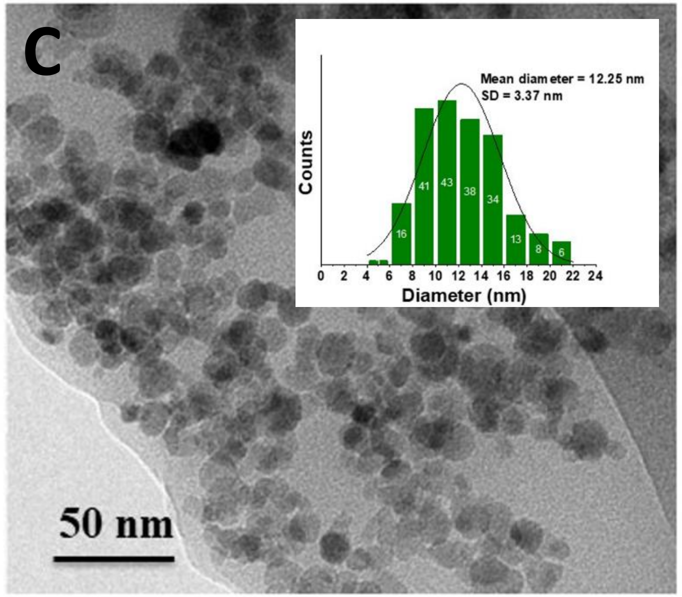


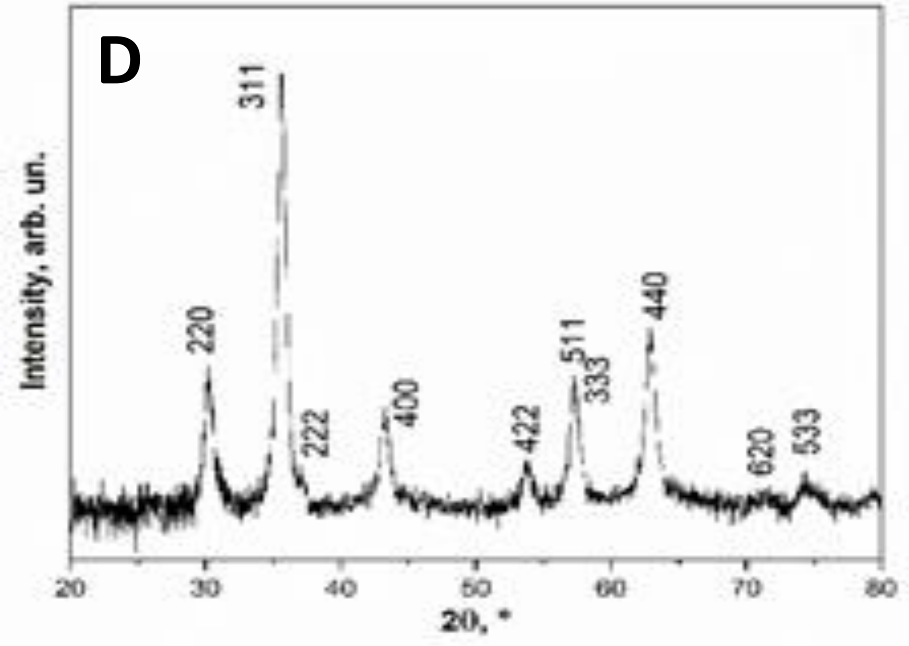


Magnetic nanoparticles synthesis and characterization









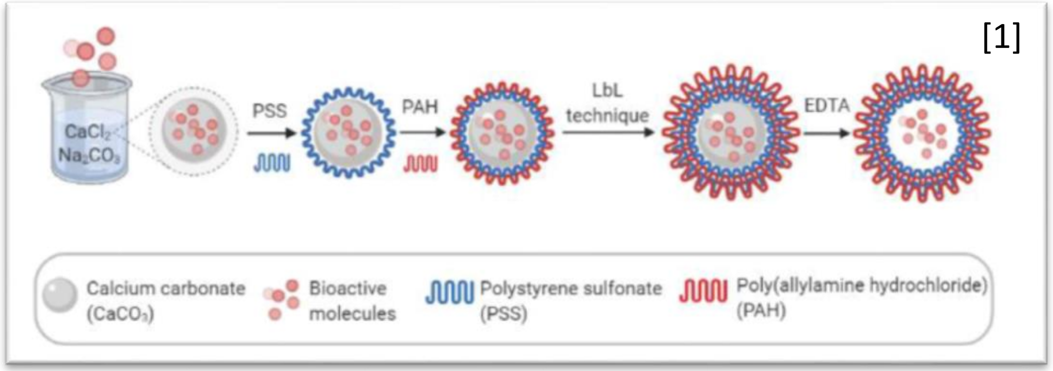
A – Scheme of synthesis of MNP (Massart method)

