Lab-On-Chip, Internet of Things, Analytics and Health Care 4.0: A synergistic future forward

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Abstract. In this era of the internet with the latest technology and rapid communication, the various fields of processes and business are led to the road of automation in recent days. The major part of this automation is that they help in the cost reduction with increased safety measures and also results in absolute portability of the equipment. To indulge in continuous processing, and also to identify the best technology, the analytical methods must be directly involved in decision making. This revolution in analytical methods is named as Analytics 4.0, which has a significant role in healthcare and diagnostics. The self-assessment and decentralization of the data acquiring can be motivated with the help of the microfluidic biosensors and biochip. It also helps in the immediate access of the information without resulting in delay. Diagnostic 4.0 helps in storing the patient details as cloud files providing high security and also analyze them through the deep learning algorithms. It also helps in constant monitoring on a broad scale and reliable assessment through monitoring apps that can shift the health care efficiency to the next notch. Hence the evolution of the healthcare sector has multiple generations listed with numerous advances which stand as the boon in this era.

1. Introduction
The industrial production, economies, and the people's social lives had been drifted due to the digital revolution that had been witnessed in recent years. This development of the healthcare sector due to digitization makes the online availability of the laboratory medicines and better communication by integrating the individual’s health with the health care sectors. This also helps in achieving the outcome with high yield and product quality enabled with the more reliable process.

In our daily routine Lab On Chip (LOC) has a vital role, and also deserves its place various fields such as to monitor the safety aspects in food science and its production process, health care improvisations, environmental safety monitoring, forensics, and life sciences research. It is evident that analytical method will become an integral part of the IoT (Internet of Things) with rapid growth in the fields of automation and networking within and of industrial processes, health care development, and also in our homes, which will contribute for decision-making process by providing analytical data.
In analyzing the amount of the data to be transferred and the quantity of data interpretation, Analytics 4.0 plays an essential role by describing these technologies that suit for the automation and connection to IT (Information Technology) and computing methodologies. In these technologies, the remote sensing areas and the cloud are associated with the decentralization of the data generation. Hence it can be stated that the unstoppable part of IoT in recent days is the evolution of the Analytics 4.0. This is being supported by integrating the analytical method straight down to the process which devoid the usage of the traditional methods such as the use of individual sensors for the purpose of decision making [1].

2. Generations
Though there is a notable level of rapid advances in big data and data analytics, the healthcare industry is way behind other industries in adopting these digital technologies due to the requirement of data security and accuracy. From figure 1, it is understood that the evolution in healthcare devices had resulted in four generations among which first two generations of the technological revolution had been adopted at its ease, but the third level of digitization was found to be a bit tougher in adopting initially owing to numerous risk factors. In the last few decades health care informatics- electronic health record systems, genomics, remote diagnosis, wireless technologies, wearable systems, context-aware computing, and cellular technologies have been dealt with higher advancements that laid the foundation for changing the level of the health care industry. The health care delivery system can face upcoming automation when they develop the ability to adapt the data analytical techniques.

Figure 1. The evolution and comparison of the analytical devices of each generation and their advantages.

In 2015 Jagannadh et al. had described the optofluidic microscope that helps in developing an automated, versatile cellular diagnostic platform. It helps in morphological analysis and automated
clinical diagnosis [2]. Though there was an easier adoption for the first and second generation of the devices, they possess some of the drawbacks that led to the development of the future advancements. Some of the disadvantages for these generations are that they devoid automation and require human resources to operate it. Hence the human error rate is considerably high when compared to the further generations. Moreover, their huge size and temporary storage of the results for future analysis made them be a failure. To get rid of these drawbacks, the evolution of the analytical equipment had resulted in the development of further generations, which includes automated devices.

The third generation devices had evolved with complete automation, and they are highly time consumable and multitasking in their working. They devoid human resources utilization and the human error rate has been eradicated as a whole. They are also supported with high storage of results that can be analyzed for the later process. Kim et al. had described a new microarchitecture in 2017 that is completely automated for sample preparation from clinical pathogen with high throughput and reduced reagent consumption with improved reproducibility [3]. Though these technologies are far upgraded than the previous generations, they could not be evolved in the real-time signal and data transmission.

