January - February 2020
ISSN: 0193 - 4120 Page No. 11232 - 11235

Lab-on-Chip Technology: A Review on Future Scope in Biomedical Applications

Dr.SU.Suganthi, M.Gayathri, S.Malathi , M.Manisha
(Associate professor)
Department of Electronics and Communication Engineering,
Sri sairam institute of technology,Chennai

Article Info
Volume 82
Page Number: 11232 - 11235
Publication Issue:
January-February 2020

Article History
***Article Received**: 18 May 2019*
***Revised**: 14 July 2019*
***Accepted**: 22 December 2019*
***Publication**: 21 February 2020*

Abstract

Lab-on-Chip (LoC) integrates various analyses such as biochemical operations, chemical synthesis, DNA sequencing onto a single chip which otherwise would have been performed in laboratory taking sufficient amount of time. Due to the miniaturization of these biochemical operations, better diagnostic speed, cost efficiency, ergonomy, sensitivity and so on can be achieved. This paper gives the detailed description of Lab-on-Chip technology including its system components. Ongoing worldwide research projects based on LoC technology have been investigated and various constraints that need to be fulfilled for designing a LoC system are presented. The biomedical applications of LoC in different fields like in diagnostics, cellomics, in environmental studies to control the effect of pathogens, to check the food quality such as for the detection of various antibiotic families in raw milk have also been discussed. Finally, the current open research issues of this technology along with the possible future research scope in the biomedical area have been presented.

Keywords: *Biomedical Systems, Biosensor, MEMS, Microfluidics, Lab-on-Chip*

1. Introduction

Lab-on-Chip technology implies those techniques that perform various laboratory operations on a miniaturized scale such as chemical synthesis and analysis on a single chip leading to a handheld and portable device. In other words, LoC is a device which is capable of scaling the single or multiple laboratory functions down to chip-format. The size of this chip ranges from millimeters to a few square centimeters. [1] Current trend shows the growth of research in this area. In many universities across the world, many groups are formed that are dedicating their research in this area. For example, BIOS in University of Twente, Mina Med in Germany, and Nanobe in Finland [2] are some of the groups. Their main motive is to understand naonofluidics and nanosensing, to connect micro/nanoeng. with biomedical and life science fields, to develop new micro and nano technologies for LOC, and to demonstrate new LOC applications.

2. Design

A **lab-on-a-chip** (**LOC**) is a device that integrates one or several laboratory functions on a single integrated circuit (commonly called a "chip") of only millimeters to a few square centimeters to achieve automation and high-throughput screening.[3]. LOCs can handle extremely small fluid volumes down to less than pico-liters. Lab-on-a-chip devices are a subset of microelectromechanical systems (MEMS) devices and sometimes called "micro total analysis systems" (µTAS). LOCs may use microfluidics, the physics, manipulation and study of minute amounts of fluids. However, strictly regarded "lab-on-a-chip" indicates generally the scaling of single or multiple lab processes down to chip-format, whereas "µTAS" is dedicated to the integration of the total sequence of lab processes to perform chemical analysis. The term "lab-on-a-chip" was introduced when it turned out that µTAS technologies were applicable for more than only analysis purposes.

January - February 2020
ISSN: 0193 - 4120 Page No. 11232 - 11235

The paper [4] presents the on-going research activities in LoC technology and recent advancements in the handling of various biological processes medical applications. The progress and success of available technological tools leads to the fabrication of Micro-Electro-Mechanical-System (MEMS) that integrate micromechanical and microelectronic structures in one system leading to interdisciplinary applications. MEMS and microelectronics differ in technological approaches inspite of the fact the MEMS have grown from microelectronics. The MEMS approach known as microflidics helps in the handling of small fluid volumes even less than picolitres. The scaling of one or several of the lab processes onto a single chip-format is known as LoC which has the capability of handling micro and nano particles by combining several laboratory functions on one chip. To perform chemical analysis, MEMS is used. Photolithography which is directly derived from microelectronic fabrication is the the basis for most LoC fabrication processes and is discussed in this paper.

A review [5] on various promising system integration techniques for microfluidics has been presented along with their merits, challenges and applications. The emerging microfluidic strategies in order to perform the effective integration of multiple microfluidic components leading to fully automated lab-on-a-chip systems are: (i) Multilayer Soft Lithography; (ii) Capillary Driven and Paper-based Microfluidics; (iii) EWOD Driven Droplet Microfluidics; (iv) Multiphase Microfluidics; (v) Centrifugal Microfluidics; (vi) Electrokinetics, and (vii) Hybrid Microfluidics. Due to on-going research in this area, fully automated microfactories can now be thought of that will have the capability of performing various biochemical analyses at a much low cost for a wide spectrum of biomedical and biological engineering applications. The obstacle in the designing of LoC or microfluidic devices for biomedical applications is that most of these applications need sensitive detection modules like thermal cyclers for PCR reactions, mass spectrometers for sample analyses, microscopes for cells, fluorescence visualization and bacteria.

