Real-Time Measurement of Cell Concentration During Bioprinting Using the Smart Syringe

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Introduction

- Bioprinted scaffolds are hindered from FDA approval due to quality control requirements involving cell-infused products.[1]
- **Destructive testing is required** to determine cellular properties such as cell concentration, resulting in specialized labor and increased production costs.[2,3]
- A non-destructive method to determine cell concentration of bioprinted constructs does not currently exist.
- Dielectric Impedance Spectroscopy (DIS) **non-destructively** determines cellular properties in 3-D cell culture by measuring cellular resistance to an electric current. [4]
- We seek to show the **repeatability and sensitivity** of the **Smart Syringe**, a device that incorporates DIS into bioprinting, at known cell concentrations in real-time.

Testing destroys printed scaffolds

Objective

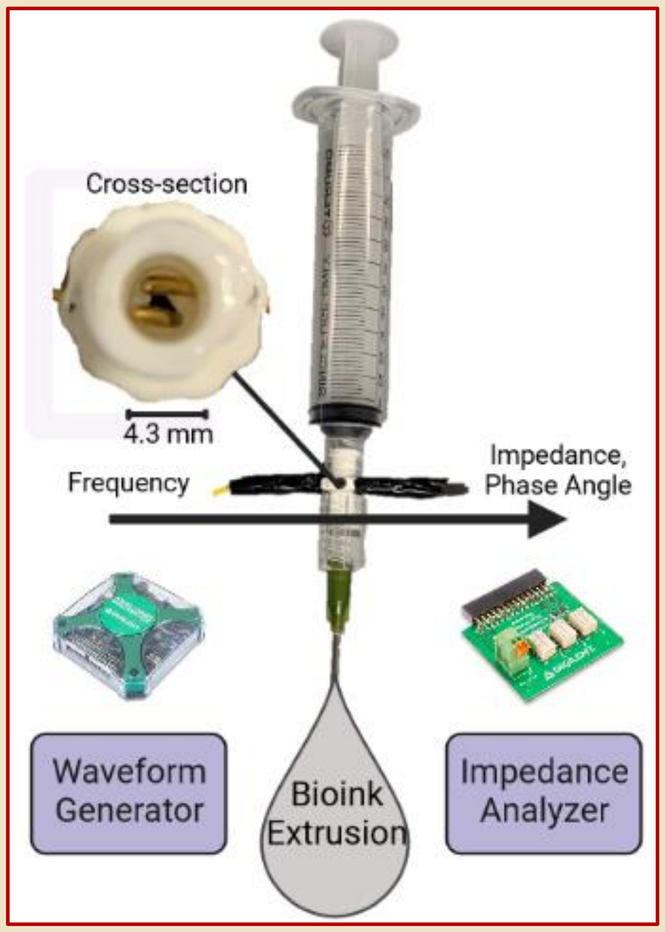
Create a device for real-time, in-line detection of cell concentration in bioinks during printing

Methods

Cell and Bioink Preparation

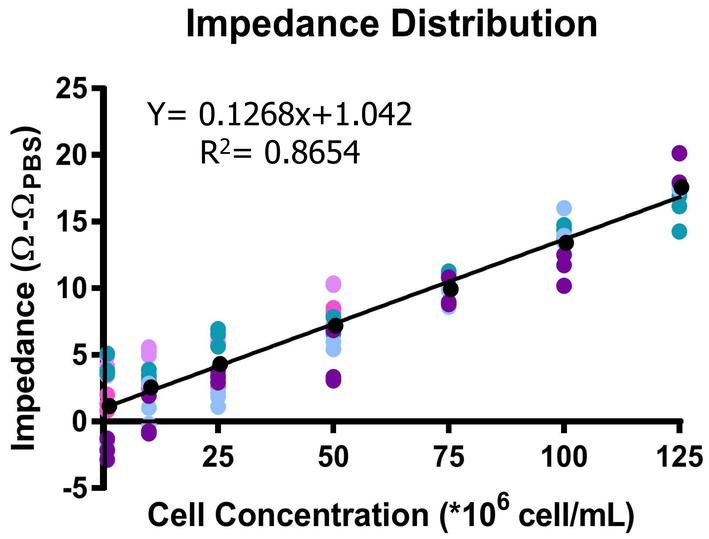
- Condyles were harvested from the femurs of 1-3 day old bovids.[2]
- Cell concentration of samples ranged from 1-125*10^6 cell/mL.
- Frequency sweeps were preformed from 0.01-25 MHz at 50 mV with a 1 kΩ resistor using the Digilent Analog Discovery 2 device.
- Experiment was conducted 5 times to access repeatability of the Smart Syringe.

