Patent protection and licensing in microfluidics

Ali K. Yetisen* and Lisa R. Volpatti* 

Microfluidic devices offer control over low-volume samples in order to achieve high-throughput analysis, and reduce turnaround time and costs. Their efficient commercialisation has implications for biomedical sciences, veterinary medicine, environmental monitoring and industrial applications. In particular, market diffusion of microfluidic laboratory and point-of-care diagnostic devices can contribute to the improvement of global health. In their commercialisation, consultancy and patent protection are essential elements that complement academic publishing. The awareness of knowledge transfer strategies can help academics to create value for their research. The aim of this article is to provide a guidance to (1) overview the terminology in patent law, (2) elucidate the process of filing a patent in the US, EU, Japan and internationally, (3) discuss strategies to licence a patent, and (4) explain tactics to defend a patent in a potential infringement. Awareness of the patent law and rights allows obtaining optimised, valid and valuable patents, while accelerating implementation to market route. Striking a balance between academic publishing, consultancy to industry and patent protection can increase commercial potential, enhance economic growth and create social impact.

Introduction

The global microfluidics market was valued at $1.59 billion in 2013 and is expected to reach $3.57 billion by 2018 and $8.64 billion by 2023. The segments primarily responsible for this growth are in vitro diagnostics, lab analytics, and drug delivery devices. The largest share of the market is currently in point-of-care (POC) diagnostics, which accounted for $257 million in sales in 2013 and is projected to reach $762 million in 2018. However, the drug delivery device segment is expected to grow at the highest CAGR with recent advancements in pharmacy-on-a-chip technologies. While their added value in POC diagnostic devices is based on miniaturisation, multiplex assays, low volumes of consumables and disposability, they also offer automation and high-throughput processing in pharmaceutical research applications. The largest market is the US, which represented 46.9% of worldwide sales in 2012. Major players in the field include F. Hoffmann-La Roche, Abbott Laboratories, Illumina, Inc., Danaher Corporation, Caliper Life Sciences, Agilent Technologies, Life Technologies, Fluidigm Corporation, Bio-Rad Laboratories, RainDance Technologies, Inc., Gyros AB and Cepheid, Inc.

Despite the abundance of research in microfluidic technologies and their obvious capabilities, few products have reached their full commercial potential. Understanding knowledge transfer strategies can maximise the benefits gained from an innovation or invention, and enable researchers to transfer their technologies from the lab to the market efficiently (Fig. 1). An important pillar of commercialisation is the protection of intellectual property (IP). University and public research patents are more frequently cited than patents held by corporations in the US, Germany, France and Japan, suggesting that knowledge may diffuse more rapidly from academic patents than industrial patents. Conversely, patenting in academia may limit the diffusion of knowledge due to exclusive licencing agreements or the high-cost of licencing fees. In transferring knowledge from academia to the industry and public, it is important for scientists and engineers to find a satisfactory compromise between academic publishing, consulting to industrial partners and protection of intellectual property to increase the social impact of their research.

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*Department of Chemical Engineering and Biotechnology, University of Cambridge, Tennis Court Road, Cambridge, CB2 1QT, UK. E-mail: ay283@cam.ac.uk; Tel: +44 (0)1223 334160

Department of Chemistry, University of Cambridge, Lensfield Road, Cambridge CB2 1EW, UK. E-mail: lv279@cam.ac.uk
Microfluidic devices in academia and industry

Journal articles on microfluidic or lab-on-a-chip (LOC) devices increased significantly between 1988 and 1990.14 The field rapidly expanded with ~600 publications in 2003 and ~3000 in 2013 (Fig. 2). Since many of these devices held potential commercial applications, there was a corresponding rise in patent protection. The first microfluidic patent application was published in 1991, with an increase to 410 patents published in 2003 and over 550 in 2013.15 The decrease in the number of patents after 2011 may have resulted from a decrease in investors’ confidence due to the limited number of products that have successfully infiltrated the market. The entities (main applicants) with the highest number of patents include Samsung, Philips, Caliper Life Sciences, the University of California, Fluidigm, and Caltech, indicating that both academia and industry play roles in the commercialisation of microfluidic devices.16

