Enhanced and super-localised magnetic hyperthermia

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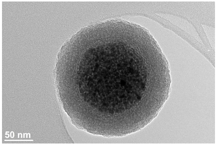
MAGNETIC NANOPARTICLE (MNP)

Magnetic nanoparticles are a class of nanoparticle that can be manipulated using magnetic fields.
MNP is in the focus of much research recently:



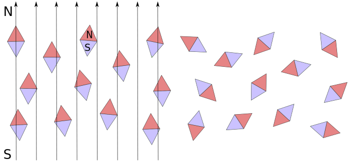
- magnetic particle imaging,
- data storage,
- medical diagnostics and treatments,
- cancer therapy
  - direkt - magnetic hyperthermia
  - indirekt - synergic effect

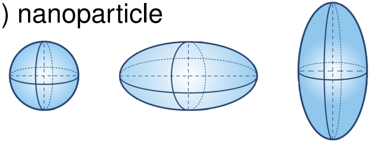
Iron oxide nanoparticles ($e.g. Fe_3O_4$) are the most explored magnetic nanoparticles up to date. –> biomedical applicition.

MAGNETIC NANOPARTICLE (MNP)

Physical properties of magnetic nanoparticles:

- superparamagnetic
- diameter $\sim 10\mathrm{nm} - 200\mathrm{nm}$
- single domain
- $T < T_{\mathrm{Curie}}$ and $T_{\mathrm{Curie}} \sim 44\,^{\circ}\mathrm{C}$
- biocompatible external coating
- shape anisotropy: λ_{eff}
  - $\lambda_{\mathrm{eff}} = 0$ spherical (isotropic) nanoparticle
  - $\lambda_{\mathrm{eff}} < 0$ oblate (lens shape) nanoparticle
  - $\lambda_{\mathrm{eff}} > 0$ prolate (cigar shape) nanoparticle





ADVANTAGES

Advantages of hyperthermia:

- well localized
- no side effects
- not toxic
- brain tumor, pleural tumor efficient treatment
- several methods exist for preparing magnetic nanoparticle

$\longrightarrow$ Charité - Universitätsmedizin Berlin

$$f \leq 100kHz, H = 18kA/m$$

GOAL OF THE RESEARCH

MNP + applied field = heat generation

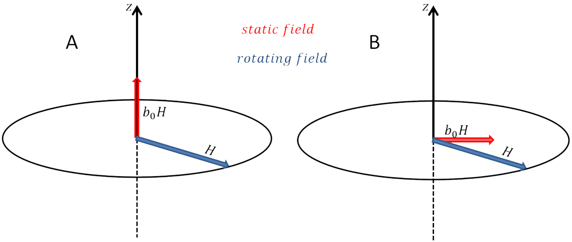
Improve efficiency! $\rightarrow$ by a new type of external field

- isotropic case, $T = 0$: rotating field $\leq$ oscillating field [1]
- isotropic case, $T \neq 0$: rotating field $\simeq$ oscillating field [2]
- $T = 0$: anisotropic rotating, (when it $\perp$ rotating field) $\leq$ isotropic rotating [3,4]

Always the oscillating is the best?

[1] P.F. de Chatel, I. Nándori, J. Hakl, S. Mészáros, K. Vad, J. Phys. Cond. Matter **21**, 124202 (2009).
[2] Yu. L. Raikher, V. I. Stepanov, Physical Review E **83**, 021401 (2011).
[3] I. Nándori, J. Rácz, Physical Review E **86**, 061404 (2012).
[4] J. Rácz, P. F. de Châtel, I. A. Szabó, L. Szunyogh, I. Nándori, Phys. Rev. E **93**, 012607 (2016).

static + rotating field



Two cases are considered: $(T = 0)$

A) $b_0 \perp$ rotating field **?** rotating field ($b_0 = 0$)

B) $b_0 \parallel$ rotating field **?** rotating field ($b_0 = 0$)

Deterministic Landau-Lifschitz-Gilbert (LLG) equation

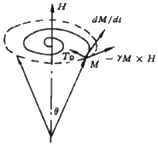
Magnetic dynamics of a single-domain MNP
(no thermal fluctuations)

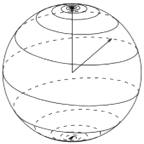
$$\frac{\mathrm{d}}{\mathrm{dt}}\mathbf{M} = -\gamma'[\mathbf{M} \times \mathbf{H}_{\mathrm{eff}}] + \alpha'[[\mathbf{M} \times \mathbf{H}_{\mathrm{eff}}] \times \mathbf{M}]$$

Magnitude is unchanged $\Rightarrow$ unit vector $\mathbf{M} = \mathbf{m}/m_S$

Parameters:

