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Trends and Recent Patents on Cellulose-Based Biosensors †

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Abstract: Research on cellulose and its derivatives as biosensors is developing rapidly through the innovation and improvement of materials, chemical synthesis, and methods of preparation and formulation. This study presents the state of the art by introducing what has been innovated and patented concerning cellulose-based biosensors between 2010 and 2020. More specifically, this form of patent analysis encapsulates information that could be used as a reference by researchers in the fields of biosensors and cellulose-based biosensing platforms, as well as those interested especially in cellulose and its derivatives. As a result, a total of 241 patent documents related to cellulose-based biosensors were found. The United States leads the patent race in this sector. Based on patent classifications, most patents and inventions are intended for chemical analysis of biological materials and testing involving biospecific ligand binding methods, as well as measuring or testing apparatus with condition measuring or sensing means. Research and development are based on the investigating or analyzing of materials by the use of electric or electrochemical means, as well as nanotechnology for interacting, sensing, or actuating, which are concentrated in most patents.

Keywords: cellulose; biosensors; patents; innovation

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1. Introduction

Materials used for fabricating biomedical devices, such as implantable biosensors, need to possess appropriate physical, chemical, and biological properties, depending on specific circumstances [1]. Among a variety of materials commonly used as biosensing platforms, cellulose and its derivatives have gained considerable attention [2,3].

Cellulose and its derivatives exhibit biological appropriate properties which make them suitable for biomedical applications [4–6]. Due to its promising physical and biological characteristics as well as chemical structure, cellulose has been demonstrated to be a versatile material, affording a high-quality platform for accomplishing the immobilization process of biologically active molecules into biosensors [7]. Nevertheless, to promote the sufficiency of cellulose in biosensing, several researchers have investigated pathways to enhance cellulose properties to meet biosensing requirements [2,8].

The first patent application concerning cellulose-based biosensors was filed in 1987 and then granted in 1991 [9]. Through this patent, Godfrey has invented methods of producing polymer-coated surfaces suitable for use as optical structures. In particular, the inventor has proposed methods of producing surfaces suitable for use in biosensors in which one of a pair of binding partners is applied to the surface of a polymer-coated optical structure to form a device for detecting the presence of the complementary component in a sample subsequently brought into contact with the surface. A claimed method in this patent suggests that the polymer is cellulose nitrate [9].

Research on cellulose and its derivatives as biosensors is developing rapidly through the innovation and improvement of raw materials, chemical synthesis, and methods of

preparation and formulation, with more than 200 organizations around the world currently involved in patent activity and filings concerning cellulose-based biosensors. This trend is justified by the several advantages that cellulose offers for biosensing and biomedical applications. This is also evident from the elevation in the number of patent applications filed each year worldwide in research and development in this area [10].

This study, in the form of patent analysis, presents the state of the art by introducing what has been patented in relation to cellulose-based biosensors between 2010 and 2020. Furthermore, a detailed analysis of the patentability has been provided by determining publication years, classifications, inventors, applicants, owners, and jurisdictions. Finally, this work, which gives an analysis of the past, present, and future trends, lead, to various recommendations that could help one to plan and innovate a research strategy.

2. Methods

2.1. Resources and Research Methods

The supported field codes used in this study were based on the Patentscope search service of the World Intellectual Property Organization (WIPO) [10,11] and The Lens patent data set [12]. During the search, different keywords and related terms were used, and patents were searched according to title, abstract, and claims. The search was then filtered to include only patent documents with a publication date between 1 January 2010 and 31 December 2020.

2.2. Analysis of the Patentability of Cellulose-Based Biosensors

After the search, 241 patent documents were found. Generally, it encompasses patent applications and granted patents. In relation to cellulose-based biosensors, the found patent documents are classified as 204 patent applications and 37 granted patents. The detailed list of these patent documents is presented in Table S1 (Supplementary Materials).

Hereinafter, the state of the art will be reviewed by introducing what has been patented concerning cellulose-based biosensors. A detailed analysis of the patentability will be provided with emphasis on the used cellulose and its derivatives, testing involving biospecific ligand binding methods, and interacting, sensing, or actuating, following the publication year, patent classifications, inventors, applicants, owners, and jurisdictions.

