What is the future of lab-on-a-chip diagnostic devices? Assessing changes in experts' expectations over time

Fabio Mota, Luiza Amara Maciel Braga, Bernardo Pereira Pereira Cabral and Carlos Gilbert Conte Filho

Fabio Mota is based at Center for Strategic Studies, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil. Luiza Amara Maciel Braga is based at Federal Fluminense University, Rio de Janeiro, Brazil and Center for Strategic Studies, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil. Bernardo Pereira Pereira Cabral is based at the Department of Economics, Federal University of Bahia, Salvador, Brazil and Center for Strategic Studies, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil. Carlos Gilbert Conte Filho is based at Center for Strategic Studies, Oswaldo Cruz Foundation, Rio de Janeiro, Brazil and the Department of Economics, Federal University of Santa Maria, Santa Maria, Brazil.

Received 4 May 2021
Revised 29 June 2021
Accepted 29 June 2021

The authors thank the Center for Strategic Studies of Oswaldo Cruz Foundation for institutional support, and all the researchers who participated in this study. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Abstract

Purpose – *Lab on-a-chip (LOC) may lead to low-cost point-of-care devices for the diagnosis of human diseases, possibly making laboratories dispensable. However, as it is still an emerging technology, very little is known about its future impact on the diagnosis of human diseases, and on the laboratory industry. Hence, the purpose of this study is to foresee possible developments of this technology through a consultation with researchers in the field in two distinct time periods.*

Design/methodology/approach – *Based on Technology Foresight, this study addresses this gap by assessing the opinions of over five hundred LOC researchers and tracking changes in their views on the future of LOC diagnostic devices. These researchers participated in a two-wave global survey with an interval of two and a half years*

Findings – *Although second-wave (2020) respondents are less optimistic than those of the first wave (2017), the results of both surveys show that LOC diagnostic devices are expected to: move from proof-of-concept demonstrations to industrial development, becoming commercially feasible worldwide; integrate all laboratory processes, delivering cheaper, faster and more reliable diagnoses than laboratories; and provide low-cost point-of-care solutions, improving access to healthcare.*

Research limitations/implications – *Although it would be desirable to collect and explore the views of different sets of stakeholders, the method of generating lists of survey respondents shows a bias toward academic/scientific circles because the respondents are authors of scientific publications. These publications may as well be authored by stakeholders from other fields but it is reasonable to assume that most of them are researchers affiliated with universities and research and development organizations. Therefore, this study lacks in providing an image of the future based on a more diverse set of respondents.*

Social implications – *The results show that these devices are expected to radically change the diagnostic testing market and the way laboratories are organized, perhaps moving to a non-laboratory-based model. In conclusion, in the coming decades, these devices may promote substantial changes in the way human diseases are diagnosed.*

Originality/value – *Only a few studies have attempted to foresee the future of LOC devices, and most are based on literature reviews. Thus, this study goes beyond the existing research by providing a broad understanding of what the future will look like from the views of researchers who are contributing to the advancement of knowledge in the field. The researchers invited to take part in this study are authors of LOC-related scientific publications indexed in the Web of Science Core Collection.*

Keywords *Technology foresight, Expert opinion, Disease diagnosis devices, Lab-on-a-chip, Two-wave survey*

Paper type *Research paper*

Introduction

Lack of diagnosis, misdiagnosis and delay in diagnosis are a global public health concern (WHO, 2018; Mahumud *et al.*, 2016). These are problems not only to populations living in remote or inaccessible areas (Path, 2005) but can be a global issue in outbreaks of novel pathogens, as in the case of the coronavirus disease 2019 (COVID-19) pandemic (Binnicker, 2020). As known, these diagnostic-related issues can lead to, e.g. medical malpractice, wrong treatment (Mahumud *et al.*, 2016), bacterial, virus resistance (Yager *et al.*, 2006), sepsis, hospital adverse events (Balogh *et al.*, 2015), virus transmission (Zhuang *et al.*, 2020) and deaths (Cheng *et al.*, 2008). Therefore, putting additional health and economic burden to society (Mahumud *et al.*, 2016). This is even more serious in the case of lower-income countries, where funds, skilled labor (physicians, nurses, etc.) and healthcare facilities (clinics, laboratories, hospitals, etc.) are often unavailable (Cheng *et al.*, 2008; Kolluri *et al.*, 2017).

Possible solutions to these diagnostic-related issues include the development of low-cost laboratories (Cheng *et al.*, 2008) and low-cost diagnostic tools (Path, 2005). In line with that, there are currently new technologies being developed in research labs that promise to tackle these problems in the future. Known as lab-on-a-chip (LOC), they are "Microdevices that combine microfluidics technology with electrical and/or mechanical functions for analyzing very small fluid volumes" (MeSH: ncbi.nlm.nih.gov/mesh/?term=lab-on-a-chip). The diagnosis of diseases is one of its most anticipated applications (Chin *et al.*, 2007; Mendes *et al.*, 2019).

In the future, LOC diagnostic devices are expected to perform and integrate all laboratory processes in a single chip (Ríos *et al.*, 2012; Romao *et al.*, 2017). When fully developed, LOC devices will likely provide low-cost point-of-care (PoC) solutions, delivering cheaper, faster and more reliable diagnoses than laboratories (Ríos *et al.*, 2012; Zhu *et al.*, 2020a; Arshavsky-Graham and Segal, 2020), but without the need for the physical infrastructure, trained personnel and specialized equipment (Casquillas *et al.*, 2016; Romao *et al.*, 2017).

In remote or difficult-to-access areas, LOCs can eliminate the time between collecting a patient's sample, transporting it to a laboratory and then delivering and communicating the diagnosis. As PoC diagnostic devices, LOCs could do the same diagnoses as laboratories in a much shorter space of time, allowing for the prompt onset of treatment (Giannitsis, 2011; Arshavsky-Graham and Segal, 2020). The time saved could increase the effectiveness of treatments, such as by avoiding bacterial and virus resistance (Yager *et al.*, 2006; Casquillas *et al.*, 2016; Kolluri *et al.*, 2017), helping to improve survival rates in these populations (Ríos *et al.*, 2012). Additionally, these devices are expected to be handled by people with little training (including patients themselves) (Casquillas *et al.*, 2016; Romao *et al.*, 2017) and perform real-time monitoring of patients' health (Martín *et al.*, 2017; Zhuang *et al.*, 2020). Therefore, in the future, LOC diagnostic devices can be of major importance not only to support public health policies aimed at facilitating access to health care of populations living in remote or difficult-to-access areas (Ríos *et al.*, 2012) but also to help stem new virus transmission and flatten the epidemic curve (Lee, 2020).

