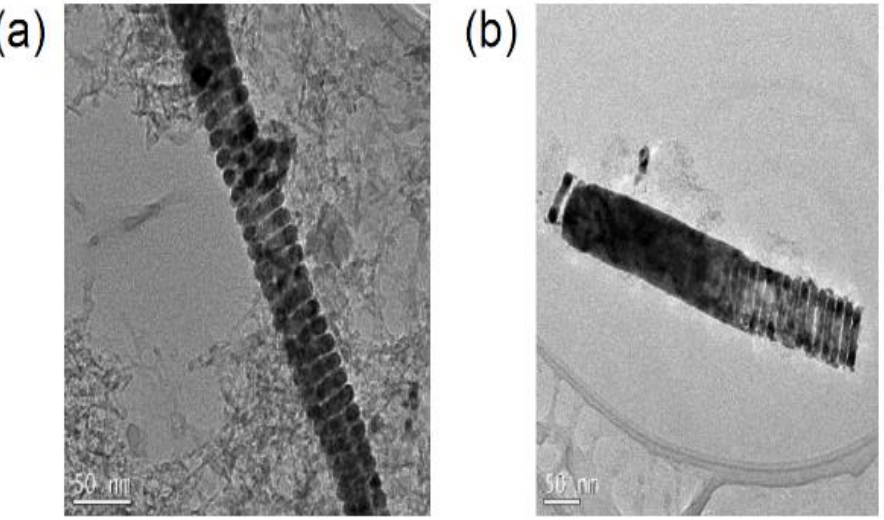
NSF NRI (1637535): Design of nanorobotics based on FePd alloy nanohelices for diagnosis and treatment of cancer



FePd nanorobot (a) nanohelix only,
(b) cylinder head and helical tail.

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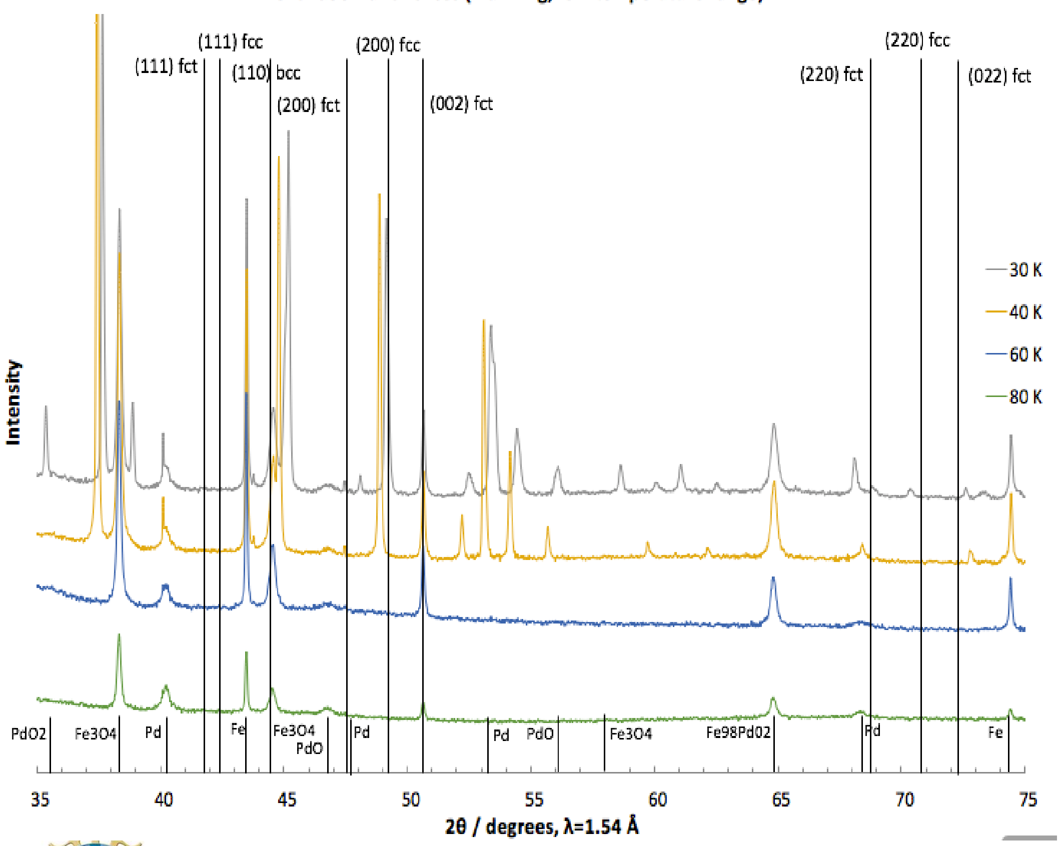
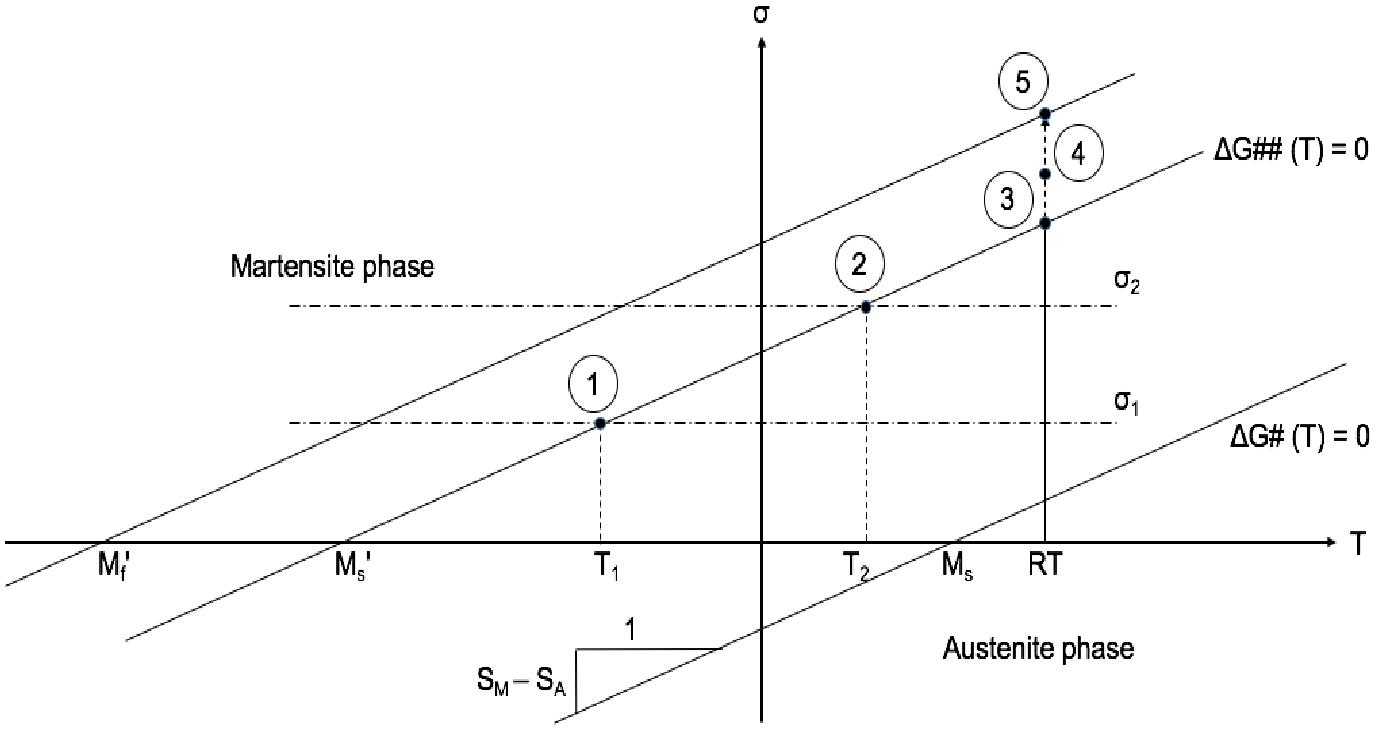
Advantages: (i) flexible and price control under magnetic field
(ii) Truly nano-size (10-100nm)
(iii) MRI signal enhancement
(iv) biocompatible
(v) Tool for applyin mechanical stress loading to cancer cells

