Graphene Research and Advances

Report May 2020

Sophie Charpentier, Johan Ek Weis and Camilla Johansson

26 May 2020

Med stöd från

VINNOVA Sveriges innovationsmyndighet

Energimyndigheten

FORMAS

Strategiska innovationsprogram

Summary

Today, graphene is produced at a large scale. The worldwide production capacity of graphene flakes equals to approximately 7000 tonnes per year. Films of graphene, such as produced by chemical vapour deposition, are produced in large roll-to-roll processes and several companies are currently scaling up their production. The synthesis of the other two-dimensional (2D) materials is a bit behind, but as shown in this report, new production methods are developed within universities These methods will likely result in increased industrial production if and when there is an increased demand for these 2D materials as well.

China owns a significant amount of the worldwide graphite resources and is known to be a country with enormous production capacity in many sectors. This can also be seen in the patent statistics as most of the patents related to graphene manufacturing are filed in China. However, it will be shown that companies might not file patents to protect their manufacturing processes but instead treat it as trade secrets.

There is a continued development of characterisation methods, where some are highlighted in this report. These methods need to be standardised and widely followed in industry in order for potential buyers to efficiently compare products and be able to use different suppliers. Standardisation is an important process where there now are opportunities to get involved in the process in Sweden and ensure that Swedish interests are taken into consideration.

Graphene has a lot of potential for biotechnology, and the path to market differs significantly (in time, investment, resources, regulatory requirements) between the different types of applications (diagnostic, implants, drug delivery etc.). The regulatory requirements, related to health and toxicity, are much more stringent in this area of application than others where graphene can have an impact (for example areas such as coatings and composites), leading to longer time to market: from 3-7 years for medical devices to more than 12 years for molecular drugs. This explains why it took a longer time for this application area to take off, compared to others like composites or energy. However, it did not stop the recent creation of a few companies, aiming at commercializing graphene-based biotechnologies. Graphene not only has the potential to enable new types biotechnological devices but could be used to enhance a vast array of already existing technologies, thanks to its multifunctionality. The application area of graphene´s antibacterial is especially effervescent, as can been seen by the very important yearly increase of the number of publications and the large number of patent applications with pending status.

Introduction

SIO Grafen's Research Intelligence Report Series, published twice a year, aims to highlight some of the most interesting research findings on graphene that have emerged during the last few months. This report focuses on two of the six areas of strength within SIO Grafen; manufacturing and biotechnology. In addition to the presentation of the latest state-of-art research, the report also includes a discussion of the patent landscape within these areas and the graphene field in general.

In the last few years, there has been a strong interest from the Swedish industry to incorporate graphene in a variety of applications, resulting in a large number of innovation projects funded through SIO Grafen, with 19 projects on manufacturing and 7 on biotechnology applications. In total, 98 innovations projects have been started within SIO Grafen since its creation in 2014. A complete list of these can be found on the SIO Grafen homepage.

A roadmap for the manufacturing area of strength within SIO Grafen is currently under development. This will include a brief description of the current status of graphene manufacturing as well as propose goals and activities for continued development.

Content:

Summary 2

Introduction 3

Content: 4

State-Of-Art Research - Manufacturing 5

Synthesis of 2D materials 5

Bottom-up production of “new” 2D materials 5

Top-down production of “new” 2D materials 6

Characterization 6

Faster Raman mapping 6

Towards standardised electrical characterisation techniques 7

State-Of-Art Research – Biomedical Technology 8

Antibacterial Composite 8

Sweat Sensors to Detect Stress Level 9

Supramolecular Biofabrication Enabled by Graphene Oxide 9

Graphene-based Sensor for Field Testing of COVID-19 10

New Commercial Ventures 10

Statistics of Scientific Publications 11

Statistics of Patents 13

Concluding Remarks 16

State-Of-Art Research - Manufacturing

There are many different types of graphene, many other 2D materials and numerous fabrication methods. New materials are produced, and established production methods are continuously improved and scaled up. A few recent developments are discussed here.

