ChE 4260: Biological Engineering

Project Presentation for Group 8

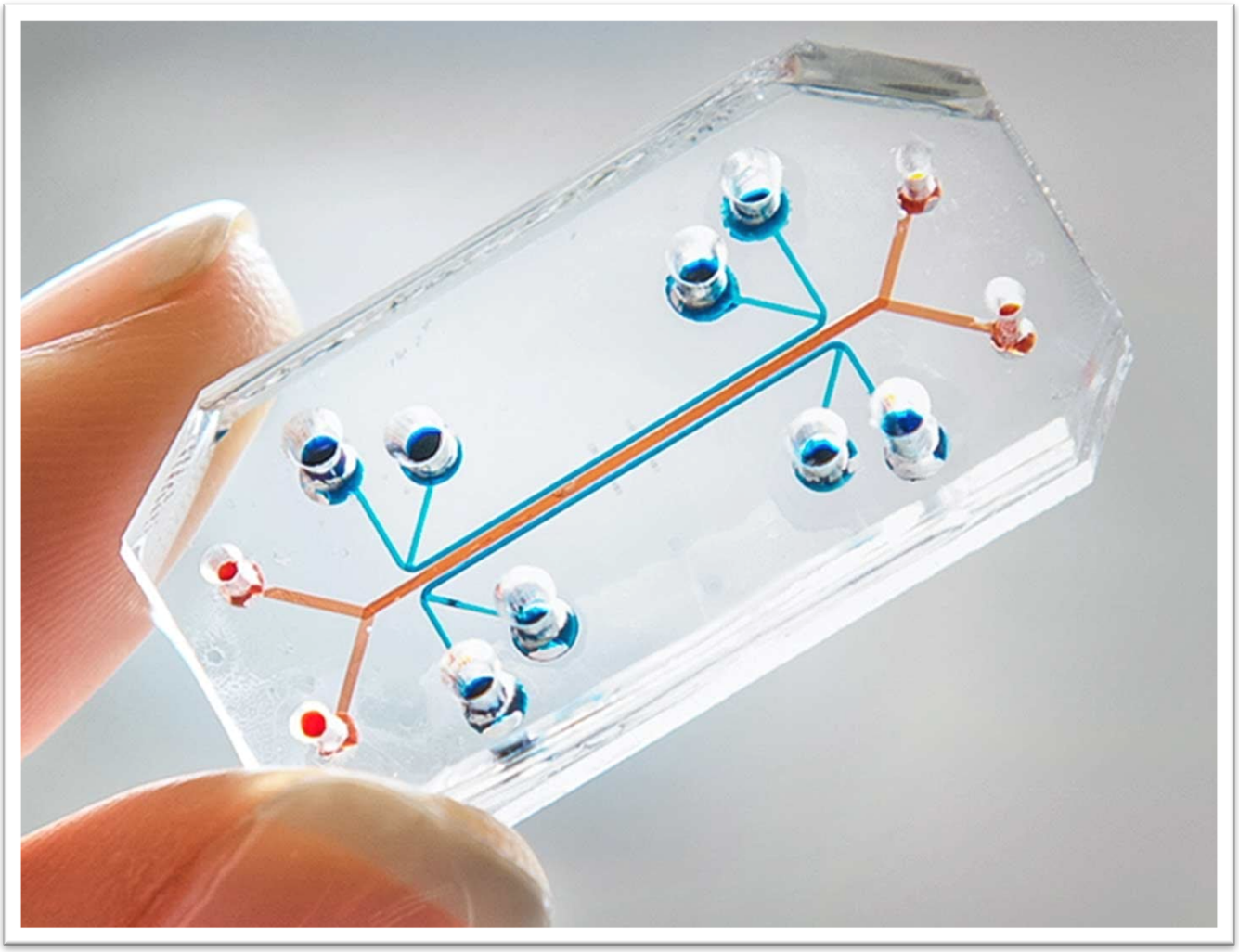

Figure 1) Lung–on–a–Chip. This microfluidics chip aims to simulate the breathing process in our lungs by lining its channels with human lung cells and capillary cells. Photograph Credit: Wyss Institute/Design Museum.

