National Institute of Biomedical Imaging and Bioengineering

Technology Platform #4

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soon to be…
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American Institute for Medical and Biological Engineering

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Concepts

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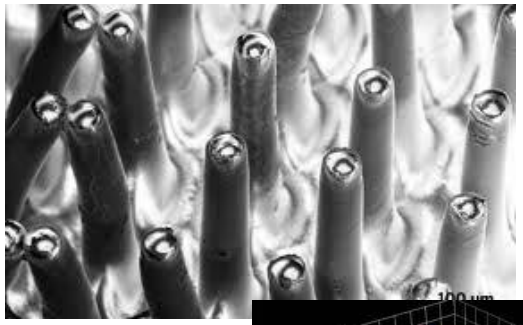
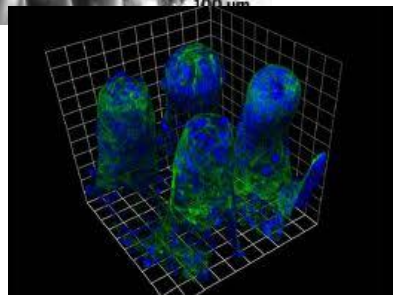
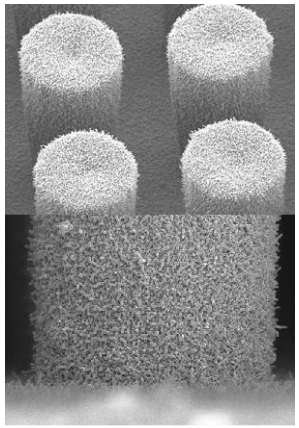
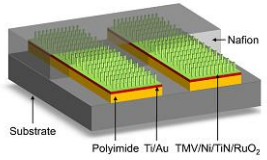
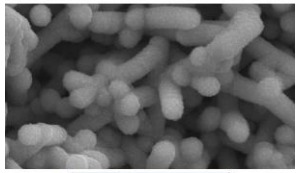