October 29, 2018

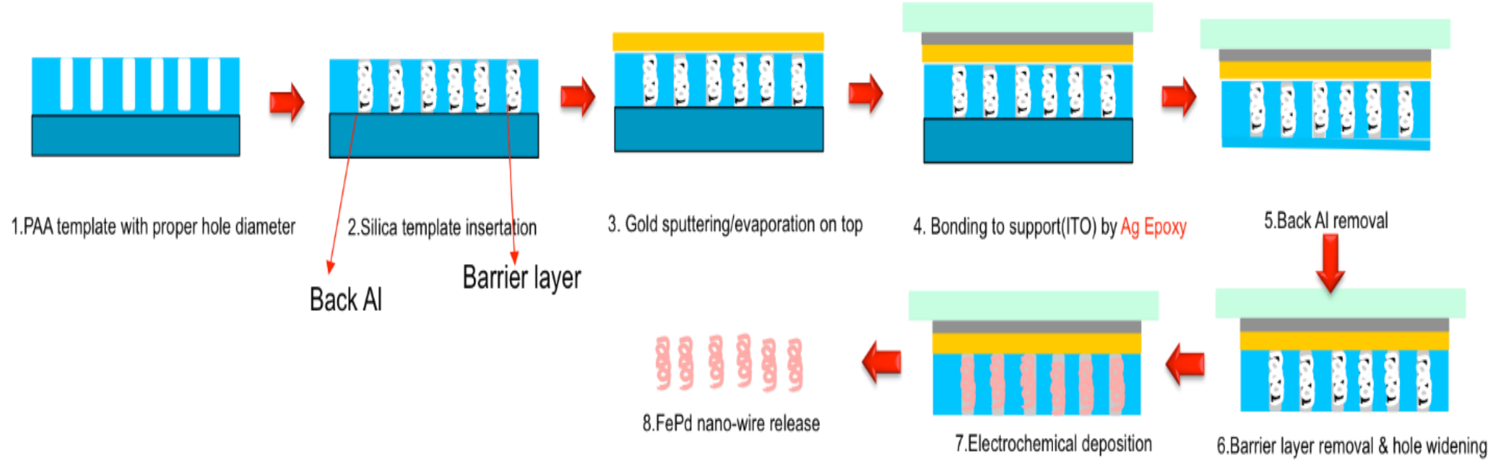
Phase Transformation Diagram of ferromagnetic shape memory alloy FePd nanomaterials,

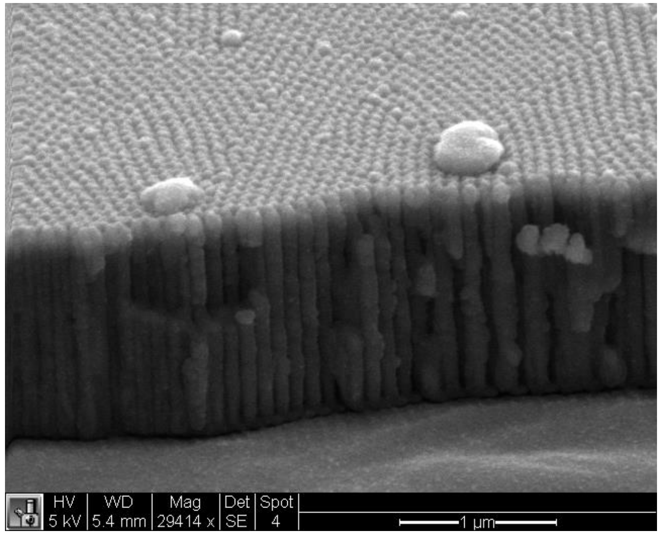
Austenite (A) to martensite(M) phase change of FePd nanohelix under decreasing temperature and increasing stress
But the A-M phase boundary line of nano-sized FePd is shifted to lower temperature, as compared with bulk sized FePd,
Whlie use of FePd nanorobots needs to be room temperature (RT), thus, pre-existing residual stress is needed to
the A-M boundary line moving upward, shown in vertical line (see Right Figure). XRD data of synchroton (Left Figure) shows the A-M
Change taking place, good news !!!



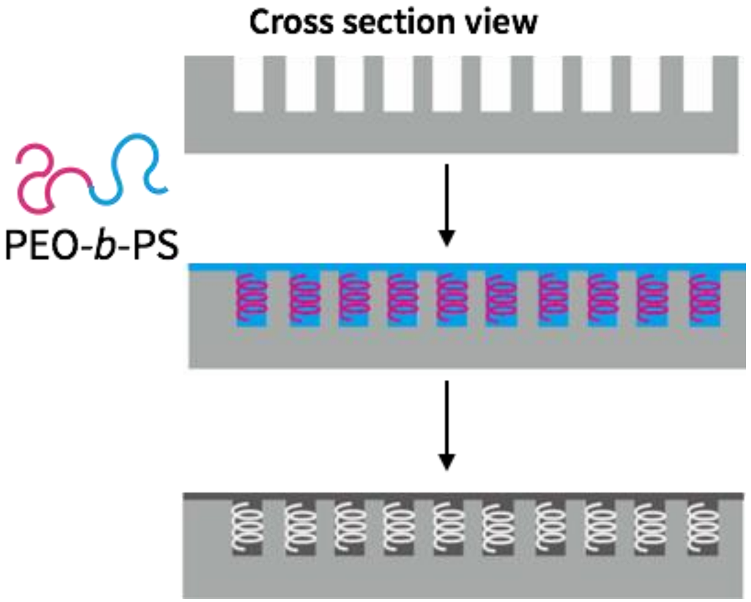


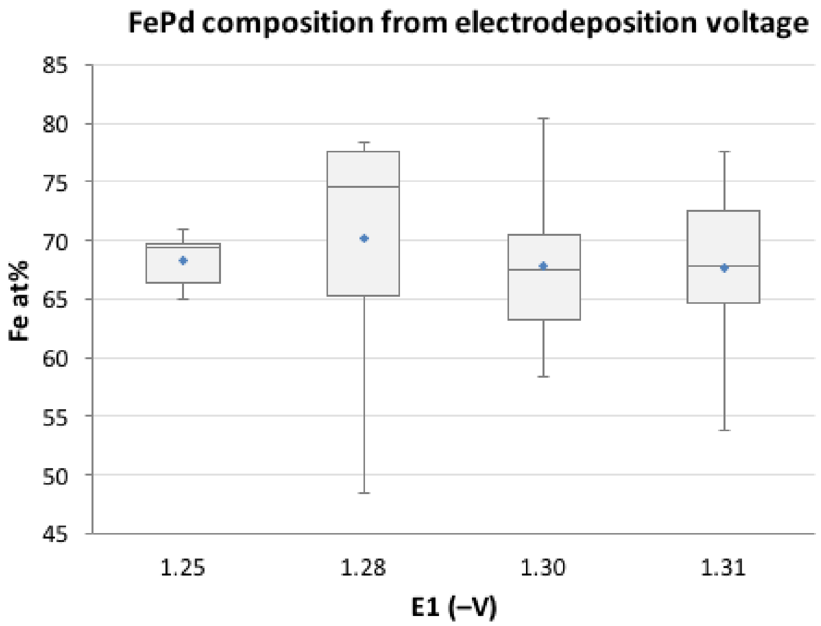
Processing of FePd nanohelices is challenging



