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TRENDS

From research to market: correlation between publications, patent filings, and investments in development and production of technological innovations in biosensors

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Abstract

As the global population grows and science and technology development evolve, fulfilling basic human needs has been even more linked to technological solutions. In this review, we present an overview of the biosensor market and discuss the factors that make certain countries more competitive than others in terms of technology and innovation and how this is reflected in the trends in publication and patent filling. Additionally, we expose briefly how the COVID-19 pandemic acts as a catalyst for the integration of research and development, business, and innovation sectors to bring solutions and ideas that have been predicted as tendencies for the future.

Keywords Biosensors · Technological innovation · Biosensor research · Biosensor market · Biosensor development

Abbreviations

POC	Point-of-care
CAGR	Compound annual growth rate
USD	United States dollars
R&D	Research and development
ACAP	Application of the absorptive capacity
WIPO	World Intellectual Property Organization
PCT	Patent Cooperation Pact
EPO	European Patent Office
IPAustralia	Intellectual Property Australia
CIPO	Canadian Intellectual Property Office
CNIPA	China National Intellectual Property Administration
JPO	Japan Patent Office
KIPO	Korean Intellectual Property Office
DPMA	German Patent and Trademark Office
GDP	Gross domestic product
USPTO	United States Patent and Trademark Office
IPO	Intellectual property owners
IPONZ	Intellectual Property New Zealand
IPI	Intellectual Property India

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Introduction

Biosensing and bioelectronics devices act as one of the most important technological solutions already developed. Nowadays, it is possible to find biosensors with multiple applications in a wide range of areas such as point-of-care (POC) monitoring of treatment and disease progression, environmental monitoring, food and biohazard control, drug discovery, forensics, and biomedical research [1]. Among all of biosensing areas, biosensors dedicated to healthcare and medical analyses are one of the most promising fields for delivering marketable and accessible biosensors, with a commercial purpose and high expectation to fulfill human needs and demands [2].

The increasing wellness market over the years is also responsible for many of the emerging biosensing technologies and innovation. This market aims to fulfill the needs of a population (with or without a diagnosed pathology) who wants to prevent a variety of consequences of aging and improve its self-esteem through body-care [3]. Recently, a McKinsey and Company report showed that consumers define the "wellness market" across six different dimensions: better health, appearance, fitness and nutrition, mindfulness, and high-quality sleep [4]. For monitoring these well-being facets, global biosensing market have invested on wearable and self-powered biosensors [5] capable of connecting with telemedicine apps working through data-driven care, *just-in-time* diagnosis, and quick symptoms monitoring [4]. In this context, a study reported that total global wearable device revenues are expected to reach USD 73 billion by 2022, especially based on the Asia Pacific fast-growing rate [6]. These statistics include not only biosensors devices, but also hybrid watches, smartwatches, and other electronic technologies that can be integrated to the biosensing assay itself.

The global biosensing devices market, by its turn, is projected to reach USD 27.1 billion by 2022, and by 2028, it is anticipated to reach a range of USD 31.5 billion [7–9]. In 2019, the global biosensors market was valued at USD 19.6 billion, expanding at a compound annual growth rate (CAGR) of 7.9% during the forecast period. In comparison, in the same period, the global pharmaceutical manufacturing market was valued at USD 324.42 billion in 2019 and is expected to grow at a CAGR of 13.7% [10]. Furthermore, the global healthcare market reached nearly USD 8.45 trillion in 2018, with a CAGR of 7.3% since 2014. This is expected to grow to nearly USD 11.9 trillion with a CAGR of 8.9% by 2022 [11].

Although the biosensors field is correlated to the pharmaceutical market and healthcare market, why does not it share the same growth as the latter markets? Perhaps the biosensor industry has difficulty in converting knowledge and applying this to technology, that is, marketable products [12, 13]. Recently, COVID-19 pandemics outbreak seemed to worse innovation purposes. A McKinsey and Company report on the impact of COVID-19 in innovation, surveyed across more than 200 companies around the world, presented that innovation is not seem anymore as a high-level priority in different industry areas during COVID-19 crisis [14]. In Medical and Health industry, which presents the majority of biosensors production companies, only approximately 30% of executives considered innovation as priority after COVID-19 outbreak, in comparison to 60% of executives considering it in precrisis moments [14]. These metrics indicate that the conversion of academic or industrial knowledge into future marketable biosensing products may be affected in the next years.

