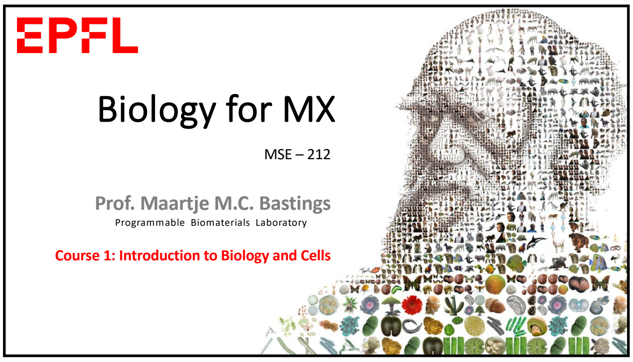
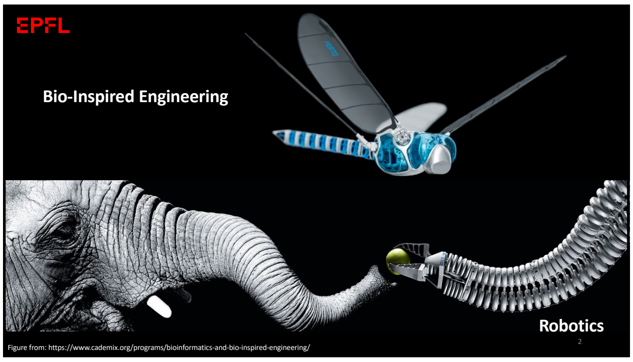
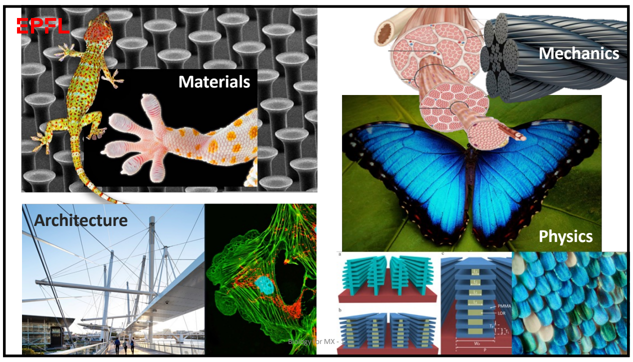

EPFL
Biology for MX
MSE – 212
Prof. Maartje M.C. Bastings
Programmable Biomaterials Laboratory
Course 1: Introduction to Biology and Cells

1


EPFL
Bio-Inspired Engineering
Robotics
Figure from: https://www.cademix.org/programs/bioinformatics-and-bio-inspired-engineering/

2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Materials
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Architecture
Physics

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Course Content

BLOCK 1: Introduction and engineering with cellular components

Lecture 1.	Intro to biology and cells	(February 21)
Lecture 2.	Proteins and protein based materials	(February 28)
Lecture 3.	DNA and DNA-based materials	(March 6)
Exercise 1.	*Proteins, peptides and DNA*	*(March 13)*

BLOCK 2: Inter- and intracellular action

Lecture 4.	ECM, adhesion and artificial matrices	(March 20)
Lecture 5.	Virus, antibodies and immune engineering	(March 27)
Lecture 6.	Bacteria	(April 10)
Exercise 2.	*Nanoparticles and Scaffolds*	*(April 17)*

BLOCK 3: Physics of biological action

Lecture 7.	Receptors and targeting	(April 24)
Lecture 8.	Endocytosis	(May 1)
Lecture 9.	Signaling and communication	(May 8)
Exercise 3.	*Engineering functionality*	*(May 15)*
Lecture 10.	Revision and conclusion	(May 22)
Open office.	*Questions, discussion, exam prep*	*(May 29)*

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Organization

Lectures 2x45 min, 3 blocks of 3 lectures, followed by 1 week of exercises – recordings (hopefully) available the week after, current recordings from 2021 available but different.

Mediaspace subscription: https://mediaspace.epfl.ch/channel/MSE-212+Biology+for+Engineers/30273/subscribe

Exercises + Q&A with TA's on 4 occasions Wednesdays 8.15-10h CE15

Virtual open office: TBA, 1 or 2 weeks before the exam

Background reading on Moodle (scientific articles) provide more depth on a subject

Exam: 3h written in final session

English: the course and exam are in English, you can ask questions in French

Preparation: This course forms the preparation for MSE 471: Biomaterials for MX

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Exercises

These help to prepare you for the exam

Answers sheets will be provided after the session.