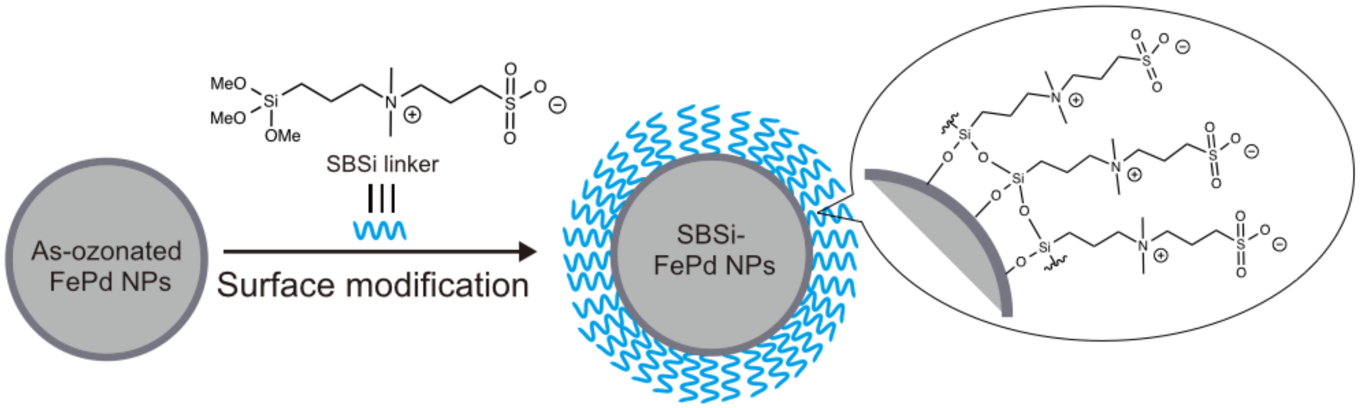


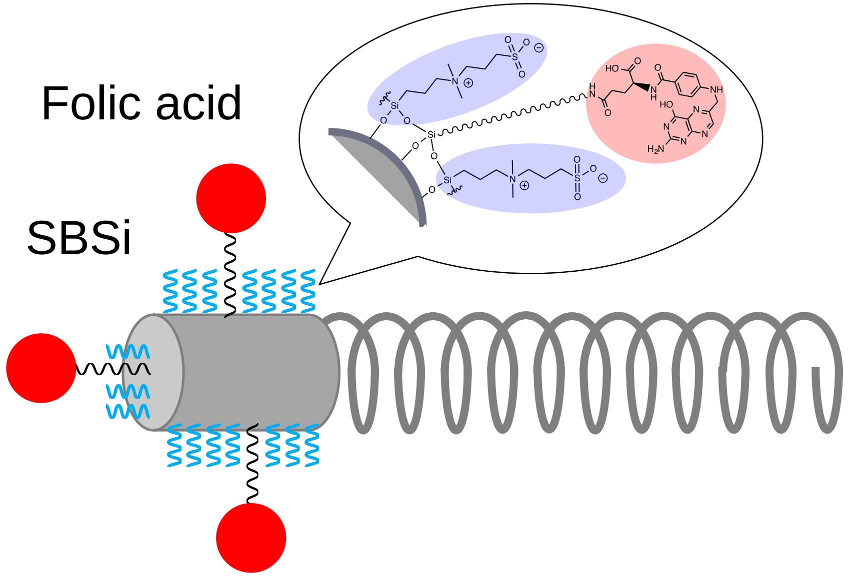
1. Need higher yield processing
2. Optimized block coplymerization for ideal nanorhelical holes in template
3. Correct stoichiometry of $Fe_{70}Pd_{30}$ for electroplating



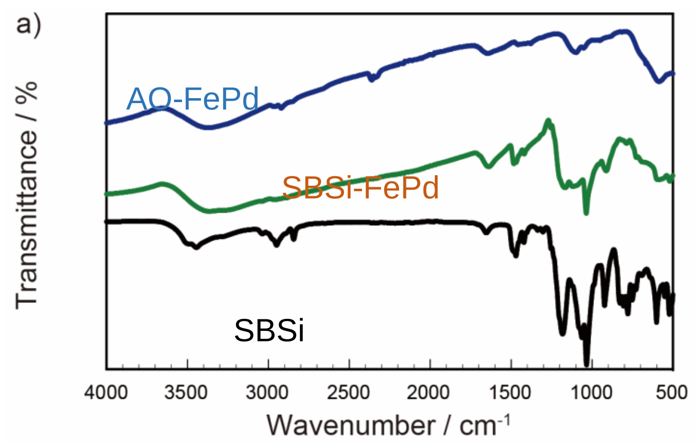


Surface coating for biocompatility and better dispersibility of FePd NRs.

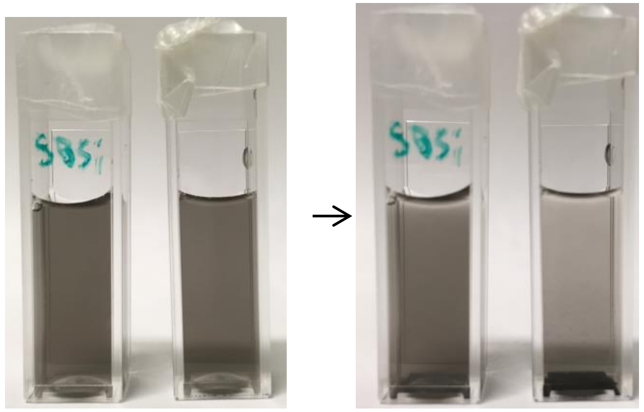




FTIR spectra



Dispersibility test



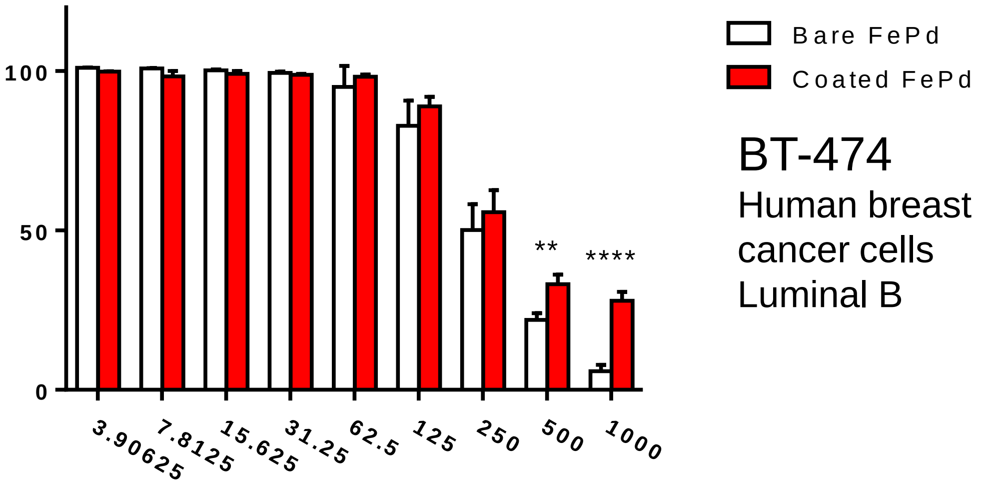
0 hour

24 hours

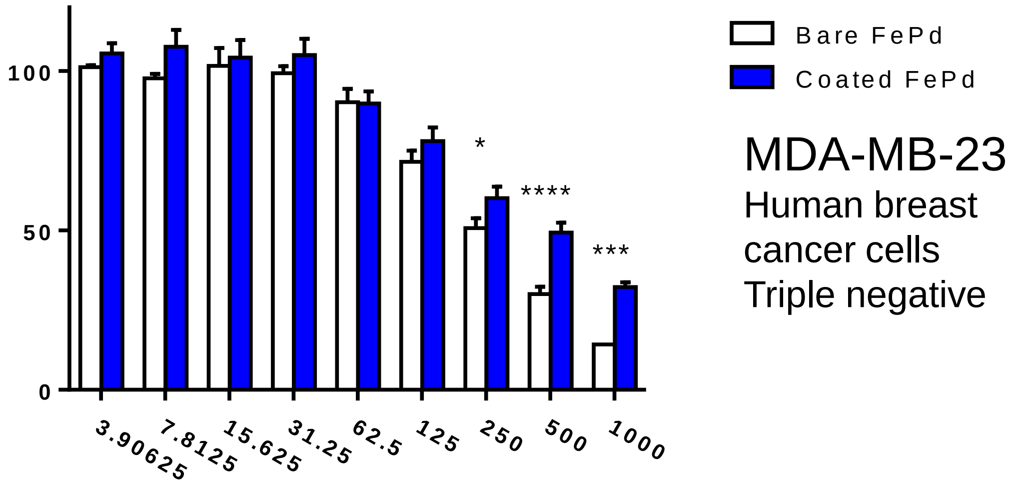
A) Illustration of the surface modification of FePd by Zwitterionic linker (SBSi) .
B) FT-IR indicated that SBSi linker can absorb on the surface of as-ozonated FePd NPs.
C) The dispersion test showed the dispersibility of FePd was improved by the surface modification with the SBSi linker.
D) Illustration of the surface modification of FePd by SBSi and folic acid. Folic acid is attracted to cancer cells which do not have specific antibody, such as in triple negative breast cancer

