INNOVATION
HUMAN BRAIN PROJECT
Newsletter

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HBP-EBRAINS STARTUPS MEETING

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START-UPS SOLUTION WORKSHOPS

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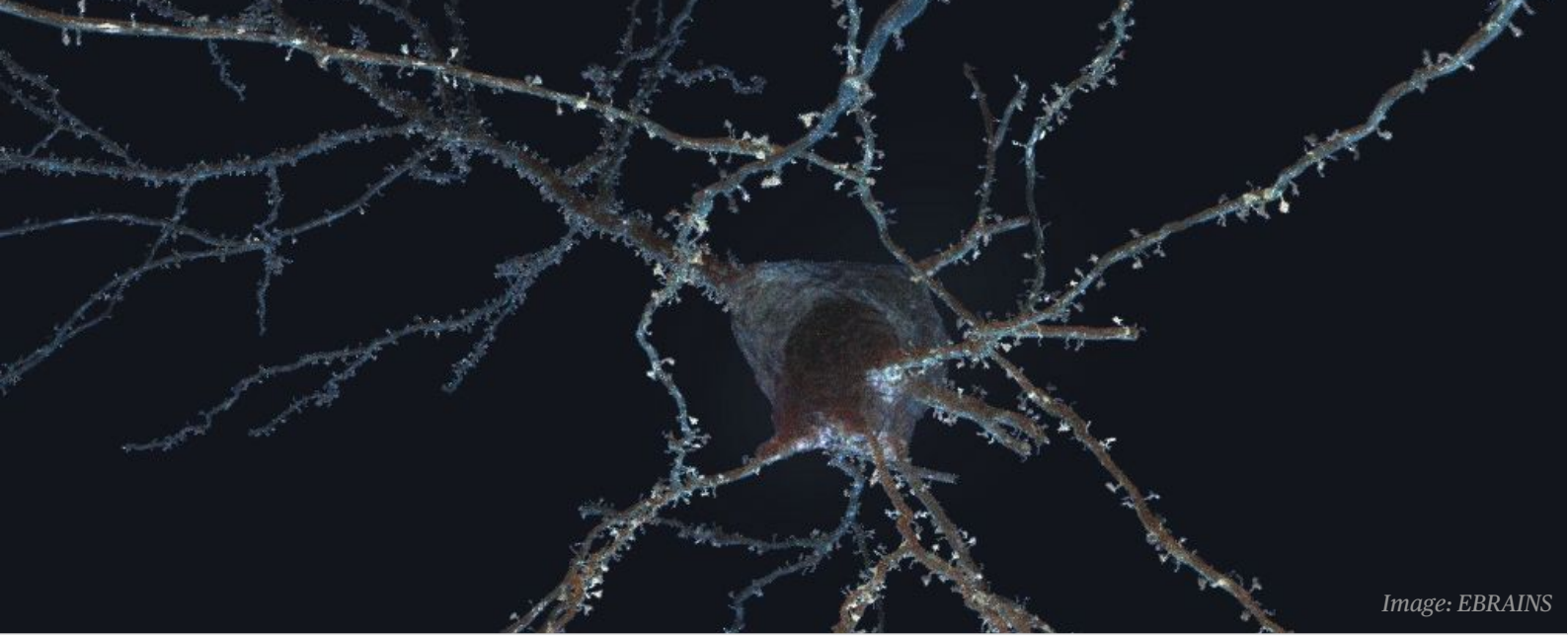

Image: EBRAINS

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UPM Innovation Team

LETTER FROM THE EDITORS

This issue of the **Innovation Newsletter** appears when the HBP SGA3 has completed its first half.It is therefore a good time to stop and review what has happened to date, assess the evolution of innovation in HBP, and present the innovation strategy to be addressed in the second half of SGA3.

During this past period, the Newsletter has reported on how innovation raised the interest for HBP participants to become a driving force for SGA3 activities. Today, the evolution of the **exploitation plans** prepared by the work packages (45 received until now) has been instrumental in involving many research groups and increasing their awareness of the way that research results could be exploited for academic, industrial, and clinical use. It is also relevant to see that a number of spin-offs are emerging from the project.

