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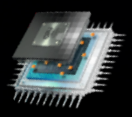
INNOVATION HUMAN BRAIN PROJECT Newsletter

N#4 · July · 2021

RECENT ADVANCEMENTS ON DEEP SPIKING NEURAL NETWORKS ALGORITHMS

EIC PATHFINDER CHALLENGE 2021

PATENT KNOWLEDGE NEWS



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FIRST HBP INNOVATION AWARD FOR VIKTOR JIRSA AND THE VEP TEAM

NEW BOOK RELEASE!
DATA-DRIVEN COMPUTATIONAL NEUROSCIENCE

COST
OPEN CALL FOR PROPOSALS

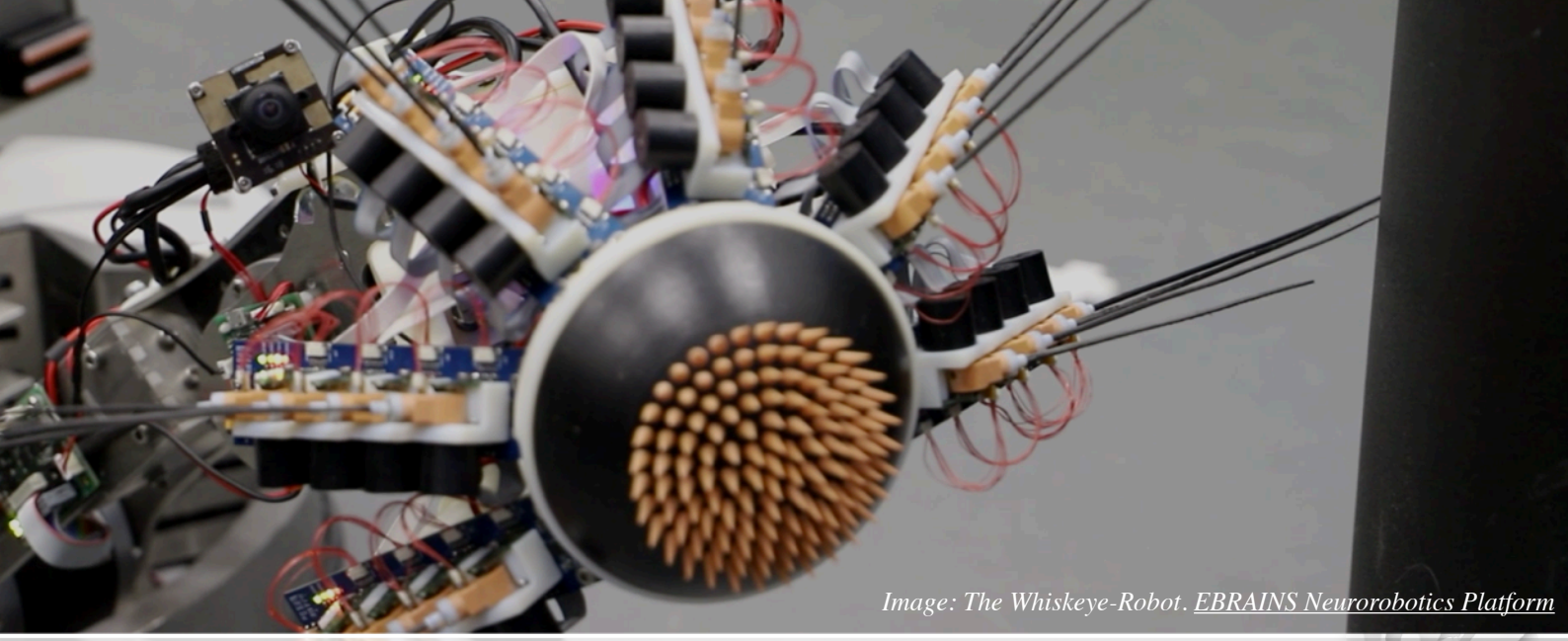

Image: The Whiskeye-Robot. EBRAINS Neurorobotics Platform

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HBP INNOVATION

BRAIN INNOVATION NEWS AND HIGHLIGHTS

FROM THE EDITORS

We have arrived at the beginning of summer 2021 with a lot of good news related to innovation in HBP. This newsletter #4 reflects the high level of innovation activities going-on and how they are playing a key role in the transition to a new phase framed in the excellent news that EBRAINS has been accepted as a new European research infrastructure in the ESFRI roadmap.

