

# Microfluidic Patch Clamp Technique for Measuring Membrane Disruption

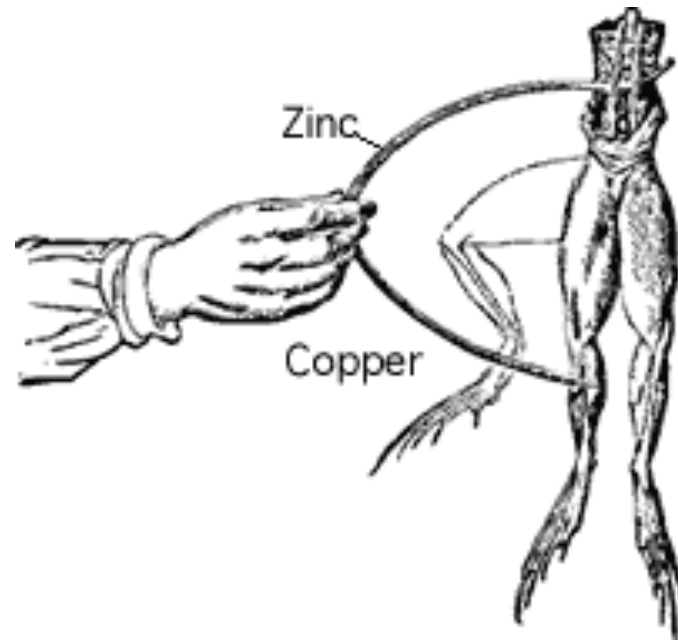
Elizabeth Gichana  
Banaszak Holl Group

# Overview

1. Background
2. Motivation
3. Data
4. Work to be done

# An Impressively Brief Background

- Luigi Galvani
  - Realization that electrical phenomena are part of animal physiology
  - ➔ Electrophysiology



- 1940's Voltage Clamp  
measures the ion currents  
across the membrane of  
excitable cells

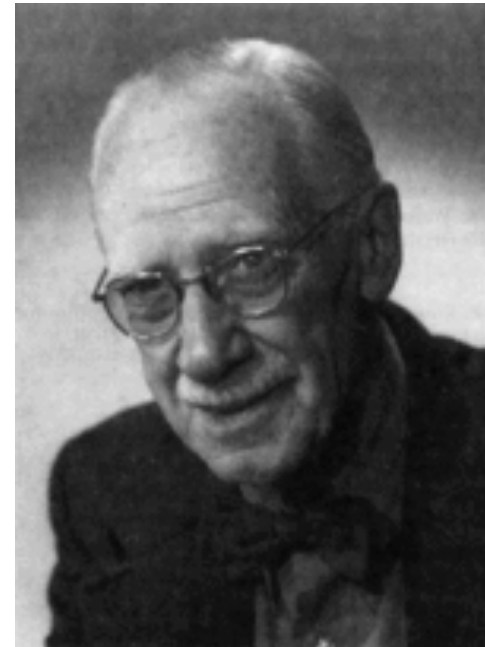
- Kenneth Stewart Cole  
“pioneer in the application  
of physical science to  
biology”

