A Shrinking Tomography System: Challenges and Application

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Abstract

This paper introduces the process of developing tomography systems onto chip-based devices. Design consideration and selection of sensor array for miniaturised devices are studied and discussed. This paper shows the electrical measurement of the miniaturised tomography system to achieve imaging of experimental sample without using optical lens equipment. The fabricated device is tested with various multiphase samples to show the feasibility of the miniaturised tomography system in reconstructing tomogram.

Keywords: Microfabrication, planar electrode array, capacitance measurement.

1. Introduction

Since the emergence of microanalysis devices in the 1990s introduced by Manz [1], this micro platform has drawn great attention from researchers of various fields. This micro platform becomes an important tool for chemical analysis, bioanalysis and cell culturing [2-3]. Currently, most of the activities within the micro platform are visualised and recorded using optical microscope. The microscope provides high-resolution images and easily available in the laboratory; however, the utilisation of the microscope can be limited when there are specific requirements of the application or reaction environment such as an incubator. Besides that, some biomedical experiments and analysis require continuous monitoring, which is time-consuming. For example, in cell culturing, the cells are placed in a cell incubator to provide stable thermal condition which conventionally microscopic observation is the commonly used method to observe the cellular activities inside the incubator that might cause limitation of working space in the incubator. Furthermore, a microscope with camera for recording needs a huge database and large storage memory.

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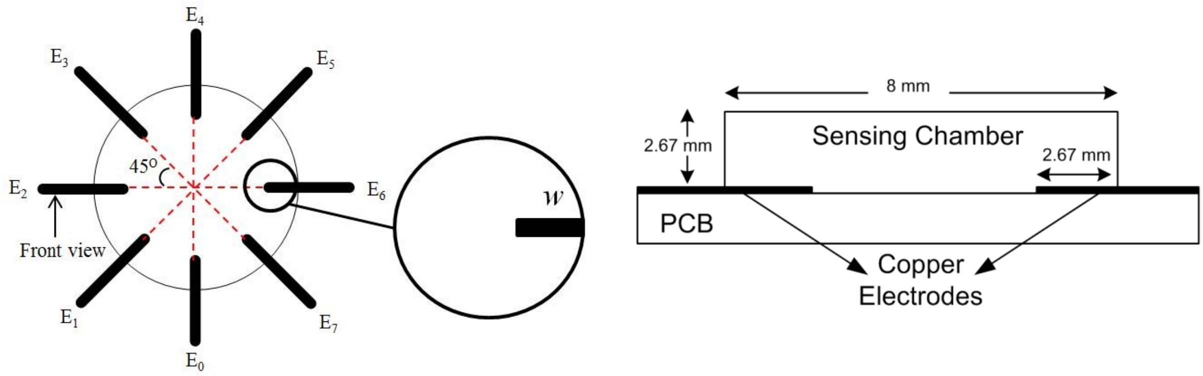
The idea is to replace tomography system within this platform to enable 2D data records without optical microscope and at the same time provides electrical measurements that can be easily stored, processed and used for data analysis. Tomography is a technique that produces cross-sectional images of human body or solid object without cutting the object. Process tomography (PT) is widely used for monitoring flow process of closed pipeline without obstructing and affecting the flow inside [4]. A typical tomography system consists of sensing array, control unit, data acquisition unit and image processing system in order to capture images of the cross-section. Various types of sensing array are used in which it defined the type of tomography systems such as Ultrasonic Tomography (UT), Electrical Resistance Tomography (ERT), Positron emission tomography (PET), Electrical Impedance Tomography (EIT) and Electrical Capacitance Tomography (ECT). The selection of PT type is based on application and purpose of the analysis. Among items to be considered are the environment, the material inside the inspection area, the size of the sample and the sensing element [5]. With microfabrication techniques, miniature sensor array such as electrodes can be integrated inside a microdevice easily as compared to ultrasound or optical sensors. Electrode-based sensors offer measurement in impedance and capacitance measurement. This microdevice with the sensor array acts as a miniature tomography system that allows the users to obtain 2D image data of the sample [6].

