FINITE ELEMENT ANALYSIS OF SINGLE CELL STIFFNESS MEASUREMENT USING PZT-INTEGRATED BUCKLING NANONEEDLE

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This project is dedicated to my beloved parents (Father and Mother) for their spiritual guidance, encouragement, caring and prayers.

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ABSTRACT

In this project, we propose a new technique for real-time single cell stiffness measurement using PZT-integrated buckling nanoneedle. The PZT and the buckling part of the nanoneedle have been modelled and validated using ABAQUS software. The two parts are integrated together to function as single unit. After calibration, the stiffness, Young's modulus, Poisson's ratio and sensitivity of the PZT-integrated buckling nanoneedle have been determined to be 0.8600 Nm^{-1}, 123.4700 GPa, 0.3000 and 0.0693 VmN^{-1} respectively. Three *Saccharomyces cerevisiae* yeast cells have been modelled using ABAQUS and validated based on compression test. We determine the average global stiffness and Young's modulus of the cells to be 10.8867 ± 0.0094 Nm^{-1} and 110.7033 ± 0.0081 MPa respectively. The nanoneedle and the cell have been assembled to measure the local stiffness of the single *Saccharomyces cerevisiae* yeast cell. An indentation force of 0.2 μN equivalent to single mode eigenvalue which causes the nanoneedle to buckle has been applied along y-axis. The local stiffness, Young's modulus and PZT output voltage of three different sizes *Saccharomyces cerevisiae* yeast cells have been determined at different environmental conditions. We investigated that, at low temperature the stiffness value is low to adapt to the change in the environmental condition as a result the cell is vulnerable to virus and bacteria attack. In future, the technique will supplement the present-day biochemical technique for diseases diagnosis.

ABSTRAK

Dalam projek ini, kami mencadangkan satu teknik baru untuk masa-nyata pengukuran kekakuan sel tunggal menggunakan Lead zirkonat Titanate (PZT)-mengintegrasikan *nanoneedle.* The PZT dan bahagian lengkokan *nanoneedle* yang telah dimodelkan dan disahkan menggunakan perisian Abaqus. Kedua-dua bahagian yang bersepadu bersama-sama berfungsi sebagai unit tunggal. Selepas penentukuran, kekakuan, Young’s modulus, nisbah Poisson dan sensitiviti lengkokan *nanoneedle* PZT telah ditentukan untuk menjadi 0,8600 Nm-1, 123,4700 GPa, 0,3000 dan 0,0693 Vmn-1. Tiga *Saccharomyces cerevisiae* sel yis telah dimodelkan menggunakan Abaqus dan disahkan berdasarkan ujian mampatan. Dengan menentukan kekukuhan purata global untuk sel-sel Young’s modulus masing-masing ialah 10.8867 ± 0.0094 Nm-1 dan 110,7033 ± 0,0081 MPa. *Nanoneedle* dan sel telah dipasang untuk mengukur kekukuhan semulajadi pada sel tunggal *Saccharomyces cerevisiae*. Satu tenaga lekukan 0.2 μN di bersamaan dengan nilai tunggal eigen mod yang menyebabkan *nanoneedle* membengkok telah digunakan di sepanjang paksi-y. Kekukuhan semulajadi, Young’s modulus dan keluaran voltage PZT dengan tiga saiz yang berbeza *Saccharomyces cerevisiae* sel yis telah ditentukan pada keadaan persekitaran yang berbeza. Dengan disiasat itu, pada suhu yang rendah nilai kekukuhan yang rendah memudahkan sel terdedah dengan menyesuaikan diri dengan perubahan sekitarnya dan boleh mengakibatkan sel terdedah kepada virus, bakteria menyerang. Pada masa akan datang, teknik ini akan menambah baik kepada teknik biokimia masa kini untuk diagnosis penyakit.

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AFM	-	Atomic Force Microscope
ESEM	-	Environmental Scanning Electron Microscope
EDS	-	Energy Dispersion Spectrometry
FE	-	Finite Element
FEA	-	Finite Element Analysis
FEM	-	Finite Element Model
FIB	-	Focused Ion Beam
PVDF	-	Polyvinylidene Fluorine
PZT	-	Lead Zirconate Titanate
SEM	-	Scanning Electron Microscope

