

Measuring the mechanical properties of three-dimensional tissue structures

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Introduction

- How do mechanical properties of cells relate to those of 3D tissue structures?
- Novel approaches are needed to study the link between mechanics and biology.

3D tissue systems

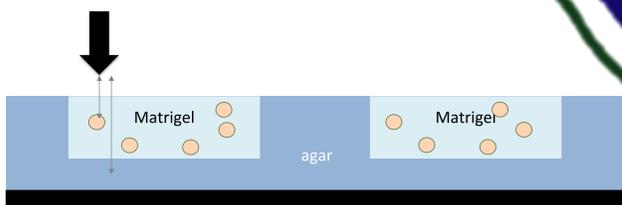
- Cells grown in a 3D matrix such as Matrigel or Collagen grow into 3D structures, also called "organoids".
- Organoids provide useful tools for research, such as drug discovery, tissue engineering and developmental cell biology.

Microultrasound (μ US)

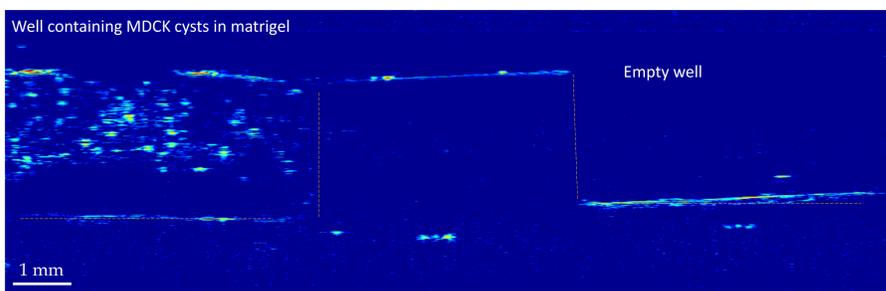
- Measurement of the backscatter of an ultrasound wave.
- Information about tissue structure from backscatter and acoustic impedance.



Samples are prepared by seeding cells in matrigel in 4.8mm diameter wells made of agar.



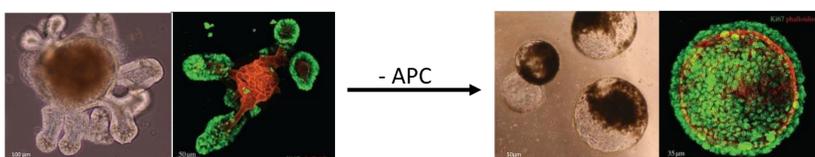
The sample is laterally scanned with a transducer to create a B-scan.



B-scan of two wells shows cysts revealing their acoustic properties.

Outlook

- Towards measuring gut organoids and looking at changes in mechanical properties during cancer progression.

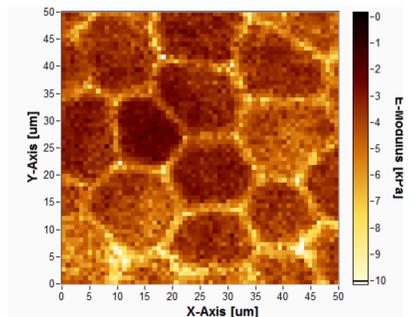
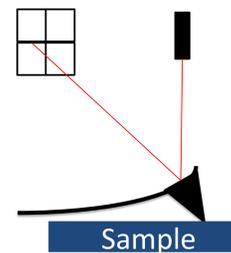


Gut organoids in health and disease. When carrying *Apc* (Adenomatous Polyposis coli) mutations, organoids lose normal structure and form round cysts. APC-mutations are common in >90% of colorectal cancers.

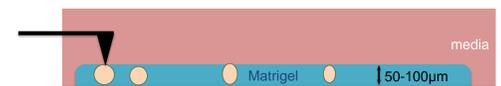
Atomic Force Microscopy (AFM)

- Measurement of *local* Young's modulus by measuring deflection of a cantilever while approaching/retracting from a sample.
- Stiffness maps of a field of cells with each pixel representing a separate stiffness measurement.

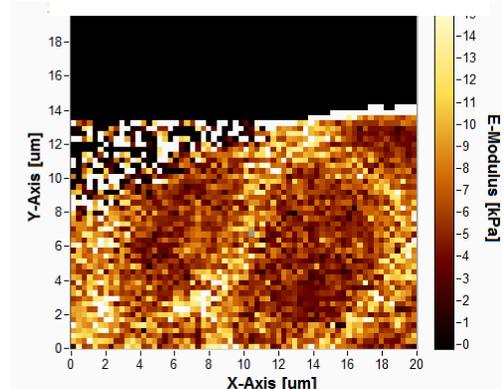
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Left: Principle of AFM. Right: A Force-volume map of a monolayer of MDCK cells. The nuclear region has a stiffness of $E = 2.0 \pm 0.56$, the cell junctions have a stiffness of $E = 5.3 \pm 2.4$.



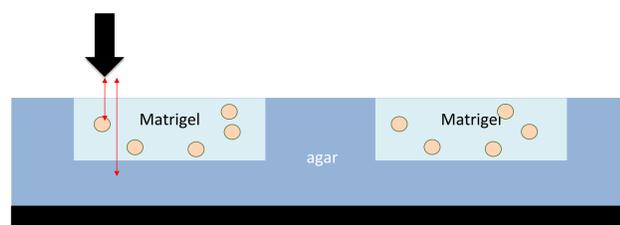
Sample setup for 3D tissue structure measurements.



Force volume map of two cells in an MDCK cyst. The nuclear region has a stiffness of $E = 4.8 \pm 1.3$, the cell junctions have a stiffness of $E = 8.3 \pm 3.8$.

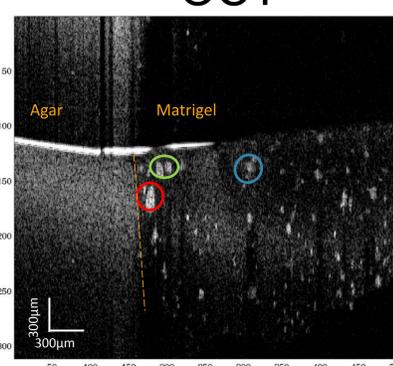
Optical Coherence Tomography (OCT) and Elastography (OCE)

- Measurement of backscatter of (near)-infrared light.
- Tomography: structural image
- Elastography: stiffness by measuring relative deformations.
- *Global* stiffness information.

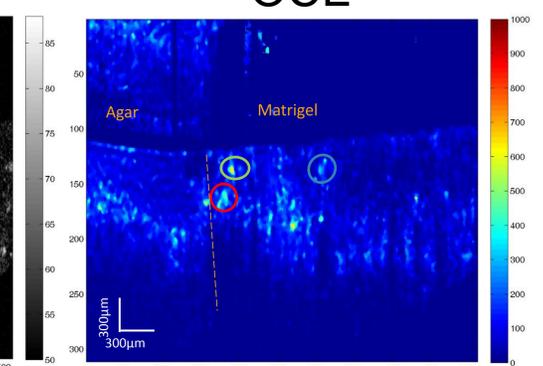


The sample is laterally scanned with a near-infrared laser to create a B-scan. Elastography images are obtained by measuring the relative deformation of the sample when subjected to a compression, in this case by vibrating the sample stage.

OCT



OCE



Resulting OCT and OCE images. The stiffness of cysts was measured to be $E = 338 \pm 21$ kPa. Matrigel had a stiffness of $E_{\text{Matrigel}} \sim 150$ kPa.

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