As a result of both industrial and academic research, a number of companies were created based on microfluidic platforms. One of the pioneers in the field, Caliper Life Sciences (now a PerkinElmer corporation) was founded in 1995.17 Caliper commercialised several microfluidic devices for applications such as diagnostics,18 and determining molecular interactions,20 diffusivity and molecular weight.21 Another leader in the field, Fluidigm® was spun out of research in the laboratory of Stephen Quake, then at Caltech, in 1999.22 Quake and colleagues developed a pneumatic valve that has served as the basis of Fluidigm®’s integrated fluidic circuit (IFC) technology, which was used to produce the first commercial digital PCR.24 Fluidigm® currently markets their BioMark™ HD System, an instrument with associated software that has a range of analytical capabilities, including protein expression, gene expression and digital PCR. Another company, BioRad has developed and commercialised a droplet digital PCR system that consists of two instruments: a generator to partition the PCR reagent mixture into nanoliter droplets and a reader to analyse the droplets after PCR has been performed on a separate thermal cycler. In addition to next generation sequencing and gene expression, BioRad’s QX200™ Droplet Digital™ PCR can also be used for applications such as environmental monitoring and testing of genetically modified organisms (GMOs). Microfluidic products have also been commercialised in POC diagnostics. For example, Abbott Laboratories markets the i-STAT® System, a handheld device that employs single-use cartridges to perform blood chemistry. Specifically, this instrument can quantify the concentrations of electrolytes, metabolites, gases, and cardiac markers in a blood sample.

Patenting a microfluidic device

The protection of IP, such as inventions, confidential information, artistic expressions, brands, designs, and images, allows innovation to flourish by providing benefits to both the inventor and the general public. IP can be protected by a trade secret or through intellectual property law in various ways, for example by a trademark, a copyright, or a patent – an exclusive right granted for a novel, useful invention.26 The concept of the patent system is based on the theory of economic incentives, providing motivation to spend resources on R&D and the marketing of inventions.27,28 However, whether patent laws actually stimulate R&D and invention remains the subject of debate. Generally, a correlation exists between strong patent laws and R&D spending; countries with stronger patent laws tend to have increased R&D funding.29 It is possible that increased R&D spending causes stronger patent laws through industry lobbying, however, leading to a loop of causality and endogeneity.29 Based on the contract or disclosure theory, the inventor provides full disclosure of the invention to the public, while the government grants exclusive rights to the inventor.30 This right enables the inventor to exclude others from making, using, or selling the patented invention for up to 20 years after the filing date.

The inventors are the original contributors to the conception of at least one of the claims of a patent application. In the case of joint inventorship, each of the inventors has full rights, meaning that each of the patent owners can make, use or sell the invention without accounting to the other inventors. While some inventors maintain the rights to the patent, it is common in academic settings for the researcher to assign their rights to the university. In 1980, the United States passed a landmark legislation, the Bayh–Dole Act, which granted recipients of federal R&D funds the right to patent inventions and licence them to firms.31 This incentive allowed the universities to set up licencing offices and contract with companies that can commercialise the inventions and make them available for the public. If the patent is issued for an innovative incremental step to an existing invention,
however, then the patent owner does not necessarily have the right to make, use or sell the product. For example, consider the situation in which a first inventor holds a patent on a pioneering invention such as a PCR chip. A second inventor is then issued a patent on an improvement of the pioneering invention, an increased performance of the PCR chip. In this case, the first inventor can stop the second inventor from making, using or selling devices containing the original PCR chip. In turn, the second inventor can stop the first inventor from making, using or selling devices containing the improved PCR chip. Due to the overlapping inventions, neither of the inventors can make, use or sell the improved PCR chip. As a result, one inventor may choose to licence, cross-licence, or sell the patent to the other.