In this context, this review aims to explore the academic research and applied technology by comparing the number of scientific publications versus patent filings. Additionally, we present a briefly overview of the integration of R&D, business, and innovation sectors to bring solutions for the COVID-19 pandemic and discuss the impact of science and technology investments that make certain countries more competitive than others in this field.

Technological innovations: publications biosensors versus biosensor patents

Since the 1970s, biosensors have attracted the interest of researchers from numerous areas, which is supported by the constant growth of scientific literature in this field, with over 150,000 articles, and numerous reviews, books, and chapters published, as can be seen in Fig. 1A. Between the 1990s and 2010, the USA was the country that published the most articles on the subject. However, because of the establishment of the *National Medium to Long-term Plan for the Development of Science and Technology* (2005–2020) [15] which represents an important milestone in China's scientific

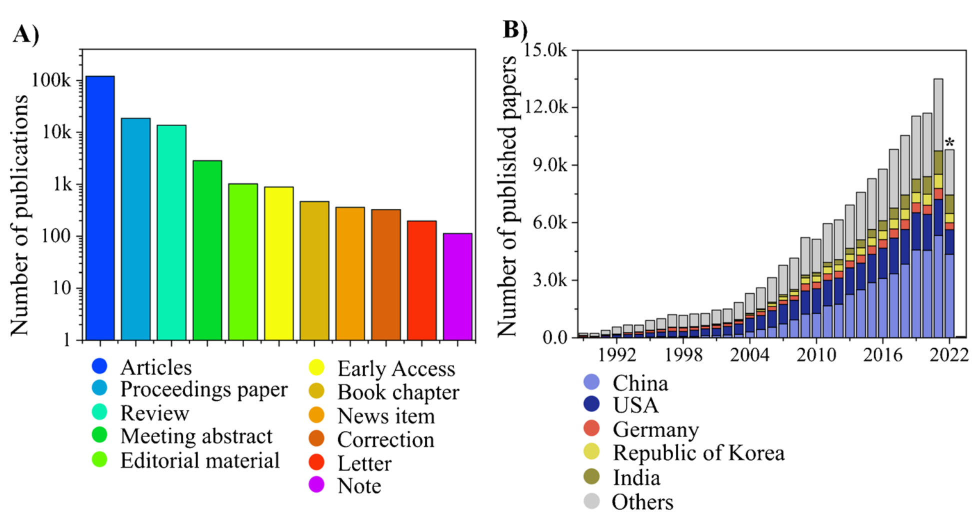

Fig. 1 **A** Types of publications found in the Web of Science for the term "biosensors" for the period from 1960 to 2022. **B** Progression of publications over the years involving biosensors to five countries that publish the most on this topic

modernization, over the last decade, the country has been leading the publication of articles on biosensors, widely surpassing countries such as the USA and Germany [16], as shown in Fig. 1B. In addition to the countries already mentioned, Korea and India are the remaining of the five main countries that publish on the subject (Web of Science database).

In turn, the number of patent applications has also been growing worldwide every year since 2004, with the sole exception of 2009 when growth decreased by 3.8% due to the financial crisis [17]. In 2018, the patent applications in all fields worldwide grew by 5.2%, representing 3.3 million patent applications. In the performed patent search in October 2022, we found around 132,056 patents in the field of biosensors had been registered at World Intellectual Property Organization (WIPO) (Fig. 2A). Of these, contrary to the trend observed in the search for scientific production, when it comes to intellectual property protection, the USA, represented by US Patent and Trademark Office (USPTO), continues to be the largest patent depositary in the biosensor field annually (55,023 patents). In second place is the Patent Cooperation Pact (PCT), which has 27,764 patents. The PCT, an agreement signed on June 19, 1970, in Washington, was created with the purpose of developing a system of patents and technology transfer to promote cooperation between industrialized and developing countries [18]. Nowadays, filing an international patent application under the PCT allows applicants to protect an invention in 153 countries simultaneously, including the largest biosensor markets in the world. Next is the European Patent Office (EPO), which protects 14,057 of patents on biosensors, followed by Intellectual Property Australia (IPAustralia, 9192) and the Canadian Intellectual Property Office (CIPO, 10,229). The China National Intellectual Property Administration (CNIPA, 4,927) showed the same trend observed in article publications, i.e., achieving some protagonism after the "National Medium to Long-term Plan for the Development of Science and Technology." The Indian Patent Office (IPI, 3,592), Japan Patent Office (JPO, 2,322), Korean Intellectual Property Office (KIPO, 1,739) (WIPO, 2022), and Intellectual Property Office of New Zealand (IPONZ, 594) finalized the ranking of the ten offices that most filed patents at WIPO up to October 2022. Germany, on the other hand, was one of the first countries to protect its intellectual property (along the USA). However, currently, it does not play a leading role in the biosensor patent scenario. Figure 2A shows the evolution of patents filed to biosensor field from 1970 to 2022 and Fig. 2B shows the patent percentages of the offices that most have registered documents at WIPO.

