Research Article.

An Electromagnetically Actuated Double-Sided Cell-Stretching Device for Mechanobiology Research

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Abstract: Cellular response to mechanical stimuli is an integral part of cell homeostasis. The interaction of the extracellular matrix with the mechanical stress plays an important role in cytoskeleton organisation and cell alignment. Insights from the response can be utilised to develop cell culture methods that achieve predefined cell patterns, which are critical for tissue remodelling and cell therapy. We report the working principle, design, simulation and characterisation of a novel electromagnetic cell stretching platform based on the double-sided axial stretching approach. The device is capable of introducing a cyclic and static strain pattern on a cell culture. The platform was tested with fibroblasts. The experimental results are consistent with the previously reported cytoskeleton reorganisation and cell reorientation induced by strain. The orientation of the cells is highly influenced by external mechanical cues. Cells reorganise their cytoskeleton to avoid external strain and to maintain intact extracellular matrix arrangements.

Keywords: Biomedical Engineering, Cell Stretching, Mechanobiology.

1. Introduction

Cells in a functioning multicellular system are continuously exposed to various mechanical forces. The ability of the cells to recognise these mechanical stimuli and transform them into chemical responses is known as mechanotransduction.[1-3] It is well known that abnormalities in mechanotransduction signalling pathways affect the cell behaviour and tissue homeostasis, consequently leading to pathogenesis.[4,5]

Mechanical forces related to cyclic deformation of soft tissues are essential for the maintenance of various physiological conditions of organs such as heart, blood vessels and lungs.[6] The connective tissues of these organs contain a significant amount of fibroblastic cell types. The mechanotransduction mechanisms in fibroblasts are crucial to modulate tissue homeostasis.[7] Fibroblasts continually perceive external mechanical stimuli, which subsequently lead to the production and remodelling of extracellular matrix (ECM) components. For instance, numerous studies have reported that under cyclic or static strain, fibroblast cells synthesise the ECM protein.[8] Fibroblasts anchor their actin cytoskeleton with ECM by linkage proteins called integrins.
Integrins act as mechanosensors that sense the physical forces applied onto the cell surface. The ECM-integrin-cytoskeleton integration plays a vital role in the functional and structural adaptation of cell to mechanical cues.[9] These mechanical signals are then transmitted to cytoskeleton by the formation of ECM-actin cytoskeleton linkage. This complex system promotes the assembly of focal adhesion, thereby induces the reconstruction of actin cytoskeleton that is necessary for cell stiffening, gripping and adherence.

The cytoskeleton reorganisation exerts adaptive response in the cell under mechanical stimuli.[10] This process enables cells to regulate the formation of new lamellipodia and to adjust their adhesion to resist physical deformation.[11,12] Thus, cell displacement has been observed for different amplitudes, types and directions of mechanical strain. For instance, cyclic stretching at high frequency aligns the cells perpendicularly to the stretching direction.[13] In contrast, static stretching induces cells to align parallel to the stretching direction.[14] Hence, better understanding of the cellular response of the fibroblast culture upon mechanical stimuli provides insight into examining how mechanical factors alter the physiology and behaviour of the fibroblasts. Thus, various techniques have been developed to introduce mechanical stimuli to the cellular microenvironment. Considering the complex *in-vivo* microenvironment of the cells, the majority of the cell stretching approaches has been developed as *in-vitro* platforms.[15-18]

Most cell stretching approaches include the use of tweezers or micropipettes to induce the mechanical stimuli.[19-22] However, commercial cell stretching platforms such as Flexcell (Flexcell International Corporation), Strex Systems for cell Stretching (STREX Inc.) and ElectroForce have been recently available.[23-25] Moreover, various customised stretching platforms have been reported in the last decade. The majority of these platforms utilises either electromagnetic, pneumatic, piezoelectric or optical actuators to deform an elastic membrane with cell cultured on it. For instance, Shimizu *et al.*[26-29] developed a microfluidic device with serially connected balloons. The authors utilised a positive pressure to inflate the balloons and directly induce strain onto the cells. Similarly, Kamotani *et al.*[30] designed a microfluidic device with a deformable membrane at the bottom and an array of piezo electrically actuated pins, which were placed below a microwell plate. Each microwell was independently actuated by the pin, which deforms the micro-well membrane with cells cultured on it. Furthermore, Huang *et al.*[31] designed a cell stretching platform with

![Fig. 1 Schematic illustration of the working principle: (a) Steps to obtain static strain; (b) ON state for cyclic stretching condition; (c) Actual cyclic cell stretching platform and the PDMS device.](image-url)
indenter and utilised a servomotor to introduce strain onto the deformable membrane. In another study, Sraj et al. [Bibliography] designed a microfluidic channel and utilised a single-mode laser (830 nm, 200 mW) to trap and deform the cells.

