Cells on chips

Emilia Peltola, D.Sc.

31.3.2021

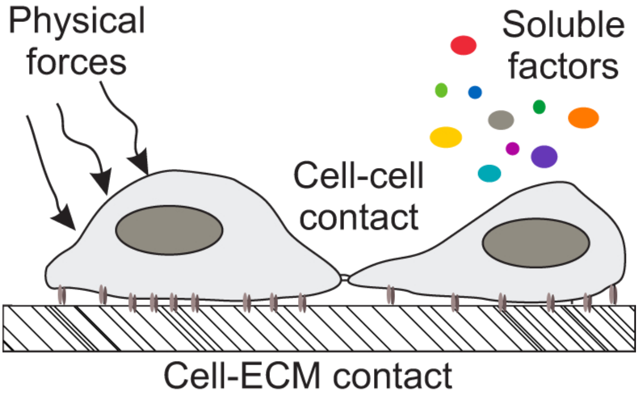
Aalto-yliopisto
Sähkötekniikan
korkeakoulu

- Why are bioMEMS great for influencing cells?
- How cells interact with materials?

Motivation

Automatic work
Accuracy
Price

Cell regulation



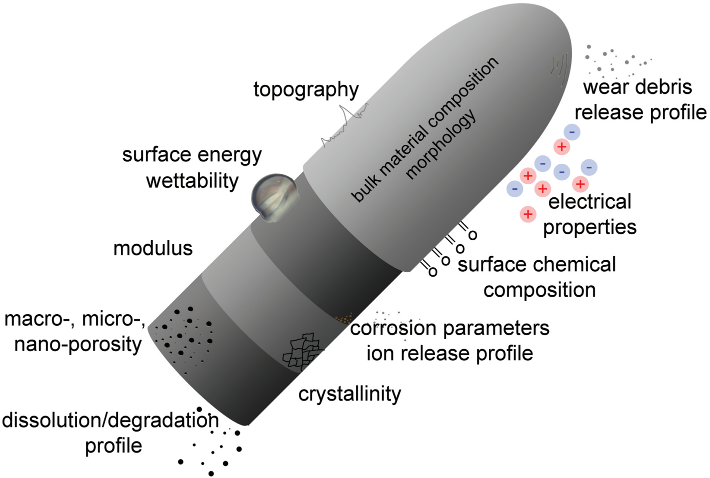
BioMEMS enable modification of all the relevant factors!

Cell-material contact

Better understanding of cell-material contact is needed for...

- tissue engineering
- implant integration
- understanding cancer
- cell-based sensors

Material properties influencing cells

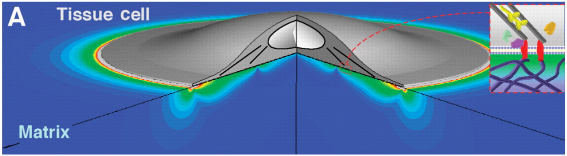


[Kaivosoja et al., 2011]

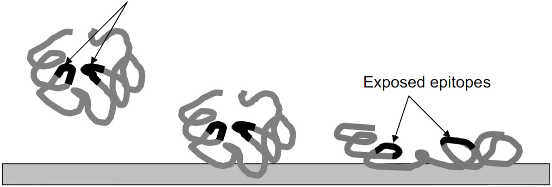
Mechanism of cell-material interaction

(3) Mechanotransduction

(2) Focal adhesion



[Discher et al., 2005]

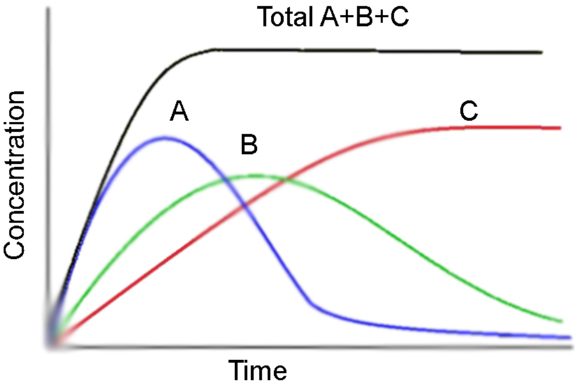


[Thevenot et al., 2008]