Concerning the registration of patents, the WIPO database makes it possible to evaluate the patent classification which depends on the type of innovation that is being protected, as shown in Table 1. With regard to the published articles, the advanced search of the *Web of Science* was used, and the words highlighted in Table 1 were inputted in the topic field together with the word "biosensor."

By analyzing the numbers of Table 1 in terms of subjects contemplated in the academic research and intellectual property protection, it can be seen that there is a relationship between the percentage of patents and published articles on biosensors in relation to fermentation processes (4.1% and 5.7%), diagnosis and identification (6.5% and 8.5%), and investigation and analysis (24.7% and 19.7%) of physical and chemical properties. Alternatively, articles involving the application of biosensors in the medical and dental fields comprised the least number of articles among the search results (3.4%), while the corresponding patents add up to 17.2% of the results found.

Based on the biosensor scenario presented, it is possible to analyze the relationship between research generated in academia and number of patents and technological transfer. The success of the innovation industry can be intricately linked to the effective technology transfer between the research and development (R&D) sectors, either in universities or industries, and the manufacturing sector. The ability of the industry to assimilate and apply the new knowledge originating from R&D allows the conception and/or maintenance of a competitive advantage. In addition, investing in research has a double effect: it develops new processes and product innovations and develops and expands the company's ability to identify, assimilate, and exploit the information available in the market [19]. In this sense, the application of the absorptive capacity (ACAP) concept is fundamental. Succinctly, ACAP is defined as the ability to

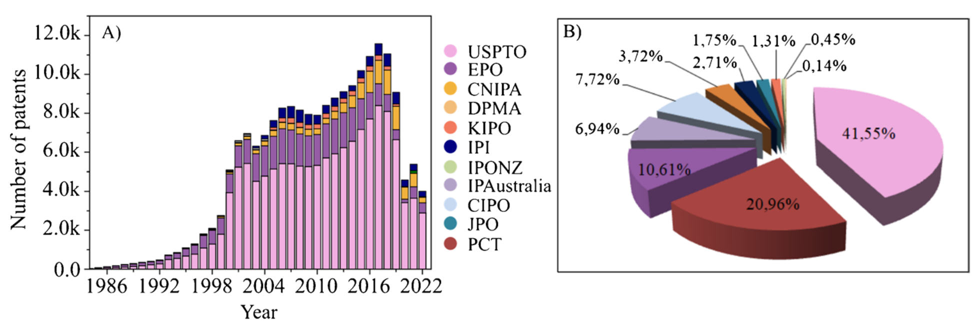

Fig. 2 **A** Evolution of patents filed to biosensor field all long the years in biosensor field and **B** patent percentages of the offices that most have registered documents at WIPO (search term: biosensor, from 1970 to 2022)

Table 1 International class of patent filed related to biosensors, from 1976 to October 2022 (WIPO database)

International class code	Patent applications (%)	Articles published in the topic (%)	Description
G01N	24.7	19.7	Investigating* or analyzing* materials by determining their chemical or physical properties
C07K	18.8	3.9	Peptides*
A61K	17.2	3.4	Preparations for medical*, dental*, or toilet purposes
C12N	11.4	21.8	Microorganisms* or enzymes*; compositions thereof; propagating, preserving, or maintaining microorganisms; mutation* or genetic engineering; culture media
C12Q	10.8	18.5	Measuring or testing processes involving enzymes*, nucleic acids*, or microorganisms
A61P	7.4	18.3	Specific therapeutic* activity of chemical compounds or medicinal* preparations
A61B	6.5	8.5	Diagnosis*; surgery*; identification
C12P	4.1	5.7	Fermentation* or enzyme-using processes to synthesize a desired chemical compound or composition or to separate* optical isomers from a racemic* mixture

*Keywords used in the advanced search field of *Web of Science* to compare patents and published papers

identify and to amass knowledge, by assimilating, internalizing, transforming, and applying it, resulting in the creation of valuable products and services for commercial purposes [20, 21].

