**Title:** Development of a low-cost on-chip PCR (polymerase chain reaction) platform for rapid nucleic acid based disease diagnosis (COVID-19).

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**Duration of the project:** 3 years *Submitted to SERB under IRHPA COVID-19 special call*

**Project summary:**

Covid-19 is pandemic to which the world is fighting. Various precautionary measures are being imposed all over the world which is affecting the routine life of an individual and also to the economy worldwide. Although, a definite vaccine is still not known to medical science but they are able to distinguish the Covid-19 from the other types of flu. Presently this is being done by detecting the SARS-CoV-2 virus using RT-PCR technique as recommended by World Health Organization (WHO) [1]. Reverse Transcription Polymerase Chain Reaction (RT-PCR) is a nucleic acid amplification test that converts the RNA into DNA and subsequently amplifies the specific DNA targets. This method was already being employed to detect the severe acute respiratory syndrome–associated coronavirus (SARS-CoV) [2]. The entire process of DNA amplification takes place in three steps: denaturation, annealing, and extension for which the sample is required to be maintained at constant temperatures of 95, 55 and 72 °C, respectively. Present techniques are marred with long turnaround time and samples need to be sent to specialized pathology laboratories. Also, cost of testing per sample is high in absence of indigenously made PCR machine. Hence, there is a dire need for point-of-care devices, which can be used on the spot allowing instantaneous diagnosis at low cost even in remote areas. Analogous to development of integrated circuits, which revolutionized miniaturization of electronics and computational devices, miniaturization of PCR technology, using microfluidics will lead to unprecedented saving in cost and time, and represents future of the wet laboratory functionality. Literature survey shows that continuous flow-through microdevice has several advantages such as homogenous mixing, instantaneous temperature switch, and lower amplification time etc. over stationary chamber PCR. However, device simplicity, portability are some areas where there is sufficient scope to improve the design and develop a micro-PCR, which will be undertaken as part of this project. The primary objective of this project is to develop a low-cost pump-less on-chip PCR. A flow-through microdevice, which has several advantages over stationary chamber PCR, will be developed and tested.

Experimental as well as numerical techniques will be employed in this work. Two different configurations as shown below have been proposed. Detailed numerical simulations will be carried out to understand the thermo-siphon flow and resulted temperature distribution in the proposed design which will help to extract the optimal geometrical, and input parameters. Microdevice will be fabricated using fabrication facility available in-house with collaborators. After initial testing, microdevice will be integrated with temperature control unit. The microdevice will be further optimized for various length template DNA molecules ranging from 1-30 kB in size. This will increase the range of applicability of the developed micro-PCR.

Outcomes of this work will be useful in the development of on-chip RT-PCR (polymerase chain reaction) for DNA amplification of SARS-CoV-2.