Biocompatibility assay of FePd NPs

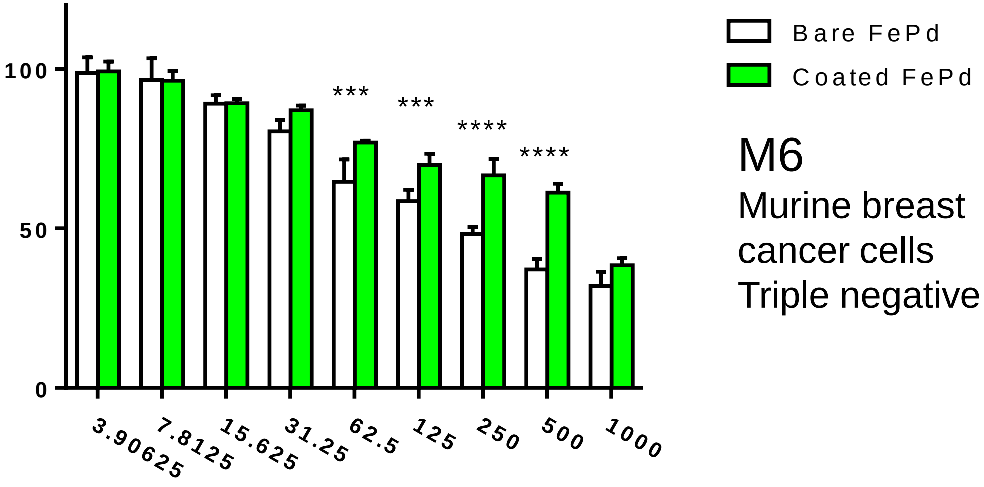
Cell viability (% Control)



BT-474
Human breast cancer cells
Luminal B



MDA-MB-231
Human breast cancer cells
Triple negative



M6
Murine breast cancer cells
Triple negative

Three cell lines were cultured with bare or SBSi-coated $Fe_{70}Pd_{30}$ NPs for 48 hr and cell viability was measured by XTT assay.

Table 1. GI50 of bare and coated $Fe_{70}Pd_{30}$ NPs (μg/ml)

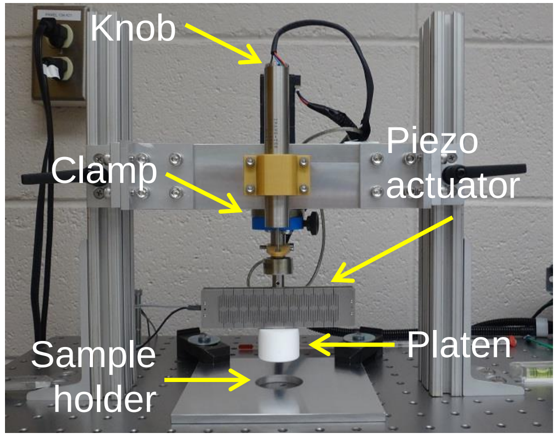
Cell line	Bare	Coated
BT-474	252	218
MDA-MB-231	217	223
M6	226	748

Concentration of bare or coated $Fe_{70}Pd_{30}$ NPs (μg/ml)

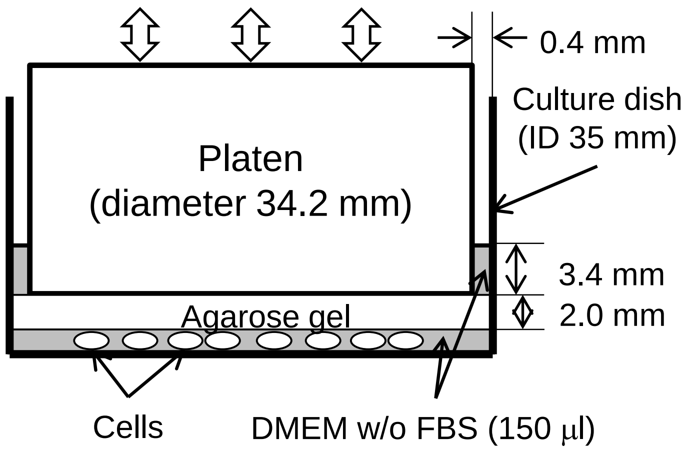
Mechanical Stress-induced Cell Death (MSICD)

Mechanical stress was applied to cancer cells macroscopically and we assessed cell damages.

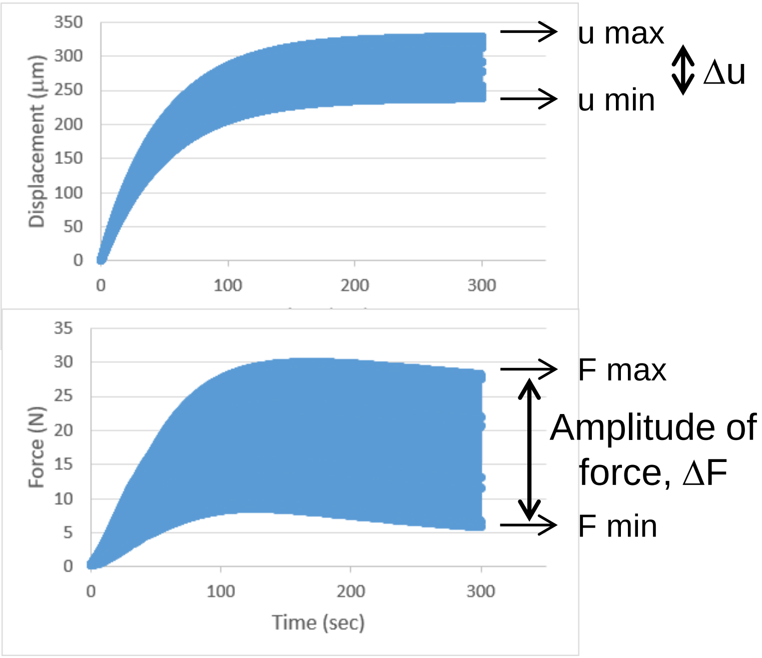
A



B



C



Equation: $\delta(t) = \alpha/2*(\sin(2*pi*f)+1)*(1-e^{(-t/\tau 1)}) + \beta*(1-e^{(-t/\tau 2)})$

Setting parameters of mechanical stress loading testing

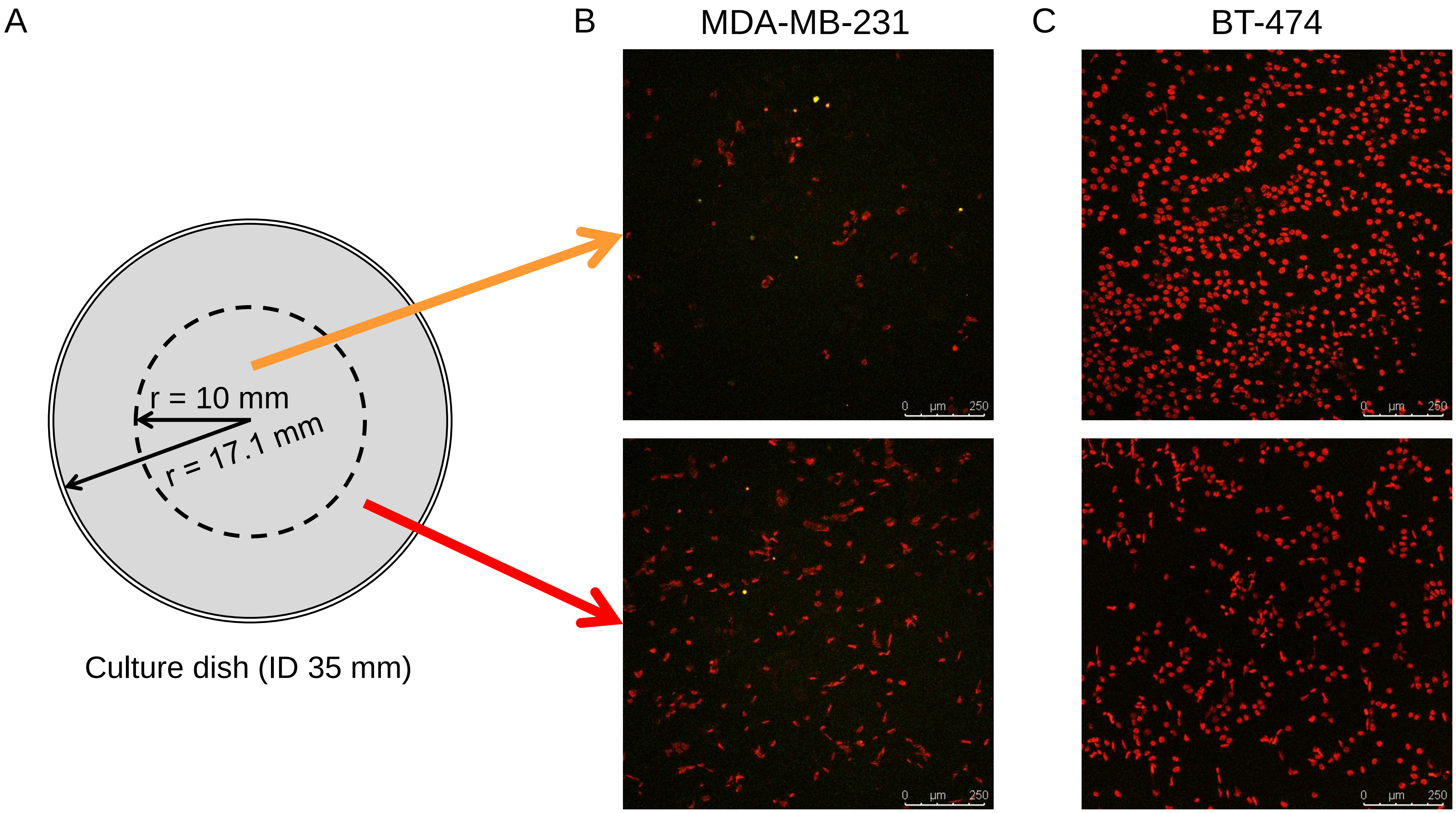
- Agarose gel: 3.0 %, ~2 mm thickness
- f: 30 Hz (the displacement frequency)
- α: 40-130 μm (the displacement amplitude)
- t: 210-450 sec (duration)
- τ1: 50 sec (the time constant for the ramp-up stage)
- τ2: 50 sec (the time constant for the additional compressive load)
- β: 200, 220 μm (the additional compressive displacement to prevent tensile loading)