Furthermore, the creation of the **Innovation Awards,** and the selection process behind them, have increased the visibility of some outstanding results within and outside the project. The two Awards delivered by the DIR in 2021 constitute an excellent sample of HBP results presented during the past HBP-EBRAINS Summit: The Virtual Epileptic Patient (VEP) and the Perturbational Complexity Index (PCI).

The **Innovation Team** has also tried to work closer to HBP researchers by providing them support in understanding key concepts on innovation and protection of their intellectual property through a set of **training seminars**, and by offering them advice for decision making towards exploitation by developing a set of **market analyses** on key results closer to the market.

The report on European brain technological start-ups developed last year was also the basis for the organisation of '**solution workshops**' where selected start-ups and HBP researchers met to find common ground for future cooperation in some areas.

The current issue of the Innovation Newsletter summarises one of the last solution workshops on neurostimulation developed last December, and the market analysis on the potential use of the HBP Brain Atlases. A general overview of the exploitation plans is also included.

The evolution and consolidation of **EBRAINS services** during the second half of SGA3 will be a catalyst for innovation. The maturity level of many of the HBP results integrated in EBRAINS services makes them ready to attract the interest of users in the three main market segments where our efforts are directed: academic researchers to accelerate their research agenda, industries to develop more advanced product and services, and clinicians to open the way towards therapeutic solutions.

To facilitate the maturation of EBRAINS, the Innovation team is engaged in assisting in the creation of a **vibrant open ecosystem** of users and entities linked to the research infrastructure, as part of our plans during the second half of SGA3 by strengthening the interaction with partnering projects (able to participate in future Innovation Awards). Through the **interaction with technology-based start-ups**, we not only encourage more projects to join us, but also motivate them to be protagonists in this journey, providing them open access to state-of-the-art technologies, data, and knowledge from hundreds of neuroscientists and informatics engineers. The meetings with highly innovative companies will provide the bases for enhanced bidirectional cooperation, by increasing the functionality of specific EBRAINS services and converting them into active users.

We are fully confident that 2022 will be a year of opportunities for HBP and EBRAINS. Hopefully, the impact of COVID-19 will be ameliorated by a continuing worldwide scientific effort, and additional funding opportunities for our brain activities at the European and national levels will allow us to accelerate research and innovation activities.

We are ready to support you in this exciting way. From the HBP Innovation Team we invite you to follow our next Newsletters and accompany us on this path of innovation and learning.

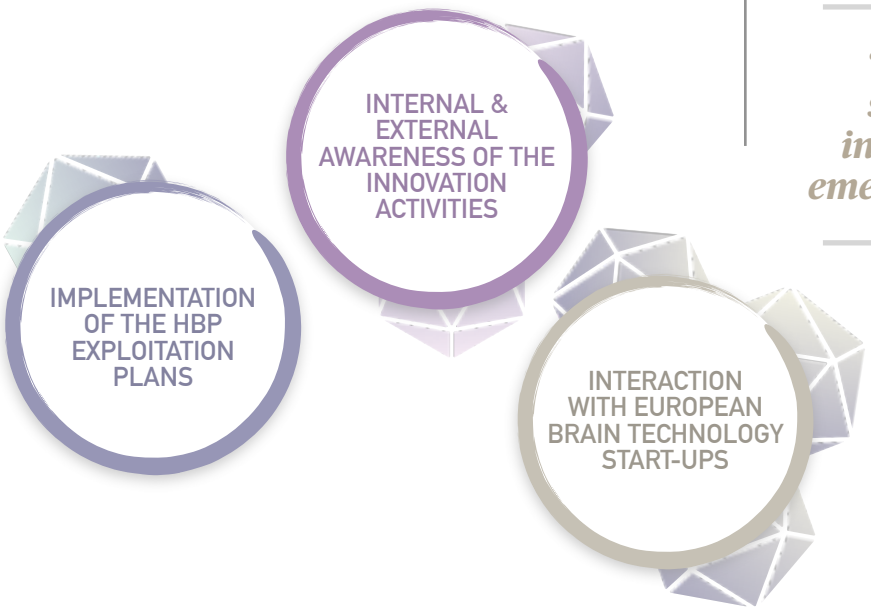
Wishing you a Happy New Year 2022!

