1. INTRODUCTION TO THE CHALLENGE

The goal of the portfolio is to develop technologies offering novel therapy and diagnosis targeting the brain and the peripheral nervous system.

Specifically, the challenge is motivated by the untapped opportunities resulting from two parallel threads of scientific and technological progress:

- Increased understanding of the electrical activity in the brain linked to (i.e. causing or resulting from) brain-related diseases.
- Progress in our ability to observe and modify low magnitude electrical/optical/mechanical phenomena, by means of rapidly improving microelectronics, microfabrication, ultrasound transducers and sensors, optical sensors and light sources, etc.

Indeed, XXIst technology hinges to a large extent on sensing, amplification, transmission and processing of signals, often electrical in nature. These ever-increasing technological capabilities to deal with low-magnitude signals align well with the clinical need to monitor and modify the patterns of electrical activity in the nervous system.

This challenge called for ideas to extract the unrealised potential of current technologies (microsensors, electronics, actuators, etc.) to diagnose and treat the brain. Please see the Challenge guide for further details.

2. SUMMARY OF THE PORTFOLIO

<table>
<thead>
<tr>
<th>NUMBER</th>
<th>MAIN OBJECTIVES</th>
<th>IMPACT ON PATIENT</th>
</tr>
</thead>
<tbody>
<tr>
<td>HYPERSTIM</td>
<td>Cortical electrical neurostimulation prosthesis for the blind. Achieve effective increase of number of electrodes by means of novel complex stimulation patterns</td>
<td>Treat blindness</td>
</tr>
<tr>
<td>MINIGRAPH</td>
<td>Fully integrated implantable DBS device including ASIC, with graphene-enhanced electrodes and closed-loop design.</td>
<td>Treat symptoms of essential tremor and Parkinson’s disease. Potentially also psychiatric disorders.</td>
</tr>
<tr>
<td>INTRECOM</td>
<td>Implantable with 128 electrodes for speech decoding.</td>
<td>Treat locked-in syndrome</td>
</tr>
<tr>
<td>NEMO BMI</td>
<td>Spinal cord stimulator.</td>
<td>Restore walking function after spinal cord injury</td>
</tr>
<tr>
<td>CITRUS</td>
<td>Non-invasive trans-cranial stimulation by ultrasound technology. Increased spatial resolution by means of closed-loop architecture.</td>
<td>Treatment for neurological and mental health conditions.</td>
</tr>
<tr>
<td>MICROVASC</td>
<td>Monitoring electrical activity by means of microbubble-enhanced ultrasound. Target both evoked and spontaneous activity.</td>
<td>Improved neurovascular diagnostics</td>
</tr>
<tr>
<td>UPSIDE</td>
<td>Epidural implantable ultrasound brain stimulator.</td>
<td>Treat depression</td>
</tr>
<tr>
<td>CROSSBRAIN</td>
<td>Microrobot swarms for endovascular implantation. Achieve local release of viral vectors and divalent ions.</td>
<td>Treat Parkinson’s and epilepsy</td>
</tr>
<tr>
<td>HYPERPROBE</td>
<td>Intraoperative hyper-spectral optical activity sensing for neurosurgery guidance.</td>
<td>Improve brain cancer neurosurgery outcomes</td>
</tr>
</tbody>
</table>
The table above summarises the portfolio, tackling the Challenge with diverse technological approaches.

**APPROACH 1**

**ELECTRICAL STIMULATION/ MONITORING OF BRAIN ACTIVITY**

HYPERSTIM, MINIGRAPH, INTRECOM and NEMO BMI focus on advanced electrical stimulation or sensing for therapeutic purposes. HYPERSTIM will aim at treating blindness by direct stimulation of the visual cortex. This patient population is characterised by a complete loss of movement function, and therefore of any means of communication with the external world. INTRECOM will seek to free these patients and convert their thoughts into speech with a new implantable device. NEMO BMI will develop a new spinal cord stimulator capable of full walk function recovery after spinal cord injury.

As a subset in the portfolio, the five projects above share the use of electrical stimulation and sensing as their core technology, yet they explore different routes to achieve major clinical impact for patients.

**APPROACH 2**

**ULTRASOUND STIMULATION/ MONITORING OF BRAIN ACTIVITY**

Projects CITRUS, MICROVASC and UPSIDE propose the use of ultrasound technology. CITRUS seeks to modulate brain activity non-invasively to treat neurological and mental health conditions whereas UPSIDE will explore an alternative approach, an implantable ultrasound emitting device, to treat depression. MICROVASC, instead, will monitor rather than stimulate, by means of ultrasound to leverage the contrast afforded by microbubbles. The main application explored will be the diagnosis of neurovascular disorders.

This subset of projects will seek to elevate the impact of existing ultrasound technology to achieve unprecedented brain treatment and diagnostic.

**APPROACH 3**

**SWARMS OF “TINY” IMPLANTABLE DEVICES**

CROSSBRAIN explores the concept of microbots implanted endovascularly. The key idea relies on the development of small-sized devices, suitable for intravascular deployment, but capable of sensing neuronal activity and delivering multimodal stimulation (e.g. electrical and optical). The clinical goal is the treatment of Parkinson’s disease and epilepsy.

**APPROACH 4**

**OPTICAL TECHNOLOGIES**

HYPERPROBE will develop hyper-spectral real-time mapping of brain activity to be used in an intra-operative setting. Neurosurgeons will use this technology as part of neuro-oncology procedures in order to better identify the tumor mass versus healthy brain tissue.
3. PORTFOLIO LEVEL ACTIVITIES

CHALLENGES AND OPPORTUNITIES

Two main sets of activities are planned:

■ joint follow-up of progress along the technological development roadmap

■ targeted actions addressing specific portfolio hurdles.

