Intracellular shear wave elastography imaging of macrophages in adherent and suspended conditions

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Date: February 3, 2022
Location: Virtual seminar 2022

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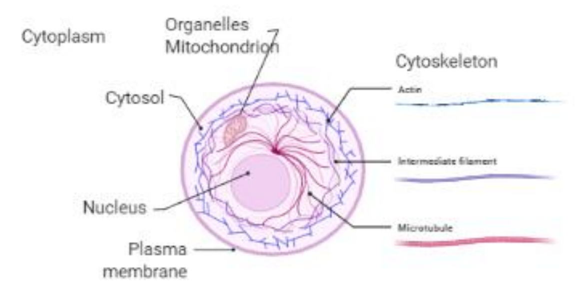
Disclosures

This work was supported by a grant from the “Quebec Bioimaging Network ” , and the “Support professoral du département de radiologie ”.

1. Introduction



• Cell mechanics

There is relation between cell’s mechanical behavior and cell function.

Cell mechanics is one of the factors determining the cell’s behavior.

Therefore, the mechanical properties has the potential to be considered as a biomarker for cell state.

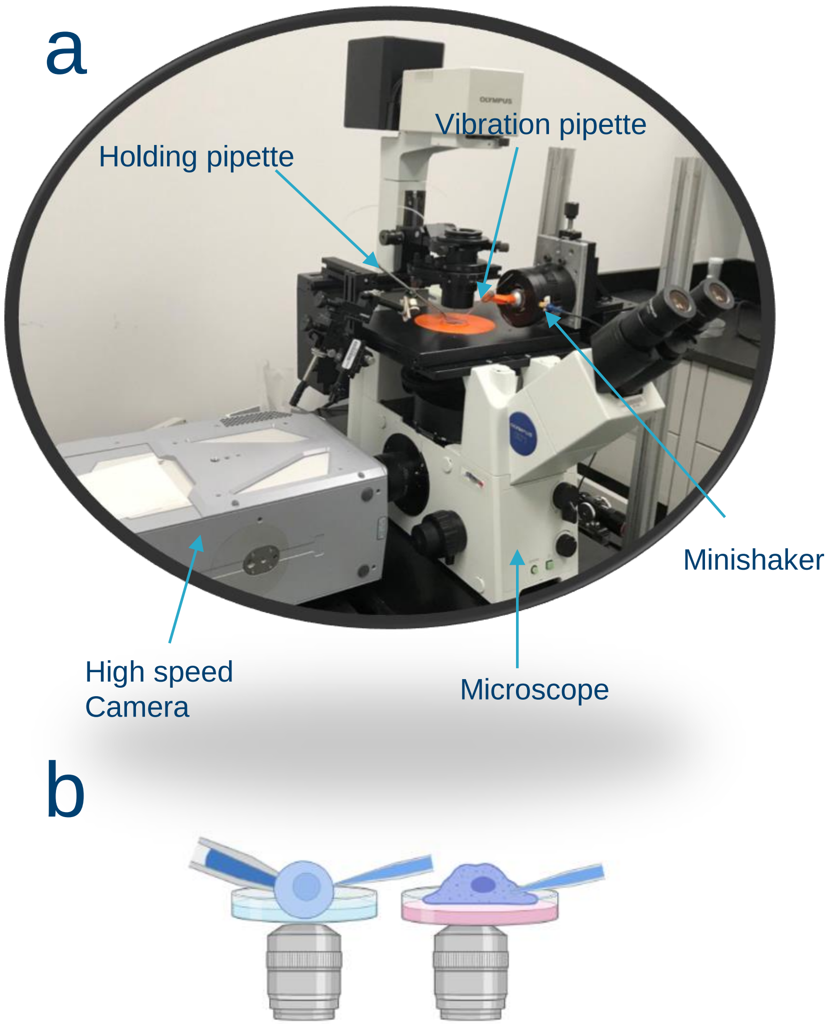
• Issue with most of the cell mechanical properties assessment methods

-Most of them require analyzing force and deformation in a local region of the cell such as surface of the cell membrane.