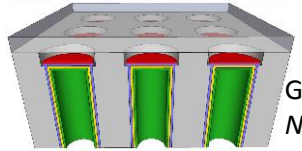


Sung *et al*, *Lab Chip,* 2011; 11, 389-392

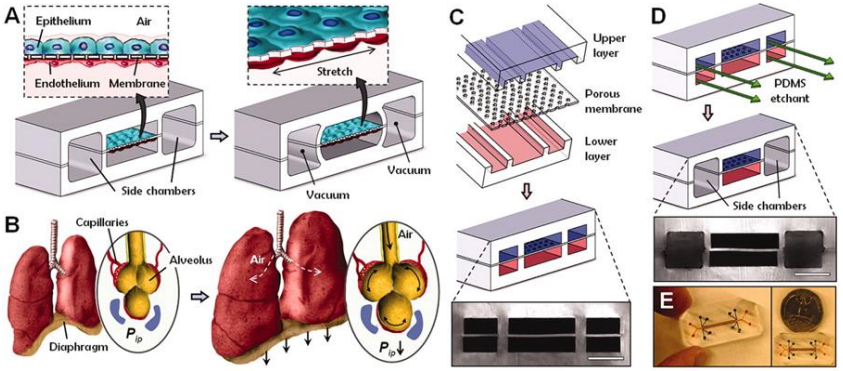




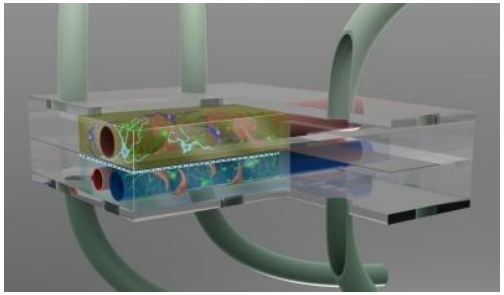




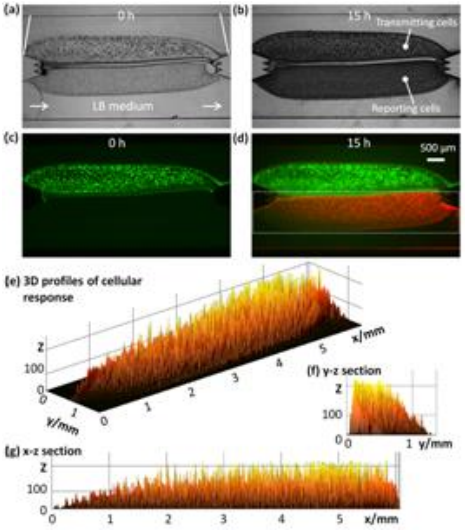
Gerasopoulos *et al*, 2012, *ACS Nano*, 6, 6422-6432



Huh et al. *Science* 2010;328:1662-1668



Wikswo *et al*, Brain Chip
Vanderbilt Institute for Integrative Biosystems Research and Education



Luo et al, 2012,
Biomaterials, 33, 5136-5143

Reproducibility

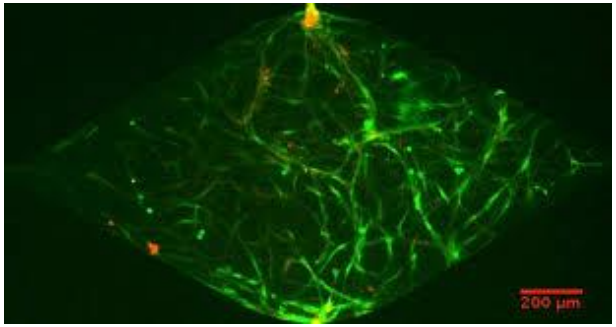
- Issues that revolve around reproducibility
  - Tissue
  - Matrix
  - Vasculature
  - Analytical Measurements

You make the mix and things assemble, but is the method derived with an idea of developmental biology? (perhaps liken to molecular biology kits…the "kit" includes the cells that are there and the system has been assembled). It might not matter how it works, but that it works in a reproducible manner. Does pharma use this? The approach to take might be "qualify" the reagents. Perhaps this in vitro "kit" is a reagent in the screening campaign. Is it measurable? Consistent?

Note 3D is very important here.

What would happen if you used cells from adult tissue? They might not work…did it with HUVEC and they work fine.

Is it a technology in search of a mission? But, can't sell it that way…need to be asked by industry.



From Anne Plant

- Repeatibilty (replicates)
- Reproducibility (different days, locations)
- Ruggedness (sensitivity to assay parameters)
- Dynamic range
- Limit of Detection
- Specificity

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Human Variability

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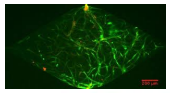
- Intra-organ variability
- Donor variability
- Personalized approach?



How many cell lines or origins are needed? What will the system be used for? For pharma company to create context. We are developing technologies based on interest in mechanisms; we need to develop context.

If you can get well controlled repeatable device into the hands of the masses, you can get these out there into the world. Perhaps move these to Agilent, Waters, etc. The device is relatively cheap.

Is this going to be amenable to finding the population that can not take Vioxx? Maybe not Vioxx, but maybe Lipitor that have accumulated toxicities or also for acute issues like cancer chemotherapies. Things that would take a year of dosing might be revealed in a shorter time.

Perhaps it's a more sensitized system…so imbalance shows up more quickly.

Perhaps you could take a tumor biopsy and seed several systems and screen anticancer drugs and go. Not making new drugs, but drugs already there and screen them.

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Number and Type of Organ Systems

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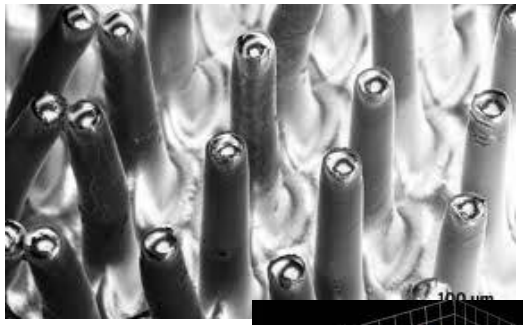