Initial platen movement was operated manually to reach the surface of gels (~0.2 N), then started the program in LabVIEW.

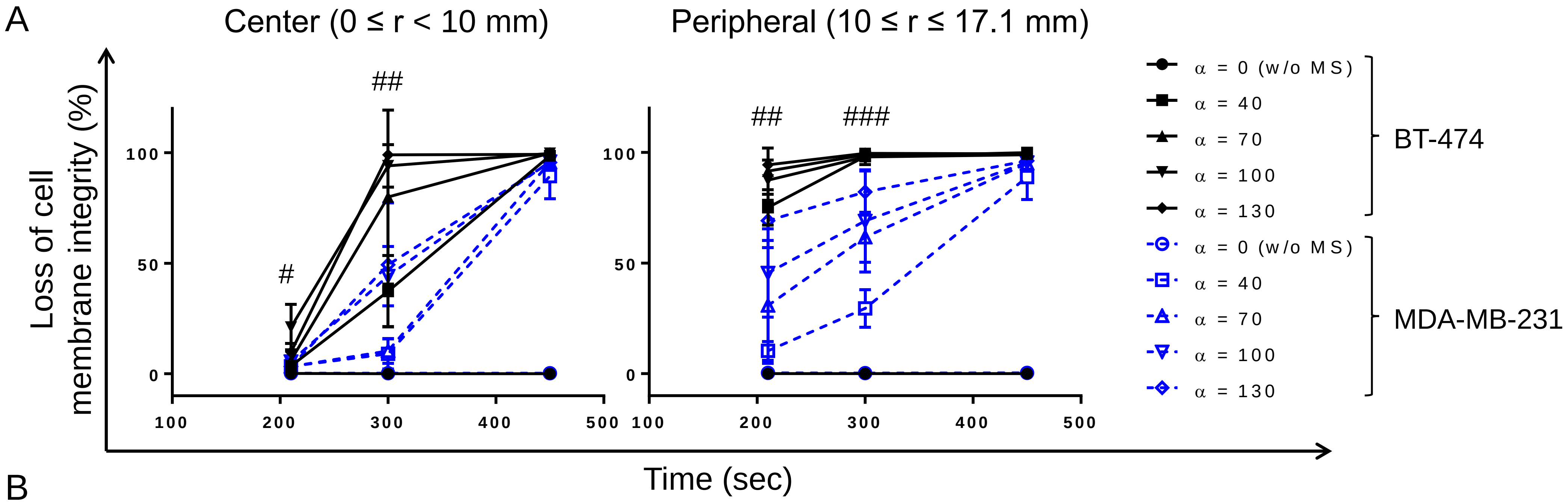
DMEM, Dulbecco's modified Eagle's medium; FBS, fetal bovine serum.

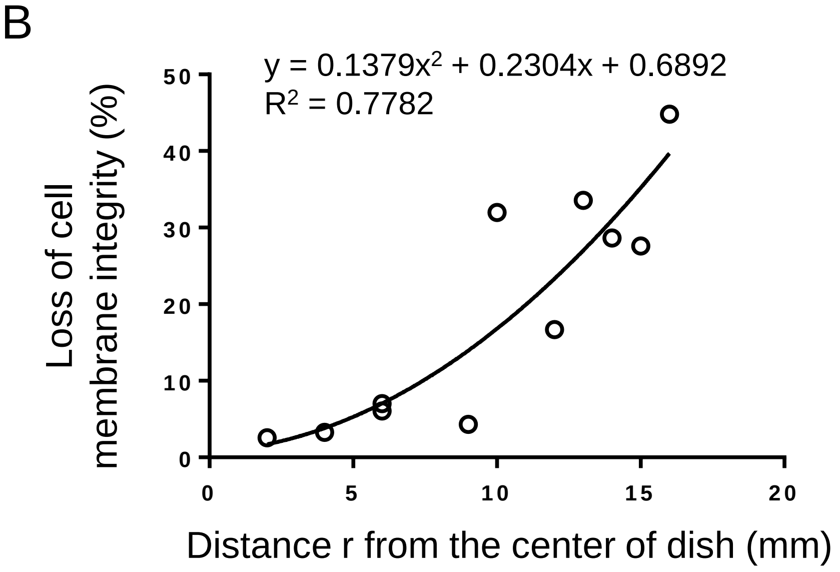
Cells used in the experiments are breast cancer cell lines, BT-474 (luminal B) and MDA-MB-231 (triple negative).

MSICD: two regions in culture dish



Necrosis-based MSICD





A
#, $p < 0.05$ for $\alpha = 40$;
##, $p < 0.01$ for $\alpha = 40, 70, 100, 130$;
###, $p < 0.01$ for $\alpha = 40, 70, 130$.

B
MDA-MB-231 treated for 300 sec with 40 μm displacement loading.

MRI relaxation time (T2= 1/R2) of FePd nanoparticles, which are found to enhance MRI signals

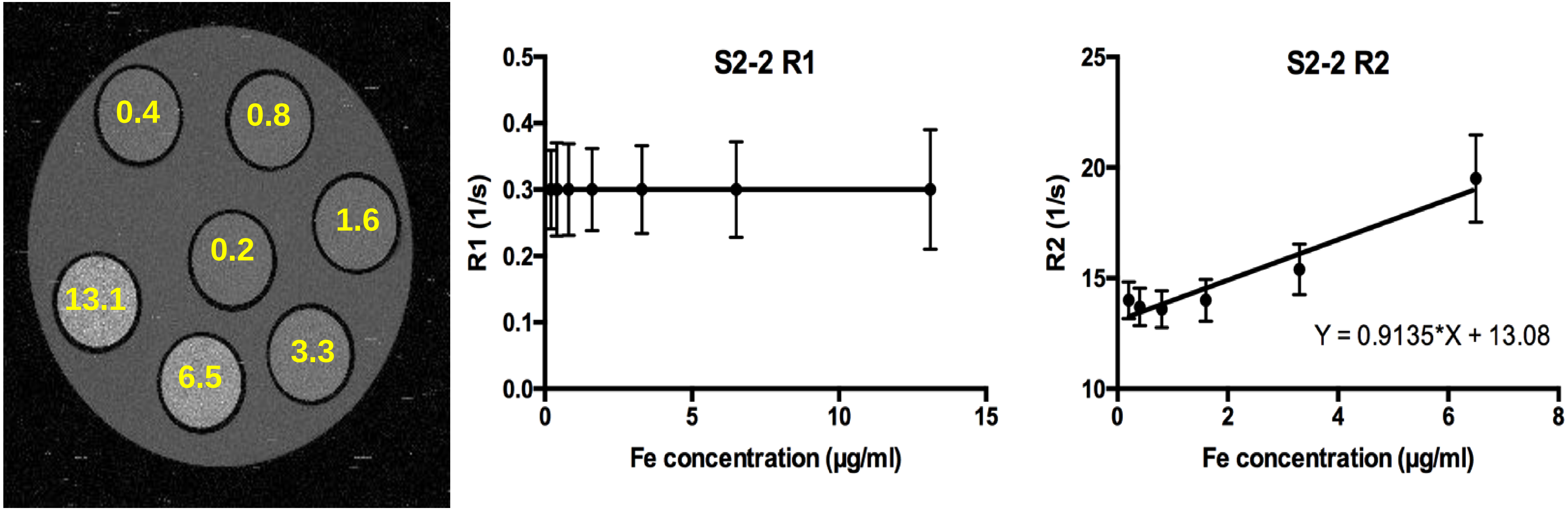


Figure #. T2 weighted images containing different iron concentrations in µg/ml (left) and R1 (middle) and R2 (right) as a function of iron concentration.