- George Marmont

- 1970-1980 – Patch  
Clamp

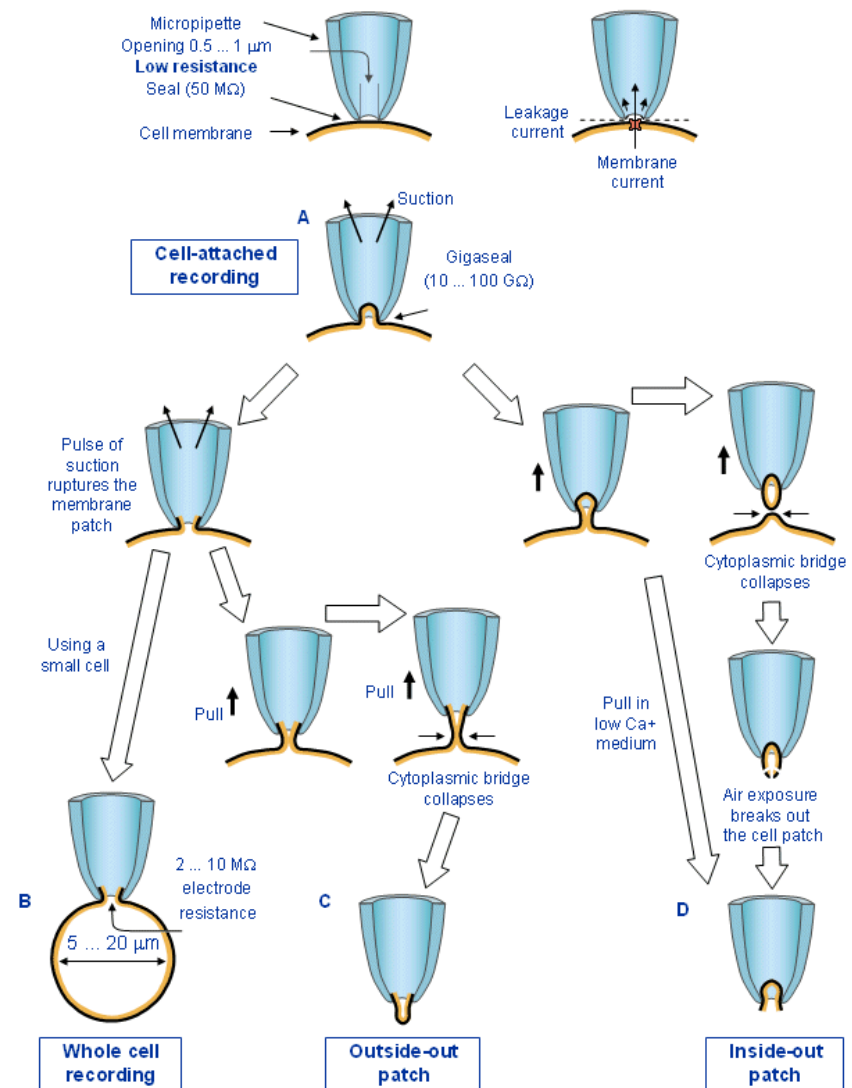
- Erwin Neher

- Bert Sakmann



# What is a patch clamp?

- “An extremely fine glass pipette with a very small opening [that] is used to make contact with a tiny area, or patch, of the cell's outer membrane.” A small amount of suction is applied through the pipette and forms a tight seal.
- Fit the pipette with a highly sensitive electrode to record very minute changes in current produced as ions flow through the clamped channel into the pipette.



# Nobel Prize!



- 1991 Nobel Prize in Physiology and Medicine
  - “conclusively proving the existence and function of ion channels.”

Hypothesis: Cationic nanoparticles induce the formation and/or growth of nanoscale defects in cell membranes, such as holes, causing cell membrane leakage.

Chen et al. *Journal of Physical Chemistry* 2009

Goal: Measure changes in  
electrical properties of  
membrane to infer  
damage





# Importance

- Applications in medicine
  - Drug and gene delivery
  - Viruses
  - Prions
    - Untreatable and fatal!
- Cytotoxicity
  - Nanoparticles

# IonFlux

- Traditional Patch Clamp
  - Slow and labor intensive
- Microfluidic Patch Clamp
  - Incredibly quick
  - “microfluidic design to provide automated cell introduction”
  - channel network that connects the wells with a series of tiny channels for cell and compound introduction.
  - pneumatic flow control



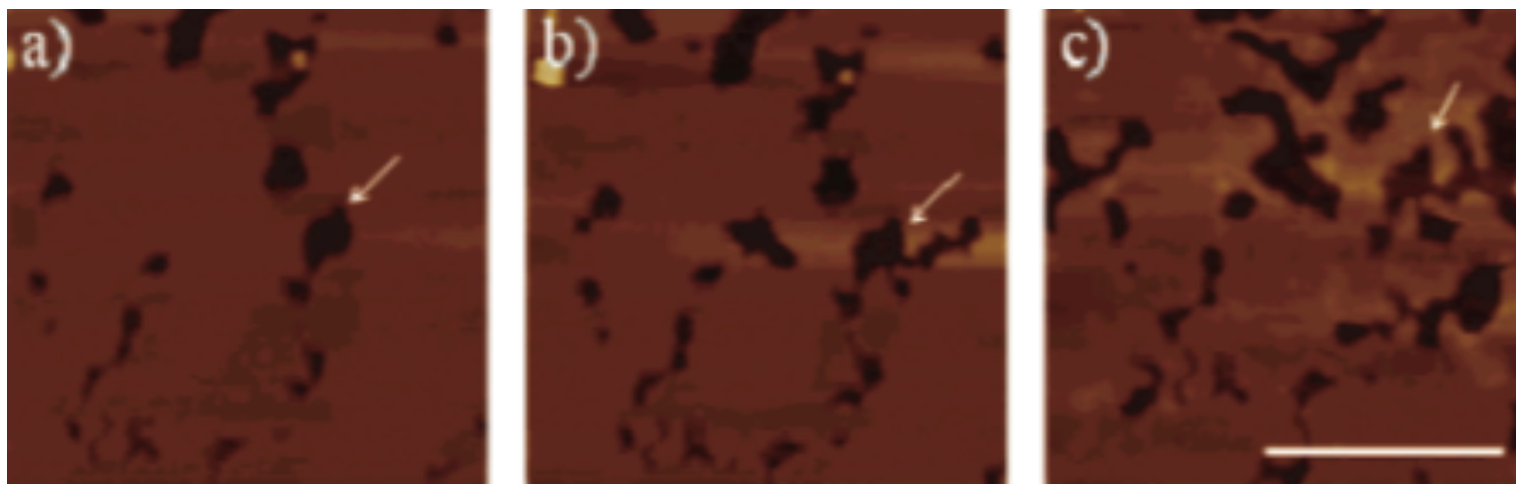
# What the Literature Says

- There haven't been any measurements of individual nanoscale hole forming events induced by cationic nanoparticles on living cell membranes
- There hasn't been characterization of the time course of the events