Image: Freepik

A GENERAL LOOK AT 2022 ACTIVITIES ON INNOVATION SUPPORT

The beginning of a new year should be the right time to think about new challenges, to reschedule past activities, and to reaffirm commitments to community progress. This vision also applies to the Innovation Team in this crucial year for HBP and EBRAINS.

The support to HBP innovation in 2022 will have ***three main milestones***: to assist the implementation of the HBP exploitation plans, to increase the internal and external awareness of the innovation activities, and to devote much more effort to raising the interaction with identified European brain technology start-ups.



After the effort made in 2021 in preparing the 45 ***exploitation plans*** created by HBP research groups from all work packages, we need to work with their proposers to advance on the implementation of exploitation plans and to contribute to make them a reality. Special focus will be placed on supporting the creation of very innovative start-ups from the HBP emerging from the exploitation plans.

This process will be supported by ***internal training courses*** on technology and market vigilance and funding opportunities. Based on the experience of 2021, we need to reach a larger number of HBP researchers, mainly those related to the exploitation plans.

> *"Special focus will be placed on supporting the creation of very innovative start-ups from the HBP emerging from the exploitation plans"*

Furthermore, it is necessary to continue to assess the ***technology*** of the identified solutions to monitor their evolution. This activity will be supported through a new set of ***market analyses*** to identify opportunities to enter the market. During 2022, we will

make public the final versions of the market analyses on ***Brain Atlases*** and ***NEST desktop***, but also a new one on ***Neurostimulation*** with a focus on medical devices and its interaction with HBP, and another one on ***risk capital funding for brain technologies***.

We also note the need to continue increasing the awareness on the innovation aspects of the project. Then, the ***Innovation Awards***, opened this year to partnering projects, will be an excellent method to achieve this goal. The use of the ***Innovation Newsletters*** throughout the year and the continuous update of the ***Innovation pages*** on the HBP websites will contribute to this goal.

> ***"During 2021 two of these workshops (on brain imaging and neurostimulation) were organised and four will take place in 2022"***

To strengthen the interaction with start-ups in their double role as potential users of EBRAINS services and as providers of additional tools to enrich the research infrastructure, we will continue with the organisation of ***"solutions workshops"*** in new areas. During 2021 two of these workshops (on brain imaging and neurostimulation) were organised and ***four will take place in 2022***. With this activity, between 20 and 30 selected start-ups will be in contact with HBP researchers. It will complement the technical developments of the HBP firms after the open calls for industry engagement monitored by the innovation team.

In addition, we will organise a set of ***meetings with identified start-ups*** in those countries where national nodes of EBRAINS are being created. The intention is two-fold: to create the basis of industrial users of EBRAINS and to help in the exploitation of HBP results. Apart from ***Spain***, where the process started last December 2021, we will meet start-ups in ***Belgium*** and ***France*** in the first quarter of 2022, and then the process will continue in ***Germany***, ***Sweden***, ***Norway***, ***Italy***, ***Greece***, ***Switzerland***, and maybe other countries joining EBRAINS.

This is a very ambitious plan, but the innovative HBP results have reached the maturity level to allow them to be moved to external exploitation in academic, industrial, and clinical markets. ***Our role and wish are to be helpful in this challenging scenario.***

MARKET ANALYSIS COLLECTION

INNOVATION NEWSLETTERS

INTERNAL TRAININGS

SOLUTION WORKSHOPS

HBP INNOVATION WEBSITE

INNOVATION AWARDS

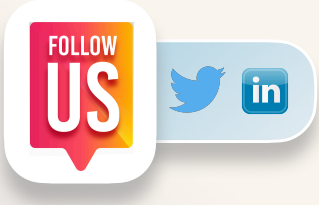
Image: Ministry of Science and Innovation, Spain. EBRAINS.

