# Analytical and mechanical modelling of a proposed hydrogel using FE software to simulate the ICSI injection process

A.M. Hajiyavand[1], M.Saadat[2] and A. Stamboulis[3]

[1]PhD Student, University of Birmingham, UK.

axh047@bham.ac.uk

[2]School of Mechanical Engineering, University of Birmingham, UK.

[3]School of Metallurgy and Material, University of Birmingham, UK.

**Abstract**

In this paper, analytical, mechanical modelling and Finite Element (FE) analysis are proposed to an artificial oocyte (fabricated gels) and then the mechanical tests are applied on fabricated samples. The results are compared to each other and after reaching the satisfaction, The FE model is used to model the real oocyte in micro size. The FE analysis is also compared with obtained results for real Mouse oocyte from literature and it shows the satisfactory results. So this software has the ability of simulating the procedure of the injection in ICSI. Moreover the alginate hydrogel which is proposed here can be a good alternative for oocyte.

## Introduction

Intra Cellular Sperm Injection (ICSI) is one of the most important applications of microinjections. There are two main factors affecting on the success rate of pregnancy from this method; one is from specific medical procedure and the other is about the method of insertion of needle into the ooplasm and the harms which is caused by this impact injection. So there are two way to reduce this harms from the oocyte; one is developing the injection procedure and the other uses a material which can have the properties of the ovum that can transfer the gene and the chromosomes in it instead of remaining them into the defective ovum. So all of these developments can be happened if the properties of the real ovum are known. Moreover, by simulating the procedure of ICSI into software, development can be reach in the injection process. There are some works done for simulating a needle insertion biological cell, but none of them has the ability of doing Finite element. There is 3D Biomechanical tensegrity model is developed in 2008 to dynamic modelling, visual/haptic display and model validation of cell injection.

Here, the first step is analysing a real oocyte analytically and mechanically. This can help to analyse the injection process and the factors affecting on it. Then the Finite Element (abaqus 6.10) of the model can be applied. This can simulate the mechanism of injection and can help to analyse different factor affecting on this mechanism. Since accessing to the real oocyte is limited, then it is proposed to use the artificial one. The artificial oocyte is made from a specific dose of alginate which is obtained by different experiments. It should be mentioned that the data used for analytical modeling and FE software is designed for alginate gel that make the situation possible for comparing. After analysing the results obtained from the analytical, FE and real test, it is concluded that the real test result on the gel is completely satisfying the FE software result and analytical result. So the FE can be used for the

real ovum with its properties to simulate the injecting procedure. This method is used to predict the results of any development in ICSI processes.

**Analytical and Mechanical modelling**

In this section, mechanical modelling will be proposed to simulate the compression or injection process and situation. This modelling is used for hydrogel to simulate an actual ovum injection. The model proposed here is an extension of Rivlin's model in the injection inside the gel application. This model was selected and developed in view of the deficient existing models. In this modelling, the Mooney-Rivlin model employs the strain energy function.
There is some assumption[1] which is applied for this model such as:

1. The gel sample is free of initial stress or residual stress.
2. The model starts with the planar circular area as the tip of injector which is in contact with the layers at the time of injection with zero residual stress.

The modelling would be applied from the point of first contact is made to where the sample punctured. This mechanical modelling can be expanded for the simulation of the ovum injection. This interval shows the dimpled profile of the ovum before the punctuation.
The figure 1 shows schematic process of injection

The first step is to write the force balance at the place of the injection in the force modelling of the injection situation. This model is known as the point load model.

$$\sum F_y = ma = m\frac{dV}{dx} \tag{1}$$

where m is the mass of Plate and $a$ is the acceleration. The plate is moving with constant velocity as assumed, so the equation of the force balance becomes as follows:

$$F - F_p - 2\sigma_d \pi r h \frac{dw}{dx} = 0 \tag{2}$$

where F is the Plate force, $F_p$ is the internal pressure acting on the outer part of the gel and $\sigma_d$ is the stress on the outer layer section of the gel (this can be the stress at the injection section at the time of injecting into the cells). Also $\frac{dw}{dx}$ is the dimple profile changing due to the changing in radius.
If the purpose is finding F, this model cannot be supported individually, because the pressure inside the gel is unknown. Therefore, the Mooney-Rivlin model must be adapted thus, by employing the strain energy function.
So the final equation would be as follows:

$$\left[\frac{2hK_1}{\lambda_1\lambda_2}\left({\lambda_1}^2 - \frac{1}{{\lambda_1}^2{\lambda_2}^2}\right)(C_1 + {\lambda_2}^2 C_2) + \frac{2hK_2}{\lambda_1\lambda_2}\left({\lambda_2}^2 - \frac{1}{{\lambda_1}^2{\lambda_2}^2}\right)(C_1 + {\lambda_1}^2 C_2)\right].\pi a^2 - F_p - 2\sigma_d \pi r h \frac{dw}{dx} = 0 \tag{3}$$

Where h is the thickness and $C_1$ and $C_2$ are material constant and would obtain from the experiment.

[1] The list of complete assumption will be in the original paper.

The variable equations would be as follows:

$$\lambda_1 = \frac{dx_1}{dx_2} \ , \ \lambda_2 = \frac{dy_1}{dy_2} \ , \ \lambda_3 = \frac{1}{\lambda_1 \lambda_2} \qquad (4)$$

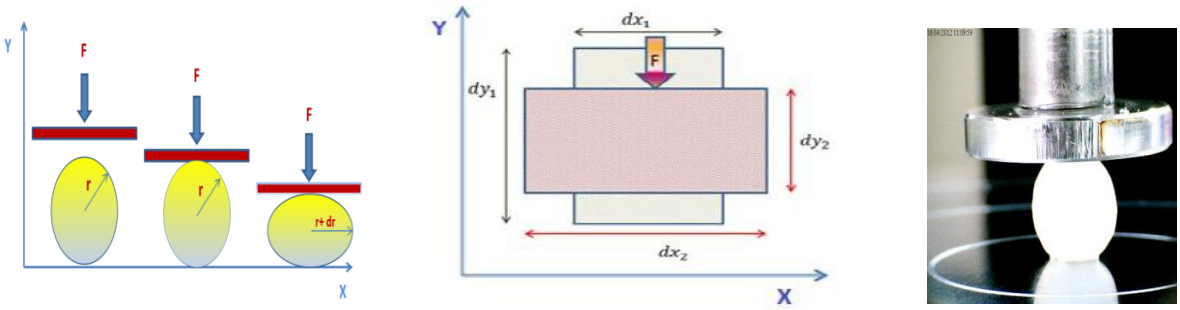


Figure 1: The compression test for the Hydrogel samples

The above picture shows the displacement of the gel in compression test in both X and Y directions[2]. Moreover, the nominal stresses can be calculated from the following equations:

$$\sigma_{11} = 2C_1 + 4C_2 + 2(C_1 + C_2)k^2 - p \qquad \sigma_{22} = 2C_1 + 4C_2 - P \qquad \textbf{(5)}$$

**The sample manufacturing (Gel Fabricating)**

The proposed gel for the samples is alginate acid sodium salt. Alginate hydrogel has varied applicability as a biomaterial, such as drug delivery, scaffolding for tissue engineering, as an implant, etc. Using this hydrogel requires control of the material properties, including mechanical stiffness, swelling, degradation, cell attachment and binding or release of bioactive molecules. The benefits of these developed alginates gels as biomaterials have been shown in many in vitro and in vivo studies. Alginate hydrogels, due to the unique biocompatibility aspects and desirable physical characteristics, are good candidates in many applications in medicine. Different doses (0.1, 0.5, and 1 M) of alginate used to understand the suitable doses for experiment. The manufactured gel is completely liquid and viscose, so the next step would be finding a suitable technique to solidifying and cross link them to obtain the required stiffness of the gel. Two different methods are applied here to crosslink the liquid gel; one is using Petri dishes and covering the top and bottom of the gel by filter papers which are wetted by the $CaCl_2$, and the other is using the spherical mould which was designed by the researcher for this purpose and instead of covering it by the filter paper, it was suggested that calcium chloride should be injected into the gel in the mould and also covering by it by wetting the inside of the mould with alginate. It should be mentioned that different doses of calcium chloride (2%, 5% and 10%) are used in this experiment. Also a C++ Programme developed here by the researcher using the gel experimental data, which can specify the doses used in this experiment by obtaining the dimension data from the user. This program can help to calculate the exact amount of $CaCl_2$ with no need for trial-and- error experimenting. This program was written by modelling of the obtained real results from gel making experiments experiment. .

