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A perspective on a white biotechnology under development: biomachining

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ABSTRACT

Biotechnology advances are traditionally associated with the biological and biohealth sectors, but these innovations have also been decisive in areas such as the mitigation of the environmental impact of industrial activities. As an example, biomachining is an alternative to the sustainable engraving of metal pieces, using microorganisms in the process, but it has yet to be implemented at industrial scale. This study focuses on the assessment and future consideration of biomachining among businesses and prospective professionals in industry. A preliminary opinion survey was conducted on the degree of acceptance of this bioprocess, with the field of application being assessed. The biomachining process was considered sustainable by the respondents, although the answers revealed a degree of apprehension about the bioprocess when the intervention of live microorganisms was mentioned. The misgivings concerning biological risk and the difficulty in automating the process are drawbacks to be overcome before its industrial implementation. The machining of metal pieces in the jewellery and craft sectors is not feasible because the materials currently required are not biomachinable. Nevertheless, biomachining can play a significant role in the future manufacture of microfluidic chips that have emerging applications in many sectors.

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INTRODUCTION

Biotechnology is a multidisciplinary and technological science that involves numerous branches and disciplines (biology, biochemistry, genetics, virology, agronomy, chemical engineering, mining, information technology and veterinary, among others). Bearing in mind the difficulty of establishing its application boundaries, there is no single definition of biotechnology. In general terms, all the possible definitions refer to the use of living microorganisms or compounds obtained from them, with the ultimate goal of achieving valuable products for improving people's quality of life; that is, to serve and benefit humanity. In a broad sense, it involves a group of innovations that use microorganisms and biological processes for producing goods and services and for conducting research activities [1-3].

After the Second World War, biotechnology acquired enormous relevance and significance with such crucial discoveries as those involving DNA. Many recent discoveries (cloning, monoclonal antibodies, sequencing of the human genome...) have unlimited implications and applications, although the research interest of the scientific community (and particularly funding organizations) has focused on three ambitious projects that cover the following objectives: the production of medicines through the use of recombinant microorganisms, the overcoming of genetic diseases through the treatment of faulty DNA in patients and the living systems developed and designed to perform a desirable function.

Biotechnology's rapid progress in many fields is poised to change the world over the coming decades, and there is a prevailing atmosphere of great expectation around it. Although one feature of this evolution is the intensive use of scientific knowledge, biotechnological innovations are appearing in the productive sector, while new discoveries are mainly being developed in research institutions and universities [4]. Interestingly, one of the most important steps in the innovation process is knowledge generation and/or acquisition, which implies research and development (R&D). It is worth mentioning that R&D is not synonymous with innovation, as the transformation of an invention or new knowledge into a useful product, technique or service to be commercialized is not always feasible [5, 6].

Research and innovation in biotechnology have played a decisive role in mitigating the environmental impact of industrial activities. Thus, living microorganisms have been used in air, solid and wastewater treatment and the biodegradation of environmental pollutants, and new biofuels have been promoted to reduce global dependence on fossil fuels [7-10].

As far as scientific and industrial applications are concerned, biotechnological tools are being increasingly used in countless processes. This diversity has prompted the need to categorize its uses into groups with common features or final uses. Thus, biotechnology can be broken down into subdisciplines according to a colour code (red, white, gray, green...) [11-14]. Nevertheless, large sectors of society seem unaware of the broad field of biotechnological applications available today.

White key technologies

White or industrial biotechnology involves industrial processes for synthesizing chemicals, or for producing and manufacturing consumer goods with biotechnological tools. Those sustainable tools are vital for mitigating the environmental impact of industry while maintaining high efficiency and applicability. Nevertheless, recent biotechnological applications are so challenging, profitable and appealing for developed countries that many mature industrial sectors are being encouraged to adapt their productive systems accordingly. In fact, the European Commission included biotechnology within Key Enabling Technologies (KETs) [15]. KETs are a group of six technologies that have applications in multiple industries and help tackle social challenges. They are knowledge-intensive and associated with high R&D intensity, rapid innovation cycles, high capital expenditure and highly skilled employment. It is worth mentioning that the collaboration between industry and universities and research institutions is crucial for overcoming the difficulties in translating the research results into a profitable business. In fact, although KETs are among the priority action lines of European industrial policy, one of their major weaknesses lies in the difficulty of translating their knowledge base into marketable goods and services. This innovation gap has been identified as the European 'Valley of Death'. European scientists are among the world's leading researchers, but Europe has lost ground to the rest of the world when it comes to putting ideas into practice [16, 17].