HBP-EBRAINS START-UPS MEETING

Last December 14th the HBP Innovation team organised a meeting where 25 start-ups working in brain technologies discussed and reflected on aspects related to the Spanish Neurotechnology innovation ecosystem. The event was held at the Spanish Ministry of Science and Innovation. The meeting was chaired by Teresa Riesgo, Secretary General for Innovation, Inmaculada Figueroa, Vice Deputy Director General for the Internationalisation of Science and Innovation, Asunción Gómez, Vice-Rector for Research, Innovation and Doctoral Studies at Universidad Politécnica de Madrid, and Gonzalo León and Guillermo Velasco, both from the Universidad Politécnica de Madrid and leaders of the innovation area at Human Brain Project.

The event aimed at presenting HBP to the companies and explaining the services offered by the research infrastructure EBRAINS, thus opening the way to potential collaborations. Furthermore, the report **"Where is European Brain-Innovation happening? The role of tech-based start-ups"**, elaborated by the HBP Innovation team was presented. Finally, there was an open debate - moderated by Lluís Blanch, coordinator of the Innovation Platform in Spanish Health (ITEMAS) - on the opportunities emerging from the ecosystem.

The participating start-ups showed great interest in the project and so far, four of these companies have already expressed their interest in engaging with HBP and joined the Spanish Innovation Community.



A MARKET ANALYSIS OF THE MULTILEVEL HUMAN BRAIN ATLAS

Today's world witnesses unprecedented advances in our understanding of the human brain. With some of the main global players investing remarkable resources in further exploring its structure, connectivity and function, Europe should not miss out. In its quest to continue at the forefront of brain mapping, an outstanding European flagship result is the EBRAINS Multilevel Human Brain Atlas.

In this market analysis (to be published in February 2022) we provide a brief introduction to the working principle of brain atlases, its templates and parcellations, to then analyze the current situation of the HBP Atlas. For this aim, we classify the Atlas content into a two-level scheme, differentiating between that exposed by the interactive 3D viewer "siibra-explorer" and that only accessible in the form of curated datasets through the EBRAINS Knowledge Graph (KG) database. We conclude that high quality datasets are offered and that notable efforts are being made to add value and integrate results from other brain initiatives (e.g., JuGEx, developed using gene expression measurements from the Allen Brain Atlas). As part of this first analysis of the Atlas we also consider its IT infrastructure, concluding the interactive possibilities offered by the 3D viewer as well as the growing need to provide programmatic access to the data, an aspect that is now addressed with the development of *siibra-python* [1] and the http interface *siibra-api*.

We conclude that high quality datasets are offered and that notable efforts are being made to add value and integrate results from other brain initiatives

The second part of this analysis explores the main brain initiatives in the world, namely those part of the International Brain Initiative (IBI). This review yields a list of other widely used and/or advanced brain atlases in the world, including the Human Connectome Project, the Allen Brain Atlas or the Harvard-Oxford Atlas. For the sake of discovering further differences between them and the HBP Atlas, we classify all into a taxonomy that results in 39 filters grouped into three broad categories, namely Content, IT Infrastructure and Other Miscellanea. All advantages and drawbacks found are then analysed through a SWOT matrix.

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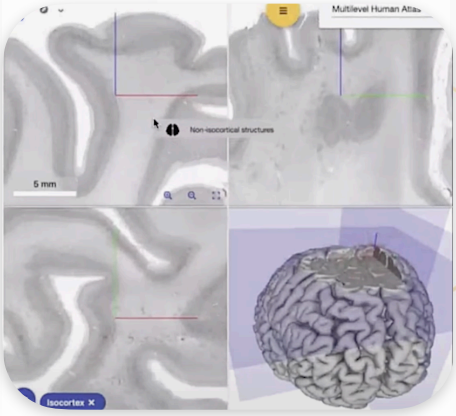
At the content level, four conclusions stand out. First, the most important brain atlases developed in the word so far do not -mostly- overlap with each other in terms of content. Second, that such avoidance of competition may be hindered when research is proved of strategic commercial interest (e.g., connectomics research for AI). Third, that nearly all atlases make use of free non-commercial licenses, with most of them -not the HBP Atlas- opting for customised licenses which enable to retain further commercial power (free non-commercial -unless granted- licenses), being this a key difference for the future exploitation possibilities of the data. Fourth, that even though the US Neuroscience Information Framework (NIF) used double resources (from multiple sources) than the EBRAINS KG, the latter seems to be the most powerful brain database available in terms of complementary services offered.