Over the next decades, LOC diagnostic devices are expected to move from research to industrial-scale production, becoming commercially viable worldwide (Gupta *et al.*, 2016; Romao *et al.*, 2017). This process can lead to radical changes in the diagnostic testing market, perhaps moving from a laboratory-based model to a non-laboratory one (Figeys and Pinto, 2000; Romao *et al.*, 2017). However, as most of LOC diagnostic devices are still at the proof-of-concept stages (Temiz *et al.*, 2015; Kolluri *et al.*, 2017; Arshavsky-Graham and Segal, 2020), very little is known about its future impact on the diagnosis of human diseases and on the laboratory industry as a whole. Our study addresses this gap by assessing the opinions of over five hundred LOC-related researchers and tracking changes in their views on the future of LOC diagnostic devices. These researchers took part in a two-wave global survey with an interval of two and a half years. The first survey was conducted in 2017 and the second in 2020.

As far as we know, only a few studies have attempted to foresee the future of LOC devices, and most are based on literature reviews (van Merkerk and Robinson, 2006; Kaur and Kaur, 2009; Craighead, 2006; Zhuang *et al.*, 2020; Thilmany, 2005). Thus, our study goes beyond the existing research by providing a broad understanding of what the future will look like from the views of researchers who are contributing to the advancement of knowledge in the field. The researchers invited to take part in this study are authors of LOC-related scientific publications indexed in the Web of Science (WoS) Core Collection.

This study is grounded in Technology Foresight (Martin, 2010; Miles, 2010; Martin, 1995; Martin and Johnston, 1999), which refers to "the process involved in systematically attempting to look into the longer-term future of science, technology, the economy and society with the aim of identifying the areas of strategic research and the emerging generic technologies likely to yield the greatest economic and social benefits" (Martin, 1995). Overall, Technology Foresight studies provide strategic information for decision-making and long-term planning in science and technology, being used to governments, organizations to prepare for the future (Martin, 2010; Miles, 2010; Martin, 1995; Martin and Johnston, 1999). As known, expert opinion surveys are one of the most used methods in Technology Foresight (Georghiou, 2008). Yet, as time goes by, advancements in scientific knowledge and technology developments may lead to changes in experts' views. Therefore, the tracking of changes in expectations about emerging technologies is of great importance to support decision-making and planning in science and technology. Thus, we hope the methods we applied can contribute to future studies aimed at tracking changes in experts' views of the future.

Technology foresight and decision-making in the health field

The term Foresight started to be used with science and technology in 1983 – at the Science Policy Research Unit, University of Sussex, UK – to refer to the studies carried out to identify or foresee the research areas that would probably lead to the greatest social and economic benefits in the future. Soon the term Technology Foresight started to be used to the researchers invested in it to mean a new future-oriented approach and also to distinguish it from Technology Forecasting – a more traditional forward-looking approach developed in the 1950s in the USA mainly by researchers at RAND Corporation. While the latter approach would de mainly predictive, the former was intended not only to look into the future of science and technology but also to shape the desired future (Martin, 2010; Miles, 2010). This purpose would be achieved not only by providing a common shared understanding of what the future may look like but by promoting networks of relevant stakeholders of the innovation systems through Foresight exercises (Martin and Johnston, 1999).

Overall, Technology Foresight is a future-oriented approach that aims to support decision-making, connect research and development (R&D) to innovation and connect the relevant actors in innovation systems. By addressing such relevant issues, Technology Foresight gained prominence as early as the 1990s as a means of supporting government decision-making in science and technology, becoming an important tool to foster the development of innovation systems (Martin and Johnston, 1999).

Most of the large and long-term government founded studies of the 1990s involved a combination of prospective studies, participatory orientation and policy-relatedness. For the most part, these studies – known as Technology Foresight Programmes or fully fledged foresight studies – gave way to a more limited type of future-oriented studies, in which some of those elements are missing (Miles, 2010). These studies are mainly "shorter-term perspectives, more conventional forecasting work, academic research with little policy engagement and desk-based studies and simulations without networking and broad knowledge bases" (Miles, 2010). In that sense, most of these studies are probably prospective exercises without connection with decision-making and planning for the future.

Yet, they have for some time now been predominant over the fully fledged foresight studies. Thus, it is certainly fair to say that these narrow Technology Foresight studies are responsible for a large part of the methodological and empirical advances in the field.

Additionally, their focused nature (covering one or a few main research subjects at a time instead of many) makes them more suitable for the study of a given technology and more feasible because they usually require low budgets, few researchers, the use of one or a few methods, etc. Thus, if the methods used are suitable for the research problem, and the results made available (e.g. through scientific publications), these studies may well be used to support decision-making and planning in governments, organizations other than the one in which they were conducted.

Materials and methods

We conducted a two-wave Web-based survey with an interval of two and a half years. The respondents of both waves were LOC-related researchers, who were identified from scientific publications involving LOCs indexed in WoS. To do that, we used the following search strategy:

TS=("lab* on a chip*" OR "lab* on chip*"))

Indexes = SCI-EXPANDED Timespan = 2010–2017 (Wave 1) and 2015–2020 (Wave 2)

The search strategy covered the two most common LOC descriptors: lab-on-a-chip and lab-on-chip. In the WoS advanced search mode, we used the tag Topic (TS) to broaden the scope of the results because it searches in the title, abstract and keywords of publications. As the target respondents were researchers from the natural sciences, we used only the Science Citation Index Expanded (SCI-EXPANDED). The publication years were limited to 2010–2017 in Wave 1 (W1) and 2015–2020 in Wave 2 (W2).

The W1 search was carried out in July 2017 and retrieved 2,788 records of publications. We performed the W2 search in March 2020 and obtained 2,107 records of publications. All the records were imported into the software VantagePoint 10.0, where we retrieved 3,205 (W1) and 2,930 (W2) authors' emails. Then we linked about 80% of the emails to their account owners using in-house Python code. The list of respondents of W1 and W2 was uploaded to the online survey platform SurveyMonkey, where we prepared the questionnaire and managed the survey. After the upload, the number of emails was reduced to 2,470 (W1) and 2,839 (W2) due to bounced emails and previously opted out contacts in SurveyMonkey.

The questionnaire was based on a literature review of LOC technology, focusing on diagnostic. It was structured into three parts and asked respondents to consider 2017–2037 (W1) and 2020–2037 (W2) as a future time horizon. The first part asks if respondents have knowledge of LOC applications in clinical analyses and diagnostic testing. Those who reported having no knowledge were disqualified from the survey and did not answer the rest of the questionnaire. The second part asks whether LOCs are still a window of opportunity for R&D organizations. The third section presents nine literature-based statements about the future of LOCs, whose likelihood and expected time of occurrence the respondents were asked to indicate (whether before or after 2037). Overall, the statements refer to the likelihood of LOCs: reaching industrial-scale production and being commercially viable worldwide; performing and integrating laboratory processes; providing low-cost PoC solutions and real-time monitoring of patients' health; and radically changing laboratories and their market. We did not include demographic questions because the demographics of the respondents (e.g. age, gender, ethnicity, employment, location) are not expected to influence the results (Cabral *et al.*, 2019a; Mota *et al.*, 2020; Cabral *et al.*, 2020). We also adjust the questionnaire to be answered within 2–3 min to avoid respondents' fatigue, skipped questions and dropout rates.