3. Chip materials and fabrication technologies

The basis for most LOC fabrication processes is photolithography. Initially most processes were in silicon, as these well-developed technologies were directly derived from semiconductor fabrication. Because of demands for e.g. specific optical characteristics, bio- or chemical compatibility, lower production costs and faster prototyping, new processes have been developed such as glass, ceramics and metal etching deposition and bonding, polydimethylsiloxane(PDMS) processing (e.g., Off-stoichiometry thiol-ene polymers (OSTEmer) processing, thick-film- and stereoli thography as well as fast replication methods via , injection molding and embossing. The demand for cheap and easy LOC prototyping resulted in a simple methodology for the fabrication of PDMS microfluidic devices: ESCARGOT (Embedded SCAffoldRemovinG Open Technology)[6]. This technique allows for the creation of microfluidic channels, in a single block of PDMS, via a dissolvable scaffold (made by e.g. 3dprinting)[7]. Furthermore, the LOC field more and more exceeds the borders between lithography-based microsystem technology, nanotechnology and precision engineering.

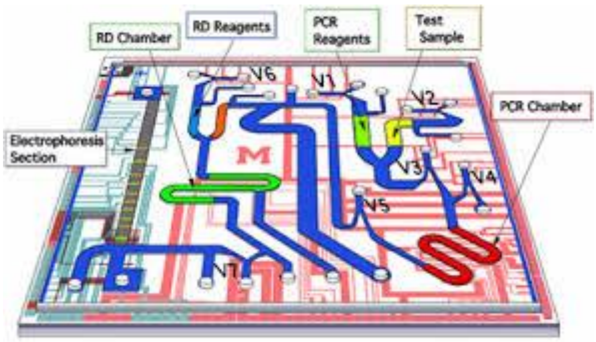

Figure1:Lab on a chip

4. Application of Lab-on-Chip Technology

The increased demand of LoC devices in many areas is due to the various technological advantages of LoC technology such as portability, automated sample handling, re-configurability etc. Immunoassay LoC for bacteria detection, Real time PCR detection chips, DNA chip, Gene Chip, Cellular Analysis chip, Flow Cytometer LoC (for HIV) etc. are some of the applications of LoC technology in the biomedical field. [8]

The review [9] presents the characteristic of microfluidic LoC to be used for meeting the requirements and improving the efficiency of Point-of-Care diagnostic systems. Since the required functional modules and working principles generally depend on target analytes, so the applications of POCT systems are categorized according to the type of analyte such as cells, proteins, metabolites and nucleic acids. POCT systems have the ability to detect specific biomarkers from these analytes. These different biomarkers require different assays, diagnostic principles and operating systems. Thus in each category, configuration of modules, detection methods and advantages and disadvantages of Lab-on-Chip based POCT diagnostic systems are reviewed.

The recent advances in the Lab-on-Chip technology and design strategies that lead to the development of universal sample-to-result microfluidic devices useful for efficient pathogen detection with high specificity and sensitivity has been presented in [10]. The main focus is given on the development of accessory-free and totally integrated self-contained microchips that will have many advantages such as point-of-care diagnosis, handling of small volumes of sample, rapid detection time, miniaturization and portability. This will help in reducing the mortality rate and in controlling the propagation of life-threatening diseases such as tuberculosis (TB), HIV and so on.

5. Advantages for lab on a chip.

- low fluid volumes consumption (less waste, lower reagents costs and less required sample volumes for diagnostics)
- faster analysis and response times due to short diffusion distances, fast heating, high surface to volume ratios, small heat capacities.
- better process control because of a faster response of the system (e.g. thermal control for exothermic chemical reactions)
- compactness of the systems due to integration of much functionality and small volumes
- massive parallelization due to compactness, which allows high-throughput analysis
- lower fabrication costs, allowing cost-effective disposable chips, fabricated in mass production[11].
- part quality may be verified automatically[12].
- safer platform for chemical, radioactive or biological studies because of integration of functionality, smaller fluid volumes and stored energies.

6. Global challenges.

For the chips to be used in areas with limited resources, many challenges must be overcome. In developed nations, the most highly valued traits for diagnostic tools include speed, sensitivity, and specificity; but in countries where the healthcare infrastructure is less well developed, attributes such as ease of use and shelf life must also be considered. The reagents that come with the chip, for example, must be designed so that they remain effective for months even if the chip is not kept in a climate controlled environment. Chip designers must also keep cost, scalability, and recyclability in mind as they choose what materials and fabrication techniques to use.