Regarding IT, almost all atlases provide a viewer specifically tailored for their own data, be it web-based or as a desktop navigator, with a shift to the former format the current trend. The 3D atlas viewer *siibra-explorer* offered by EBRAINS seems to be the most advanced, broadly usable web-based viewer to date. Regarding programmatic access, most atlases do provide it. Some even offer a complementary suite of applications, a software kit sometimes integrated within existing software (such as the JuBrain Anatomy Toolbox v3.0, included in the SPM suite). Until the recent development of the siibra-toolsuite, the lack of such programmatic access was found to be the greatest disadvantage with respect to its IT infrastructure. Competition between brain initiatives does exist in the IT realm, as they don't depend on each other to progress.



"The multilevel human brain atlas in EBRAINS: Features, use cases and future perspectives" by Timo Dickscheid. Watch it here

We rely on the opinion of several experts whose insights shed light on applied research, clinical and educational exploitation possibilities

The third and last part of the analysis concerns the exploitation of the Atlas. There we rely on the opinion of several experts whose insights shed light on applied research, clinical and educational exploitation possibilities. Some observations include how to transition from the information given in the atlas to its application in patients, or the need to have a platform that integrates information from multiple sources. For the latter, several interviewees agreed on the high potential of the data curation offer, as well as on the importance of creating needs in potential users, showcasing them that using the HBP Atlas could be of great benefit.

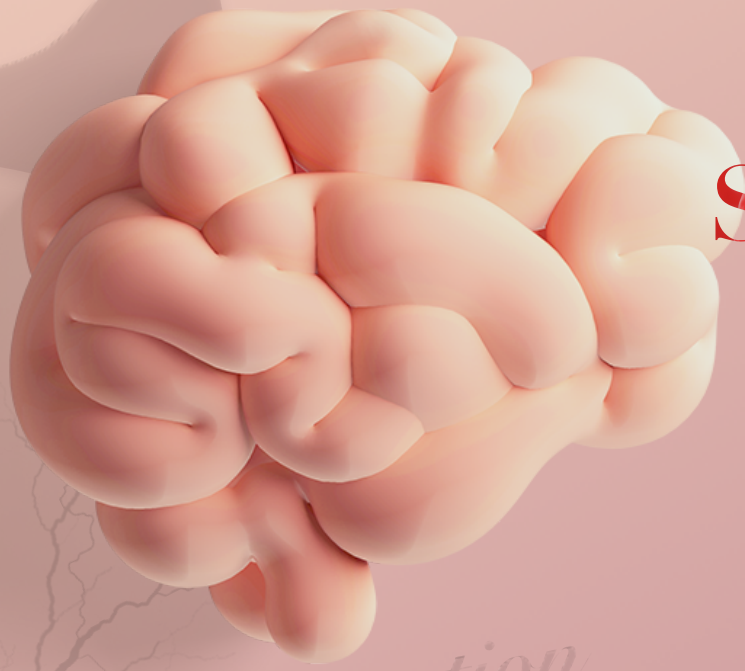
The UPM Innovation Team supports market analysis and exploitation plans for the Multilevel Human Brain Atlas* and other HBP technologies:

- Spiking network modelling and Training
- The Virtual Epileptic Patient (VEP)
- The Medical Informatics Platform (MIP)
- Brain Simulation & NEST

*Fernández, A., Velasco, G., León, G., Strange, B. (2021). The Multilevel Human Brain Atlas: A Market Analysis of the Technology. Human Brain Project.