To verify how the industry concentrates the knowledge generated in R&D, patents have become the standard measure for innovation in most fields [22]. However, there are those who argue that this is not the most appropriate method, especially because some patents are never commercialized, or some companies use patenting to prevent others from entering their field [23]. Nevertheless, the filing of patents is still a widely used indicator to assess the capacity for technological innovation [24]. Based on that, this indicator was chosen to discuss the innovations coming from university and private initiative in the present work.

In WIPO database, we perform a search using the terms “biosensor” and patent applicant (PA). As a result, it obtained a total of the 17% of patents with universities or institutes as applicants. The other results (83% of the total patents) were considered to be originated from private initiative. Analyzing individually each patent office was found the following percentages of patents considered academic: 17.2% from USPTO, 7.2% from JPO and IPI, 15.8% from CIPO, 14.6% from IPAustralia, 22.3% from PCT, and 0.3% from EPO. CNIPA and KIPO, patent offices from China and Republic of Korea, presented almost the same percentage of patents filed among academy (46.8% CNIPA and 44.2% KIPO) and private initiative (53.2% CNIPA and 55.8% KIPO). Figure 3 presents the percentages related to the search for patent academic and private initiative.

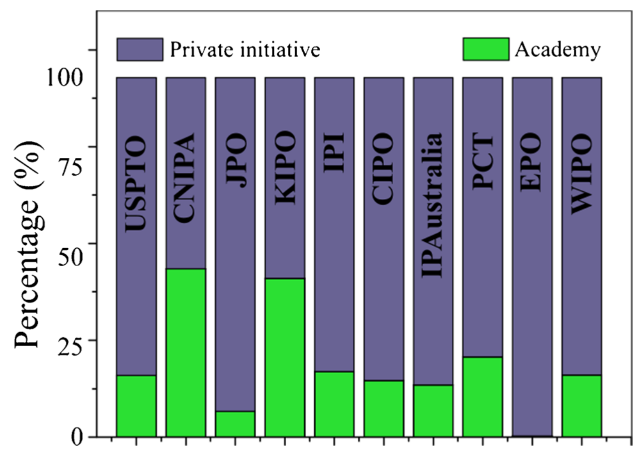

Fig. 3 Percentages related to patent academic and private initiative in WIPO database (search term: biosensor and PA (university or institute); October 2022)

In terms of technologic transfer, the numbers presented through search in WIPO database indicates that there is still a gap between the knowledge production carried out by the academy and its conversion into technological innovation (evaluated here in terms of the filing of patents involving biosensors). This discrepancy can be associated with the fact that not all research developed at universities will be converted into technological innovation, often because the knowledge generated is more focused on unknown phenomena or fundamental research. Another issue is the difficulty in the development of research involving these areas, such as aspects of the structure necessary for this type of research, as well as the stringent measures imposed by the ethics committees. Furthermore, it may be difficult for researchers in academic centers to contemplate and meet the needs of the market, with the appropriate speed to face the problem in question, partially due to its volatility, or even due to not being in direct contact with such demands, or because some of these research centers think that this is not the primary role of academia. Thus, it is imperative to establish effective communication between representatives of the private sector (aware of market demands) and leading researchers of groups in the area of biosensors (holders of know-how), so that the transfer of technology is carried out successfully, and the needs of the general population are met.

In contrast, the private initiative holds most of the patents filed at WIPO, because it is important for a company to have patented products in its portfolio to maintain its market share, its current net worth, its sale value when going public, and many other factors. Furthermore, companies use intellectual protection not only to protect the original idea, but also to protect newer versions of the same product, which ends up creating a family of patents. Therefore, this could compromise the idea of using patent numbers as an indicator of technology transfer. However, when performing a new search in WIPO using the term "biosensor" only with the "patent families" field checked, we found a total of 44,713 filed patents. The same search was performed using the term "biosensor and PA (university or institute)," obtaining the value of 9501 filed patents. From these numbers, we obtain the percentage of 21.2% of academic patents and 79.8% of patents from the private sector, values that are not very far from the percentage found for "single patents" (17.2% and 82.8%, respectively).