(1) Macromolecule adsorption

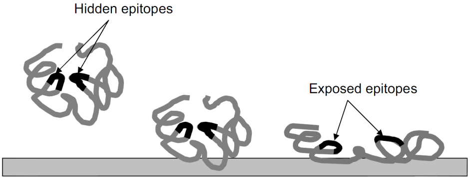
(1) Macromolecule adsorption

Type and amount



(1) Macromolecule adsorption

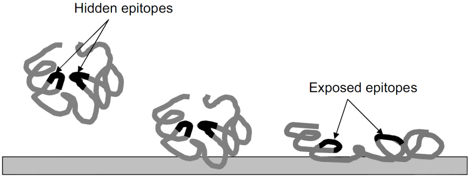
Functionality



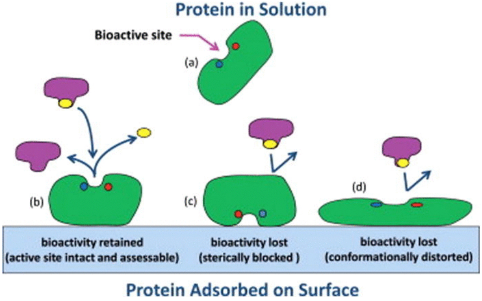
[Thevenot et al., 2008]

(1) Macromolecule adsorption

Functionality



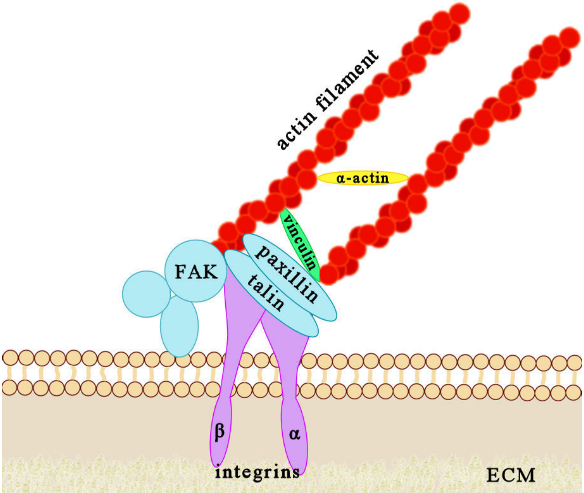
[Thevenot et al., 2008]



[Thyparambil et al., 2015]

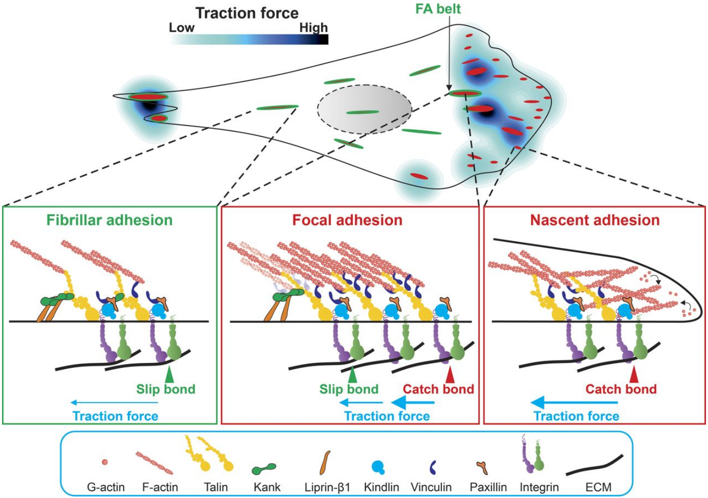
(2) Focal adhesion

Size range from 10 nm to 10 µm



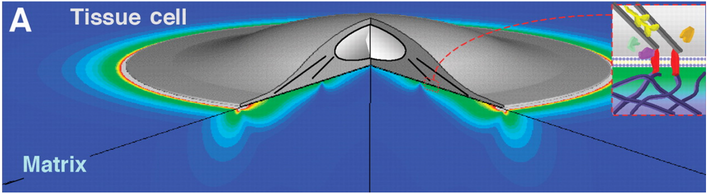
[Kaivosoja, 2008]