Characterisation is very important with so many different types of materials. A new development which has allowed significantly faster analysis using Raman spectroscopy is highlighted together with a new study on characterisation of the electrical properties of graphene which aims at laying the foundation to new standards.

Synthesis of 2D materials

A large review over the synthesis of 2D materials was recently published. The focus is on the many kinds of graphene, but also other 2D materials are discussed. It is a comprehensive overview with 1800 references that aims to provide practical details and procedures of the main techniques for production and processing of graphene.

Backes et al., 2D Mater. 7, 022001 (2020)

Bottom-up production of "new" 2D materials

There are over 5 000 layered materials and many of these can be transformed into 2D materials with new properties similarly to how graphite is the bulk version of graphene. The production of graphene is in general a few years ahead of all other kinds of 2D materials. Boron Nitride (BN) has been produced and available on the market for some time, but otherwise it is very limited. However, a few studies have recently showed that it should be possible to produce many other 2D materials at larger scales.

Transition metal dichalcogenides (TMDs) are one interesting class of 2D materials. These have a band gap, in contrast to graphene, and can therefore for example be used in transistors in electronics or as emitters and detectors in optics. This type of material consists of one transition metal (M) (Mo, W etc.) and a chalcogen (X) (S, Se or Te) in the form MX_2.

A study led by scientists in Denmark demonstrated a method to produce a range of this kind of 2D materials. A bottom-up approach was used for production of well-studied crystals (such as MoS_2) and for completely new compounds. The basic idea of the method is to use a catalyst layer of gold to both limit the synthesis to few-atom thick layers and make the 2D material epitaxially aligned to the gold.

The technique is easier and safer than many alternative methods and uses readily available raw materials. The technique can be used to fabricate many kinds of 2D materials, around 20 were showcased, and can result in high quality material.

A. Shivayogimath *et al.*, Nature Communications 10:2957 (2019)

Top-down production of "new" 2D materials

Another recent study instead used a top-down approach to produce a different kind of 2D material. The technique used hydrofluoric and hydrochloric acids to etch away parts of a ceramic precursor in order to create a nanometer thin material. The method was used to fabricate $Ti_3C_2T_x$ but the authors believe it could be applied to other similarly structured 2D materials. The yield was better than 50% and it was shown that the process could be scaled up from 1 g to 50 g per batch resulting in identical material. The researchers stress that new technical challenges might need to be solved in order to scale up even further, but also that the 50 g produced can already be used to create more than 200 000 microsupercapacitors or about 11 m^2 of electromagnetic interference shielding.

C. E. Shuck *et al.*, *Adv. Eng. Mater.* **22**, 1901241 (2020)

Characterization

Faster Raman mapping

Raman spectroscopy is one of the most used characterisation techniques for analysing graphene and other 2D materials. It can give information of the quality, defects, number of layers, crystal boundary, doping and strain, oxidation state and electron-phonon interactions. However, the Raman scattering efficiency is very low, and the laser power has to be kept low in order to not damage the sample. The integration time of a single spot is therefore typically hundreds of milliseconds to tens of seconds. Although this might seem fast, it also means that mapping out a 50 x 50 μm^2 region with high resolution typically takes half a day.

A new article shows how the Raman mapping speed can be increased by 50 times using principal component analysis (PCA). PCA is a mathematical algorithm which is used in signal processing and machine learning to find common features in the dataset. PCA can distinguish signal features from noise and thus also increase the signal to noise level significantly. The method was demonstrated by analysing graphene oxide (GO) using a very low laser power (5 μW) and short integration time 10 ms, which prevents any reduction of the GO. The technique can obviously also be used on other materials and was shown for MoS_2, WS_2, and BN.

S. Nair *et al.*, National Science Review, nwz177, https://doi.org/10.1093/nsr/nwz177 (2019)

Towards standardised electrical characterisation techniques

CVD graphene (that is graphene produced by chemical vapour deposition) is showing great promises for applications in electronics, especially in radio-frequency electronics, integrated circuits and optoelectronics. The material can be produced at large scale, but there is a lack of standardised electrical characterisation techniques for important parameters – such as carrier concentration, mobility and sheet resistance – that often are used as figures-of-merit of the quality.