7. Future Scope

It is widely discussed that Microfluidic LoCs have great potential to revolutionize the biomedical field and possess the capability to give a boost to healthcare sector. But still this LoC technology would seem to be a dream especially in developing countries. In the low-resource areas such as developing countries, efforts are still required to improve the business model under which LoC devices are produced and to make people aware about their efficient use.

Many infectious diseases are there such as malaria, HIV and AIDS, measles, TB, lower respiratory conditions and so on that require timely diagnosis and treatment so as to reduce the mortality rate [13].

Now-a-days, Swine Flu, Zika Virus and Ebola Virus are killing thousands of people and causing the risk of epidemic. For all these diseases, LoCs diagnostics are desperately needed because of their ability to provide diagnosis in real time so as to improve the disease-management landscape. Moreover, this technology can proven to be useful for finding a novel way to treat central nervous system disorders such as Parkinson's disease and spinal cord injury with the help of extracting sufficient cerebrospinal fluid needed to perform conventional assays [14]. The potential of this technology can further be explored for autoimmune joint diseases like rheumatoid arthritis.

8. Conclusion

Based on the survey, it is seen that LoC devices have wide range of applications. Research in this technology mainly focuses on chemical synthesis, DNA analysis and human diagnostics. They can be used in different areas such as in diagnostics, bioanalysis, and biosensing, for environmental monitoring including testing of water and food quality, for testing of different drugs, in pharmaceutics and so on.

REFERENCES

[1] Lisa R. Volpatti and Ali K. Yetisen, "Commercialization of microfluidic devices", Trends in biotechnology, vol. 32, no. 7, **(2014)**, pp. 347-350.

[2] "Microfluidics, Lab-On-Chip", http://lab-on-chip.gene quantification.info, accessed 29 June 2016.

[3]Volpatti, L. R.; Yetisen, A. K. (Jul 2014). "Commercialization of microfluidic devices". Trends in Biotechnology. **32** (7): 347–350. doi:10.1016/j.tibtech.2014.04.010

PMID 24954000

[4] B. Y. Majlis, "MEMS and lab on chip: Interfacing macro to nano world", Proceedings of IEEE Regional Symposium on Micro and Nanoelectronics (RSM), Langkawi, **(2013)**, September 25-27.

[5] Sin, Mandy LY, JianGao, Joseph C. Liao, and Pak Kin Wong, "System integration-A major step toward lab on a chip", Journal of biological engineering, vol. 5, no. 1, **(2011)**. [6]Saggiomo, V.; Velders, H. A. (Jul 2015). "Simple 3D Printed Scaffold-Removal Method for the Fabrication of Intricate Microfluidic Devices". Advanced Science. 2 (8): X. doi:10.1002/advs.201500125. PMC 5115388. PMID 27709002.

[7]Vittorio Saggiomo (17 July 2015). "Simple fabrication of complex microfluidic devices (ESCARGOT)" – via YouTube.

[8] C.D. Chin, Vincent Linder and S.K. Samuel. "Commercialization of microfluidic point-of-care

diagnostic devices", Lab on a Chip Journal, vol. 12, no. 12, **(2012)**, pp. 2118-2134.

[9] Jung, Wooseok, Jungyoup Han, Jin-Woo Choi, and Chong H. Ahn, "Point-of-care testing (POCT) diagnostic systems using microfluidic lab-on-a-chip technologies", Microelectronic Engineering Journal, vol. 132, **(2015)**, pp. 46-57.

[10] Foudeh, Amir M., TohidFatanatDidar, TeodorVeres, and Maryam Tabrizian,

"Microfluidic designs and techniques using lab-on-a-chip devices for pathogen detection for point-of-care diagnostics", Lab on a Chip Journal, vol. 12, no. 18, **(2012)**, pp. 3249-3266.

[11]Ryan S. Pawell, David W. Inglis, Tracie J. Barber, and Robert A. Taylor, *Manufacturing and wetting low-cost microfluidic cell separation devices*, Biomicrofluidics 7, 056501 (2013); doi:10.1063/1.4821315

[12]Pawell, Ryan S.; Taylor, Robert A.; Morris, Kevin V.; Barber, Tracie J. (2015). "Automating microfluidic part verification". *Microfluidics and Nanofluidics*. **18** (4): 657–665.

[13] "Where the chips fall– lab-on-chip diagnostics", http://www.medicaldevice-developments.com/features/featurewhere-the-chips-fall-lab-on-chip-diagnostics-4212684/, accessed 24 June 2016

[14] "Lab-on-a-Chip' Technology Cuts Costs of Lab Tests for HIV, Lyme Disease, Other Diseases", http://news.rutgers.edu/research-news/%E2%80%98lab-chip%E2%80%99-technology-cuts-costs-lab-tests-hiv-lyme-disease-other-diseases/20150910#.VtWeUPl97IU, accessed 15 June 2016.