7,404
histological sections of the BigBrain model

20 μm
cellular resolution of the BigBrain model



NEURO-STIMULATION SOLUTION *Workshop*

Innovation Team

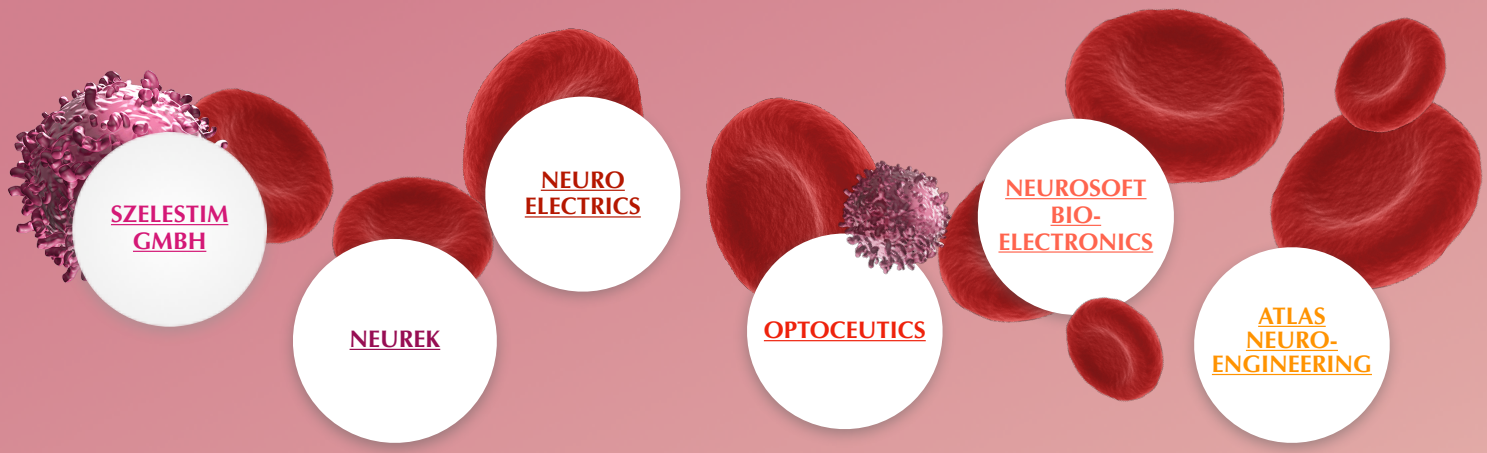
Last December 1st, the HBP Innovation team has organised the 2nd Solution Workshop, with a special focus in Neurostimulation technologies. As we announced in previous releases, these thematic workshops have been conceived to facilitate the interaction of HBP researchers and developers with a selection of start-ups working in specific brain-technology areas.

We firmly believe that engaging young tech companies to EBRAINS will contribute to the growth and sustainability of the infrastructure beyond HBP

The selection process drew on the recently published work done by the Innovation team: "*Where is European Brain Innovation Happening? The role of tech-based start-ups*". The elaboration of this report implied the searching and mapping of around 400 brain technology start-ups worldwide. A meticulous analysis that allowed a deeper understanding of the activities in which these projects stand-out, the trends for each area of specialty, and the possibilities that EBRAINS services offer to support their technology developments.

Seven HBP leaders were invited to the workshop to present the EBRAINS Data services, Knowledge Graph, QUINT, Multilevel Human Brain Atlas, the EBRAINS Modelling & Simulation tools, the Virtual Epileptic Patient, the Medical Informatics Platform, Elephant, and the EBRAINS registering and supporting process.

Six start-ups with excellent achievements in neurostimulation participated in the event: *Neuroelectrics* explores the circuit-based electrical nature of brain diseases, trying to adjust dosages dynamically and target specific brain regions to personalise therapies. *Neurek* is specialised in non-invasive brain stimulation and clinical applications of Transcranial static magnetic field stimulation (tSMS) devices. *Optoceutics* provides solutions to Alzheimer's, memory problems, anxiety, and depression by utilising non-invasive light tech-