Sensor array is an important element within a tomography system. To integrate suitable sensor array without interrupting the microfluidic platform, planar sensor array using electrodes are chosen. Besides that, optical sensors and acoustic sensors are difficult to be integrated in micro platform due to fabrication limitation. Other than that, based on the Beer-Lambert Law, the optical detection scale with path length which limits the sensitivity of this sensor. Therefore, the structure of the sensor array for microdevice platform is different with the conventional process tomography system. Planar sensor array is proposed and tested for the feasibility in microdevice platform tomography. Planar electrodes are feasible for impedance [7,8] and capacitance measurement [9].

This paper discusses the design and fabrication considerations for miniaturizing tomography system within a chip-based platform. Furthermore, the overall development of the miniaturized tomography system with 2D tomograms of the sample being monitored in the sensing area is discussed as well.

2. Design and Fabrication

Due to the suitability of sensor integration within small device platform, electrodes are often chosen for the sensor array. The configuration of the sensors design is shown in Figure 1.



(a) (b)

Figure 1. The sensing chamber and sensor array (a) Top View (b) Front View

The electrode array is fabricated using a standard copper coated printed circuit board (PCB), the design of the electrodes are designed using computer-aided design program and the design is then transferred to PCB through UV exposure. The exposed PCB is developed by etching with ferric chloride ($FeCl_3.6H_2O$). The developed PCB with copper electrodes is shown in Figure 2.

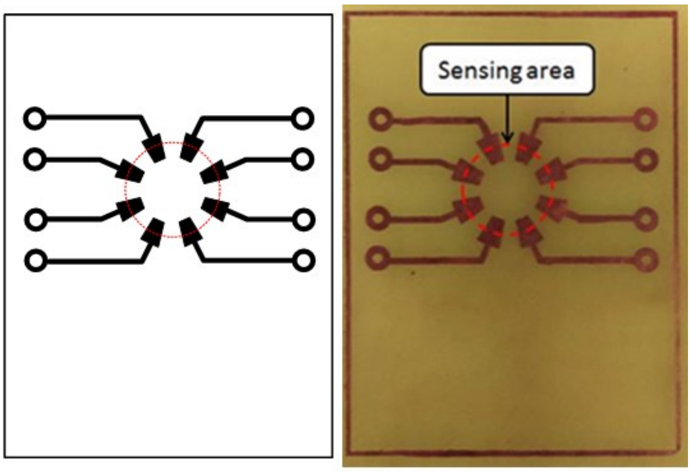


Figure 2. Electrode array design and development on PCB

The sensing chamber is fabricated using the casting method similar to microfabrication process. Figure 3 shows the fabrication and developed polymer chamber.

