A Magnetic Actuator-Based Platform for Functional Assessment of 3D Human Skeletal Muscle Bioengineered Tissues in Myotonic Dystrophy

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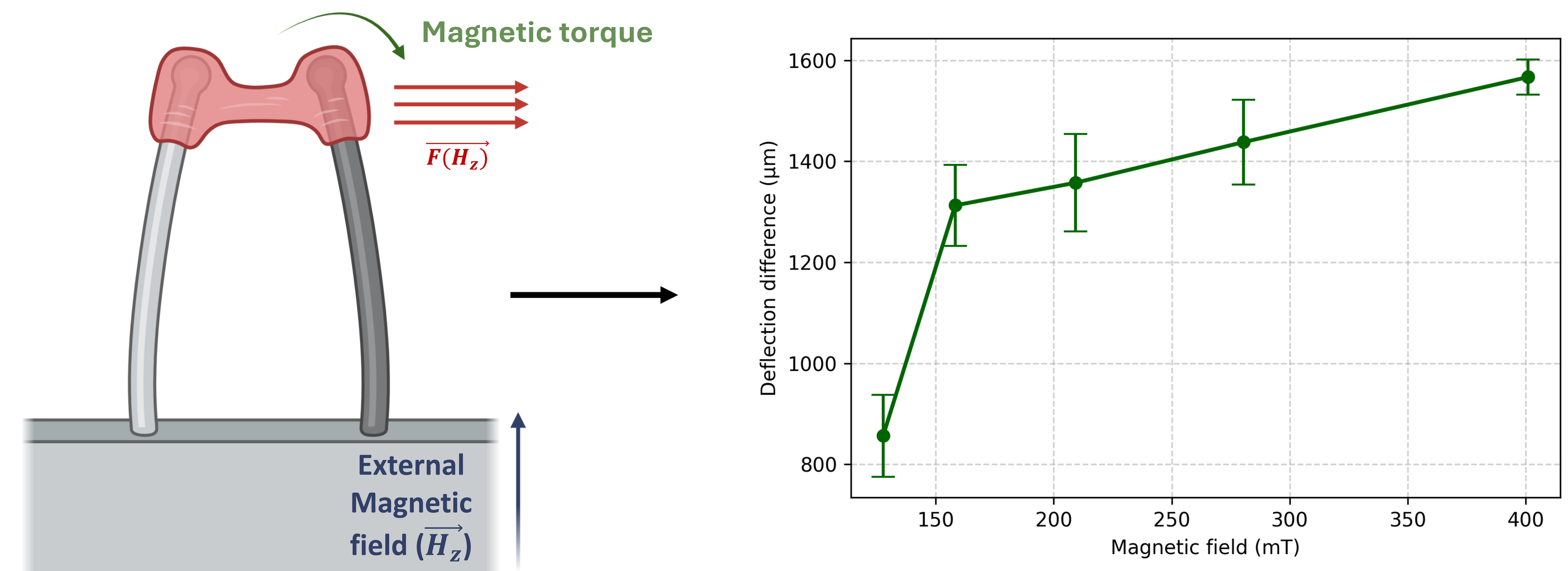
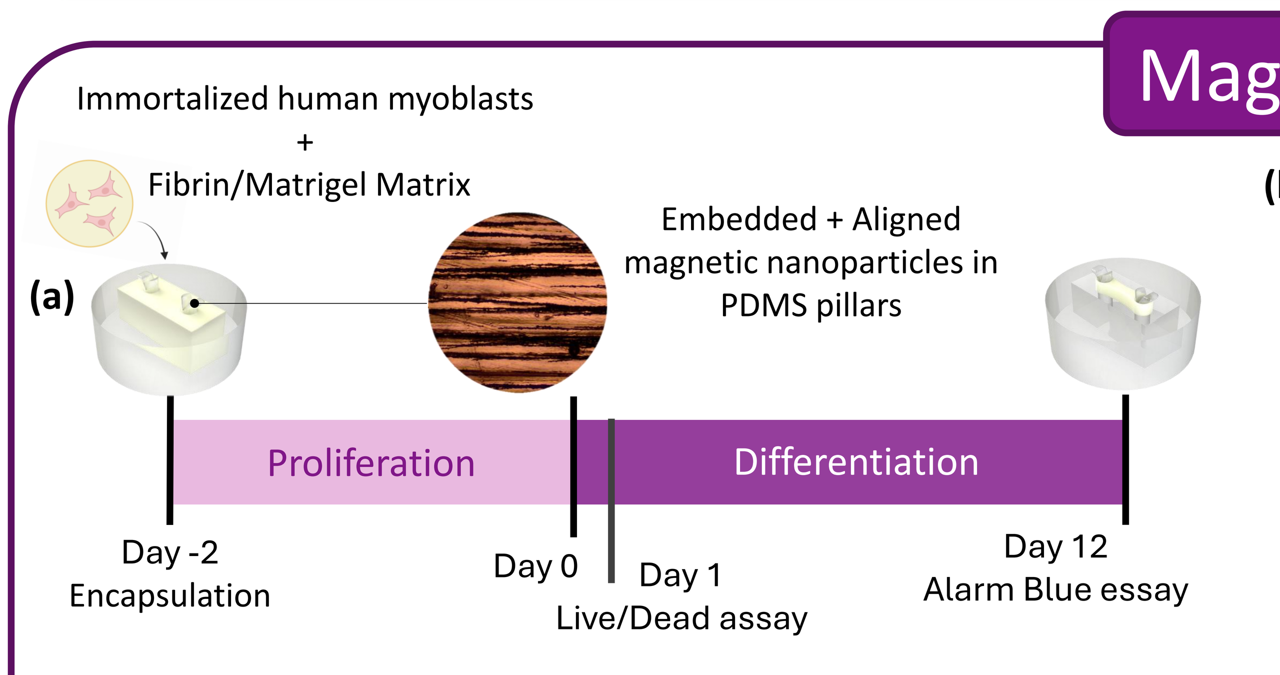
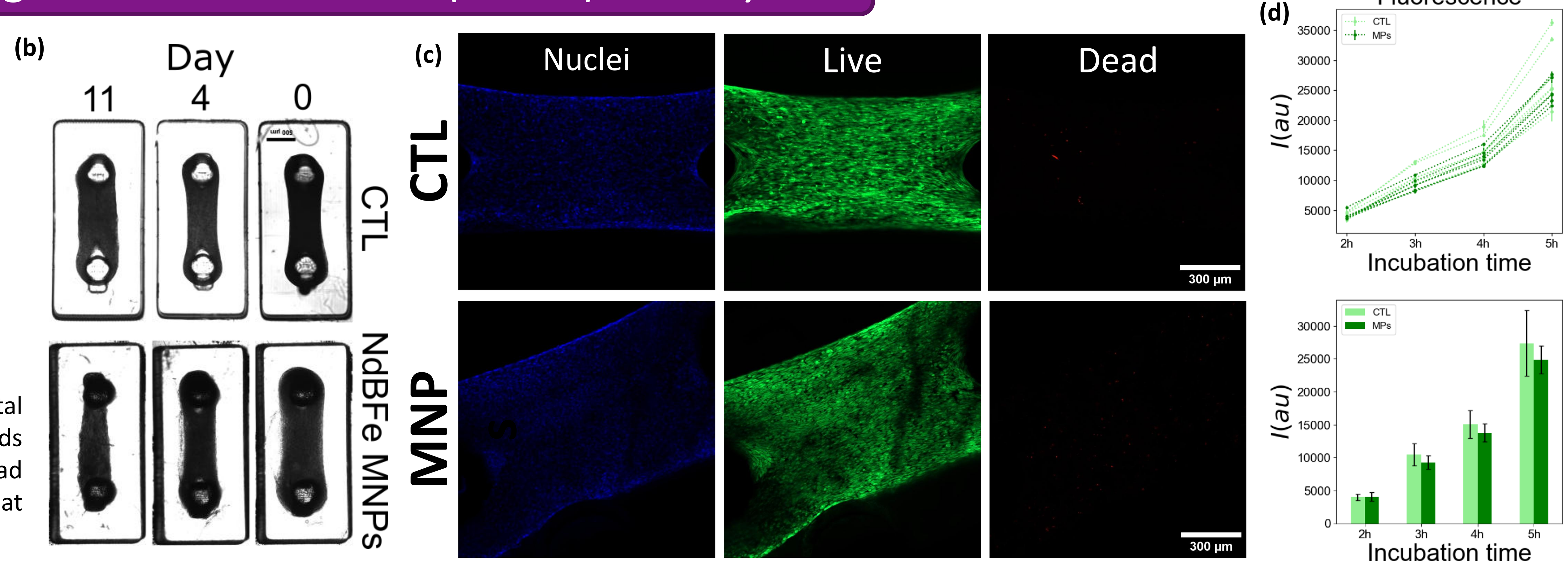
Background:

3D bioengineered tissues has emerged as a relevant approach to devellop more relevant biological models compared to traditional 2D cultures. It has previously been demonstrated that controlling the cellular microenvironment can enhance tissue morphogenesis, cell differentiation, and functionality. We aim to devellop magnetic actuator-based platforms that can reproduce DM1 phenotypes and induce percussive myopathy. To achieve this, we are designing chips with flexible pillars with magnetic nanoparticles to support 3D tissues and to generate this deflection, we are developing a magnetic actuation system based on electromagnets.



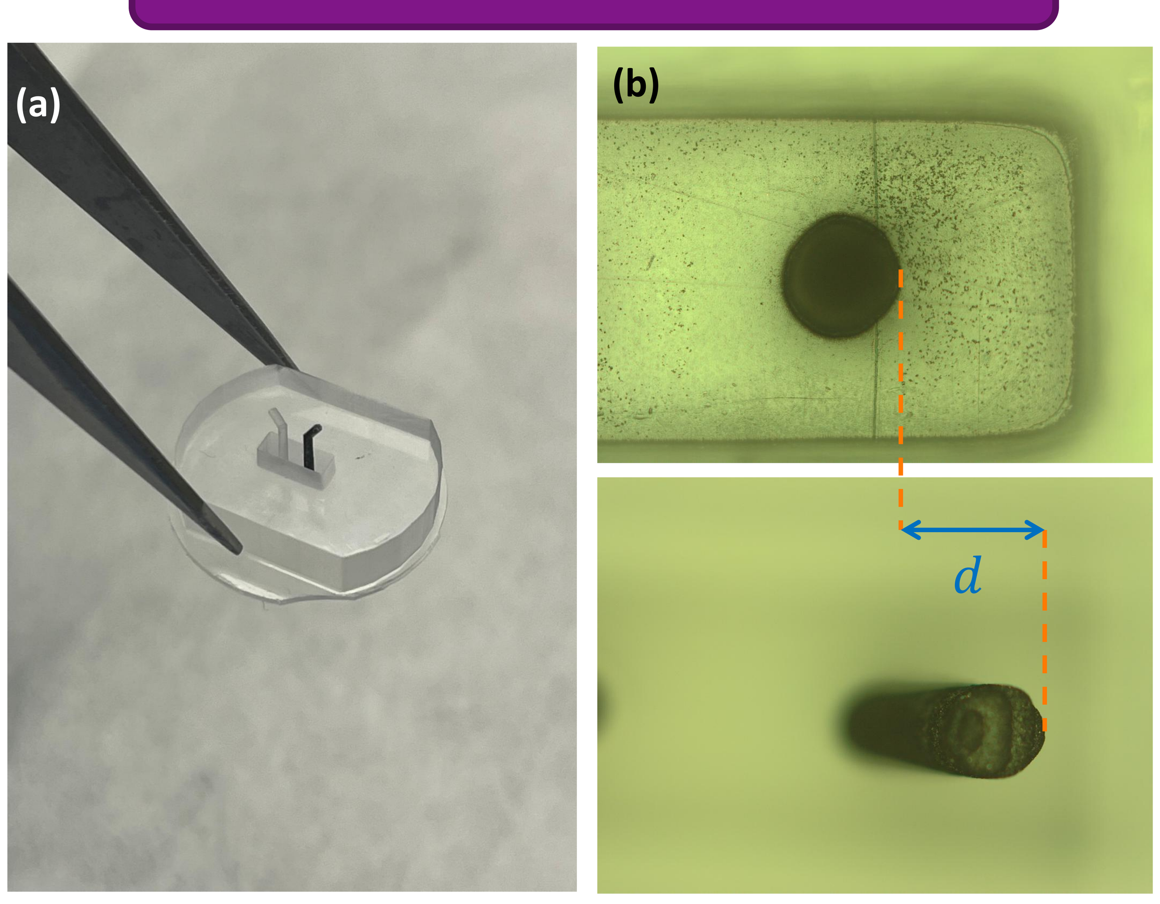
Magnetic NanoParticles (MNPs) toxicity test

