OCTiCell by ChromoLogic

Continuous non-invasive, non-contact, real-time in-line monitoring of bioreactors

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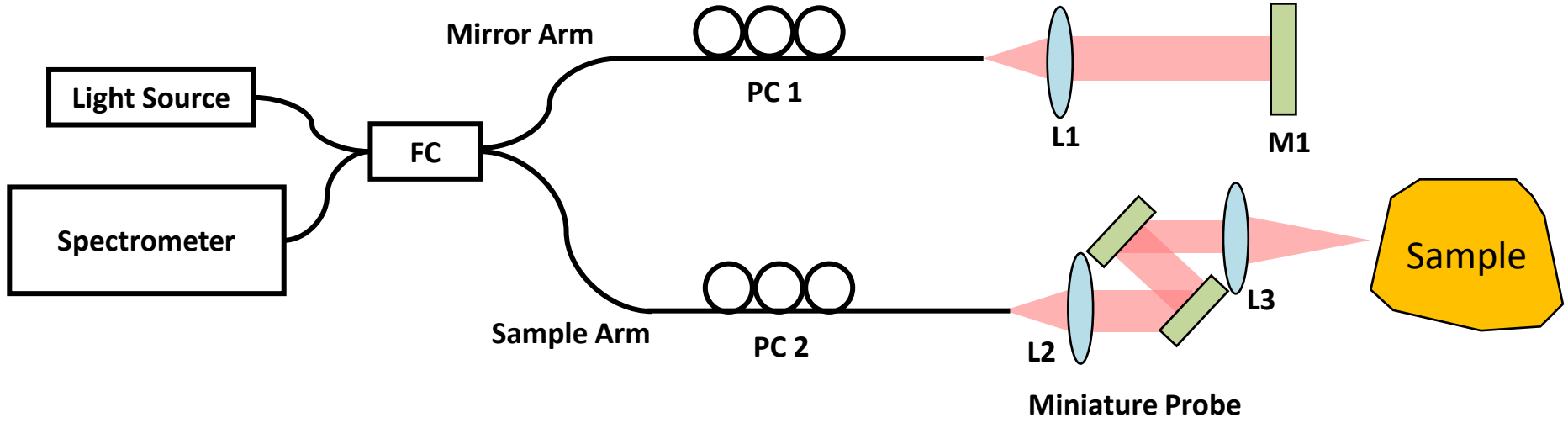
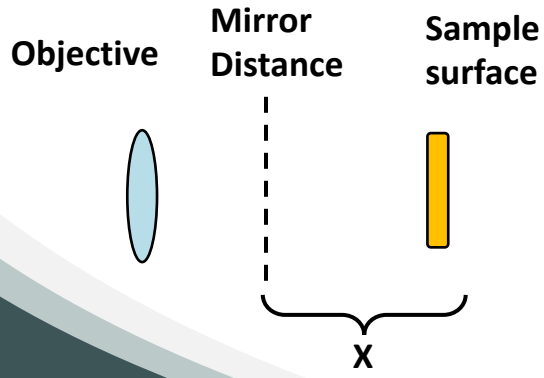
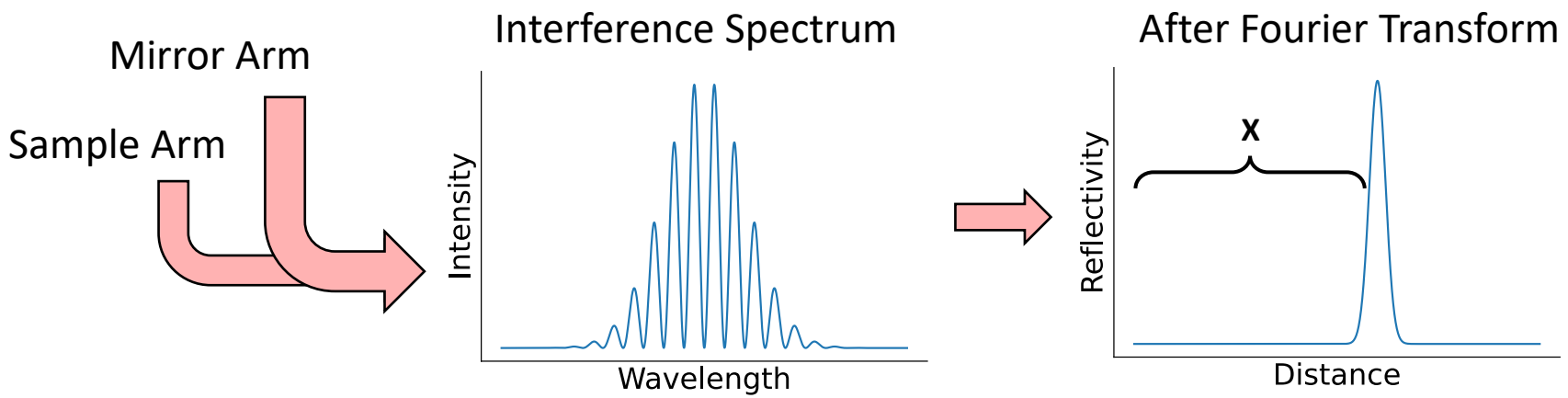
Motivation