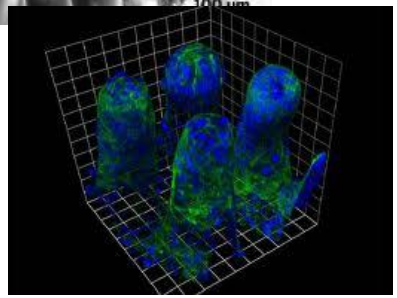

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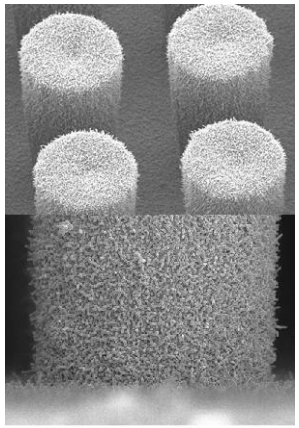

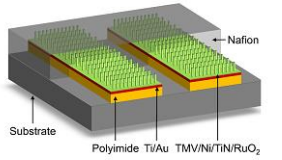

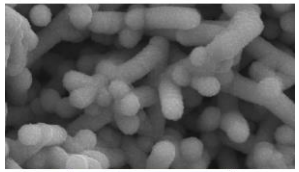

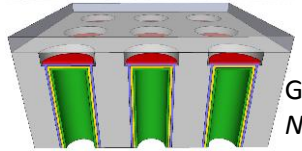

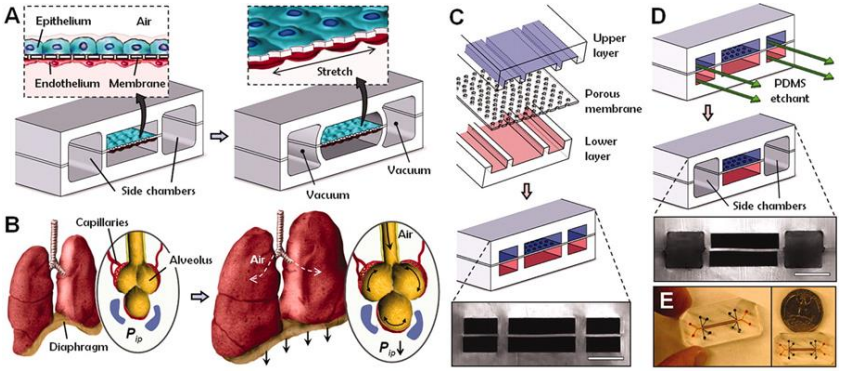

Lung
Huh et al. *Science* 2010;328:1662-1668

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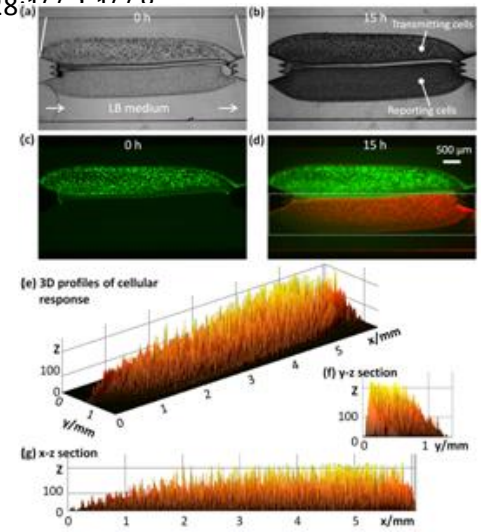
Number?

Priority?

Missing?

Liver?

Gerasopoulos *et al*, 2012, *ACS Nano*, 6, 6422-6432



Microbiome
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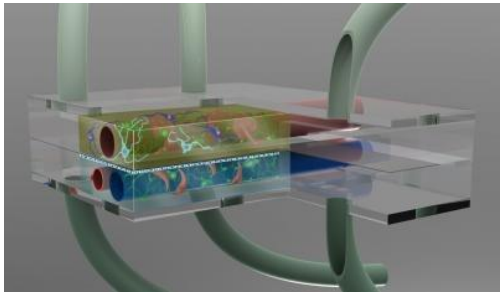

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Number and Type of Organ Systems

Represent all the organs or tissues? Generate metabolites…they get dissolved in the medium, then liquid to cell ratio needs to be incorporated. Fat can be represented by a polymer that absorbs.