Therefore, based on the concept that technology transfer is a set of steps that describe the formal transfer of inventions resulting from scientific research conducted by the R&D sector (which include universities) to the productive sector [25], the indicators (quantity of patents) presented above demonstrate that, for the biosensors field, the technological flow is better consolidated in the private sector. In an ideal scenario, if technology acquisition came through transfer between academia and the private sector, it would allow companies to acquire new products, processes, or technology without the need to participate in the initial, expensive, and volatile stages of research and development [26], enabling the sharing of risks and costs with other institutions.

Science and applied technology as result of innovation investments

From 2013 to 2019, UNESCO (United Nations Educational, Scientific and Cultural Organization) has gathered statistical data regarding science, technology, and innovation investment patterns for more than 200 countries [27]. Data were organized either according to the percentage of gross domestic product (GDP) of the country that is allotted to R&D (research & development) or the total invested amount. The obtained trends found for the first 15 countries, in both scenarios, are shown in Table 2.

Generally, countries attempt to allot a fixed percentage of the total GDP to fund science, technology, and innovation, considering R&D as an important business sector of its national economy [27]. However, the GDP percentage allotted to this business sector (Table 2) is still low and dependent on a series of factors, such as working population size, the economic performance of each country in the global market, transparency and political issues, and unemployment rates [28]. Despite being dependent on these factors, there is a consensus in literature that R&D expenditure leads to long-term productivity growth for the country [29]. This is due to the direct correlation between science, technology, and innovation investments and the technological development and independence of countries. These relationships are

Table 2 Data on R&D funding of the 15 countries that have the highest investments in R&D according to UNESCO's statistical study conducted from 2013 to 2019 [27]

Country	Percentage of GDP allotted for R&D	Country	Total investment in R&D (USD, billions)
Republic of Korea	4.1%	USA	476
Japan	3.4%	China	346
Switzerland	3.2%	Japan	170
Austria	3.1%	Germany	110
Finland	3.1%	Republic of Korea	73
Sweden	3.1%	France	61
Denmark	2.9%	India	48
Germany	2.9%	UK	44
USA	2.7%	Brazil	41
Slovenia	2.4%	Russian Federation	40
Belgium	2.4%	Italy	29
France	2.3%	Canada	28
Australia	2.2%	Australia	23
Singapore	2.1%	Spain	19
Czechia	2.0%	Netherlands	16

supported by two main arguments: (i) the higher the R&D expenditure, the greater the technology transferred through science and innovation; and (ii) these expenditures directly affect the industrial innovation potential [29].

The investments of a country in science, technology, and innovation are reflected by the trends in its publication. According to a statistical study carried out by NSF (National Scientific Foundation) in 2018, the five countries that contributed the most to publications in science- and engineering-related academic articles and conference proceedings were 1st China; 2nd USA, 3rd India, 4th Germany, and 5th Japan [30, 31]. Interestingly, except for India, all these countries are part of the top five nations that have the biggest total investment in R&D reported in Table 2. Concerning research on biosensors, the top five in terms of activity in publishing articles under this field in scientific databases (Web of Science and PubMed) until 2020 were 1st China, 2nd USA, 3rd Germany, 4th South Korea, and 5th India. These countries were listed according to the first author's affiliation, considering the countries with 500 or more publications based on author's affiliation. This ranking is correlated to the total investment of the first five countries presented in Table 2 (under the R&D column), and this relationship is presented in Fig. 4. The Republic of Korea and UK were also added as they were ranked 5th in terms of total investment and biosensing publication rankings. Four out of the top five most active countries in biosensing literature are among the five countries with the highest investments in science and technology in general. Among them, China is one of the most prominent nations due to its rapid and remarkable economic and scientific growth [16], whereas the other countries have kept similar positions in the past years. The contributions made by the Republic of Korea are also significant and may be attributed to its massive investments in general education over the years [32]. These data are also consistent with the percentage of GDP allotted to the R&D business sector. Moreover, Republic of Korea has the largest ratio of researches per inhabitants, resulting from their recent policies on education and innovation [27]. For a more critical review of publication trends in biosensing according to other kinds of classifications, as well as publication counts for other countries, please see the Olson and Bae report [33].

