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Lab-on-a-chip—fostering a sustainable future

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KEYWORDS

lab-on-a-chip, sustainability, lab efficiency assessment framework, my green lab, life cycle assessment, environmental impact analysis

1 Introduction

Every year, bench scientists in the biomedical and agricultural fields consume approximately 1,000 kg of plastic (Urbina et al., 2015), 30 times the average person in Europe (Eurostat, 2018). The climate crisis has urged laboratories to strive to improve sustainability practices and programs such as 'My Green Lab' (Green Lab Certification, 2013) and "Lab Efficiency Assessment Framework" (LEAF, 2018) are supporting laboratory changes through education, resources, and certifications. Lab-on-a-chip (LoC) technologies enable miniaturized laboratory analyses including drug screening, clinical diagnostics, and environmental and food safety monitoring. By their nature, they bring important advantages compared to macro-scale counterparts, including low sample volume and reagent consumption, rapid reactions, high throughput, and small dimensions allowing to use less material for manufacturing and providing portability (Agrawal et al., 2022). However, most commercially available microfluidic devices comprise non-biodegradable plastics with significant carbon dioxide equivalent (CO₂-eq) (Eurostat, 2014) footprints. More than half of the published diagnostic LoC devices are made of polydimethylsiloxane (PDMS), preventing scaling and efficient production (Ongaro et al., 2022). Their portability has the potential to facilitate their use in remote areas, outside laboratory settings, raising concerns around health and environmental risks due to impractical, unavailable, or challenging waste disposal regulations and practices. Recent studies have investigated possible sustainable materials and reagent alternatives (Agrawal et al., 2022; Ongaro et al., 2022), however the environmental burden of LoC devices throughout their life cycle remains largely unexamined. Whilst substantial efforts in choosing LoC materials to reduce single-use non-biodegradable plastics are required to enable efficient scalability and reduce toxic chemicals, similarly, design and (bio)physical principles used to develop LoC need to be considered. Innovation in manufacturing technologies and the incorporation of life cycle assessments (LCA) from the outset of new LoC research can reduce downstream human health and environmental impacts (Visotsky et al., 2017). However, the lack of systematic studies on the non-green aspects of LoC systems limits our understanding and ability to improve their environmental performance effectively. Further research is needed to address this gap and provide guidance for the design and implementation of sustainable LoCs.

In this paper, I explore recent achievements around LoC sustainability and potential LoC life cycle sustainable improvements. I also propose that environmental impact analyses and sustainable materials should take center stage in new LoC research.

2 Environmental impact analysis

A product's environmental hotspots can be identified using several tools (Table 1), but the most comprehensive is LCA (Luz et al., 2018). LCA quantifies potential impacts on the natural environment, human health, and resources during each step of the product life cycle (Caro, 2019). Since the LoC market is anticipated to grow by 20% year-on-year (Sridhar et al., 2022), there is an important need for guidelines to develop and dispose these technologies. The basis of a sustainable 'self-assessment' is incorporated into a 'Design for Sustainability' approach (Clark et al., 2009; Ceschin and Gaziulusoy, 2016) that can be integrated from the early stages of LoC design. These new initiatives could focus on reducing non-renewable energy and water consumption, waste production and harmful chemicals, and on developing longerlasting designs (Ongaro et al., 2022). Such approaches, however, focus mainly on the consumable elements of LoCs (Agrawal et al., 2022; Ongaro et al., 2022), i.e., the materials and reagents involved, and their disposal. Therefore, LCA covering all cradle-to-grave aspects (Figure 1) should be advocated by the scientific community and encouraged by policymakers. Usually, LCA assesses products' effects after their design and implementation, but embedding LCA into the initial stage of product design can significantly enhance the overall product's sustainability (Visotsky et al., 2017). Luz et al. (2018) have recently proposed a novel approach to integrate LCA into the product development process, which can enhance the strategic planning of activities.