Many conventional or mature industrial sectors dealing with the manufacture of plastics, shoes, clothes, chemicals, food, detergents, fuels... include biotechnological tools in their productive chains, although they are not classified as biotechnological companies. The use of those innovations can differentiate between companies in the same sector and, additionally, the environmental benefit is a valuable asset in current industrial policy, as many industries focus their efforts not only on improving productivity but also on complying with environmental regulations (while also promoting an eco-efficient and eco-friendly image). Those companies are in a position to develop new products and patentable innovations while improving quality and productivity.

Biomachining of metal pieces: Innovation processes

The metal industry has been forced to search for technological alternatives that allow processing metal pieces in a more sustainable manner. Biotechnological tools help to mitigate the environmental impact of the machining industry and reduce the consumption of energy and chemicals [18, 19]. Although the technology related to machining has undergone far-reaching changes in recent years, improvement still plays an important role through the application of new innovations and the optimization of processes based on new knowledge.

The biotechnological alternative to be analyzed in this study is called biomachining and involves the use of microorganisms within the process of machining metal pieces. The microorganisms' role is to continuously bio-regenerate the oxidizing agent (Fe^{3+}) responsible for the chemical dissolution of the metal (Equations 1 and 2). Theoretically, the oxidant is never depleted and machining continues as long as the microbial performance is maintained. Consequently, the oxidizing agent does not have to be supplied by chemical addition, with the consequent economic and environmental advantages. One of the drawbacks is that the process is slower than the chemical one [20].

Chemical process for machining copper pieces

$$Cu^{o}\,(s) + 2\,Fe^{3+}\,(ac) \rightarrow Cu^{2+}\,(ac) + 2Fe^{2+}\,(ac) \qquad \text{(Eq. 1)}$$

$$Fe^{2+}\,(ac) + O_2\,(g) + 4H^{+}\,(ac) \rightarrow Fe^{3+}\,(ac) + 2H_2O\,(ac)$$

Biochemical regeneration of the oxidant Fe^{3+} (Eq. 2)

Based on the successful performance of biomachining at lab scale, it may compete with other processes in the near future, although intensive further research is required before it can be launched onto the market. In fact, innovation is related not only to innovation performance but also to financial and marketing performance [21].

This work focuses on the assessment and future outlook of biomachining among entrepreneurs and future professionals in industry. This alternative is a combination of chemical and biological processes for machining metal pieces. It has not been implemented in industry so far because it still requires R&D to guarantee its performance, and it is relatively unknown. A preliminary opinion survey was conducted on the degree of acceptance of this bioprocess that uses microorganisms as a biotechnological tool. The future field of application was also assessed. The interviewees' population was a group of university students and staff with a technical profile.

METHODOLOGY

Bearing in mind this work's objective and the "science and technology" driving force for biomachining, a consistent three-step methodology was used:

1. Opinion survey on the implementation of a biological process at productive/industrial level. A questionnaire was administered with multiple-choice items.
2. Formulation of the biomachining concept map. The concept map was created as a visual tool or diagram that depicted relationships between key concepts. It helped to organize and analyse all the process's inputs and stakeholders.
3. Company selection. This step focused on analyzing the market by selecting possible competitors or business niches.

It is worth mentioning that these steps are not consecutive, and the results attained in each one can be used as feedback for the others.

Biomachining relies on the ability microorganisms have to regenerate the oxidizing agent responsible for metal dissolution. Nevertheless, and bearing in mind the possible misgivings and hazards involved in the use of bacteria in this type of innovation, a preliminary opinion survey among a technical population was conducted within the first step of this methodology. The study involved staff and students in various engineering degrees at the University of the Basque Country (UPV/EHU) (Spain) and the Fachhochschule Dortmund University of Applied Sciences and Arts (Germany). A total of 127 interviewees took part in the study in February and April 2017-2018. The variables related to the different educational systems and industry markets in both countries were taken into account for processing the results and reaching the conclusions.

As a sustainable and cyclic process, biomachining is clearly an emerging biotechnology, but the public reluctance to accept biological hazards and other misgivings and misunderstandings can be major obstacles for successfully adopting bio-innovations in industry. Therefore, the initial perception of the bioprocess among technical staff and future engineers can be decisive for successfully introducing the future technology to businesses, stakeholders and managers.

