An Integrated microfluidic system for automatic drug cocktails screening of antibiotics and their applications for personalized medicine

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Abstract

Multi-drug resistance of bacterial strains resulting from misuse and inappropriate use of antibiotics have been an important global issue. In order to assist physicians with better antibiotic administration for rapid and effective treatment of patients, we developed a portable microfluidic system which can be used to automatically perform antibiotic screening with single antibiotic, two antibiotic combinations and even three antibiotic combinations on clinically isolated bacteria strains. With the incorporation of the integrated pneumatically-driven microfluidic chip, a pneumatic control module, a temperature control module, and an optical detection module, the developed microfluidic system was capable of achieving antimicrobial susceptibility test and evaluation of efficacy of drug combinations via colorimetric results within 6 hours.

Features

1. Automatically perform antimicrobial susceptibility test (AST) against multi-drug resistance of bacterial strains.
2. Achieve on-chip bacteria/antibiotics manipulation and interpret minimum inhibitory concentration (MIC) of antibiotics for drug cocktails screening.
3. Substantially reduce complicated manual operation and human errors
4. Increase the accuracy and flexibility of AST for precision medicine of antibiotics.

Methods

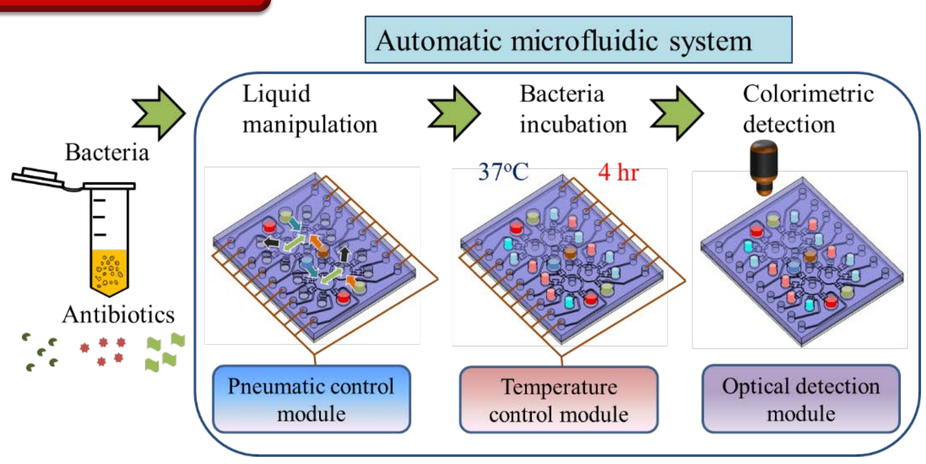

Figure 1: Schematic illustration of on-chip AST with antibiotic combinations.

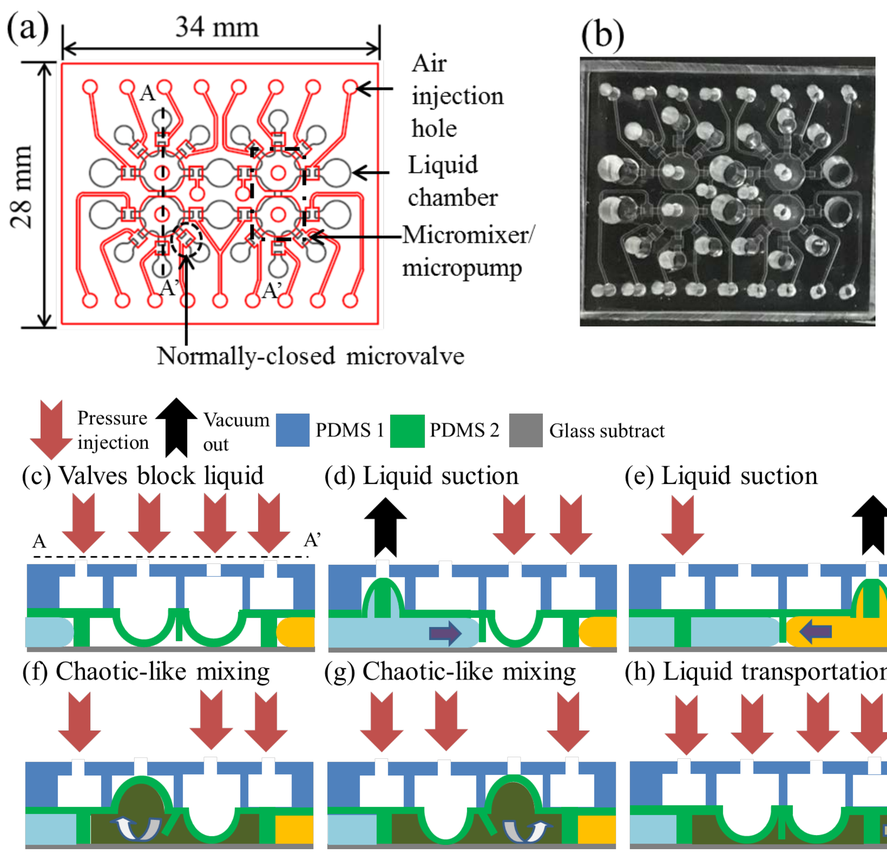

Figure 2: (a) Detailed microfluidic components and (b) a photograph of the chip. (c) The working principle of the chip.