3 Sustainable consumables for LoC

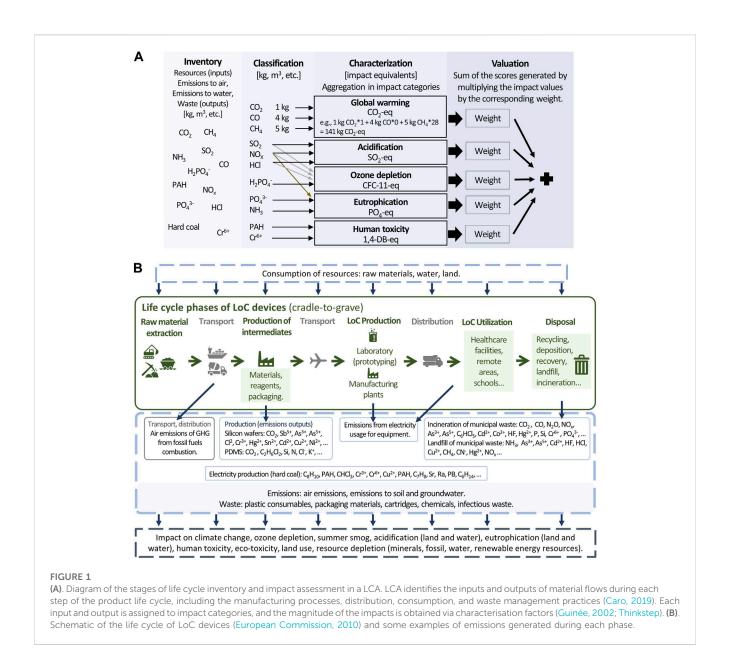
3.1 Current materials and possible alternatives

Following the advent of microelectronics in the 1960s, the first substrate used for fabrication of LoCs was silicon (Foret et al., 2013).

TABLE 1 Summary of environmental analysis tools, including environmental impact analysis (Wackernagel and Rees, 1996), carbon footprint analysis (ISO, 2018), carbon emissions reduction potential (Yang, 2010) and LCA (ISO, 2006a; 2006b). LCA offers a global view of the product's impacts on the natural environment, human health and resource depletion, and is the most powerful tool to support decision-makers (Luz et al., 2018; Torabi and Ahmadi, 2020).

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Environmental impact analysis (EIA)		
Scope and Purpose	Advantages	Disadvantages
Systematic assessment of the potential environmental, social and economic impacts of proposed projects, policies, or plans at a specific location EIA informs decision-makers, regulators, and stakeholders about the project's potential impacts to support the implementation of mitigation measures	Applicable to a variety of projects Can inform economic analysis	 Short assessment period is usually limited to the project's lifespan. Focused on a specific location. Project-oriented
Carbon footprint analysis		
Scope and Purpose	Advantages	Disadvantages
Measure of the amount of greenhouse gases (GHG) released directly and indirectly within the spatial and temporal boundary of the population, system, or activity of interest	Can be reduced to a single score	Focus only on impacts related to global warming and climate change (limited view)
This indicator can be used to compare the climate-relevant impacts of different individuals, products, companies, countries by distinguishing activities, and to identify the activities with a high and low footprint.*		
Carbon emissions reduction potential		
Scope and Purpose	Advantages	Disadvantages
Measure of the amount of GHG emissions that can be avoided or reduced by implementing a specific technology or practice	Can be reduced to a single score	Focus only on impacts related to global warming and climate change (limited view)
It can help identify areas where emissions can be reduced and provide a basis for setting targets for reducing emissions over a specific time-period.*		
Life cycle assessment (LCA)		
Scope and Purpose	Advantages	Disadvantages
Systematic analysis of the environmental impacts of a product, process, or system throughout the entire life cycle, from raw material extraction, to manufacturing, use and end-of-life. LCA can support decision-making and identify opportunities for improvement	Looks at the entire life cycle of a product or system Considers the long-term environmental and human impacts LCA considers a full variety of environmental impact categories Can inform economic analysis	 Time-consuming. Cannot be reduced to a single score. No single method

^{*}Emissions are expressed in carbon dioxide equivalent (CO₂-eq). Major GHG, include CO₂, CH₄, N₂O, SF₆, HFCs, PFCs, NF₃.