The main information to be collected in the questionnaire was related to the following items:

- Personal opinion or misgivings on the use of a biotechnology outside the bio-health discipline.
- Personal assessment of the use of biomachining at industrial scale.
- Level of proactive attitude when making a decision about selecting a biotechnological alternative.

A total of 127 questionnaires were completed.

Each item was developed in three structured question blocks that were carefully drafted to avoid misunderstanding. In the first group, the respondents were asked to classify any machining process in which microorganisms play a significant role, and other related questions. The second group of questions focused on measuring the level of knowledge on the biomachining process, operating problems, drawbacks and advantages that could be predicted at real scale. Thus, the respondents were asked to rank the following advantages: compliance with environmental legislation, reduction in the consumption of chemicals, feasible treatment of wastes, low requirements for specialized personnel and savings in the overall cost of the process.

Finally, two specific questions were included in the third group. The first one asked the respondents to choose between a conventional technology and a more innovative and creative alternative, assuming the same efficiency in both cases. In the last question, the interviewees were asked to propose a commercial name for launching the biomechanical process in a professional and business environment.

RESULTS AND DISCUSSION

The results of the survey show that 58.1% of the respondents rated any process involving microorganisms as ecological. Regarding the selection of a label (adjective) for the bioprocess, the adjective "sustainable" was chosen by 37.3% of those interviewed, who preferred this description to other ones such as "competitive", "affordable", and "appealing" (Figure 1).

As far as the disadvantages of biomachining are concerned, there is a proven reluctance to make a decision about the extensive use of bacteria as a supporting bio-tool. As expected, the threat of a biological hazard and the difficulty in automating the process (selected by 46.6% and 25.4% of the respondents, respectively) were highlighted as possible drawbacks for its industrial implementation.

As far as the second group of questions is concerned, it is worth mentioning that only 87.4% of the population (111) completed the whole item, assigning a numerical priority to each advantage. The priority scale was from 1 to 5, but three score groups were established; 1 or 2 points out of 5 for very high and high priority, respectively, 3 points out of 5 for a neutral or undefined opinion, and 4 or 5 points out of 5 for low and very low priority, respectively (Table 1).

The advantage related to the reduction in the use of chemicals was classified as a major priority by 70 interviewees (63%). Compliance with environmental legislation and the viable treatment

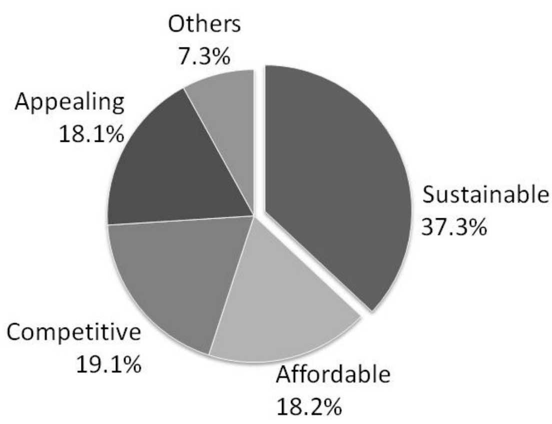

Figure 1. Labels for the biomachining process.

Table 1. Priority score on the advantages of biomachining (n = 111).

Advantage of biomachining over the conventional process	Number of answers according to the priority scale (percentage)		
	1 + 2 High	3 Undefined	4 + 5 Low
Reduction in the use of chemicals	70 (63%)	21 (19%)	20 (18%)
Compliance with environmental legislation	54 (49%)	28 (25%)	29 (26%)
Reduction in the process cost	38 (34%)	21 (19%)	52 (47%)
Viable treatment of wastes	45 (40%)	34 (30%)	34 (30%)
Low requirements for personnel training	17 (15%)	7 (6%)	87 (79%)

of wastes were also scored 1 or 2 by 49% and 40% of the respondents, respectively. Conversely, a majority of the interviewees (79%) stated that the low requirement for personnel training was not a relevant advantage of the bioprocess. Surprisingly, the process cost did not seem to be crucial for 52 respondents out of 111 (47%). In sum, the sustainable factor (reduction in chemicals and waste treatment) and legal compliance were particularly highly valued.