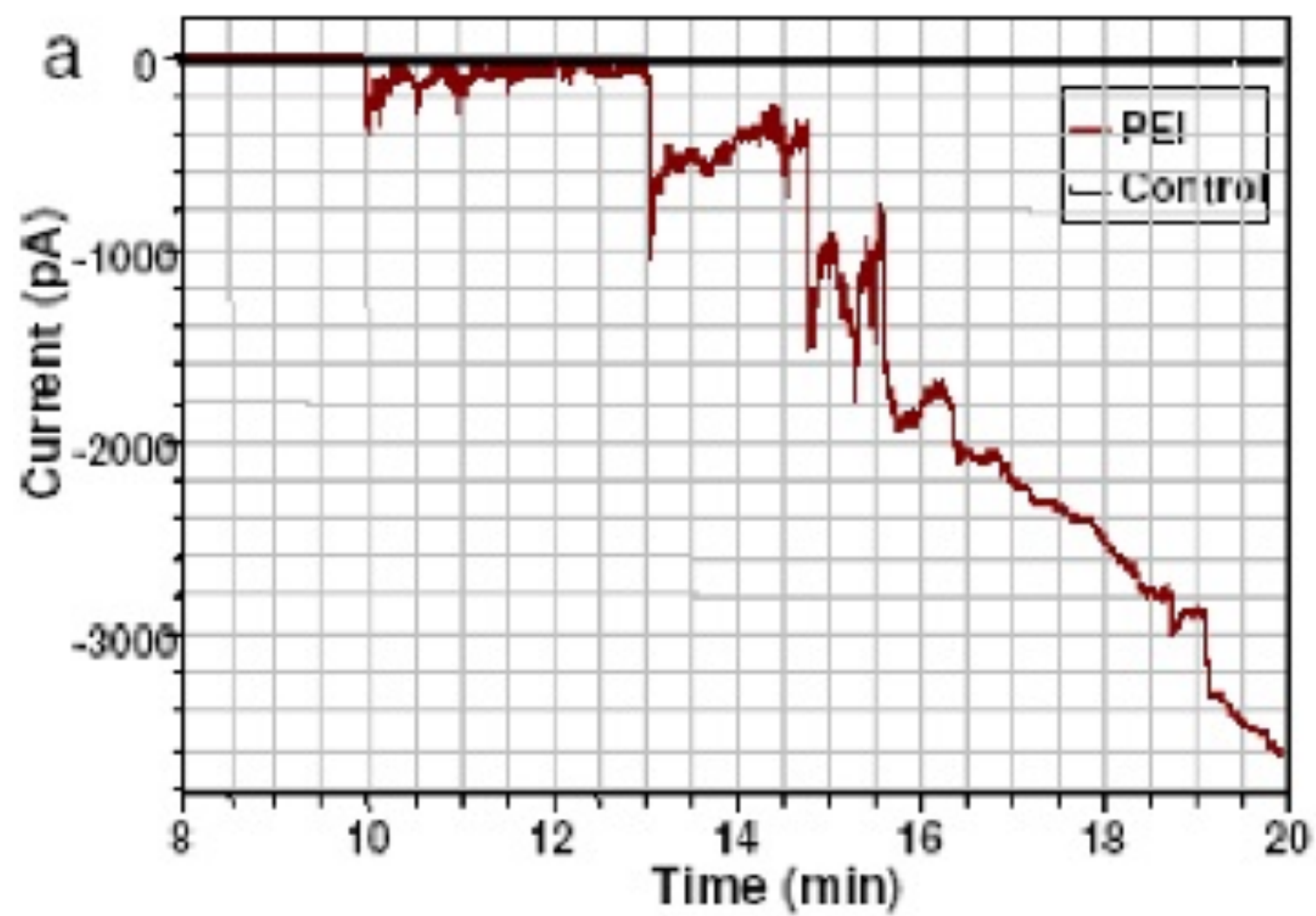
Chen et al. Journal of Physical Chemistry 2009

# Paper Results

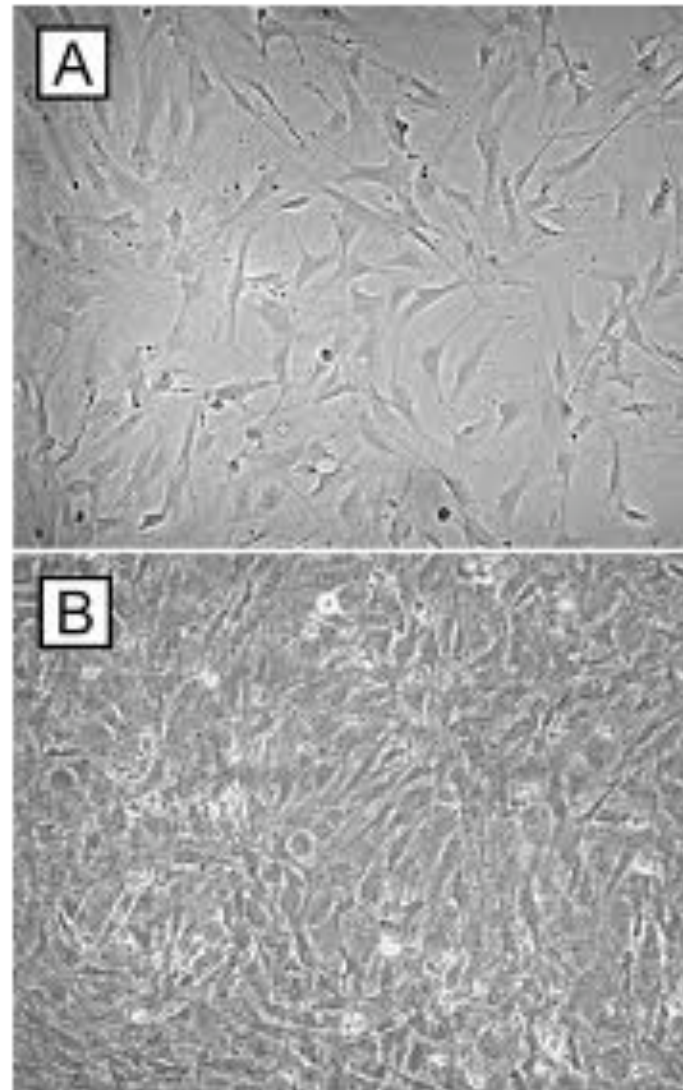
- 1. “Exposure of cells to noncytotoxic levels of cationic nanoparticles results in the formation of defects that enhance conductance through the cellular membrane”
- 2. “These defects can recover over time allowing a decrease in transmembrane conductance toward it’s original value.”