TAs = Pauline Hendrickx (pauline.hendrickx@epfl.ch)
Pitt Meyer (pitt.meyer@epfl.ch)
Shujie Li (shujie.li@epfl.ch)

Pauline

Pitt

Shujie

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Demonstrations - recorded

BLOCK 1: Introduction and engineering with cellular components
Lecture 1 DEMO: Microscopy of cells
Lecture 3 DEMO: DNA and DNA-based materials

BLOCK 2: Inter- and intracellular action
Lecture 4 DEMO: Cytoskeleton and tensegrity

BLOCK 3: Physics of biological action
Lecture 8 DEMO: Endocytosis
Lecture 9 DEMO: Bacteria in action

https://mediaspace.epfl.ch/channel/MSE-212+Biology+for+Engineers/30273/subscribe)

https://mediaspace.epfl.ch/media/DEMO%201%2C%20Demo%201%3A%20cell%20division%20and%20organelle%20staining%20/0_039ck1ur

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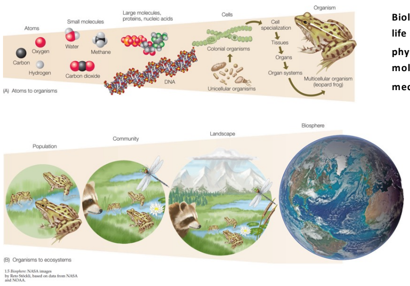
Biology



Biology is the natural science that studies **life** and **living organisms**, including their **physical structure**, **chemical processes**, **molecular interactions**, **physiological mechanisms**, **development** and **evolution**.

Despite the complexity of the science, certain unifying concepts consolidate it into a single, coherent field.

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Objectives of this Course

In this course, we explore the concepts and fundamentals needed to understand how **biology** can be used to **draw inspiration** from for **materials engineering challenges**. Through touching the basics of (cell) biology and the physics of biological phenomena, you will be equipped for future more nuanced and detailed (bio)materials discussions. This course is foundational for MSE 471: Biomaterials for MX

BLOCK 1: Introduction and engineering with cellular components
We learn about the main components found in cells and how they are used as synthetic bioinspired materials

BLOCK 2: Inter- and intracellular action
We explore physical phenomena that give the cell mechanical properties and how this translates to materials design.

BLOCK 3: Physics of biological action
We learn about the interaction of cells with other biological entities and their importance for materials engineering.

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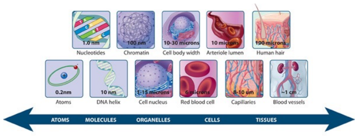
Cells

A Cell is the basic membrane-bound unit that contains the fundamental molecules of life and of which all living things are composed. A single cell can be a complete organism in itself, such as a bacterium or yeast. Other **cells** acquire specialized functions as they mature and form tissues.



Cells can vary between **1 micrometer (µm) and hundreds of micrometers** in diameter. Within a cell, DNA (chromatin) is approximately 100 nanometers (nm) wide, whereas the nucleus that encloses this DNA can be approximately 100 times bigger (about 10 µm).

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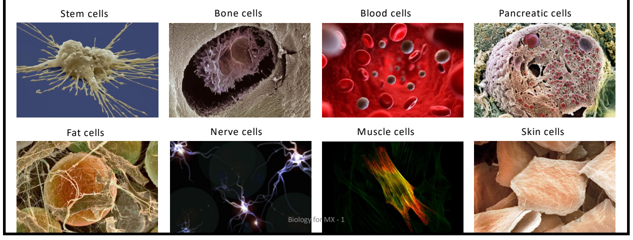
Cells in Numbers

The average human is made up of approximately **37.2 trillion cells**

37 million-million : 37.000.000.000.000

There are about **200 different cell types**, for example:



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What can engineers do?

"the most complicated watch in the world"

2,800+ components

Swiss watchmaker
Vacheron Constantin

A single car:

about **30,000 parts**, counting down to the smallest screws.

JumboJet

A jumbo airplane has about **5,000,000 parts**

A computer

the independent electronic parts range in the **thousands** and if you count single transistors as a part in itself you get ***millions*** of parts.

