# Vision Guided Robotic Cell Micromanipulation

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**PROJECT DESCRIPTION:**

Since the inception of the life science era in the past decade, the science and art of nuclear reprogramming has been one the most intriguing stories, captivating scientists and the man in the street alike. Among others, nuclear programming promises the possibility of therapeutic cloning, a technique that reproduces spare tissue and organs for the patient from his or her own somatic cells. The current approach requires the removal of the nucleus from the recipient's egg and replaces it with a donor's nucleus, all performed manually.

This highlights the dependence of numerous cell microinjection tasks in life science research and applications on the skill of experienced lab operators. The success rates of cell microinjection tasks have been reported to range from a marginally acceptable 40-70% in microinjection applications (e.g. intracytoplasmic sperm injection in In-Vitro fertilization) to a measly 1-4% in transgenic work for plant, animal, and human embryonic or stem cells. Besides putting the blame on intrinsic genetic defects and reasons not yet known, a certain part of this inefficiency can be traced back to the manual imprecision and inconsistency of the operator.

We are proposing a novel vision-guided robotic approach to replace human intervention. A three degree-of-freedom piezoelectric-driven robotic manipulator is used to hold a micropipette. A high speed camera with a embedded processor captures images of the cells and the micropipette tip under a conventional microscope, processes the images, and controls the robotic manipulator in real-time to perform the intended task.

The proposed approach holds the potential of revolutionizing microinjection standards and protocols for cells and microorganisms in life science research and applications. It may also allow microbiologists to attempt experiments and new procedures that are otherwise hindered by the inherent limitation of human in manual manipulation at the microscopic level.

As an example, in the research to uncover the molecular mechanism of early embryonic cells, the microbiologists have great interest in the study of key cell-cell signaling and interaction using sea urchin as a model. One important experiment involves dissecting of sea urchin embryonic cells at their 16-cell stage to remove and transplant the four micromeres, which are responsible for the growing of limbs, to the embryonic cells of other sea creatures. Successful dissection of the micromeres requires manipulation accuracy of less than 5μm, which is practically impossible to achieve manually.

**GRANT:**
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**PUBLICATIONS:**

***Refereed Journal (Published/In Press):***

1. Y. L. Zhang, M. L. Han, M. Y. Yu, C. Y. Shee, and W. T. Ang, "Automatic hysteresis modeling of piezoelectric micromanipulator in vision-guided cell micromanipulation systems," IEEE/ASME Trans. Mechatronics, vol. 17, no. 3, pp. 547 – 553, 2012.
2. M. L. Han, Y. L. Zhang, M. Y. Yu, C. Y. Shee, and W. T. Ang, "Non-contact force sensing for real-time stressing of biological cells," Micro Nano Lett., vol. 6, no. 5, pp. 306 – 310, May 2011
3. Y. L. Zhang, M. L. Han, J. Vidyalakshmi, C. Y. Shee, and W. T. Ang, "Automatic control of mechanical forces acting on cellbiomembranes using a vision-guided microrobotic system," J. Microscopy, vol. 236, no. 1, pp. 70 – 78, 2009.
4. Y. L. Zhang, M. L. Han, C. Y. Shee, T. F. Chia, and W. T. Ang, "Self-calibration method for vision-guided cell micromanipulation systems," J. Microscopy, vol. 233, no. 2, pp. 340 – 345, 2009.

***Refereed Conference (Published/In Press):***

1. M. Han, Y. L. Zhang, M. Y. Yu, C. Y. Shee, and W. T. Ang, "Real-time modeling and control of the circular cell membranes strain," in Proc. IEEE Intl. Conf. Robotics and Automation, Shanghai, China, Dec. 2011, pp. 4115 – 4120.
2. M. Yu, M. L. Han, C. Y. Shee, and W. T. Ang, "Autofocusing algorithm comparison in bright field microscopy for automatic vision aided cell micromanipulation," in Proc. IEEE Intl. Conf. Nano/Molecular Medicine and Eng., Hong Kong, Dec. 2010, pp. 88–92.
3. M. L. Han, Y. L. Zhang, M. Yu, C. Y. Shee, and W. T. Ang, "Real-time stressing and force sensing on biological cells," in Proc. IEEE Intl. Conf. Nano/Molecular Medicine and Eng., Hong Kong, Dec. 2010, pp. 16–20.
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5. M. Han, Y. Zhang, C. Y. Shee, and W. T. Ang, "Estimation of the cell deformation," in Proc. 1st Intl. Conf. Intelligent Robotics and Applications, vol. 5315 LNAI, no. Part 2, Wuhan, China, Oct. 2008, pp. 217 – 223.

6. M. Han, Y. Zhang, C. Y. Shee, T. F. Chia, and W. T. Ang, “Plant cell injection based on autofocusing algorithm,” in 2008 IEEE Conf. Robotics, Automation and Mechatronics, Chengdu, China, Sep. 2008, pp. 439 – 443.
7. Y. Zhang, M. Han, C. Y. Shee, and W. T. Ang, “Calibration of piezoelectric actuator-based vision guided cell microinjection system,” in 2008 IEEE/ASME Intl. Conf. Advanced Intelligent Mechatronics, Xi’an, China, Jul. 2008, pp. 808 – 812.
8. Y. Zhang, M. Han, C. Y. Shee, T. F. Chia, and W. T. Ang, “Automatic vision guided small cell injection: Feature detection, positioning, penetration and injection,” in Proc. 2007 IEEE Intl. Conf. Mechatronics and Automation, Harbin, China, Aug. 2007, pp. 2518 – 2523.
9. Y. Zhang, M. Han, C. Y. Shee, T. F. Chia, and W. T. Ang, “Position control using 2D-to-2D feature correspondences in vision guided cell micromanipulation,” in Proc. 29th Annu. Intl. Conf. IEEE Engineering in Medicine and Biology Society, Lyon, France, Aug. 2007, pp. 1449 – 1452.

***Non-Refereed Conference (Published/In-Press):***

1. M. L. Han, Y. Zhang, C. Y. Shee, and W. T. Ang, “Injection of microbiological cells using microscopic focus method,” in 3rd Asian Conf. Computer Aided Surgery, Singapore, Dec. 2007.