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CHAPTER 1

INTRODUCTION

1.1 Introduction

Nanotechnology has thrown more light on how to enhance the standard of living [1]. As a result it made the study of single cell mechanics possible. Moreover, it provides room to analyse the mechanical properties of single cell [2], which is the basic structural and functional unit of life in all living things [1,3]. As a matter of fact, mechanical properties such as elastic modulus of a cell is one of the most important property used for cell stiffness characterisation [4]. The idea of determining the stiffness of a single cell can be associated with the health condition peculiar to that cell [5]. Indeed, parasite attack to a particular cell changes the elastic modulus of that cell by altering the structure and molecular configuration of the cell [5]. Furthermore, several dangerous diseases such as cancer results from changes occur at cell level rather than tissue or organ level [5]. In point of fact, the idea of a single cell stiffness measurement will gives more accurate and reliable result than average result obtain using biological processes, which may lead to the wrong conclusion [5]. Conversely, the mechanics of cell wall, which contribute immensely for understanding of the mechanical properties of the cell, is an area of "near-total darkness" [6]. This made the knowledge of cell mechanical properties of great interest. Because of the considerable information derived for better understanding of disease diagnosis, infection and many more upcoming applications in biomedical field [6,7].

Traditional procedure used to determine the modulus of elasticity of a material practically cannot be directly applied to the structures at micro and nano level, for example nano fibres, biological cells etc. To determine the mechanical properties of a single cell accurately without causing considerable harm to the cell a suitable nano force sensor is required. At this stage the use of nanoneedle as a nano force sensing device is unavoidable. Nanoneedle can be fabricated at a various uneven locations with suitable orientation on either Atomic Force Microscope (AFM). Depends on the applications, a suitable material such as silicon, silicon dioxide [8], silicon nitride or tungsten can be chosen for the nanoneedle fabrication [9]. Because there are many strategic locations under study at nano level in which even standard AFM probes are difficult to be used. Nanoneedle can be used for many applications, not only as nano force sensor, but also can be used for drug delivery to a single cell, cell surgery, cell growth, study of a single cell electrical properties etc. [9]. Furthermore, it can also be used to mechanically examine other structures, materials at nano level etc. [10]. It can either be rigid or soft. Soft nanoneedles are those that can buckle on contact with a stiff surface when force is applied to it, while on the other hand rigid nanoneedles are strong which can even penetrate soft materials. Rigid nanoneedle is not preferred as a nano force sensor for single cell stiffness measurement, because it causes severe damage to the cell. For this reason buckling nanoneedle is the solution. Despite the fact that, measurement of nano Newton force using buckling nanoneedle require special instrumentation [11]. A buckled nanoneedle used as a force sensor to mechanically examine a suspended nano fibre and cell stiffness characterisation is shown in Figure 1.1 and Figure 1.2. In point of fact, the used of buckling nanoneedle as a force sensor for single cell stiffness measurement will serve as a quick and accurate process to diagnosis diseases at early stage in a cell for effective treatment [2,12]. For this reason, the technique will supplement the present-day biochemical technique, which could be a great contribution in the field of medicine as well as biology [2,4].

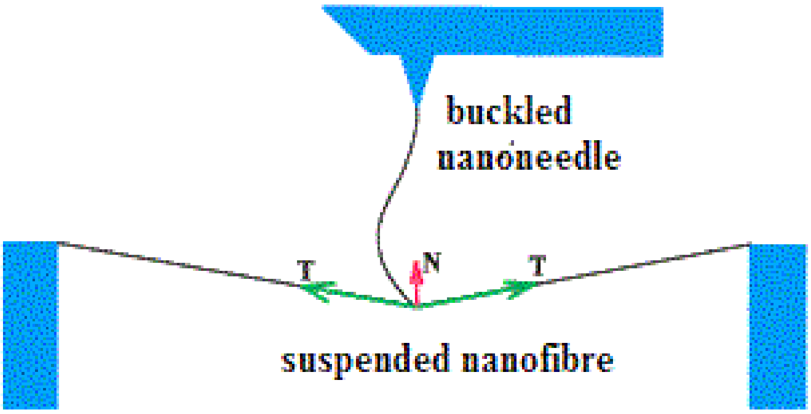

Figure 1.1 Buckling nanoneedle used as a force sensor to mechanically examine a suspended nano fibre [10]

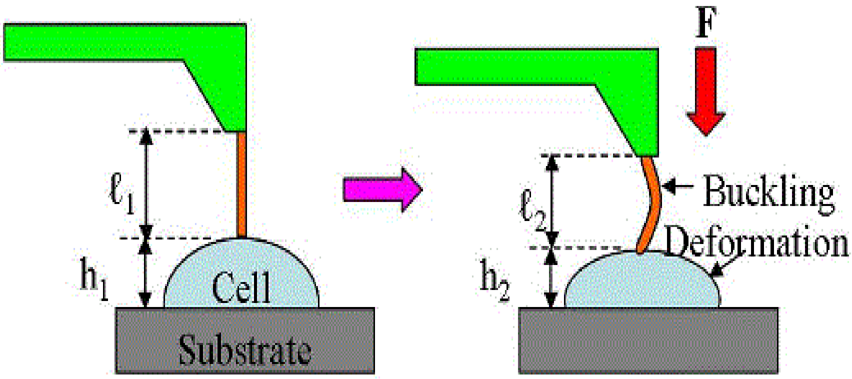

Figure 1.2 Buckled Nanoneedle used for cell stiffness characterisation [2]