- dimensionless damping factor: α
- gyromagnetic ratio:
  $\gamma_0 = 1.76 \times 10^{11}$ Am^2/Js
- permeability of free space:
  $\mu_0 = 4\pi \times 10^{-7}$ Tm/A (or N/A^2)
- $\Rightarrow \gamma' = \mu_0\gamma_0/(1+\alpha^2)$
- $\Rightarrow \alpha' = \alpha\mu_0\gamma_0/(1+\alpha^2)$





Rotating, static magnetic field and the effect of anisotropy:

$$\text{A)} \quad \mathbf{H}_{\mathrm{eff}} = \mathrm{H}_0 \left(\cos(\omega \mathrm{t}), \sin(\omega \mathrm{t}), \lambda_{\mathrm{eff}} \mathrm{M_z} + \mathrm{b}_0\right),$$

$$\text{B)} \quad \mathbf{H}_{\mathrm{eff}} = \mathrm{H}_0 \left(\cos(\omega \mathrm{t}) + \mathrm{b}_0 + \lambda_{\mathrm{eff}} \mathrm{M_z}, \sin(\omega \mathrm{t}), 0\right),$$

- ω angular frequency,
- M_z z-component of the magnetization,
- λ_{eff} anisotropy parameter
- b_0 stands for the static stabilising field

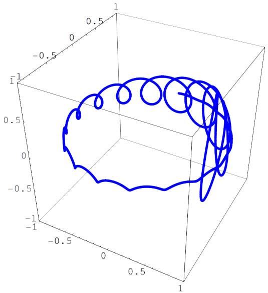
Dimensionless parameters for hyperthermia: ($t_0 = 0.5 \times 10^{-10}$s, $\omega_L = H_0\gamma'$, $\alpha_N = H_0\alpha'$)

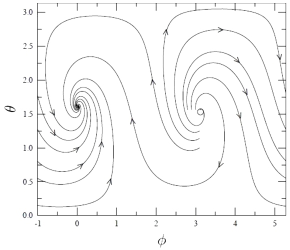
$$\begin{aligned} \omega \rightarrow \omega t_0 &= 2.5 \times 10^{-5}, \\ \omega_L \rightarrow \omega_L t_0 &= 0.2, \\ \alpha_N \rightarrow \alpha_N t_0 &= 0.02 \end{aligned}$$

STEADY STATE

LLG equation has attracitve steady state solutions. We can rewrite LLG equation in polar coordinates in a rotating frame $(M, \theta, \varphi) \rightarrow$ but $M =$ constant.

$\Rightarrow$ fixed points in the rotating frame, i.e., in the (θ, ϕ) plane:

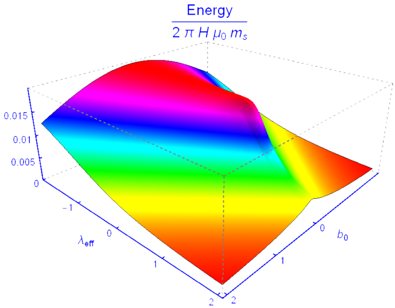




Loss energy in a single cycle (steady state solutions)

$$E = \mu_0 m_S \int_0^{\frac{2\pi}{\omega}} \mathrm{d}t \left(\mathbf{H}_{\mathrm{eff}} \cdot \frac{d\mathbf{M}}{dt} \right) \Rightarrow E(\lambda_{\mathrm{eff}}, b_0, \omega, \alpha_N, \omega_L)$$

A) Static field perpendicular to the plane of rotation

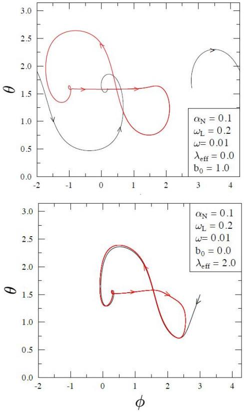


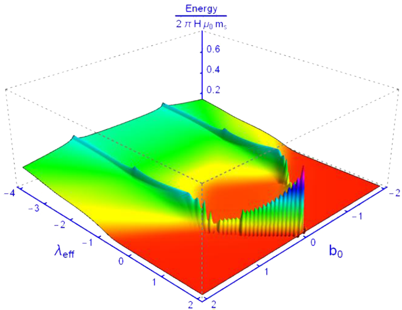
Any static field (b_0) decreases the energy loss!

$\longrightarrow$ **NEGATIVE RESULT**

B) Static field in the plane of rotation

No fixed point solutions, but attractive limit cycles! The limit cycle depends on the strength of the static applied field and the strength of the anisotropy parameter.
$\longrightarrow$ The change in the shape is enhanced when $|b_0| \sim 1, \lambda_{\text{eff}} \sim 2$.