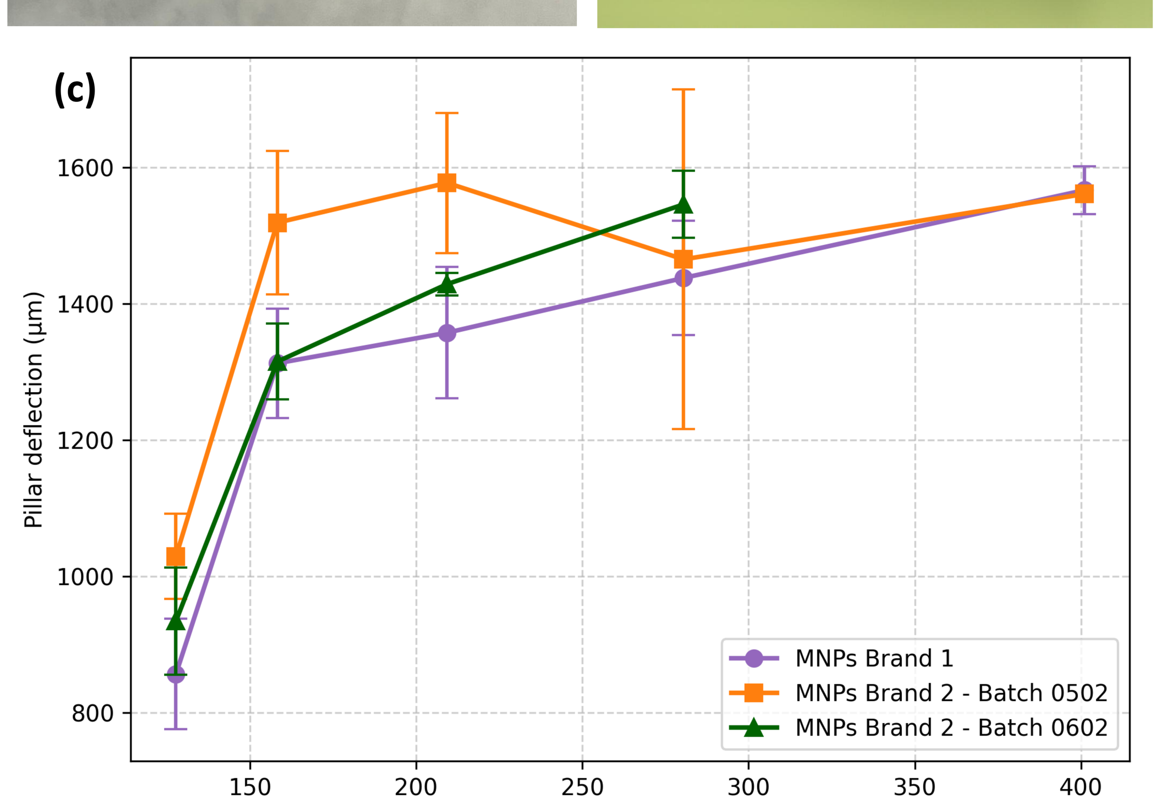




(a) Timeline of the experiment. (b) Brightfield images of the 3D skeletal muscle tissues. CTL in standard molds and NdBFe MNPs in casting molds which have embedded magnetic particles in the pillars. (c) Live/Dead assay of encapsulated immortalized myoblasts. (d) Alamar Blue assay at day 12 . $N_{CTL} = 6$, $N_{NdBFe\ MNPs} = 7$.

Deflection characterization