(2) (Focal) adhesion



[Sun et al., 2016]

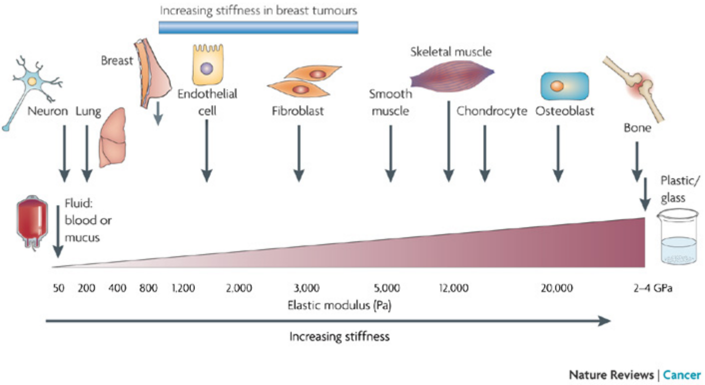
(3) Mechanotransduction



[Discher et al., 2005]

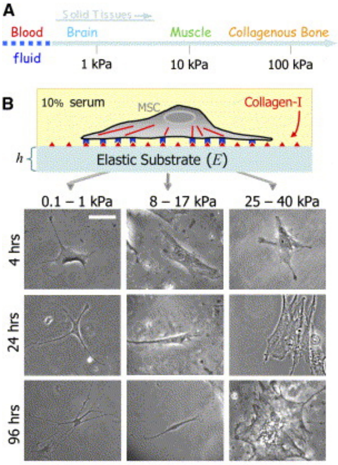
= mechanisms by which cells convert mechanical stimulus into chemical activity.

(3) Mechanotransduction



[Butcher et al., 2009]

(3) Mechanotransduction

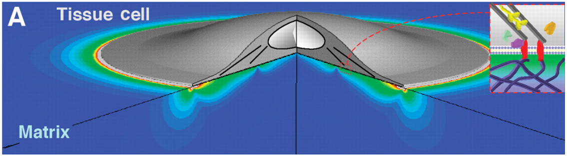


[Engler et al., 2006]

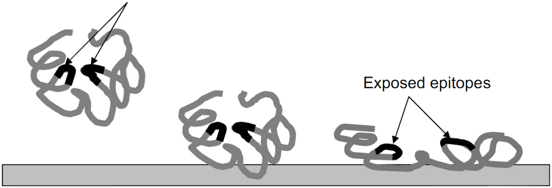
Mechanism of cell-material interaction

(3) Mechanotransduction

(2) Focal adhesion



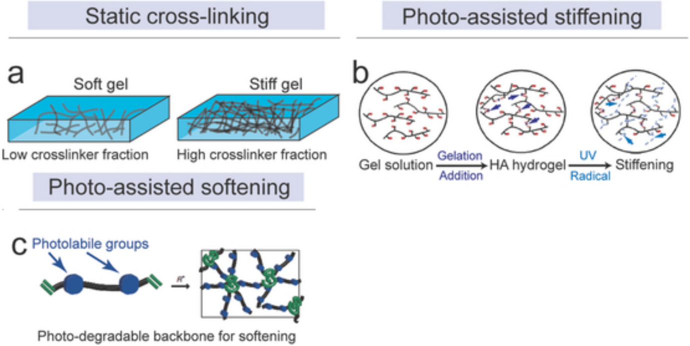
[Discher et al., 2005]



[Thevenot et al., 2008]

