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# Clinical translation of graphene-based medical technology

Kostas Kostarelos<sup>1,2,3,4</sup>, Carolina Aguilar<sup>5</sup> and Jose A. Garrido<sup>1,2†</sup>

<sup>1</sup> Catalan Institute of Nanoscience and Nanotechnology (ICN2), CSIC and BIST, Campus UAB, Bellaterra, Spain

<sup>2</sup> Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain

<sup>3</sup> Centre for Nanotechnology in Medicine, Faculty of Biology, Medicine & Health, The University of Manchester, Manchester, UK

<sup>4</sup> Institute of Neuroscience, Universitat Autònoma de Barcelona, Barcelona, Spain

<sup>5</sup> INBRAIN Neuroelectronics, Barcelona, Spain

†e-mail: [joseantonio.garrido@icn2.cat](mailto:joseantonio.garrido@icn2.cat)

**Standfirst** | Many promising technologies born in academic laboratories struggle to transition to industry because of rapid research direction shifts, funding constraints, and complex challenges, hindering their full development. Here, the founders of *INBRAIN Neuroelectronics*, a startup working on graphene-based neural interfaces, describe how a different outcome is possible.

Many scientific articles, even some written by us, conclude with a future-looking statements of this sort “...this technology has the potential to ...”. Particularly in academic laboratories, the bitter reality is that, in (perhaps) most cases, research projects and funding move on rapidly in the quest for the next high-impact, high-novelty finding. As a result, a lot of truly promising technologies never transcend from the laboratory realm to the world of industrial development and do not mature to their full potential. There can be many reasons for such unaccomplished ‘promises’. A central one is the implicit understanding that the path from a lab demonstrator to a marketed device is full of multifaceted challenges. Apart from requiring enormous dedication, these projects usually necessitate considerable financial resources and, needless to say, a big portion of good luck. Furthermore, if the technology in question is based on a novel material platform for which no industrial standards exist, or worse, a novel *nanomaterial* that may not even be compatible with the established industrial methodologies, then the challenges compound dramatically, and could easily be perceived as insurmountable. Yet, in some rare cases, inventors and developers may manage to find the right combination of expertise that allows their innovations to find a way out of the laboratory, on to a track towards industrialization.

Such could be the story of [INBRAIN Neuroelectronics](#), a startup aiming at the industrialization and commercialization of clinical-grade graphene-based neural interfaces in the form of thin film technology for the treatment of neurological disorders. *INBRAIN Neuroelectronics* develops graphene-based implantable platforms able to record, decode and modulate neural signals in high resolution and real time, both for central and peripheral nervous system applications.

It all started during the Graphene Flagship, a visionary 10 year-long European Commission funded initiative for the industrialization and adoption of graphene and other 2D material technologies [1]. In the space of biomedicine, the research program converged to the development of neural interface medical technologies [2], and the technology pipeline was

designed around two main device concepts: electrodes and transistors. The transistor technology was built upon the extraordinary electronic properties of chemical vapor deposited graphene [3], and it aimed to enable a future generation of high channel count brain-computer interfaces with expanded frequency range of recorded brain signals [4,5]. The electrode technology took advantage of the electrochemical properties of reduced graphene oxide (rGO) and aimed to build bidirectional neural interfaces capable of high spatial resolution modulation and recording of neural activity [6].

The success of initial *in vivo* pilot studies brought a first challenge: neuroscientists required many devices (dozens, quickly reaching hundred devices per year) with high level of homogeneity and reproducibility. However, R&D academic labs are ill-suited to produce devices with this level of maturity, since most of their research activity is conducted by PhDs candidates or postdoctoral researcher, whose main objective is to complete an academic training, write papers or gain skills. For the first time, we were confronted with the need to establish a dedicated vehicle for the industrialization of the newly developed technology. At the same time, the demonstration of graphene-based neural interfaces in preclinical studies triggered interest from clinicians and industry in exploring these new technologies. However, the maturity level of the technology was not yet ready for direct industrial adoption. Early interaction with industry revealed another challenge: knowledge and intellectual property (IP) was shared among several academic organizations across Europe, that could result in long and non-efficient negotiations for IP licensing.

