

MRI-Compatible Bioreactor for Cancer Cells

➤ Team Members:

- Jeff Hlinka (Team Leader)
- Sam Paulsen (Communicator)
- Sarah Reichert (BWIG)
- John Byce (BSAC)


➤ Client:

- Dr. Sean Fain

➤ Advisor:

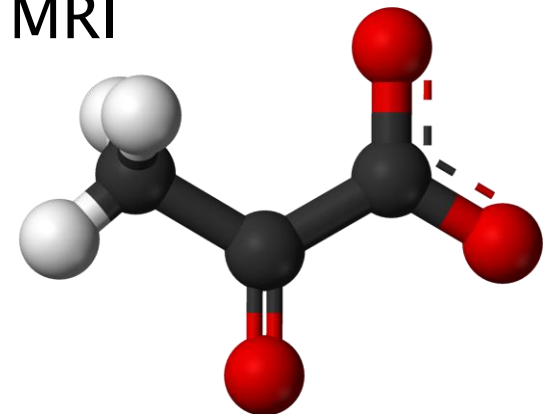
- Dr. Brenda Ogle

Outline

- ▶ Client Description
 - ▶ Motivation
 - ▶ Problem Statement
 - ▶ Current Devices
 - ▶ Design Specifications
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- 

Client Description

- ▶ Sean Fain
 - Associate Professor, Dept. of Medical Physics
 - UW School of Medicine and Public Health
- ▶ Research: tracking cell metabolic rates
 - Uses ^{13}C pyruvate to visualize with MRI



http://en.wikipedia.org/wiki/Pyruvic_acid


Motivation

- ▶ Tracking metabolic rates using ^{13}C pyruvate
 - Describes severity and extent of malignancy
 - Aids treatment planning and prognoses
- ▶ Technique must first be verified *in vitro*



<http://medicineworld.org/stories/lead/11-2009/predictive-value-of-lung-cancer.html/>

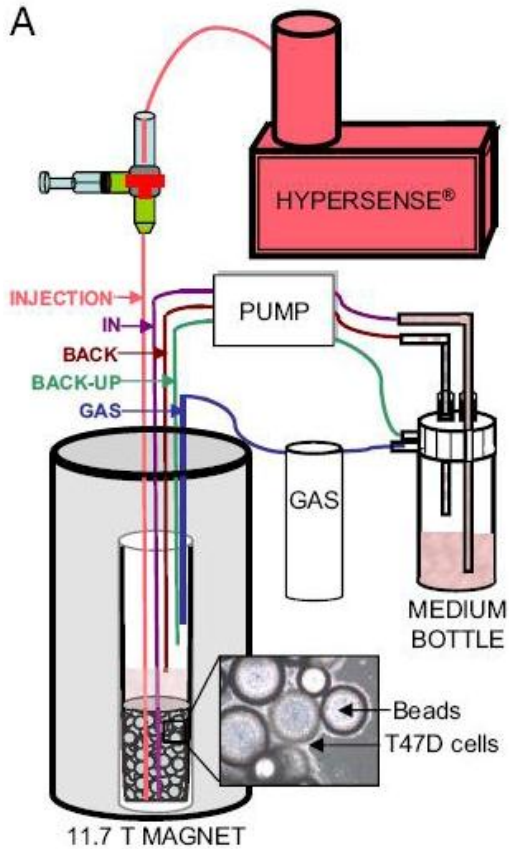
Problem Statement

- ▶ Create MRI-compatible bioreactor to support cell culture
 - Pump system
 - Sensing system
 - Heating mechanism
 - Injection port for gases and substances
 - ▶ Provide essential nutrients for high cell densities
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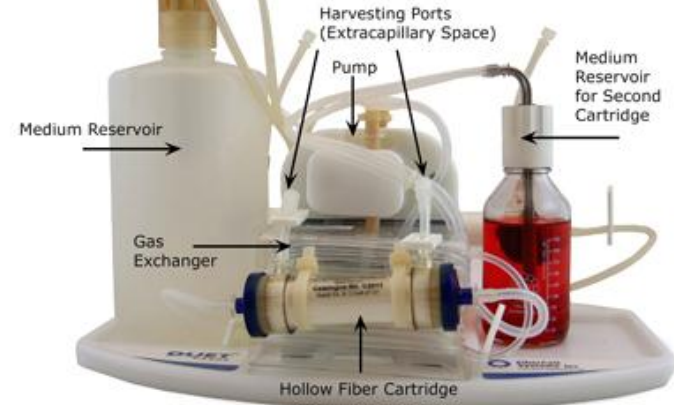
Current Devices