To circumvent the hazardous chemicals involved during fabrication and fulfil the high demand for low-cost devices, several polymers, including PDMS and poly (methyl methacrylate) (PMMA) have been used for their simple prototyping. Most commercially-available microfluidic devices are currently composed of these (and others) non-biodegradable plastics that have a large CO₂-eq footprints (Ongaro et al., 2022). In the past decade, a variety of sustainable alternatives have been proposed (Keçili and Hussain, 2021; Damiati et al., 2022; Ongaro et al., 2022), but more research on how designs could be modified to accommodate different material strategies should take place.

Bio-derived and biodegradable (B&B) polymers such as polylactide (PLA) (Bettinger and Borenstein, 2010; Wang et al., 2010; Ongaro et al., 2020; 2018), polyDL-lactic-co-glycolide (PLGA) (Domachuk et al., 2010), zein (maize proteins) (Hsiao and Luecha, 2011; Luecha et al., 2011), shellac (Lausecker et al., 2016), and silk fibroin (Bettinger et al., 2007), have been

successfully used both in biomedical and environmental applications. Other low-cost and biodegradable materials, such as paper and cotton, have been extensively used for detection of bioanalytes and pathogens (Agustini et al., 2021). Gelatin has also been used as a bio-based and biodegradable microfluidic platform in cell culture (Paguirigan and Beebe, 2006) and, most recently, as casing for lateral flow strips in a water-dispersible SARS-CoV-2 antigen test (Okos diagnostics, 2020). Interestingly, wood has been introduced in microfabrication processes, but some limitations around mechanical and chemical properties still need to be addressed (Ongaro et al., 2022).

3.2 Chemical and waste reduction

The impact of LoC does not simply arise from substrates, casing and cartridges. Greener options for solvents, like chloroform or

acetone, and reagents, should be used in the future (Keçili and Hussain, 2021; Agrawal et al., 2022; Ongaro et al., 2022). For chemical analysis, green solvents include ionic liquids, deep eutectic solvents, and supercritical fluids (Keçili and Hussain, 2021; Agrawal et al., 2022). Clinical diagnostic assays often require chaotropic reagents, highly toxic to humans and marine life, with specific, high CO₂-eq disposal procedures. Promising new methods have recently been introduced at a macroscale level in laboratory settings, e.g., by Merck (Merk), or integrated into microfluidic platforms for DNA extraction from *E. coli* or whole blood (Yoza et al., 2002; Nakagawa et al., 2005; Hagan et al., 2009).

A significant benefit of LoCs is the reduction in sample and reagents volumes, but also packaging material, compared to equivalent macroscale analytical processes. Importantly, LoCs allow automation, and it is critical to increase access to such capability so that researchers and users are able to harness benefits arising from increased reproducibility and lower number of analyses required in optimization processes (Keçili and Hussain, 2021).

4 Beyond consumables for LoC

4.1 Environmental considerations concerning bio-based and bioderived plastics, and fabrication methods

Using materials that are recycled or derived from biological sources for single-use LoCs can help to reduce CO2-eq emissions and plastic pollution at the point of use. However, material selection should also consider how the material is produced and disposed. For example, while B&B polymers, such as PLA, are praised substitutes for regular plastics, their production competes with food production, they require specific conditions for degradation, and generate methane gas during composting (Atiwesh et al., 2021). The same applies to cotton, whose crops are water-intensive and often use fertilizers with ecotoxicological effects (Naderi Mahdei et al., 2022). Consequently, not all the suggested alternatives are necessarily better for the environment than conventional plastics at all stages of their life cycle, Supplementary Materials (Walker and Rothman, 2020; Naser et al., 2021; Rosenboom et al., 2022). Moreover, fabrication processes, such as photolithography, laser printing, wax printing, hot embossing, and plasma oxidation (Ongaro et al., 2022; Sridhar et al., 2022), make use of chemicals and energy sources that contribute to the overall environmental impact of LoCs. For example, if gelatin represents a natural and biodegradable alternative to plastics, gelatin devices are often generated using photolithography (Paguirigan and Beebe, 2006), which uses chemicals that are toxic, carcinogenic, or derived from non-renewable sources (Mullen and Morris, 2021).

Substrates' impact during the whole life cycle should be part of the design process before integrating specific materials in LoCs. Nonetheless, this task is complex and, importantly, not integrated in the training of LoC scientists or in their collaborative networks. There is therefore a urgent need to

identify and compare the environmental hotspots of LoC substrates, and specific fabrication methodologies through LCA.