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Results

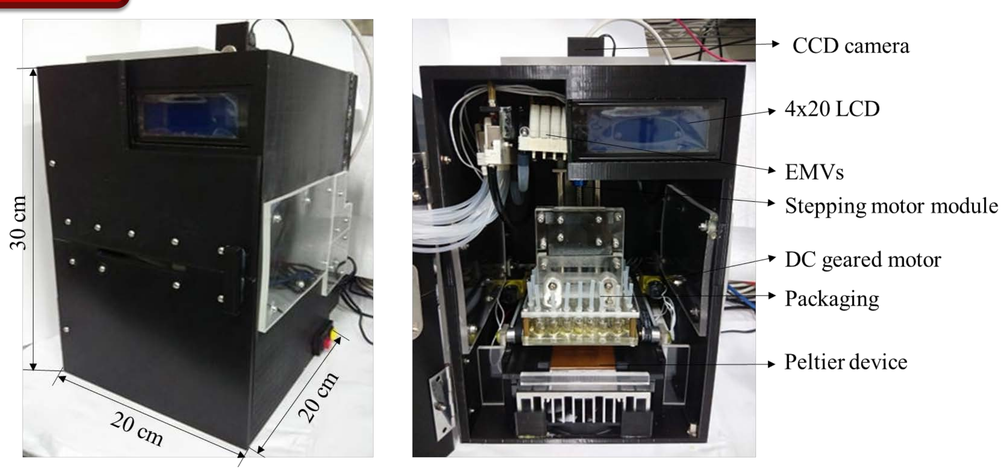

Figure 3: A portable device for automatic drug cocktails screening of antibiotics.

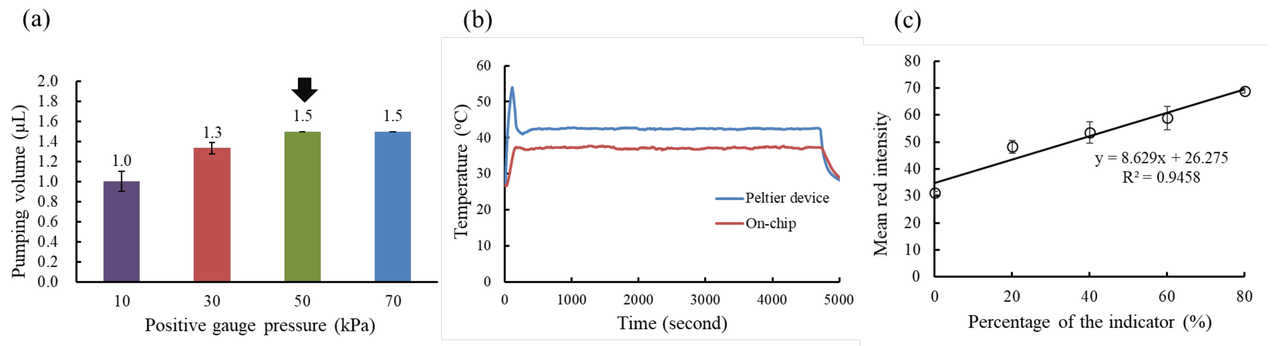

Figure 4: (a) Pumping volumes by the pneumatic control module. (b) The temperature profile of the temperature control module. (c) The calibration curve between the concentration of the bacteria viable indicator and the red color intensity measured by a CCD.

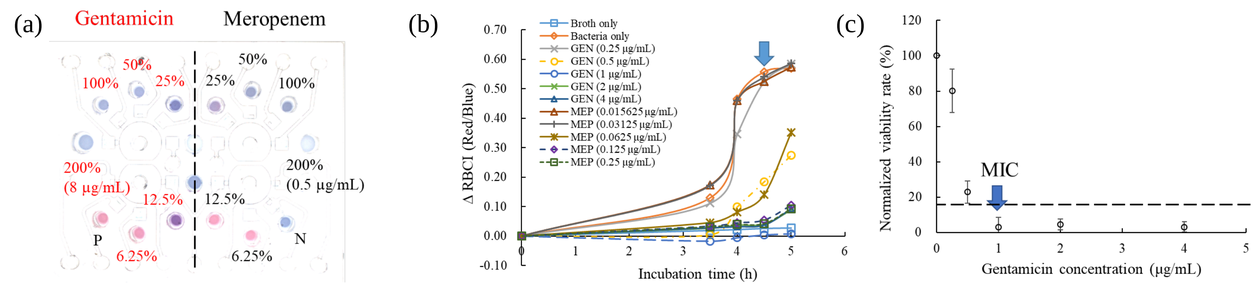

Figure 5: Colorimetric images of on-chip AST with GEN and MEP against CRE. coli at (a) two single drugs and (b) the relationship between relative red/blue color intensity and incubation time, (c) MIC measured between normalized bacteria viability rate and antibiotic concentrations.

Table 1 Tested results of broth microdilution vs. the developed microfluidic device for three common antibiotics, including ceftazidime (C), gentamicin (G), and meropenem (M).

Bacteria strains	Antibiotics	Minimum inhibitory concentration (MIC, μg/mL)		Incubation time (hr)	
		Broth microdilution	Developed system	Broth microdilution	Developed system
CRE. coli	CAZ (C)	>32	>32	24	4.5
	GEN (G)	2	1		
	MEP (M)	0.25	0.125		

Table 2 AST results of two and three antibiotic combinations against CRE. coli using the developed microfluidic system.

Bacteria strains	Antibiotics combination	Fractional inhibitory concentration index (FICI)	Combination effect
CRE.coli	GEN (G) + MEP(M)	1	Additive
	CAZ (C)+GEN (G) + MEP(M)	>0.75 and ≤0.78	Additive

Conclusions

- We have demonstrated a portable device on which rapid and automatic AST of antibiotics against clinical isolated bacteria could be successfully performed.
- The developed device was equipped with a pneumatic control, a temperature control and an optical detection modules.
- MICs and Interaction effects of antibiotic combinations could be determined by implementing the whole AST assay.

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