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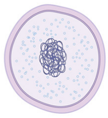
Size and Growth

As a cell **grows**, its **volume** increases much more rapidly than its **surface** area. Since the **surface** of the cell is what allows the entry of **oxygen**, large cells cannot get as much oxygen as they would need to support themselves.

In other words, as a cell grows, it becomes less efficient.

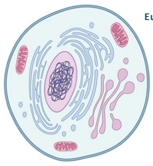
One way to become more efficient is to **divide**; another way is to **develop organelles that perform specific tasks**.

These adaptations lead to the development of more sophisticated cells called **eukaryotic cells**.



Prokaryotic

Bacteria and single cell organisms



Eukaryotic

Animals and plants

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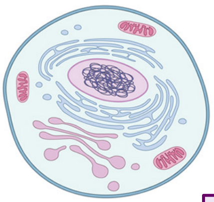
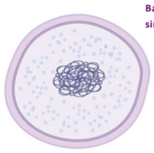
Eukaryotic vs Prokaryotic Cells

Animals and plants



Bacteria and single cell organisms



A **eukaryotic cell** has membrane-enclosed DNA, which forms a structure called the **nucleus** (note the purple DNA enclosed in the pink nucleus). A typical eukaryotic cell also has additional membrane-bound **organelles** of varying shapes and sizes

Prokaryotes are unicellular organisms that lack organelles or other internal membrane-bound structures. Therefore, they do not have a nucleus, but, instead, generally have a single chromosome: a piece of circular, double-stranded DNA located in an area of the cell called the nucleoid.

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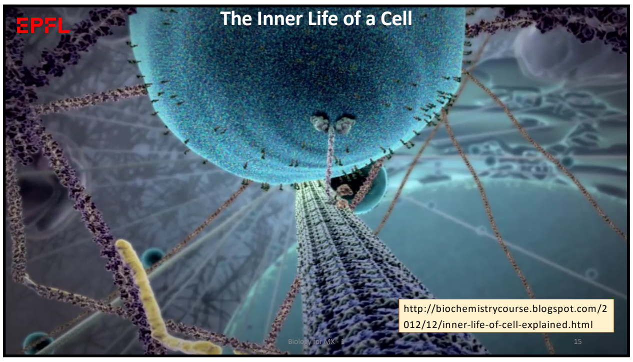

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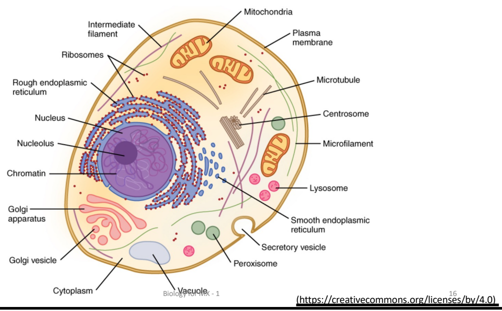
The Cell



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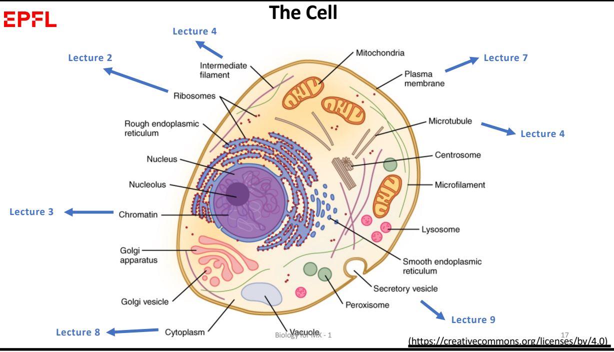
The Cell



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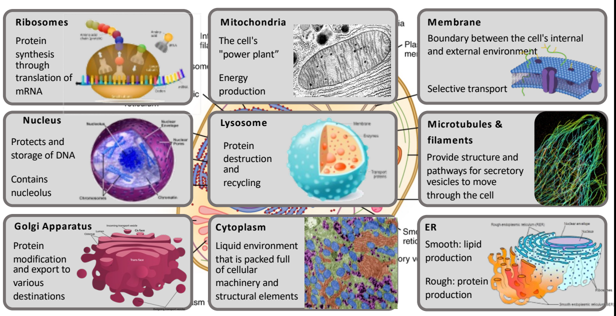
The Cell



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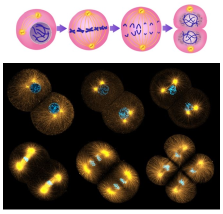
DEMO: The Cell in Action

TA: Armand Kurum

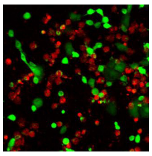
DEMO 1:

Cell division



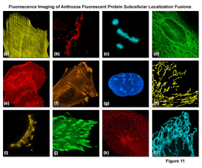
Cell viability

What could kill a cell?