The data shown above confirm what is already known in the research and innovation community: the higher the R&D expenditure, the greater its projection in the number of academic publications in a certain nation. Regarding biosensing technology, these trends are still valid. This is one of the most important factors that influence the innovation stats of a nation. Furthermore, the information from a research article shared with the scientific community, for example, can also be converted into an innovative commercial biosensor, depending on the stage of this research. In this context, a country with several academic biosensing publications has the potential to lead in terms of biosensor innovation globally, if other social and technological barriers are successfully surpassed with a short research-innovation conversion time.

COVID-19 pandemics: how has it influenced business, R&D, and innovation for biosensing market?

The COVID-19 pandemic outbreak in February of 2020 led to a worldwide public health crisis which evidenced different social and technological limitations and inequalities of society in this scope [34]. For example, we have seen the facility of access that developed communities had in relation

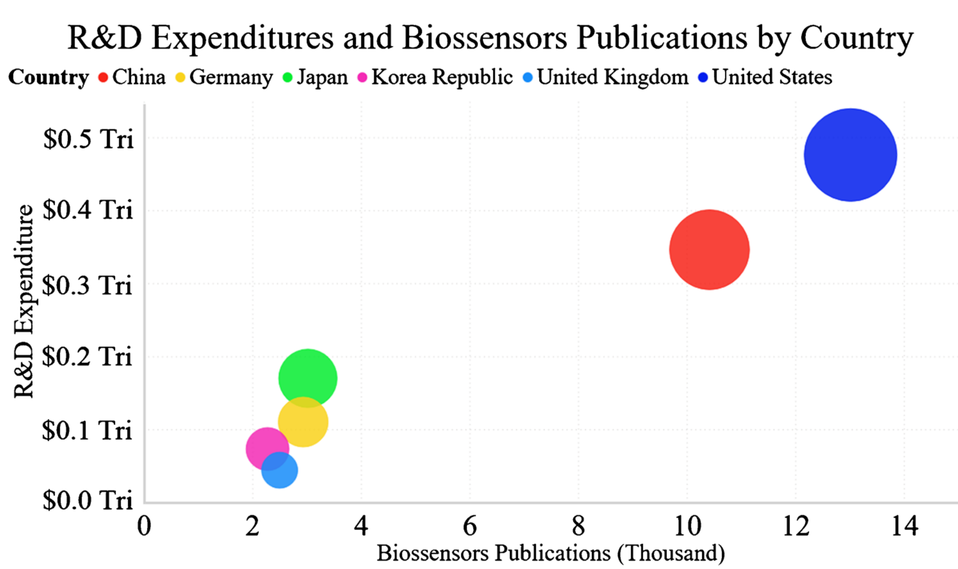

Fig. 4 R&D and biosensor publication trends for the top five most active countries in these fields. Data from the Republic of Korea were added as it is ranked 5th in terms of total R&D expenditure in billions of dollars. Circle sizes are proportional to the total R&D expenditures presented in Table 2

to vaccines and high-quality hospitals in contrast to the precarious conditions of public health systems and disorganized pandemic control strategies of emerging and non-developed countries.

Despite these social aspects, COVID-19 pandemics also brought challenges for R&D, business, and innovation, which directly or indirectly affected biosensing market (and others) and led to the need of further integration between these areas. In 2020, they were rapidly mobilized to provide solutions for pandemic control in order to fulfill a main human need with social, political, and economic implications: reducing social distancing. For this, science, technology, and innovation gained much attention from governments and worldwide organizations, and, as a result, billions of dollars were mobilized for researching solutions [35].

In this sense, innovation was considered one of the pillars for pandemic control and overcoming, as the demand for it remarkably increased. Despite the executives' pessimism toward innovation during pandemics previously discussed in the "Introduction" section [14], a variety of policies was adopted to ease some barriers frequently faced during innovation process, such as regulatory flexibilities, stimulation of collaborations between startups, industries and academic institutions, hackathons and competitions, and fast-track support [35]. According to an OECD report, the result of these efforts was reflected on the expressive rapidness of vaccine development. As of November 2020, approximately 10 months after pandemic outbreak, it was reported more than 200 vaccine candidates under development, according to WHO data [35]. Moreover, alternative COVID-19 treatments and diagnosis methodologies were also rapidly studied and proposed. As of April 2020, the WHO had more than 200 reports of it [35]. However, the impressive rapidness of innovation seen, especially during 2020, is also a reflection from integration with R&D institutions, which also faced some facilities that improved its performance, as knowledge diffusion through research made publicly available, extensive adoption of preprint publication, access to critical research infrastructure in some institutions, and others [35].

