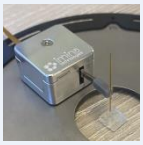


Microrobotic sample transfer for high throughput drug screening

Ziwei Dang, Jang Ah Kim, Meysam Keshavarz, Alex Thompson
The Hamlyn Center, Institute of Global Health Innovation, Imperial College London, UK.

HAMLYN SYMPOSIUM ON MEDICAL ROBOTICS 2021

Abstract

In this project, a microwell plate and a microrobotic sample transfer mechanism will be developed. The transfer mechanism will be based on capillary action to allow transfer of micro-liter volumes, and this will be controlled automatically based on visual feedback via a magnetic micromanipulation platform (Imina).

Introduction

Background: The development of a new drug takes a long time (about 12-15 years) and needs large financial support (about 1 billion dollars). On average, only one molecule out of more than one million screened will be studied in late-stage clinical trials and eventually used by patients. In early 1990s, high throughput screening took the place of conventional techniques for early-stage drug discovery [1] to save time and enhance efficiency. Meanwhile, fluorescence-based assays have become a practical technique for drug screening. Real-time molecular and cellular analysis plays a significant role in drug discovery.

Limitation:
Large-scale pipetting robots: Usually includes x-y drives, plus sometimes a z drive, to control the translational motion of the end-effector [2]. Inappropriate for real-time imaging and control at the micro-scale. Not capable of targeting individual or small groups of cells.
Microfluidic systems: Restrictive for cellular cultures [3].

Solutions: Develop a microrobotic sample transfer mechanism to facilitate high throughput imaging under standard and commercially available microscopes.

Method

Design and fabricate microwell plates

- Negative models design (with draft angle; different type) & 3d printing
- PDMS (Polydimethylsiloxane) microwell plate (test different concentration)
  advantages: elasticity, optical permeability, biocompatibility, inexpensive.

Capillary action liquid transfer

- Experiment setup

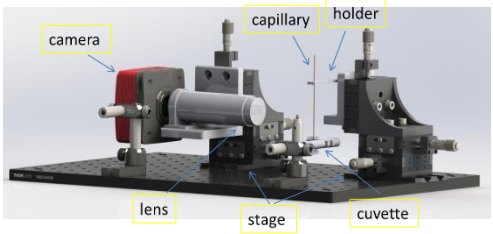


Figure 1 - Experiment setup

- Prediction and measurement of liquid rise rate

Control of imina microrobots

- Acquire and import real-time image from zeiss microscope (screenshot)
- Imina microrobots tracking and microwell plate detection
- Computer vision-based control
  calibration (direction & speed), visual feedback.

Results

Microwell plate

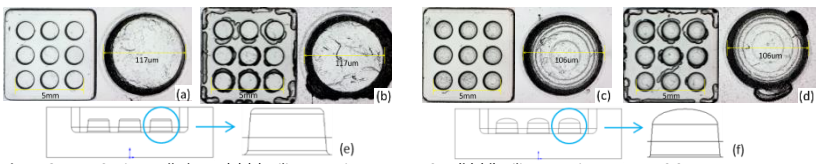


Figure 2 - PDMS microwell plates. (a) (c): silicone:curing agent = 10:1; (b) (d): silicone:curing agent = 10:2; (a) flat bottom; (b) flat bottom; (c) round bottom; (d) round bottom; (e) negative models example (flat bottom); (f) negative models example (round bottom).

Capillary action

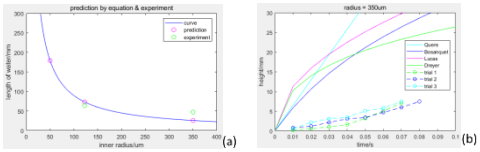


Figure 3 - (a) relationship between inner radius and maximum height; (b) liquid rise rate (prediction and experiment).

Imina microrobots tracking, microwell plate detection, calibration (direction)

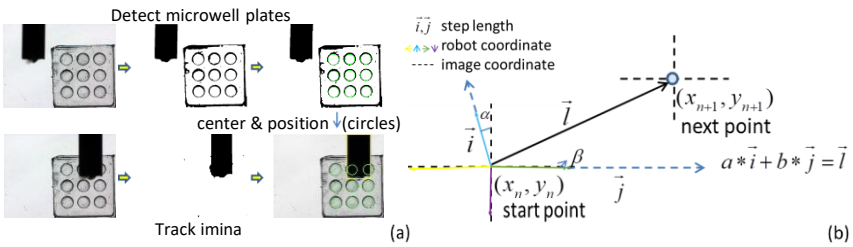


Figure 4 – (a) detect microwell plates and imina tracking; (b) image and robots coordinate (direction calibration).

Future plan

Microwell plates

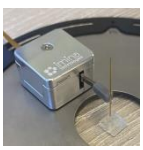
- Test the minimum size achievable using PDMS moulding
- Further test fabrication: silicone moulding and 2-photon polymerisation

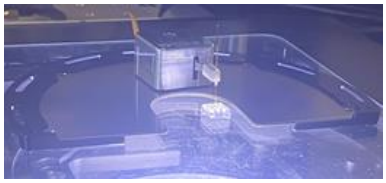
Control of imina microrobots

- Calibration
- X-Y plane: computer vision-based control
- Z plane: set parameters in advance

Liquid release approach

- Micropump
- By passively diffusion (eg. contact with hydrogel)





References

[1]B. Liu, S. Li, and J. Hu, "Technological Advances in High-Throughput Screening," American Journal Pharmacogenomics, vol. 4, pp. 263–276, August 2004.
[2]F. Kong, L. Yuan, Y. F. Zheng, and W. Chen, "Automatic liquid handling for life science: a critical review of the current state of the art," Journal of Laboratory Automation, vol. 17, no.3, pp. 169-185, 2012.
[3]E. E. Hunter, E. B. Steager, A. Hsu, A. Wong-Foy, R. Pelrine and V. Kumar, "Nanoliter Fluid Handling for Microbiology Via Levitated Magnetic Microrobots," in IEEE Robotics and Automation Letters, vol. 4, no. 2, pp. 997-1004, April 2019.