Cell compartments

- Mitochondria
- Membrane
- Nucleus
- Actin Filaments



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After the break:

How can MATERIALS be used for the:

Engineering of Artificial Cells… ?

Engineering of Artificial Organs… ?

Engineering of Artificial Humans… ?

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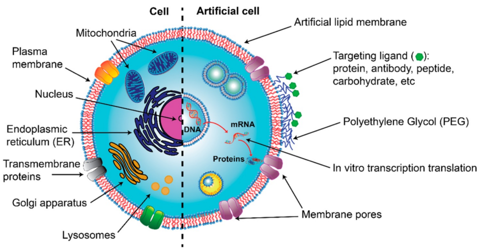
Engineering of Artificial Cells… ?



https://doi.org/10.1021/acsnano.7b03245

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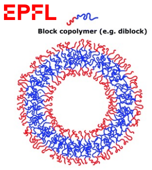
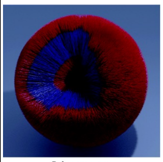
Polymersomes

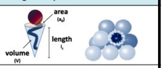
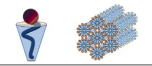
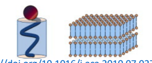



Polymersome

Comparable to lipids, **synthetic block co-polymers** can be made with hydrophilic / hydrophobic molecules.

Polymersomes are artificial vesicles with radii ranging from 50 nm to 5 µm or more.

They are made using **amphiphilic** synthetic block co-polymers to form the vesicle membrane and have a hydrophilic centre.

Aggregate type	Packing parameter	Surfactant geometry	Aggregate structure
Spherical Micelles	$\frac{V}{a_a l_c} < \frac{1}{3}$		
Cylindrical Micelles	$\frac{1}{3} < \frac{V}{a_a l_c} > \frac{1}{2}$		
Flexible Bilayers or Vesicles	$\frac{1}{2} < \frac{V}{a_a l_c} < 1$		
Planar Bilayers	$\frac{V}{a_a l_c} \sim 1$		

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https://doi.org/10.1016/j.aca.2010.07.027

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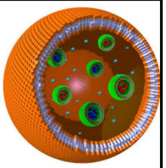
Artificial Organelles?



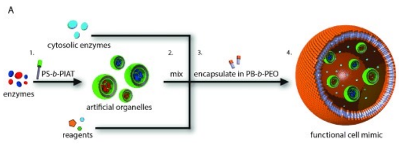
The concept of an artificial cell mimic:

(1) initial **encapsulation** of **different enzymes** in small polymersome nanoreactors

(1) mixing of the **organelle mimics, cytosolic enzymes, and reagents**

(2) encapsulation of the reaction mixture in big polymersome vesicles

(3) the functional cell mimic inside which enzymatic multicompartment catalysis takes place.



https://doi.org/10.1002/anie.201308141

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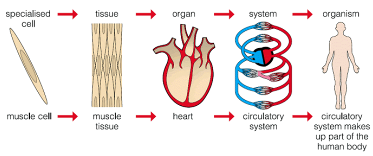
Cellular Organization

Cells in multicellular organisms **organize** themselves in such a way that enables a **greater structure** and **function**. Cells differentiate into **specific structures and functions**, and organize themselves as such into **tissues**. The different tissues can then form **organs** with yet a **higher level of structure and function**, and organs can work together in certain broad areas of the organism's structure and function by taking part in **organ systems**.



Does engineering these in the lab require materials with hierarchical organization?