To validate the questionnaire, get feedback from respondents and assess the study protocol, we conducted a pilot study in W1 with an aleatory sample of about 11% (275) of the authors' emails. The 19 respondents who participated in the pilot study did not suggest any changes. Thus, neither the questionnaire nor the study protocol was modified. Their answers were then included in the results. The formal surveys took place in August and October 2017 (W1) and March 2020 (W2). The respondents were informed about the study during the data collection period, first in an invitation and then in reminder emails. The questionnaire was available for completion for eight days after the invitation was sent. During this time, up to three reminders were sent to non-responders. The participation was voluntary, no personal or sensitive data were asked, and the data collected were anonymized in the results. Overall, the procedures adopted in this study are in line with part of the specialized Web-based survey literature (Sauermann and Roach, 2013). The methods applied to identify and collect respondents from scientific publications in WoS, and the design and conduction of the Web-based survey are based on recent future-oriented studies (Cabral *et al.*, 2020; Cabral *et al.*, 2019b; Mota *et al.*, 2020; Cabral *et al.*, 2019a).

Results

The response rate of W1 and W2 were, respectively, 10.36% and 12.47%. Of the 256 (W1) and 354 (W2) researchers who accepted to participate in this study, 12 (W1) and 16 (W2) were disqualified because they declared no knowledge of LOC applications in clinical analyses and diagnostic testing. A total of 549 individual qualified researchers participated in this study, 33 of them in both waves. The descriptive statistics of data collected in W1 and W2 are depicted along with the results of non-parametric tests of marginal homogeneity with a 5% significance level. Confidence levels and margin of errors were calculated for each question. At a 95% confidence level, the margin of error for the W1 sample was between 6.0% and 6.2%, and for the W2 was between 5.0% and 5.3%. The frequency distribution of the medians is described only in cases where there were changes in the results of W2 compared to W1. All statistical analysis of the study is available as Supplementary Material.

According to the respondents' emails' internet protocol, researchers from 46 countries participated in W1 and 49 in W2 (Figure 1). In W1, the highest proportion of respondents was from the USA (15.63%), followed by Italy (10.55%), India (6.64%) and France (5.86%). In W2, the largest share of respondents was also from the USA (14.69%), followed by Italy (9.32%), India (9.04%) and China (9.04%).

In W1 and W2, respectively, 96.22% and 97.31% of the respondents reported that LOCs still represent a window of opportunity for R&D organizations (Figure 2). The non-parametric test suggests that W1 and W2 responses are homogeneous at a 5% significance level. The probability of supporting the homogeneity was 49.6%, meaning that there was no statistically significant change in respondents' expectations between W1 and W2.

According to 90.83% of the respondents of W1 and 85.99% of W2, LOC devices will likely move from bench research and proof-of-concept demonstrations to industrial-scale production before 2037 (Figure 3). In W1, less than 10% of respondents believed that this result would not occur until after 2037, against 12.42% in W2. The non-parametric test of W1 and W2 responses shows that there was no statistically significant change in respondents' expectations, as the probability of supporting the homogeneity hypothesis was 19.9%.

LOC devices will likely be successfully commercialized worldwide before 2037 according to 83.91% of W1 respondents (Figure 3). In W2, the percentage dropped to 71.34%. On the other hand, the percentage of respondents who believe that it would be successfully commercialized after 2037 increased from 16.09% (W1) to 26.75% (W2). This change in the perception of the respondents is confirmed by the non-parametric test of marginal homogeneity, which shows that the probability of accepting the homogeneity hypothesis is 0.3%. In other words, it can be said that, in 2020, the respondents expect that more time will be needed for LOCs to be successfully commercialized globally. The heterogeneity of the results of the two waves was also verified in the analysis of the frequency distribution of the median. While in W1 the frequency distribution of the median is the same in the three quartiles analyzed (1/4, 1/2 and 3/4), it is observed that in

Figure 1 Global distribution of respondents

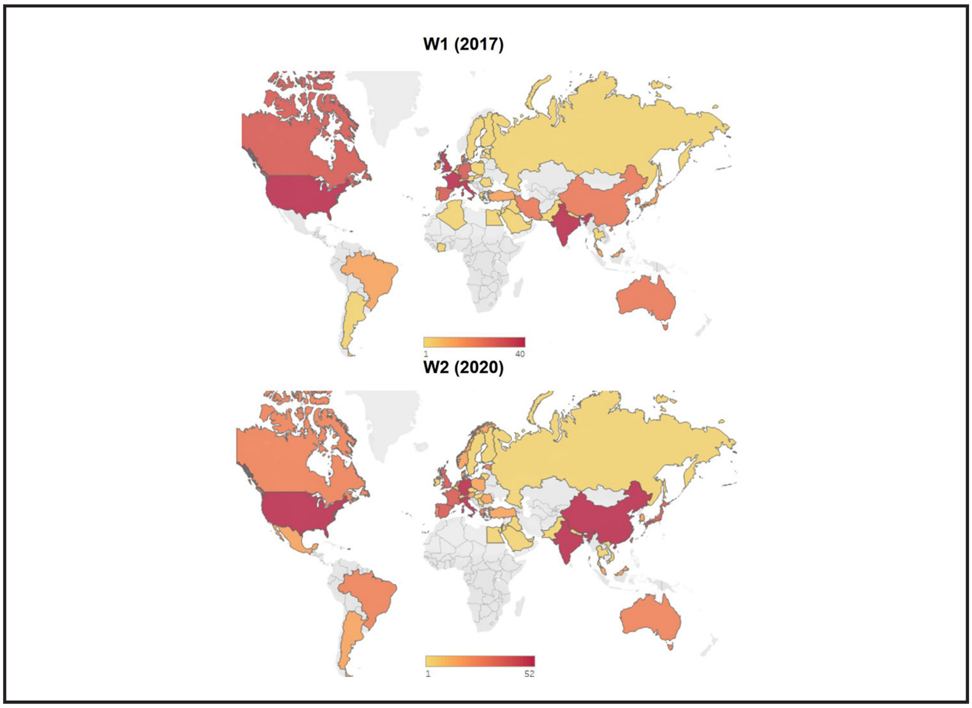
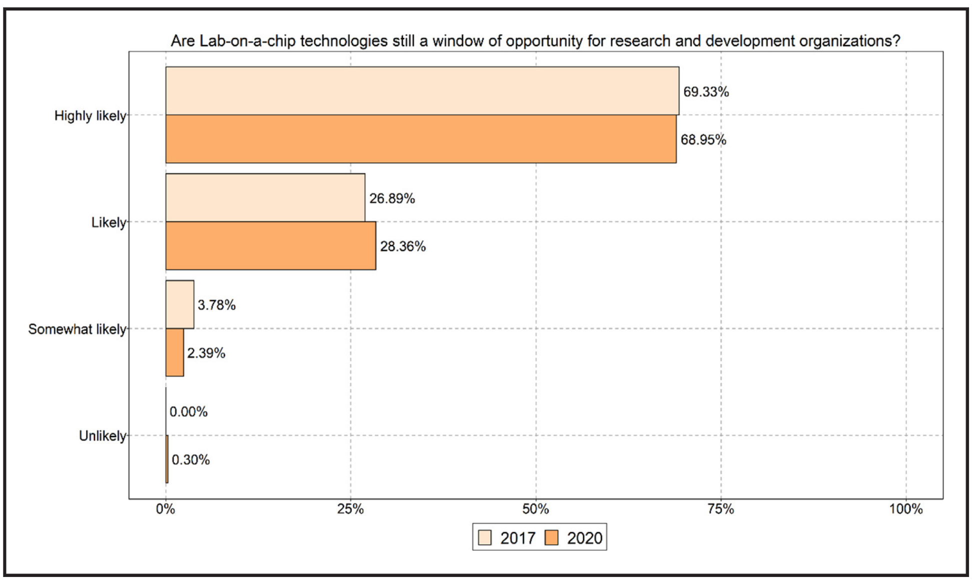