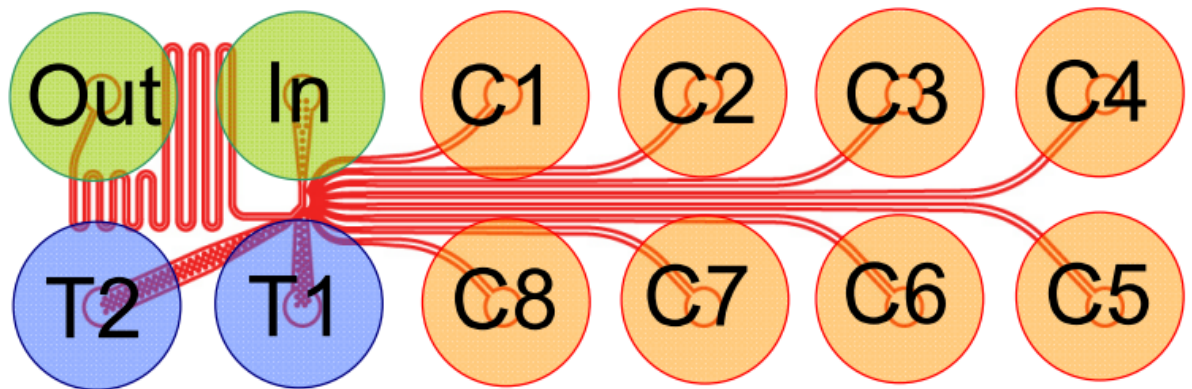
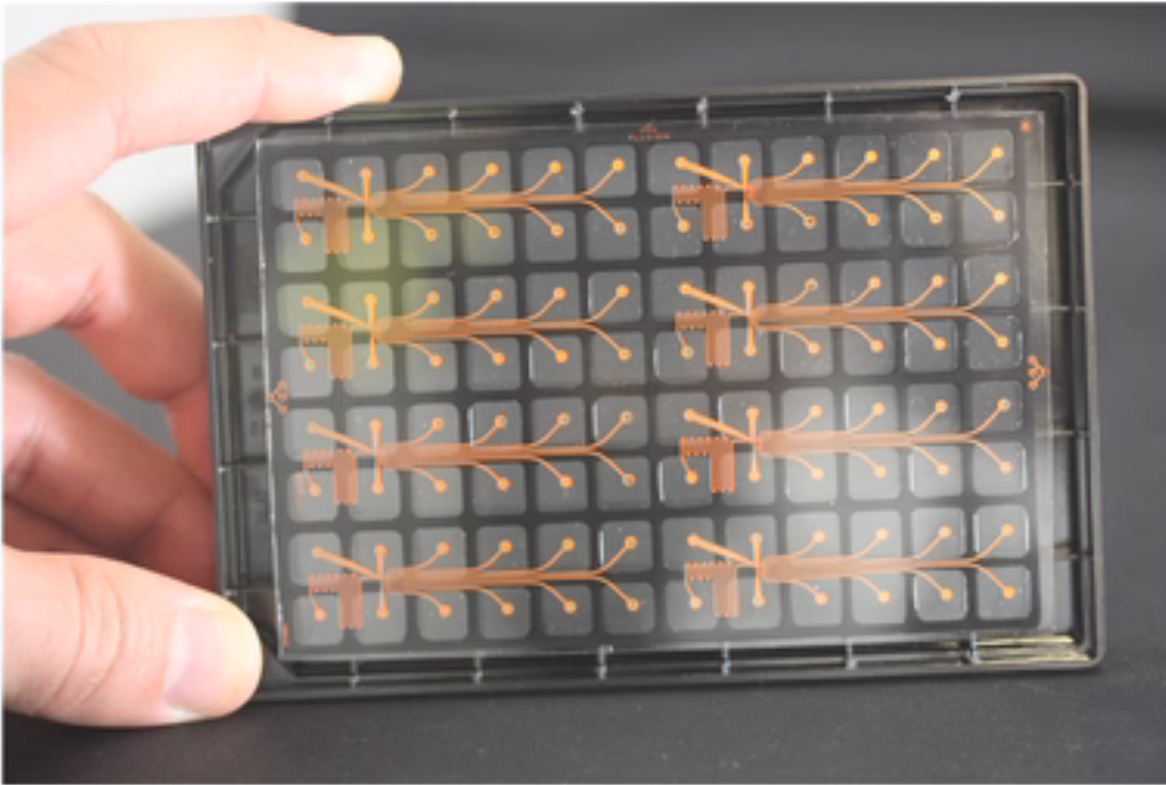
Hong, et. Al. *Bioconjugate Chemistry* 2006



