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WIRELESS OPTICAL MICROSCOPE ON DISC FOR CELL CULTURE MONITORING

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Decision-making time of antibiotics implementation strongly correlates patient survival rate in hospitals. Traditional antibiotic resistance evaluation uses disc diffusion on solid agar, which requires hours and trained personal to evaluate the results with an optical microscope. Moreover, the solid agar doesn't reflect bacterial natural growth environment. To fulfill the demand of *in vitro* cell culture and real-time antibiotics evaluation, we integrate a miniaturized wireless optical microscope into a centrifugal lab-on-a-disc (LoD) [1] based cell culture platform in a compact size and scalable format.

Figure 1 shows the miniaturized optical microscope, which integrates a 2.4GHz Wi-Fi transmitter, a complementary metal-oxide-semiconductor (CMOS, 1920 x 1080 pixels) sensor, with a high numerical aperture optics and a wireless inductive "Qi" energy transmission interface [2]. Cells are incubated in a cell culture chamber which is sealed by a lid layer. The cell clusters can be imaged by the CMOS sensor, while the real-time photo and video can be wirelessly displayed and stored on a smart phone or PC through Wi-Fi transmitter. The Qi interface ensures stable power supply for the functioning of the wireless microscope for the full incubation period. Other microscope parameters such as imaging resolution (1080p/720p), exposure time, modes switching and photo/video capture time interval (from 15 minutes to 24 hours) can also be controlled by the mobile application.

A known width MEMS structure characterizes imaging resolution of the microscope, as shown in Figure 2. The present optics setup enables 2±0.187 μm per pixel resolution, which is sufficient for observing cell clusters in the perfusion chamber. Figures 3 show microscopic images of magnetic microbeads clusters, which mimic the size of bacterial clusters, at different spinning speed. The centrifugal force shifts the cluster at higher RPM (150, 300 and 450 RPM). However, the cluster completely moved out of the imaging field beyond 600 rpm.

The wireless optical microscope combined with the cell culture disc spun in a 30º C controlled environment (Figure 4.) for culturing *Pseudomonas aeruginosa*. Figure 5(a) shows floating *Pseudomonas aeruginosa* cell cultures imaged by the wireless microscope. The same cell cultures were imaged by a confocal microscope, as shown in Figure 5(b). The wireless microscope has a depth of focus c.a. 6 μm, which will be beneficial to integrate focusing mechanism in the future to image both cells in suspension and within the biofilm. The modular nature of the platform additionally provides the possibility for integration impedimetric quantification of the cells. This can be achieved by combining interdigitated electrodes in the cell growth chamber and measured by a wireless potentiostat with Electrochemical impedance spectroscopy (EIS) module integrated on the disc. The combination of wireless imaging complemented with EIS can provide new insights into the stages of biofilm development.

The goal of this small and handy platform is to replace bulky pumps, tubing, valves [3] and standalone optical microscope for sample to answer antibiotics resistance, food safety and environmental monitoring in the future.

Word Count: 483

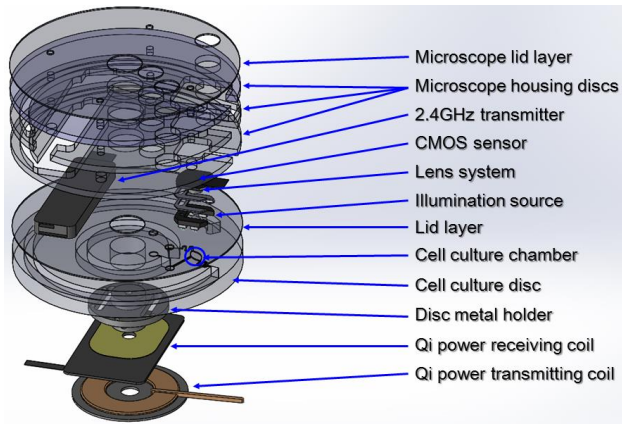

Figure 1. A wireless microscope integrated into a cell culture platform.