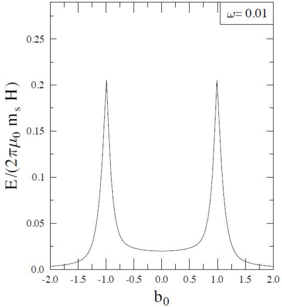




The energy loss depends on the strenght of the static applied field and the anisotropy. For positive anisotropy the energy loss over the limit cycle has been enhanced only if b_0 and λ_{eff} fulfil the following relation.

$$\boxed{|b_0| + \frac{1}{2}\lambda_{\text{eff}} - 1 = 0}$$

The energy loss has a very large maximum ($\lambda_{\text{eff}} = 0$). [5]



This can be used to
"SUPER-LOCALISE"
the heat transfer.

$\longrightarrow$ **POSITIVE RESULT**

[5] Zs. Iszály, K. Lovász, I. Nagy, I. G. Márián, J. Rácz, I. A. Szabó, L. Tóth, N. F. Vas, V. Vékony, I. Nándori, JMMM **466**, 452-462 (2018).

Stochastic Landau-Lifschitz-Gilbert (LLG) equation

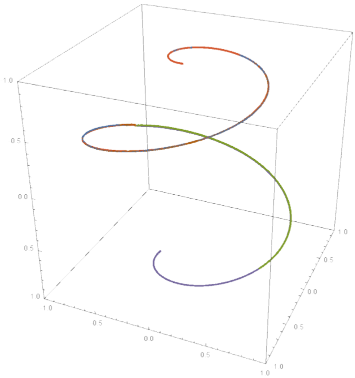
For experimental realisation it is a necessary to consider the influence of thermal fluctuations.

$$\frac{\mathrm{d}}{\mathrm{dt}}\mathbf{M} = -\gamma'[\mathbf{M} \times (\mathbf{H}_{\mathrm{eff}} + \mathbf{H})] + \alpha'[[\mathbf{M} \times (\mathbf{H}_{\mathrm{eff}} + \mathbf{H})] \times \mathbf{M}]$$

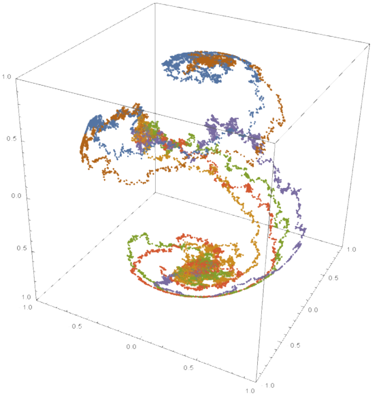
where the stochastic field, $\mathbf{H} = (\mathrm{H_x}; \mathrm{H_y}; \mathrm{H_z})$ consists of Cartesian components which are independent Gaussian white noise variables.

STOCHASTIC LLG RESULT

When the anisotropy field is assumed to be parallel to the z-axis.



$T = 0$

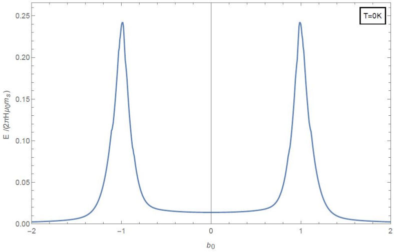


$T \neq 0$

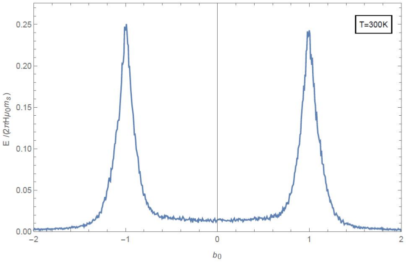
THE INFLUENCE OF THERMAL FLUCTUATIONS

Stochastic LLG equation in the presence of the applied magnetic field which is a combination of static and rotating ones (in plane). The effective applied field (isotropic nanoparticle):

$$\mathbf{H}_{\text{eff}} = H_0 \left(\cos(\omega t) + b_0, \sin(\omega t), 0\right)$$



$T = 0$



$T \neq 0$

$\longrightarrow$ Thermal fluctuations do not violate the enhancement and super-localisation effect!

Summary

If the static applied field is in the plane of rotation and the magnitudes of the static and rotating fields have a certain ratio (should be the same for isotropic case)
$\Rightarrow$ significant increase in the energy loss/cycle is observed;
$\Rightarrow$ it can be used to "super-localise" and enhanced the heat transfere!

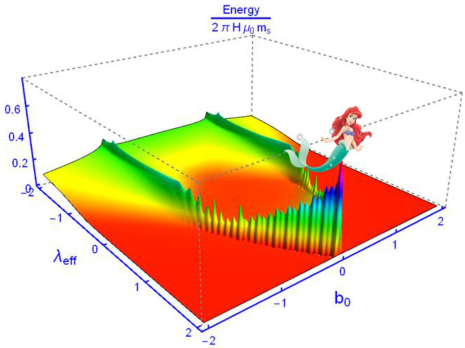
In case of an inhomogeneous applied static field, tissues are heated up only where the magnitudes of the static and rotating fields are equal to each other.

$\Rightarrow$ experiments in progress...

REFERENCES

Thank you for your attention!

https://youtu.be/v5z_HB1WzCc



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