Hyperpolarized ^{13}C Spectroscopy

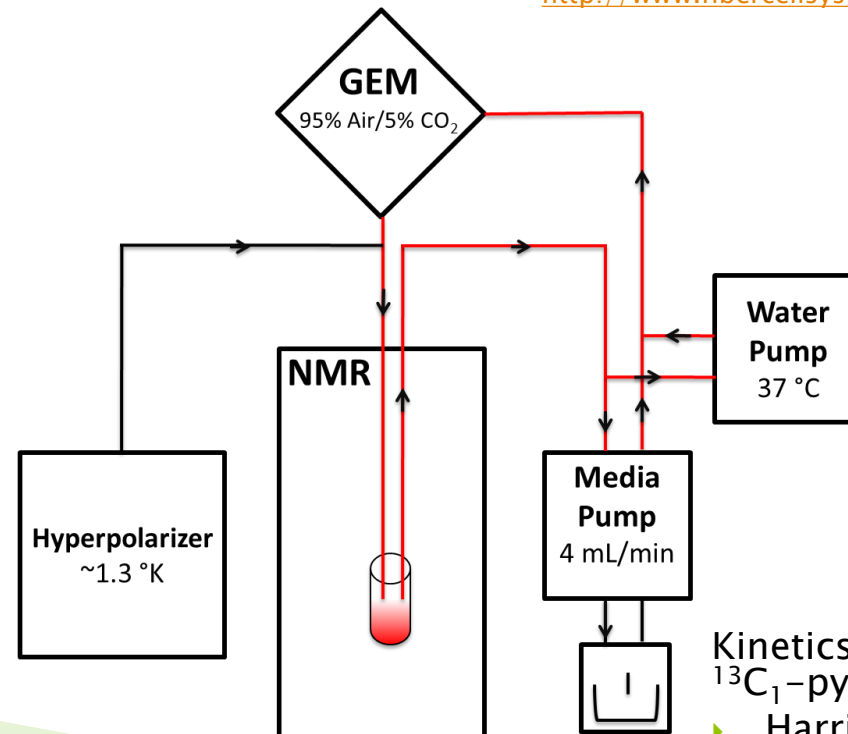
► Keshari et al., 2010



Fiber Cell System




<http://www.fibercellsystems.com/>



Kinetics of Hyperpolarized $^{13}\text{C}_1$ -pyruvate

► Harris et al., 2009

Design Specifications

- ▶ Compatible with horizontal MRI configuration
 - ▶ Maximum cartridge diameter: 10.8 cm
 - ▶ Compatible with cell culture
 - ▶ Senses and controls cellular conditions
 - pO_2 , pCO_2 , pH, temperature
 - ▶ Even dispersal of injected substances
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Design Alternatives

▶ Sensing system

- Electrodes
- Mass flow controller
- Flow through monitor

▶ Pumping system

- Diaphragm
- Peristaltic
- Duet
- Syringe

Sensing System: Electrodes

- ▶ pO_2
 - Reaction produces current $\propto [O_2]$
 - Range: 0–50 mg/L
 - Accuracy: $\pm 5\%$
- ▶ pH
 - Ion-specific with H^+ membrane
 - Range: 0–14 pH
 - Accuracy: ± 0.01