- Growing large volumes of cells usually requires suspended cultures.
- GMP/GLP environments require tight monitoring of every stage in the manufacturing process.
- Need to measure viable cell density in order to determine when the growth is complete.

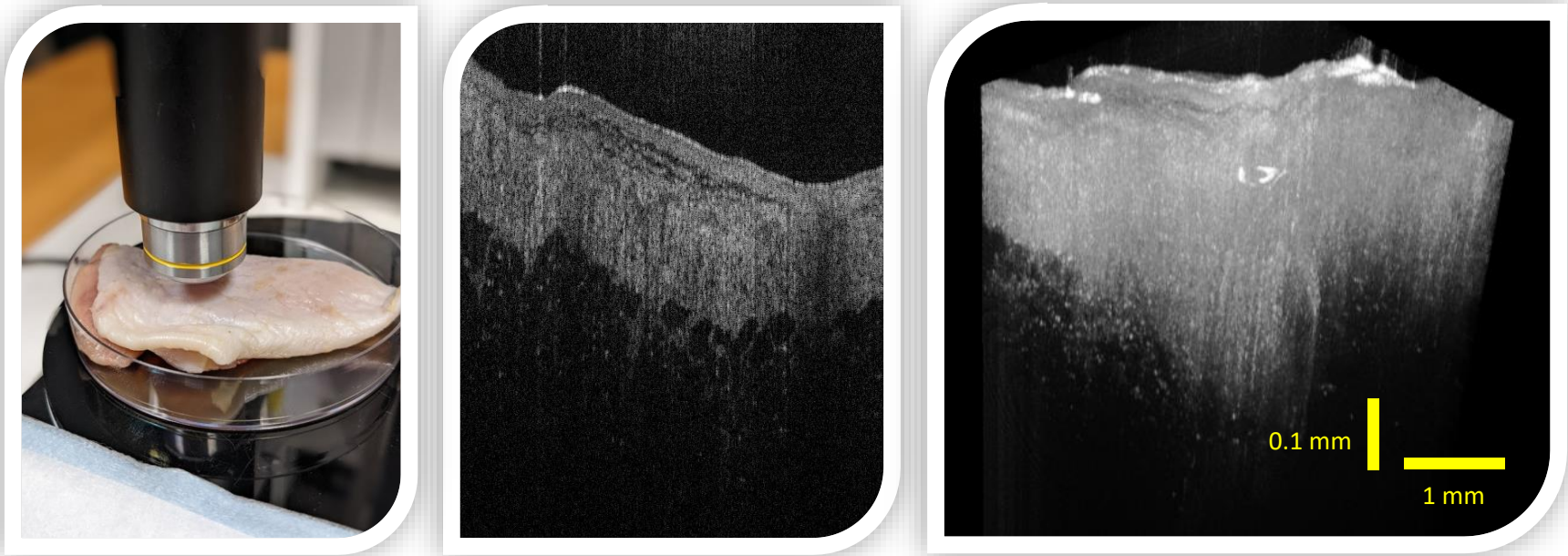
Optical Coherence Tomography







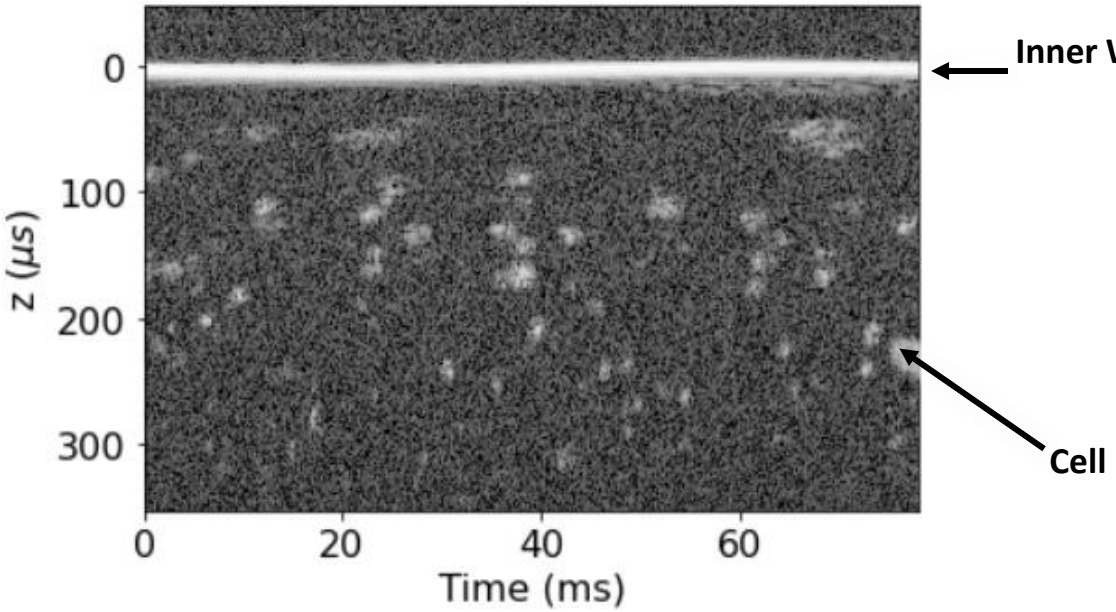
Traditional OCT Imaging

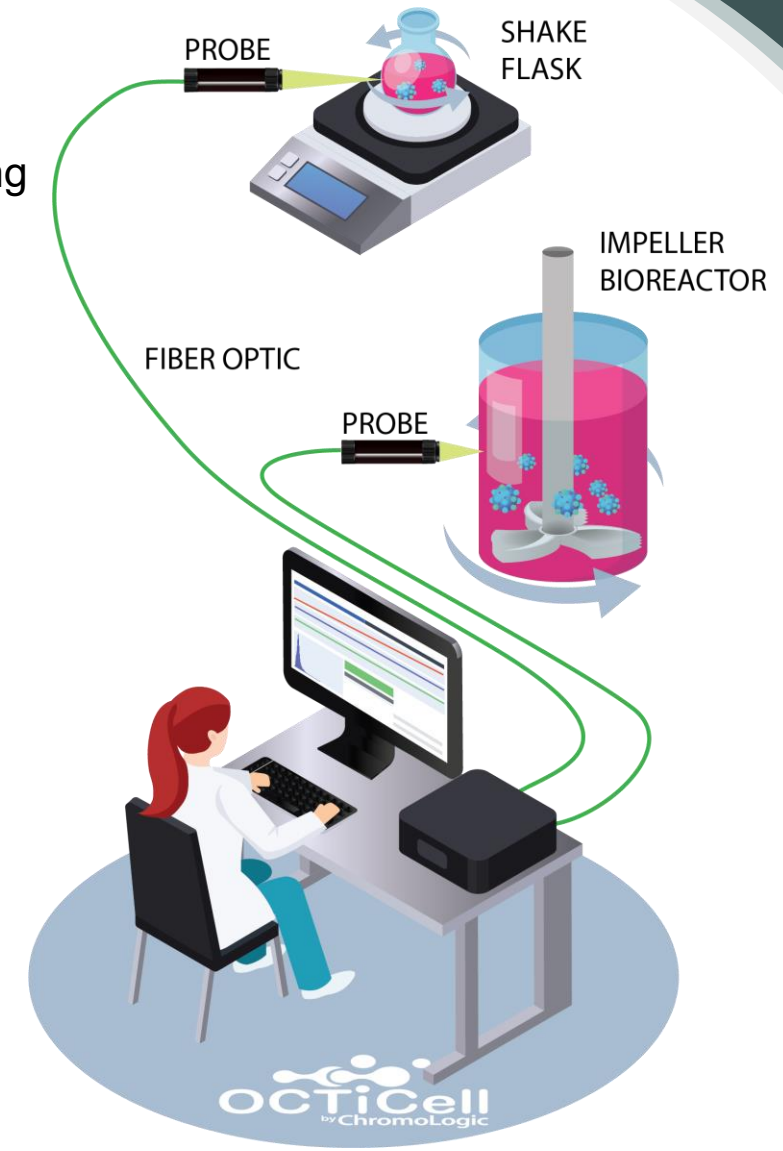


- Fast scanning mirrors used to generate 3D images of a sample