The slope of R2- concentration graph is higher than that of R1, thus, use of R2 data is better suited for our FePd nanorobots to detect their location inside mice or human.

Nanorobot Swimming Speed and Swim Time Model

$$F = VM * \nabla H_x$$
$$T = VM * H$$

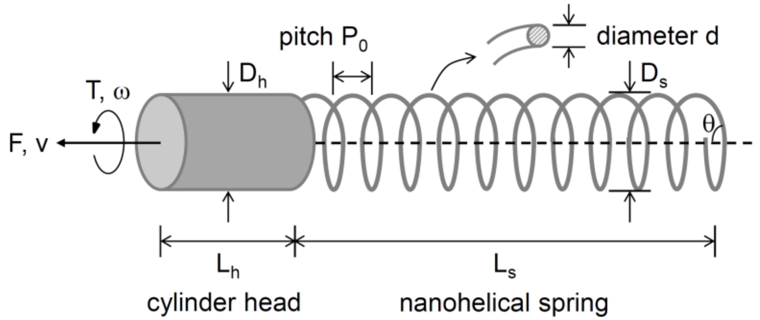
Where, $H \cong H_y \cong H_z$ $(Rotational\ EM\ Field)$
and relationship (34)

$$\begin{bmatrix} V \\ T \end{bmatrix} = \begin{bmatrix} \alpha & \beta \\ -\beta & \gamma \end{bmatrix} \begin{bmatrix} F \\ \omega \end{bmatrix}$$

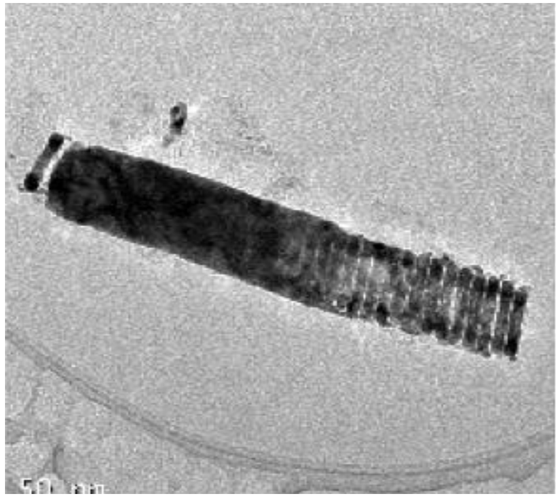
With respective element computed by definition result in:

$$\begin{pmatrix} V \\ T \end{pmatrix} = \begin{bmatrix} 1.76 \times 10^7 \left[\frac{m}{N.s}\right] & 1.391 \times 10^{-9}[m] \\ -1.391 \times 10^{-9}[m] & 3.378 \times 10^{-23}[N.s.m] \end{bmatrix} \begin{pmatrix} F \\ \omega \end{pmatrix}$$

With F and T computed we can obtain $\omega_{step\ out}$ as 51,125 rad/s. Thus exceeding the step out angular velocity is impossible
for our driver system to achieve due to high induction and overheating from flux leakage.



Geometric definition of NR composed of head and nanohelix tail.

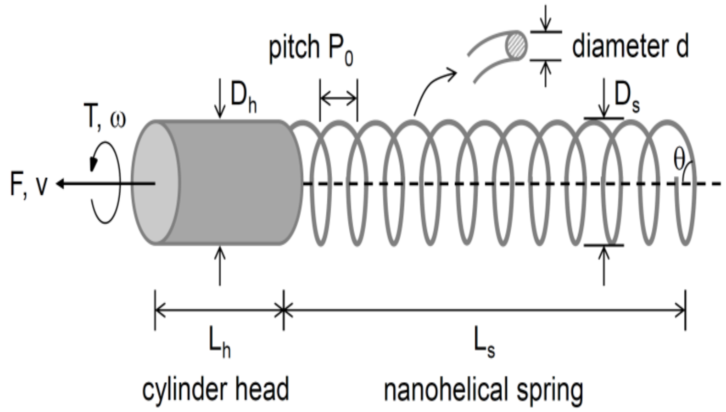

TEM photo of a FePd nanorobot made of cylinder head and nanohelix tail.

Nanorobot Swimming Model: velocity and spring constant

Case	D_h (nm)	$L_h (nm)$	D_s (nm)	$d = 2r$(nm)	L_s (nm)	n	Velocity (mm/s)	Swim Time (Hours)	k_{mart} (N/m)	k_{aust} (N/m)
0	60	200	60	10	250	16	0.000525	12.7	0.00392	0.01305
1	60	200	200	20	1000	19	0.00161	3.46	0.00141	0.00470
2	60	200	1000	50	20000	76	0.0086	0.65	0.00011	0.000367
3	200	600	200	20	1000	19	0.00157	3.53	0.00141	0.00470
4	1000	3000	1000	50	20000	76	0.00854	0.65	0.00011	0.000367
5	1000	3000	2000	50	10000	19	0.018	0.32	0.000055	0.000184
6	1000	3000	1000	50	10000	38	0.0085	0.65	0.00022	0.000734

Comparison of swimming velocity of NRs and Swim time of NRs of different cases are done based on similar EM driving condition assumed for all cases which are:

- $f = 50Hz$ rotational EM field, $l = 2cm$ swimming length,
- $14mT$ rotational maximum magnetic field density and
- $0.2\ T/m$ magnetic field density gradient.

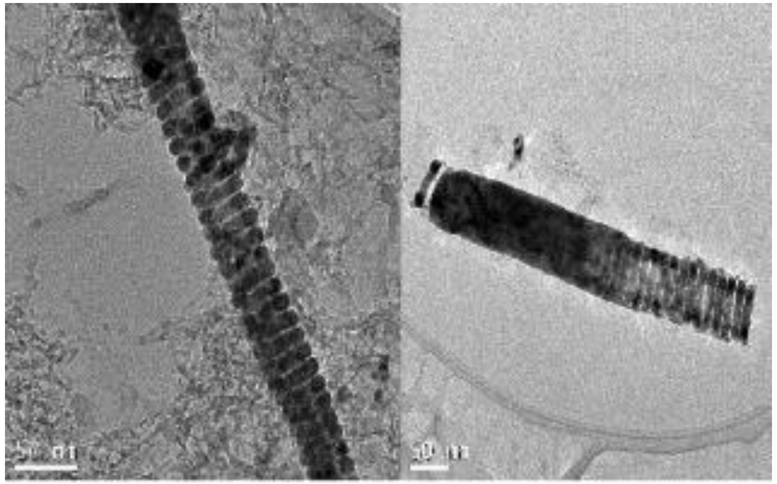


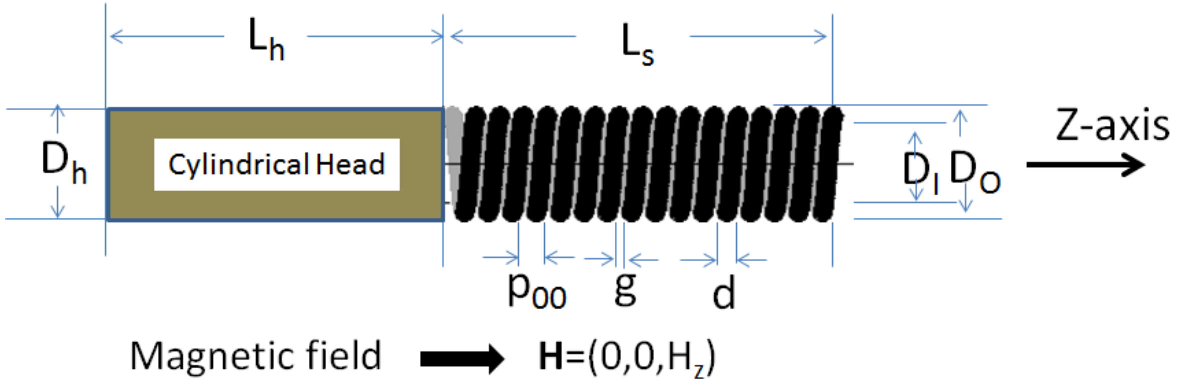
Predict the effective stiffness, k of the nanohelix along its symmetric axis.

$$k = \frac{d^4 G}{8 D_s^3 n}$$

G can be either martensitic or austentic shear modulus of the FePd which is dependent on its shape memory effect.