[2] The comprehensive modelling will be present in the original paper

**Test**

In this section the mechanical testing of the hydrogel would be analysed. This test is known as compression test and was done in two parts; one with plate to simulate the software and compare the result of the experiment with software, the other is with needle to simulate the ICSI process. The force is variable and reported in this test, as can be seen from the graphs and collected data. A constant velocity was applied to the samples - 5 mm/min. Hence, the force increased as the displacement increased. The output data from this machine concern force, displacement, work and time of experiment.

**Results**

The results present in this paper are divided into different sections; the first one is comparing the different doses of the $CaCl_2$ which has the role of stiffness and also different method of the $CaCl_2$ deliveries. The other is the result of comparing the FE modelling results and the actual testing of the gels. Also the comparison between a prediction in FE software and a real test on mouse oocyte is shown a good satisfactory of the FE software design here (see figure 2). Moreover, the money reviling analytical modelling needs two $C_1$ and $C_2$ two model the injection into the MATLAB. These constants are obtained from the FE software.

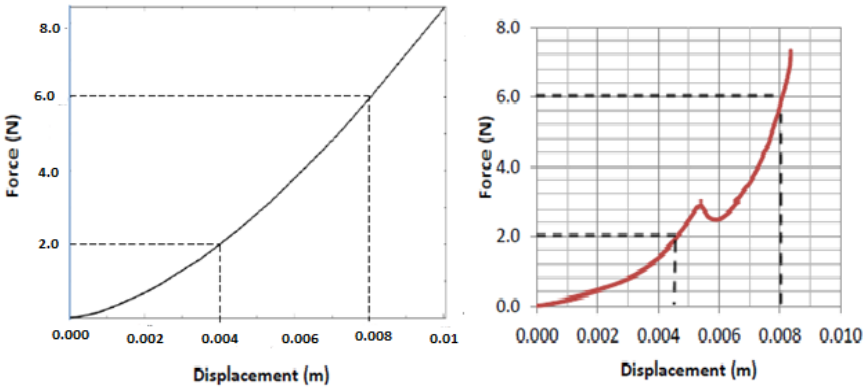


Figure 2: The comparison between the FE result and real cell test

Table 1:The obtained displacement and force feedback from software and experiment

| Type | DATA | before puncturing | puncturing point | after puncturing point |
|---|---|---|---|---|
| FEA Model | displacement (mm) | 4.2 | NA | 8.4 |
| | force (N) | 2 | NA | 6 |
| Experimental result | displacement (mm) | 4.64 | 5.19 | 8.09 |
| | force (N) | 2 | 2.75 | 6 |

**Conclusion**:

From this section, it can be concluded that the proposed gel has the closest mechanical properties and behaviour under the compression and injection to the real cell. This is obtained by using multiscale modelling and testing which is gained from macro scale testing and modelling and is predicted in micro scale using the FE software. Also the prediction in FE software is compared to the actual experiment done in a literature and the results shows the satisfaction of the FE.

**References**

Youhua Tan, Dong Sun and Wenhao Huang, February 2009. A Mechanical Model of Biological Cells in Microinjection. *International Conference on Robotics and Biomimetics*, Issue 2008 IEEE.

Yu Sun, Kai-Tak Wan, Kenneth P. Roberts, John C. Bischof and Bradley J. Nelson, DECEMBER 2003. Mechanical Property Characterization of mouse zona pellucida. *IEEE TRANSACTIONS ON NANOBIOSCIENCE, VOL. 2, NO. 4, DECEMBER 2003,* VOL. 2, NO. 4,(IEEE).

R.SKALAK, A.TOZEREN, R. P. ZARDA and S. CHIEN, 1973. Strain Energy Function of the red blood cell membranes. *Biophysical* , 13 (Columbia University, New York), pp. 245-264.

Sarthak Misra, Allison M. Okamura, and K. T. Ramesh. Force Feedback is Noticeably Different for Linear versus Nonlinear Elastic Tissue Models. *Department of Mechanical Engineering, The Johns Hopkins University*