http://www.coleparmer.com/catalog/product_view.asp?sku=3580100&pfx



http://www.instrumart.com/assets/108/Extech-DO705_200

Sensing System: Mass Flow Controller

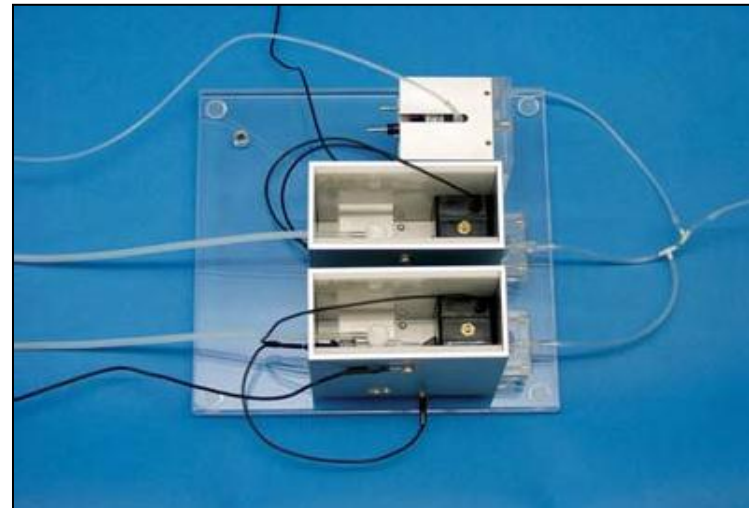
- ▶ Senses and controls pO_2 , pCO_2 , and pH
- ▶ Accuracy: $\pm 3\%$
- ▶ Flow rate: 0 to 3,000 mL/hr
- ▶ Requires external electrodes



<http://www.bioreactors.eu/en/instruments/massflow/>

Sensing System: Flow Through Monitor

- ▶ Monitors pO_2 , pCO_2 , pH, and temperature
- ▶ Accuracy: $\pm 0.2\%$
- ▶ Response time: < 90 s
- ▶ Can be autoclaved
- ▶ Closed loop system

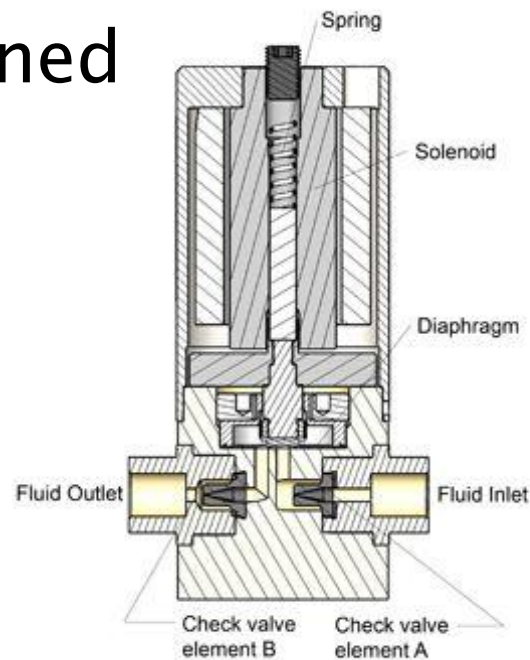


Sensing System Design Matrix

	Electrodes	Mass Flow Control	Flow Through Monitor
Cost (30)	30	12	0
Accuracy (20)	18	17	15
Precision (20)	16	17	18
Cytotoxicity/ Sterilizability (20)	13	15	19
Feasibility (10)	7	4	9
Total	84	65	61

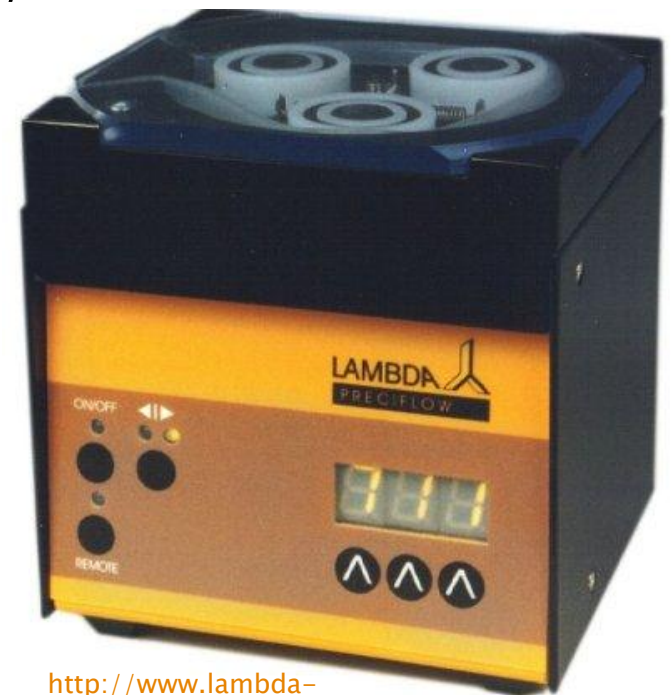
Pumping System: Diaphragm

- ▶ Suctions and pressurizes
- ▶ Material: fluorinated polymers
- ▶ Flow rate: predetermined
 - 288, 360 or 432 mL/hr