We have also decided to focus this issue on five activities which will be continued after the summer to target higher visibility during the HBP-EBRAINS Summit in Brussels next October, and beyond.

First, you can find an interview with Viktor Jirsa. Dr Jirsa and his VEP (Virtual Epileptic Patient) team were awarded last May with the first HBP Innovation Award. Congratulations from the Innovation team for the excellent work on VEP. The Award will be officially delivered during the next Summit in Brussels. The interview demonstrates how excellent collaborative research conducted over many years in the HBP has produced very innovative results which are reinforced by the on-going clinical trial and the first steps taken towards the creation of a start-up to exploit this innovative tool.

This issue also includes a summary of the main findings from a market analysis on deep spiking neural networks (SNNs) algorithms and their implementation on neuromorphic chips, developed by the Innovation Team in cooperation with the SpiNNaker and BrainScaleS groups. The report describes how the interest in this field is growing in its different approaches and how it will become a key driver to accelerate the training of SNNs. The elaboration of market analyses will gain momentum with the completion of the NEST desktop report, focused on Education markets, the Brain Atlases analysis, and the study made on the exploitation possibilities of the Medical Innovation Platform (MIP). Furthermore, an analysis of the pharma industry trends and needs and its relationship with EBRAINS services in also under way. All of these studies will be presented in the coming months.

One relevant activity which demonstrates the growing activity in innovation in HBP has been the preparation of 29 exploitation plans of HBP-EBRAINS specific tools. Among other multiple aspects, the plans include the market readiness expected of the results by 2023. In fact, some of these plans have started their implementation phase while others will gather speed during the next years. Globally, they reflect the HBP partners' strong commitment to move their research results to society through commercial and non-commercial products and services.

Another key activity during the last three months has been the analysis of European start-ups working on brain technologies. The intention was to classify their offers in terms of products and services which could have a relationship with EBRAINS. Understanding their challenges may serve as an input for the development and/or adaptation of future EBRAINS services, and as an instrument to approach them as potential EBRAINS users. More than 400 start-ups were analysed and categorised during the last months.

A specific outcome of this effort on start-ups has been the successful organisation of a "Solution workshop", with the cooperation of several HBP scientific leaders and the AISBL EBRAINS team. This represents the first of a series of thematic workshops, where a select number of start-ups (*Pixyl, Qubiotech, Mag4Health and Ti-Com*) related to the field of neuroimaging presented and discussed their offer and technology needs. The dialogues with the companies and the lessons learned before and during these events should serve to give continuity to this interaction and to explore ways of eventual collaborations.

The underlying intention of this initiative is to facilitate and increase the utilisation of EBRAINS services by external users. In this sense, the recent incorporation of seven companies through the HBP open calls has also demonstrated our firm commitment to co-create and cooperate with the industrial sector.

Finally, the newsletter offers some other relevant news around EBRAINS open calls, textbooks, and innovations. We are living exciting times within the brain research and innovation ecosystem, and we are sure that the EBRAINS infrastructure will become a key part of it.

The Innovation team is fully committed to bridge the gap between research and innovation, and I am sure that the HBP community will gladly support it. Enjoy this Innovation Newsletter!

Gonzalo León

HBP Innovation Team Coordinator
Innovation & Technology Transfer Node

Image: Freepik, @jcomp

FIRST HBP INNOVATION AWARD FOR VIKTOR JIRSA AND THE VEP TEAM

One more step towards a highly personalised medicine in epilepsy with the VEP. The scientific leader shares with us some of the experiences gained in the exciting and challenging journey of this fantastic technology.

UPM Innovation Team

Innovation does not just require new technologies and products, but also new applications, solutions. New product, process, and distribution technologies provide powerful levers for creating competitive value. With the proposal to promote innovation the Innovation Team and DIR created the "Innovation Awards" to recognize the on-going efforts made in innovation activities by HBP researchers and teams.

After the evolution of brilliant candidates, the DIR made the decision to grant the first Innovation Award to Viktor Jirsa and the Virtual Epileptic Patient (VEP) team. Here we would like to present the interview with Viktor Jirsa.

What is the problem addressed and the advantages of the solution provided? Please explain the contribution of the technology to the potential of EBRAINS.