A recent study showed how a combination of characterisation techniques can be used to extract this information and do it at the macro-, micro- and nanoscale. A combination of contact and contactless methods was used with good reproducibility. The investigated methods were magneto-transport in the van der Pauw geometry, THz time-domain spectroscopy mapping and calibrated Kelvin probe force microscopy.

This allowed fast and large-area mapping of the electrical properties, which is required in any industrial application. The authors further report that the results will become part of Good Practice Guides and will lay the foundation to proposals for new standards.

C. Melios *et al. Scientific Reports* **10,** 3223 (2020)

State-Of-Art Research – Biomedical Technology

Thanks to its unique properties such as large surface area and electron mobility as well as functionalisation potential, graphene is paving the way for novel diagnosis and treatments. For example, the large surface area of graphene makes an excellent platform for drug delivery whereas its good conductivity makes it attractive in biosensors. Graphene is also biocompatible and can be made into scaffolds, and its conductivity makes it a good material for tissue engineering. Graphene-based polymer could even be used to make very sensitive electromechanical sensors that can be used to make improved deep brain implants.

Antibacterial Composite

In a previous edition of the Research Intelligence Report (no 1, 2018), a study by a multidisciplinary team of researchers at Chalmers University of Technology demonstrated that it is possible to create an effective antibacterial coating using graphene. In their study, the researchers showed that an antibacterial coating is created when the graphene flakes are perpendicular to the bacteria. This coating seemed promising but producing is expensive, and its production, not readily scalable.

In a more recent study, other researchers joined the same team, which was able to achieve the same outstanding antibacterial effect by using a composite consisting of relatively inexpensive thin (6-8 nm) graphite nanoplatelets (GNPs) in a matrix of low-density polyethylene (LDPE). The composite was extruded in conditions that enabled to control the orientation of the GNPs. The GNPs were later exposed by etching the surface of the composite and the antibacterial activity was then evaluated. The best results were obtained with relatively high loadings (15-20% of GNPs) and oriented GNPs. Not only did the coating decrease the bacterial viability by 4 orders of magnitudes, it also prevent bacterial colonization, which reduces the numbers of dead cells on the surface – a key advantage for longer-term biomedical applications where cleaning is usually required. It is also worth to mention that the composite, in the same way as the coating studied in the previous study, is biocompatible: the nanoplatelets prevent bacterial infection but without damaging healthy human cells.

S. Pandit *et al. Small* **1904756**, 1 (2020)

Sweat Sensors to Detect Stress Level

In a recent article, researchers at Caltech (USA) took advantage of the flexibility and sensitivity of graphene to fabricate a fully integrated wireless mobile health sensor system to detect stress level. The common methods currently used to assess stress level are either subjective or invasive and the results are available after several hours. The system developed, based on laser-induced graphene electrodes, can quickly (in few minutes) assess stress level by monitoring small variation (few ng/mL) in the cortisol level excreted in sweat. Not only can these small variations in the cortisol level help to analyse acute external stimuli-triggered stress response, it can also help monitoring circadian rhythms. The production of the system is also rapid, scalable and low-cost.

In October 2019, NASA announced that the lead researcher of this project was one of six selected to participate in studies of the health of humans in space. The goal is to develop this sensor technology into a system for monitoring the stress and anxiety of astronauts during deep-space missions.

R. M. Torrente-Rodríguez *et al. Matter* **2**, 1 (2020)

Supramolecular Biofabrication Enabled by Graphene Oxide

The ability to engineer tissue will increase the potential for regenerative medicine. Graphene has been shown to display biocompatibility with mammalian cells necessary for use as a scaffold structure for tissue engineering. In a recent article, researchers used graphene oxide (GO) in combination with a protein (elastin-like recombinamers, ELRs) to produce hierarchical self-assembling system that organise into tubular structures replicating some properties of vascular tissue. When solutions of GO and ELRs are put in contact, a multilayer membrane develops at the interfaces. Loading the ELRs solution in an injecting tip and injecting it in a GO solutions enables the creation of a circular membrane. By controlling the injection, layer by layer, one can therefore 3D print a tube.