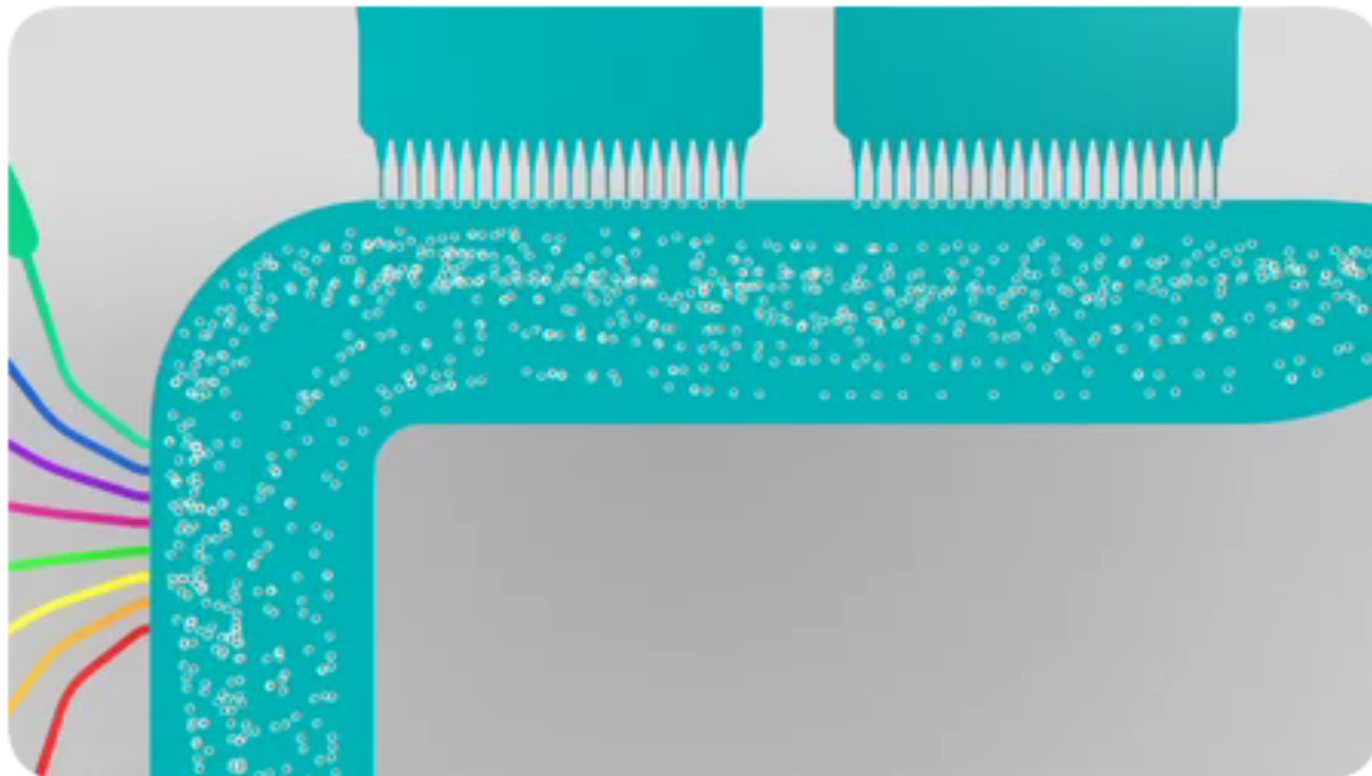
# Cells...



