COMPUTER CONTROLLED PIEZO MICROMANIPULATION SYSTEM FOR BIOMEDICAL APPLICATIONS

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Abstract: In this paper, the development of a computer controlled piezo manipulation system for biomedical applications such as intra-cytoplasmic sperm injection (ICSI) is presented. The hardware setup and the control strategies will be described in full details to illustrate the advantages of this approach as compared to other manual-based injection methods.

Keywords: Precision measurements, control precision, actuators, speed control, biomedical control systems.

1.INTRODUCTION

ICSI is a human-assisted method for animal or human reproduction, which is first introduced by Palermo et al. (1992) and it has since been used throughout the world. However, the survival and fertilization rates of oocytes from the ICSI process are still widely varying among practicing hospitals and institutions. Reported survival rates have ranged from 80 to 90%, and fertilization rates of intact oocytes have ranged from 45 to 70%.

There are two main factors affecting the success rate. One of these is due to the specific medical processes used in the actual processing of oocytes and spermatozoa. The other is due to the method used in the insertion of the needle into the ooplasm, and the impact caused to the oocytes during the insertion process. In this paper, we are mainly concerned with addressing the latter cause. It is possible that the initial orientation of oocytes and spermatozoa can be carried out using a fixed procedure before the actual micromanipulation, . Thus, the actual placement of the spermatozoa within the oocytes constitutes a very important factor for the survival and fertilization rates of ICSI. Traditionally, a successful ICSI mostly relies on the manual operation of experienced doctors. But, it is still very difficult, even for a highly experienced doctor, to be able to repeat the process precisely and consistently, inevitably resulting in undue trauma and damage caused to the oocyte.

In this paper, we develop a systematic and operator friendly, yet sophisticated method, to assist the operator to execute the ICSI process at a high oocyte survival rate. The method is based on the use of a precisely-guided piezo actuator. This actuator offers the operator highly repeatable motion at both very high speed and ultra-fine resolution. These contradictory yet desirable end objectives are unachievable with the manual approach. A library of basic piezo movements is developed to enable the operator to experiment and construct a sequence of optimal mechanical movements for the ICSI operation. Investigation results are documented on the construction of an optimal injection profile to execute the ICSI process at minimal trauma and damage to the oocyte.

2. THE STRUCTURE OF OOCYTES

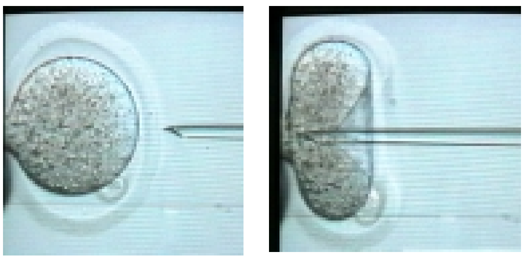

Fig. 1: The structure of oocytes

From the engineering viewpoint, the oocyte is composed of three parts: the zona pellucida, the cytoplasm or vitelline, and the vitelline membrane or oolemma. The zona pellucida is a thick transparent membrane surrounding the ovum. The vitelline membrane, which is located between the vitelline and zona pellucida, is a protective membrane formed around cytoplasm, acting as an obstruction to the entry of sperm. Usually, the zona pellucida and oolemma is very elastic and it can be difficult to be pierced at low speed as illustrated in Fig. 1.

The main objective of ICSI is to pierce a needle, holding the sperm, through the zona pellucida and oolemma, and release the sperm in the deep area of cytoplasm. Minimum deformation of the oocyte should be achieved to maximize the survival of the egg after the artificial ICSI process.

3. OPERATIONAL PRINCIPLES OF PIEZO-MICROMANIPULATOR

A piezo-micromanipulator is constructed from appropriately positioned piezoelectric materials, which can convert electrical energy into mechanical energy and vice versa. For nanopositioning applications, the precise motion, which results when an electric field is applied to a piezoelectric material, is of a great value. Piezo-actuation is now widely used in highly precise semiconductor processes, nano-metrology and sub-micrometer positioning and assembly automation.

Figure 2 shows a common configuration in the form of a piezo stack actuator, which can achieve a very minute δL deformation when a voltage is applied.

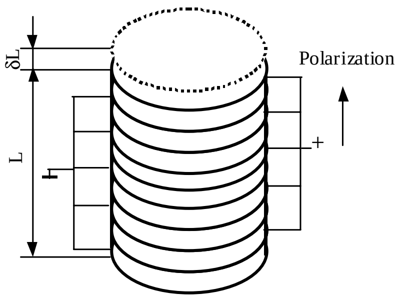

Fig. 2: Piezo stack actuator

The main advantages of piezo actuators are:

Unlimited Resolution. A piezoelectric actuator can produce extremely fine position changes down to the subnanometer range. The smallest changes in operating voltage are converted into smooth movements. Motion is not influenced by stiction/friction or threshold voltages.