- Line-scan rate is ~6kHz
- Not fast enough for 3D or 2D imaging cells as they are moving in suspended cell bioreactors

OCTiCell: OCT Cell Monitoring

- OCTiCell solution:
  - Keep the imaging beam fixed: Use the cell's own motion for imaging



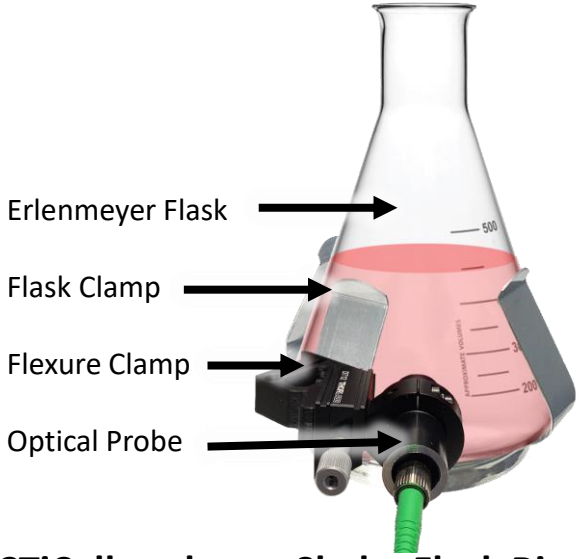


Advantages

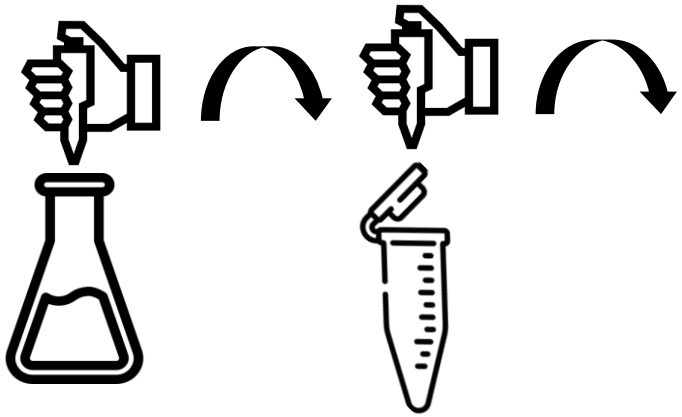
- Completely non-invasive
  - No risk of contamination
- Automated measurements
- No consumables
- Continuous measurements
- Measures cell concentration
- Measures cell viability
- Measures cell size
- Adapts to different bioreactor types
  - Glass/plastic
- Web interface allows for remote monitoring and operation

Monitoring Cell Growths

- Worked with Jost Vielmetter, PhD, Director of the Caltech Protein Expression Center
- Grew HEK293-6E Cells over 6 days.
- Cells typically passed at 3 days
- Concentration, viability and size measurements were compared to Cedex automated cell counter.
- Probe adapted to shake flask bioreactor.