Molecular Dynamics Model Simulation for Nano-motions of FePd nanohelix robots under applied magnetic field



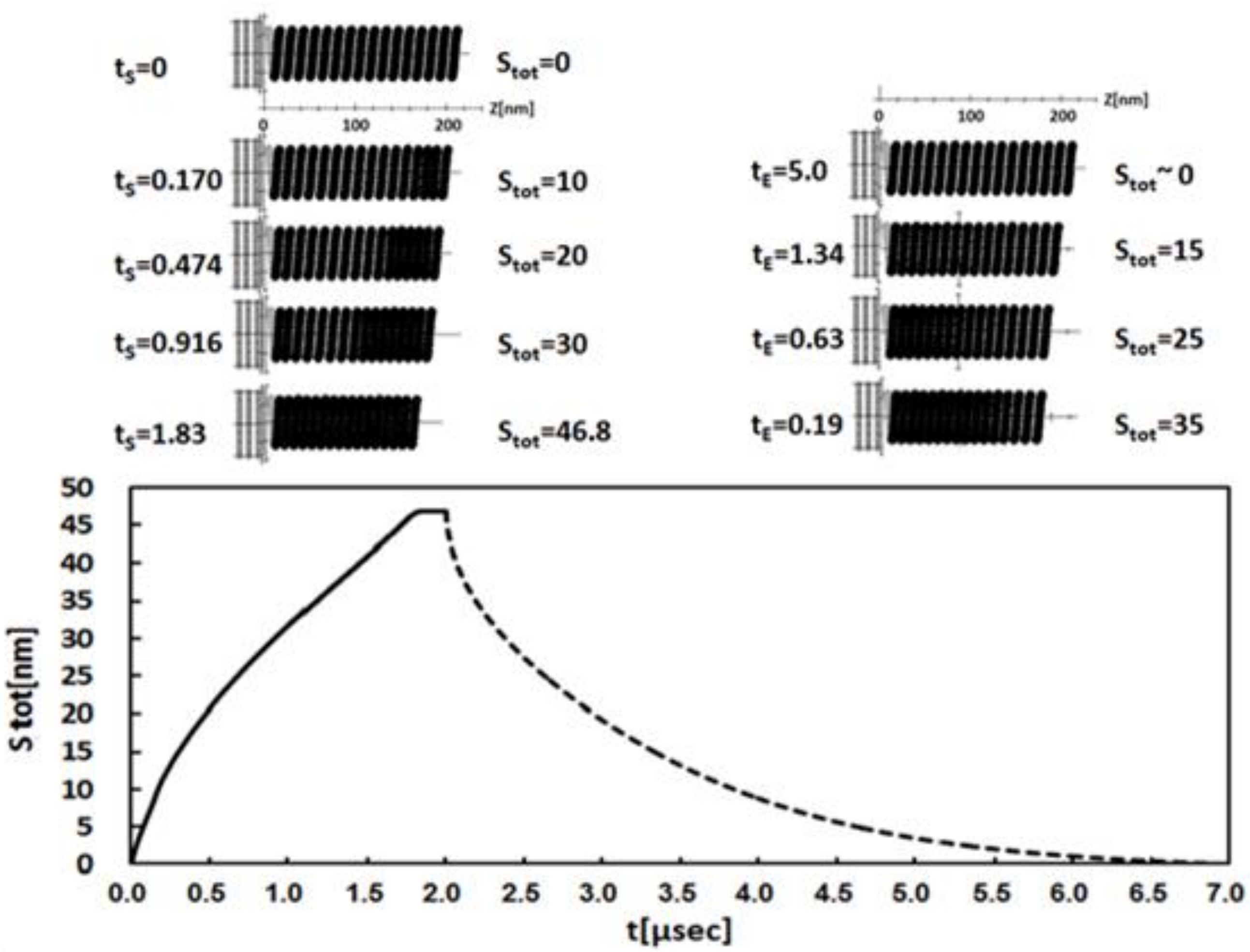


Left : nanohelix only
Right: nanorod(head) connected to nanohelix(tail)

Molecular dynamics model is developed to simulate the nano-motions of FePd nanorobots under applied magnetic field, for two cases, (i) on-aixs magnetic field, and (ii) off-axis magnetic field

Taya et al (2017), J. Appl. Phys., **121**, 154302

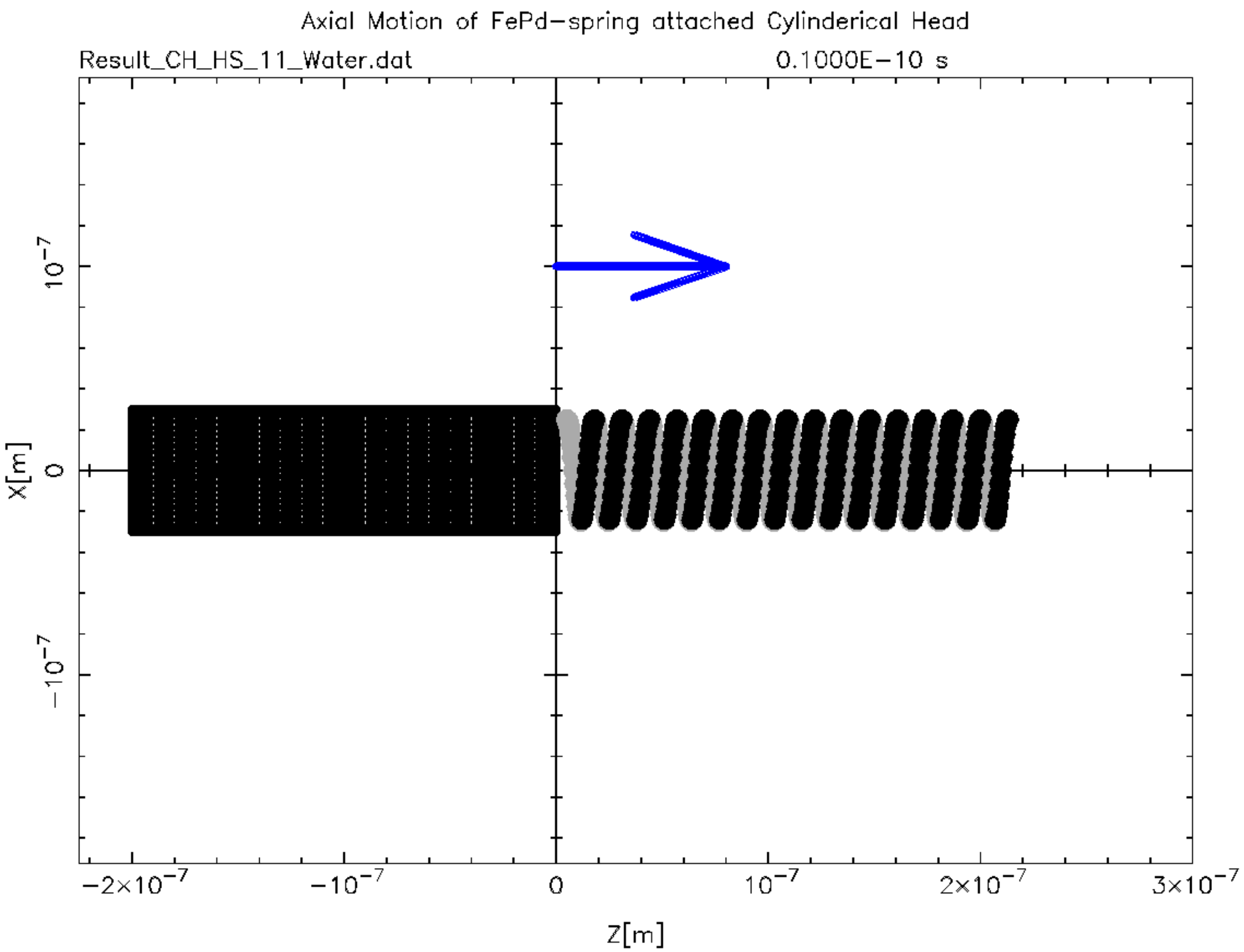
Molecular dynamics (MD) model Simulations for the robot made of nanorod and nanohelix with left end fixed under on-axis magnetic field