Epilepsy is a disorder that affects 1% of the world population. 30-40% of epilepsy patients are drug resistant and candidate for resective surgery. In these cases, it is of great importance to know well the epileptogenic zone, which is the target of surgery. Our technology, the Virtual Epileptic Patient (VEP), provides the clinician with a computational tool for better decision making. VEP combines information from highly heterogeneous sources in a patient-specific brain model. For instance, the patient's own MRI data are used to reconstruct his/her brain connectivity and link it to computational models running on EBRAINS. Machine Learning techniques allow to further personalize the brain model to the patient's own brain imaging data.

"VEP combines information from highly heterogeneous sources in a patient-specific brain model"

The advantage of VEP is that it provides a balanced judgement of the contribution of the various factors influencing seizures, including regional epileptogenicity, the patient's brain connectivity, but also electrode placements. Furthermore, it can simulate brain activity, test clinical interventions, and reveal brain activity, which is not accessible otherwise. For instance, sometimes a clinician would like to have an extra electrode in the patient's brain, which could not be implanted originally, and VEP can simulate the electrode and generate the missing data.

How was the innovation conceived and by whom? We would like to know the role played by HBP in this conception.

I am the scientific leader of The Virtual Brain (TVB), a full-brain simulation platform, which was first released in 2012 as part of the efforts of the Brain Network Recovery Group (2005-2015), coordinated by Randy McIntosh and with participation of Petra Ritter. When I joined HBP in 2014, there was a crossing of three streams of development, that is my efforts in TVB, mean field theory building in HBP (*SP4), and the availability of stereotactic EEG epilepsy patient data in HBP (*SP3) and my home institution at Aix-Marseille University. When I tried to integrate these efforts, it became evident that they will be useful for the patient only, if we manage to render predictions patient-specific. With my colleagues from neurobiology, Christophe Bernard, and clinics, Fabrice Bartolomei and Maxime Guye, we then designed the steps for a workflow that leads from

Image: Viktor Jirsa
Institut de Neurosciences des Systèmes
Aix- Marseille University
Reference: "Virtual Brain Modeling for Epilepsy: The Next Generation"

the patient's data to the individual brain model and back to the patient and clinical decision making. TVB engineers Marmaduke Woodman and Huifang Wang did all the initial engineering. Every single step, such as epileptic mean field modeling (Epileptor), TVB seizure modeling, personalization of brain model through inference, was a task in HBP work packages during **SGA1, SGA2, SGA3, ultimately leading to what we know today as VEP workflow. All the colleagues above (except CB) are today members of HBP and have grown into a strong and engaged team working in the HBP ecosystem.

What are in your opinion the most impactful applications of the technology? How is the technology positioned in relation to other trends and solutions in the area?

Now, the immediate application of VEP is its diagnostic use in epilepsy, aiding in better identifying the epileptogenic zone of a patient. We use Monte Carlo Markov Chain (MCMC) techniques for the estimation of model parameters, which are powerful as they provide many diagnostics for reliability and confidence testing, but they are also notoriously difficult to use. Other technical solutions are easier to use (such as frequentist approaches) but provide no information on "how right or wrong they are" and do not allow to integrate prior knowledge (such as anomalies visible in the MRI). In our judgement, we think that the advantages of MCMC out-perform its difficulties. But the most impactful application in the long term will be the use of the generative modelling capacity of VEP, in which the patient-specific brain model is used to simulate brain activity under new conditions, other than the ones used to build it. This allows, for instance, to explore novel clinical interventions such as brain stimulation, which can be optimized to the patient's brain. I consider this the most original and distinguishing feature of VEP compared to other trends and technologies, which rather emphasize the data analysis than the data generation. It is also very much in the spirit of HBP.

The VEP team: (Outer circle clock-wise starting from the top) Jayant Jha, Spase Petkoski, Maxime Guye, Borana Dollomaja, Meysam Hashemi, Huifang Wang, Anuska Stoka, Lisa Otten, Marmaduke Woodman, Fabrice Bartolomei. (Inner circle clock-wise starting from the top right) Jean-Didier LeMarechal, Samuel Medina, Julia Scholly, Jan-Paul Triebkorn.

"This allows, for instance, to explore novel clinical interventions such as brain stimulation, which can be optimized to the patient's brain."

INNOVATION MANAGEMENT

What is the market potential of the technology? What type of users could be interested in utilizing it? Are there many users of the tool registered today?