The article shows it is possible to obtain tubes with inner diameters from 50 µm, 10 µm wall thickness and length up to 10 cm able to withstand flow of up to 12.5 mL/min for at least 24 hours and within 60 minutes of formation. The researchers also added suspending human umbilical vascular endothelial cells (hUVECs) to the ELRs solution before printing. These cells were shown to grow on the structure for several days after printing, suggesting that the hybrid material is cell friendly in vitro.

Y. Wu *et al. Nat. Commun.* **11**, 1182 (2020)

Graphene-based Sensor for Field Testing of COVID-19

Due to its large specific area, high electronic conductivity and high carrier mobility, graphene is a useful material for sensing applications. In a graphene-based FET biosensor, the graphene part is functionalized to make it sensitive to the target molecule which allows it to become an ultrasensitive and low-noise detector. In a recent article, researchers fabricated such a device able to detect the SARS-CoV-2, the virus causing the COVID-19 pandemic disease. At the time of publishing their results, diagnostic tests for this disease relied on a technique called real-time reverse transcription-polymerase chain reaction (RT-PCR), which requires the analysis of the collected patient swabs using laboratory equipment and at least 3 hours.

The graphene-based FET sensor was functionalised to detect the SARS-CoV-2 spike protein and the presence of the virus, when it attaches to the sensor, it changed the conductivity of the graphene enabling detection. This sensor can analyse patient samples directly from the samples, without any additional preparation steps and under a minute.

G. Seo *et al. ACS Nano* (2020)

New Commercial Ventures

Even if the commercialisation of graphene-based biotechnology is slightly behind other areas of applications, mainly due to regulations and health aspects, it is still a fast growing and very dynamic area. Two companies were recently created with the goal of commercialising graphene-based biotechnologies.

InBrain Neuroelectronics, a spin-off from ICN2 in Barcelona (Spain), aiming to develop a graphene-based neural interfaces for deep-brain stimulation, allowing a better signal resolution while being flexible and using smaller electrodes.

Grapheal, a spin-off from Neel Institute CNRS Grenoble (France), develops a graphene-based wearable patch that monitor and promotes the healing of chronic wounds. The patch is also very sensitive and flexible. The first human trials are about to begin and the launch is planned for 2023.

Statistics of Scientific Publications

Manufacturing

It is difficult to get a clear image of the development of the number of publications specifically related to manufacturing of graphene since most studies of graphene includes at least a description of the material, regardless of whether the manufacturing itself was studied or not. Numerous different search strings were used in Web of Science. The trends of for example how many scientific articles that are published each year and where the authors are based can be discussed, although the searches therefore likely include a large number of articles that better fits into other areas of strength within SIO Grafen.

The publication rate of scientific articles mentioning graphene manufacturing increased rapidly until around 2014 and has since then been quite stable, see figure 1. This is in stark contrast to the total number of articles published about graphene where the publication rate has more than doubled since 2014. One reason could be that a lot of the development within this area now becomes patents or company secrets instead of openly published within the scientific community.