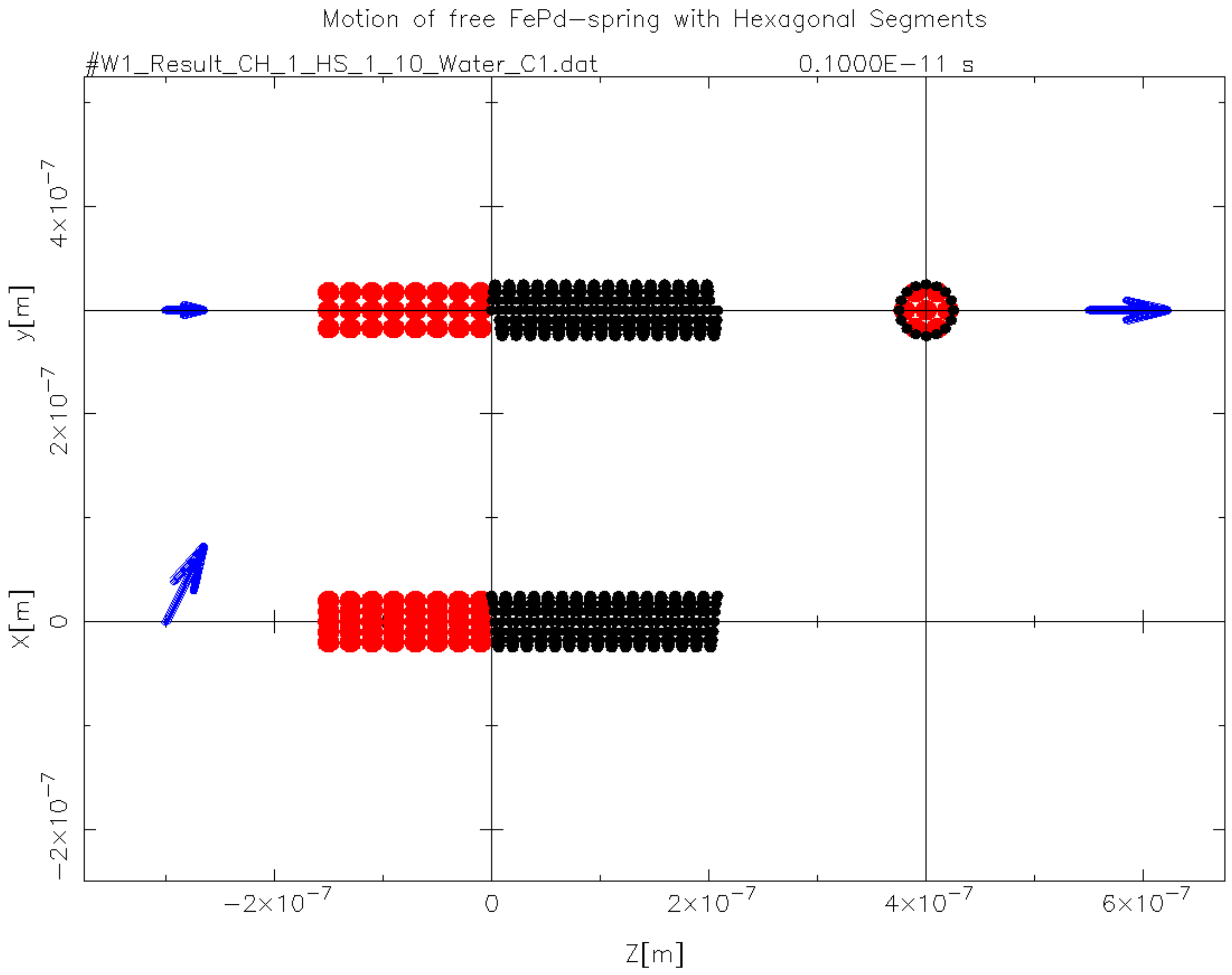
Fast nano-motions of FePd NRs under applied magnetic field on(solid curve in left graph) and off (dashed curve)

Taya et al (2017), J. Appl. Phys., **121**, 154302

Video: Molecular Dynamics model simulation of FePd NR under on-axis magnetic field

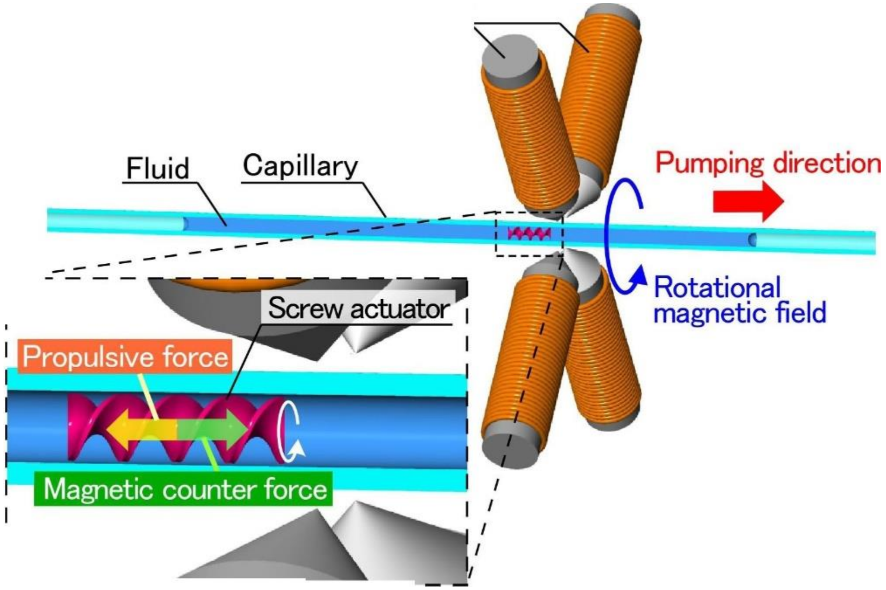


Video: Molecular dynamics model to simulate the nano-motions of FePd nanorobots under off-axis applied magnetic field



2D Helmholtz coil system for swimming of FePd nanorobots

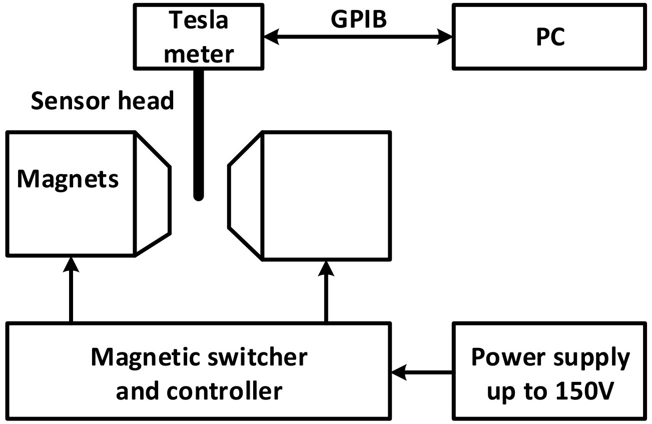
Use of lower frequency is better for more accurate control and also adequate for inducing cancer cell death

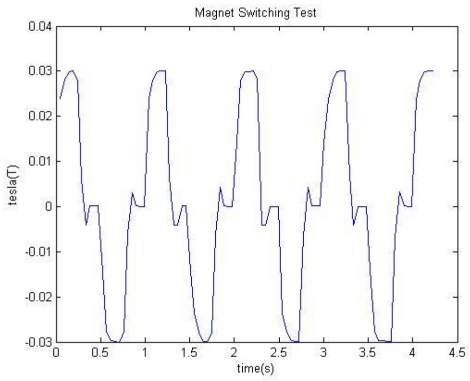


Conceptual diagram

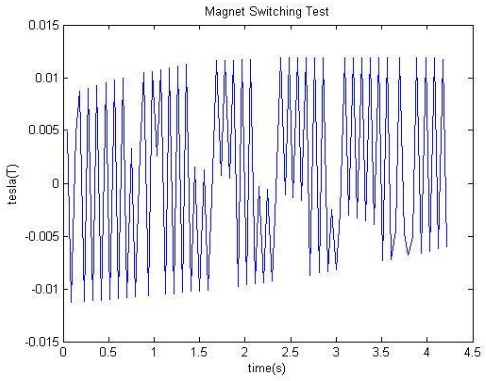
Kobayashi, K and Ikuta, K (2009)

Setup for testing





Response: 1 Hz



Response: 10 Hz

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UW collaborators:
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Graduate students: S. Morgan (Chem E), C. Chiew (ME)
Undergraduate students: T.Niiyama(ME), A. Hoffman(EE)

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Dr. S. Kawaguchi, Spring 8, Hyogo, Japan

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