B – Magnetic hysteresis loop of MNP

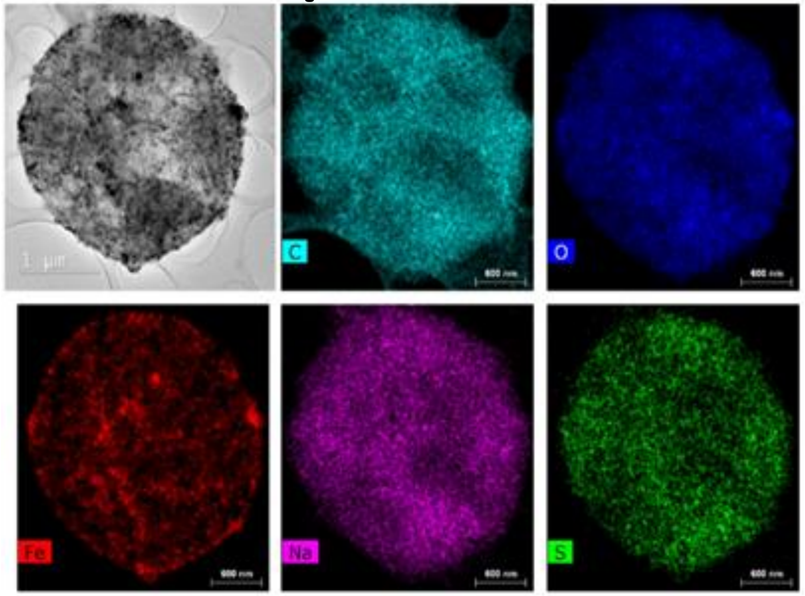
C – TEM image of MNP in microcapsules shell and size distribution. Average diameter of MNP – 12 ± 1 nm

D – XRD of MNP

Polyelectrolyte magneto-sensitive microcapsules



Microcapsules were prepared by the layer-by-layer method.
Colloid particles: $CaCO_3$ + TRITC-dextran

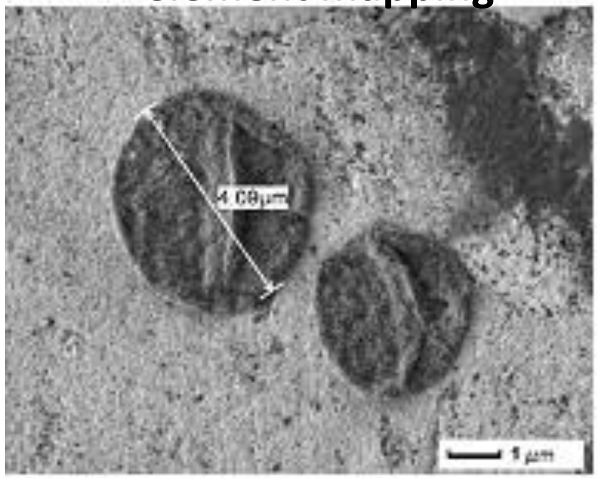


TEM image of microcapsules and element mapping

The shell structure of polyelectrolyte microcapsules was as follows: **PAH/PSS/PAH/MNP/PSS/PAH/PSS**

Poly(styrene sulfonate) (**PSS**), Poly(allylamine hydrochloride)(**PAH**), **MNP** – magnetic nanoparticles