(a) Picture of a magnetic chips. (b) Reflective microscope images of the chips for deflection calculation. (c) Mean pillar deflection in function of magnetic field intensity. $N_{MNPs\text{-}Brand\ 1} = 8$, $N_{MNPs\text{-}Brand\ 1} = 5$, $N_{MNPs\text{-}Brand\ 1} = 5$

Geometry checking for tissues force calculation

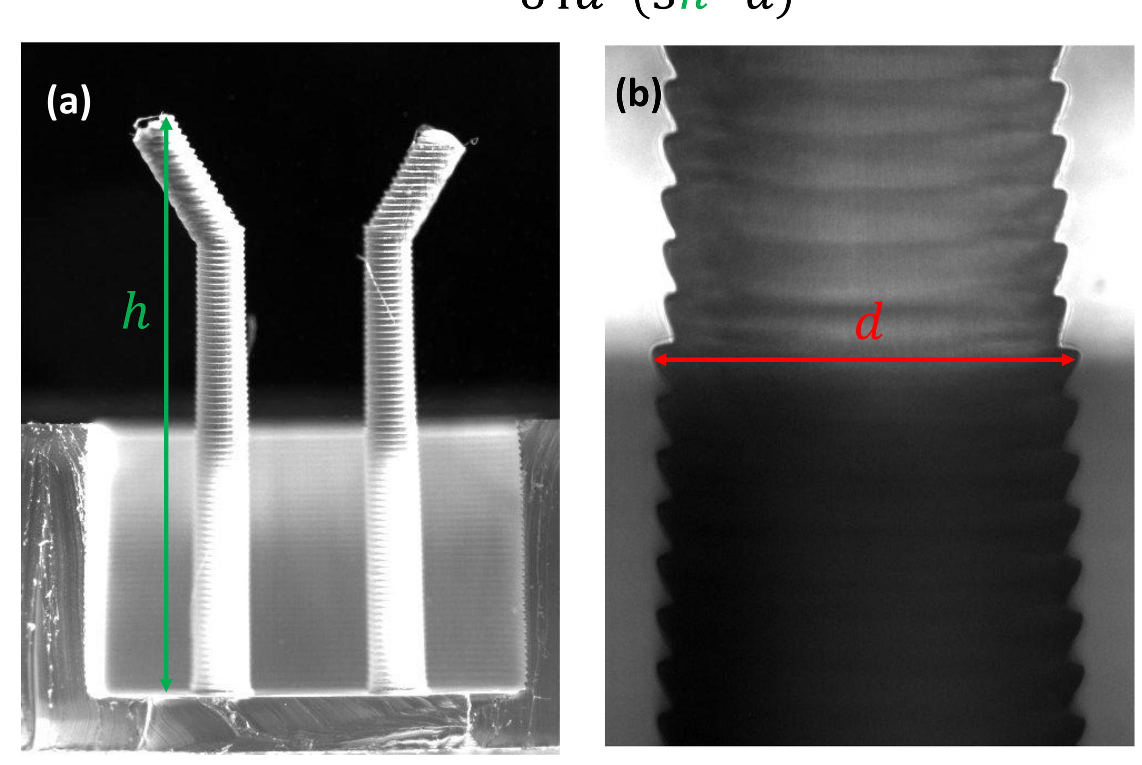
Applied force :