***Structure* and *Function* through hierarchical organization of components**

https://thealevelbiologist.co.uk/organisation-under-the-microscope-cells-tissues-organs/

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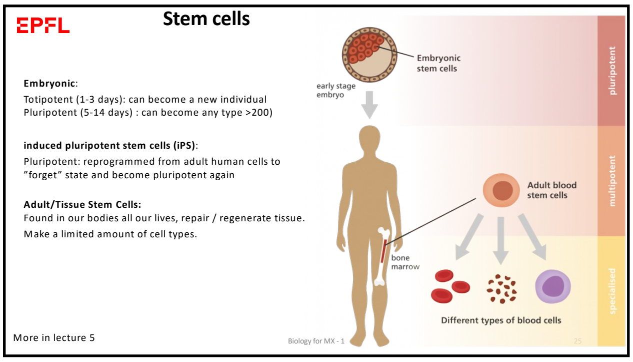
EPFL
Stem cells
Embryonic:
Totipotent (1-3 days): can become a new individual
Pluripotent (5-14 days) : can become any type >200)
induced pluripotent stem cells (iPS):
Pluripotent: reprogrammed from adult human cells to "forget" state and become pluripotent again
Adult/Tissue Stem Cells:
Found in our bodies all our lives, repair / regenerate tissue.
Make a limited amount of cell types.
More in lecture 5
early stage embryo
Embryonic stem cells
Adult blood stem cells
bone marrow
Different types of blood cells
pluripotent
multipotent
specialised
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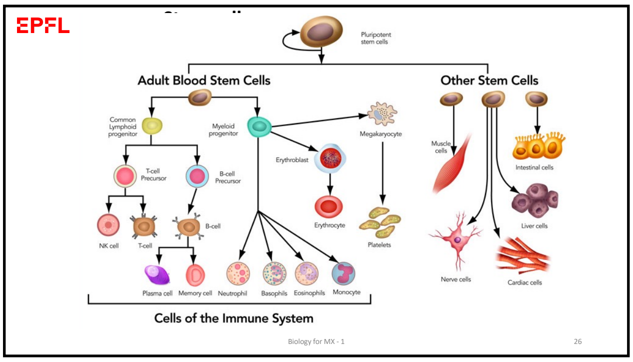
EPFL
Pluripotent stem cells
Adult Blood Stem Cells
Other Stem Cells
Common Lymphoid progenitor
Myeloid progenitor
Megakaryocyte
Erythroblast
T-cell Precursor
B-cell Precursor
Erythrocyte
Platelets
NK cell
T-cell
B-cell
Plasma cell
Memory cell
Neutrophil
Basophils
Eosinophils
Monocyte
Cells of the Immune System
Muscle cells
Intestinal cells
Liver cells
Nerve cells
Cardiac cells
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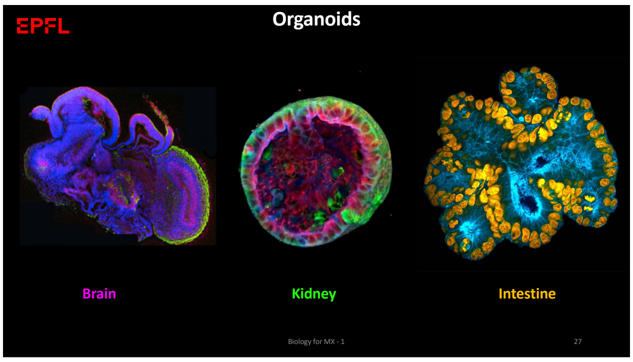
EPFL
Organoids
Brain
Kidney
Intestine
Biology for MX - 1
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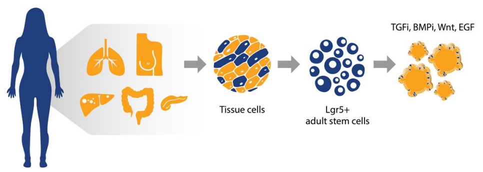
Engineering of cellular organization: Organoids

An **organoid** is a **miniaturized** and **simplified** version of an organ produced *in vitro* in three dimensions that shows **realistic micro-anatomy**.

Production of Organoids



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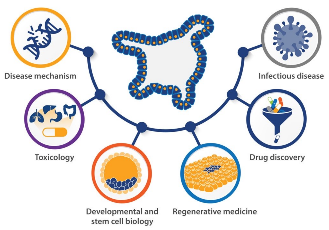
Engineering of cellular organization: Organoids

Applications in Engineering and Healthcare



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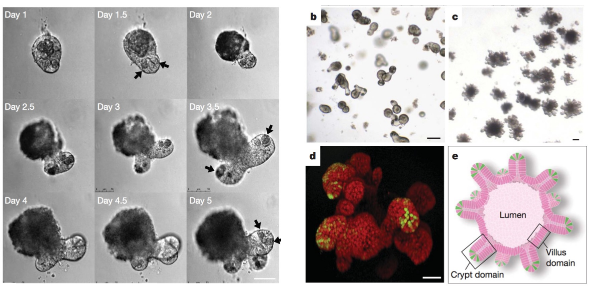
Intestinal Organoids



