A Micro Force Measurement, Transmission and Control System for Biomechanics Studies

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Abstract

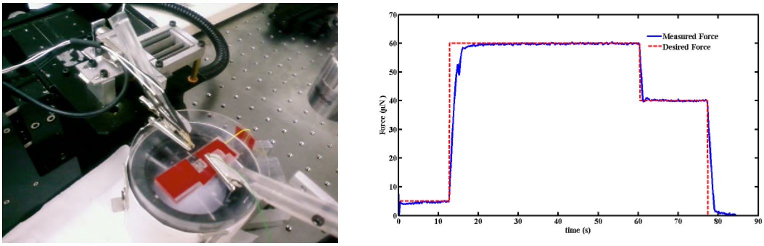
This paper describes the development of a micro force measurement, transmission and control system, which is able to precisely regulate the force exerting on a zebrafish embryo with ±5 μN accuracy. The system serves as a platform to characterise the viscoelastic properties of zebrafish embryo membranes and to study the effect of mechanical forces on the change of the zebrafish embryo impedance.

1 Introduction

Various approaches [1-2] have been reported to apply external forces on cellular organisms. These approaches include mechanical, optical, and magnetic based micromanipulation methods. Techniques based on microfluidics, surface patterning, and MEMS tools are under intensive development for regulating cellular microenvironments and enabling accurate, quantitative measurements of cellular response in high throughput manner. All these techniques normally involve deforming a cellular organism and simultaneously measuring the induced forces. An engineering challenge remains in precisely control the applied force to achieve force regulation and trajectory tracking. This paper presents a micro force measurement, transmission, and control system, enabling precise control of the forces exerted on zebrafish embryos and the generation of any desired force trajectories. Its application on biomechanics studies has also been described.

2 Micro Force Measurement, Transmission and Control System

A one-axis piezoresistive micro force sensor (AE801, SensorOne Technologies Corporation) was modified to measure the force exerted on the embryo. The sensor measures up to 200mN force with ±2µN resolution. A compound flexure stage is designed to transmit forces generated by a linear voice coil actuator (LA-05-000A, BEI). The stage consists of a movable platform supported by four leaf springs. The stage is able to transmit forces with 0.575µN resolution. The force controller was decomposed into a model based portion and a servo portion. The model based portion made use of the mass-spring-damping model of the stage, while the servo portion is a rule based multiple step PID controller whose parameters are selected according to the difference between the measured and the desired forces. The multiple step PID controller works to avoid both the overshoot of the force and the jerk of the micro force sensor and the pipette attached. The developed system and its force response results are shown in figure 1. The control results are as follows: overshoot < 1µN, stabilization time < 5 seconds, and force variation < 5µN.



(a) (b)

Figure 1: (a) The developed system and (b) force response results

3 Viscoelastic Model of Zebrafish Embryo Membrane

Force relaxation experiments on zebrafish embryo membranes were conducted using the developed system. The embryos were deformed of X_0=300µm in 0.3 second and the deformation was kept for some time before releasing. The measured force relaxation curves for 5 different embryos are plotted in figure 2 (solid lines). The force relaxation has two phases, a sharp decreasing and a more flat decreasing phase. A generalized Maxwell-Weichert model is found to be suitable to fit the force relaxation process of the embryos [3]. The model has two Maxwell elements and one spring connected in parallel with parameters of k_1, k_2, k_3, b_2, and b_3. Thus the force relaxation can be described as:

$$F = (k_1 + k_2(1 - e^{-\frac{k_2}{b_2}t}) + k_3(1 - e^{-\frac{k_3}{b_3}t}))X_0 \tag{1}$$

The fitting results are also drawn in figure 2 (dash lines). The viscoelastic parameters of the 5 different embryos are given in table 1. Different embryos have comparable but different viscoelastic parameters, indicating that these parameters can be used to characterise the status of embryos.

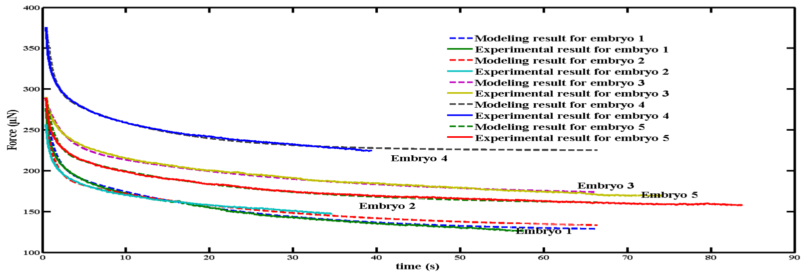


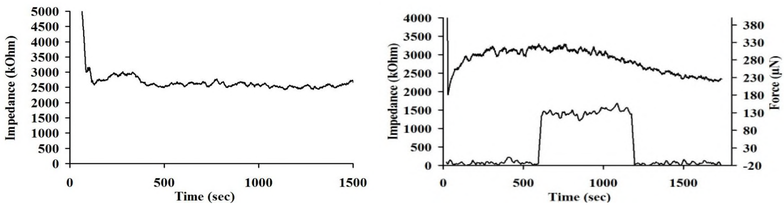
Figure 2: Force relaxation curves and fitting results for 5 embryos

Table1 1: Viscoelastic parameters of different embryos

	k_1 (N/m)	k_2 (N/m)	k_3 (N/m)	b_2 (Ns/m)	b_3 (Ns/m)
Embryo 1	0.42	0.245	0.26	0.25	5.2
Embryo 2	0.43	0.22	0.21	0.22	5.2
Embryo 3	0.56	0.2	0.21	0.4	5.8
Embryo 4	0.75	0.26	0.25	0.21	3.0
Embryo 5	0.53	0.22	0.22	0.22	4.4

4 Effect of Mechanical Force on Embryo Impedance

The developed system was also used to study whether external forces affect embryos' impedance. A force of 100μN was applied on the chorion of an embryo for about 600 seconds. The embryo's impedance with and without the force exertion was measured and given in figure 3. The results showed that the application of a properly controlled external force leads to significant change of the zebrafish embryo's impedance.



(a) (b)

Figure 3: Embryo's impedance without (a) and with (b) a force application

Structurally zebrafish chorion has three electron dense layers [4] as illustrated in figure 4. The middle and inner layers are penetrated with pore canals. Pore plugs on the outer layer block the pore canals to the outside environment. The application of an external force may dislodge the pore plugs, opening a path for ions to move in or out of the chorion across the membrane. Such ionic movements in pore canals may offer a possible explanation to embryo's impedance change with force application. Further research will be needed to better understand the mechanism linking external forces and ionic movement in pore canals in the chorion of zebrafish embryos.

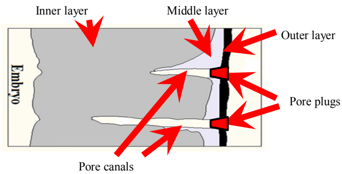


Figure 4: Structure of the zebrafish chorion

5 Conclusions

A micro force measurement, transmission and control system is developed to precisely regulate the forces exerting on zebrafish embryos with ±5μN accuracy. The system enables the characterisation of the viscoelastic parameters of zebrafish embryo membranes and the finding that mechanical forces change the zebrafish embryo's impedance.

References:

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