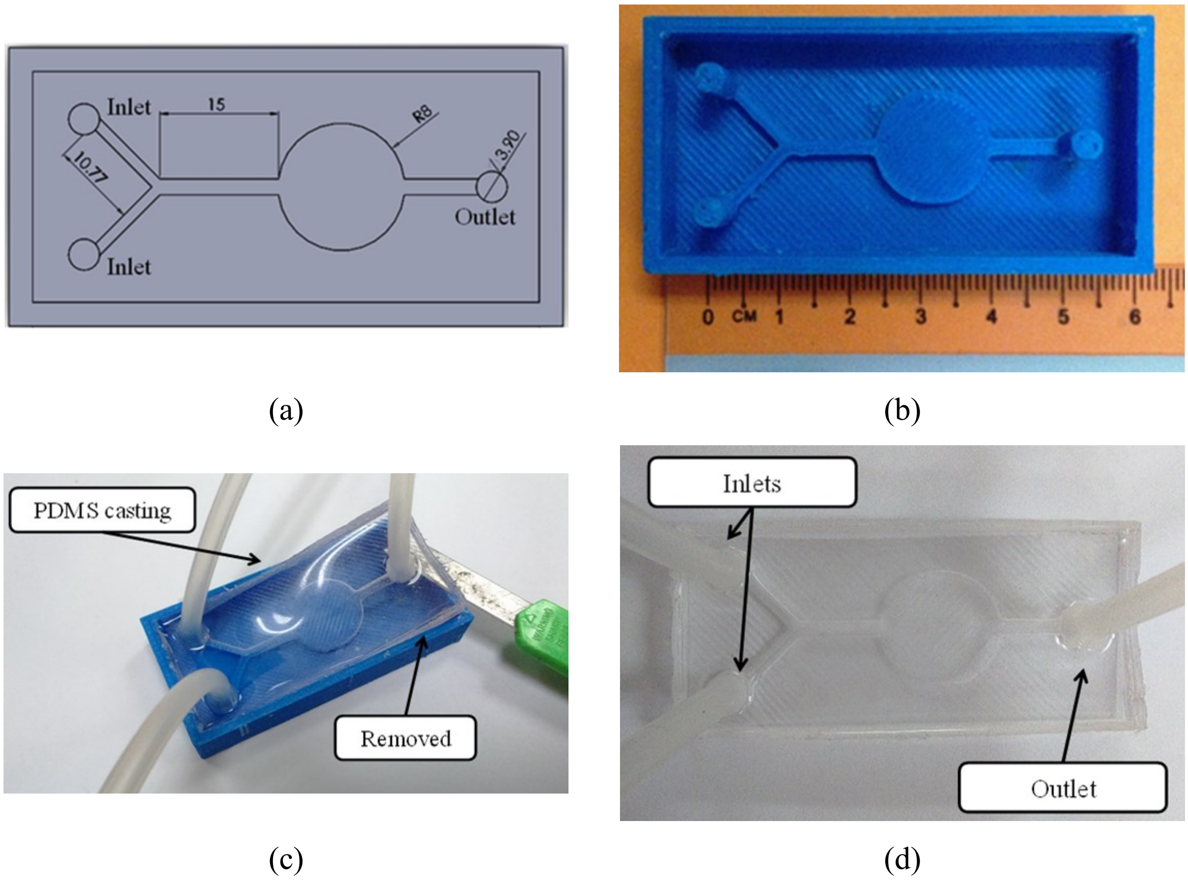


Figure 3. Sensing chamber fabrication (a) CAD drawing (b) 3D printing master template (c) cured PDMS casting (d) fabricated PDMS channel and chamber

A negative casting replica of the microchannel and sensing chamber is designed with CAD software (Solidworks®). The replica acts as the master template for rapid prototype of a Y-shape channel design so that 2 different fluid samples can flow into the chamber at the same time to produce two-phase fluid flow sample.The overall size of the fabricated 3D master template is 70 mm × 35 mm × 10 mm (length × width × height). The width and the height of the microchannel is 3 mm × 2.67 mm respectively. The 3D master template is printed by using3D printer (MakerBot Replicator) where this mater template is used for casting the polymer resin (PDMS elastomer by Dow Corning's Sylgard® 184). Polymer resin is prepared according to the elastomer recipe and poured into the master template with silicon tubing attached to all the inlets and outlet beforehand. The resin together the master template is cured in a research oven at 60°C for 60 minutes and then left overnight at room temperature. Finally, the PDMS microchannel is removed carefully from the master template.The cured PDMS microchannel is assembled on the developed PCB shown in Figure 4.