The last part of the questionnaire was devoted to the proposal of a commercial name for the bioprocess, and as many as 65% of the interviewees did their best to provide a creative name. Some of the proposals coincided, others were appealing, and others were not enthusiastic. As an example, some of them were Ferrobacter, Bactomec, Mecabacter, Bacteriomachining, Biomachining, Cobim, Bioetching, CopperTech or Ecomachining. The first four names referred to the particular use of bacteria for machining metal pieces, as they included the word “bacto”, “bacter” or similar. Other names such as Biomachining, Ecomachining and Bioetching included a reference to the sustainable or biological nature of the process in which bacteria played a relevant role, and the reduction in chemical use is noteworthy. The last name proposed, Bioetching, caught our attention as it jointly highlighted the biological aspect and the engraving process.

Bearing in mind that the respondents at both universities were students with a technical (engineering) profile or university staff with no particular training in biological processes, the results were very similar in the two groups, which revealed that their different nationalities, teaching systems or industrial development did not constitute a distinguishing factor. All the respondents appeared open-minded to innovations and their opinions did not differ according to nationality.

The biomachining process was considered sustainable by the majority of the respondents, who also proposed the adjectives “feasible”, “appealing”, and “competitive”. Nevertheless, the answers revealed a degree of apprehension over the bioprocess when the intervention of live microorganisms was mentioned. The concern about biological hazard was also pointed out, which will have to be taken into account when launching the process onto the market. As expected, the threat of biological hazard and the difficulty in automating the process are possible drawbacks for its industrial implementation. The collaboration between businesses and researchers will be decisive for overcoming the second disadvantage, although future research is required.

As far as advantages are concerned, a high value was given to the reduction in the consumption of chemicals, and compliance with environmental regulations that are becoming increasingly more restrictive. In fact, compliance with environmental regulations and the viable treatment of wastes were flagged as the other main advantages, highlighting the sustainable features of bioprocesses.

As a result of today’s rapid pace of progress, technologies are continuously being substituted or improved, but an innovation is accepted only if it means a significant improvement in a product or service with a profitable result. In this study, the population's average age was between 21 and 39 and, accordingly, they were expected to be open-minded and receptive toward new technological challenges. Nevertheless, they were cautious when making a decision about a technology substitution, as half the respondents preferred a conventional (but sustainable) option.

The search for a commercial name for the bioprocess rendered a combination of two words; one referred to the microorganisms and the other one to the mechanical application (Bactomec, biomachining etc). Although none of the proposals was accepted as-is, the final name selected for future marketing was also composed of two words: eco, referring to its sustainable nature and the word etching, referring to the mechanical action for creating pieces by selective metal removal: Ecoetching.

The concept map of biomachining

The successful performance of biomachining at production and marketing level involves three main steps that can be summarized as knowledge generation and/or acquisition, preparation for production, and preparation for marketing. Nevertheless, the innovation process can start with any one of the three steps, and they may record numerous interactions until the innovation process has been completed. There is a circular interaction among the three steps [22].

Knowledge generation and/or acquisition (innovation block) involves R&D. Although biological processes are set to become part of future industrial procedures for sustainable development, the biomachining process has yet to be developed and implemented in continuous industrial production, as only small-scale studies have been reported in the literature [23-26]. As an example, Figure 2 shows the overall design of a new biomachining pilot plant for the continuous production of etched microparts. The bioreactor consists of several consecutive adiabatic vessels, with temperature, redox potential and pH control being ensured by remote-controlled electrodes. A sulfuric acid solution for pH adjustment is fed automatically in response to a signal from the pH electrode. Another additional two solutions (sodium chloride and hydrogen peroxide) are required for waste liquid treatment. Continuous mixing systems are assembled in all the vessels. An electronic arm is programmed for immersing the parts in the active vessels, and biomass regeneration periods (stand-by periods) are optimized.

Regarding the preparation for production (target sectors and competitors' block), industrial processes in which biomachining can play a role