The success of R&D, business, and innovation integration was also reflected on the generation of new technologies and implementation of past knowledge into emerging solutions. Besides, in some cases, COVID-19 pandemic outbreak acts as a catalyst to solutions and ideas that have been forecasted as tendencies for the future. As an example, the rise of digital healthcare and telemedicine [36, 37] for patient self-care in a social isolation context has been predicted by several authors in literature since, at least, the 2010s, as a future trend for medical area [38]. On the other hand, viral screening in a population was adopted as one of the most important strategies for pandemic control, relying on mass-testing by employing rapid, easy-to-handle and accessible biosensors and POC assays [39], as lateral flow immunochromatographic devices (LFIDs). This sort of device has already been largely studied over the years [40], since its first conceptualizations in the 1960s [41], and a large number of patents have been deposited since then. Therefore, in this context, the successful integration of R&D efforts over the past years with LFID market knowledge was of great usefulness for guiding the rapid development of COVID-19 rapid lateral flow tests. Moreover, the swiftness of the conversion of research into marketable products seen in COVID-19 LFIDs can be attributed to the previous market and industry experience, as, for example, with pregnancy immunochromatographic rapid tests and other technologies based on the same working principles.

Concluding remarks

After analysis of the databases, it is possible to conclude that a country's investment in science, technology, and innovation is reflected by the trends in its publication. This was evidently seen when the top five countries in terms of activity in a publication related to biosensors were the same five countries which invested the most in science and technology. However, there is still some gap between scientific research and technological innovation which hinders the production of a commercially viable biosensor and its introduction into the market. This highlights the need for researchers to better understand consumer behavior and the importance of interactions between researchers from different fields (chemistry, biology, medicine, and engineering, for example) as well as between the academy and companies. Government and/or private financial investments remain essential to the development of translational research. An alliance of experts with different backgrounds and significant R&D investments will provide high-impact scientific production, which consequently leads to the filing of patents for new high-impact products in the market. However, the entire process of technological innovation is not simple and involves several steps. Furthermore, in light of the present review, there is a perception that a lack of well-established methodology in conjunction with ineffective communication between the involved parts, hinders, even more, the innovative technological transfer. Thus, the transfer of technological innovation between universities and the biosensors market is a field of research to be explored with the possibility of carrying out future studies.

Outlook

Studies have been conducted with the goal of developing biosensors in different fields of application. Many of these projects are deposited in important patent offices. In the other hand, only few patent projects became commercial products. This scenery tends to change with integralization of the sectors. In other words, by the technology transfer between academic areas (as engineering, chemistry, materials science, and computation) and industry. Countries that invest in multidisciplinary teams will be a step ahead when it comes to resolving technological barriers that often prevent the launch of new products. This makes them emerge as leaders in the main biosensor market segments. In addition, in the emergence of unexpected demands, as in the case of the COVID-19 pandemic, these research centers will be able to develop solutions to control the spread of disease through rapid diagnose using specific biosensors. Furthermore, there are other areas that need strategic attention, such as the segment of cancer biomarkers. Many researches are carried out and patents are filed; however, there are few commercial products. In such cases, there are problems that need to be solved, whether regulatory or technological, and once solved; the demands of a vast portion of the market can be met.

Author contribution Giovana Cagnani: Conceptualization; visualization; writing, original draft; writing, review and editing; formal analysis; investigation

Thiago Oliveira: Conceptualization; visualization; writing, original draft; writing, review and editing; formal analysis; investigation

Isabela Mattioli: Conceptualization; visualization; writing, original draft; writing, review and editing

Graziela Sedenho: Visualization; writing, original draft; formal analysis; investigation

Karla Castro: Writing, original draft; investigation

Frank Crespilho: Conceptualization; resources, supervision

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Declarations

Conflict of interest The authors declare no competing interests.

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