Besides the above mentioned actuation approaches, electrothermal, electrostatic and dielectrophoretic actuations have recently been adapted to introduce mechanical force onto the cells.[34-36] All cell stretching approaches reported in the literature have their specific advantages. However, very few platforms provide the main features of a robust cell stretching tool such as standardised strain pattern, a wide range of imaging options and high-throughput capability. This paper presents a novel cell stretching platform with a double-sided uniaxial magnetically actuated stretching approach to introduce both homogeneous cyclic or static strain onto the cell culture. The cell stretching platform provides homogenous and a wide range of strain values, cyclic and static stretching modes, compatibility with general clinical tools and imaging options. Thus, our system is suitable for long-term cell stretching studies. The present paper discusses in details the modelling, fabrication and characterisation of the cell stretching platform and provides preliminary observation of the response of fibroblasts under cyclic, static stretching and non-stretching conditions.

2. Materials and Methods

2.1 Device design and working principle

Figure 1 illustrates the schematic of the stretching platform. The platform consists of the PDMS device with embedded permanent magnets, holding clip for the static strain condition and a mounting stage with electromagnets for cyclic strain condition. The PDMS device has two NdFeB disc magnet (15mm diameter and 2mm thickness) embedded in the front and back walls, which are 4 mm thick and placed 8 mm apart from each other.

The permanent magnets are positioned along the actuation axis, such that the north poles of both magnets are facing each other to induce the repulsive force and to deform the front and back walls of the PDMS device. This active magnetic repulsion was utilised to introduce the static strain onto the deformable membrane. The custom made 3D printed holding clip was used to overcome the active magnetic repulsive force and to maintain the PDMS device in a predefined position. The 200-µm thick deformable membrane was then bonded at the bottom of the device after oxygen plasma treatment. Removing the holding clip results in the desired static strain on cells cultured on the deformable membrane, Fig. 1a. This simple but effective strategy allows for achieving a wide range of predefined strain onto the deformable membrane, simply by controlling the initial and final position of the holding clip during the bonding process of the deformable membrane and the PDMS body.

For cyclic strain, two axially aligned electromagnet (JL Magnet) controlled by a DC power supply (MK Power) was used simultaneously to externally actuate the magnets embedded in the PDMS device. The mounting platform was 3D printed to introduce the necessary constraint onto the PDMS device and to provide axial alignment for the permanent magnets (PMs) and electromagnets (EMs). Upon actuation, the magnetic forces generated by the EMs and the PMs deform the front and the back wall of the PDMS device. This force is further transferred to the deformable membrane, which in turn induces a well-defined strain onto the cells cultured there, Fig.1b. Fig. 1c shows the actual developed cell stretching device capable of inducing homogeneous cyclic strain onto cells cultured on a deformable membrane for studying the cell behaviour.

2.2 Modelling and fabrication

Finite element analysis (FEA) model of the PDMS device was formulated in COMSOL Multiphysics 5.2 (COMSOL, Inc.) to understand and to optimise the stretching device. We modified and updated the previously reported FEA model to achieve the necessary parametric optimisation of the device.[37] The grade of the permanent magnets (PMs) was the key optimisation parameter,
which was taken under consideration to manipulate the active magnetic repulsive force to obtain optimised static strain condition for the PDMS device without physically damaging the device. To start with, a reference FEA model was formulated in COMSOL to understand the magnetic field requirement. The two PMs were defined at the axial distance of 8 mm and the diameter and thickness of the PMs were defined as 15 mm and 2 mm, respectively. The NdFeB material was assigned for the adapted geometry and the PMs were modelled using Maxwell-Amperes law.

\[
\nabla \times \mathbf{H} = \mathbf{J}, \quad \mathbf{B} = \nabla \times \mathbf{A}, \quad \mathbf{J} = \sigma \mathbf{E} \mathbf{B}
\]

(1)

where \( \mathbf{B} \) is magnetic flux density in T, \( \mathbf{E} \) is an electric field in V/m, \( \mathbf{A} \) is a magnetic vector and \( \mathbf{H} \) is the magnetic field strength in A/m.