Determining patentability

Before filing a patent application, the applicant needs to determine if the invention is patentable. In the US, inventions must be useful and contain an element of novelty that would not be obvious to a person reasonably skilled in the art. In addition, “theoretical” inventions that have never actually been created are still patentable. To file a patent in the European Patent Office (EPO), the invention must be new, contain an inventive step, and be “susceptible of industrial application.” Japanese patent law formally defines an invention as “the highly advanced creation of technical ideas by which a law of nature is utilized.” To verify whether an invention is novel, a patentability search of academic literature and existing and pending patents must be conducted, which allows the inventor to identify past inventive concepts and deduce the potential availability of the scope of the present invention. Searches of these patents can be conducted through patent search engines, using keywords and classifications. In the US Patent and Trademark Office (USPTO), microfluidic devices fall under class 422 for chemical apparatuses, subclass 502, and are defined broadly as apparatuses that are used for “precisely controlling and manipulating a liquid or gas which is constrained to a small, typically sub-microliter scale.” In PATENTSCOPE, most patents for microfluidic devices fall under the international classification B01L 3/00, pertaining to “containers or dishes for laboratory use.” After identifying the appropriate classification, keywords can be used to search relevant issued patents and published patent applications. Secondary search tools include inventor assignee searches and iterative citation searches. An iterative search process involves (i) searching the keywords in the abstracts of the issued patents, (ii) noting the classifications of the most relevant issued patents, (iii) reviewing the class definitions of the three most relevant classes or subclasses, (iv) identifying the references to important patents and subsequent patents that cite the relevant patent, and (v) searching the issued patents by the same inventor or company.

At this stage, the inventor should also determine the potential commercial success by evaluating whether the invention is likely to acquire a patent and generate revenue. Issues such as patenting costs, production costs, competitors and demand for the product should be considered. The inventor should also research the potential market for the product to validate the marketability and assess whether the benefit will outweigh the expense of a patent.

National and international patent offices

Upon establishing that the technology is novel, the inventor must decide in which country or countries to file the patent. Intellectual property laws are territorial; they do not extend beyond the border of an individual country or region. Therefore, either of the inventors or a third party in the preceding example can make, use, or sell the improved PCR chip in a country other than the one in which the patent was granted. If the inventor is seeking patent protection in a single country, s/he should file a patent application in a national patent office, such as the USPTO or the Japan Patent Office (JPO). An inventor can also opt to file a patent in an international office. For example, the European Patent Convention established a single procedure through the EPO for protecting inventions in any of the 38 contracting states. Moreover, the Patent Cooperation Treaty (PCT) allows for a patent to be filed in single language and paid for in a single currency to be considered by any number of the 148 member countries indexed in the World Intellectual Property Organisation (WIPO). “Worldwide patents” do not currently exist, however, and a patent must be independently approved by the local patent office according to IP law in each corresponding country.

Fig. 3 illustrates the number of patents granted in 2012 in selected countries according to the residency status of the applicant. The countries with the highest number of granted patents are Japan, US and China, respectively. While Japan and China have a significantly higher percentage of resident applicants than non-resident or abroad, patents granted in the US are evenly split between the three categories. Moreover, a significantly larger number of foreign inventors wish to protect their IP in Japan and the US than in China. This may be attributed to the ineffective enforcement of IP rights in China. It is also important to note that an applicant has around a 75% probability of successfully obtaining a patent, a grant rate that is comparable across USPTO, EPO and JPO.