3. Results and Discussion

3.1. Publication Year

A patent publication is the step when the patent document (i.e., patent application, granted patent, etc.) is made available to the public, to which a publication number and a publication date have been assigned by a patent authority. In other words, the date on which a patent document is published, thereby making it part of the state-of-the-art [13].

Concerning cellulose-based biosensors, 241 patent documents have been found between 2010 and 2020. The results encompass 204 patent applications and 37 granted patents. In the year 2010, we registered five patent documents. In contrast, the year 2020 recorded 34 patent documents. The maximum number of granted patents (8) was recorded in 2018. Furthermore, the year 2020 was the year with the maximum patent applications or patent documents, with 27 and 34, respectively (Figure 1).

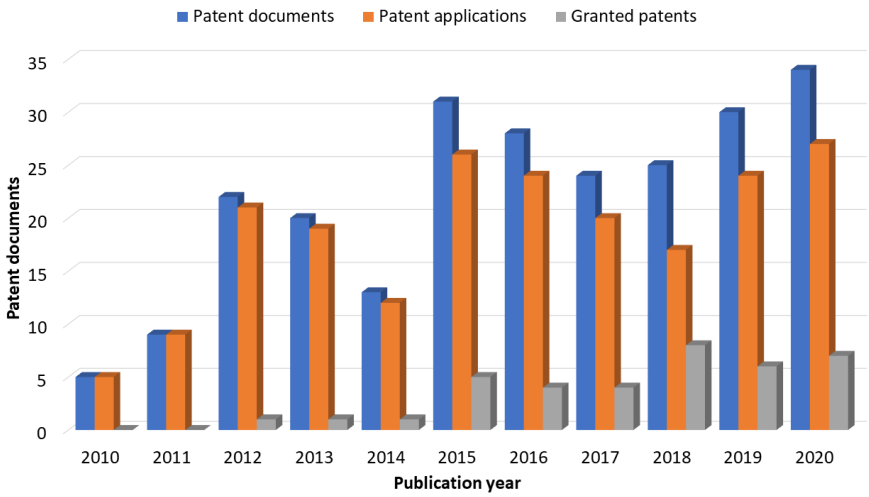

Figure 1. Evolution of patent documents (i.e., patent applications and granted patents) as a function of the published date of cellulose-based biosensors between 2010 and 2020.

3.2. Patent Classifications

The International Patent Classification (IPC) is a hierarchical system in the form of codes, which divides all technology areas into a range of sections, classes, subclasses, groups, and subgroups. It is an international classification system that provides standard information to categorize inventions and evaluate their technological uniqueness [14,15].

Concerning cellulose-based biosensors, the top 10 IPC codes between 2010 and 2020 are presented in Figure 2. The most IPC code corresponds to G01N27/327, which is a subgroup of investigating or analyzing materials by the use of electric or electrochemical means, such as biochemical electrodes. This subgroup recorded, alone, 60 patent documents. The second IPC code corresponds to C12Q1/00, which is a group of measuring or testing processes involving enzymes, nucleic acids, or microorganisms. It concerns measuring or testing apparatus with condition-measuring or sensing means. This group has recorded 45 patent documents. For more details concerning these top 10, a description of each IPC code is shown in Table 1.

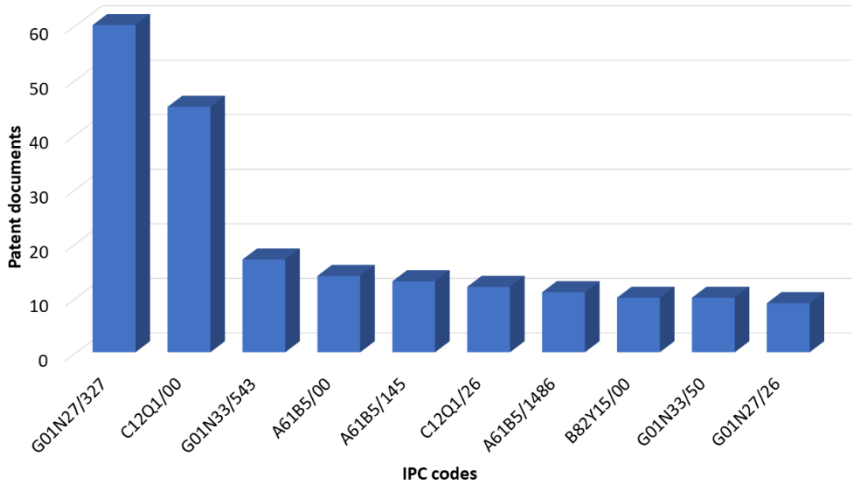

Figure 2. IPC codes (top 10) of the resulted patents as a function of patent documents of cellulose-based biosensors between 2010 and 2020.

