Miniaturized nucleic acid amplification system for multiplex detection of pathogens in complex biological samples

Proposers

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Introduction

The miniaturization of biological and chemical analytical systems has gained fundamental importance on the development of autonomous and self-sufficient devices included in the point-of-care (PoC) concept. PoC devices have the potential to improve the management of various diseases and conditions, especially in resource-limited settings where healthcare infrastructure is weak and access to quality and timely medical care is a challenge. A valuable application of PoC systems is in the detection of viral infections that represent an important portion of global public health concerns with thousands of deaths annually. Nucleic acid amplification tests (NAAT) are very popular in the diagnosis and management of viral infections because they allow determination of the viral load. In other terms, quantitation of the viral nucleic acid by amplifying the target sequence thousands-fold. In most cases, they are now considered a reference, or 'gold standard' method for diagnostic practices. The most common approach is PCR thermocycling technology which requires a demanding temperature control for on-chip systems. To overcome this constraint, isothermal amplification is reported to improve the stability and sensitivity of on-site assays. The challenge is to achieve a single stranded product and a multiplexed reaction to overcome the need for post-processing and multi-well reactions for different target analytes, respectively. Despite steady advances over the last decades and the existence of numerous instruments capable of automating this amplification process, its integration in fully automated devices still needs to be exploited. The integration process of such an amplification system within a LoC platform is the objective of this PhD proposal.

Project outline/goal

Project outline:

The proposed project will address the development and optimization of an isothermal amplification unit for the detection of arbovirus, focusing in:

- Design, simulation and fabrication of a thermocycling unit.
- Temperature control system development.
- Characterization and testing the on-chip thermocycler
- Establishment of amplification conditions comparing with a standard thermocycler.
- Assessing the limit of detection and dynamic range of the system for genomic extracts.

- Integration of the thermocycling unit with an existent detection platform and sample preparation unit
- Studying the hybridization efficiency of the generated amplicons with specific oligo probes.

Main goals are:

1 - Development of on-chip multiplexed nucleic-acids amplification module.

2 – Achieve modules assemblage in a self-contained device.

Partner 1 – INESC-MN

INESC-MN detains all the facilities, tools and experience required to develop spintronic based devices for sensors and chip microfabrication. A microfluidics lab with know-how in the microfabrication of plastic and polymeric micro-structures for sample preparation structures is also available. Presently, a bioengineering laboratory is being installed at INESC-MN premises to accommodate bioanalytical bench top equipment that will allow testing, comparison and validation of the in-house generated systems.

Partner 2 – INESC-ID

INESC-ID, in particular SIPS group has a long tradition in high level research in the areas of signal processing, electronics and high-performance processing systems. INESC-ID for the last decades have been in strictly collaboration with INESC-MN to develop cutting-edge research and development in the area of electronic platforms for biochip read-out. The developed system involves the biochip reading, control and signal processing, as well as digital communication ports to outside. The capabilities to support and pursue this project in its electronics component for system automation and control are therefore, secured at all levels.

System Integration – INESC-MN and INESC-ID

INESC-MN and INESC-ID are two R&D institutions working on the development of integrated electronic bioanalytical devices for almost two decades. Experience, know-how and relevant preliminary data have been generated and gathered as scientific documents, patents, trained personnel, demonstrators and prototypes, and in the format of a spin-off company. Magnomics S.A. is the result of this fruitful collaboration between these two complementary institutions in the fields of electronics and spintronics/nanotechnology. In this ecosystem, the development of an autonomous and compact bioanalytical device targeting fully autonomy and easiness of operation is being pursued.

Student profile

Profile sought: enthusiastic and motivated person with an Engineering background in Biomedical, BioNano, or Physics and interest in bioelectronics.