NON-CONTACT MEASUREMENT OF YOUNG’S MODULUS OF SINGLE LIVING CELL USING HYDROSTATIC PRESSURE IN A MICROCHAMBER

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ABSTRACT

This paper introduces a biochip which contains a microchamber for measuring the mechanical properties of cells without physically touching them. Unlike previous methods, dissipative forces such as friction are avoidable increasing the accuracy of our measurements. This can be used for cancer detection at an early stage based on the fact that cancerous cells are more elastic than normal cells as well as for studying the effects of hydrostatic pressure on the biochemical pathways in the cell.

Keywords: Biochip, light scattering theory, living cell, Young’s modulus

1. INTRODUCTION

Ever since the first attempt to study the mechanical properties of biological membranes in the 1930s using sea urchin eggs [1], the field of cell mechanics gained increasing focus of interest due to the importance of studying the mechanical interaction of the cell with its surroundings and how this can ultimately lead to diagnosis between normal and infected or cancerous cells. Currently, the more popular methods used to measure the cell’s mechanical properties include micropipette aspiration studies, compression studies using atomic force microscopy, glass microneedles and cell poker [2]. Limitations of these methods are that only one cell can be measured at a time, only sections of a cell are being used for measurement and deviations arise at different sections where the measurements are made such as in the close proximity of the nucleus and other bulky organelles. This paper introduces a simple and precise method for generating uniform force around the cell and allows for measurement of many cells simultaneously, hence increasing the accuracy of the measurements.

2. MEASUREMENT PRINCIPLES

The strain could be measured via principles of light scattering. When a monochromatic laser source of wavelength 524 nm passes through a cell, scattering fringes are formed and their position is directly dependent on the instantaneous geometrical shape of the cell. Hence, any changes caused by compression on the cell could

Figure 1. Principle of the optical detection
be measured by observing the fringe shift as illustrated in figure 1. The Young’s modulus can be calculated via the equations derived from the constitutive Hooke’s law and tensor analysis:

\[
E = \frac{-P}{tr\varepsilon_{ij}} (1 - 2\nu) \quad (1)
\]

\[
\varepsilon_{ij} = \frac{1}{2} \begin{pmatrix}
  x_1^2 - 1 & 0 \\
  0 & x_2^2 - 1
\end{pmatrix} \quad (2)
\]

Where \( E \) is the Young’s Modulus, \( P \) is the pressure exerted, \( \varepsilon_{ij} \) is the strain tensor, \( tr \) refers to the trace function from matrix algebra, \( \nu \) is the Poisson’s ratio and \( x_1 \) and \( x_2 \) are the ratio between the instantaneous radius and the initial radius of the horizontal and vertical components of the cell respectively.

The biochip’s design is illustrated in figure 2 and consists of three parts, the microfluidic structure, a sample chamber and a pressure generator. The microfluidic structure is used for the input of the cells together with their culture medium and oil into the sample chamber. The purpose of the oil is to prevent the cell culture medium to mix with the water generating the pressure. The sample chamber is where the cell is contained and where optical measurement is made. The pressure is generated using hydrostatic pressure via a pressure column which is placed at the inlet and outlet after the cells and the oil are loaded into the sample chamber. As the pressure can be varied in intervals as small as 0.0001 atm, the exact stress the cell is subjected to can be determined to a high accuracy and also more data points can be generated. The device is made up of PMMA annealed to a glass substrate coated with MgF₂ so as to allow clear and distinct scattering fringes.

![Figure 2. Schematics and photograph of the biochip](image)

**3. EXPERIMENTAL RESULTS AND DISCUSSIONS**

The cells were loaded to the microchamber. Experiments were done on MDCK( Madin Darby Canine kidney cell) with the size of 15-20 µm and the zebrafish embryo choroid of size 856 µm. The pressure was varied at intervals of 100 Pa. Micrographs as seen in figure 3 were taken for every 10 minute intervals when equilibrium had been established with each pressure variations and the shift in the fringes processed to determine the extent of compression and hence the strain of the cells. The results obtained were plotted as seen in figure 4.

![Figure 3. Photomicrograph of a MDCK cell with its fringes](image)
Figure 4. Experimental and theoretical compression vs pressure plot for (a) MDCK cell line; and (b) Zebrafish embryo chorion for 100 samples each

The Poisson’s ratio can be estimated by a DICM height measurement method [3] and is found to be around 0.48 for the Zebrafish Embryo and 0.45 for the MDCK cells. Assuming a linear correlation between the pressure and the strain for simplicity, the Young’s modulus of the MDCK is calculated to be around 6.2 – 0.031 kPa compared with earlier calculated results of 6.2 – 1.2 kPa [4] and that of the Choroid is calculated to be 1.32 – 0.013 MPa which correlates well with previously published results of 0.98 – 1.51 MPa [5].

4. CONCLUSIONS

This paper introduced a method capable of measuring the mechanical properties of many living cells simultaneously. As the cells are not destroyed during the process, they could be reused for other purposes, which is extremely useful for valuable cell types. Moreover, in the absence of detrimental forces, it increases the accuracy and reliability of the measurements.

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REFERENCES