Pumping System: Peristaltic

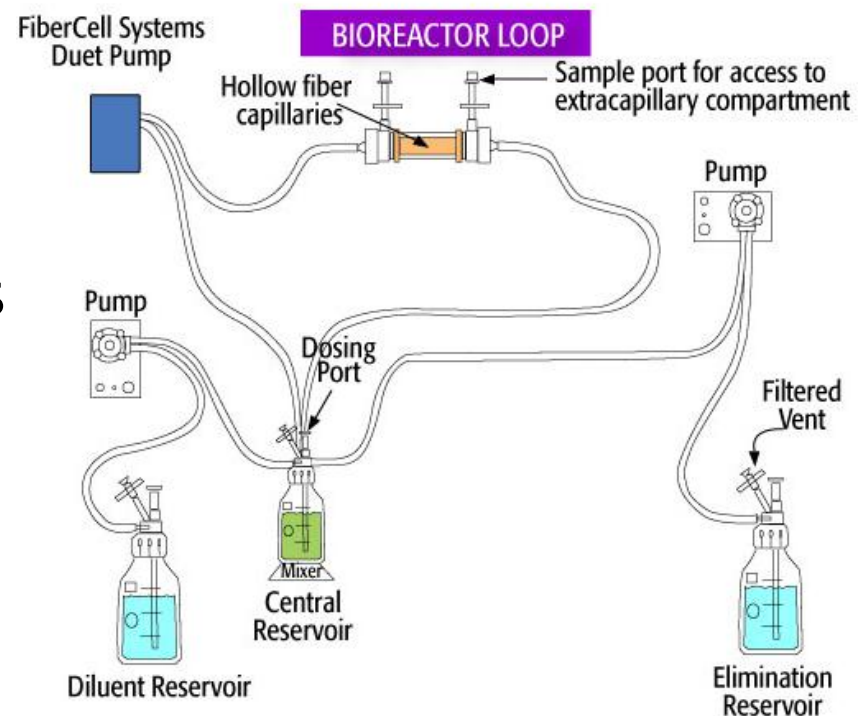
- ▶ Positive pressure displacement
 - Rollers compress tube to cause flow
- ▶ Flow rate: 0.01 to 3,000 mL/hr
- ▶ Low shear force
- ▶ Only tubing contacts fluids



<http://www.lambda-instruments.com/pdf/LAMBDA-peristaltic-pumps.pdf>

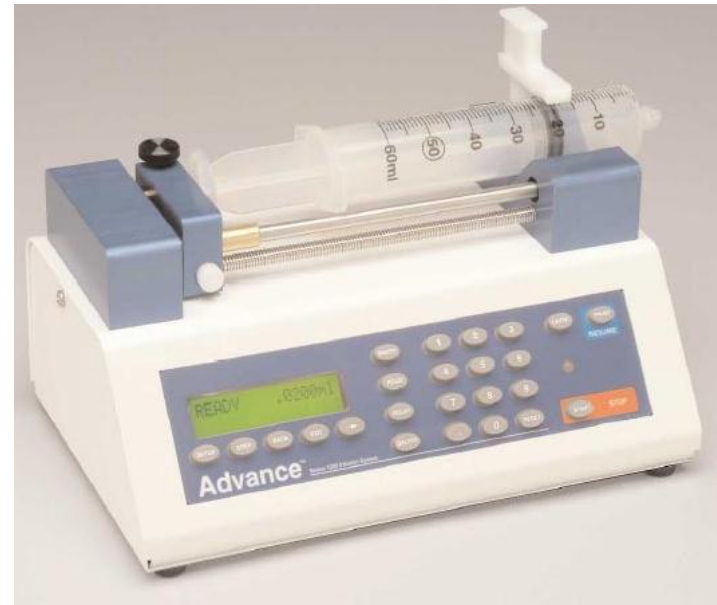
Pumping System: Duet

- ▶ Hybrid of diaphragm and peristaltic
- ▶ Flow rate: 60 to 8,400 mL/hr
- ▶ Frictionless pumping
 - Squeeze tubing
 - Two one-way check valves
- ▶ Continuous flow



