Modeling Cellular Contraction on Biohybrid Devices using Thermal Contraction Capabilities of Finite Element Analysis Tools

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Introduction

Biohybrid Devices

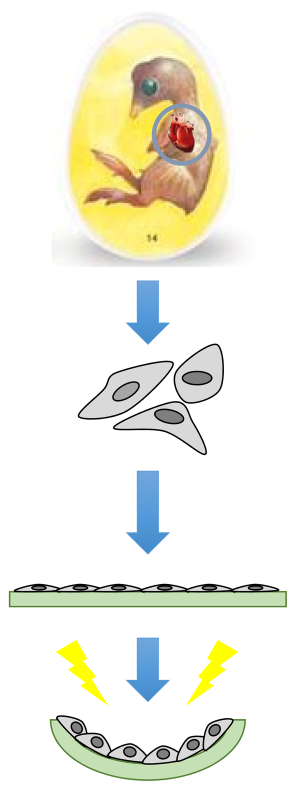
- Fabricated using biocompatible substrates, actuated by muscle cells

Modeling Techniques

- Existing techniques use FEA with individual forces and device specific models
- Engineering models are needed which are computationally efficient and reduce access barriers for new researchers

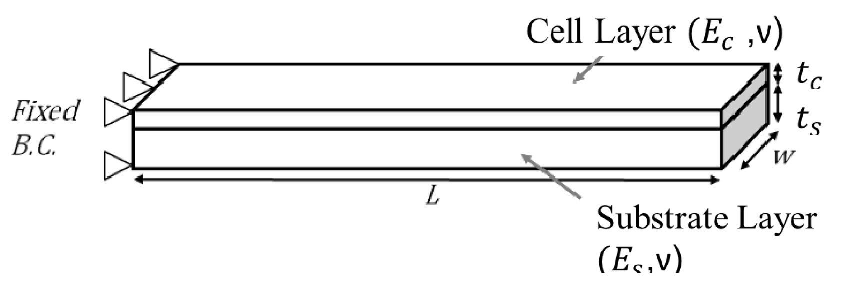
Purpose

- To Identify Thermal Expansion Coefficient (TEC) that can be used to emulate cell induced contractions in Finite Element Analysis (FEA)



Methods

Determine stress from experimental biohybrid cantilevers

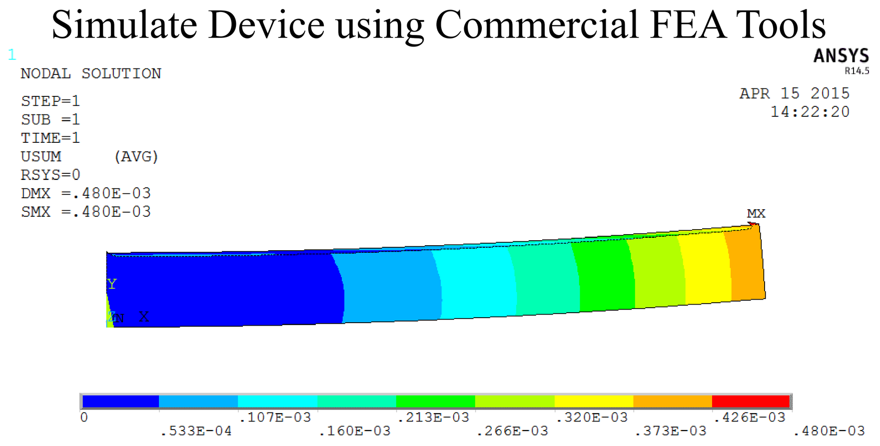


$$\sigma_c = (1+\delta^3\gamma)\frac{1}{6Rt_c}\left(\frac{E_s t_s^3}{((1-\nu)(t_s+t_c))}+\frac{E_c t_c^3}{((1-\nu)(t_s+t_c))}\right)$$

R : experimentally measured radius of curvature of the beam
ν : Poisson's ratio
t_c and t_s : thicknesses of the cell and substrate layers, respectively
E_c and E_s : moduli of the cells and substrate, respectively
$\gamma = E_c'/E_s'$
$E' = E/(1-\nu)$
$\delta = t_c/t_s$

Calculate Thermal Expansion Coefficient (TEC) $\alpha\Delta T = \frac{\sigma_c}{E_c}$

Simulate Device using Commercial FEA Tools



- Calibrated TEC values from 7 cantilever models from 3 studies in existing literature [1,3,5]
- Wide range of geometric and material properties
  - Thickness: 0.02 – 0.45 mm
  - Length: 0.25 – 10 mm
  - Width: 0.1 – 20 mm
  - Substrate Modulus: 17.82 – 1500 kPa
  - Cell Modulus: 10-188 kPa