Fat speroids…can you kill fat cells and not muscle?

Personalized treatments...where you find optimal combinations of drugs to treat a tumor. Will insurance companies pay for it?

Could you test biomaterials using these systems. Prosthetic tissue? The challenge these normally take a long time to materialize. Biocompatibility is a major issue.

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In situ Measurements

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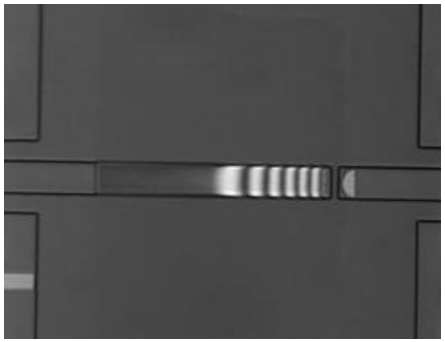
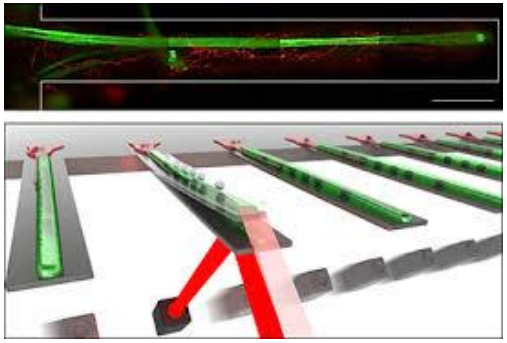
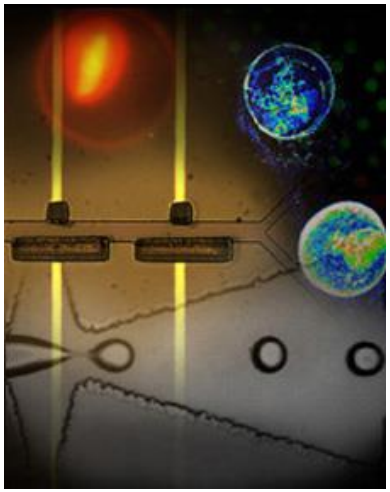
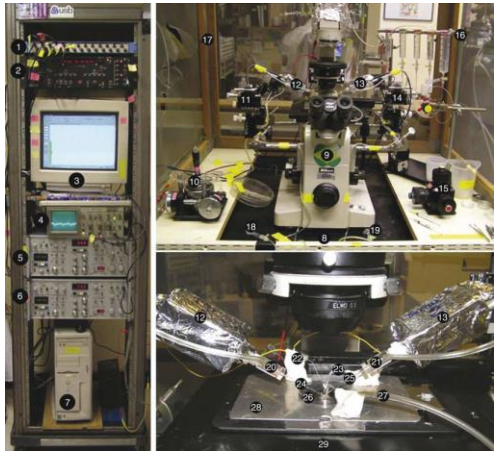
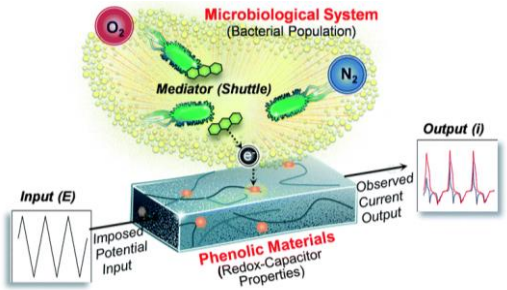








Beyond fluorescence –
What are issues?
Can they be placed in best locations?
Are they flexible and sensitive?



In situ Measurements

In line measurements…small chip with equipment that is large. Needs to go into the biosensing world. Either implant in tissue and then record information.

Enzymes? Separate line of investigation. Need to evaluate gene and protein expression, we don't have it.

Need to rethink indicator systems in matrix? FRET or optical based approaches for collagen. Biomarkers could be co-expressed.

John Wikswo – micro MS fingerprinting approach.

Fluorescently labeled cell types..put these into the system. Take a reading of all three colors each day.