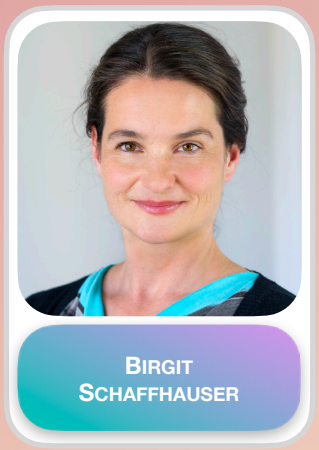


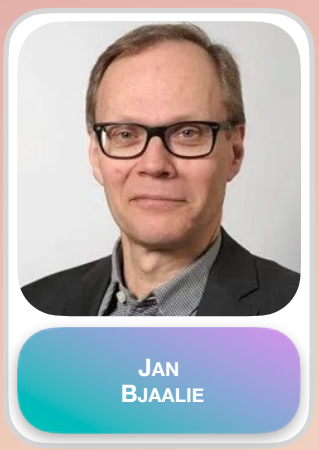
Start-ups participants

nologies. *Neurosoft Bioelectronics* is developing the next generation of seamless implantable electrodes to interface with the human nervous system. *Szelestim* is developing the first chronic pain management system based on auricular vagus nerve stimulation. And finally, the company *Atlas Neuro-Engineering* is focused on electrode micro-fabrication for in-vivo preclinical electrophysiology.

We firmly believe that engaging young tech companies to EBRAINS will contribute to the growth and sustainability of the infrastructure beyond HBP. For that reason, four other workshops will be organised during 2022. We look forward to being again, in those occasions, so brilliantly assisted by our HBP leaders' colleagues and observing in participant firms the same level of enthusiasm.

EBRAINS leaders present at the last solution workshop


Birgit Schaffhauser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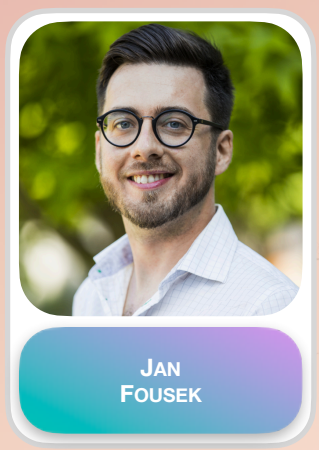
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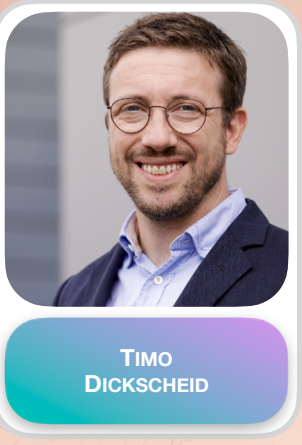
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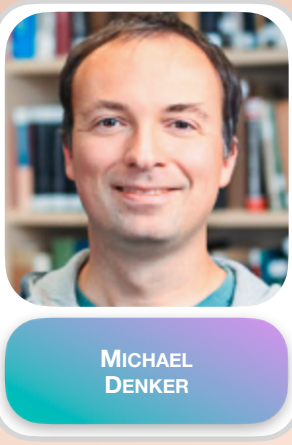
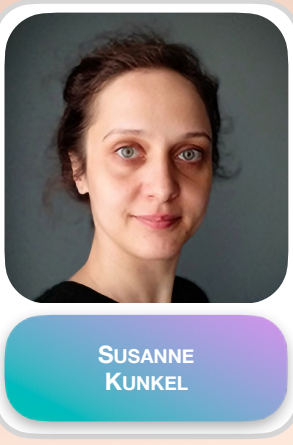

Michael Denker


Susanne Kunkel

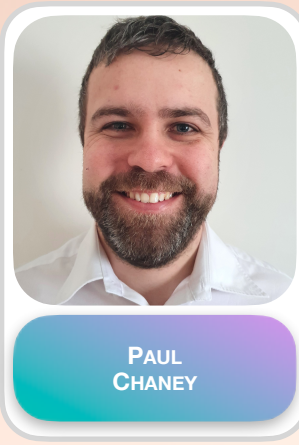

Paul Chaney

Image: Pexels/Gustavo Fring

EBRAINS: TOWARDS A NEW AVENUE IN NEUROSTIMULATION

Millions of people suffer from often debilitating and treatment-refractory neurological conditions -or neurological diseases for which there are currently no established effective treatments- including neurodegenerative diseases, brain injuries and mental health disorders. Worldwide, there are estimated to be 50 million people suffering from Alzheimer's disease and related disorders, the most common class of neurodegenerative diseases. Existing treatments for these diseases are limited in efficacy and mainly address symptoms rather than the cause or the progressive course.