To overcome these intricacies, the fourth generation of devices had evolved. In 2018 Xu et al. had presented a review about the smartphone-based microfluidic biosensor system, which also imparted knowledge about the structure, analytical methods, and sensing modalities. They hold a special place in the biomedical sensing for their fullest potential in the POCT (Point Of Care Tests) [4]. Mercer et al. had described the miniaturization of the equipment with the use of the Arduino microcontroller, which leads to automated assay protocol with high throughput detection in POCT [5]. The remarkable advantages of this generation are they were provided with high cloud storage with peak security and involved in real-time signal and data transmission to the health care sector. Also, they provide a high rate of accuracy in the analysis of the data with suitable methods. Moreover, the emergence of deep learning paved the successful way in the data-mining field, where the retrieval of new and useful information from the existing information is possible. This evolution has made health care to shift to its next level of success.

3. Recent advances

Advancements, along with the adoption of developing technologies, play an important role in the success of the implementation of the analytical methods in the healthcare sector. Such newly developed devices in the healthcare sector with the recently updated technologies are represented in figure 2 and 3. In 2015, Matthijs et al. had presented guidelines on the Next Generation Sequencing (NGS) to develop a rating system based diagnostic test, which was considered as the new feature. The authors had also performed the analysis with the group of geneticists and bioinformaticians along with the suggestions received from the representatives and the clinicians, where 37 statements of guidelines were described in the article [6]. Later on, Mc Nerney threw light upon the requirement for the promotion of innovative ideas to develop the rapid assays in the diagnostics. This has also paved the way for the further upliftment of the diagnostics in an evolutionary path. It also concentrated on accelerating premarket approval of the devices [7]. In the year 2016, Matthijset al. had represented an article based on the spectroscopic methods along with their suitability in order to monitor the chemical synthesis process routine, which helps in the line up of production. Hence it can be said that the overall process controls related to the automated analytical chemical technology. They also illustrated that the large scale production could be achieved by the detailed analysis integrated small scale solutions. The outcome of the entire process was directly influenced by the with the up and down streaming decision making steps that were coupled to it [8].
In 2018 Mayer et al. had given a detailed review of the direct involvement of the analytical chemistry procedures along with the set of Process Analytical Technologies (PAT) in the decision-making process. Human interaction is the only needed reaction in the passive sensing element. This paves the pathway for the completely automated system. The authors also added a note that the communication between the distributed sensors and the networked analytical labs to make automated decisions that stood as the initiation towards the internet of analytical things [1]. Neumaier had described the digitalization of patient data with higher visibility that also helps in enhancing the patient-physician-laboratory relationship. The authors had also mentioned that preventive healthcare had been supported by deep learning algorithms. Hence all-time online availability of health services results in strengthening healthcare. Along with this, the recent automation and the data exchange that paved the way for the industry 4.0 had been mentioned by the authors [15]. Rahmani et al. had listed out and worked on the few healthcare applications in order to enhance the different characteristics of IoT architectures along with their characteristics through fog computing-based solution. The analysis was made through Geo-distributed fashion at the edge of the network which results in predicting the Easy Warning Score (EWS) where the EWS has been utilized for the patients with acute illness [16].
Figure 3. (a) Compatible and continuous monitoring device for monitoring the vital parameters [17], (b) Smart contact lens to detect the level of glucose with increased accuracy [18], (c) and (d) Entire outlook of the automated operation theatres that pave the way for the integration of IoT in healthcare technologies [19], (e) Robotic arm employed in the automated surgical procedures with high success rates [20], (f) Utilisation of ultrasound technology to detect the vein accurately for surgical procedures [21].

Pang et al. represented an article with three main reasons, which includes future research and applications. Moreover, the other motive was to list out the industrial requirements along with the research technologies. Also, the last motive was to provide a review of the biomedical engineering and automation in the health care informatics. The authors had also stated that the interaction between human intentions and the environment leads to the development of powerful equipment for the rehabilitation. Also, they threw light upon the development of the technologists and the engineers with valuable knowledge plays an important role, and it relays on the universities and professional schools to make them more knowledgeable [22]. Kamble et al. had presented a review about the rapid automation in industries of manufacturing the healthcare devices and the state of research at the current topics like experimentation, prototype preparation. The authors had also described the limitations, which include the missing of relevant articles that could not be covered within the selected database [23]. Another new technology known as Fog Computing (FC) was proposed by Kumari et al. that deals with various challenges such as data management, security, and privacy. This helps in decreasing the delay in comparison during the protection of sensitive data [24]. It involves three layers of patient-driven architecture to provide a better analysis. In 2019, Silveria et al. had represented a systematic literature review on the technologies that can be used in the hospitals along with the qualitative and explanatory variables. It is also stated that improvisation can be adopted with the satisfaction of the principles of the health care sector [25].