Patent applications

A key question in pursing patent protection is when to file the initial application. If the application is filed too early when the invention is still at the idea stage, the patent may be denied on the basis that there is not sufficient experimental evidence to support the patentability requirements. Moreover, evolved designs and drawings might not reflect the original patent application. On the other hand, if a patent is filed too late, the inventor takes the risk that a competitor may patent a similar invention in the interim. Therefore, a balance must be reached between filing early to secure the
filing date and ensuring that there is enough experimental support. Hence, the provisional application should be as complete as a full patent application. While it is possible to file a patent based solely on a hypothetical example and retrospectively submit experimental evidence to the EPO to illustrate that the example is practical, the inventor runs the risk that the hypothetical example may not work as described in the application.58 However, it is not possible to submit technical support after the filing date if the application is denied due to a fundamental insufficiency of evidence.

In the US, inventors have the option of filing either a provisional patent application or a full (non-provisional) patent application. A provisional patent application sets an effective filing date for the subsequent non-provisional patent application and allows for a one year pendency period without requiring formal claims.49 Advantages of a provisional patent include a less extensive application and reservation of a filing date. It also extends the lifetime of the eventual non-provisional patent by one year, which can be valuable considering the time necessary to commercialise a new technology. A provisional application may be filed when (i) there is insufficient time to prepare a full patent application, (ii) there is a lack of financial resources, or (iii) the technology will undergo significant modifications.50 By filing a provisional application, the applicant can also postpone the fees associated with the more costly non-provisional application. If the provisional application is abandoned after a year, the application is not published, and the patentee can opt for a trade secret. However, the patentee should not pursue both a patent and a trade secret for the same invention.51

The provisional application consists of several sections: an abstract, a background to the invention, a detailed description of the invention with drawings, and references to related prior art. Prior art includes public information on the Internet, public talks, conference proceedings, journal articles, technical publications, prior patents, and local and international commercial products. A provisional application should be intended to support the claims of the non-provisional application with the inclusion of a substantive technical specification section. This section consists of drawings and a description of the invention. It should include (i) expected use, (ii) existing problems, (iii) advantages of the technology, (iv) essential elements, (v) alternatives for each essential element, and (vi) the relation of these elements. If the technical specifications section is not sufficiently detailed, the patent may not be granted or revoked after it is challenged in a court action.

A priority date is granted to the inventor upon receipt of a provisional or non-provisional application. The USPTO switched from the first-to-invent to a first-inventor-to-file provision in March 201352 to standardise US patent laws according to those in EU and Japan.53 Therefore, the priority date is especially important in all countries because it disqualifies other patent applications filed after this date. Although filing a provisional application delays the filing of a non-provisional patent application for a year, it does not count toward the 20 year term of the patent.

A non-provisional (regular) application in the US is similar to patent applications in other patent offices, including the PCT, the EPO and the JPO. It involves all the components of a provisional application and the claims. The claims are the most important section of a patent application.32 They comprise the “legal section” of the patent, and indicate the scope and the coverage of the patent. A wide scope of patent claims has been shown to enhance functionality development and increase productivity of the technology.54-56 For this reason, and to prevent patent infringement, patent claims are typically worded as extensively as possible without being overly broad. It should be noted that the success of the entire patent may be jeopardised by keeping the claims too broad. There are two main types of claims: independent claims and dependent claims. While an independent claim can include any number of elements and their characteristics, a dependent claim is based on a previously listed claim. If the claims are poorly drafted, a competitor can circumvent or design around the patent.

The application is a stand-alone piece of work, which covers the subject matter and teaches someone skilled in the art how to make or use the invention. The patent application may also indicate the best mode or embodiment of the invention that the inventor considered the best at the time of filing the application. It is a common practice to leave out the best mode in the patent application to prevent others from replicating the invention at the highest quality. In the US, due to Leahy-Smith America Invents Act (effective since 2011),52 failure to disclose a best mode is not a basis for invalidating or rendering unenforceable an issued patent.57

Steps and costs of obtaining a patent

While the following steps of obtaining a patent relate to the USPTO, they are broadly relevant to patenting an invention in
other countries such as Japan or through the EPO. Key differences of these patent offices include the option of filing a provisional application in the USPTO, and the presence of a request lag in the JPO and EPO in which the applicant receives the benefits associated with “patent-pending” before requesting a formal examination. Fig. 4 illustrates the timelines of US and PCT patents. Although the publication date and validity of the patent are the same across most patent offices, the average pendency period for successful patent applications is ~3 years in the US, while the duration of patent examination (after submission of an examination request) is on average 4.3 years in the EPO and 2.9 years in the JPO.

