Bacteria-on-a-chip: Towards deciphering antimicrobial resistance worldwide in E. coli

Summary

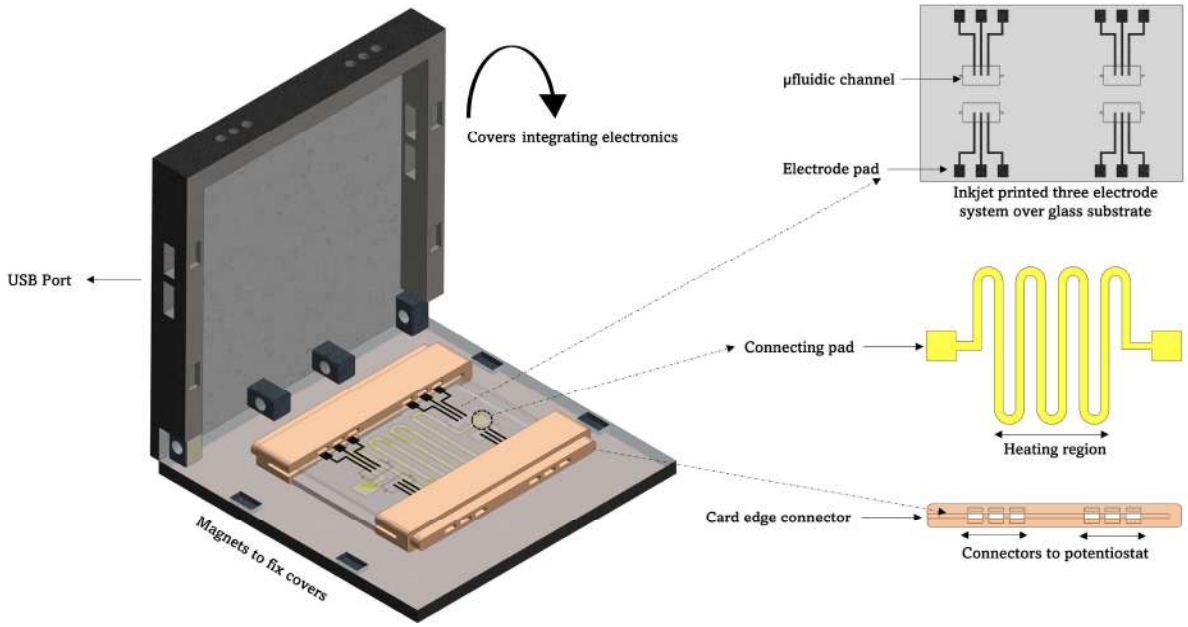
Bacterial infections pose serious risks to human health worldwide, and their resistance to antimicrobials has worsened the prevailing conditions. Antimicrobial resistance (AMR) is considered a global health concern, especially in developing countries, and is responsible for significant morbidity/mortality, increasing the economic burden on healthcare settings. Although there are advancements in detecting pathogenic bacteria, the challenge exists to develop methods that can perform quantification accurately, rapidly, and sensitively with cost-effectiveness. In addition to this, the existing approaches are laborious, time-consuming, lack accuracy, and require manual interventions, affecting the overall treatment of bacterial infections at an early stage. Lab-on-chip-based devices are being developed as novel probes to detect low concentrations of pathogenic bacteria as they allow rapid analysis using point-of-care (POC) techniques.

The presented work aims to develop a lab-on-a-chip device for simultaneous detection, culturing, and resistance testing. Hence, this work consists of four major parts: (i) the development of microfluidic components for lab-on-a-chip device, (ii) the fabrication and integration of heating element with a microfluidic chip, (iii) the functionalization of working electrodes with Graphitized Mesoporous Carbon (GMC) and their electrochemical detection for bacteria, and (iv) the development of a multiplexed device for antibiotic susceptibility study. This work involved designing and fabricating a microfluidic reservoir and its integration with screen-printed electrodes for the development of a Lab-on-a-Chip device. The electrode was printed on the glass substrate using a screen-printed method, and the microfluidic reservoir was fabricated using a soft photolithography process. The LIG heater was fabricated in-house using CO_2 laser ablation over a polyamide substrate and used for bacterial incubation. The temperature required for the growth of bacteria was controlled by a DC-DC voltage regulator. The achieved temperature required for bacteria incubation, i.e., 37°C, was recorded using a thermal camera.

The sensitive detection of pathogenic bacteria can be achieved by modifying the surface of the working electrode with GMC. The GMC increases the effective surface area needed for bacterial cell trapping. The prepared bacterial culture (*E. coli*) was injected inside the

microfluidic chip. A constant temperature of 37°C was supplied for the incubation of bacteria. An electrochemical analysis for bacterial detection was carried out using Potentiostat. The change in the current response with time signifies the growth of bacteria. The obtained result was validated with the conventional method, which showed that the growth of bacteria in the microfluidic device was more than in the conventional incubator. The concentration effect was carried out to find the number of bacteria present in the sample. The viability study was performed to determine the sample's ratio of live and dead bacteria. Along with this, metabolic activity was studied using microbial fuel cells.

In the antibiotic susceptibility study, different concentration of antibiotic was used. The specificity of the developed device was checked by using different bacterial pathogens. Finally, studies were conducted with the developed microfluidic system to establish the on-chip testing. Real samples were tested with the lab-on-chip device to prove the suitability of the device for point-of-care applications.



Developed a Bacteria-on-a-chip platform for combatting antimicrobial resistance

Applicant: Sonal Fande

Supervisor: Prof. D Sriram