Table 1. Meaning of IPC codes concerning the resultant patents of cellulose-based biosensors [14].

IPC Codes	Description
G01N27/327	Investigating or analyzing materials by the use of electric or electrochemical means, such as biochemical electrodes.
C12Q1/00	Measuring or testing processes involving enzymes, nucleic acids or microorganisms (measuring or testing apparatus with condition-measuring or sensing means).
G01N33/543	Immunoassay and biospecific binding assay with an insoluble carrier for immobilizing immunochemicals.
A61B5/00	Measuring for diagnostic purposes.
A61B5/145	Measuring characteristics of blood in vivo (e.g., gas concentration, pH-value, etc.).
C12Q1/26	Measuring or testing processes involving oxidoreductase.
A61B5/1486	Measuring characteristics of blood in vivo by using enzyme electrodes (e.g., with immobilized oxidase).
B82Y15/00	Nanotechnology for interacting, sensing or actuating.
G01N33/50	Chemical analysis of biological material (e.g., blood, urine, etc.); Testing involving biospecific ligand binding methods; Immunological testing.
G01N27/26	Investigating or analyzing materials by the use of electric or electrochemical means by investigating electrochemical variables or by using electrolysis or electrophoresis.

3.3. Inventors

An inventor is a natural person designated for a patent application. In several cases, the inventor can also be the applicant, and in some cases, there may be more than one inventor per patent application [13].

Concerning cellulose-based biosensors, the top 10 inventors between 2010 and 2020 are presented in Figure 3. Jung Sung-Kwon from the Republic of Korea is ranked as the first inventor who has recorded 15 patent documents. The inventors, Cha Geun Sig and Nam Hakhyun, from the Republic of Korea, tied for second place with 11 patent documents each.

All found patent documents by these three above inventors concern the healthcare companies i-Sens Inc. (Seoul, Republic of Korea) and Osang Healthcare Co. Ltd. (Dongan-gu Anyang, Republic of Korea) as applicants and/or owners (Figures 4 and 5). i-Sens Inc. is a healthcare company that develops, produces, and distributes medical devices. The company's main products include blood glucose monitoring systems, electrolyte and gas analyzers, and immunosensors [16]. However, Osang Healthcare Co., Ltd. is a healthcare company that manufactures and distributes medical supplies. The company produces diagnostic biosensors for blood glucose measurements, cholesterol-measuring devices, and other related products [17].

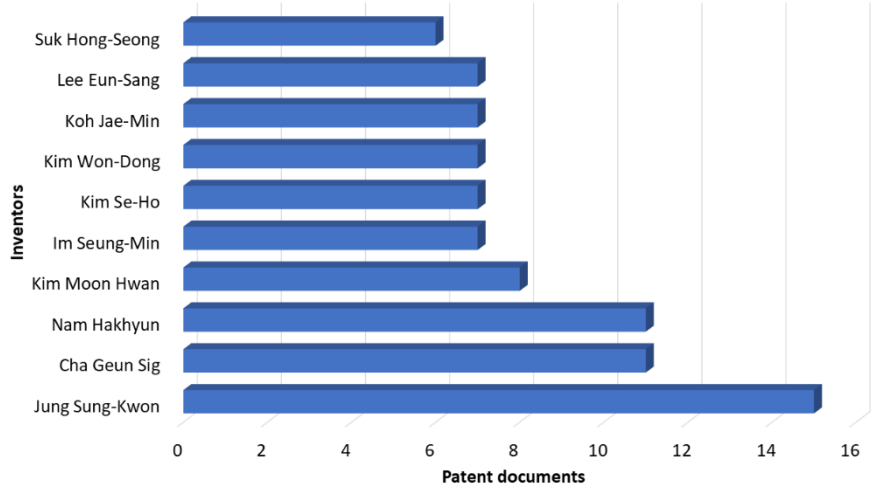

Figure 3. Inventors (top 10) of the resulted patents as a function of patent documents of cellulose-based biosensors between 2010 and 2020.