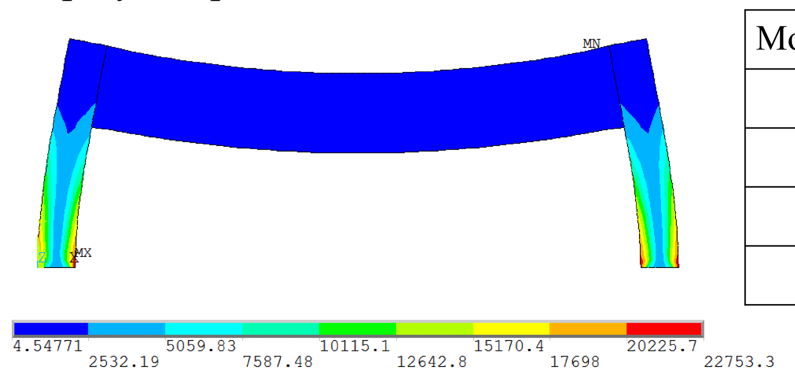
Results

Calibration

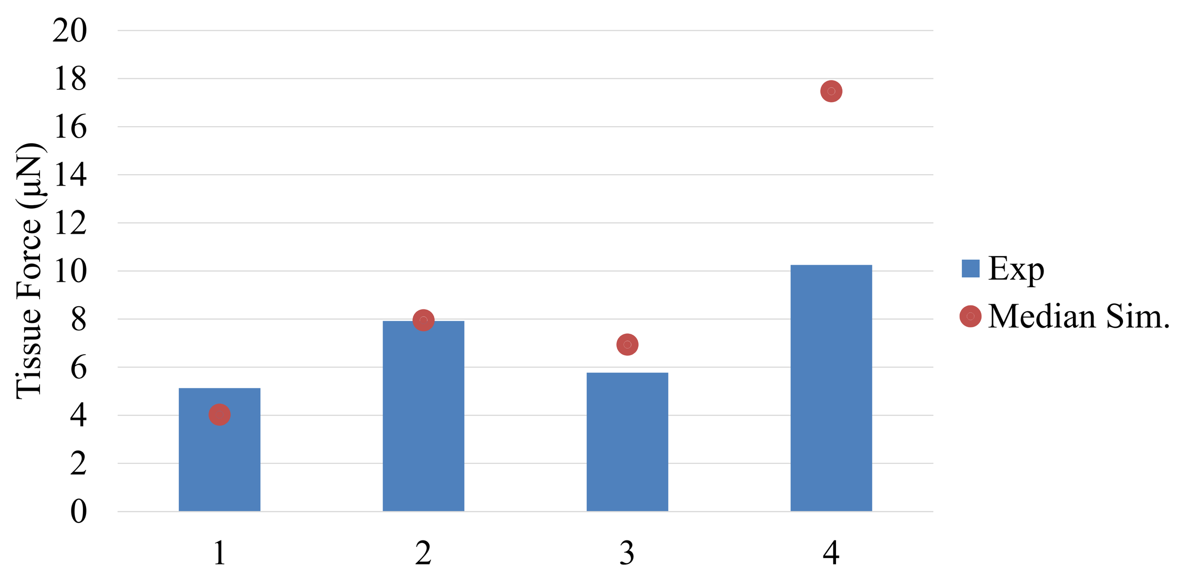
- Resulted in range of $\alpha\Delta T$: -0.009 to -0.423

Micropillars [2]

- 2-D simulation of contracting microtissue between two synthetic polymer pillars



Model	E (kPa)	k (μN/μm)
1	5	0.098
2	5	0.397
3	25	0.098
4	25	0.397

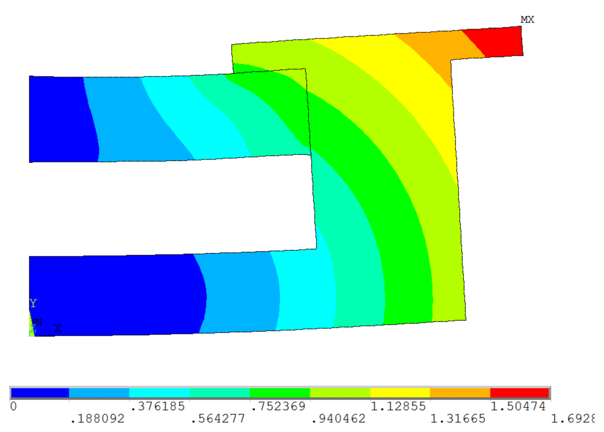


Top Left: FEA simulation (stress) of micropillar array based on Legant et al. 2009[2].