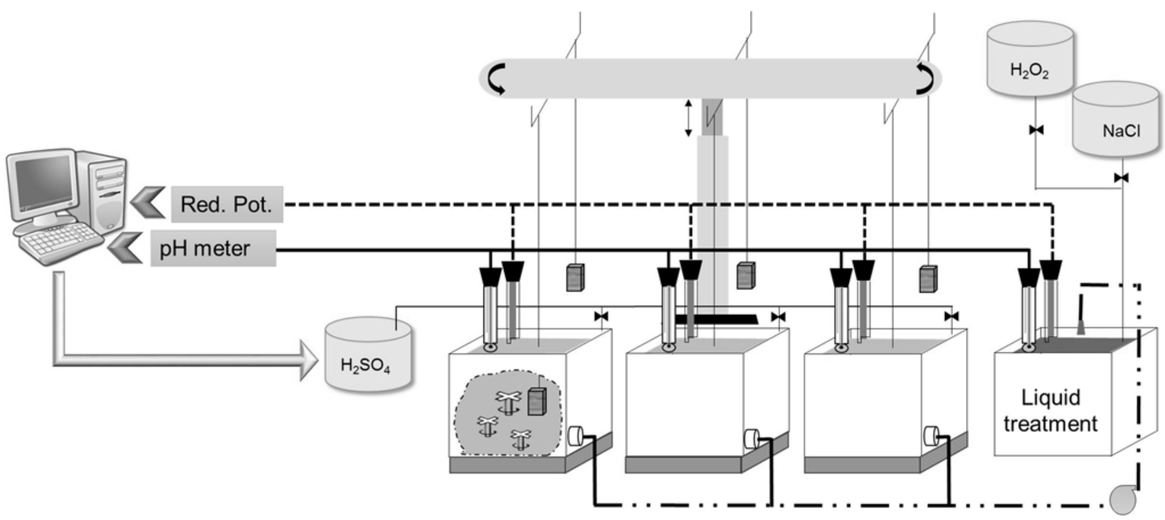

Figure 2. Layout of the preliminary design of a biomachining pilot plant.

(target market) and competitors (conventional or alternative processes) should be carefully assessed. Thus, the collaboration between businesses and researchers is crucial for developing and producing a competitive product (process).

Regarding the preparation for marketing, it is worth mentioning that marketing is based on thinking about the business in terms of customer demands and their satisfaction. Biomachining is the result of technological research conducted by corporate R&D activities and, consequently, in this case a ‘‘science and technology push’’ is responsible for the marketing [21].

With a view to connecting the three steps in the biomachining innovation process, a concept map was created (Figure 3). Thus, this visual illustration depicting the concepts and relationships among the different steps around the innovation process is composed of four blocks, because the preparation for production step has been divided into two blocks: one block devoted to the processes in competition with biomachining and the other one devoted to the production market.

Company selection and future market

The final part of this study has focused on contacting companies working with metal machining or etching, particularly on copper pieces. The first step was to look for local companies in the Basque Country (Spain) involved in artistic etching (one of the target sectors on the concept map of biomachining in Figure 3; jewellery, watch making, and craft working, among others).

A total of 16 registered companies were visited and interviewed, and information about their etching process type, market demand for copper etched pieces, sales market and preliminary assessment of the biomachining to be integrated into the enterprise was kindly provided. The names of the companies are confidential. Among these companies, only seven used chemical machining.

The first conclusions reveal that as far as the materials for artistic etching are concerned (plates for the automobile sector and domestic electrical appliances, memorial events...), steel and aluminium are the most popular ones (98% and 90% of the companies used them, respectively). Copper-etched

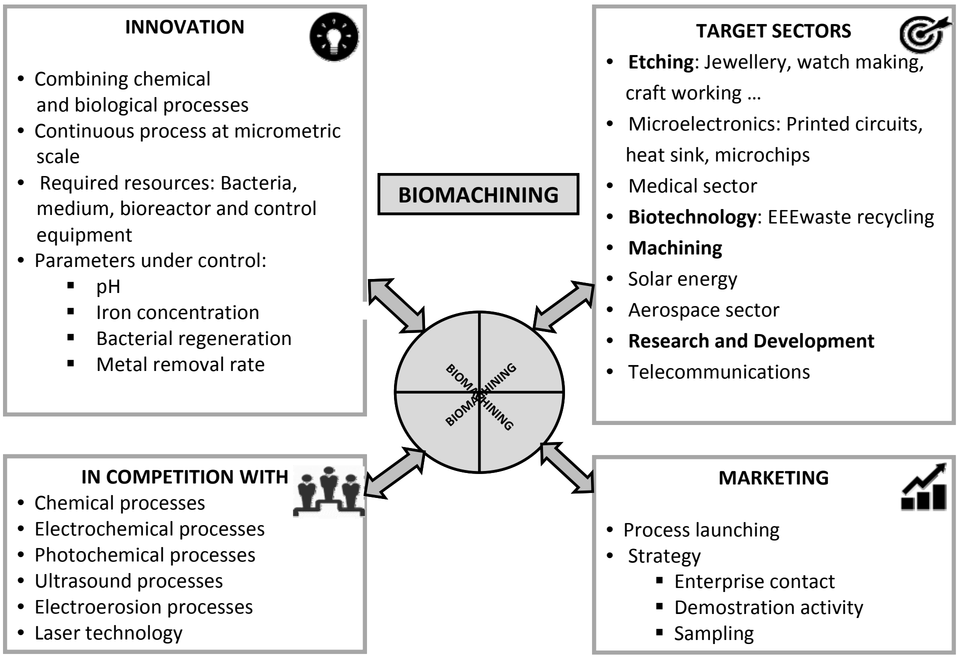

Figure 3. Concept map of biomachining.

pieces have been largely replaced by these materials or even by plastics such as polycarbonates, polyesters or vinyl. Copper is now only used for certain specific and unique jobs with a very small and occasional sales market.