3.4. Applicants

In the case of a patent application, an applicant is a person (i.e., a natural person) or an organization (i.e., a legal entity) that has filed a patent application. In several cases, the applicant can also be the inventor, and there may be more than one applicant per patent application [13].

Concerning cellulose-based biosensors, the top 10 applicants between 2010 and 2020 are presented in Figure 4. Regarding this top 10, all applicants are considered as people or organizations (companies and universities). As a legal entity, the healthcare company i-Sens Inc. (Seoul, Republic of Korea) is ranked as the first applicant that has recorded 9 patent documents.

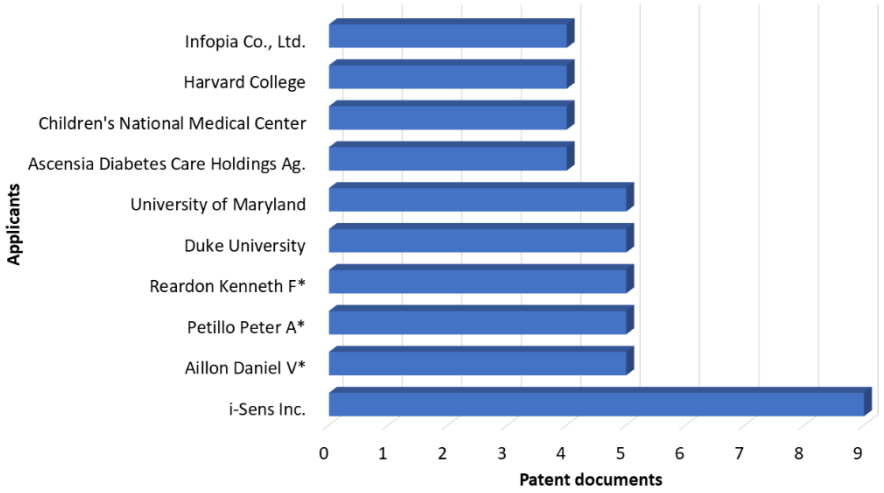

Figure 4. Applicants (top 10) of the resulted patents as a function of patent documents of cellulose-based biosensors between 2010 and 2020. *The applicant is a natural person.

3.5. Owners

An assignee, or patent owner, is a person (i.e., a natural person) or an organization (i.e., a legal entity) to whom the inventor or applicant assigned the right to a patent. The patent owner has the right, for a period limited to the duration of the patent term, to pro-

tect his brainchild. The patent system stops others from making, using, or selling the invention without his permission, or requires others to use the invention under agreed terms with the inventor [18,19].

Concerning cellulose-based biosensors, the top 10 owners between 2010 and 2020 are presented in Figure 5. The healthcare companies Ascensia Diabetes Care Holdings Ag. (Basel, Switzerland) and Bayer Healthcare Llc. (Emeryville, CA, United States), as legal entities, are ranked as the first owners who have recorded 6 patent documents each.

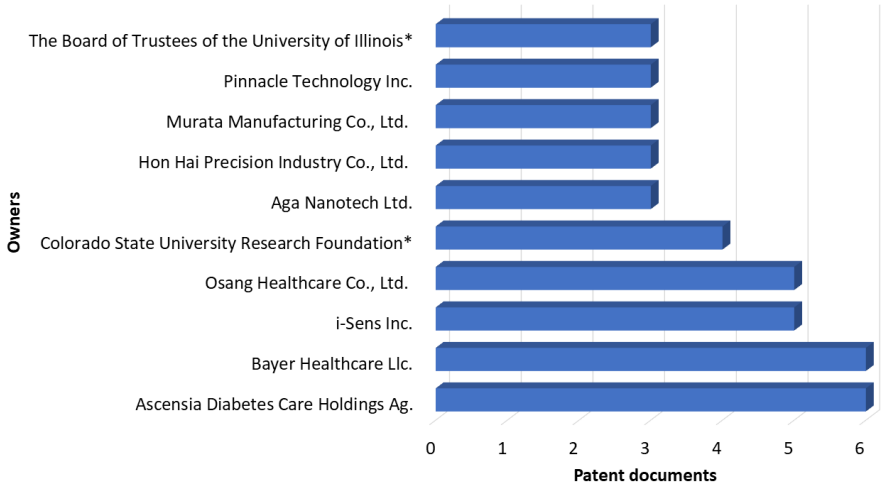

Figure 5. Owners (top 10) of the resulted patents as a function of patent documents of cellulose-based biosensors between 2010 and 2020. *The owner is a foundation or a governing body.