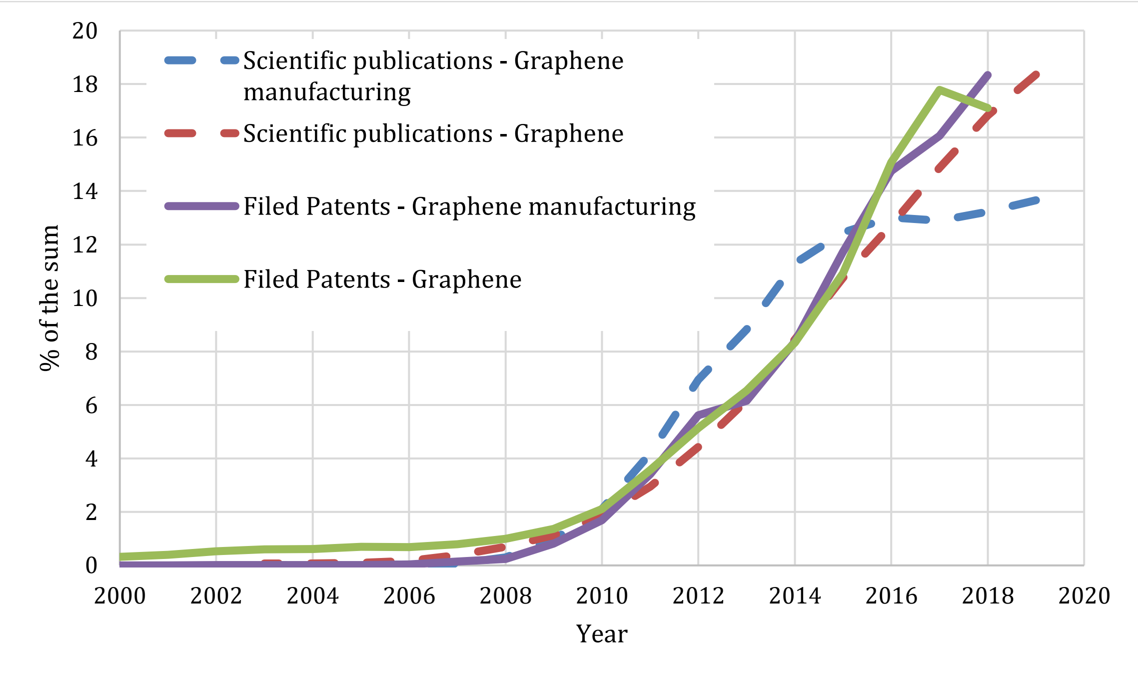

Figure 1 Total number of scientific publications per year for graphene and graphene manufacturing compared to the number of filed patents per year related to graphene manufacturing and all graphene patents. The curves presented are rescaled and expressed as a percentage of the sum to allow comparison of the trend over time. Data from Web of Science, March 2020.

Biotechnology

The analysis performed on the data collected from searches on Web of Science shows that the number of scientific publications on graphene in the application area of biotechnology shows a steady increase, see Figure 2. Several other application areas related to biotechnology were also investigated, such as drug/gene delivery, prostheses and implants, neural interfaces etc. All had a very low number of publications and the trend over time is therefore not presented. One area of application, antibacterial, was selected and plotted also in Figure 2. The trend is clearly different than the one for graphene: the area is younger (no publications before 2008) and the number of publications shows a steeper increase, a general trend also observed for other biomedical topics with few publications. It is not surprising that it took longer for areas of applications where graphene is inside or in direct contact with biological tissue to gain interest, as they are submitted to more rules and regulations. The steep increase in the number of applications is however demonstrating that the interest and potential is important.