Furthermore, the optimisation was carried out by varying one parameter while maintaining the other parameters constant. Maintaining the geometrical parameters constant, the magnetic remanence (\( Br \)) of the PMs were varied over the range of 0.05 T to 2 T with the step of 0.05 T using parametric sweep function to model the variation of the NdFeB magnet grade. The inset in Fig. 2 shows the results for the FEA model with an input magnetic remanence (\( Br \)) of 1.2 T. In the next step, to measure the corresponding deformation, the FEA model geometry of the PDMS device was built with the front and back wall thickness of 4 mm, the side wall thickness of 2 mm, deformable membrane thickness of 0.2 mm and axially aligned PMs with 15 mm diameter and 2 mm thickness embedded into the front and back wall. The total volume of the geometry formulated in COMSOL was 30x25x12 mm³.

Next, the study of structural mechanics and the magnetic force was coupled in COMSOL to estimate the outward force acting on the front and back walls for various values of magnetic remanence. The appropriate material properties (750 kPa Young’s modulus and 0.49 Poisson’s ratio for 10:1 PDMS-cross linker mixture) were selected to match the real device. All four corners of the device were fixed to maintain the necessary boundary conditions. Figure 2 shows the average displacement versus the magnetic remanence of the PMs along the actuation axis. The parametric optimisation suggested that an 1.2-T magnetic remanence (Grade N35) yields a magnetic flux of 103 mT at the surface of the PM and generated an average displacement of 0.788 mm between the

Fig. 2 Simulated axial displacement versus magnetic remanence. (Inset: FEA results with \( Br=1.2 \) T, selected NdFeB grade N35 magnet, PDMS device with static strain condition).
two embedded PMs along the actuation axis. Thus, for the static condition, the magnetic repulsion facilitated a maximum static strain of 9.85% onto the membrane. Considering the experimental requirement, a NdFeB magnet of grade N35 was selected for the cell stretching system.

The next step was the fabrication of the optimised design. The fabrication process involved the fabrication of a master mould, mounting platform, and PDMS device. To start with, the aluminium master mould was designed and fabricated to replicate the PDMS device with the optimised geometry. The mounting platform and holding clip was designed in SolidWorks 2013 to achieve the necessary constrain and axial alignments. Finally, the optimised mounting platform and holding clip design was 3D printed using Eden 260V printer (Stratasys Ltd.). In the final step, the PDMS device and the deformable 200 µm membrane was fabricated.

![Fig. 3 Magnetic force over the voltage range of 1-30V (Inset: Experimental setup and FEA model for PDMS device).](image)

For the fabrication of the PDMS device, 20 g of degassed mixture of PDMS and cross linker (Sylgard 184 elastomer kit, Dow Corning, USA) was prepared with a volume ratio of 20:1. The mixture was poured into the master mould and was again degassed for 15 minutes to remove any remaining air bubbles. The mould was then carefully closed to cure the PDMS mixture for 2 hrs at 80°C in a vacuum oven. Once cured, the mould was carefully opened and the PMs were placed into the created cavities such that the north pole of both magnets facing each other to achieve active magnetic repulsion condition. To fix the magnets in position, a small amount of PDMS-cross linker mixture (10:1 volume ratio) was coated onto the PMs. The mould was then carefully closed and cured for another 30 minutes at 80°C in a vacuum oven to ensure the proper placement of the PMs. The cured PDMS device was then inspected and carefully removed from the mould. Finally, the PDMS device was cleaned with isopropanol and DI water. In the next step, a degassed PDMS-cross linker mixture with volume ratio of 10:1 was spin coated at 4000 rpm for two minutes and cured at 80°C for two hours to achieve the 0.2-mm thick deformable membrane. The cured membrane was inspected to confirm the uniform thickness and then cleaned with isopropanol and DI water. In the last step, the PDMS device was plasma bonded with the deformable membrane and cured for one hour at 80°C.
2.3 Cell culture

Fibroblast cells were cultured in DMEM/F12 (Gibco, Thermo Fisher Scientific) medium with 10% FBS and 1% penicillin at 37°C and 5% CO₂ in a standard incubator. To sterilise the device, the device was treated with 80% ethanol and washed three times with 1X PBS followed by UV exposure for 20 minutes. Before seeding the cells, the device was treated with fresh media and incubated for one hour under standard condition (37°C and 5% CO₂) to further ensure its biocompatibility. For seeding the device, 80% confluence was reached and the cells were harvested at the optimised density of 7.5x10³ Cells/250 μl. In order to achieve an optimal adherence and growth of the cells onto the membrane, the device was incubated at 37°C and 5% CO₂ for 24 hours before the mechanical strain was applied.