Fast Expansion. Piezo actuators offer the fastest response time available (microsecond time constants). Acceleration rates of more than 10,000 g's can be obtained.

No Magnetic Fields. The piezo effect is related to electrical fields. Piezo actuators do not produce magnetic fields nor are they affected by magnetic fields. Thus, they do not exhibit rippling or cogging force characteristics found in permanent magnet linear motors. They are specially well suited for applications where influence from magnetic fields cannot be tolerated.

No Wear and Tear. A piezo actuator has neither gears nor rotating shafts. Its displacement is based on solid state dynamics and shows no wear and tear. Endurance tests conducted on piezo actuators have shown no change in performance even after several billion cycles.

Vacuum and Clean Room Compatible. Piezo actuators are ceramic elements that do not need any lubricants and show no wear and abrasion. Thus, they are cleanroom compatible and ideally suited for Ultra High Vacuum (UHV) applications.

4. PRECISE MECHANICAL GUIDING SYSTEM

In certain applications with more stringent geometrical requirements (such as ICSI), a stack actuator alone is not sufficient to achieve the desirable end objectives. For example, when precisely straight motion is needed, and only nanometric deviation from the ideal trajectory can be tolerated, a stack translator cannot be used because it may deviate as much as a few tens of arcseconds from the straight path while expanding. If the stack and the part to be moved are decoupled and a precision guiding system is employed, exceptional trajectory control can be achieved. The best guiding precision can be achieved with flexures as shown in Fig. 3. This guiding system is used in the overall construction of the injection system reported in this paper.

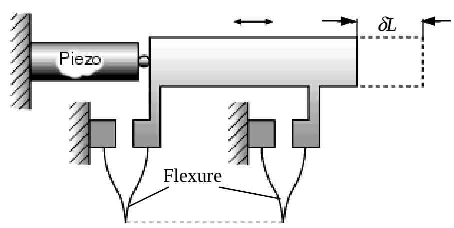

Fig. 3: Flexure guided piezo actuator

The figure shows the structure of a piezo driven flexure stage with an integrated flexure guiding system. An integrated 3:1 lever driven by a piezo stack actuator pushing a spherical tip constructed integrally to the lever is used to enlarge the piezo movement.

The lever is connected to the platform by a flat spring, which is very stiff in the push/pull direction but flexible in the lateral direction. This flexibility ensures straight stage motion with minimum tilt and lateral deviation. The system runout and flatness are less than 5 nanometers and even this low figure can be reduced with a larger flexure base. The flexure design is not limited to single axis stages; systems with up to six degrees of freedom can be constructed based on flexures.

5. PIEZO INJECTION SYSTEM

5.1. Hardware Configuration

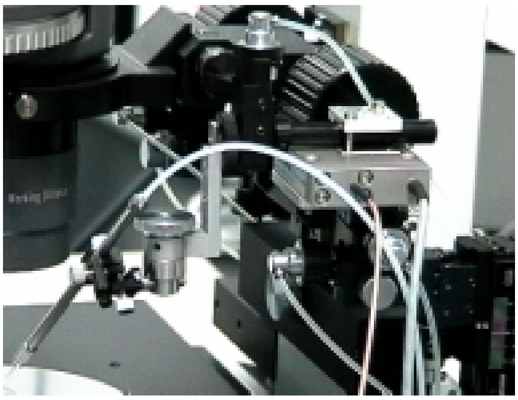

Fig. 4: Photograph of the piezo injection system

The photograph depicted in Fig. 4 shows the hardware structure of the piezo injection system developed. The main hardware configuration of the manipulator is shown in Fig. 5.

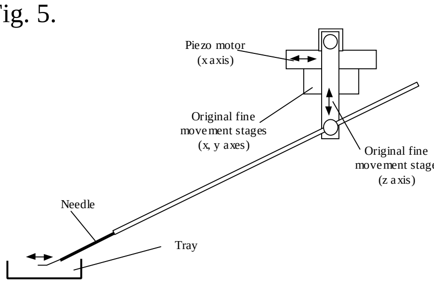

Fig. 5: Hardware configuration

A flexures-guided piezo stage is used to drive the needle in the desired piercing direction. The original microscope, onto which the piezo injection system is integrated, is already equipped with a hydraulically-driven fine and coarse movement stages manufactured by Narishiga. A special mechanical fixture is designed to mount the piezo actuator to the system. In this way, the operator can still use all original functions without any additional difficulties after the piezo linear motor is added.