A New Type of Artificial Organ

Topic K: Organ – on – a – Chip

Presentation Group 8 includes:

Evan Casper, Mason Phelps, & Griffin Rose

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Introduction

Background. There is an unfathomable amount of complexity within just one cell. Biologists have spent decades studying and trying to understand a cell's inner workings. Cells compose tissues, tissues compose organs, and organs compose an organism. The complexity only increases in orders of magnitude as you go. For this reason, it is impossible to simulate organs on computer chips. Why fight a losing battle? Instead, biologists are beginning to physically simulate entire organs on microfluids chips.

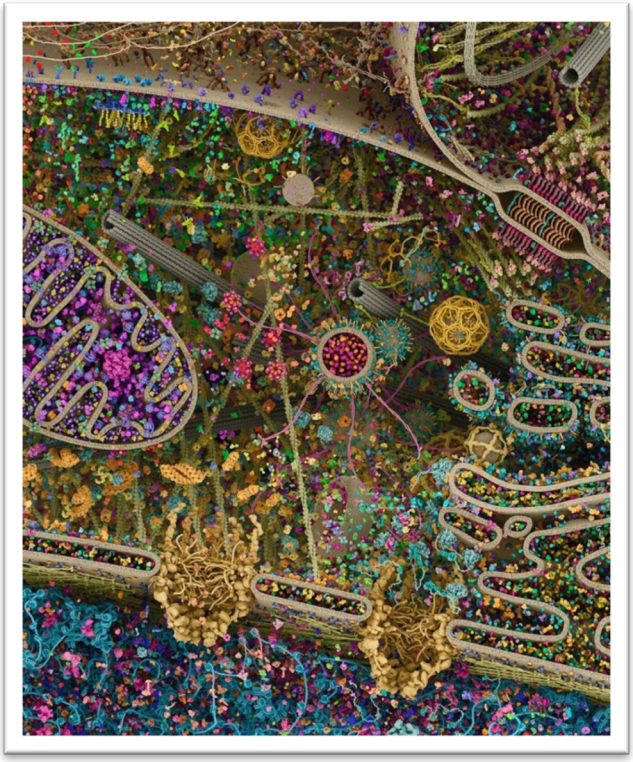

Figure 2) The Most Complete Model of A Cell. Created using datasets from X-Ray, NMR, and cryoelectron microscopy. NASA.

Why not study in-vivo? A common question that arises is why wouldn't we simply observe the organs provided by nature? There are a few reasons:

1. _____: It is difficult to study the cellular detail of how organs operate while they are within the organism they originate. Organs are an opaque mélange of tissues and fluids all clouding our perception of the organ.
2. _____: Even with minimally invasive techniques there is a risk of introducing contaminants that is better avoided with humans.

Brainstorming Activity: Discuss with your neighbors or in the chat on additional complications that may arise with in-vivo study.

Origins. Before organs, researchers were trying to develop laboratory on a chip devices (LOCs). As early as 1979, researchers were able to make a gas chromatograph on silicon wafers. The development of Organ–on–a–Chip devices was inspired by the benefits demonstrated by LOCs such as:

1. _____: lower volume of reagents and materials, and less waste.
2. _____: quicker thermo-chemical reactions.
3. _____.

Organ–on–a–Chip Devices *[YouTube Video]*

What are they? Organ–on–a–Chip devices (OOCs) are ____-_____ cell cultures that use hollow _____ lined with human organ cells to _____ simulate the complexity of organs.

Brainstorming Activity: Discuss with your neighbors or in the chat about possible complications that could arise when developing an organ-on-a-chip device.

Why do we care? Within the early stage of drug development, animal models are the default way of gathering in-vivo data that would predict human _____. In many cases, however, these animal tests are long, costly, and most of all controversial. OOCs provide an alternative to phase out animal drug testing completely. Eventually, _____ devices may end animal testing of products like make-up as well. By allowing researchers see what is happening as contaminants are introduced into the system, OOCs will expedite drug development most of all.

Lung–on–a–Chip

Modeling. The function of the lungs is most notably _____ between blood and air. Any model attempting to recreate this would need to reproduce key properties of the human alveolar-capillary interface such as

1. _____ Properties: separates two fluids, blood and air, via a membrane.
2. _____ Properties: facilitating gas exchange.
3. _____ Properties: being able to expand and contract with air inhalation.