(1) Macromolecule adsorption

Modulation of substrate mechanics

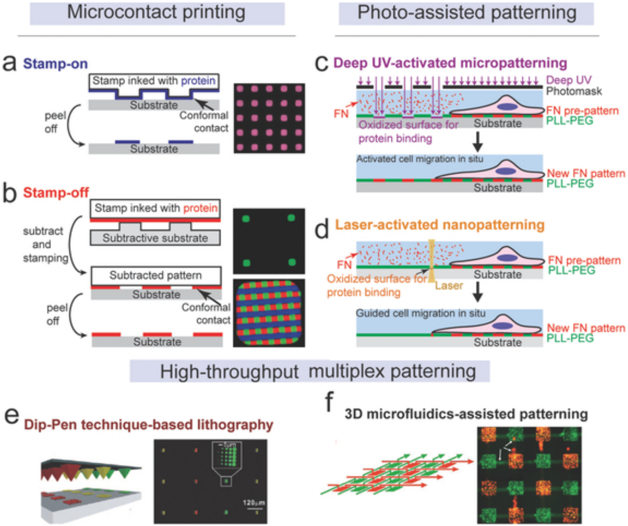


[Shao and Fu, 2014]

Surface features

Shape: pillars, pits, gratings, etc.
Dimensions: size, spacing, height
Arrangement: regular / irregular / random, isotropic / anisotropic

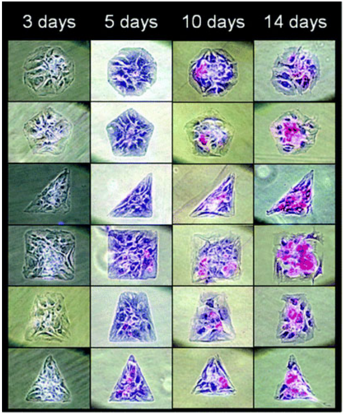
Generating adhesive cues



[Shao and Fu, 2014]

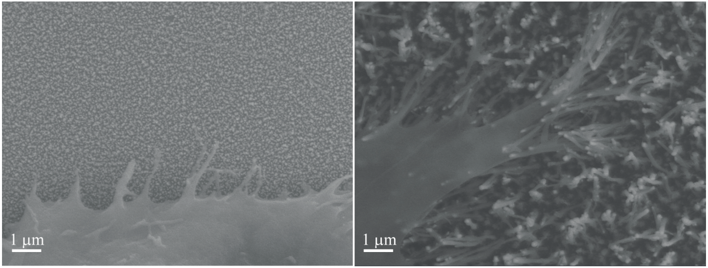
Examples: Shape

Understanding how to control stem cell fate using micro–fabricated surfaces:



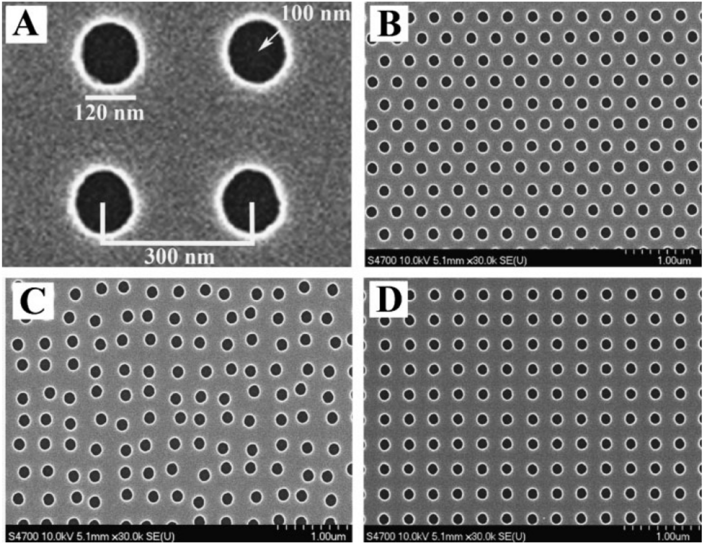
[Luo et al., 2008]