The market potential of VEP is quite significant in a mid and longer-term perspective.

The entry point, the first functionality developed and meant to reach the market, is a pre-operative planning tool for the surgery of drug-resistant

epileptic patients. The patients' population eligible for surgery represents 10% of the global population of epileptic patients.

This first application of the technology is currently tested in a clinical Trial (EPINOV) including 13 of the most prominent reference centres of epilepsy surgery in France. The clinicians involved in EPINOV are today the main users of VEP. It essentially means that (i) the targeted future users are already using it in a prospective clinical trial environment, and (ii) we can reasonably believe that we are close to a commercial market release of the VEP soon.

As we progress and develop less invasive options (like the minimally invasive VEP), and develop or co-develop new functionalities (diagnostic, prognostic, therapeutic options with the neurostimulation, ...), the corresponding market potential will evolve and become more important. To be specific, there are now approximately 16.5 million drug-resistant epilepsy patients globally, and 1.2 of which in the United Sates, one of the markets we have obviously targeted for the future commercial release.

The next step, after the progressive penetration of the epilepsy market, will be to consider other types of neurologic and neurodegenerative diseases that TVB will help address. We will then switch to a much larger market potential and will be in a position to offer new alternatives to the neurologists, in an area where the clinical needs are largely unmet.

"Scientists and researchers, through partnerships that could be promoted, organized, or coordinated by EBRAINS, but also industry or clinical research consortia"

Beyond the clinical applications of the tool, other types of users will find a great interest in using TVB. I think here of scientists and researchers, through partnerships that could be promoted, organized, or coordinated by EBRAINS, but also industry or clinical research consortia, which could likely benefit from a tool like the VEP first, and its generalizations to other diseases later, for instance to optimize the findings and outcome of patients included in clinical trials in their domains. Although these are projections and aspirations for the future, they are becoming more concrete now.

How is the technology currently used or tested by researchers and other industrial or medical users? May you briefly describe your experience with the clinical trials?

A first version of the VEP technology is currently tested by medical users within the clinical trial EPINOV. The trial study is conducted in 13 hospital centers in France and has started in June 2019. The study will last four years and aims at guiding therapeutic strategies to improve surgical prognosis. It will include about 400 prospective patients (adults and children over 12) who have been diagnosed with drug-resistant epilepsy and identified as potential candidates for resective epilepsy surgery. The EPINOV Trial is the largest randomized multi-site trial ever conducted in epilepsy surgery and has been funded by the French scientific excellence program "Investissements d'Avenir" (Investment in the Future) entitled « Recherche Hospitalo-Universitaire en santé » (RHU) operated by the National Research Agency (ANR). The conditions in the past two years were challenging due to the sanitary situation, with intermittent closures of surgery centers, but as of today we have included more than 180 patients, of which 120 were randomized and virtualized. EPINOV is thus on track despite the difficult conditions.

What market-oriented steps you will take during the next two years? and after the finalisation of HBP? (Licensing, patenting selling, cross licensing, services, facilities, consultancy, personnel exchange, start-ups, joint ventures, etc.)

The decision to exploit the research and development around VEP and TVB has been made some time ago and the creation of a dedicated start-up, VB-Tech (VB-Tech for Virtual Brain Technologies), is now imminent. Its future CEO, Jean Marc Ferrier, drafted an ambitious and aggressive business plan and organized an international initial shareholders' group ready to support the project. You will probably hear more about this in the coming weeks. The start-up will coordinate and implement the technology transfer strategy, including the industrialization of the technology in a Quality Assurance environment, obtaining the CE mark for Europe and the 510(k) clearance for the US market as first priorities, and construction of the relevant commercial strategy to reach the market. As far as the possible options to reach the market are considered, several are on the table at this point: direct exploitation, licensing and distribution agreements, and co-developments with partners presenting synergetic technologies with the VEP/TVB.

Have you explored any venture capital (or similar) investing options to get funding?

Yes, of course we did. The first pre-seed and non-dilutive funding plan is in place, the SEED round is already planned as early as in 2022. The SEED round is the first capital opening to investors, in other words the first dilutive funding operation.

Early contacts have been made with several VCs, some in France, others in Europe, anticipating the future significant financial rounds (series A, B, ...) that will take place in the midterm. We will pay special attention to the choice of VCs that will accompany VB-Tech, as the quality of the relationship and the trust between investors on one side, and the management and science-engineering team on the other side, will be a critical success factor for the start-up. Essentially, we will be looking for investors clearly motivated and passionate about the project, and able to support us on the long term.

