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Imaging of live cells during application of mechanical stress

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Many cells in the human body are exposed to mechanical stress. The stress triggers a response in mechanosensitive ion channels (e.g. Piezo1 [1] and TRP-channels [2]), which are embedded in the cell walls. Mechanosensitive ion channels are correlated to diseases such as deafness [2], osteoporosis [3] and heart failure [4]. Therefore, it is important to examine these channels and their reaction to stress in detail. The ion channels can be tagged for example with GFP (green fluorescent protein) and thus be studied using fluorescence microscopy. Another possibility is to use ion indicators like Fluo-4 (for calcium), to study the ion influx into living cells during experiments.
For this purpose, a device was developed at the Institute of Medical Biotechnology (FAU), the *IsoStretcher* (see fig. 1A), which applies isotropic stretch to a PDMS membrane [5]. Adherent cells (such as HEK cells) can be cultivated on this membrane, will stick to it and can thus be stretched. The stretching of non-adherent cells (such as cardiomyocytes) is possible through embedding the cells in a hydrogel, which will stick to the PDMS membrane and transmit the stretch to the cells [6].
The PDMS chamber (see fig. 1B) gets fixed on the six pins of the *IsoStretcher*, which are driven apart radially by a stepper motor. The device can be operated using a LabView User-Interface, which communicates with an Arduino and provides two different work modes, a live mode and a continuous mode.
The *IsoStretcher* was implemented in the modular bioreactor system of the company Ospin (see fig. 1D) and can therefore be part of a custom-made bioreactor.
In order to have visual control over the sample in the device, different optical solutions were added. There is a compact fluorescence microscope as well as a bright field and phase contrast microscope. They had to be custom-built in order to fit the confined space available in the bioreactor (see fig. 1E) and also provide a sufficient image quality to examine biological samples.

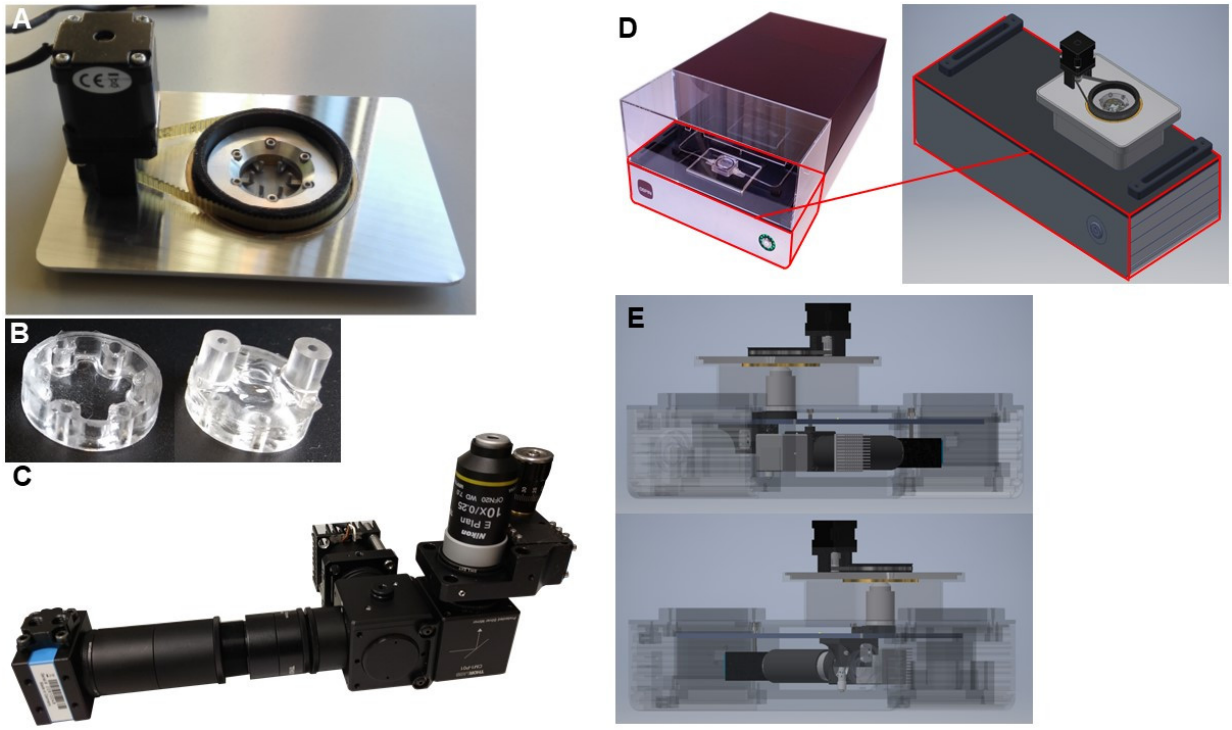

Fig. 1: **A** is showing the *IsoStretcher*, the motor on the left drives the device via a v-belt, which is connected to a belt wheel. The two different PDMS chamber designs (open chamber and chamber with a lid and tubing connections) are shown in **B**. A preliminary design of the fluorescence microscope is depicted in **C**. Ospin's bioreactor is shown in **D** (https://ospin.de/bioreactorplatform-5/), including the CAD drawing of the front part, carrying the *IsoStretcher*. **E** shows the implementation of the stretching device and the fluorescence microscope in the bioreactor as a CAD drawing (for better visibility the reactor and the platform holding the *IsoStretcher* are transparent).

References (Arial, 10pt)

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