Upon filing a patent application in the US, the applicant must pay the associated fees of $2600 (as of May 2014), although small entities and micro entities receive a 50% and 75% fee reduction, respectively. USPTO then publishes patent applications 18 months after the earliest priority date. The issue of patentability may arise if the invention is disclosed publicly before the application is published. Furthermore, the disclosure before the publication of the patent limits the patentee to further modify the scope of the patent. These cases include (i) narrowing the scope of the patent protection to include specific features not fully disclosed in the provisional application, and (ii) amending the scope of the protection sought. If the invention needs to be shown to the others during this time, an non-disclosure (confidentiality) agreement (NDA) should be sought. An NDA can be one-way or mutual; one or both parties involved in the agreement can disclose information. For example, if a startup discloses proprietary information to a non-competitor and the non-competitor uses this information merely to evaluate a business arrangement, a one-way NDA should be employed. On the other hand, a mutual NDA should be used when both the startup and non-competitor disclose confidential information that is mutually beneficial, such as a discussion on the improvement of the technology.

An NDA should include several key elements such as a definition and scope of the confidential information, obligations of parties, an effective time period, and any additional provisions in the agreement. It is recommended that the inventor file a patent and reach the patent-pending stage before disclosing the invention under an NDA. If the third party, such as an investor, is not willing to sign an NDA, then the patentee should only disclose information regarding the business arrangement (the outcome and the use). The publication of a patent does not grant any patent rights until the pending application is granted or issued. However, at this point the inventor can publish experimental evidence or speak about the invention at a conference without forfeiting patentability due to public disclosure. After receiving an application, the patent office conducts a substantive examination to determine the prior art and ensure that the application satisfies patentability requirements. After the examination of the application, the results are sent to the applicant in a document called “office action”. This may include several rejections including presence of prior art (novelty requirement); the invention is an obvious combination of prior art (non-obviousness requirement); or the description is not clear for someone to make and use the invention (enablement requirement). Other grounds for challenging patents include written description, indefiniteness, utility and double patenting. Based on the office action, the applicant may choose to modify the claims in an office action response, present an argument for the rejections, or a combination of both. This process, known as prosecution, may repeat multiple times until the application is accepted or rejected.

![Fig. 4 Estimated timelines for obtaining and maintaining a non-provisional patent in the US, and filing a patent through the PCT if the inventor opts to pursue patent protection in multiple countries.](image-url)
While the novelty requirement is objective, the non-obviousness requirement is subjective. Therefore, almost all patent appeals deal with obviousness. The obviousness rejection may be overcome in a number of ways by arguing that (i) the combination of the references do not teach or disclose every element of the rejected claim; (ii) none of the references provide any motivation for the combination; (iii) the secondary considerations might provide a secondary evidence (showing that the invention had unexpected properties, has commercial success or it solved a long-standing problem in the field); and (iv) modifying the rejected claim to include another element not taught by the combination. The applicant may choose to change the scope of the claims as long as the originally filed specification supports the changes. Inaccuracies of description, unnecessary words, and drawings can be modified. However, new matter beyond the originally-filed specification cannot be added to the application.