> ***"We will be looking for investors clearly motivated and passionate about the project, and able to support us on the long term."***

Could you summarise what have been, in general, the most important difficulties and barriers found (technical, economic, ethical issues, etc.)?

The technical development of the core technology has obviously been a great challenge. Here, dealing with the intra- and inter-patient variability in clinical real-world scenarios poses immense technical challenges and the VEP engineering team has been fantastic in this respect. In HBP today, two of its showcases are directly dedicated to this problem of variability. If you read texts of Daniel Kahneman, it is precisely such low-validity environments where algorithmic approaches should be used and can have the most impact.

Among the other difficulties encountered, one of the main challenges has been to build a highly multidisciplinary team including clinicians, neurologists and radiologists, data scientists, engineers, etc... who are critical in a project like ours to allow for an optimal transition from a purely scientific project to a translational activity, with the chance to have this technology benefit the patients one day.

If we further consider that the project has matured for a long time, involving different stake-holders and partners at various stages of the project and multiple funding sources, it is inevitable that interests have evolved heterogeneously, sometimes generating political tensions, conflicts of interests and divergent claims of ownership, and even pressure as the project evolves and

approaches the market. The management of this "project heritage", and the necessity to address and clarify all the pre-existing situations have definitely caused difficulties that I believe have been overcome by now.

CONCLUSIONS

What recommendations would you give to young scientists and researchers in terms of innovation and entrepreneurship?

If your aspirations as a scientist and researchers are geared towards clinical translation, I strongly recommend considering the equivalent of a science strategy of market pull, rather than techno push. Essentially, it means that you identify and analyse the challenges in the clinical real-world environment, and then derive the appropriate technology from your science to solve the actual problem. I often hear the comment that I got lucky with my clinical colleagues, but luck may not have played the major role. My clinical colleagues are outstanding (see my next point), but most importantly, they are engaged because VEP addresses one of their most important needs in clinical routine.

Next, bring on board the right partners, in relation with your final objective. As an example, if you plan to develop a new therapeutic innovative solution, you need a clinician in your team, who

"Identify and analyse the challenges in the clinical real-world environment, and then derive the appropriate technology from your science to solve the actual problem"

VIKTOR JIRSA-
RESEARCH LEADER WP1-
HBP - HUMAN MULTISCALE
BRAIN CONNECTOME

Read more about the Virtual Epileptic Patient

is an undisputable expert in the field. This needs to happen early to give the right orientation in your technical development. Not only this clinical partner will help you develop the right positioning for your technology, but he/she will be your first partner to evaluate clinically the technology you developed together.

Importantly, reach first a certain level of maturity and proof of concept before considering a transfer to the market, to be in a better position to attract early investors, and to negotiate their entry in the project in optimal conditions. As an example, in our project, the SATT SE (the Aix-Marseille University Technical Transfer Office (TTO)), has supported us efficiently in the (costly and time-consuming) maturation effort, which allows us today to consider the market transfer in very good conditions, with several strong assets (patents), with a prototype already developed, with the possibility to show an initial proof of concept, and with a technology already in the clinical phase of validation. Finally, if you consider bringing your innovative technology to the market, bring the relevant management resources on board early, as the entrepreneurial process is a more

and more complex one. The main two characteristics of the management resources you should be looking for are: experience, and personal fit between you and him/her. The HBP Innovation Team at UPM (Universidad Politécnica de Madrid) led by Gonzalo León and participation of Guillermo Velasco played an important role in supporting the development of these plans. Earlier this year they provided a state-of-the-art professional market review focusing on the VEP, including supplementary documents covering the top 5 collaboration opportunities and a list of potential VEP lead customers. This input was critical guidance for us in constructing the foundations of the start-up and its business model. It also demonstrates the high degree of dedication of HBP to accompany translation.

"This input was critical guidance for us in constructing the foundations of the start-up and its business model"

16.5

million drug-resistant epilepsy patients globally

- The UPM Innovation Team supports market analysis and exploitation plans for the VEP* and other HBP technologies:

- Spiking network modelling and Training
- HBP applications and tools for hospitals
- Brain Simulation & NEST
- Brain Atlases
- The Medical Informatics Platform (MIP)

*Duran, T., Velasco, G., León, G., Strange, B. (2020). VEP Market Review. Human Brain Project.