2.4 Application of strain on fibroblasts

Two stretching modes were tested: cyclic and static axial stretching and compared to the non-stretching (control) condition for this study. Cyclic stretching was applied to cells with 1.4% strain at 0.01 Hz and 50% duty cycle. Under the static condition, 1.4% strain was applied to the fibroblast cell culture. The strain was introduced onto the cells over 5 different time instances (0.5 hr, 1 hr, 2 hr, 3 hr and 4 hr) for a maximum of 4 hours. Cell characteristics such as area, aspect ratio and orientation was observed after stretching and compared to the control. For the analysis, the central region of the membrane was imaged with an inverted microscope (Nikon Eclipse Ts2). Biological triplicates were performed.

2.5 Cell fixing, immunofluorescence staining and imaging

The stretched cells were fixed after stretching 4% PFA for 15 minutes followed by the three 10-minute washes with PBS. The deformable membranes with fixed cells were stored in the PBS solution at 4°C. For actin and nuclei observation, cells were incubated with ActinGreen™ 488 and NucBlue™ ReadyProbe™ Reagent (ThermoFisher Scientific) for 30 minutes followed by the three post-staining washes with PBS. Images of the cell nuclei and actin fibres were finally obtained with a fluorescent microscope (Olympus DX50) using 10X and 20X magnification.

2.6 Image analysis

For the image analysis, three separate locations within the central region i.e. the region of interests (ROI) with homogenous strain, were captured. Each image was enhanced using post processing with Image J (NIH), which mainly included FFT bandpass filtering, sharpening, enhancing image contrast and thresholding. For quantification, the captured cells were analysed to estimate the averaged area, aspect ratio and orientation of the cells in ROI at each time instance.

3. Results and Discussion

3.1 Force calculation

For estimating the experimental magnetic force, we utilised a similar approach as reported in our previous work.[38] The optimised FEA model of the PDMS device was utilised to obtain the spring constant for the experimental condition. Considering the stretching condition, the magnetic actuation is modelled in COMSOL by introducing an outward force onto the PMs to deform the front and back walls of the PDMS device. The force was varied over the range of 0.5 N to 1 N in steps of 0.5 N to observe the corresponding displacement of the PMs. Considering the material properties, we assumed the Hooke’s law to obtain the spring constant k for this study:

\[
F = -k \cdot x
\]

where, k is the spring constant in N/mm, F is the force in N and x in the displacement in mm.
The next step was to experimentally obtain the displacement of the PMs over the applied voltage. Both EMs were simultaneously actuated by supplying the voltage ranging from 1 V to 30 V. The corresponding displacement of the marked points on the PDMS device wall along the actuation axis was recorded for each step using a digital camera (EO Edmund Optics). Furthermore, our particle tracking algorithm based on digital image correlation and Matlab image processing toolbox was utilised to detect and measure the displacement of the randomly marked points.[38] Finally, the obtained average displacement was used to calculate the force using the spring constant of 2.41N/mm determined by the FEA simulation.

We modified and updated our previously reported FEA model to calculate the magnetic force between PM and EM[37] and to validate the experimental data. We considered the symmetric nature of the system and obtained the magnetic force at the PM surface along the actuation axis over the voltage range of 1V - 30V.[37] The simulation results were verified with the experimental data, Fig. 3. As expected, a linear force-voltage relationship can be clearly observed from Figure 3. The simulation agrees well with the experimental data. The results provide an acceptable error variance of 9.42% over the range of 9 V to 30 V between experimental and simulation data.

3.2 Strain calculation

Characterisation of strain applied to the deformable membrane was observed using both experiments and simulation. For measuring the strain experimentally, the membrane deformation was recorded with a digital camera (EO Edmund) over the voltage range of 1 V to 30 V. The particle detection and displacement measurement algorithm based on digital image correlation and Matlab image processing toolbox was further utilised to calculate the offset displacement of the marked points. For reliable experimental data, the membrane of each recorded image was divided into the 2x5 regions. A minimum of three marked samples from central region (M1, M3, M2, M3) was observed. Finally, to warrant the repeatability of the results, three experimentally obtained results were averaged to represent the displacement of the region. The inset of Fig. 4 depicts the experimental setup and example of the particle detection and tracking algorithm result.