At this stage, we decided to launch *INBRAIN Neuroelectronics*, a vehicle that could drive through the challenges of technology industrialization. Being independent from its parent academic organizations, the startup could eventually attract capital from venture investors [7] to mature the technology into a product and to design a solid business pathway. The early phase of a startup is extremely critical. Many of the decisions related to the incorporation of the company, such as the partnership agreements with the parent organization(s) and the choice of experts and entrepreneurs responsible for reshaping the vision and driving the technology and the company forward are key to its success. In the case of *INBRAIN Neuroelectronics*, we almost serendipitously found the right combination of expertise to generate confidence among potential investors: scientific founders able to provide a deep technology understanding, industrial founders experienced in translating early technologies into industrial prototypes, and business founders to guide the commercialization vision.

Another critical challenge for most academic-originated startups is the complex transition from academic to the industry mindset, for which process documentation and standardization are needed at a completely different level, almost at odds with academic ingenuity and flexibility. With a core technology that needed production of graphene-based devices in semiconductor cleanrooms, the challenge for *INBRAIN Neuroelectronics* was even higher: the low maturity of groundbreaking technology together with the use of a novel nanomaterial, like graphene, created a challenge of access to industrial cleanrooms. This challenge is part of what is called the *Lab-to-Fab gap*. For us, the most convenient solution was to mature the technology in the existing R&D cleanroom infrastructure; however, in such environment, the implementation of the rigorous quality controls and procedures required y for industrial production of medical devices is not straightforward.

Despite all the above challenges, *INBRAIN Neuroelectronics* has made tremendous progress. Since its foundation in December 2019, the company established efficient partnerships to mature and industrialize the technology, including the upgrading of R&D cleanrooms to industrial quality standards via ISO certifications. *INBRAIN Neuroelectronics* also succeeded in nourishing and attracting talent, supported by different funding vehicles, including private venture capital funds, as well as public funding dedicated to innovation (from the Spanish government and the European Commission, the later via funding from the European Innovation Council). Thanks to this, *INBRAIN Neuroelectronic* has been recently granted Food and Drug Administration (FDA) Breakthrough designation for its therapeutic platform for Parkinson's disease [8]. Almost at the same time, *INBRAIN Neuroelectronic* has partnered with the University of Manchester and the NHS Salford Royal Hospital in the UK to run the first-in-human clinical investigation study using a graphene-based medical device. This is a major milestone towards the regulatory approval for the use of graphene technology in any clinical setting worldwide. In addition, *INBRAIN*, through its subsidiary *INNERVIA Bioelectronics*, has partnered with the pharma company Merck KGaA (Germany) to explore therapeutic neuromodulation of the peripheral nervous system for the treatment of systemic and metabolic diseases [9], an area coined as bioelectronic medicines or electroceuticals [10].

Here, we highlighted the challenges of the Lab-To-Fab journey for graphene-based neural interfaces, since they can serve other colleagues considering or attempting the translation of advanced materials into medical devices at industry level. The timeline of under 10 years for graphene-based neural interfaces from academic labs to the scale and quality required for human clinical use is somewhat extraordinary. The first transistor prototype in our laboratories was only reported in 2011 [3]. By 2021 we had a device prototype for a graphene-based clinical neural probe. Such progress can be attributed to a variety of factors: a) sustained research funding, primarily by the European Commission Graphene Flagship project, that kept the teams together; b) multi-disciplinary sharing of expertise that enabled effective synergies and progress; c) timely involvement of non-academic experts motivated to take the technology forward; d) institutional support to commercialize graphene; e) a booming landscape where neurotechnology, medical devices and deep-tech are merged, and that facilitated venture capital funding.

The creation of *INBRAIN Neuroelectronics* was pivotal to accelerate the transition of graphene technology from research to industrial standards and to facilitate a clinical pathway. Based on our particular experience, the translation of advanced materials (such as 2D nanomaterials) into medical products could only be achieved through the focus, expertise and dynamism that a startup commercial entity can offer.

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### **Related links**

INBRAIN Neuroelectronics: <https://inbrain-neuroelectronics.com/>

### **Competing interests statement**

The authors declare that they hold interest in INBRAIN Neuroelectronics, which has licensed technology described in this article.