3.1 PORTFOLIO TECHNOLOGY DEVELOPMENT ROADMAP AND JOINT FOLLOW-UP

An important element of portfolio-level management is the clear specification and follow up of technological milestones achieved by individual projects contributing to the common goals of the challenge.

To this end, a roadmap with quarterly objectives has been agreed jointly with each project coordinator. The set of nine roadmaps makes up the global time-line of the portfolio.

The portfolio beneficiaries will meet regularly to collectively, as an EIC challenge community, share their progress along the project roadmaps and to debate achievements and hurdles encountered.

The first gathering including all the teams in the portfolio took place in Brussels on the 7th of December 2022 in the context of the annual EIC Summit.

As an example see an anonymised example of a single project below.
Operational details:

- POs receive individual roadmaps from all coordinators. PM assembles from them the global portfolio roadmap.
- POs and PM coordinate with project coordinators date/time for all-project portfolio meetings.
- During the meeting, PM asks coordinators to share with the portfolio community the progress achieved along the time-line of the roadmap.
- PM, POs, project coordinators and project partners interact to, collectively, identify achieved milestones and discuss solutions to encountered hurdles (technical, regulatory, clinical, organisation, financial, etc.).

Planned Portfolio Plenaries and Project Events

- When: Q1 (Fall 2022)  Purpose: Portfolio kick-off event
  At the time of writing (Oct 2023), this meeting has already taken place as a satellite event of the 2022 EIC summit in Brussels. Each project team presented their objectives and main strategies to achieve them during the execution of their workplans.
- When: Q5 (Fall 2023-Winter 2024)  Purpose: Individual follow-up of the progress achieved by each project.
- When: Q6 (Spring 2024)  Purpose: Joint all-projects analysis of device development progress and identification of shared challenges for collective co-design of solution paths.
- When: Q8 (Fall 2024)  Purpose: Joint analysis of version 1 of the prototype devices/instruments and joint planning of the upcoming safety and efficacy validation phase.
- When: Q10 (Spring 2025)  Purpose: Joint all-projects analysis of progress towards safety and efficacy validation. Identification of shared challenges for collective co-design of solution paths.

When: Q16 (Fall 2026)  Purpose: Joint analysis of portfolio maturity level and prioritisation of the technologies for Transition to market. Joint design of the strategy for the upcoming Transition phase (from Q16 onwards).

TOPIC-FOCUSED SATELLITE WORKING GROUPS

Portfolio projects will benefit from interaction within smaller groups. These workgroups will focus on a specific technical goal, a common clinical indication or a narrowly defined topic-specific hurdle.

The budget provided to each project for portfolio level activities can be used to organize these satellite activities around specific interests. The creation of these events, meetings, internal demos, etc. will be carried out by the beneficiaries.

Operational details:

Beneficiaries communicate to PO and PM their willingness to create a working group within the portfolio. PO/PM accepts working group.

If requested by beneficiaries, PO provides contact details of other projects in the topic area to help the promoter of the working group in identifying partners.

Beneficiaries in a working group self-organise (meetings, visits, negotiation of potential collaborations, etc.). PO and PM can be invited to meetings of working groups.

Throughout the execution of the projects, the PM will identify common hurdles affecting all projects and setup an activity to address them. At the time of writing, two such bottlenecks have already been identified and according to actions have been designed, one has been implemented already as of June 2023.

3.2 EIC-DRIVEN ACTIONS TO ADDRESS COMMON HURDLES AS A COMMUNITY

A. CE MARKING HELPDESK

Virtually all neurotech projects face the challenge of progressing towards regulatory approval, CE marking. Particularly at early stage of technology development, within academic labs, questions arise regarding the regulatory path in the future. Moreover, early decisions in the development route will have a major impact on the speed at which the technology can be brought to patient through the appropriate regulatory channel once the technology has achieved the required level of performance and clinical validation.

To facilitate this path we have created a CE marking helpdesk, already active in June 2023 on the EIC Community Platform.
Our portfolio beneficiaries can log into the EIC community platform, and submit questions about CE marking. Regulatory experts are engaged to answer these questions. Further, these Q&A dynamics will be used to trigger interaction amongst portfolio beneficiaries on regulatory issues.

**Operational details:**

- Portfolio projects access EIC medtech community platform and submit CE marking questions.
- Experts engaged by EIC provide answers.
- Portfolio community can debate on the forum, or off-forum, and support each other’s efforts with previous experience. The CE marking helpdesk will function as a catalyst of interaction around regulatory topics when the need arises.

**B. RECEIVING CLINICAL AND/OR INDUSTRIAL FEEDBACK AND GUIDANCE**

An additional problem encountered by neurotech projects is product-market fit.

For a technology developed at EIC to reach patients, it must be perceived by clinicians and industry as advantageous for the patient, economically viable, regulation-wise acceptable, etc.

There is a risk of developing core technologies requiring deep academic knowledge but missing features or attributes perceived by clinicians and patients as necessary. These features are not easily identified by academic or SME beneficiaries who typically have a focus on tech development.

To address this potential hurdle, and in addition to the CE marking helpdesk, the neurotech portfolio will be offered opportunities to interact with industrial partners, clinicians and possibly patient associations.

**Operational details:**

The PM, PO and PM-experts, and others, will seek to identify partners (e.g. industry associations, hospital networks, patient groups, etc.) willing to provide the input required.

With the help of POs, PM will facilitate the interaction between these groups and our portfolio. Budget for said interactions will be sourced from the project’s budget for portfolio interaction.

In practice this means discussion meetings with e.g. clinicians, patients, etc. and beneficiaries, moderated by PMs.