Several non-pharmacological interventions have been shown to be effective and accepted by patients. For example, interventions may include nutrition, exercise, or neuromodulation/neurostimulation. Recent advances in neurostimulation research suggests its potential to harness endogenous neural plasticity, broadening the therapeutic possibilities to a diverse range of motor disorders. Early clinical successes hint at the power of this approach. Neurostimulation also help in the treatment of neurologic disorders that aid in the delivery of electrical stimulation to the intended parts of the patient's brain, peripheral nervous system, and spinal cord. These are particularly used for the treatment of various diseases, such as movement disorders, epilepsy, Parkinson's disease, chronic pain, and depression.

Neurostimulation is representing a major and very quick growth part of the neurotechnology market whose key players are giant medical device companies Medtronic, Boston Scientific, or Abbott (formerly Saint-Jude Medical) taking most of the market share. However, during the last seven years, market shares are moving slightly due to technology improvement in neurostimulation with smaller players bringing new technologies. Consequently, the number of different start-ups across EU and USA have increased during these last years.

Neurostimulation is representing a major and very quick growth part of the neurotechnology market whose key players are giant medical device companies

Some of the key factors driving the neurostimulation devices market include the growing elderly population, the introduction of technologically advanced products, escalating product demand as add-on therapy, and increasing incidence of chronic diseases, such as migraine and epilepsy, and the presence of highly unmet medical needs in these disease segments. On the other side, high prevalence of chronic pain disorders and growing product usage for pain management as a result of their high therapeutic value are also the key factors driving the growth of innovative devices.

In the face of these global issues, it is urgent to continue innovating in increasingly effective and specialised applications, which promote collaborative

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What technologies of this infrastructure stand-out to accelerate advances in neurostimulation?

and open science, but above all that they help to reduce some of the concerns that arise in clinical practice. In this context, during interactions between HBP/EBRAINS and healthcare industry and start-ups, questions arise such as: What technologies of this infrastructure stand-out to accelerate advances in neurostimulation? Which of these would facilitate the drug development and personalised treatments in this digital age against the offer of international initiatives?

We cannot know with certainty the global impact that these applications will have on the future in terms of neurostimulation or the pharmaceutical industry. However, our innovation team has worked together with their developers, clinical experts, leaders of start-ups in neurotechnologies, lecturers, among other actors, in an attempt to understand how HBP/EBRAINS can contribute further to reducing the technological, ethical, data, and other gaps that arise in medical research in these sectors that in one way or another are transferred to the market. Barriers that often limit the ability of the neuroscientific community and start-ups to generate greater social benefit while the prevalence of neurodegenerative diseases is increasing.

For a long time, we have advanced in a better understanding of the benefits of these technologies at the market level (through market analysis, evaluations of exploitation plans, market vigilance, etc.), scientific level (interviews, conversations with experts), intellectual property level (consultation to IP experts, business leaders), and clinic level (questionnaires, interviews), mainly. From the perspective of neurostimulation and with an open innovation approach, it has been useful to address how these solutions fit with the needs of some market players, and the increasing interest in these areas.

For example, understand how the Virtual Epileptic Patient (VEP), may improve neurostimulation therapies or surgical intervention strategies in patients with refractory epilepsy by identifying the brain regions that trigger epileptic crisis. Other tools such as the Multilevel Human Brain Atlas -*open access and based on the Julich-Brain Atlas*- are useful by allowing the integration of other software, exploring data at the molecular level (see the previous article) to support surgical planning. Another interesting achievements of the project, such as the Perturbational Complexity Index (PCI) or the transcranial direct current stimulation (tDCS), and the administration of apomorphine to patients with disorders of conscious (DOC) (Sanz et al, 2019), complete a non-exhaustive sample of the scientific efforts of HBP groups and how they are preparing to face the challenges in this area of neurostimulation and drug development.

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León, G., Velasco, G., Strange, B., Kireev, R., Gasset, B., Beltrán, A., Durán, T., Beltrán, B., Fernández, A., Chrayah,.M