3.6. Jurisdictions

An applicant, or the first mentioned applicant in the case of joint applicants, can file an application for a patent at the appropriate patent office under whose jurisdiction he normally resides, has his domicile, has a place of business, or the place from where the invention actually originated. Furthermore, related patent applications could be filed in multiple jurisdictions by applicants seeking to protect their inventions in multiple jurisdictions [20,21].

Concerning cellulose-based biosensors, the top 10 jurisdictions between 2010 and 2020 are presented in Figure 6. The United States through the USPTO (United States Patent and Trademark Office) encompasses 110 patent documents with a higher patent contribution per total of ~46%. On the other hand, the global system for filing patent applications, known as the Patent Cooperation Treaty (PCT) and administered by WIPO, encompasses 73 patent documents with a patent contribution per total of ~30%, as well as China, through the CNIPA (China National Intellectual Property Administration), encompasses 27 patent documents with a patent contribution per total of ~11%. Finally, the EPO (European Patent Office), through which patent applications are filed regionally (Europe), encompasses 23 patent documents with a patent contribution per total of ~10%.

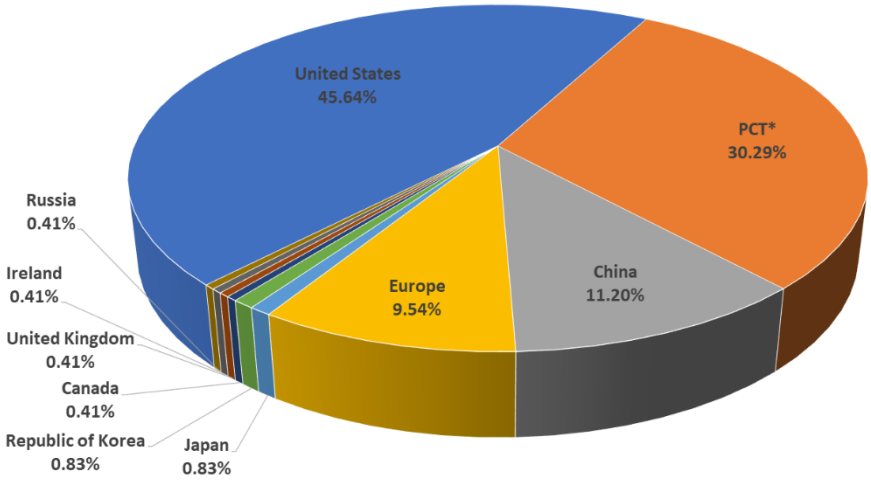

Figure 6. Patent contribution (%) as a function of jurisdiction of filed patent applications and granted patents of cellulose-based biosensors between 2010 and 2020. *The global system for filing patent applications, known as the Patent Cooperation Treaty (PCT) and administered by WIPO.

4. Selection of Relevant Patents

Cellulose-based biosensors are a technological innovation in the field of nanotechnology for sensing and analyzing by the use of electrochemical means. These cellulose-based biosensors are developing rapidly through the improvement of materials, chemical synthesis, and methods of preparation and formulation.

Table 2 presents examples of innovation and utilization of cellulose-based biosensors as demonstrated by inventions and patents. To clarify the real status of such patents in this area, the ones described herein are the most relevant patents focused on cellulose-based biosensors between 2010 and 2020. The choice of these selected patent documents is based on the most prolific countries patenting on cellulose-based biosensors as well as the patenting levels (national, regional, and international). However, the detailed list of all patent documents is presented in Table S1 (Supplementary Materials).

In 2010, Baker et al. invented a novel sensor mechanism based on the aggregation of nanoparticles for target molecule detection and quantification. The signal-enhanced biosensor system according to this patent was made with a substrate that was selected from a group consisting of, among other things, a cellulose substrate or a nitrocellulose substrate [22].

In 2012, Kim invented a disposable biosensor made of tin oxide-cellulose nanocomposite. The invented biosensor was biodegradable, biocompatible, and flexible. It was obtained by coating tin oxide on the surface of a regenerated cellulose film and fixing the biochemical receptor (e.g., glucose oxidase, glutaminase, asparaginase, penicillinase, nitrate reductase, etc.) by a conventional method, such as encapsulation, covalent binding, crosslinking, and adsorption [23].