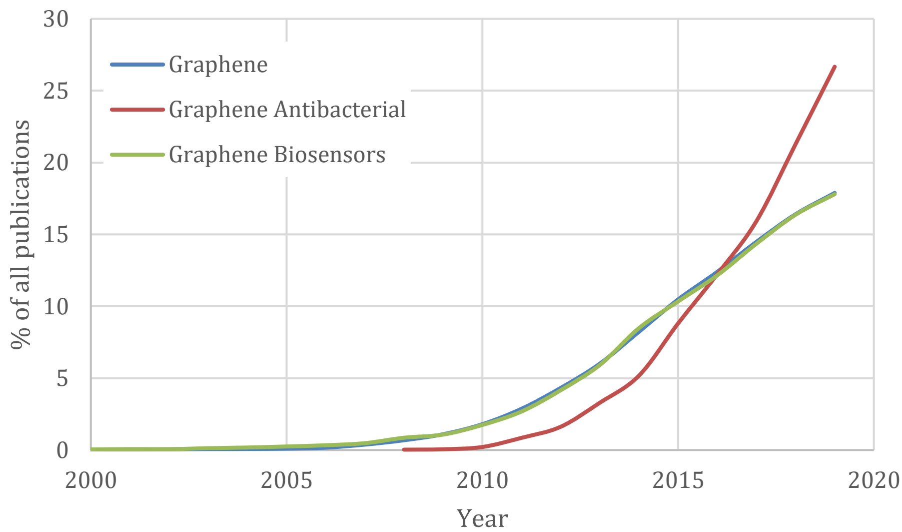

Figure 2: Total number of scientific publications per year for graphene, graphene and antibacterial and biosensors. The curves presented are rescaled and expressed as a percentage of the total amount of publications for each application area in order to allow comparison of the trend over time. Data from Web of Science, March 2020. Keyword searches for topic were employed, also including derivatives, such as bioimaging.

Chinese organisations are dominating, with almost half of the publications on graphene. This is also true of the other areas of applications presented. Other prominent countries are especially USA (with around 15% of the total number of publications on graphene and on biomedical applications and 12% on graphene manufacturing) but also South Korea (around

10% of the total number of publications on graphene and regarding graphene manufacturing) and India (almost 10% for biomedical applications and for graphene manufacturing).

Only one of the top 50 most published organizations on biosensors is European (CNRS).

Statistics of Patents

The patent searches presented below were performed using the patent database Orbit Intelligence, a global patent database comprising more than 50 million patent families (itself comprising more than 100 million patent and patent applications). Please note that there are patents and patent applications which due to different reasons do not appear when performing this search. For example, this may be due to that a patent applications does not become public until 18 months after filing, or due to mistakes which have been made when translating a patent or a patent application.

Manufacturing

The search was made using keywords [a]. A number of synonyms for manufacturing was listed and that any of those should be found in close proximity to the word graphene in either title, abstract or claims of the patent or patent application.

The trend of how many patents that are filed per year for graphene manufacturing closely follows the trend for the whole graphene area, see figure 1. These trends are also very similar to the trend for all publications related to graphene, although the rate of filed patents have increased a bit more than the scientific publications have over the last few years.

Approximately 40% of the filed and published applications have been granted. Another 40% are still pending. This number is similar to the ratio for filed applications and granted patents for graphene in general. The remaining 20% are dead patents, which include patents that have not been renewed etc.

[a] The following keywords were used for searches within titles, abstracts and claims for biotechnology: manufacturing: (((preparation OR preparing OR production OR producing OR manufactur+ OR growth OR exfoliat+ OR centrifugation OR deposit+ OR synth+) 5W graphen+)).

Looking at the geographical distribution, around 80% of all patent families has one member which has been filed in China, significantly more than the second largest which is South Korea (9%). Only 4% of the filed patent applications are “worldwide”, so called PCT-applications[b] and even fewer are filed as EP-applications at the European patent office (0.5%).

When looking at these numbers, it should be noted that even if it is possible to patent a method for e.g. producing graphene, it is often hard to determine if anyone is infringing on such a patent. Therefore, it is common that companies do not patent their methods. They keep it as a trade secret or know-how instead of protecting it with a patent application. The vast majority of the patent holders are universities, which implies that many of the patents not necessarily hold a significant commercial value but are used for academic reasons.

Biotechnology

This search was also made using keywords[c], which keywords should be found in the title, abstract or claims of any patent or patent application. The same keywords were used as for the search for scientific publications.

For the application area of biosensors, the trends for the number of patent families which have been filed every year, are very similar to the trends for scientific publications, c.f. Figure 3 left. The trends for the application area of antibacterial (c.f. Figure 3 right) is slightly different, with a pronounced increase in 2016.

The distribution of legal statuses for the subfield of biosensors and bioimaging is very similar for graphene in general as well as for graphene manufacturing (approximately 40% of the filed and published applications have been granted and 40% are still pending). For the field of antibacterial, only 25% of the filed and published applications have been granted, and 52% are pending. The fact that the number of pending applications is so large is a clear sign that

[b] A PCT-application is an international patent application which makes it possible to seek patent protection for an invention simultaneously in a large number of countries by filing a single application instead of filing several separate national or regional applications. The granting of patents remains under the control of the national or regional patent Offices in what is called the “national phase”.

