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# The design of a rotating bioreactor for use in multi-sample loading regimes

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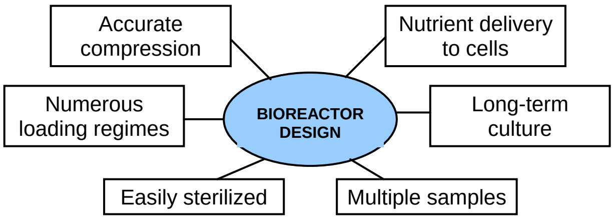
**INTRODUCTION:** Mechanical forces, spatial environment and biochemical stimuli influence the differentiation of mesenchymal stem cells (MSCs) *in vivo*[1]. These types of stimuli can be applied *in vitro* to MSCs whilst they are incorporated in a 3D scaffold, which can then be placed in a bioreactor. We have designed a novel bioreactor which will enable the application of numerous loading regimes to multiple samples.

**METHODS**:




**RESULTS:** Nutrient delivery and long-term culture: To achieve this the bioreactor was designed to hold approximately 700mls of culture media and was fitted with a circular stand to enable the bioreactor to be horizontally rotated at 5 RPM for up to 4 weeks, Figure 1A. Multiple samples: To compress multiple samples simultaneously a flexible holder was designed out of silicone rubber, Figure 1B. Sterilisation: The materials were chosen to enable the bioreactor to be autoclaved. The main body of the bioreactor is made out of glass and the lid is made out of stainless steel. Application of loading regimes: A loading rig was designed, Figure 2, and Labview software was used to enable the application of varying ranges of compressive displacement ranging from 1 – 20% strain when applied to a 4mm height scaffold (40 - 800µm) with varying frequencies and cycle numbers. Accurate compression of scaffolds: The original start position prior to compression was determined over 60 minutes. It showed that pre-conditioning the stepper motor for 30 minutes prior to use reduces the variability, Figure 3.

**DISCUSSION & CONCLUSIONS:** Most of the design objectives have been achieved. The completed bioreactor is capable of rotating whilst remaining sterile and allows the application of compression loading with various regimes to numerous samples. Initial displacement measurements suggest that the stepper motor has

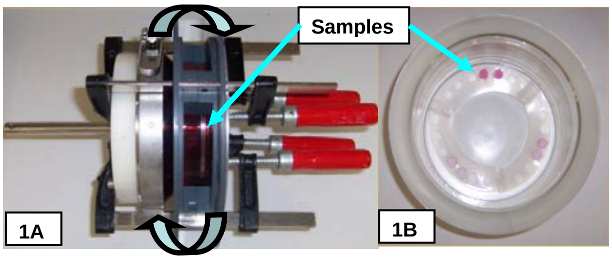



*Figure 1A: The bioreactor during rotation 1B: The samples held in a silicone rubber ring*

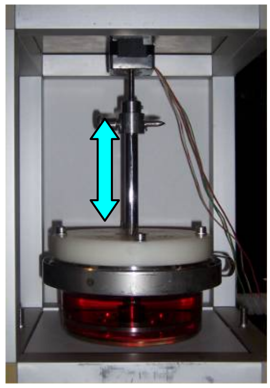


*Figure 2: The bioreactor in the loading rig. The arrow shows the direction of the stepper motor*

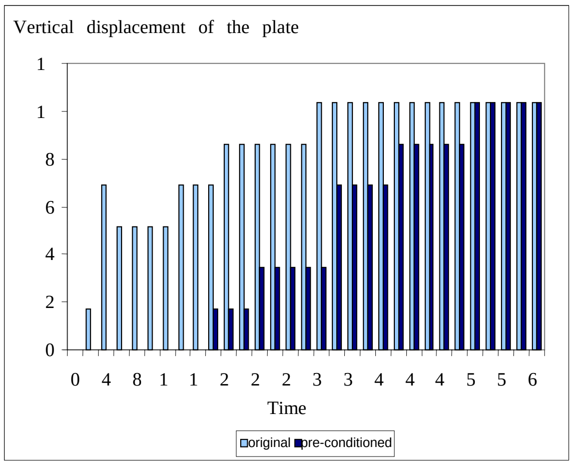



*Figure 3: The displacement of the plate over a 60 minute period of compression. Pre-conditioning of the stepper motor for 30 minutes prior to sample loading reduces the variability in the displacement*

backlash due to the metric thread of the axis. To overcome this problem a displacement sensor will be added to the system. Further studies are also needed to characterise the shear stresses being applied via the culture media during rotation.

**REFERENCES:** [1] *A Katsumi et al (2004) J. Biol Chem 279:12001-12004* **ACKNOWLEDGEMENTS:** I would like to thank the EPSRC: GR/S11510/01 and the Welcome Trust: 067743/Z/02/Z for funding, the North Staffs Hospital workshop & E. Lillyman for kindly providing me with my laptop