Examples: Dimensions



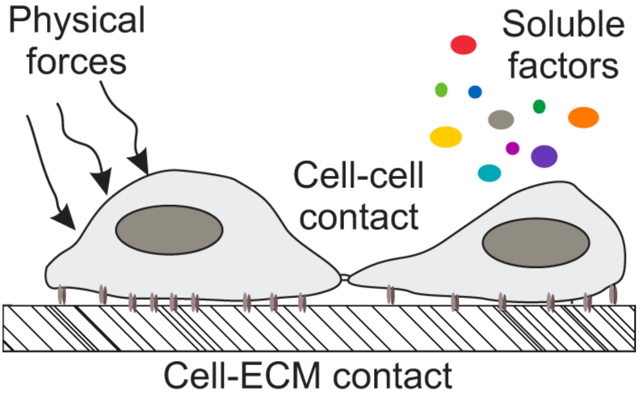
[Isoaho et al., 2018]

Examples: Surface arrangement



[Biggs et al., 2007]

Analyzing cells



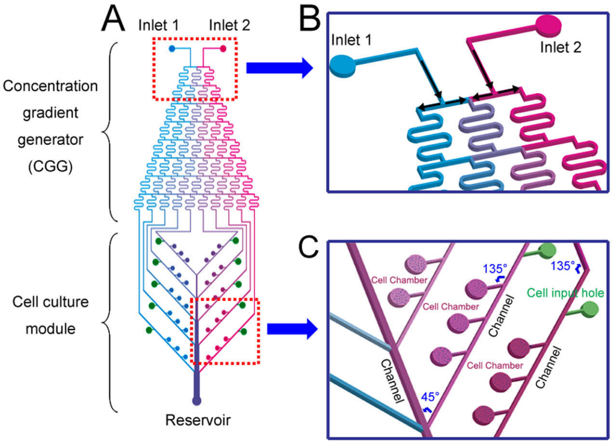
Why to control all of these?

Soluble factors

The control of soluble factors is useful for...

- drug screening
- optimizing cocktails for stem cell differentiation

Concentration gradient generator



[Tian et al., 2012]

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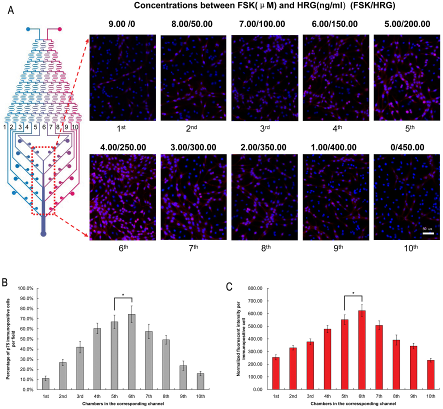
Concentration gradient generator

Stem cell differentiation into Schwann cells

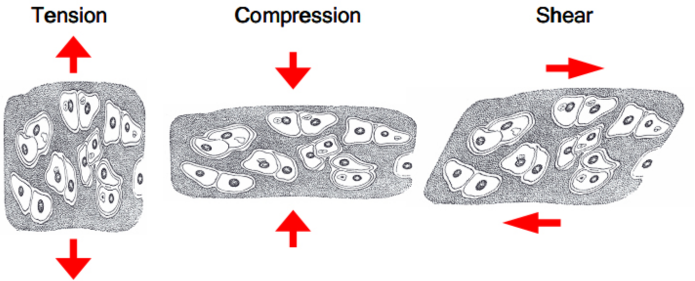


Concentration gradients of forskolin (FSK) and β-heregulin and the amount of positive Schwann cells
[Tian et al., 2012]

Physical forces

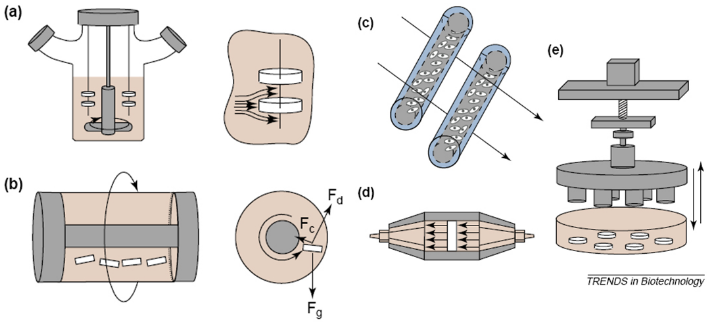
The control of physical forces is useful for...