One such model was created by Wyss Institute for Biologically Inspired Engineering at Harvard. Their fabrication was composed of three microchannels created using microchip fabrication techniques. In the center channel, a porous, flexible membrane 10 microns thick divides the center channel into two. One side of the membrane is lined with human _____ (lung) cells, while the other with human _____ (capillary blood vessel) cells. The lung cell-lined side of the membrane has air pumped through it, while the blood vessel cell-line side of the membrane has a fluid mimicking blood pumped through it. Pumps are used to expand and contract the outer channels which mimic the breathing of real lungs.

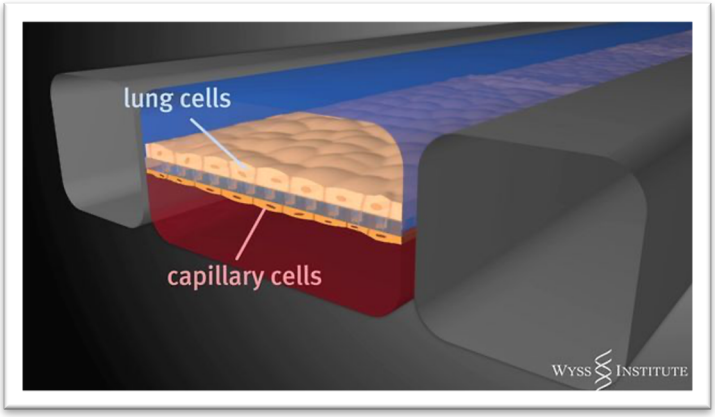

Figure 3) Lung–on–a–Chip. The human alveolar-capillary interface model developed by Wyss Institute.

Validation. Researchers inflicted injuries to the cells to fully evaluate the biological accuracy of their model.

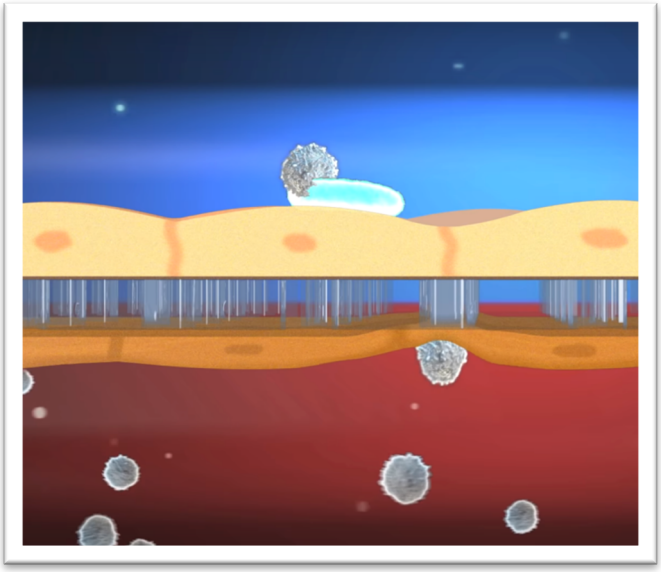

Figure 4) Pulmonary Infection. Leukocytes transmigrating to phagocytize a bacterium. Wyss Institute.

- _____: When the Wyss researchers injected E–coli bacteria into the air channel and white blood cells into the blood channel, neutrophils were detected in the blood compartment three hours later. This means the white blood cells had successfully transmigrated from the vascular microchannel to the alveolar channel where they then phagocytized the bacteria.

Application. Researchers believe the potential value of this lung-on-a-chip system will be in the detection of possible harmful compounds. For example, researchers hope to learn more about the health risks of nanoparticles by observing the model's response.

Shortcomings. While this model is much more accurate than previous simplified models, the researchers admit their model doesn't fully reproduce native alveolar epithelial cell responses. One criticism from pharmaceutical companies is that bodily processes and organs are isolated when using a singular chip and will not capture the _____ that an animal test might.

THINKING BIG FOR THE FUTURE

Brainstorming Activity: With the advancement of technology that will come in the future, what are possible improvements that can be made to the organ–on–a–chip process? Discuss with your neighbors or in the chat.

Human–on–a–Chip. As more accurate OOCs are developed and the field matures, milestones in research would be to create organ _____ and eventually an entire Human–on–a–Chip simulation. This would allow testing to be done for treatments that might be too risky for human trials. This chip would take the individual organs on a chip and incorporate them to work with one another to create a system that better represents the human body as a whole. This provides great advantages in the process of _____ _____ as scientists would be able to see how a drug reacts within the entire body. They might be able to point out possible issues or side effects that could arise when everything is incorporated.

PUBLICATIONS CITED

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