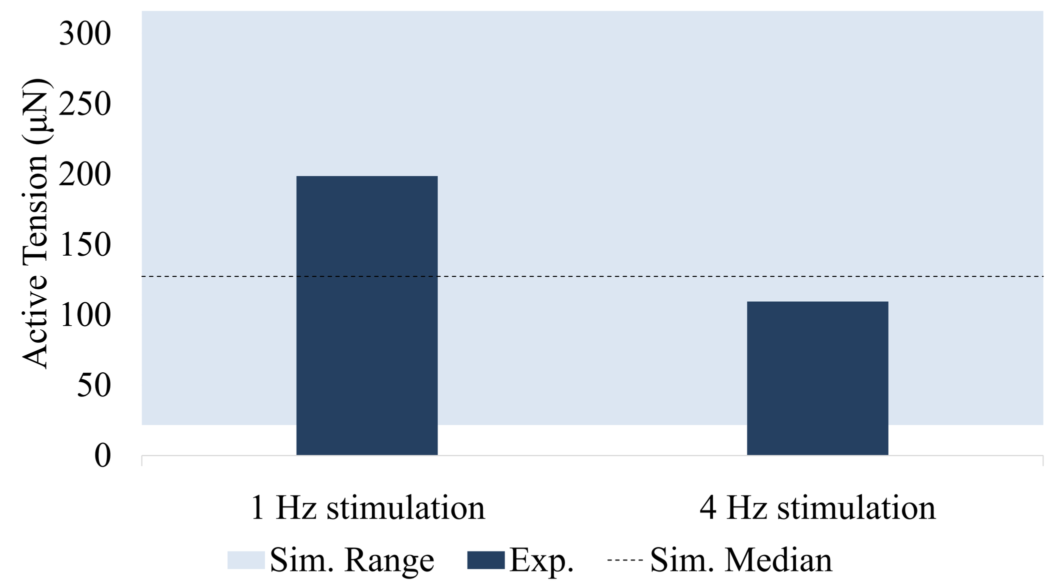
Top Right: Material properties for the four models simulated

Bottom: A comparison of the tissue force reported by Legant et al. and simulation results

Biohybrid Walker [4]



- 2-D symmetric simulation of biohybrid device activated by tissue construct



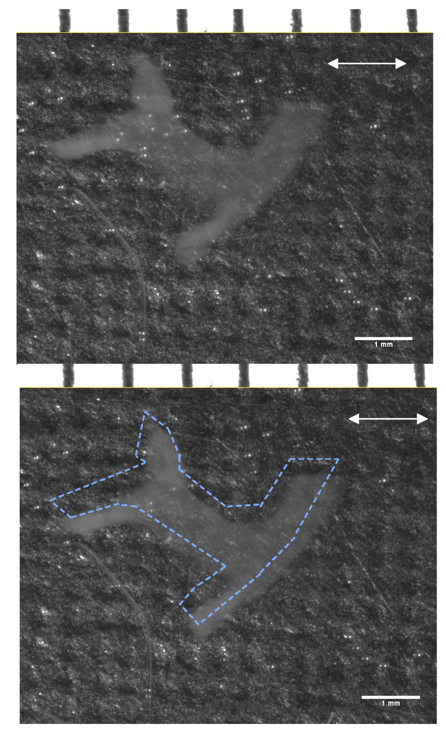
Top: FEA simulation (deflection) of one half of a biohybrid walker based on Cvetkovic et al. 2014[4] . Bottom: a comparison of the active tension reported by Cvetkovic et al. and simulation results

Conclusions

- Utilizing thermal contraction improves simulation run-time
  - 78% reduction for 10 mm cantilever
- An initial range of TEC values of -0.061 to -0.152 can be used to simulate cellular contraction
- Scatter in the available data leads to scatter in the calibration results
- Potential sources of scatter:
  - Constitutive values assumed rather than measured directly (i.e. cell layer modulus)
  - Large range of substrate moduli
    - Substrate modulus effects cell function[10,11]
- Based on preliminary calibration
  - For models with higher cell moduli, a lower TEC value should be used
  - For models with low cell modulus and low substrate modulus a higher TEC value should be used
- Modeling technique provides guidance for taking the necessary data to predict device behavior

Future Work

- Improve model calibration
  - Perform systematic experiments
  - Measure substrate modulus, cell layer modulus, and thickness directly
- Develop multi-scale simulations of biohybrid devices and living machines
  - Incorporate FEA simulations and discrete rigid body dynamic simulations to improve living machine design



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References

[1] J. Park et al. *Anal. Chem.*, vol. 77, pp. 6571–80, Oct. 2005.
[2] W. Legant et al. *PNAS*, vol. 106, no. 25, pp. 10097–102, 2009.
[3] A. Feinberg et al. *Science*, vol. 317, pp. 1366–70, Sep. 2007.
[4] C. Cvetkovic et al. *PNAS*, vol. 111, no. 28, pp. 10125–30, Jun. 2014.
[5] V. Chan et al. *Lab Chip*, vol. 12, pp. 88–98, Jan. 2012.
[6] K. Wilson et al. *PLoS One*, vol. 5, no. 6, p. e11042, Jan. 2010.
[7] A. Atkinson. *Br. Ceram. Proc.*, vol. 54, no. 1, 1995.
[8] C. Klein. *J. Appl. Phys.*, vol. 88, no. 9, p. 5487, 2000.
[9] K. Na et al. *NSTI-Nanotech*, 2008, vol. 3, p. 737–740.
[10] Engler et al. J. Cell Science, 2008, 121, 3794-3802.
[11] Bhana et al. Biotechnol Bioeng, 2010, 105(6), 1148-60.

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