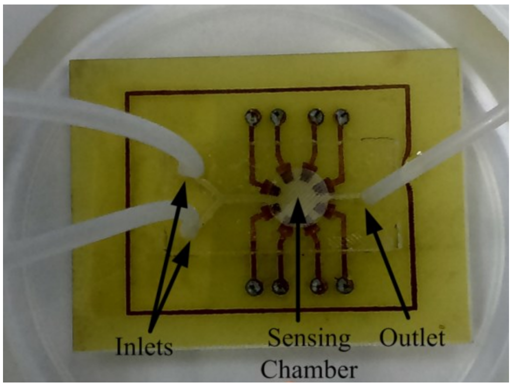


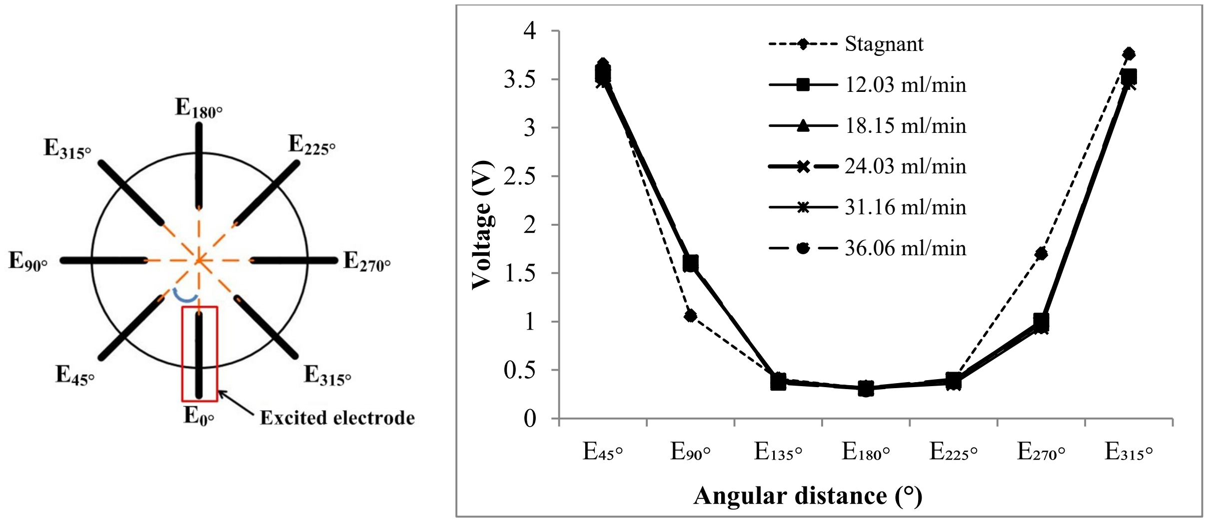
Figure 4. Micro sensing chamber and sensor array

The PDMS chamber is then adhered on the PCB by applying a thin layer of the same PDMS elastomer polymer resin on the PCB and the PDMS chamber. The device is then cured in the oven at 60°C for 30 minutes.

3. Electrical Measurement

Similar to process tomography system, the electrical signal measurement is conditioned and processed for image reconstruction. An analysis on the effect of volumetric flow rate of the sample on electrical signal measurement of miniaturized planar electrode array has been conducted. The volumetric flow rate is controlled by a peristaltic dosing pump (Myquastore, China) that operate at 7.8 V to maximum 12 V where the maximum flow range is 100 ml/min. Five flow rates have been identified and were tested with the developed device to study the effect of volumetric flow rate of sample inside the sensing chamber. A single phase sample using deionized water is flowed into the microdevice until fully filled up the sensing area. The configuration of the electrode array and the voltage measurement of the microdevice with different flow rate is presented in Figure 5.

From Figure 5(a), excited electrode at each cycle is labelled as $E_{0°}$, and the first adjacent electrode in clockwise will be labelled as $E_{45°}$. The excitation cycle of the electrode is controlled by a control unit by supplying $5V_{ac}$ with 100 kHz. From the obtained voltage measurement, it shows that the measured voltage has similar trend for stagnant and all different flow rates.



(a) (b)

Figure 5. Voltage measurement (a) electrode configuration based on excited electrode (b) stagnant and various flow rates within chamber.

Another voltage measurement analysis is conducted by using different liquid-based materials such as water, oil, 0.3 M glucose and ethanol with similar excitation voltage input at 12.03 ml/min. Figure 6 shows the voltage measured for four types of liquid.

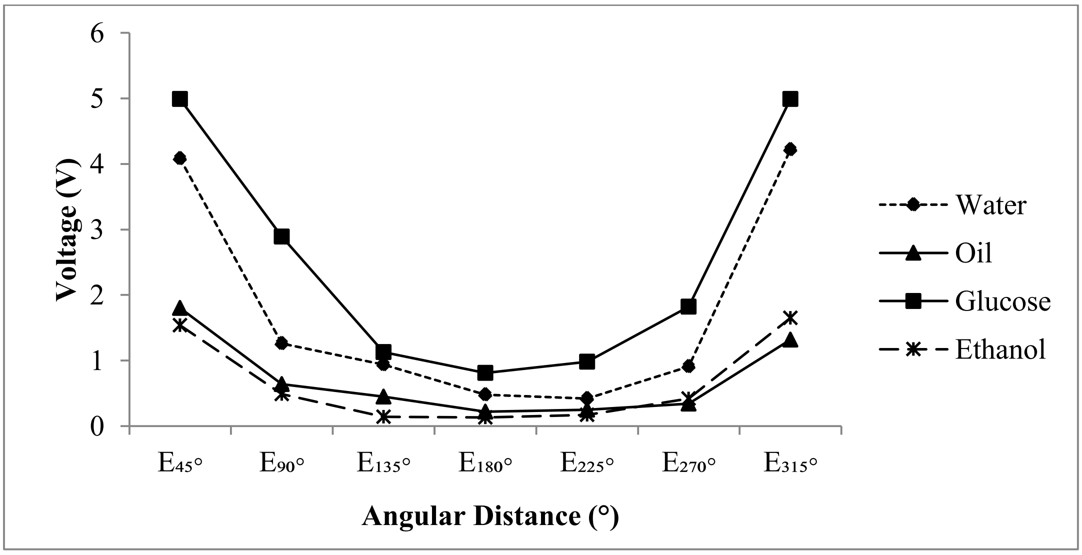


Figure 6. Voltage measurement for different liquid-based material.