LEARN MORE

1%

of the world's population is diagnosed with epilepsy

*SP: supbproject (units in which the project was formerly organised)
**SGA1, SGA2, SGA3: phases of the HBP project (Specific Grant Agreements)

RECENT ADVANCEMENTS ON DEEP SPIKING NEURAL NETWORKS ALGORITHMS AND THEIR IMPLEMENTATION ON NEUROMORPHIC CHIPS

Advanced Spiking Neural Network (SNN) training algorithms are essential for the commercial utilisation of neuromorphic technologies. Recent advancements in the field are indeed inspiring new developments on adaptive artificial intelligence (AI). In this sense, we are proud to see how recent contributions of HBP to SNN learning algorithms are already adding value to the deployment of AI functions on neuromorphic devices. These algorithms improve the efficiency and accuracy of deep learning applications on brain-inspired chips and provide an efficient solution for on-device training. The maturity of these algorithms, together with the integration of emerging memories and event-based sensors, will surely open new and exciting opportunities in the edge intelligence sector.

Involving capital investors in the practical utilisation of SNN advances in industrial applications would contribute to creating a more solid and unified European voice in the area

This report presents a review of existing SNN training methodologies and their related technologies. It describes advancements within and outside the Human Brain Project, and identifies those components needed for an efficient, effective, and scalable training. A patent-application analysis has been conducted to reveal trends and actors, with the potential of SNNs and neuromorphic technologies discussed from the perspective of an emerging and impactful new market.

UPM Innovation Team

From a global point of view, the analysis reveals to what extent research efforts and investments on SNNs are accompanying the emergence of new AI industrial applications. While European scientific institutions are playing an increasingly important role as global leaders in the generation and dissemination of new knowledge in the discipline, we have also to assume that Europe is lagging behind other world regions in terms of industrial applications, to a large extent due to the reduced number of investment initiatives. USA and China are in fact showing more intense financial efforts and higher policy interest. Intel's and IBM's collaborations with European scientists as well as the acquisitions of European start-ups by Chinese and Japanese companies are evidence of such efforts. There is a risk, in sum, that talent drain processes start, since European researchers and developers could eventually choose to sign collaboration agreements overseas with companies that better guarantee the commercial exploitation of their technology advances and most attractive innovations. Involving capital investors to the practical utilisation of SNN advances in industrial applications would contribute to create a more solid and unified European voice in the area.

Image: Freepik @pressfoto

You can download the report “Recent Advancements on Deep Spiking Neural Networks algorithms and their implementation on neuromorphic chips: an emerging new market” in the following link:

LEARN MORE

It is a pleasure to include in this issue of the Innovation Newsletter a reference to the new book recently published by our HBP colleagues Concha Bielza and Pedro Larrañaga. It is a textbook with a lot of information for STEM advanced undergraduate or graduate courses on computational biology.

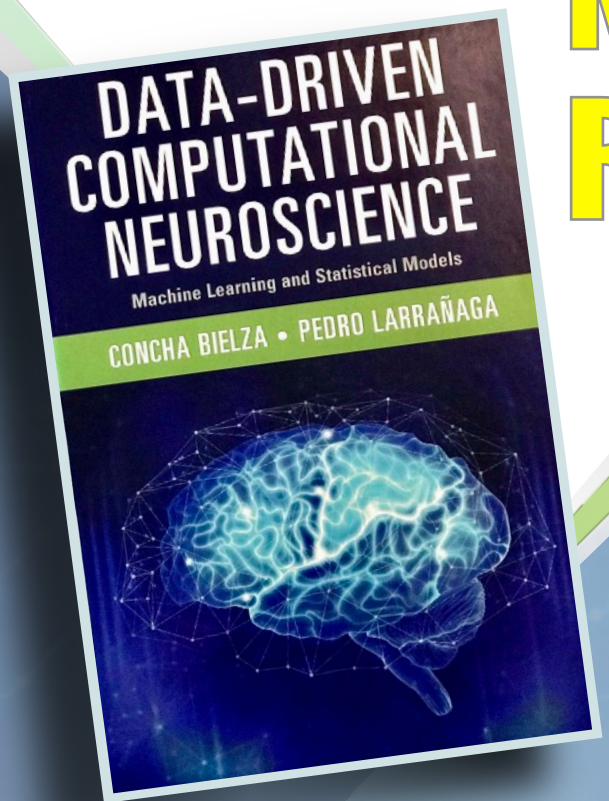
The book has been prepared in the context of the Human Brain Project as a very detailed diffusion of methods used today to process brain information by using machine learning algorithms. For the authors, a revolution in neuroscience must go hand in hand with statistics and machine learning, forming the data-driven computational neuro-science alliance. I fully agree on that, and the evolution of EBRAINS services and tools is an example in that direction where this book will help in the diffusion of techniques.