When a patent is issued, it can be corrected or amended through a certificate of correction, a reissue application, or a reexamination of the patent. The certificate of correction is used for typographical errors. On the other hand, the reissue application corrects the issues that make the patent inoperative or invalid (too broad or narrow claims). If there is a newly discovered prior art, the patent owner or another entity (competitor) may choose to raise the issue of potential unpatentability. Significantly, the rates of opposition at the JPO (4%) and EPO (6–8%) are twenty and thirty times higher than the rate of reexamination at the USPTO (0.2%), respectively. Once the patent is granted after the payment of an additional issue fee, the patent can be maintained and enforced for the remainder of the 20 year protection period in order to ensure its efficacy. In the US, the maintenance fees occur 3.5 years, 7.5 years, and of the 20 year protection period in order to ensure its efficacy. In addition to manufacturing the invention or licencing out the product, the patentee has the third option of selling the patent claims to another entity (competitor) may choose to raise the issue of potential unpatentability. Significantly, the rates of opposition at the JPO (4%) and EPO (6–8%) are twenty and thirty times higher than the rate of reexamination at the USPTO (0.2%), respectively. Once the patent is granted after the payment of an additional issue fee, the patent can be maintained and enforced for the remainder of the 20 year protection period in order to ensure its efficacy. In the US, the maintenance fees occur 3.5 years, 7.5 years, and of the 20 year protection period in order to ensure its efficacy. In the US, the maintenance fees occur 3.5 years, 7.5 years, and 11.5 years after the date the patent is granted and constitute over 80% of the total cost of the patent, which is ~$15,000, or equivalently $7600 or $3800 for small and micro entities.

If the inventor chooses to pursue a PCT application, s/he must file the international application and pay the filing fee of 1330 Swiss Francs (~$1500 as of 2014) within 12 months of filing a regional patent (Fig. 4). Within an additional four months, an international search report is issued upon payment of a search fee which can vary from around $500 to $2500 depending on the selected International Searching Authority. The patent is published internationally 18 months after the priority filing date. From this point, the inventor has an 12 months to re-enter the national phase. Thus, filing a PCT application provides the inventor with an additional 18 months to decide in which foreign countries to seek patent protection and prepare the applications for their local offices.

Due to the high costs and time required to build up and maintain an IP portfolio, startups often experience financial burden in maintaining their patents and may lose them as a result. One pitfall of spending resources to create an extensive patent portfolio is the potential for a competitor to design a similar invention that circumvents the claims of the original patents. Therefore, it is beneficial to include a method of use in the patent in addition to a physical microfluidic device.

**Employing a patent**

If a patentee decides to manufacture his/her invention (e.g. a microfluidic device), s/he should conduct a full freedom-to-operate search, which ensures that no aspect of the production infringes upon the IP rights of others. In addition to obtaining the exclusive right to manufacturing and selling the invention, there are several other reasons to file a patent: (i) restraining others to patent the technology; (ii) protecting a competitive advantage; (iii) generating licencing revenue from a non-competitor; (iv) stimulating an acquisition or an investment; (v) advertising technical or creative ability and increasing credibility; and (vi) deterring an infringement lawsuit.

To ensure a competitive advantage, startups often file patents to protect their core technologies, thus requiring another company that intends to enter the market to spend additional resources designing around their patents. If their core technology is appropriate to another company’s products in a different market, it can be licenced out to a non-competitor without negatively effecting the patent owner’s competitive position. With this strategy, startups can generate additional revenue while focusing on their core technology.

Investors view IP as an asset, which might stimulate an investment in the company or a future acquisition to access an essential piece of an IP. Inventors can strategically employ patents to gain the upper hand in negotiations, a practice commonly used in Japan. Competitors as well as investors in the market find startups more credible if they have an IP portfolio, while it also establishes credibility in the market by signalling that the startup’s product is unique.

In addition to manufacturing the invention or licencing out the product, the patentee has the third option of selling the exclusive right to the invention to another corporation or individual who will then become the new patent owner. However, once the 20 year patent period ends and the patent expires, the invention enters the public domain, can be freely made, used and sold, and the same invention cannot be re-patented at any point in the future.