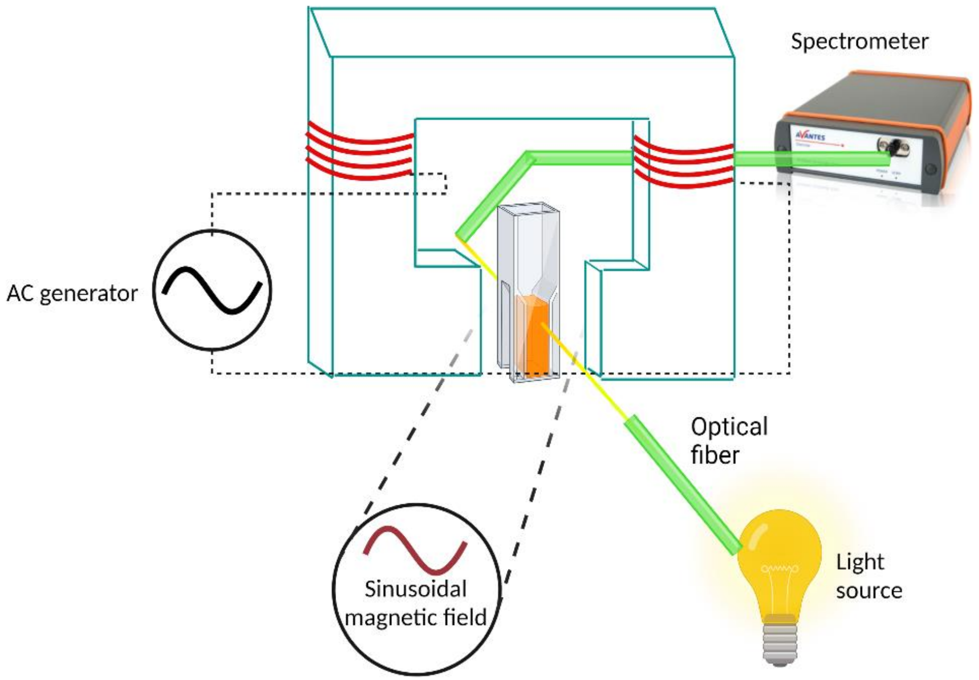
TRITC-dextran with a molecular weight of 65–85 kDa was used as a model substance.



SEM image of microcapsules.

[1] Raluca Ghiman , Roxana Pop, Dumitrita Rugina, Monica Focsan - Recent progress in preparation of microcapsules with tailored structures for bio-medical applications// Journal of Molecular Structure, Volume 1248, 15 January 2022, 131366, https://doi.org/10.1016/j.molstruc.2021.131366

Exposition in low frequency magnetic field



The *in situ* release of TRITC-dextran from the microcapsules was evaluated by measuring the optical density during the influence of magnetic field. For this, magnetic field generator with built-in light source and spectrometer were used. The scheme of the set-up is presented in Figure.

The samples were placed into the magnetic field generator in a glass cuvette with the total volume of each sample of 0.4 mL.

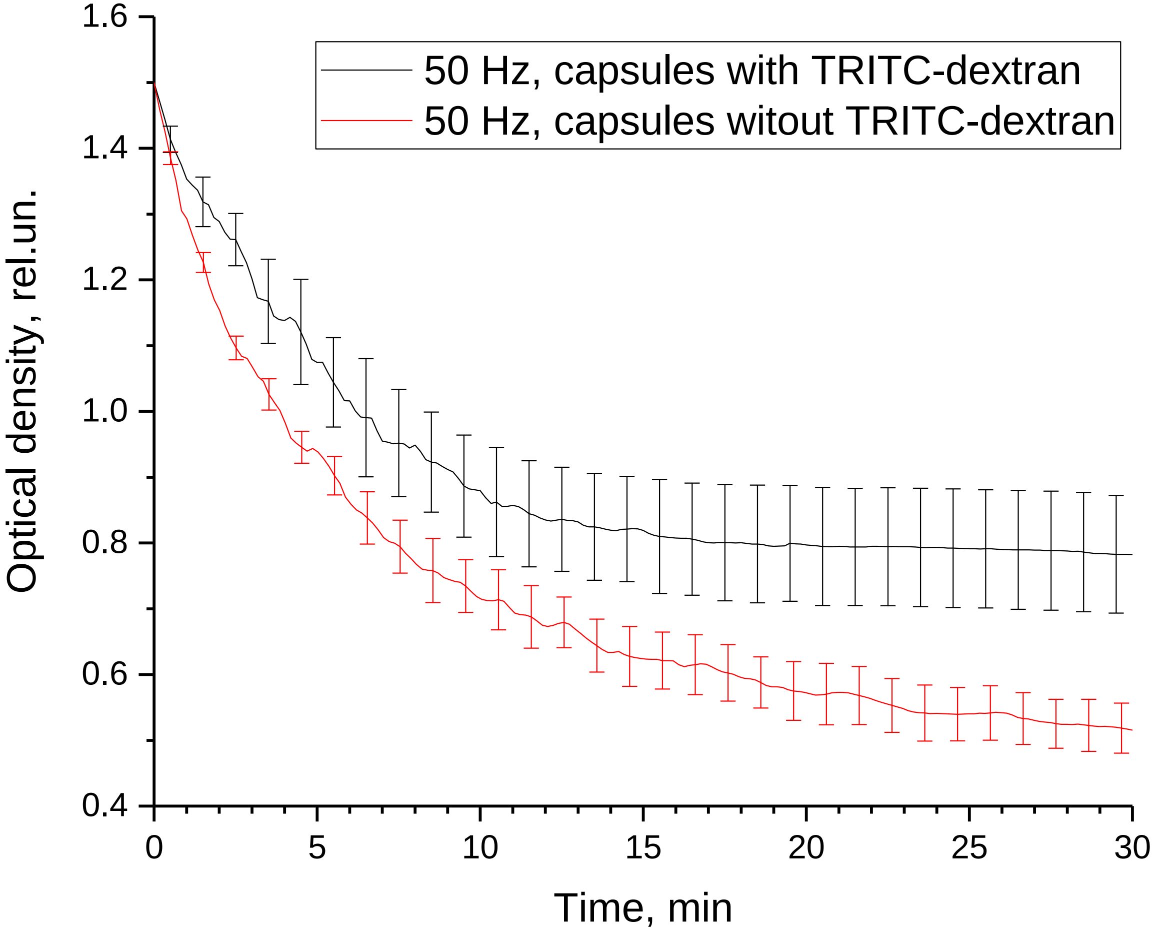
Evolution of optical density was measured at the wavelength 520 nm corresponding to TRITC-dextran absorption maximum.