The obtained data for each type of samples show similar trends which are U-shape graphs. Glucose solution has the highest voltage measured as compared to other samples which is between 5 V to 0.81 V followed by water sample where the voltage measured is between 4.22 V to 0.42 V. The lowest voltage is obtained using oil sample where the voltage measured is between 1.8 V to 0.22 V. There is a significant difference between oil sample to other liquid which due to differences in material permittivity as shown in equation (1).

$$C_X = \frac{2\varepsilon_r \varepsilon_o \ell}{\pi} \ln\left[1 + \frac{w}{a} + \sqrt{\left(1 + \frac{w}{a}\right)^2 - 1}\right] \quad (1)$$

where ε_r is the relative permittivity, $\varepsilon_o$is the electric constant, ℓ is the length of electrodes, w is the width of the electrode, and a is the half gap of the electrode. As each sample show differences in voltage measurement for different material, capacitance measurement can be utilized for tomogram reconstruction.

3.1 Image reconstruction

As in microdevice measurement requires fast data acquisition and short computational time, the simplest linear back projection (LBP) is suggested and a 16 × 16 sensitivity map is utilized for image reconstruction purposes.

The device is tested with liquid-gas and liquid-liquid samples. Each sample is loaded into the sensing chamber via the inlet. The mixing pattern is changing continuously and the image is reconstructed based on the measured electrical signal. The lowest flow rate at 12.03 ml/min is set at the micropump and it is continuously feeding into the sensing chamber. The reconstructed tomogram is compared to the real image of the sensing chamber using camera. Figure 7 shows the real image and reconstructed tomogram for three multiphase samples within the sensing chamber of the microdevice.

From Figure 7, for liquid-gas and immiscible liquid-liquid samples, the tomogram can clearly show the materials with different colour code. However as for miscible liquid-liquid sample, due to convection within the chamber, water and glucose is mixed up and it is indistinguishable from each other. Besides that, from the voltage measurement in Figure 6 shows that water and glucose has very similar reading which makes it difficult to be differentiated.

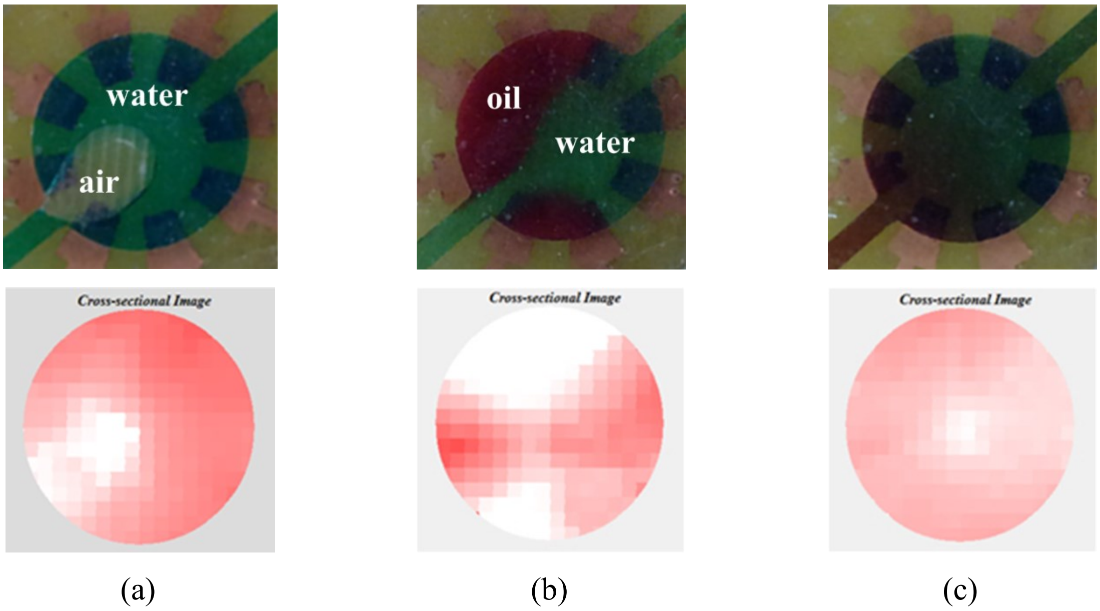


Figure 7. Real image versus reconstructed tomogram (a) liquid-gas: water-air (b) Immiscible liquid-liquid: oil-water (c) Miscible liquid-liquid: water – 0.3 M glucose.