Vol 459|14 May 2009|doi:10.1038/nature07935

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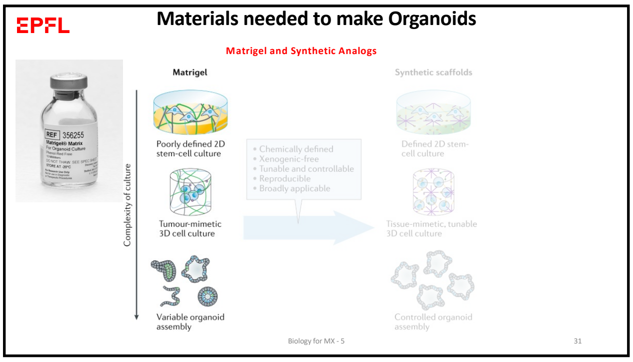
EPFL
Materials needed to make Organoids
Matrigel and Synthetic Analogs
Matrigel
Synthetic scaffolds
Poorly defined 2D stem-cell culture
Chemically defined
Xenogenic-free
Tunable and controllable
Reproducible
Broadly applicable
Defined 2D stem-cell culture
Complexity of culture
Tumour-mimetic 3D cell culture
Tissue-mimetic, tunable 3D cell culture
Variable organoid assembly
Controlled organoid assembly
Biology for MX - 5
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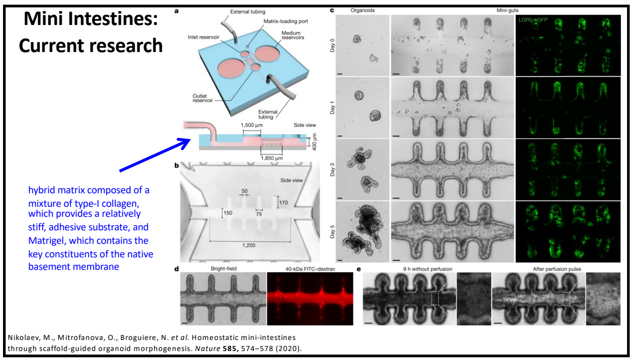
Mini Intestines:
Current research
hybrid matrix composed of a mixture of type-I collagen, which provides a relatively stiff, adhesive substrate, and Matrigel, which contains the key constituents of the native basement membrane
External tubing
Matrix-loading port
Inlet reservoir
Medium reservoirs
Outlet reservoir
Side view
Organoids
Mini-guts
Bright-field
40-kDa FITC-dextran
9 h without perfusion
After perfusion pulse
Nikolaev, M., Mitrofanova, O., Broguiere, N. et al. Homeostatic mini-intestines through scaffold-guided organoid morphogenesis. Nature 585, 574–578 (2020).

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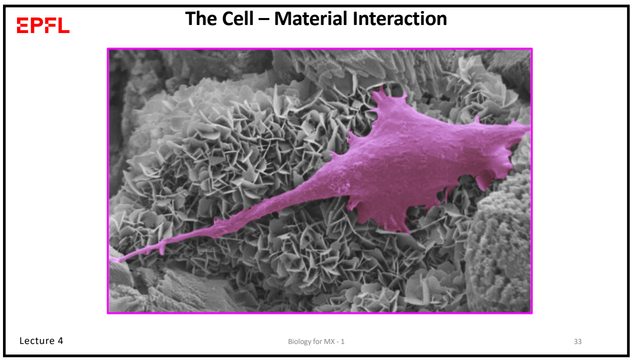
EPFL
The Cell – Material Interaction
Lecture 4
Biology for MX - 1
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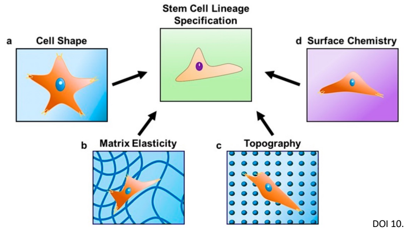
Engineering Challenges

Stem cell fate decisions can be affected by properties inherent to materials near the cell/material interface:



DOI 10.3390/gels2030020.