OCTiCell probe on Shake-Flask Bioreactor



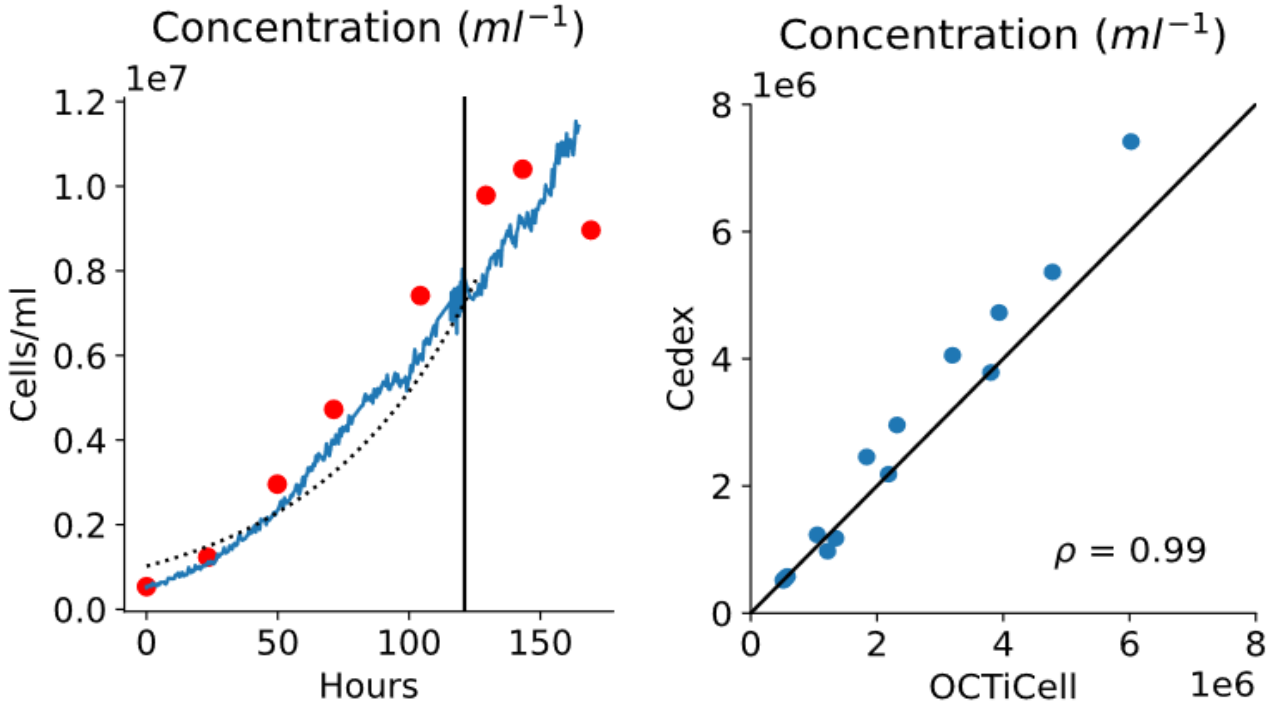
Subsample

Add Trypan Blue

Cedex Automated Cell Counter

Cell Concentration Measurements

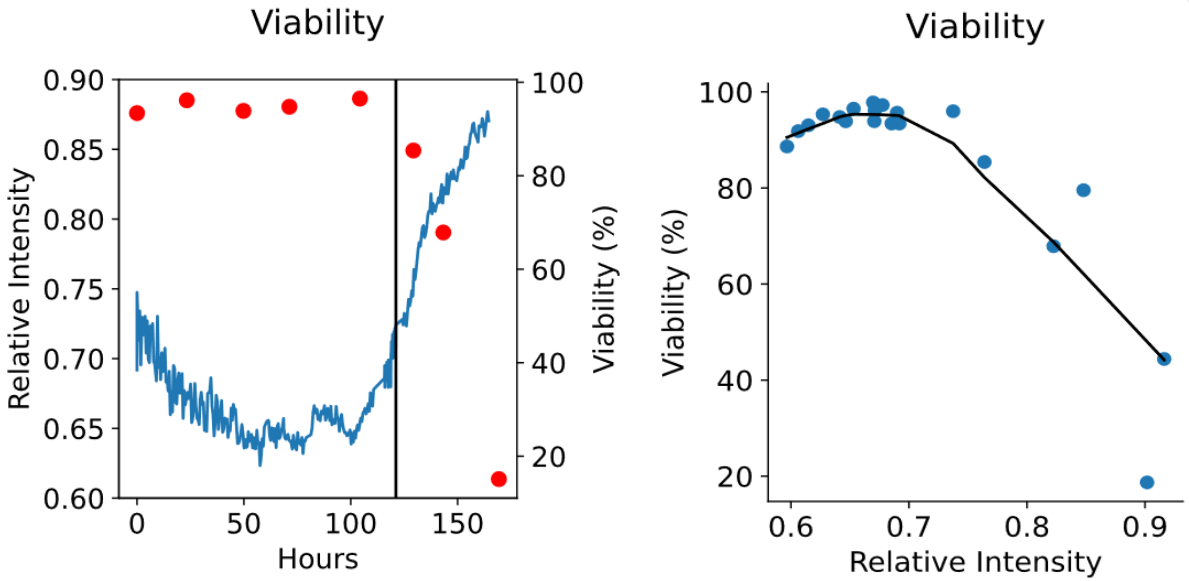
- Users specify starting concentration at the start of a measurement.
- Measurements taken every 30 minutes for 160 hours.
- Strong correlation between OCTiCell and Cedex cell counter measurements when viability was high (<100 hours).
- Correlation falls off as cells begin to die.
- 3 replicates showed similar results.
- Restricted counts to only objects >10µm
- Each measurement detected 135—6456 cells depending on concentration



Brehove M. *et al*, Cytotherapy (2022)

Cell Viability Measurements

- Backscatter intensity as measured by OCTiCell dramatically increased as cells began to die after 100 hours.
- Smoothing allows us to predict cell viability based on backscatter intensity relative to starting value.
- Observed in CHO and HEK293
- Relationship between backscatter intensity and viability is likely to vary between cell types and require individual calibration