Figure 2 Likelihood of LOCs still being a window of opportunity for R&D organizations



W2 this distribution changes. Sorting in increasing order, the first 25% of the distribution goes from likely before 2037 in W1 to likely after 2037 in W2.

The type of LOC device expected to integrate the totality of laboratory processes is generally known as Micro Total Analysis Systems (μTAS). According to 66.20% of W1 respondents, μTAS will likely integrate the totality of laboratory processes before 2037

(Figure 4). In W2, the percentage dropped to 50.00%. The respondents that believe that this outcome would occur only after 2037 increased from 24.54% (W1) to 38.54% (W1). From 2017 to 2020, the number of respondents who disbelieve that this outcome would happen at any point in the future also increased, from 9.26% (W1) to 11.46% (W2). The responses indicate a change in researchers' expectations regarding the ability of these devices to integrate all laboratory processes, whether concerning feasibility or the time required. This is confirmed by the non-parametric test of marginal homogeneity, which shows that the probability of accepting the hypothesis of homogeneity of responses in both waves is 1.2%. This change in perception is also observed in the frequency distribution of the median.

Figure 3 Likelihood of LOCs reaching industrial-scale production and being commercially viable worldwide

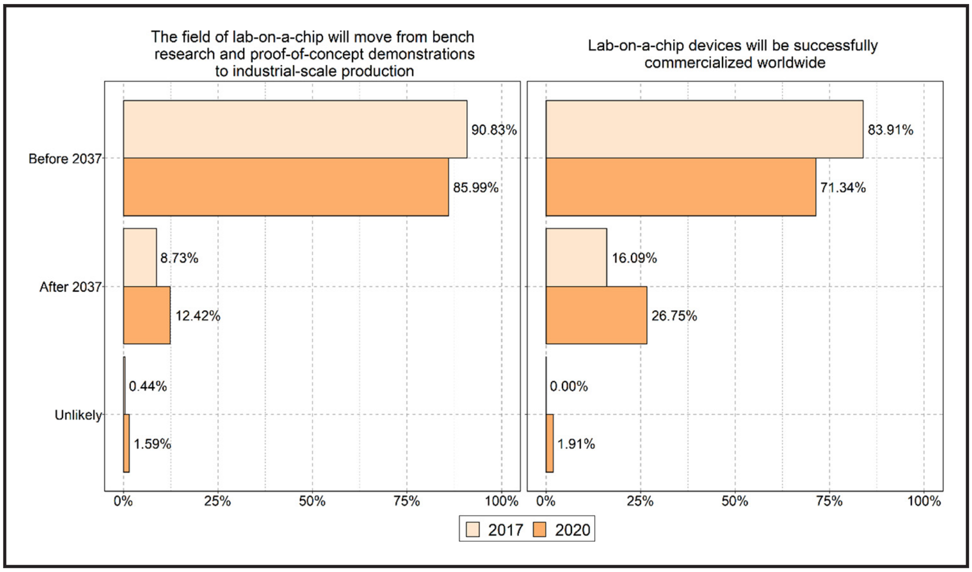
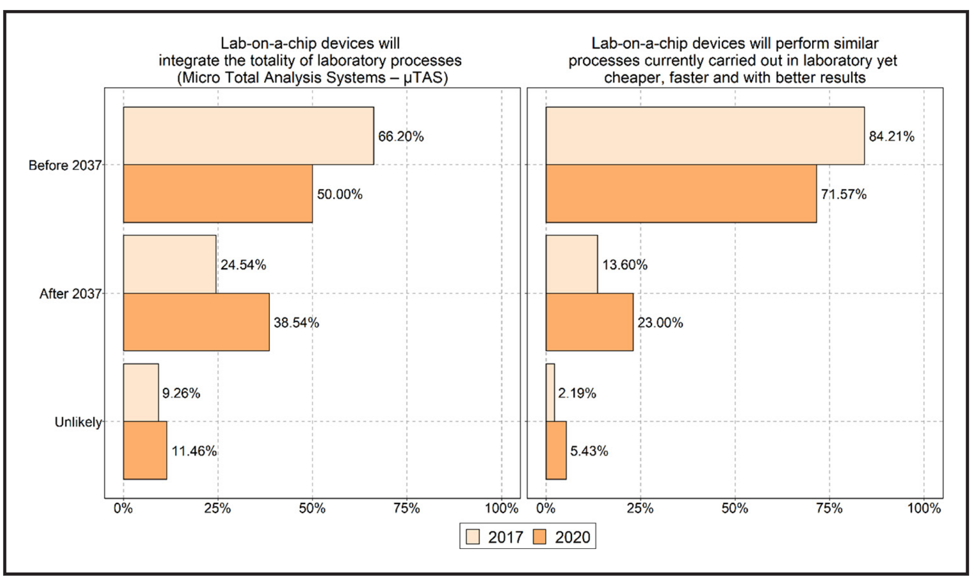