- The cell should be in one condition (suspended or adherent).
- Not consistent and it is not possible to compare
- Time consuming

2. Method

2.1 Set-up



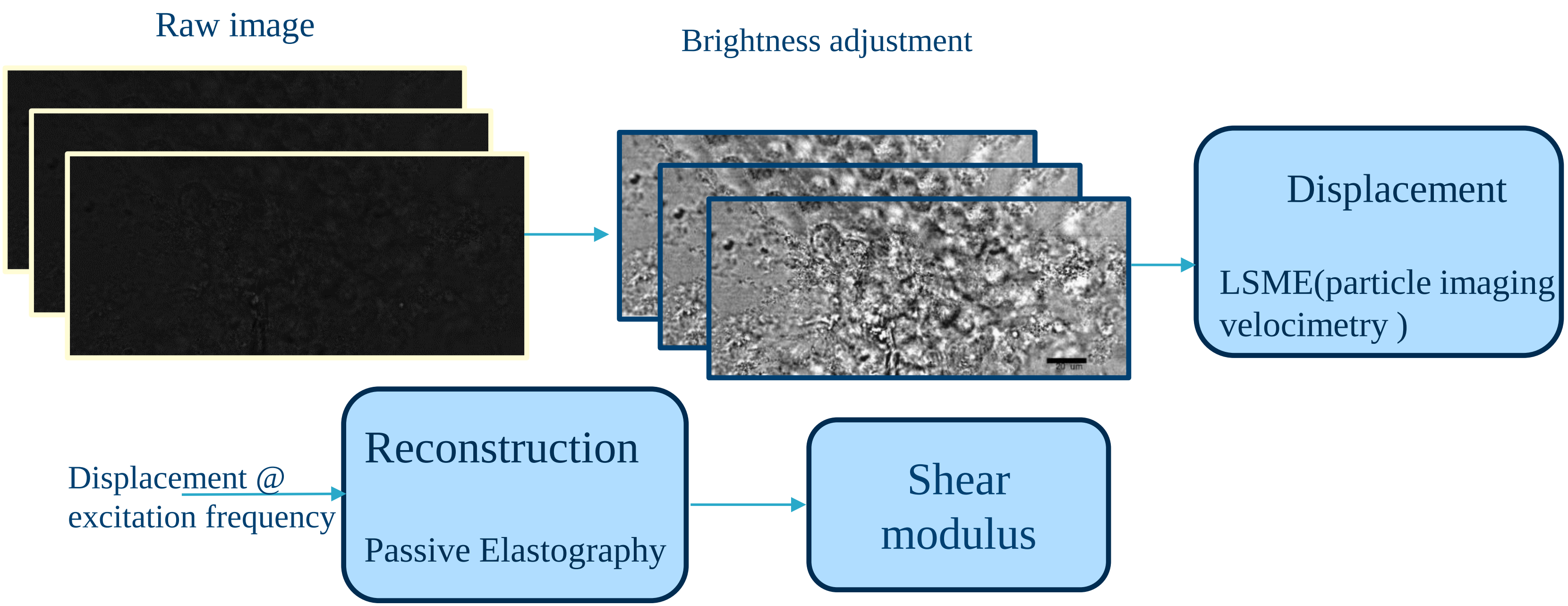
Experimental setup:

a) An inverted microscope and a high-speed camera coupled to it to capture the wave. For generating a wave, we utilize a micropipette as the cell vibrator, we attach a micropipette holder to the mini-shaker to vibrate the micropipette at a desired frequency and attach all this system to a micromanipulator to be able to move the micropipette to the desired location near the cell. To be able to fix the suspended cell, we utilize another micropipette attached to the micromanipulator.

b)Schematic diagram of the cell and micropipette's position.

2. Method

2.2 How to calculate shear modulus



Schematic process of finding shear modulus:

we employ a high frequency vibrating micropipette to produce shear waves and a high-speed camera coupled to a microscope to capture the wave propagation. Then, a displacement map is obtained by using a speckle tracking method from captured images. For solving the inverse problem and finding the shear modulus distribution within a cell, we use the passive elastography algorithm inspired by the seismology field to reconstruct elasticity images.