5.2. Library of Basic Motion Function Blocks

A set each of five basic motion function blocks is developed for the forward and reverse motion of the piezo motor respectively. Fig. 6 shows these motion function blocks. The operator can change the key parameters associated with each of these blocks such as ramp velocity, step size etc. via the software interface. Complex motion can be configured from these basic motion blocks. Additional motion blocks can be easily configured to the library according to the actual application and requirements.

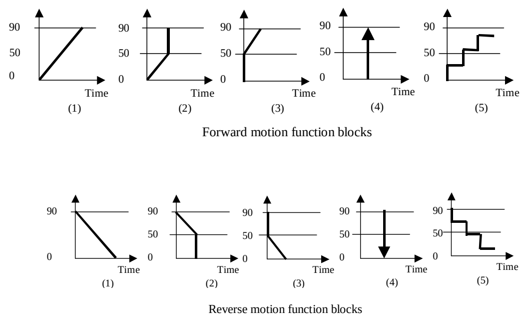

Fig. 6: Basic motion function blocks

5.3. Forward Motion with Vibration

In addition to the abovementioned motion function blocks, a short axial vibration can be added to the needle tip. The frequency and the amplitude of the vibration can be adjusted through the interface shown in Fig. 7. Two types of vibrations can be selected through the interface. The PULSE 1 vibration mode allows for vibration with same forward and backward amplitude and velocity. The other mode, PULSE 2, can vibrate the needle tip with different forward and backward amplitude and velocity. It will move the tip forward with maximum speed, but backward slowly. When tip vibration is not needed, it can be disabled via the STOP button.

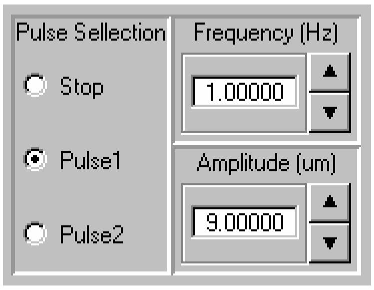

Fig. 7: Vibration modes

5.3. Operator Interface

The direction of motion can be easily selected by the operator via a special customized three-buttons mouse. The forward motion is activated via the left button, and the reverse motion is activated via the right button. The middle button is used to activate a step jump where the step direction follows the last motion. This means the middle button will manipulate the piezo actuator to step forward/reverse if the last executed motion is forward /reverse.

The step size, ramp velocity and acceleration can all be adjusted directly via the sliders of a windows-based operator software interface as shown in Fig. 8. The current position of the actuator is also shown on the software interface.

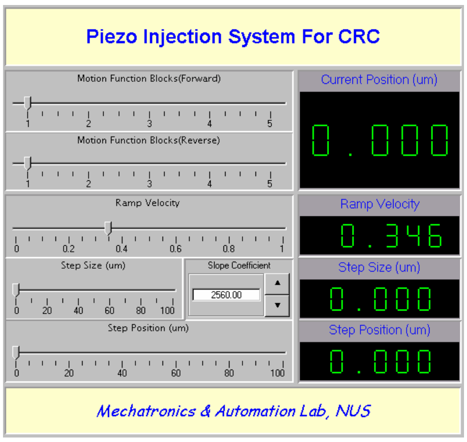

Fig. 8: Windows-based operator interface

5.4. Vibration Issue

While a large acceleration is desirable at the piercing instance, it may also lead to undue vibration which will cause as much damage to the oocyte. Experiments show that stiff mechanical fixture and a proper needle holder design can reduce this problem. The control system can also help to alleviate the vibration problem by terminating signal transmission at the vibration and resonant frequencies using notch filters. To further reduce the vibration phenomenon, an Ependorf micromanipulator is used to bear the piezo motor. In this situation, the distance from the needle tip to the driving point of the needle holder is shorten considerably. So, the tip radial vibration is reduced to a very small level, even if n=1. The structure is shown in Fig. 9.

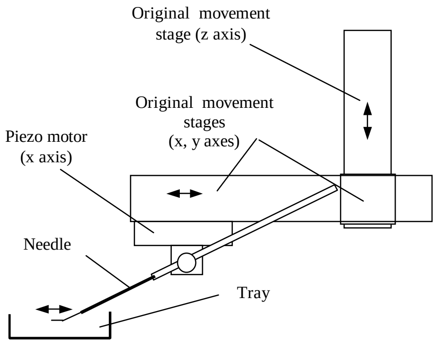

Fig. 9: Mechanical fixture to reduce vibration

6. CONCLUSIONS

The development of a computer controlled piezo manipulation system for biomedical applications such as intra-cytoplasmic sperm injection (ICSI) has been presented in the paper. The hardware setup and the control strategies are designed with a view to carry out the required process with better efficiency as compared to other manual-based injection methods.

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