LOC technology paved the way for advancements in the field of cardiac sciences, which led to the development in vitro cardiac tissue models in an inexpensive manner [26]. As the need for improvisation increased an in vivo method of recapitulating the tissue had been developed, and it led to the evolution named as tissue-on-a-chip [27]. Recent advances in microfluidics and LOC has put forward to the development of tissue on a child for drug discovery. Wherein the biosensing elements could enable real-time sensing [28]. The important aspect of the development in the Organ-on-Chip (OoC) has continuously headed with the development of technology. Therefore drug development for individual
patients can be listed with the proper design of OoC [29]. In the effective method of investigating the short span physiological and disease processing, the microarchitecture plays an essential role in the cell positions in OoC [30]. The aim of developing a high throughput drug screening systems, in the field of growing in-vitro tissue culture methods was an advancement in OoC [31]. To replicate the better function of the existing individual engineering technologies had included the transformative combination of real humans, which could lead to the development of the integrated living systems [32]. When a bioreactor has been interfaced with the OoC to develop an automated high throughput screening systems in bioprinting, it could also be used for the cell response treatment with the use of acute acetaminophen [33]. A completely implantable device based on the passive chip biosensors that can be extended in healthcare applications such as the detection of human plasma [34]. Employing the biomimicry technique, for the construction of the microfluidic Heart-on-a-Chip with personalized stem cell technologies is considered as one the advancements in LOC techniques [35]. A remote control process utilizing the liver-on-a-chip and heart-on-a-chip, the data from the biosensors were transferred to the google glass which helps in predicting the morphology of the liver and heart along with its temperature and pH [36].

The simultaneous and selective measure of sweat metabolites, such as glucose and lactate, and electrolytes, such as sodium and potassium ions along with the skin temperature by Gao et al. for the analysis of multiplexed in situ perspiration by a wearable, flexible integrated sensing array (FISA). The flexible printed circuit board (FPCB) with signal transduction, conditioning, and wireless transmission was used for real-time physiological and clinical studies [37]. In addition to this, the continuous monitoring of glucose level was performed through microneedle-based minimally invasive glucose biosensor [38]. Android interface in the field of medical evolution has a major role to play with the diagnostic tests. One such important aspect is the detection of blood glucose by the electrodeposition method and real-time data transmission through the app called BlueCells, where the acquired data is stored in external memories [39]. Most of the liquid samples are tested using the principle of calorimetry, which involves the use of laboratory equipment. Yuan Chena et al. utilizes a 3D printed attachment and ambient light sensor of a smartphone to measure light intensities of transmitted through a liquid colorimetric substrate. This kit provides accurate results for several liquid colorimetric assays, including ELISA kits, biochemical assay kits, aptamer biosensors, DNAzyme-based sensors [40]. Not only in earth’s environment but also these technologies are available in an entirely different environment like International Space Station (ISS) for the crew and station health and also to provide specific measurements in research facilities [41].

4. Conclusion and future perspectives
In this work, the major concentrated part is to give a glimpse of the evolution of the analytical devices and also a comparison between their efficient working. The evolution of the healthcare 4.0 devices is the result Analytics 4.0, which acts as a step towards an Internet of Analytical Things. The upgraded analytical methods help in automated decision making, which stands as the major advantage of this evolution. Application areas include health care sector and its divisions, smart homes and development, food and agricultural supporting systems, environmental monitoring, and industrial processes. It will be a highly relevant, important, and necessary resource for the goal of solving ubiquitous challenges in our societies.

A few years ago, there was a lag in the digital revolution in the field of medicine. The reasons may be listed as shielding of the patient's data due to resistive nature. However, in recent days, they were broken, and the data were openly accessed at any time through the cloud networks with proper security features. As a development, the researchers can extend their work in performing an analysis on the individual’s requirement and the employee's empowerment in the medical institutions in order to develop the healthcare products into result in the newer revolution era. Along with this, the researchers can also consider the complete automation of all the available devices, which may result in better analysis, accurate results in considerably lesser time.
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