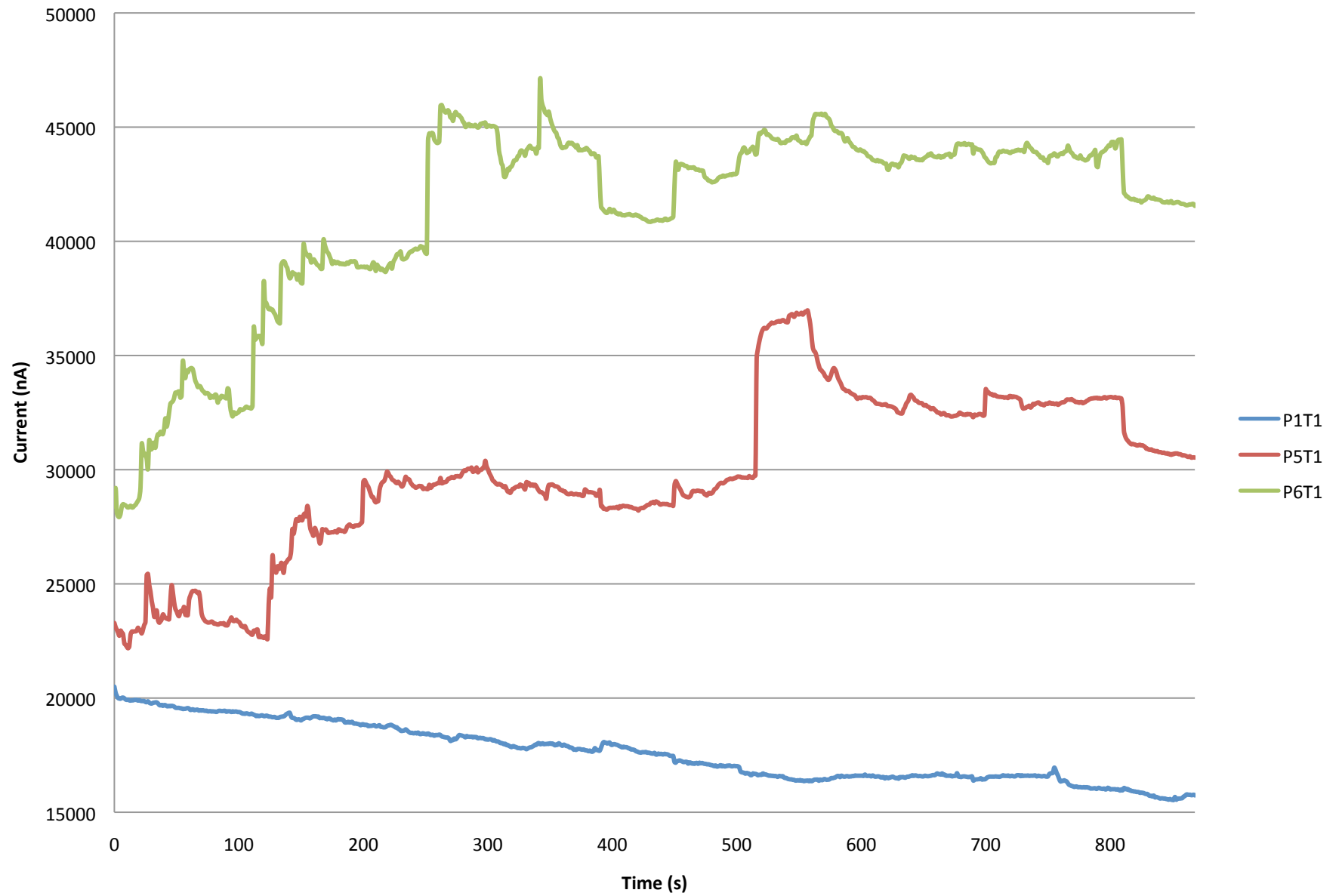
# Setup



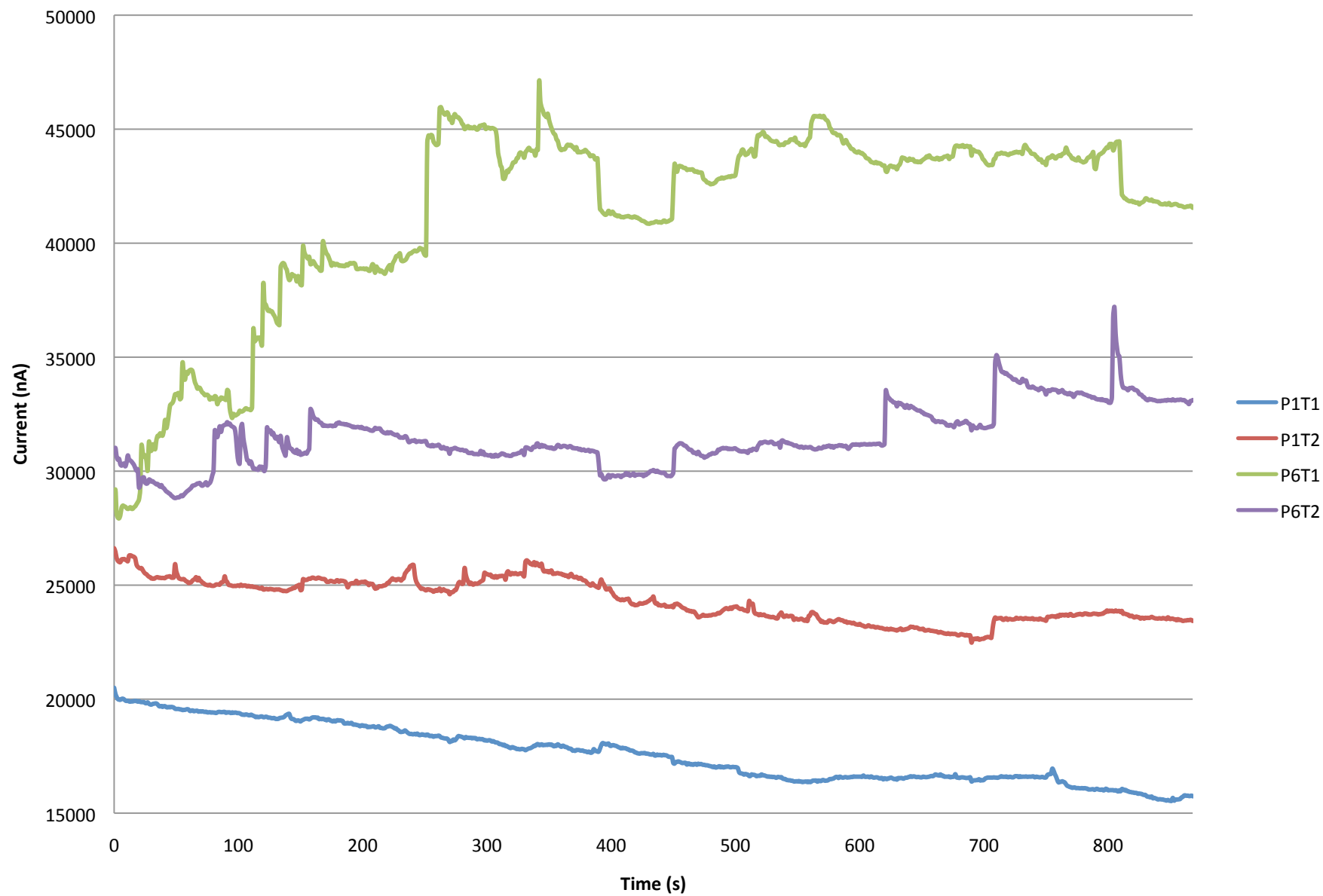