Figure 4 Likelihood of LOCs performing and integrating laboratory processes

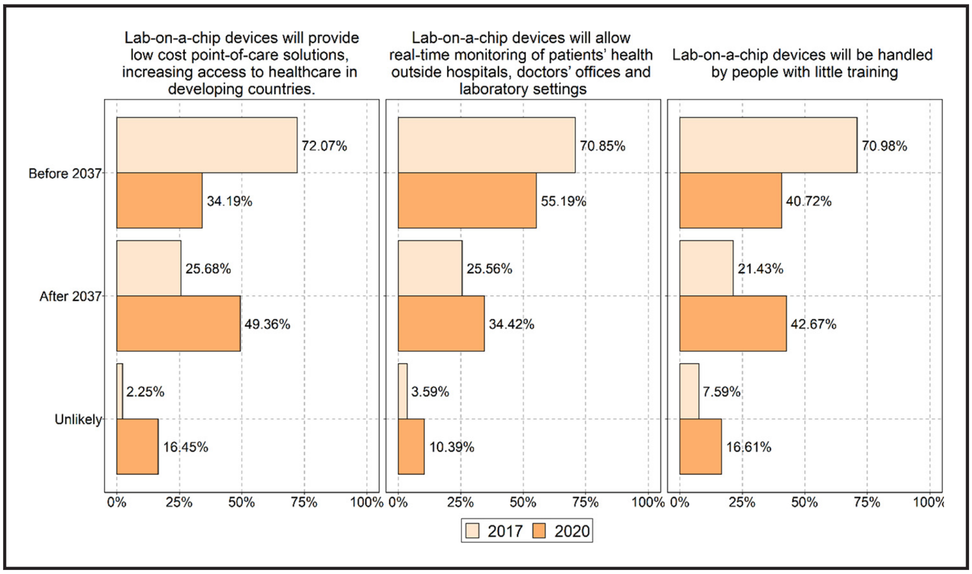


While in W1 the frequency distribution of the median is the same in the three quartiles considered (1/4, 1/2 and 3/4), this distribution changes in W2. Ranking in ascending order, the first 25% of the distribution change from likely before 2037 in W1 to likely after 2037 in W2. Therefore, it can be said that, compared to W1, the respondents of W2 believe that more time will be needed for LOC devices to fully integrate all laboratory processes.

In 2017, 84.21% of the respondents expected that, before 2037, LOC devices would perform similar processes to those carried out in laboratories, but more quickly, at a lower cost and with more reliable results (Figure 4), while in 2020 the percentage was reduced to 71.57%. On the other hand, the percentage of respondents who believe that this result would only be achieved after 2037 or that it would never be achieved has increased. In the former case it grew from 13.60% (W1) to 23.00% (W2), and in the latter case from 2.19% (W1) to 5.43% (W2). The probability of accepting the hypothesis of homogeneity of responses in both waves is 2.2%, confirming a change in respondents' expectations. The heterogeneity of the results of both waves can also be seen through the frequency distribution of the median. While in W1 the frequency distribution of the median is the same in the three quartiles examined (1/4, 1/2 and 3/4), it changes in W2. Sorting in ascending order, the first 25% of the distribution changes from likely before 2037 in W1 to likely after 2037 in W2. Thus, compared to W1, respondents in W2 consider that more time will be needed for LOC devices to perform similar processes currently performed in laboratories but cheaper, faster and with better results.

According to 72.07% of W1 respondents, LOC devices will likely provide low-cost PoC solutions before 2037, increasing access to health care in developing countries (Figure 5). From 2017 to 2020, however, expectations for such an outcome have significantly reduced, as only 34.19% of respondents chose this option. The percentage of respondents who believe that outcome may be seen only after 2037 or that it is unlikely to happen has also grown significantly between surveys. In 2020, 49.36% of W2 respondents reported that this is likely only after 2037, compared to 25.68% of W1 and 16.45% that it will not occur, compared to 2.25% of the first survey. The perception that there has been a change in expectations regarding feasibility or the time needed is confirmed by the marginal homogeneity test, which shows that the probability of accepting the hypothesis of homogeneity of responses in both waves is 0.0%. The analysis of the frequency distribution

Figure 5 Likelihood of LOCs providing low-cost point-of-care solutions, real-time monitoring of patients' health and be handled by people with little training



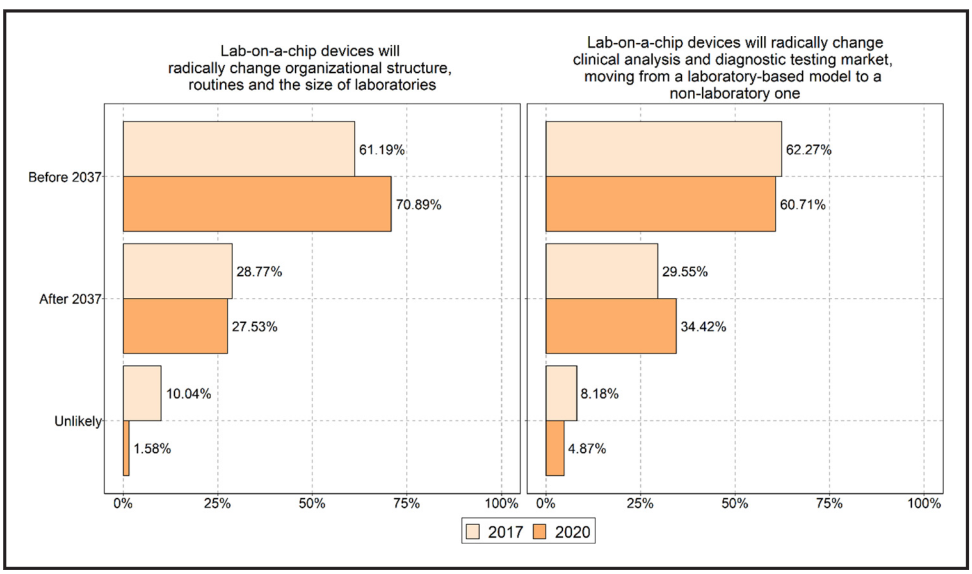
of the median also points to a change in the perception of respondents. Dividing the sample into two parts, the predominant result in W1 is that LOC devices will provide low-cost PoC solutions likely before 2037, while in W2 it changes to likely after 2037.

Overall, the results for the other two statements on the future of LOC devices depicted in Figure 5 follows the same pattern as above, including changes in researchers' expectations regarding feasibility and time needed. Between 2017 and 2020, there was a reduction in the percentage of respondents who believe the suggested outcome would occur before 2037, whereas there was an increase of those who believe it would occur only after 2037 or it would never happen in the future. The perception of changes in expectations from W1 to W2 is confirmed by the marginal homogeneity tests. The probability of accepting the hypothesis of homogeneity of responses in both waves was 0.0% for the statement that LOC devices would be handled by people with little training and 0.2% for the statement that LOC devices would allow real-time monitoring of patients' health outside hospitals, doctors' offices and laboratory settings. As for the frequency distribution of the median, dividing the sample into two parts, the predominant result is that LOC devices will likely be handled by people with little training before 2037 in W1 and after 2037 in W2.

By 2037, LOC devices will likely radically change the organizational structures, routines and size of laboratories according to 61.19% (W1) and 70.89% (W2) of the respondents (Figure 6). From 2017 to 2020, the percentage of respondents who believe this outcome would only happen after 2037 was slightly reduced, from 28.77% (W1) to 27.53% (W2). For its part, the percentage of those who disbelieve in such an outcome was significantly reduced, from 10.04% to 1.58%. Comparing the responses of both waves, it can be seen that the 2020 respondents are more optimistic about the speed at which such changes may occur. This is confirmed by the non-parametric test, as the probability of accepting the hypothesis of homogeneity was 0.0%.