[c] c The following keywords were used for searches within titles, abstracts and claims for biotechnology: (biosens+ of bioimag+) and (+bacter+).

the area is still growing. This number could be higher as patent applications filed in the last 18 months are not necessarily public yet.

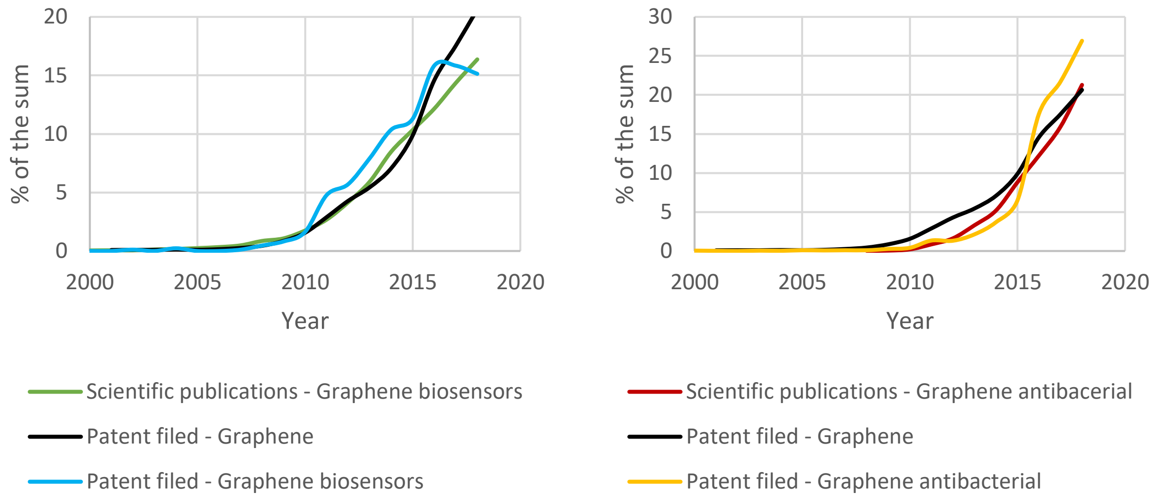

Figure 3 The percentage of all patent families filed as a function of the priority year for graphene and the application area of biosensors (left) and antibacterial (right), as well as the % of all scientific publications per year for the same application area.

For biosensors, approximately half of all patent families has one member which has been filed in China, significantly more than the second and third largest, Korea (15%) and USA (10%) respectively. The dominance of China is even more pronounced for the application area of antibacterial, where around 80% of all patent families has one member which has been filed there, significantly more than the second largest, USA (4%).

Around 2% of the investigated biotechnology patents and patent applications are published at the European patent office, which is less than half than for graphene patents in general. In addition to these, almost 10% of all graphene patent applications are worldwide PCT[d] applications. For graphene biosensors, around 10% of patent applications are worldwide PCT, and about 5% for graphene antibacterial.

[d] A PCT-application is an international patent application which makes it possible to seek patent protection for an invention simultaneously in many countries by filing a single application instead of filing several separate national or regional applications. The granting of patents remains under the control of the national or regional patent Offices in what is called the “national phase”.

Concluding Remarks

SIO Grafen's Research Intelligence Report Series is published twice a year and aims to highlight some of the most interesting research findings on graphene that have emerged during the last few months. In the last 3 editions of the report, the scope of the reports was slightly updated. Instead of discussing a few of the most interesting articles from the last six months of all six areas of strength, the reports focused on two of the six areas of strength within SIO Grafen; electronics and coatings in June 2019, then energy and composites in December 2019 and finally, manufacturing and biotechnology in the current report, May 2020. In addition to the usual state-of-art research presentation, the reports also included a discussion of the patent statistics within these areas and the graphene field in general.

In the continuation of this series, the plan is to change the format and ensure that all areas of strength are covered in every issue (and not only every 18 months like in the current format). The patent statistics could be updated in a separate report which could also go in more depth and give a better overview of the landscape.