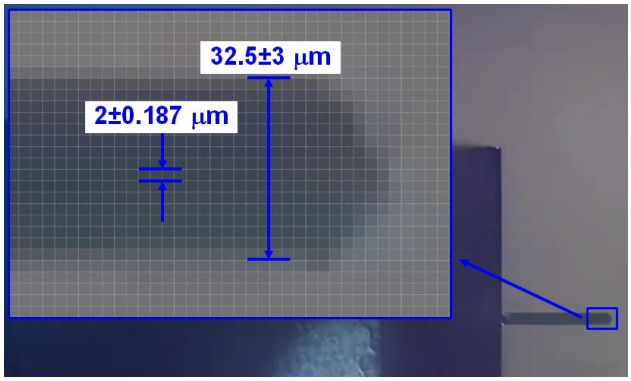

Figure 2. A known dimension MEMS structure (atomic force microscope probe CSC-38) for imaging resolution calibration. Each pixel has ~2 μm resolution.

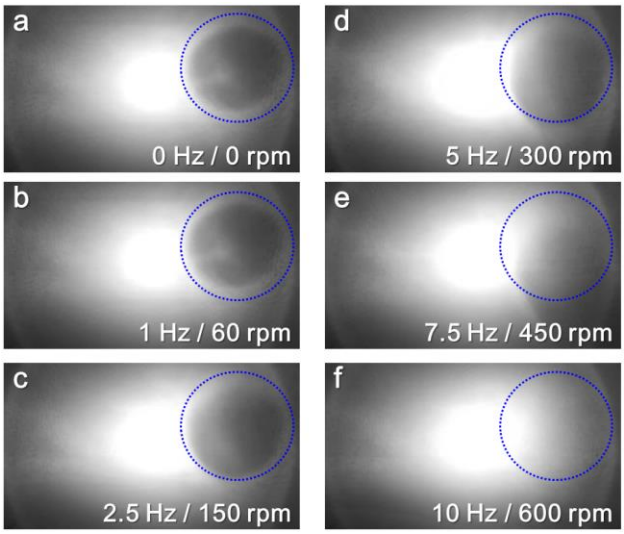

Figure 3 A magnetic micro beads cluster imaged by the wireless microscope at the different spinning speed of 0, 150, 300, 450 and 600 rpm.

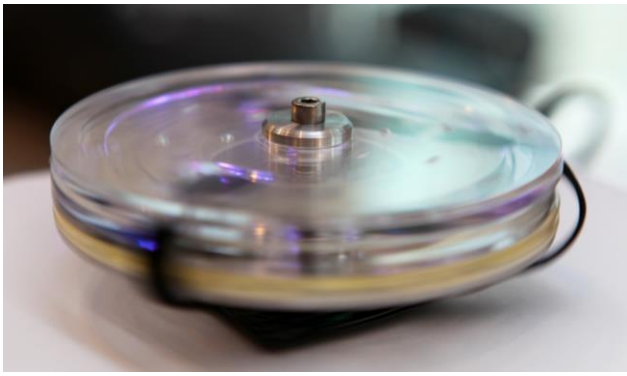

Figure 4. The platform spun at 22.5~67.5 rpm (0.375~1.125Hz) in a temperature controlled environment.

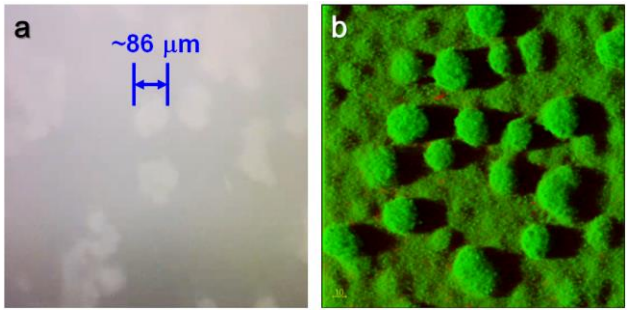

Figure 5. Pseudomonas aeruginosa cell cultures imaged by (a) wireless microscope, (b) confocal microscope.

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