4.2 IT and digitalization

The integration of cloud computing and artificial intelligence potentiates LoC functionality, usability, and performance, particularly outside centralized laboratory facilities. For example, for healthcare applications, mobile technologies can support local decision making, offer guidelines for treatment, and accelerate the implementation of surveillance programs and global health policies (Fleming et al., 2021; Guo et al., 2021). Digitally connected LoCs can minimize the need for transportation, infrastructure, and logistics commonly associated with transporting individuals or specialized personnel (doctors, technicians) to centralized facilities (Ongaro et al., 2022). This potentially reduces the greenhouse gases emissions of LoC significantly. In the future, the advancement of wearable devices for continuous monitoring of biosignals will further reduce transport-related emissions.

Nevertheless, while mobile solutions are a key part of our emissions management strategy to achieve the United Nations Sustainable Development Goals (UN, 2015; Fleming et al., 2021), internet and digital tools have a significant environmental footprint, as they require precious/rare metals for production, consume large amounts of energy for the operation of data centers, and generate e-waste that is not properly recycled (UNEP, 2022). Therefore, the environmental impact of digital platforms, challenges around security, and the interoperability of data generated by LoC analysis should be key considerations. It is essential to encourage service providers, users, and policymakers to adopt more sustainable practices for their digital platforms.

4.3 Laboratory assessment frameworks

Research laboratories, where LoC devices are first conceived, are energy intensive and produce high levels of chemical and/or hazardous waste, when compared to regular office buildings (Lopez et al., 2017). This has prompted local actions and the creation of certification programs to incentivize greener practices, such as minimizing waste, optimizing energy use, choosing greener alternatives for reagents and consumables, and optimizing people management and research quality.

A recent report efficiently grouped all the sustainable initiatives that have been embraced by different research institutes (Winter et al., 2023), in an effort to increase awareness and education. Accreditation programs like LEAF and My Green Lab have boosted the implementation of these sustainable practices and created positive feedback loops and multiplying effects, that could reach also higher levels of society (Winter et al., 2023). Researchers should advocate institutional policies that support and incentivize sustainability, such as carbon budgeting, green procurement, and CO₂-eq offsetting.

5 Discussion

Miniaturized LoC technologies have several advantages compared to their macroscale counterparts, stretching from reducing the amounts of sample and toxic chemicals, to minimization of packaging materials and better controlled energy transfer. However, the Lancet Commission for Pollution and Health reported that as many as one in six deaths worldwide since 2015 have arisen from a contaminated environment (with more than 90% of these deaths in low- and middle-income countries, which have borne the greatest economic and social burden (Fuller et al., 2022)). If, as a community, we want to increase access to chemical analysis and diagnostics to promote efficiency and reduce mortality and morbidity/illness, then we need to commit to a holistic approach for the reduction of LoC environmental impacts. Advocating for policy changes could speed up the shift to a low-carbon economy by promoting environmental practices in companies, through incentives like subsidies, clear emissions reduction goals that companies must meet, and strong national waste management infrastructures. Promoting sustainable informed choices can be institutionally supported, as illustrated by the European Union digital "product passport" (CIRPASS, 2023) that will make available to businesses, governments and consumers the information on a product's origin, durability, composition, environmental and carbon footprint, reuse, repair and dismantling possibilities, and end-of-life handling.

The possibility of creating a circular economy to minimize raw materials use in LoCs is still a way away, but it would be a game-changer for waste management in the sector (Ongaro et al., 2022). As scientists, our mission includes preventing unnecessary deaths and creating a better planet, not just for ourselves but for future generations and for all creatures and life. To do this, we need to stimulate conversation and persist until sustainability becomes an integral attribute in the delivery of green products.

Author contributions

GC conceptualized and wrote the manuscript.

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Conflict of interest

The author declares that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/frlct.2023.1239134/full#supplementary-material

SUPPLEMENTARY MATERIAL S1

Examples of studies that compare different textile materials and plastics under different aspects, in terms of global warming potential impact category in kg CO_2 -equivalents.

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