As for the statement of LOC devices leading to a laboratory-free model in the future (Figure 6), the results of 2017 and 2020 are quite similar, with the majority of respondents reporting that this outcome may happen before 2037 – 62.27% (W1) and 60.71% (W2). The most marked change occurred among those who consider the transition to a non-laboratory based model unlikely, dropping from 8.18% (W1) to 4.87% (W2). Although the results seem to suggest that the respondents of 2020 are more optimistic than those of 2017, the non-

Figure 6 Likelihood of LOCs radically changing laboratories and their market



parametric test indicates that there is no statistically significant difference in their perceptions of the future, as the probability of accepting the homogeneity hypothesis was 28.7%.

Discussion

Overall, the respondents of both waves consider that LOCs are still a window of opportunity for R&D organizations interested in investing in this technology. This is perhaps because LOCs are in the early stages of development (Arshavsky-Graham and Segal, 2020). In other words, an emerging technology at the beginning of its life cycle. As known, the life cycle of a technology is usually divided into four phases: introduction, initial growth, final growth and maturity. Due to relatively low entry requirements, the introduction phase would be the best moment for an organization to enter in a new technological system. In this phase, much of the knowledge required for entry is public and the skills to deal with the technological novelty need to be created through learning-by-doing (Freeman and Soete, 1997; Perez and Soete, 1988).

On the other hand, a technology that reaches the market and proves commercially viable is at a later stage of its life cycle (OECD, 1992). The later stages usually involve higher barriers to entry, especially knowledge-related barriers. This is because much of the scientific, technological and industrial knowledge will already have been appropriated by the organizations that entered the new technological system earlier in its life cycle (Freeman and Soete, 1997; Perez and Soete, 1988). Thus, in the later phases, late entry R&D organizations will likely not be able to take advantage of LOC technologies. Although it may remain after 2037 for about 30% of W2 researchers, our results suggest that this window of opportunity for R&D organizations to enter the LOC technological system may close before 2037. In any case, R&D organizations willing to enter the LOC technological system may have the chance of benefiting from a growing market that is expected to reach a little over USD 9bn by 2024 (Market Data Forecast, 2020).

Yet, moving from bench research and proof-of-concept demonstrations to the industrial phase is a major challenge that needs to be overcome before LOCs can reach the market (Casquillas *et al.*, 2016; Abdul Aleem Baig, 2020). For most of W1 and W2 researchers, LOCs are expected both to move from research to industrial-scale production and be successfully commercialized worldwide before 2037. So far, companies such as Abbot Laboratories, Bio-Rad Laboratories, Agilent Technologies, Fluid Corporation and Thermo Fischer Scientific are the leading players in this market and most of its efforts have been geared toward the North American market (Mordor Intelligence, 2020). This comes from its quick adoption of technological developments, whereas in Europe and Asia the driving force is the rise in investments by governments in hospitals (Market Data Forecast, 2020).

There was, however, an increase of researchers reporting that moving from research to production and achieving global commercialization would be likely only after 2037, which may mirror challenges not yet overcome, related, e.g. to the scalability of complex microfluid structures (Arshavsky-Graham and Segal, 2020). Nevertheless, the expectation is that 3D printing technology will solve these problems soon, as it can print plastic-based microfluidics (Arshavsky-Graham and Segal, 2020). There are also some concerns with high initial purchasing cost and with the lack of awareness regarding LOC devices among the middle-income countries (Data Bridge Market Research, 2020).

The greater the number of processes performed on a chip, the greater the number of circuits and electrical connections required, which increases the complexity of LOCs and the risk of failure (Trietsch *et al.*, 2011). Today, the full integration of laboratory processes into a single device (μTAS) is still a goal not achieved (Măriuţa *et al.*, 2020), as well as the development of low cost, highly effective and fast LOC devices (Zhu *et al.*, 2020a; Zhuang *et al.*, 2020). Yet, although respondents were less optimistic in W2 than in W1, our results indicate that, before 2037, LOCs are expected to both integrate all laboratory processes and perform similar processes to those currently carried out in laboratories, but at a lower cost, more quickly and with more reliable results.

One of the most anticipated applications of LOC technologies is the development of low-cost PoC diagnostic devices. Having lower costs is a prerequisite for them to become a feasible alternative to diagnostic laboratories, otherwise they will probably not be widely adopted (Kraft *et al.*, 2011). Their PoC feature could also be particularly relevant for diagnosing patients living in remote or difficult-to-access areas (Ríos *et al.*, 2012), facilitating access to health care where clinics, laboratories and hospitals are usually unavailable. In part, that is why developing countries are expected to become a major market for these devices (Kaur and Kaur, 2009). In W1 most researchers suggested that, before 2037, LOC devices would provide low-cost PoC diagnostics, facilitating the diagnosis of patients living in remote or difficult-to-access areas. Thus, helping to improve access to healthcare, especially in developing countries. In W2, most of them suggested that this would occur only after 2037 and 16.45% of them opted for "unlikely". This change in expectation may be related to the fact that, for LOCs to be considered PoC devices, they should be user-friendly and equipment free in addition to other attributes like low cost, fast speed and robustness (Zhuang *et al.*, 2020). Yet, a device with all these attributes has not succeeded in becoming commercially available (Abdul Aleem Baig, 2020).

In the future, LOC devices are also expected to perform real-time monitoring of patients, transmitting their health status via, e.g. mobile devices (Martín *et al.*, 2017). This would enable the diagnosis of a disease to be known even before the patient presented clinical symptoms, allowing the early onset of treatment (Kraft *et al.*, 2011). Despite the reduction in optimism in W2, our results suggest that LOCs providing real-time monitoring of patients' health would be likely before 2037. Thus, in the coming years, we may expect LOC devices to be integrated into peoples' daily lives. For example, to control their glucose and lactic acid levels (Martín *et al.*, 2017). A recent advance includes a wearable microfluidic device to detect the Zika virus (Zhuang *et al.*, 2020), this same device, which is similar to a bandage, could be adapted for tumor diagnosis in the future (Yang *et al.*, 2019). After the COVID-19 pandemic, the need for PoC devices that could provide rapid and robust diagnosis has risen (Arshavsky-Graham and Segal, 2020; Binnicker, 2020). The motivation of researchers and the willingness of companies to invest in the development of these technologies has also increased (Zhu *et al.*, 2020b), which may accelerate the development of diagnostic LOC devices.

It is expected that people with little to no training will be able to use LOC devices (Casquillas *et al.*, 2016), including the patients themselves (Yager *et al.*, 2006). In W1, most of the respondents suggested that people with little training would use LOC diagnostic devices before 2037, but in W2 most of them opted for after 2037. "Unlikely" also increased. Although it is an expected feature in the future, especially with the awaited integration between LOCs and smartphones (Zhu *et al.*, 2020a), currently, the use of LOCs still depends on specific knowledge and skills (Abdul Aleem Baig, 2020).