2. Method

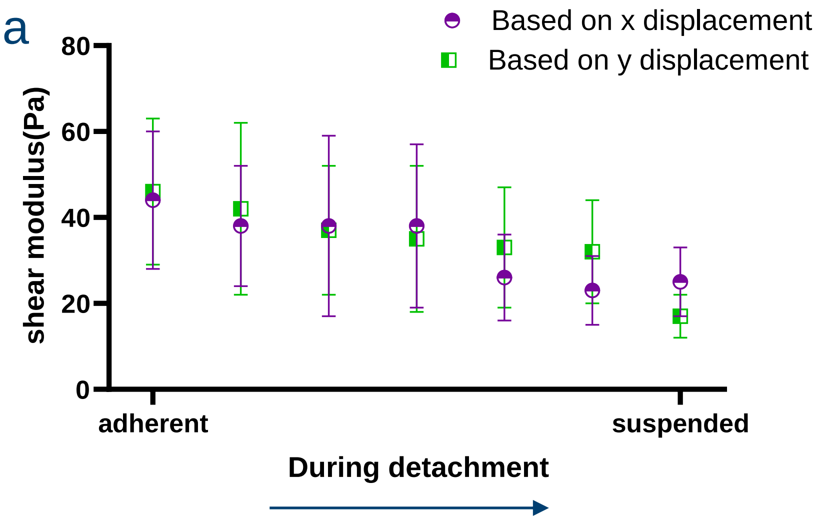
2.3 adherent and suspended cell

RAW264.7 murine macrophage cell line, were cultured in T25 flask and grown in a medium containing RPMI 1640, 10% fetal Bovine serum FBS, 1% penicillin-streptavidin (Wisent Inc., St-Bruno, Québec) and incubated at 5% CO_2 at 37 ° C. Before each experiment, cells were passaged to a glass bottom Petri dish and incubated for 24 hours. For the adherent and suspended cell conditions with RAW 264.7 macrophages, the micropipette was used to oscillate one part of the cell to induce vibrations inside the cell. For the suspended condition, the cell was detached from the petri dish before the measurement.

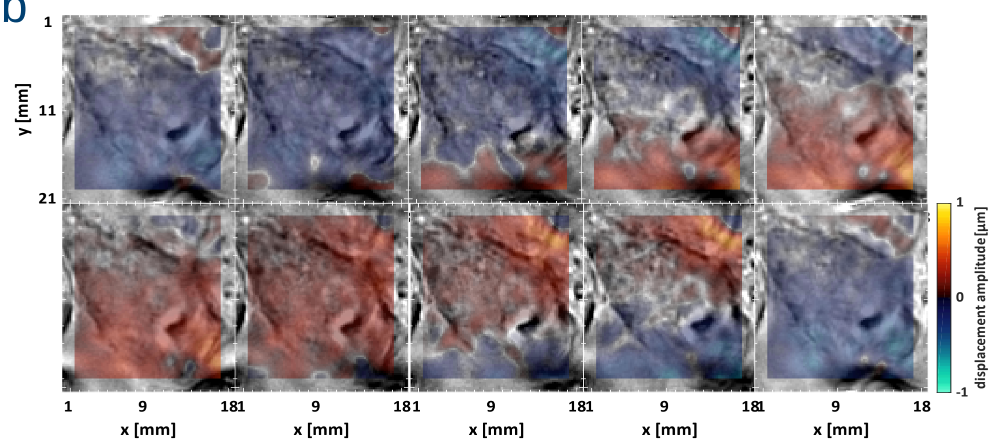
3. Results

3.1 *changing the shear modulus during the detachment*

a



b



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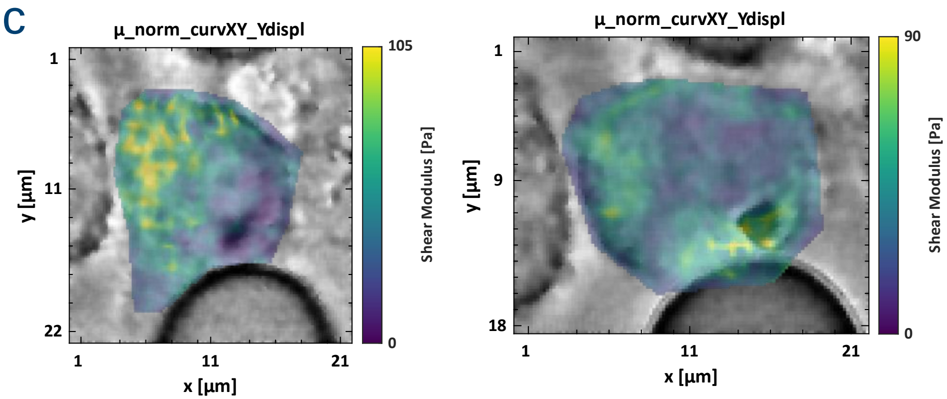