By looking closely on the tomogram in Figure 7(c), some pixels show small differences in the tomogram which indicating there is different material in the sensing chamber as to compare a 100% glucose and 100% water filled up the sensing chamber the reference tomogram is shown as Figure 8.

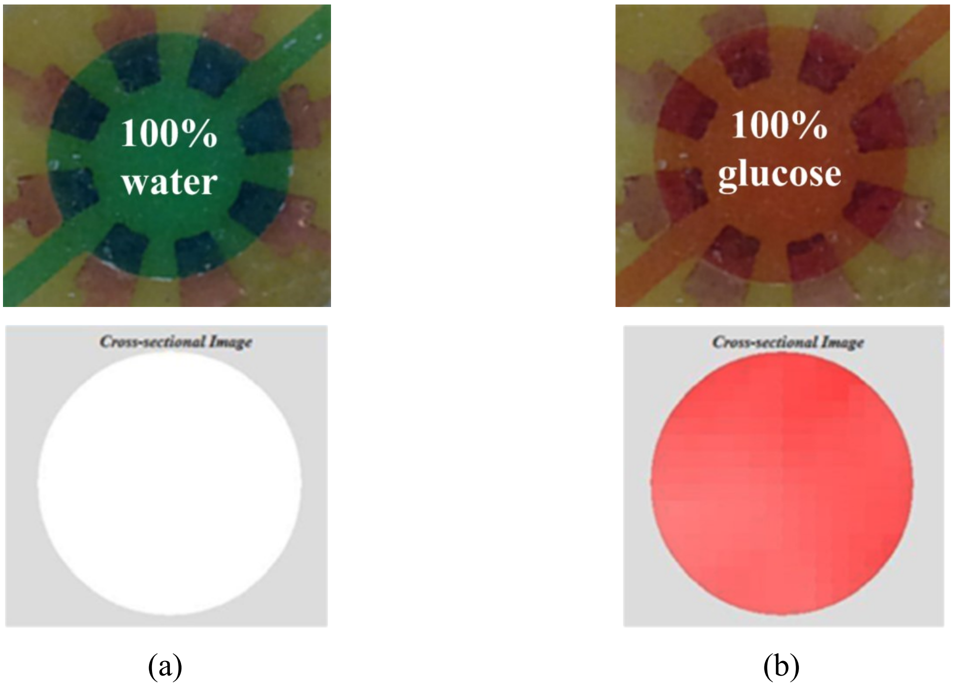
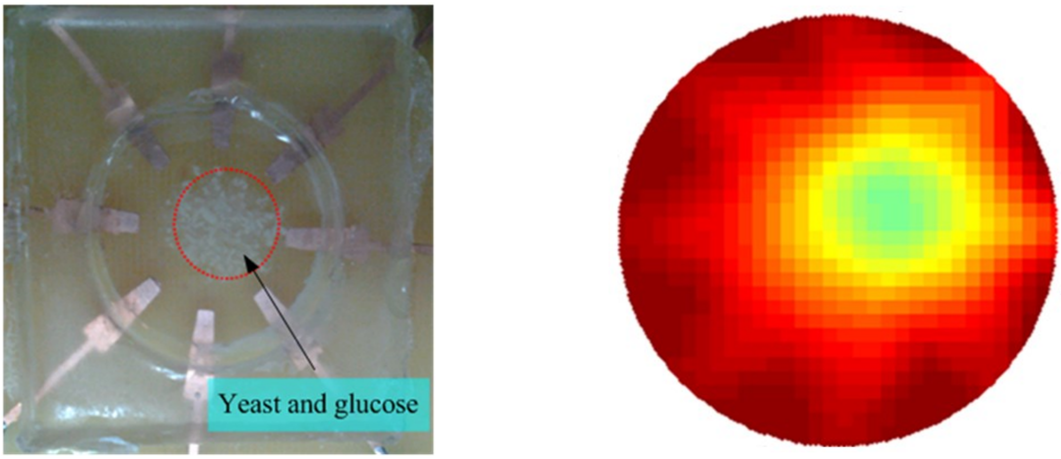


Figure 8. Reference Calibration for (a) water (b) 0.3 M glucose

Refer to Figure 8, the sensing electrode array is calibrated with the sample before the real measurement. In the miscible liquid-liquid measurement, the 100% water and glucose show significant differences in the tomograms.