Finally, LOC devices are expected to change laboratory routines (Ríos *et al.*, 2012), as in the case of the "chip in a lab" (Jung *et al.*, 2015), where microfluidic devices are used on the laboratory bench to replace part of the laboratory processes (Mohammed *et al.*, 2015). LOC devices are also expected to compete with the diagnostic laboratories in the market or even replace them. In this case, the market would move from a laboratory-based to a non-laboratory-based model (Figeys and Pinto, 2000). In line with that, our findings suggest that, before 2037, LOCs may radically change not only laboratories as we know them today, but the whole diagnostics market, perhaps moving to a non-laboratory-based model. This perception of the respondents may be related to the fact that microfluidic chips are already being used in research laboratories before they even become commercial (Nascetti *et al.*, 2019). Additionally, there is a tendency to shift from the traditional lab-centralized diagnostics to PoC settings, which was accentuated by the COVID-19 outbreak (Arshavsky-Graham and Segal, 2020).

Final remarks

This study presented the results of a two-wave global survey of researchers about the future of LOC diagnostic devices and assessed changes in researchers' expectations between Waves 1 (2017) and 2 (2020). Comparing the results of both waves, one can see a reduction in respondents' optimism about the future of LOCs. In part, the reduction in optimism may be related to the fact that most of the challenges faced by scientists in 2017 are still present in 2020. At present, e.g. scientists are still pursuing a material that is suitable for the complexity of LOC devices, which is both scalable and low cost (Arshavsky-Graham and Segal, 2020). Some examples are the use of polydimethylsiloxane (PDMS), which is suitable for the complexity of the devices but not yet scalable, and the use of paper, which is scalable and low-cost but not as suitable as PDMS for the complexity of LOC devices (Arshavsky-Graham and Segal, 2020).

In most statements, the rate of researchers who chose "after 2037" and "unlikely" increased in W2. However, for none of the questions did the "unlikely" option outperform the "likely" options, either before or after 2037. Moreover, in almost all questions, more researchers chose "before 2037" than "after 2037." This means that although W2 researchers are less optimistic compared to W1 researchers, they can be considered optimistic about the future of LOC diagnostic devices. Thus, taken together, the results of 2017 and 2020 suggest that LOCs diagnostic devices are still a window of opportunity for R&D organizations; they may integrate all laboratory processes and perform similar processes to those currently carried out in laboratories, but at a lower cost, more quickly and with more reliable results; they may provide low-cost PoC diagnostics, facilitating the diagnosis of patients living in remote or difficult-to-access areas, improving access to healthcare; and they may change not only laboratories as we know them today but the whole diagnostics market, perhaps moving to a non-laboratory-based model.

In summary, our findings seem to confirm several expectations about the future of LOC diagnostic devices, as pointed out in the reviewed literature, suggesting that they may lead to substantial changes in the way human diseases are diagnosed and health conditions are monitored. Preparing for the future is, therefore, a necessity, but especially for those involved in diagnostic testing, health-care provision, public health interventions.

References

Abdul Aleem Baig, M. (2020), "mHealth-based microfluidic lab-on-a-chip for international health security", *Contemporary Developments and Perspectives in International Health Security*, Vol. 1, IntechOpen, London, pp. 1-15.

Arshavsky-Graham, S. and Segal, E. (2020), "Lab-on-a-chip devices for point-of-care medical diagnostics", *Adv Biochem Eng Biotechnol*, pp. 1-19.

Balogh, E.P., Miller, B.T. and Ball, J.R. (Eds) (2015), *Improving Diagnosis in Health Care*, National Academies Press, Washington, DC.

Binnicker, M.J. (2020), "Emergence of a novel coronavirus disease (COVID-19) and the importance of diagnostic testing: why partnership between clinical laboratories, public health agencies, and industry is essential to control the outbreak", *Clinical Chemistry*, Vol. 66 No. 5, pp. 664-666.

Cabral, B., da Graça Derengowski Fonseca, M. and Mota, F.B. (2019a), "Long term prevention and vector control of arboviral diseases: what does the future hold?", *International Journal of Infectious Diseases IJID Diseases*, Vol. 89, pp. 169-174.

Cabral, B.P., Bonventre, J.V., Wieringa, F. and Mota, F.B. (2020), "Probing expert opinions on the future of kidney replacement therapies", *Artificial Organs*, pp. 1-24.

Cabral, B.P., da Graça Derengowski Fonseca, M. and Mota, F.B. (2019b), "What is the future of cancer care? A technology foresight assessment of experts' expectations", *Economics of Innovation and New Technology*, Vol. 28 No. 6, pp. 635-652.

Casquillas, G.V., Houssin, T. and Durieux, L. (2016), "Introduction to lab on a chip 2015: review, history and future", *Elveflow*, Vol. 1 No. 4, pp. 1-5.

Cheng, A.C., West, T.E., Limmathurotsakul, D. and Peacock, S.J. (2008), "Strategies to reduce mortality from bacterial sepsis in adults in developing countries", *PLoS Medicine*, Vol. 5 No. 8, pp. 1173-1179.

Chin, C.D., Linder, V. and Sia, S.K. (2007), "Lab-on-a-chip devices for global health: past studies and future opportunities", *Lab Chip*, Vol. 7 No. 1, pp. 41-57.

Craighead, H. (2006), "Future lab-on-a-chip technologies for interrogating individual molecules", *Nature*, Vol. 442 No. 7101, pp. 387-393.

Data Bridge Market Research (2020), Lab-On-A-Chip Market 2020 Industry Analysis Report.

Figeys, D. and Pinto, D. (2000), "Lab-on-a-Chip: a revolution in biological and medical sciences", *Analytical Chemistry*, Vol. 72 No. 9, pp. 330 A-335 A.

Freeman, C. and Soete, L. (1997), *The Economics of Industrial Innovation*, 3rd rev. and expanded ed., Pinter, London.

Georghiou, L. (2008), *The Handbook of Technology Foresight: Concepts and Practice, Prime Series on Research and Innovation Policy*, Elgar, Cheltenham, Northampton, MA.

Giannitsis, A.T. (2011), "Microfabrication of biomedical lab-on-chip devices. A review", *Estonian Journal of Engineering*, Vol. 17 No. 2, pp. 109-139.

Gupta, S., Ramesh, K., Ahmed, S. and Kakkar, V. (2016), "Lab-on-Chip technology: a review on design trends and future scope in biomedical applications", *International Journal of Bio-Science and Bio-Technology*, Vol. 8 No. 5, pp. 311-322.

Jung, W., Han, J., Choi, J.-W. and Ahn, C.H. (2015), "Point-of-care testing (POCT) diagnostic systems using microfluidic lab-on-a-chip technologies", *Microelectronic Engineering*, Vol. 132, pp. 46-57.

Kaur, E. and Kaur, J. (2009), *Opportunities and Future of Lab-on-A-Chip Technology in Diagnostics*, Singapore.

Kolluri, N., Klapperich, C.M. and Cabodi, M. (2017), "Toward lab-on-a-chip diagnostics for malaria elimination", *Lab on a Chip*, Vol. 18 No. 1, pp. 75-94.