- stem cell differentiation, tissue engineering



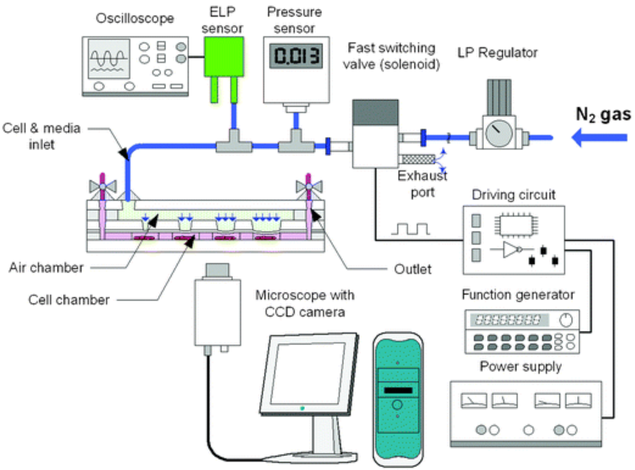
Cells are subjected to many forces *in vivo*

Conventional bioreactors



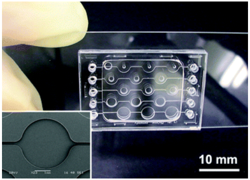
[Martin et al., 2004]

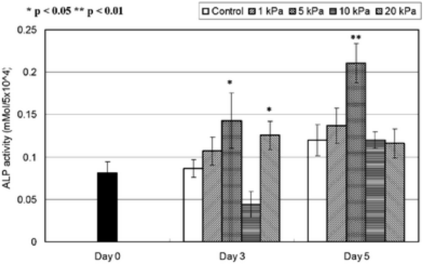
Example: Effect of pressure on bone formation



[Sim et al., 2007]

Example: Effect of pressure on bone formation





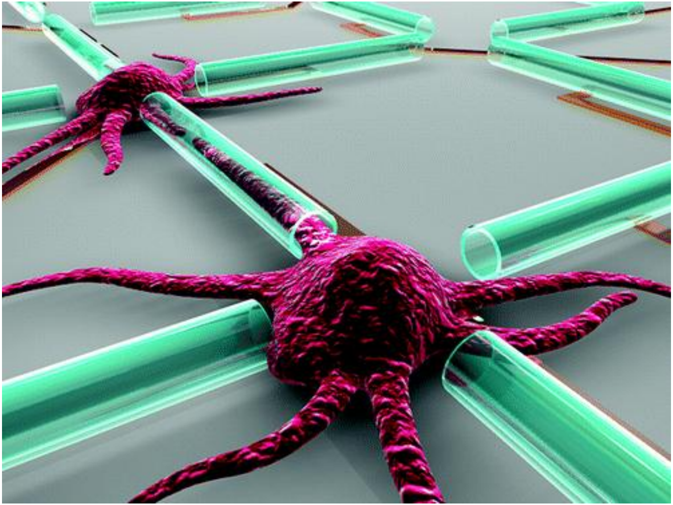
[Sim et al., 2007]

Cell-cell contacts

Why is regulation of cell-cell contacts interesting?

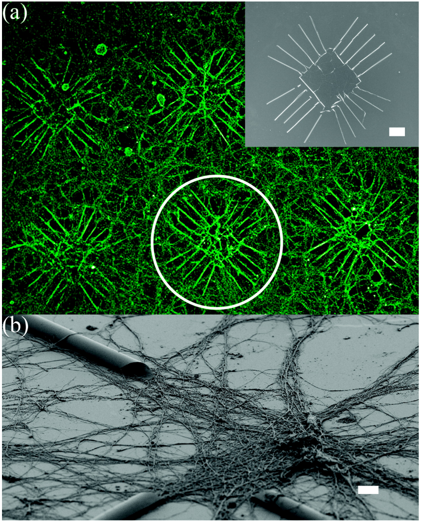
- triggering cellular behavior, such as growth, migration and differentiation
- drug and toxicology screening
- tissue regeneration