3.2 Yeast Cell Image Reconstruction

This micro-tomography device is tested with yeast sample immersed in glucose solution. Figure 9 shows the reconstructed tomogram of the sample above.



(a) (b)

Figure 9. Yeast cell and glucose within tomography microdevice (a) real image (b) reconstructed tomogram

From Figure 9, the glucose is filled up the whole chamber and 0.2 g of instant dried yeast is added into the glucose solution within the chamber. The dried yeast was seemed to be slowly immersed in the glucose water and the tomogram was taken after 15 minutes of idle time. It shows that the planar electrodes are capable to differentiate the accumulated yeast within the sensing area. As for cell culturing processes, the flow rate within the sensing area is mostly stagnant and the growing processes of the cell might take longer time within incubator, by using tomography method, images of the growing process can be recorded electrically and the signal can be used as input for post-process analysis such as artificial neural network algorithm.

4. Conclusion

The miniaturized tomography device shows that planar electrodes are feasible for image reconstruction for stagnant of hydrodynamic samples. Multiphase samples have been tested and the obtained tomograms show closed relation as compared to the real image of the sample within the sensing chamber. This project shows that there is other potential of tomography within a smaller platform and also contribution towards microfluidics research.

Acknowledgement

The authors would like to thank the Universiti Teknologi Malaysia for all the supports in various forms. This research study is indirectly supported by the Research University Grant (Q.J130000.2523.15H88).

References

[1] Manz, A., Graber, N. and Widmer, H. M. "Miniaturized Total Chemical Analysis Systems: A Novel Concept for Chemical Sensing.," *Sensors and Actuators B: Chemical,* 1, no. 6,pp.244-248, 1990.

[2] J.K. Kim, A.M. Stockton, E. Jensen and R. A. Mathies, "Pneumatically actuated microvalve circuits for programmable automation of chemical and biochemical analysis," *Lab Chip*, 16, pp.812-819, 2016.

[3] J. Kieninger, A. Weltin, H. Flamm and Gerald A. Urban, "Microsensor systems for cell metabolism – from 2D culture to organ-on-chip," *Lab Chip,* 18, pp. 1274 – 1291, 2018.

[4] M. S. Beck, T. Dyakowski, and R. A. Williams, "Process Tomography - The State of the Art," *Transactions of the Institute of Measurement and Control*, vol. 20, no. 4, pp. 163-177, 2016.

[5] M. S. Beck, T. Dyakowski, and R. A. Williams, "Process Tomography - The State of the Art," *Transactions of the Institute of Measurement and Control,* vol. 20, no. 4, pp. 163-177, 2016.

[6] Sun, T., Tsuda, S., Zauner, K. P. and Morgan, H. Single Cell Imaging using Electrical Impedance Tomography. *4th IEEE International Conference on Nano/Micro Engineered and Molecular Systems*. January 5-8, 2009. Shenzen, China: IEEE 2009,pp. 858–863, 2009.

[7] Sun, T., Tsuda, S., Zauner, K. P. and Morgan, H. On-chip Electrical Impedance Tomography for Imaging Biological Cells. *Biosensors & Bioelectronics*, 25 no. 5, pp. 1109-1115, 2010.

[8] Ali Zarafshani ; Chris Chatwin ; Thomas Bach ; Bin Zheng, "Using planar electrical impedance tomography as a structural health monitoring method to detect and evaluate the damage to CFRP composite," *2016 IEEE National Aerospace and Electronics Conference (NAECON) and Ohio Innovation Summit (OIS)*, July 25-29 2016, Dayton, OH, USA, pp. 74-79, 2016.

[9] Azmi, A. Miniaturized Planar Capacitance Tomography System Using Fan Beam Projection Technique For Stagnant Sample Visualization. Master Thesis. Universiti Teknologi Malaysia; 2015.