**Patent litigation**

If a patent is infringed upon during the period of protection, the patent owner must determine whether the commercial advantage is worth the time and costs of the litigation, which can become costly as technological complexity may require expert witness(es) and/or additional experiments. A patent infringement lawsuit averages between $100 K and $500 K in the EU and may cost an average of $2.8 M in the US. These costs are comparable for both the patent owner and the accused infringer.

It is also necessary that the patent owner ensures that the patent claims are valid and their wording encompasses the potentially infringing product before entering court. Since the claims are used as a basis to determine whether the accused product or method infringes the patent, the interpretation and evaluation of the claims constitutes the first step.
in an infringement case.\textsuperscript{75} If a patent is found to be infringed, the patent owner is entitled to remedies through granting injunctions and damages.\textsuperscript{76} Injunctions are court orders that prevent a particular party from using, making, or selling the claimed subject matter while damages cover the lost profits of the inventor. The accused party has a number of options: (i) licence the technology from the inventor or sign a royalty agreement, (ii) prove that the product omits an element of the claims, or (iii) invalidate the patent by demonstrating the existence of prior art and/or that the invention is obvious. Since the defendant generally adds a counterclaim of invalidity to the defence of non-infringement,\textsuperscript{76} patent attorneys can be beneficial when drafting an application to ensure sufficient scope and validity of the patent. Patents owned by individuals or smaller firms in newer, dynamic technologies have been shown to possess a relatively higher risk of litigation,\textsuperscript{77} as these patents are associated with increased uncertainty about patent validity and scope.\textsuperscript{78} If a large company brings a patent infringement lawsuit, the smaller company or individual is often advised to settle out-of-court with a cross-licencing agreement to avoid the high costs of patent litigation.\textsuperscript{79} Some studies suggested that plaintiffs win only 25\% of cases litigated to judgment in the US\textsuperscript{75} while others estimated closer to 45\%.\textsuperscript{80} The majority of patent infringement cases are won by the defendant in part due to invalidity of the patent and in part because of noninfringement.

**Conclusions**

Limited microfluidic devices have been commercialised in both large pharma and emerging companies founded purely upon microfluidic technologies. While microfluidics has the potential to make commercial advancements in biotechnology and healthcare, especially in the developing world, devices that can easily be applied to solve current challenges in the market are lacking.\textsuperscript{81–87} This disconnect between the microfluidic technology in the laboratory and in the market needs to be overcome by integrating academic and industrial efforts.\textsuperscript{88,89} Although the potential of patent protection has been widely recognised in the context of dynamic innovation, the effects of aggressive patenting by academics is the subject of much debate. There is uncertainty about whether patenting in academia stimulates innovation and leads to increased commercialisation of university inventions. However, academics can also contribute to innovation by consulting with existing microfluidics companies rather than patenting.

Awareness of patent law enables academics to pursue patent protection efficiently and effectively, and to attain the optimal balance between academic publishing, consulting, and patenting. The commercialisation of the academic research needs to be evaluated on a case-by-case basis to determine the feasibility of patenting or diffusing the existing knowledge through consulting. Such efforts will benefit not only the inventors, industrial partners and investors, but also increase the economic growth and social impact of microfluidics.

**Note**

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14. Journal publication searches were conducted through PubMed and Web of Science and included articles with one or more of the following words found in the title: Microfluidics, microfluidic, micro-fluidics, micro-fluidic, lab-on-a-chip, or lab on a chip. Articles that contained “microfluidics” or variations of the term only in the abstract or main text were omitted from this search. Therefore, this search represents an underestimation of the number of published articles in this field.
15. Patent searches were conducted through PATENTSCOPE and included patents with one or more of the following words found in the title: Microfluidics, microfluidic, micro-fluidics, micro-fluidic, lab-on-a-chip, or lab on a chip. Patents that contained “microfluidics” or variations of the term only in the abstract or main text were omitted from this search.

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