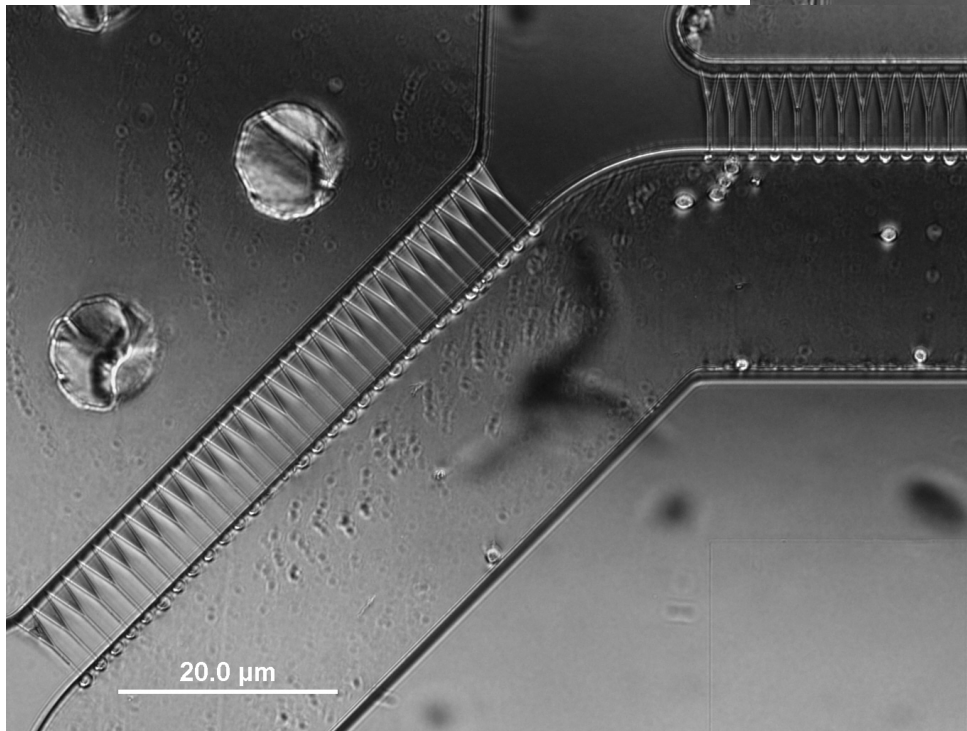
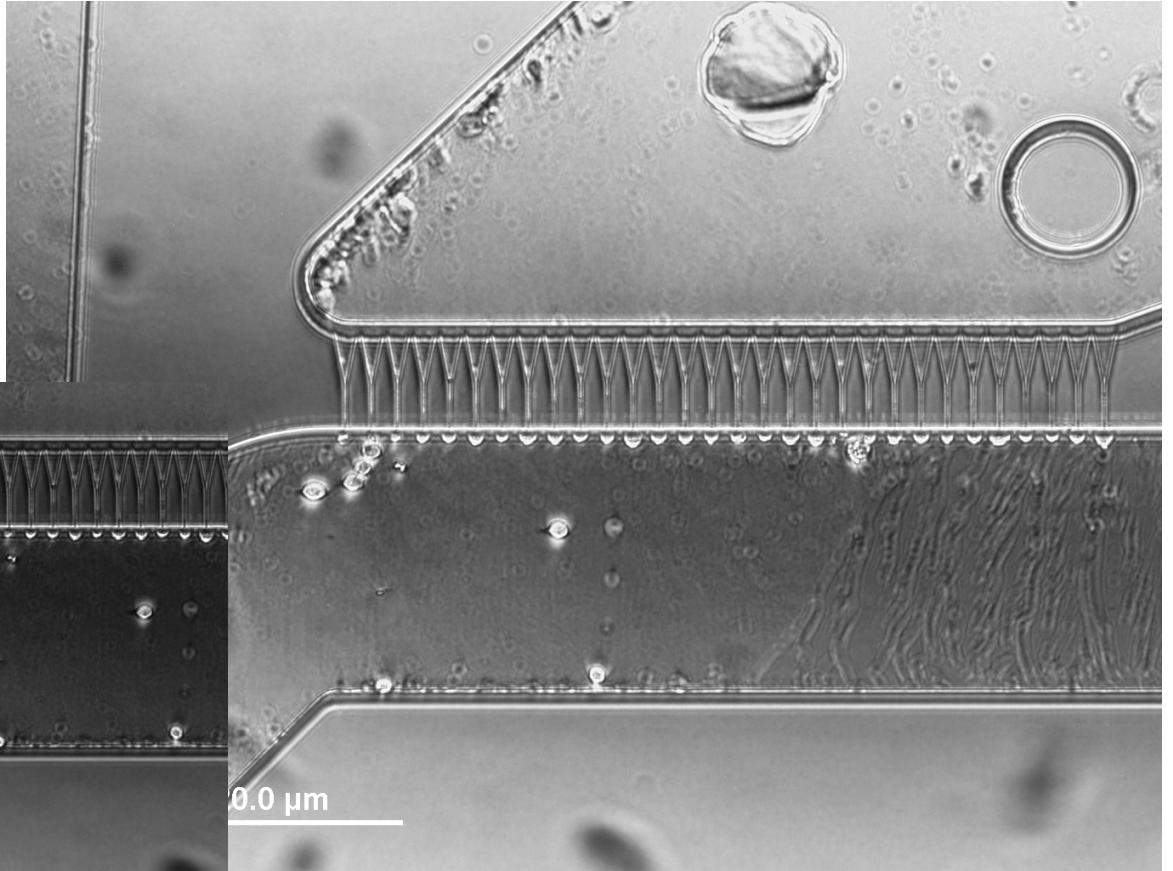
## Data Acquisition, T1