1.2 Background of the Study

There are a number of well-proved techniques for single cell stiffness measurement, which include the development of nanoneedle with buffering beam for single cell stiffness measurement by nanorobotic manipulators inside Environmental Scanning Electron Microscope (ESEM) in which a nanoneedle was fabricate on a buffering beam by etching process using focused ion beam on AFM cantilever [13]. As a result, when the nanoneedle tip comes in contact with the cell the buffering beam deformed which is modelled as a single rectangular beam with a point load at the centre. But the main drawback of the technique is that high accuracy image processing, total concentration and careful observation of the image obtained, stiffness of the buffering beam is fixed and real time stiffness measurement cannot be obtained. Another major example of the techniques for single cell stiffness characterisation is buckling nanoneedle inside ESEM to measure the stiffness of single cell, which is model together with the cell for which its stiffness is to be considered as two springs connected in series. Similarly the drawback of the technique include, it required very high details of the image of the experimental set up, total concentration and careful observation particularly on the nanoneedle as well as real time stiffness measurement cannot be obtained. The project was in depth investigated single cell stiffness measurement by using finite element-based approach.

1.3 Motivation

Single cell analysis such as single cell mechanics is becoming dominant in the field of medicine, agriculture, biotechnology, botany, zoology and pharmacy because of the considerable information derived, which is useful for single cell surgery, single cell drug delivery as well as quick and accurate diseases diagnosis for effective treatment. But all the aforementioned applications cannot be achieved without a nano tool (nanoneedle) that can acts as force sensor to accurately measure force at cell level.

1.4 Problem Statement

The current conventional method of diseases diagnosis cannot detect diseases at early stage. As a result the effect of treatment reduces by 40-50% because the disease has reached a certain level. Early diseases detection is only possible at a cell level. Nanoneedle can detect diseases at cell level. But current proposed nanoneedle cannot provide real-time force/stiffness data, stiffness measurement at certain conditions and causes significant damage to the cell. For this reason, the need arises for PZT-integrated buckling nanoneedle that will provide real time force/stiffness measurement with minimal or no damage to the cell.

1.5 Aim and Objectives of the Project

This research is aimed at modelling and simulation of PZT-integrated buckling nanoneedle for single cell measurement stiffness based on finite element analysis. This aim can be achieved through the following objectives:

- To model and validate PZT-integrated buckling nanoneedle using ABAQUS.
- To calibrate PZT-integrated buckling nanoneedle using ABAQUS.
- To model and validate cell using ABAQUS.
- To measure the global stiffness of the cell using ABAQUS.

- To investigate the effect of temperature and pressure on the morphological behaviour of the cell by measuring local stiffness of the cell using ABAQUS.

1.6 Scope of the Project

The scope of the work in fulfilling the project objectives are:

- PZT-5H material properties were used as the PZT-integrated buckling nanoneedle material properties.
- Silicon material properties were used for the buckling nanoneedle and cell slab.
- *Saccharomyces carevisiae W303* yeast cell was used as sample model of the cell.
- In this project only calibration, modelling and simulation with the aid of commercially available ABAQUS (finite element software) were considered. The results were validated using experimental data.

1.7 Significances and Contributions of This Project

The main contribution of this work is to provide new, valid, efficient and accurate force sensor model. The model produced can be fabricated in future and it will serve as a tool for quick and accurate diseases diagnosis at early stage for effective treatment at cellular level. For this reason, the technique will supplement the present-day biochemical technique, which could be a great contribution in the field of medicine.

1.8 Project Report Structure and Organization

This project report is organized in five chapters. Chapter one gives an overview of the system, objectives and scope of the project and also gives introduction regarding the problem to be solved. Chapter two reviews some previous research and literatures related to this project. Chapter three provides steps of the methodology and description of each procedure to be followed in order to solve the problem at in view. Chapter four gives a detailed explanation of the results obtained from simulation and discuss the outcomes from the followed methodology. And finally chapter five presents conclusion on the achievements in the project and also set forth some recommendations for further future works.

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