a)Shear modulus of macrophage during detachment (from adherent to partially detached and finally completely detached states)

b) Representative example of displacement propagation through an adherent cell at t=5.5 to 55 us each ten time step(5.55 us) superimpose on the optical image

c) Representative example of shear modulus map of macrophage during detachment

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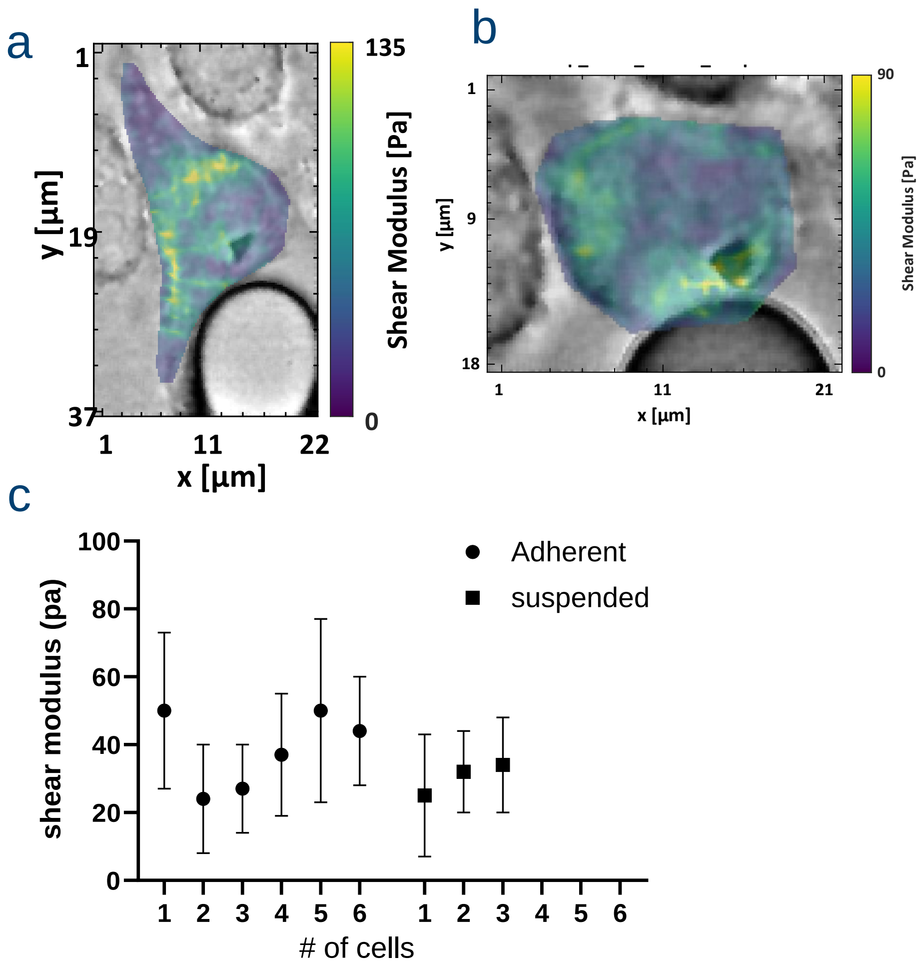
3. Results

3.2 comparison of the suspended and adherent shear modulus



a)Representative example of shear modulus of an adherent macrophages b) and a suspended macrophages, and c) Plot of the average shear modulus for N=6 adherent cells and N=3 suspended cells.

4. Conclusion

1. Our technique has the ability to measure the **intracellular cell mechanics in adherent and suspended states**.
2. Our technique has the ability to assess the **whole cell mechanics within a few ms** acquisition.
3. The shear modulus of the **adherent cells are higher than the suspended cells** and our technique is capable to show its decrease during detachment.