The irradiation time for each measurement was approximately 30 minutes, which was optimal to reach the constant values of the optical density curves. First 3-4 points was measured without LFMF, then LFMF switching on, and all the other points was measured under the irradiation.

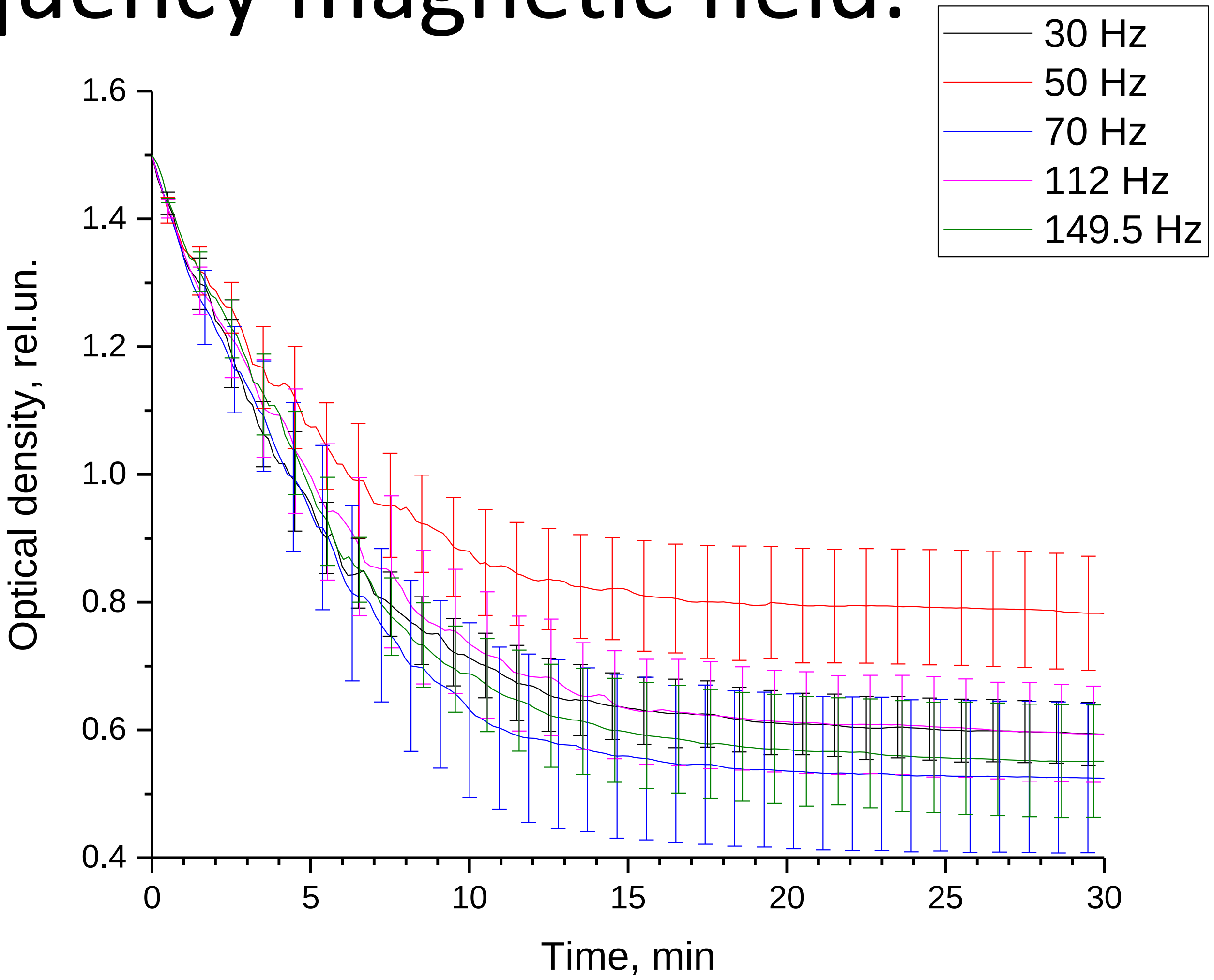
In our experiments we used 2 types of samples: unloaded capsules and capsules loaded with TRITC-dextran.
We used magnetic field with different frequency: 30, 50, 70, 112 and 149.5 Hz for both samples types.
For each samples and regime we collected 3 optical density curves.