Kraft, K., Krafczyk-Korth, J., Muehlan, H., Schmidt, S. and Hoffmann, W. (2011), "An epidemiology of care approach to lab-on-a-chip systems in individualized medicine?", *Personalized Medicine*, Vol. 8 No. 5, pp. 587-590.

Lee, A.P. (2020), "2020 vision: celebrating the 20th year of lab on a chip", *Lab on a Chip*, Vol. 20 No. 11, pp. 1889-1890.

Mahumud, R.A., Sultana, M., Sheikh, N., Ali, M.N., Mitra, D.K. and Sarker, A.R. (2016), "Diagnostic errors in low and middle-income countries: future health and economic burden for patient safety", *Austin Emerg Med*, Vol. 2 No. 8, pp. 1-3.

Măriuţ a, D., Colin, S., Barrot-Lattes, C., Le Calvé, S., Korvink, J.G., Baldas, L. and Brandner, J.J. (2020), "Miniaturization of fluorescence sensing in optofluidic devices", *Microfluidics and Nanofluidics*, Vol. 24 No. 9, pp. 1-28.

Market Data Forecast (2020), Global Lab On a Chip Market Analysis.

Martín, A., Kim, J., Kurniawan, J.F., Sempionatto, J.R., Moreto, J.R., Tang, G., Campbell, A.S., Shin, A., Lee, M.Y., Liu, X. and Wang, J. (2017), "Epidermal microfluidic electrochemical detection system: enhanced sweat sampling and metabolite detection", *ACS Sensors*, Vol. 2 No. 12, pp. 1860-1868.

Martin, B.R. (1995), "Foresight in science and technology", *Technology Analysis & Strategic Management*, Vol. 7 No. 2, pp. 139-168.

Martin, B.R. (2010), "The origins of the concept of 'foresight' in science and technology: an insider's perspective", *Technological Forecasting and Social Change*, Vol. 77 No. 9, pp. 1438-1447.

Martin, B.R. and Johnston, R. (1999), "Technology foresight for wiring up the national innovation system", *Technological Forecasting and Social Change*, Vol. 60 No. 1, pp. 37-54.

Mendes, F.M.L., Castor, K., Monteiro, R., Mota, F.B. and Rocha, L.F.M. (2019), "Mapping the lab-on-a-chip patent landscape through bibliometric techniques", *World Patent Information*, Vol. 58, pp. 1-9.

Miles, I. (2010), "The development of technology foresight: a review", *Technological Forecasting and Social Change*, Vol. 77 No. 9, pp. 1448-1456.

Mohammed, M.I., Haswell, S. and Gibson, I. (2015), "Lab-on-a-chip or Chip-in-a-lab: challenges of commercialization lost in translation", *Procedia Technology*, Vol. 20, pp. 54-59.

Mordor Intelligence (2020), Lab-on-a-chip and microarrays (biochip) market: Growth, trends, and forecast (2020-2025).

Mota, F., Braga, L., Rocha, L. and Cabral, B. (2020), "3D and 4D bioprinted human model patenting and the future of drug development", *Nature Biotechnology*, Vol. 38 No. 6, pp. 689-694.

Nascetti, A., Mirasoli, M., Marchegiani, E., Zangheri, M., Costantini, F., Porchetta, A., Iannascoli, L., Lovecchio, N., Caputo, D., Cesare, G. D., Pirrotta, S. and Roda, A. (2019), "Integrated chemiluminescence-based lab-on-chip for detection of life markers in extraterrestrial environments", *Biosensors and Bioelectronics*, Vol. 123, pp. 195-203.

OECD (1992), Technological innovation: some definitions and building blocks, Technology/Economy Programme (TEP), Background Report, Paris.

Path (2005), Diagnostics for neglected tropical diseases: Defining the best tools through target product profile, Seattle.

Perez, C. and Soete, L. (Eds) (1988), *Catching up in Technology: Entry Barriers and Windows of Opportunity*, Pinter, London.

Ríos, Á., Zougagh, M. and Avila, M. (2012), "Miniaturization through lab-on-a-chip: utopia or reality for routine laboratories? A review", *Analytica Chimica Acta*, Vol. 740, pp. 1-11.

Romao, V.C., Martins, S.A.M., Germano, J., Cardoso, F.A., Cardoso, S. and Freitas, P.P. (2017), "Lab-on-Chip devices: gaining ground losing size", *ACS Nano*, Vol. 11 No. 11, pp. 10659-10664.

Sauermann, H. and Roach, M. (2013), "Increasing web survey response rates in innovation research: an experimental study of static and dynamic contact design features", *Research Policy*, Vol. 42 No. 1, pp. 273-286.

Temiz, Y., Lovchik, R.D., Kaigala, G.V. and Delamarche, E. (2015), "Lab-on-a-chip devices: how to close and plug the lab?", *Microelectronic Engineering*, Vol. 132, pp. 156-175.

Thilmany, J. (2005), "Think small", *EMBO Reports*, Vol. 6 No. 10, pp. 913-916.

Trietsch, S.J., Hankemeier, T. and van der Linden, H.J. (2011), "Lab-on-a-chip technologies for massive parallel data generation in the life sciences: a review", *Chemometrics and Intelligent Laboratory Systems*, Vol. 108 No. 1, pp. 64-75.

van Merkerk, R.O. and Robinson, D.K.R. (2006), "Characterizing the emergence of a technological field: expectations, agendas and networks in lab-on-a-chip technologies", *Technology Analysis & Strategic Management*, Vol. 18 Nos 3/4, pp. 411-428.

WHO (2018), Technical series on primary health care: Quality in primary health care, Technical series.

Yager, P., Edwards, T., Fu, E., Helton, K., Nelson, K., Tam, M.R. and Weigl, B.H. (2006), "Microfluidic diagnostic technologies for global public health", *Nature*, Vol. 442 No. 7101, pp. 412-418.

Yang, B., Kong, J. and Fang, X. (2019), "Bandage-like wearable flexible microfluidic recombinase polymerase amplification sensor for the rapid visual detection of nucleic acids", *Talanta*, Vol. 204, pp. 685-692.

Zhuang, J., Yin, J., Lv, S., Wang, B. and Mu, Y. (2020), "Advanced 'lab-on-a-chip' to detect viruses – current challenges and future perspectives", *Biosensors & Bioelectronics*, Vol. 163, pp. 1-13.

Zhu, H., Fohlerová, Z., Pekárek, J., Basova, E. and Neužil, P. (2020a), “Recent advances in lab-on-a-chip technologies for viral diagnosis”, *Biosensors & Bioelectronics*, Vol. 153, pp. 1-14.

Zhu, H., Zhang, H., Ni, S., Korabečná, M., Yobas, L. and Neuzil, P. (2020b), “The vision of point-of-care PCR tests for the COVID-19 pandemic and beyond”, *TrAC Trends in Analytical Chemistry*, Vol. 130, pp. 1-19.

Corresponding author

Fabio Mota can be contacted at: fabio.mota@fiocruz.br