Novel *in vitro* Microfluidic Platforms for Osteocyte Mechanotransduction Studies

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Introduction

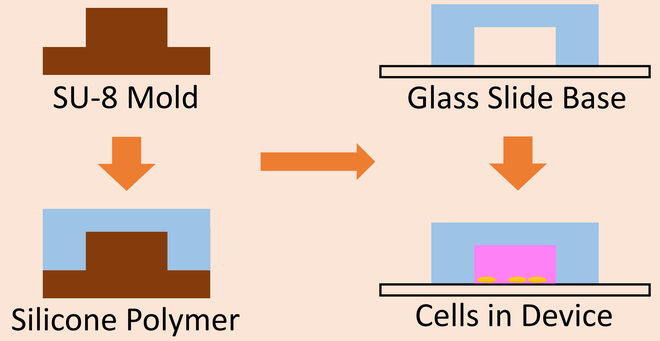
- Better understanding of osteocyte mechanobiology is key to unlocking solution to bone diseases
- Current *in vitro* platforms are expensive and lack physiological relevance [1]
- Microfluidic devices offer a new approach to *in vitro* experiments that drastically increase cost-efficiency and provide physiologically relevant physical environment for bone cell studies [2]
- Combining with on-chip protein detection methods [3], co-culture experiments in microfluidic devices can provide new insight to cellular interaction in numerous loading and disease conditions

Objective

- Design and fabrication of single microfluidic device with multi-shear flow and co-culture channels
- Test the new OCY454 osteocyte cell line and adapt it to the microfluidic device
- Integrate microfluidic platform with novel detection tools to monitor real-time cellular response

Method

- Shear-stress levels within microfluidic channels are based on channel dimensions
- Prototype devices are fabricated using a SU-8 silicone mold and soft silicone polymer
- One hertz oscillatory fluid flow within microfluidic devices generated with in-house pump
- MLO-Y4 osteocytes are seeded within the device to validate cellular response to different shear stress
- Cell response is measured by RANKL ELISA protein quantification 24 hours after flow

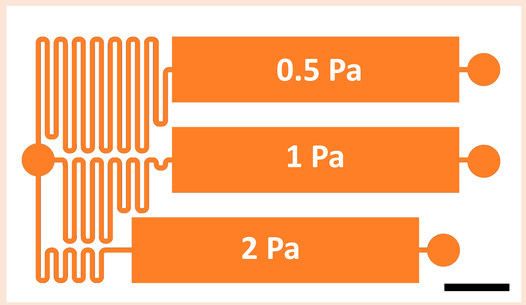


Device Design

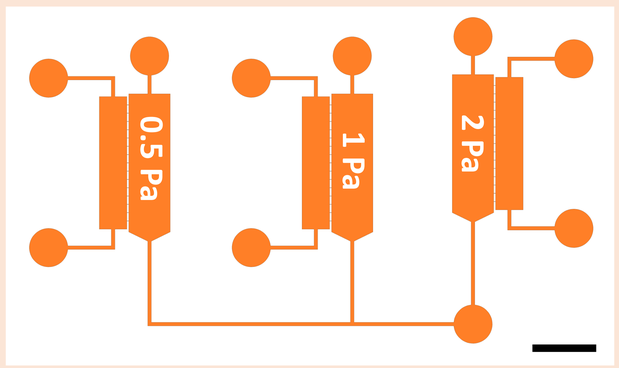
- Shear stress in microfluidic devices are based on the flow velocity profile:

$$\tau = \mu \frac{\partial u}{\partial y}$$

- When sharing a common inlet, channel resistance (proportional to its dimensions) is directly correlated to the flow velocity



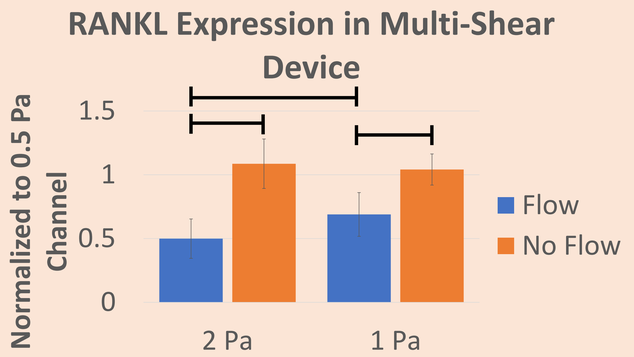
Multi-shear stress device, shear stresses correspond to levels experienced *in* vivo. Scale bar equals 3.5 mm



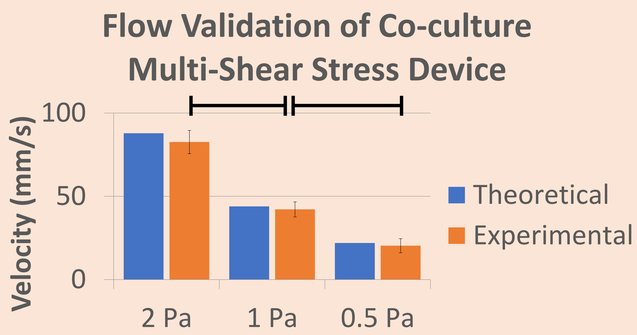
Co-culture multi-shear stress device, scale bar equals 4.5 mm

Preliminary Results

- Osteocytes reduce RANKL protein expression when exposed to flow
- RANKL affects osteoclast differentiation; can be used in validation of co-culture device
- Cells are exposed to oscillatory fluid flow for 2 hours



Data normalized to the RANKL measurement obtained from 0.5 Pa channel of respective devices. N=10, $p<0.05$



Validation for co-culture device. Communication pores have minimal effect on flow rate. N=3, $p<0.05$

Discussion and Next Step

- Results show that osteocytes respond to different oscillatory fluid flow within the same microfluidic device
- Continue testing of cellular response in co-culture platform with osteocytes and osteoclasts
- Future integration of on-chip sensors will allow for temporal monitoring of cellular response to different flow conditions

Acknowledgement

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References

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[2]Wei C., Fan B., Chen D., Liu C., Wei Y., Huo B., You L., Wang J., Chen J. "Osteocyte culture in microfluidic devices" Biomicrofluidics, vol. 9, pp 014109, Jan 2015
[3]Song P.F., Wang Y.H., Liu X.Y., "Flexible physical sensors made from paper substrates integrated with zinc oxide nanostructures," Flexible and Printed Electronics, Vol. 2, No. 3, pp 13, 2017