In 2013, Wilsey invented a method for determining the concentration of glucose in a blood sample by using sample volumes of less than a microliter and test times within about eight seconds of the application of the sample. The invention is related to an electrochemical sensor comprising an array of micro-electrodes disposed on a flexible substrate. The sensor includes a chemical coating made up of a binder and contains a set of chemicals (e.g., methylcellulose, hydroxyethylcellulose, carboxymethylcellulose, microcrystalline cellulose, etc.) that react to produce an electroactive reaction product [24].

In 2015, Jeon et al. invented a reagent composition for a biosensor having high sensitivity, which is capable of improving analysis linearity and detecting the concentration of a small amount of the analyte such as glucose by reacting with an oxidoreductase. The invented biosensor reagent composition according to patent claims encompasses, among

others, a water-soluble polymer such as hydroxyethyl cellulose, hydroxypropyl cellulose, carboxy methyl cellulose, and cellulose acetate [25].

In 2018, Agarwal et al. invented a biosensor for detecting the presence of a target analyte in a sample. Disclosed in the patent is a biosensor device for the real-time detection of a target analyte that includes a receptor component operatively connected to a transducer component which is adapted to interpret and transmit a detectable signal. The claimed biosensor uses a sensing element that comprises a polymer and was selected from a group consisting of, among others, carboxymethyl cellulose and derivatives [26].

In 2020, Pu et al. invented a flexible skin electrochemical biosensor based on a conductive cellulose-based hydrogel. The newly invented biosensor comprised a reference electrode, a counter electrode, a working electrode, and a signal wire, which were arranged on the conductive hydrogel film substrate layer. The formulation of the conductive hydrogel film substrate layer comprises mixing a zwitterionic polymer monomer, a nanocellulose solution, a thermal initiator, and a crosslinking agent. The working electrode was used for measuring biomolecules, and the signal wire was connected to external equipment. The invention improved the requirements for target molecule detection performance and wearing comfort [27].

Table 2. Selection of relevant patents for cellulose-based biosensors between 2010 and 2020.

Patent	Publication	Title	References
WO 2010/124270 A1 Application No: 2010032329	2010-10-28	Functionalized polymer biosensor	[22]
KR 20120050359 A Application No: 20100111810	2012-05-18	Disposable biosensors made with tin oxide-cellulose nanocomposite, manufacturing method of the same and measuring method using the same	[23]
US 8,349,168 B2 Application No: 201213433779	2013-01-08	Determination of blood glucose in a small volume and in a short test time using a chemical coating including binders and very short read potentials	[24]
EP 2,821,497 A2 Application No: 14175390	2015-01-07	Reagent composition for biosensor and biosensor having the same	[25]
US 2018/0271423 A1 Application No: 201615764627	2018-09-27	A biosensor device to detect target analytes in situ, in vivo, and/or in real time, and methods of making and using the same	[26]
CN 111,839,532 A Application No: 202010675959	2020-10-30	Flexible epidermal electrochemical biosensor based on conductive hydrogel	[27]

5. Conclusions

This study provided patentability and patent analysis of cellulose-based biosensors. The detailed analysis concerned the period between 2010 and 2020. The publication year of 2020 was the year with the highest patent registration, with 34 patent documents. Moreover, the United States was ranked first with 110 patent documents. Based on the IPC codes, all filed patents concerned chemical analysis of biological materials and testing involving biospecific ligand binding methods, as well as measuring or testing apparatus with condition measuring or sensing means. In addition, this study demonstrated that the

inventions included in the patents concern cellulose formulation and the process for preparing it, as well as devices and apparatus for manufacturing cellulose-based biosensors. The knowledge clusters and expert driving factors of this patent analysis indicate that the research and development are based on the investigating or analyzing of materials by the use of electric or electrochemical means, as well as nanotechnology for interacting, sensing, or actuating, which are concentrated in most patents.

Supplementary Materials: The following supporting information can be downloaded at: www.mdpi.com/xxx/s1, Table S1: Detailed list of all patent documents of cellulose-based biosensors between 2010 and 2020.

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Conflicts of Interest: The author declares that the content of this article has no conflict of interest. The author has no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in this article.

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