For cross validating the experimental data, we utilised a reference FEA model. The magnetic force obtained from the force calculation (Section 3.1) over the voltage range of 1-30 V was used as the input for the FEA model. The central region of the membrane was considered as the region of interest (ROI).

![Fig. 4](image_url) Strain on the deformable membrane over the voltage range of 1-30V. (Inset: Experimental arrangement, the membrane in ON and OFF state, an example for the particle detection and tracking.)

![Fig. 5](image_url) Strain pattern on the membrane with a selected input of 27 V: (a) Experimental results; (b) Simulation results.
An average strain across the membrane was obtained for the operating voltage range i.e. 1 V to 30 V. Figure 2 compares the average strain over the ROI from both simulation and experiments. The experimental and simulation results agree well. An average error variance of 7.89% was observed over the voltage range of 9 V to 30 V. Based on the strain characterisation, we selected an input voltage of 27 V for both actuators, which provided an average homogeneous cyclic strain of 1.38±0.021% over the central region of the membrane.

For understanding of the membrane deformation and strain pattern with the selected input voltage of 27 V, we utilised the same experimental platform and obtained the image sequence for the membrane deformation. The images were analysed using the existing particle detection and tracking algorithm to obtain the strain pattern over the 2x5 region matrix. A minimum of three marked points from each subregion was evaluated to obtain reliable results. Finally, the average value was utilised to represent the strain over each predefined subregion. Furthermore, three experiments were conducted for each set of data. Figure 5 shows the obtained strain deformation pattern from the experiment (a) and the simulation (b). The expected, homogenous strain pattern over the central region of the membrane is evident from the results. Experiment and simulation agree well and provide an average strain of 1.38±0.021% and 1.49%, respectively.

The results provide a better understanding of the membrane deformation and confirm the homogenous strain pattern for the subsequent cell stretching experiments. Figure 5 clearly shows that we could expect a homogenous strain pattern that in the central region of the membrane. Thus, it can be assumed that cells located in this region will experience an equal amount of the strain.

### 3.3 Cell area and aspect ratio

Figure 6 shows the obtained averaged cell area and aspect ratio for each predefined time point. The results show the gradual decrease in the cell area for cyclic stretching as a result of cell displacement and aggregation. The cell aspect ratio for the over stretching duration for a maximum of 4 hours also decreased which was in line with the previously reported observations.[39-42] The morphological observation suggests that both cyclic and static stretching led to significant changes in fibroblast adherence. However, we focused more on the cyclic stretching as native tissues within the body are more exposed to a cyclic strain rather than static strain. Under cyclic strain, mechanotransduction and intercellular physiology involving cytoskeletal elements and adhesion molecules drive the morphogenetic process of cells.[43] The cells respond adaptively against external stress transmission and reorganize their cytoskeleton integrity by reconstructing the actin stress fibres.[44,45] We also observed that cyclic stretching of the fibroblast cell culture triggered the formation stress fibres, and over time cells enhanced their cell-cell connection and formed cell clusters.

The reorganization of actin stress fibres seems to promote cell adhesion dynamic and to change cell morphology.[46] Furthermore, it was interesting to note that after two hours of cyclic stretching, significant formation of cell clusters was observed. The stronger cell connections and the formation of cell clusters explain how individual cell sense and transmit the physical forces to neighbouring cell by binding of adhesion molecules to expand cell-cell cohesion.[47]

Furthermore, it is interesting to address the question why stretching induces cell rearrangement and adhesion of the cells into clusters. Generally, cells on a substrate surface are dynamic in nature and are constantly reorganizing their actin filament network to retract and extend protrusions (the formation of lamellipodia and filopodia). At the cellular level, changes in the surface topology lead to the underlying processes involved in the maintenance of mechanical homeostasis.[48] The stress fibres are projecting tension-bearing bundles of actin filaments, which act as a non-muscle sarcomeres.[49] Cyclic stretching seems to trigger actin fibres to realign and to establish stronger adhesive cell-cell connections to resist the strain.[50] Thus, we hypothesise that actin organization under stress is critical for promoting cell adhesion dynamics to form cell aggregates and to withstand the applied strain.
In contrast, cell area and aspect ratio for the static stretching did not change significantly. The cells did not spread and promoted the formation of actin stress fibres under static strain as compared with cyclic strain, Fig. 6. Additionally, no significant cell clusters were observed in static strain mode. This discrepancy further suggests that prolonged static stretching imposes different effect on the regulation of ECM and adhesion proteins. Previous investigations of the effect of static strains alone on ECM synthesis showed the degradation of ECM and adhesion molecules.[51] In a recent study, Cui et al. showed that cytoskeleton organization differs for cyclic and static and indicated that cyclic stretching promote actin fibre formation and cell spreading.[52] Moreover, as expected for non-stretching (control) condition, the actin stress fibres were randomly distributed and no significant changes in cell area and aspect ratio was observed.