Induction of magnetic field – 100 mT

Exposition in low frequency magnetic field.



Optical density curves for suspension of capsules loaded with TRITC-dextran and for control sample under exposure of LFMF



Optical density curves for suspension of capsules loaded with TRITC-dextran under exposure of LFMF with different frequency

On slide demonstrates the changes in optical density due to release of TRITC-dextran from the capsules under the LFMF exposure. optical density decreases in time for all studied LFMF frequencies from 30 to 150 Hz, which is associated with the gradual precipitation of the composite capsules to the electromagnet poles. The curve corresponding to the exposure to 50 Hz LFMF differs from the whole bunch of curves indicating the presence of another process besides attraction.

Exposition in low frequency magnetic field. Fitting function

$$\mathbf{Y} = \boldsymbol{B} * \boldsymbol{e}^{v_2 * t} + \boldsymbol{A}(1 - \boldsymbol{e}^{v_1 * t}) + \boldsymbol{S} \qquad (1)$$

Y – optical density
S – background
v_1, v_2 - speed of changes of concentration
t – time
A – amount of released TRITC-dextran
B – scattering from microcapsules

The dependences can be described by a function that includes 3 components: a component describing the **attraction of microcapsules to the walls of the cuvette bordering the electromagnet poles**, a component describing the **release of TRITC-dextran from microcapsules** and constant **background** value of optical density.

Obtained curves was fitted by the function (1) Parameters S and B don't depend on frequency of magnetic field. The calculated values of those parameters are S = 0.585 ± 0.002, B = 0.831 ± 0.005. The goodness of fit was evaluated by adjusted r-squared parameter

Frequency, Hz	A, rel.un.	v_1, s^{-1}	v_2, s^{-1}
30	0.097 ± 0.001	0.221 ± 0.012	0.191 ± 0.003
50	0.184 ± 0.003	0.159 ± 0.010	0.160± 0.002
70	0.085 ± 0.008	0.111 ± 0.028	0.175 ± 0.002
112	0.014 ± 0.004	0.140 ± 0.136	0.150 ± 0.002
149.5	0.078 ± 0.005	0.200 ± 0.051	0.137 ± 0.002

adjusted r-square	Capsules without TRITC-dextran	Capsules with TRITC-dextran
30 Hz	0.999999991	0.999999499
50 Hz	0.999999984	0.999999379
70 Hz	0.999999987	0.999985792
112 Hz	0.999999988	0.999389104
149.5 Hz	0.999999985	0.999985281

Results

- The magnetic nanoparticles obtained in this work were characterized by various methods. Based on the data on the size and magnetic properties of nanoparticles, it can be concluded that they are single-domain magnetic nanoparticles.
- Using SEM and TEM methods, polyelectrolyte microcapsules with magnetic nanoparticles in a shell were characterized. From the data obtained, it can be concluded that magnetic nanoparticles are efficiently incorporated into the shell of microcapsules. The distribution of nanoparticles over the shell of the microcapsule is close to uniform, which ensures the effect of a magnetic field on the entire shell of the capsule.
- From the data obtained, it can be seen that the highest optical density, after 30 minutes of irradiation, is possessed by a sample irradiated with a magnetic field with a frequency of 50 Hz. This means that the rotational motion of MNPs in the shell of microcapsules has the resonant character.

Conclusions

The low frequency magnetic field has been applied to induce magneto-mechanical actuation of MNPs disturbing the walls of the multilayer polymer capsule. Increased optical density due release of TRITC-dextran from microcapsules, proves the perspectives of using these nanoparticles for initiating the controlled shell permeability changes. The Brown mechanism significantly accelerates the relaxation of the shell structure, causing a microstructural evolution which may be beneficial for loading or releasing substances from the capsules.

Acknowledgment

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