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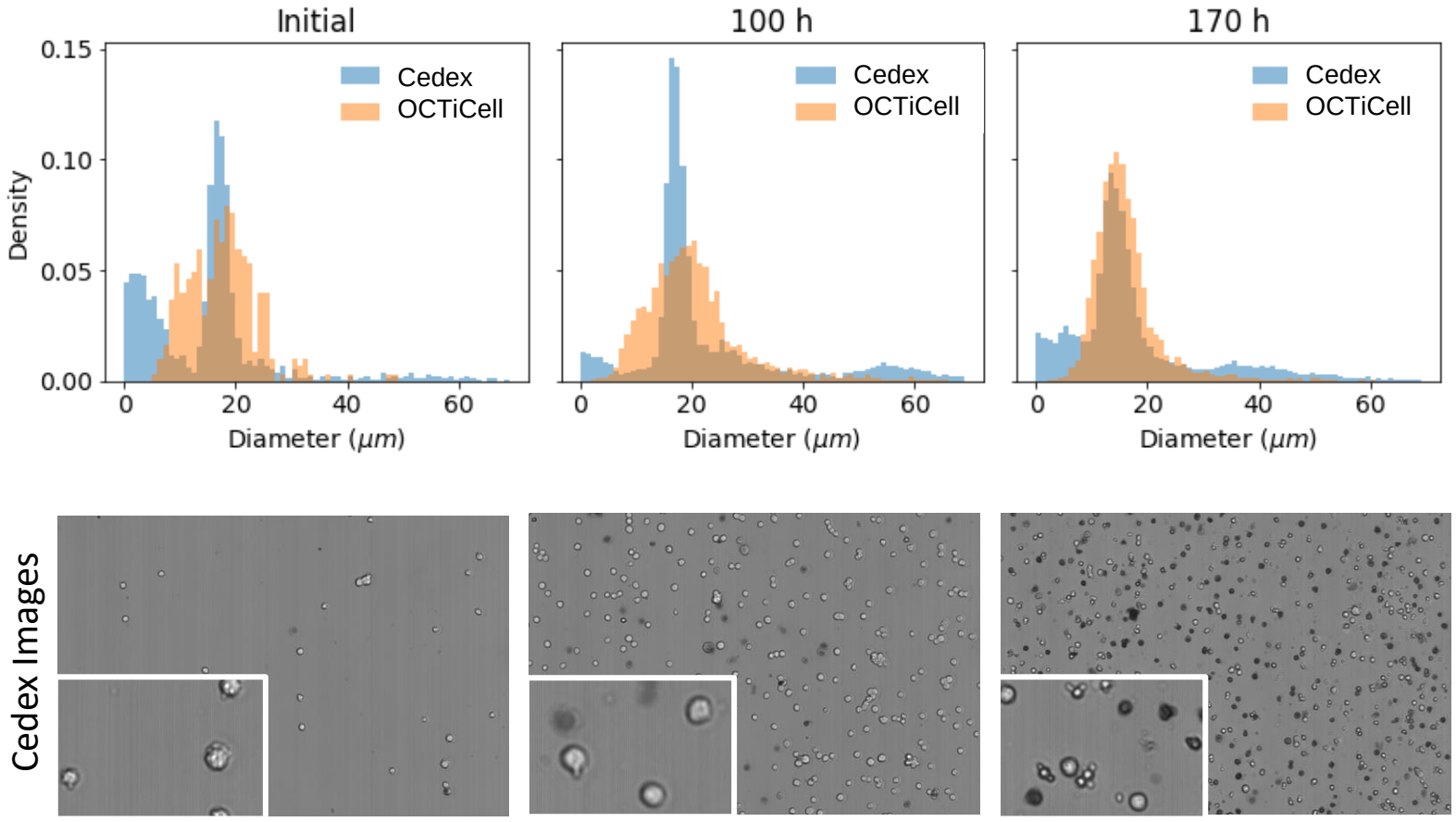
Cell Size Measurements

- OCTiCell size measurements were compared with Cedex all-object diameters.
- OCTiCell size peak matches Cedex