There are two main reasons for this: the price of copper is considerably higher than that of other materials (as an example, the prices of copper and aluminium on the London Metal Exchange (LME) on 28 December 2018 were 5,990 US$/tonne and 1,898 US$/tonne respectively), and last but not least, chemical etching is being replaced by laser etching, as in terms of small volume production or prototyping, laser machining can be more cost-effective than chemical etching. Nevertheless, according to the company managers interviewed, the quality of chemically machined pieces may be higher than laser etched ones, and bigger pieces can be treated simultaneously (depending on the vessel or tank volume). Chemical treatment can be more affordable only when the volume of production is high, although biomachinable metals such as copper still have a very low demand for etching purposes. Unfortunately, common materials in etching such as steel and aluminium cannot be engraved using the biological process.

On the basis of these results, another sector for biomachining application was sought. Microfluidics appeared to be a promising target sector. Microfluidics is both the science that studies the behaviour of fluids through micro-channels, and the technology for manufacturing microminiaturized devices containing chambers and tunnels through which fluids flow or are confined. The fluid inside the channels is moved by a pump at a rate ranging from 1 μL/minute to 10,000 μL/minute, and chemical or physical reactions can occur inside. Thus, this miniaturized device integrates onto a single chip one or several analytical processes that are traditionally carried out in a laboratory [27]. They have new and innovative applications in biomedical diagnostics, environmental analysis, chemistry, sports science, biology and medicine, although their market launch still depends on overcoming certain limitations [28-30].

The chips are usually transparent and their length or width ranges from 1 cm to 10 cm. Their thickness ranges from about 0.5 mm to 5 mm, and they are usually made of polymeric materials such as polydimethylsiloxane [31, 32]. When the manufacturing of a negative molding is needed for device fabrication, the microchannels network is generated as the negative of the structures engraved in the mold. The mold can be fabricated using different protocols, for instance, using a photo-curable resin and a mask that must be manufactured each time the channel pattern changes. This manufacturing process requires a comprehensive equipment, which is not available in most laboratories.

The biomachining process can replace this equipment, as the channels in the negative cast can be etched onto a thin copper surface immersed into an oxidant medium that is regenerated by microorganisms. Suwandi *et al*. [33] have combined a modified conventional photolithography method and biomachining, by applying a maskless process. The profiles were created by computers, and then directly transmitted to the material that had previously been coated with a photoresistant resin through a Digital-Light Processing projector. They combined maskless photolithography and biomachining to create gears, letters, and printed circuit-board tracks, and thus showcase this new method's applications, which could be used for manufacturing the negative mold for the chips [18]. This maskless method overcomes the cost and timesaving issues of the conventional method, although it is at an early stage.

The applications of microfluidic chips composed of biosensors and actuators are emerging in many sectors, and biomachining can play a significant role in their future manufacturing. Although further intensive technological and market research is required, biomachining as a complementary tool for the manufacture of microfluidic chips could be a sustainable alternative.

CONCLUSIONS

The biotechnological tools applied to industrial production are not as popular as the advances in biohealth. As far as the machining of metal pieces is concerned, the substitution of certain conventional methods by microorganism-assisted processes such as biomachining is undergoing research and development, although the use of bacteria to extract metals from their respective ores (biomining) has its roots in antiquity.

According to the information collected from a survey involving respondents with a technical profile in Spain and Germany, the sustainable nature of biomachining was highlighted by the majority of the interviewees (it is a valuable issue in current industrial policy), but there is a proven reluctance to make a decision about the extensive use of bacteria as a supporting bio-tool, which is attributed to the threat of biological hazard and other limitations of the bioprocess. Regarding the future market, biomachining can contribute to the sustainable manufacturing of microfluidic chips that is an emerging sector with numerous potential applications.

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CONFLICT OF INTEREST STATEMENT

The authors declare that they have no conflict of interest.

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