Pumping System: Syringe

- ▶ Infuses and withdraws fluid
- ▶ Flow rate: 0.001 μL to 8,400 mL/hr
- ▶ Not continuous flow



<http://www.southpointesurgical.com/infusion.aspx>

Pumping System Design Matrix

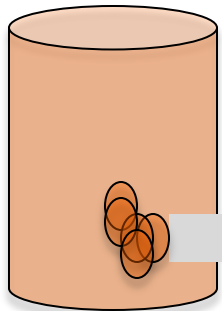
	Diaphragm	Peristaltic	Duet	Syringe
Cost (25)	20	22	12	16
Cytotoxicity/ Sterilizability (25)	20	23	25	25
Ease of Use (10)	7	8	9	7
Flow (Continuity & Rate) (20)	12	15	18	8
Physiologic Stress (20)	12	17	18	8
Total	71	85	82	64

Final Design

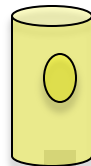
▶ Components

- Sensing system: electrode probes
 - Using LabVIEW to analyze data (open loop system)
- Pump: peristaltic pump

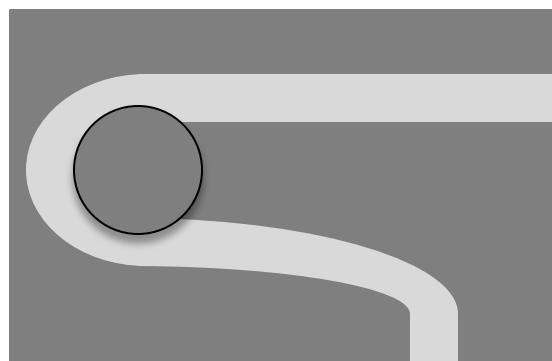
Oxygen Pump



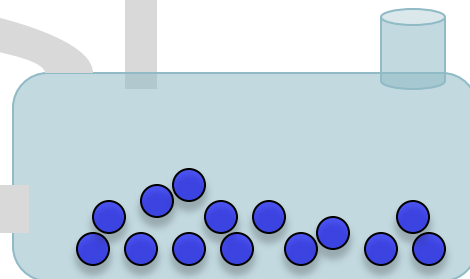
Pyruvate Injection Port



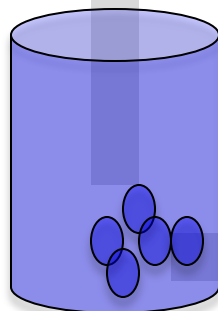
Sensing Electrodes



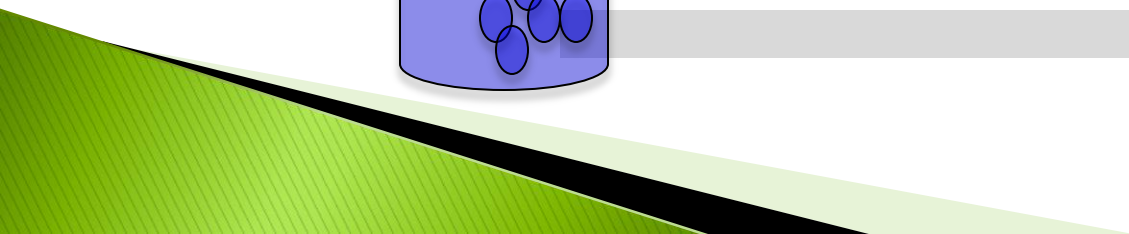
Peristaltic Pump



Bioreactor Cartridge



Cell Culture Media



Future Work

- ▶ Constant temperature system
- ▶ Testing
 - Sensing accuracy
 - Using known standards
 - Compare with other devices
 - Dispersion
 - Using colored dyes

Projected Costs

Item	Cost
Electrodes	\$310.00
Electrode Circuitry	\$125.00
Peristaltic Pump	\$350.00
Bioreactor Cartridge	\$250.00
Tubing and Connectors	\$100.00
Total	\$1,135.00

Acknowledgements

- ▶ Dr. Brenda Ogle
 - ▶ Dr. Sean Fain
 - ▶ Matt Smith
 - ▶ Jeremy Gordon
 - ▶ Cell Scaffold Team
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Questions?