Example: Neurons on a chip



[Yu et al., 2011]
3D microenvironment

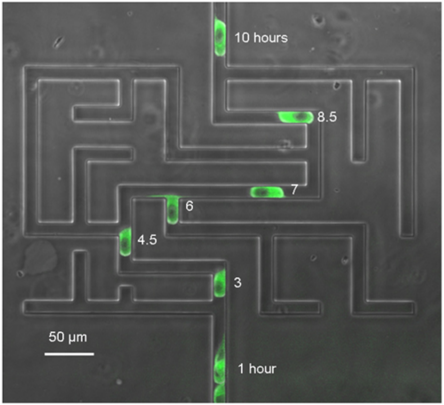
Example: Neurons on a chip



[Yu et al., 2011]
3D microenvironment

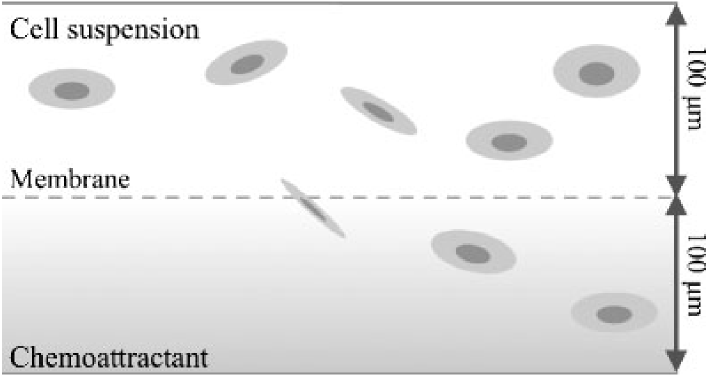
Understanding migration

Why is regulation of migration interesting?



[Perkel, 2012] Cell in a labyrint

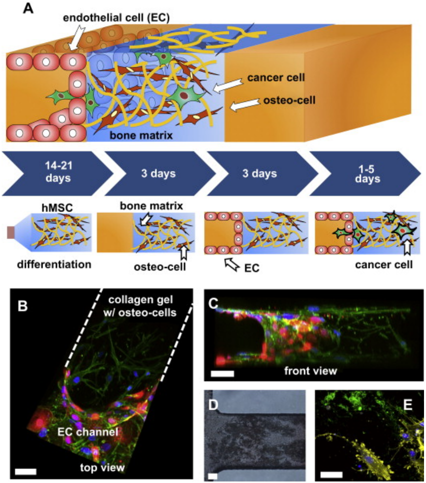
Example: Boyden Chamber + flow chamber



[Kwasny et al., 2011]

Mimics physiological shear flow conditions in blood vessel

Example: Metastasis



[Bersini et al., 2014]

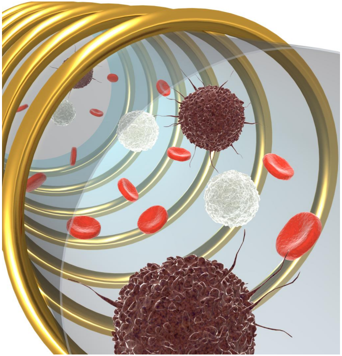
Cell trapping and sorting

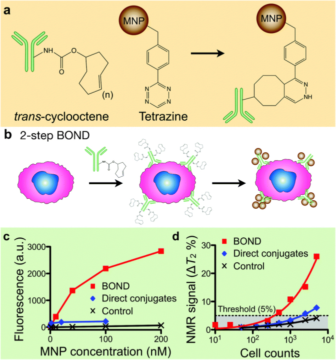
Why do we want to sort cells?