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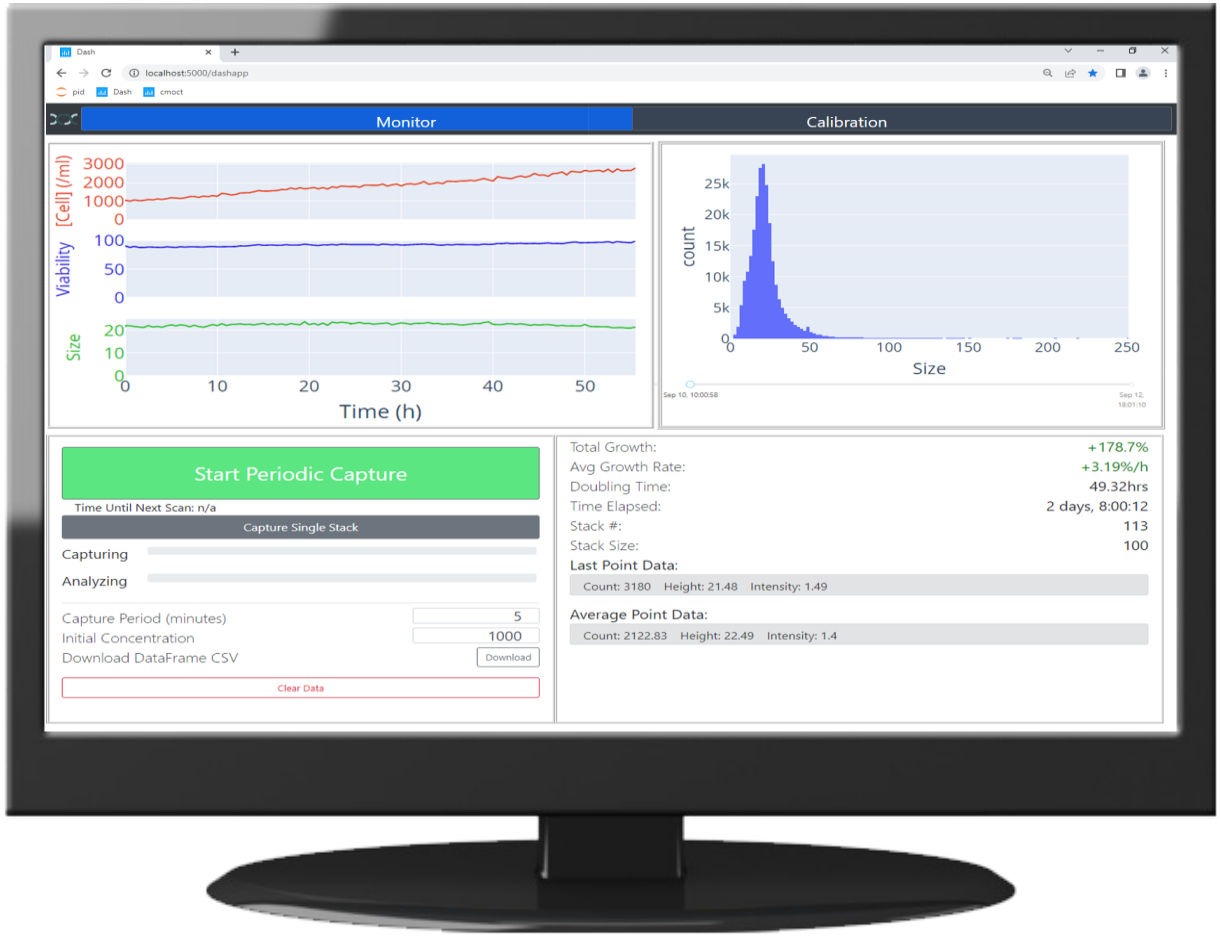
OCTiCell Interface

OCTiCell shows

- Cell counts over time
- Cell viability over time
- Average cell size over time
- Size distribution
- User controls
- Growth Statistics

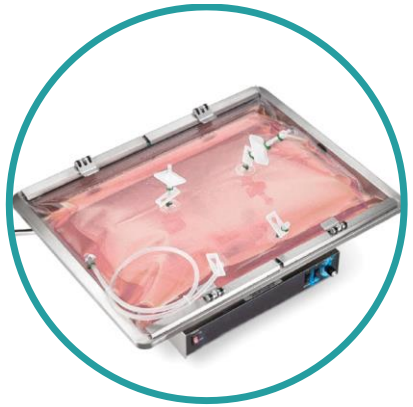


Moving forward

- OCTiCell system can be adapted to many different kinds of bioreactors including small scale bioreactors like shake flasks that cannot accommodate other monitoring methods.
- Add capability to attach multiple probes to a single system for multi-reactor monitoring
- ChromoLogic is looking for applications that can benefit the most from OCTiCell's unique advantages.

Shake Flask Bioreactor

Impeller Flask Bioreactor



Rocking Bioreactor

PBS Bioreactor

Acknowledgements

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- Paul Minor, PhD
- Naresh Menon, PhD

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- Jost Vielmetter, PhD
- Annie Lam

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