Let me reproduce here the comment made on this book by Rafael Yuste (Columbia University) a very well-known researcher heavily involved in the US BRAIN Initiative: "With admirable zeal, Bielza and Larrañaga have digested and summarized an entire field, the machine learning methods in computational neuro-science.

The critical importance of computational tools to analyze neural data and decipher the neural code has been emphasized by the US and international BRAIN Initiatives, and this book provides a sure and solid step in this direction."

"The book conveys practical content because we aim at solving real problems, and it is our wish that neuroscience practitioners understand, dare and use these techniques"
Bielza and Larrañaga

NEW BOOK RELEASE!



Concha Bielza and Pedro Larrañaga. Data-driven Computational neuroscience. Machine learning and statistical models. Cambridge University Press. 2021. ISBN: 978-1-108-49370-3

MERCK STIMULATES INNOVATION RESEARCH

Image: Adobe Stock, @James Thew

In 2021, **Merck KGaA, Darmstadt, Germany** is offering a series of research grants to stimulate innovative research in challenging areas of future importance. Grants of 40,000 € - 450,000 € per year for up to 3 years are available in the areas as further specified below.

- **Drug Discovery** - 3 grants comprising 350,000 €/year for 3 years with the option of extension.
- **Real time testing and sensors** - grant comprising between 100,000 - 500,000 $/year for 2 years with the option of extension.
- **Digital Innovation** - 3 grants comprising 40,000 - 100,000 € for 1 year with the option of extension.
- **Bioelectronics** - grant comprising 150,000 €/year for 3 years.

Submission deadline is 31 August 2021.

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EIC PATHFINDER CHALLENGE 2021

This call, launched by the European Innovation Council, has the aims of building new cutting-edge directions in the field of science and technology, creating new market fields or creating new innovative technological solutions based on high-risk / high-profit research. The European Innovation Council will finance technological solutions that are in the initial stages of development **(TRL 2-4).**

Applications may be submitted by a single entity or by constituent consortia by at least two independent entities belonging to member countries or associated with the EU.

Within the topic or thematic areas established by the call, we highlight the following related to the field of health:

- **Awareness inside:** New concepts of awareness that are applicable to systems other than human.
- **Tools to measure & stimulate activity in brain tissue:** A full device with unique features and/or new or nascent physical principles/methodologies that could be the basis for future brain sensing and/or stimulation technologies.

Image: Adobe Stock, @James Thew

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PATENT KNOWLEDGE NEWS

Image: epo.org

The European Patent Office (EPO) has launched a new online magazine called **Patent Knowledge News**, which will feature news, updates and facts relating to patent knowledge from the EPO and beyond. New articles will be published every two weeks in a dedicated section of epo.org and in the EPO newsletter. Topics to be covered by Patent Knowledge News will include - among others:

- ❖ Tips and tricks on how best to use Espacenet, PATSTAT, Global Patent Index and many other services in everyday business life;
- ❖ Articles about interesting aspects of patent searching;
- ❖The latest trends in game-changing and future and emerging technologies.

READ MORE

EUROPEAN COOPERATION IN SCIENCE AND TECHNOLOGY (COST) OPEN CALL FOR PROPOSALS.

Image: cost.eu

COST is a funding program for research and innovation networks aimed at connecting research initiatives across Europe and beyond, and enabling researchers and innovators to grow their ideas in any science and technology field by sharing them with their peers. COST Actions are networks with a duration of four years that boost research, innovation, and careers. Participants are invited to submit COST Action proposals contributing to the scientific, technological, economic knowledge advancement and development of Europe. Multi- and interdisciplinary proposals are encouraged.

Deadline: 29 October 2021.

HUMAN BRAIN PROJECT

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