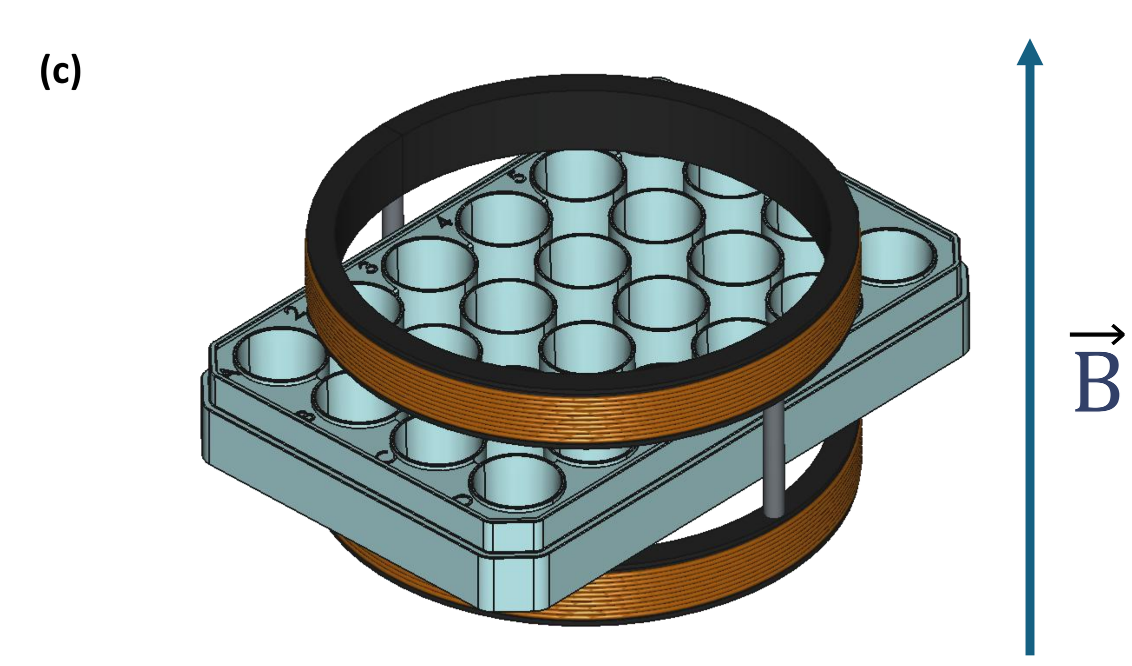
$$F = k\Delta x = \frac{6\pi E d^4}{64a^2(3h-a)}\Delta x(a)$$

Deflection mecanism : With :

$$\Delta x = k_1 \vec{B}$$
$$\vec{B} = k_2 I$$

E = Young modulus
a = tissue height position
I = Current





Chips geometry checking for muscle force calculation and for monitoring deflection mechanism (a) Microscope images of the chips for pillar height checking, N = 12. (b) Microscope images of the chips for pillar diameter checking, N = 12. (c) 3D schematic of a Helmotz coil system, which induce uniform magnetic field, for dynamic studies

Conclusions and future works

- Magnetic Nanoparticles do not present toxicity in our 3D human skeletal muscle model.
- We successfully fabricated magnetic pillars that can be deflected with different magnetic fields.
- By checking the geometry of the chips, we can calculate the force induce by the muscle contraction.
- Controlling the current through Helmotz coil system led us to control magnetic field intensity and so pillar deflection in order to monitor tissues stretching.
- Future work : We aim by using magnetic chips and magnetic platform to perform static and dynamic studies on 3D bioengineered tissues in order to increase muscle differentiation and maturation.

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