Lecture 4 Biology for MX - 1 34

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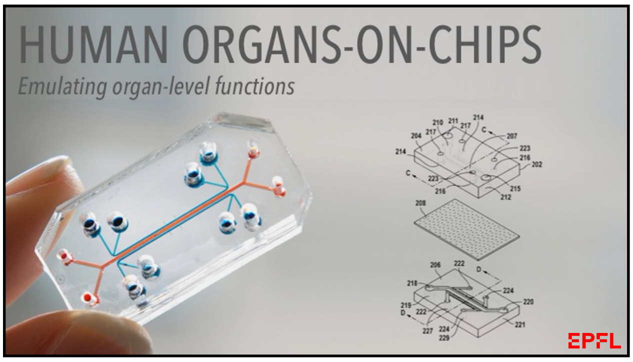

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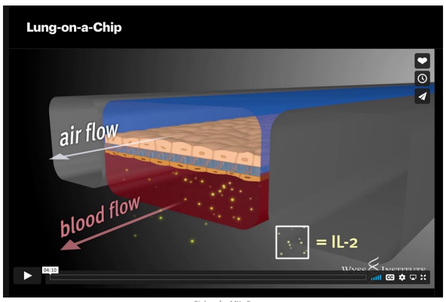
Lung on a Chip



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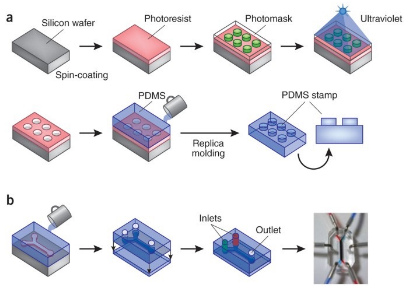
Lung on a Chip



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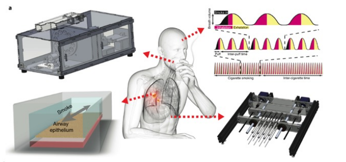
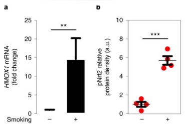
Effect of Smoking on a Chip





a,**b**, Real-time PCR and western blot analysis of induced antioxidant *HMOX1* gene expression (**a**) and increased phosphorylation of the regulator Nrf2 (**b**) with smoke exposure in mucociliated human bronchiolar epithelial cells on-chip.

Nat Protoc **15**, 183–206 (2020).
https://doi.org/10.1038/s41596-019-0230-y

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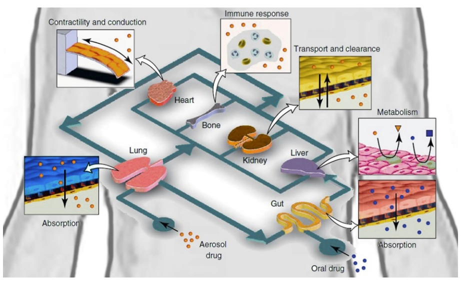
Human on a Chip?



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Impact of "on a chip" research

As an alternative to conventional cell culture and animal models, human organs-on-chips could **transform many areas of basic research and drug development**.

They could be applied to research on **molecular mechanisms** of organ development and disease, on **organ-organ coupling** and on the **interactions** of the body with stimuli such as **drugs, environmental agents, consumer products and medical devices.**

Fundamental questions

1) How microenvironmental cues regulate cell differentiation, tissue development and disease
2) how tissues heal and regenerate (e.g., mechanisms of control of angiogenic sprouting and epithelial sheet migration)
3) how different types of immune cells and cytokines contribute to toxicity, inflammation, infection and multi-organ failure.

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Conclusion

Biology is a **highly diverse field**, and we will cover only a very small subsection in this course.

We can learn enormous amounts from the **engineering efficacy** seen in natural materials.

Nature has **billion years of experience** in design optimization, it would be **foolish** not to draw inspiration from it.

Many **engineering solutions** can be found in **nature**.

It is therefore crucial as (material) engineers to **know some basics** of biology.

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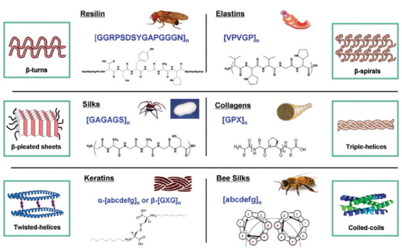
Next week

Lecture 2. Proteins and protein based materials



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