3.4 Cell orientation

![Fig. 6](image)

**Fig. 6** Analysis results of cell area and aspect ratio for cyclic, static and no stretch conditions over the predefined time points (Inset: fluorescent images of the fibroblast cells with 20x objective for corresponding time points with 50-µm scale bar).
The orientation range of 0°-180° was considered for the cell orientation analysis, which was further divided into six equal angular regions in 30° increments. For quantitative analysis of the cell orientation, the 0° to 180° was set along the stretching direction in anti-clockwise direction and total number of 900 samples from the three images of the ROI were analysed using ImageJ for each time instance. Figure 7 shows the distribution of the cell orientation for each time instance. It was interesting to observe distinct cell orientation trend for cyclic and static stretching modes. Under cyclic stretching mode, the cell orientation showed two distinct peaks over 30-60° and 120-150° range. The prominent cell orientation was observed after 1 hour of cyclic stretching. Whereas, under the static stretching condition two distinct peaks were observed over 0-30° and 150-180° range. Furthermore, it was interesting to observe that the prominence of the cell orientation under the static stretching.

**Fig. 7** Cell orientation analysis results for cyclic stretching (1.4%·0.01Hz,50% Duty Cycle), static stretching (1.4%) and no stretching condition at 0 hr, 0.5 hrs, 1 hrs, 2 hrs, 3 hrs and 4 hrs. (Inset: fluorescent images of the fibroblast cells with 10x objective for 0 hr (a-c), 0.5 hrs (d-f), 1 hrs (g-i), 2 hrs (j-l), 3 hrs (m-n) and 4 hrs (p-r) with 100-µm scale bar).
stretching conditions increased over the time. From this observation, we can conclude that most of the cells are oriented approximately either at 45° or 135° under cyclic stretching and at 15° or 165° under static stretching condition (Fig. 7 inset depicted by arrows).

Furthermore, as expected for the non-stretching condition, random distribution of the cell orientation was observed. Two distinct and almost symmetric peaks were observed for both cyclic and static stretching modes. This observation provides important evidence on the ability of the fibroblast cells to recognize and respond not only to the applied strain but also to the strain direction.[53-55] We found that fibroblasts reorient in an optimal angle to avoid the strain. Moreover, actin stress fibres arrangement is clearly involved in the realignment of the cells under strain. Our observation agrees with previous studies which reported that cells reorient and align themselves due to external strain.[53,56-61]

The adhesion dynamic of cells are guided by cytoskeleton rearrangement and was believed to be responsible for the cell alignment.[50,54] The cell–ECM connections are established by association between actin stress fibres and the focal adhesion which endows cells to form stronger ECM connections and cell-cell adhesion.[62,63] The focal adhesion is responsible for reorienting cells to a direction where cells can maintain their stability. [54] In line with this hypothesis, we also observed a cytoskeleton organisation and a distinct cell orientation under both cyclic and static stretching conditions. In contrast, the non-stretching (control) conditions led to random distribution of the cell orientation.

5. Conclusions

In summary, we developed a simple yet effective cell stretching platform capable of introducing homogeneous cyclic and static strain onto the cell culture. The characterisation of the developed platform provides a clear understanding of the device function. Furthermore, effectiveness of the developed platform was tested with stretching assays of fibroblasts. Our preliminary analysis suggested that the orientation of the cells is highly influenced by external mechanical cues. The cell aggregation observed in the cyclic stretching mode suggests that the cells reorganise their cytoskeleton to avoid external strain and to maintain intact extracellular matrix arrangements. The developed cell stretching platform may serve as a tool to investigate the cell behaviour for a wide range of strain with cyclic or static stretching conditions. Considering these preliminary results, the platform may facilitate the active manipulation of the fibroblasts to achieve the desired cell arrangements. This alternative cell culture method will have a broad range of applications in the field of tissue remodelling and regenerative medicine. Furthermore, it is also important to note that cells can be harvested after stretching using general clinical tools to perform standard biology analysis which could be critical for clinical diagnosis and subsequent therapeutic screening.

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