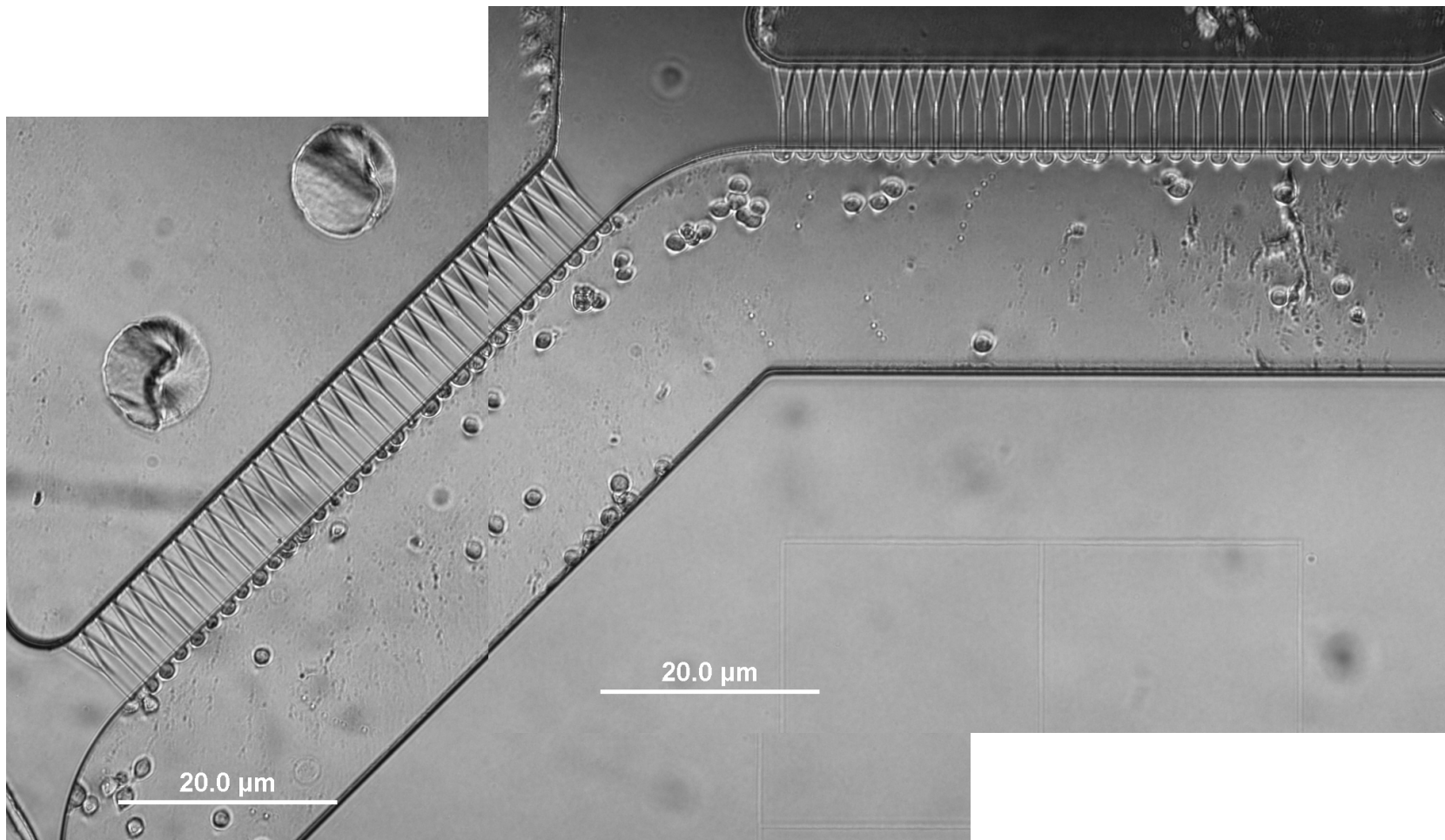


## Data Acquisition



# Images





# Future Work

- Quantify current fluctuations
- How to treat data
- PAMAM Dendrimers
  - Nanoscale drug delivery

# Works Cited

- Petit-Zeman, Sophie. "The Nobel Prize in Physiology or Medicine 1991 - Speed Read." *Nobelprize.org*. Sept.-Oct. 2006. Web. 07 Aug. 2011. <[http://nobelprize.org/nobel\\_prizes/medicine/laureates/1991/speedread.html](http://nobelprize.org/nobel_prizes/medicine/laureates/1991/speedread.html)>.
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- <http://www.bem.fi/book/04/04.htm>
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Questions?