- diagnosis of health disorders, especially blood cancers
- isolation of stem cells for research & tissue engineering

Cancer diagnostics

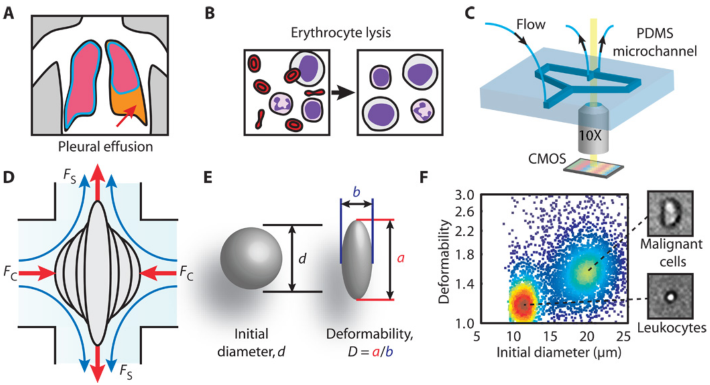
Miniaturized nuclear magnetic resonance platform for detection and profiling of circulating tumor cells





[Castro et al., 2014]

Cancer typing – benign or malignant?

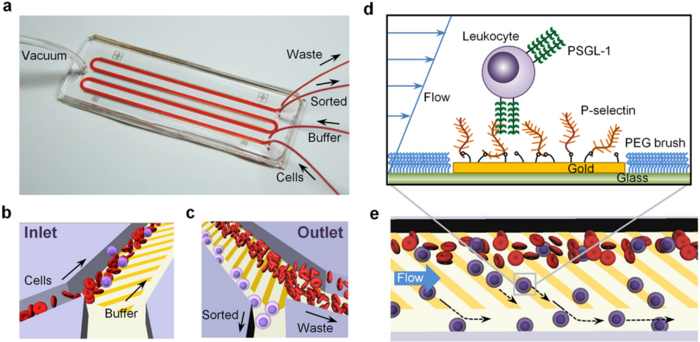


[Tse et al., 2013]

An approach that relies on microfluidic forces to diagnose pleural effusion samples as malignant, or no

Leucocyte separation from whole blood

Affinity flow fractionation



[Bose et al., 2013]

Video example of neutrophile separation from blood

Cells as sensors

The idea of using living creatures as sensors is not new: canaries used to detect toxic gases in mines already in 18^{th} century

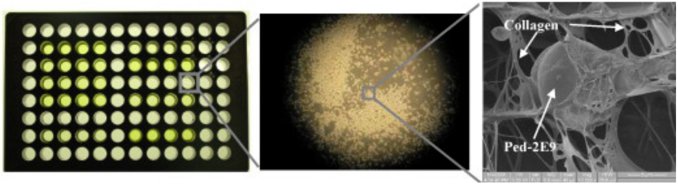
Cells based sensors are used for...

- detection of toxins and pathogens
- drug screening

Listeria detection with lymphocytes

Food safety testing
- able to distinguish pathogenic from non-pathogenic

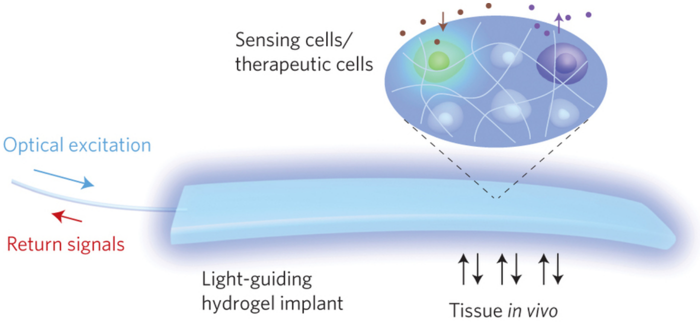
(A)



[Banerjee and Bhunia, 2010]

Example: Sensing & therapeutics

- optogenetic, glucagon-like peptide-1 secreting cells
- light-controlled therapy to obtain improved glucose homeostasis



[Choi et al., 2013]

Summary

- Why are bioMEMS great for influencing cells?
- How cells interact with materials?

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