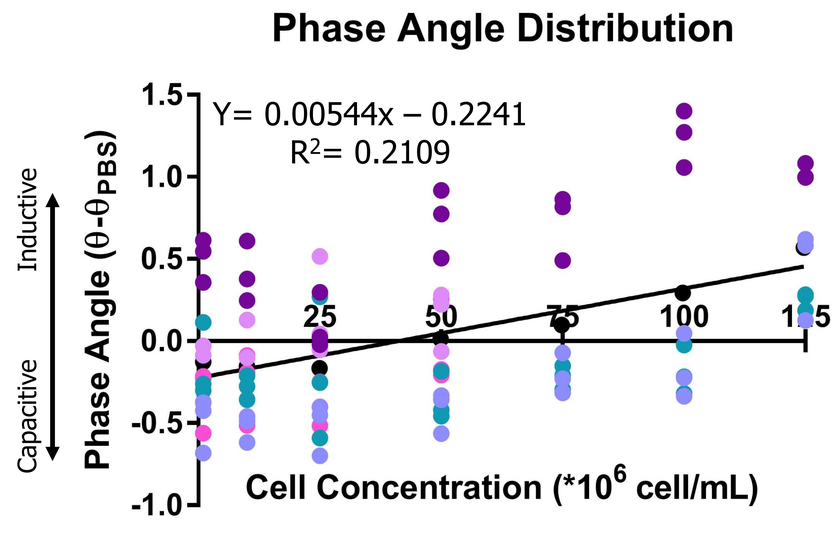
Smart Syringe Information Workflow



Results

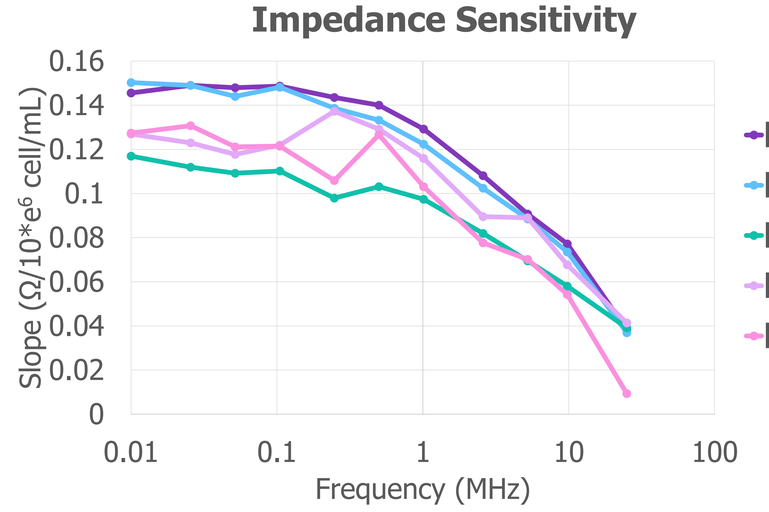
1. Impedance is suitable for estimation of cell concentration

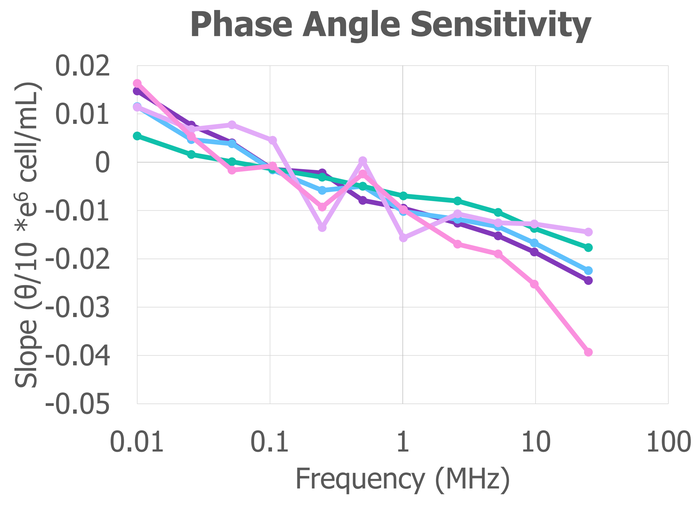




*Data shown at 0.025 MHz

2. Low frequencies demonstrate increased device sensitivity





Discussion & Conclusions

- Impedance revealed a **linear calibration curve**, showing the repeatability and consistency of data across 5 experiments.
- Phase angle calibration curve indicated that the capacitive effect on cells caused by the device is low. In fact, inductivity slightly increased with concentration.
- Both impedance and phase angle displayed dependence on frequency with highest dependence occurring at ≤0.1 MHz.
- Impedance is preferable to phase angle for in-line detection of cell concentration.
- The Smart Syringe **non-destructively distinguished** between samples of varying cell concentration from 1-125*10^6 cell/mL based on impedance measurements read in real-time in static fluid flow studies.

Significance

The Smart Syringe non-destructively detects cell concentration of bioinks in real-time.

References

1. Haring AP + 2020. 2. Diamantides N + 2019. 3. Osidak EO + 2019. 4. Narayanan LK + 2018.

Acknowledgments

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