HORIZON 2020

Ionic Neuromodulation For Epilepsy Treatment

Rendicontazione

Informazioni relative al progetto

IN-FET

ID dell'accordo di sovvenzione: 862882

DOI
10.3030/862882

Progetto chiuso

Data della firma CE
24 Settembre 2019

Data di avvio
1 Gennaio 2020

Data di completamento
31 Marzo 2024

Finanziato da
EXCELLENT SCIENCE - Future and Emerging Technologies (FET)

Costo totale
€ 3 369 758,75

Contributo UE
€ 3 369 758,75

Coordinato da
SCUOLA INTERNAZIONALE SUPERIORE DI STUDI AVANZATI DI TRIESTE
Italy

Periodic Reporting for period 2 - IN-FET (Ionic Neuromodulation For Epilepsy Treatment)

Periodo di rendicontazione: 2021-01-01 al 2022-12-31

Sintesi del contesto e degli obiettivi generali del progetto

Conventional therapeutic interventions, proposed for regulating nerve cell activity in brain dysfunctions, suffer from severe limitations and side-effects. With specific regards to the treatment of Epilepsy, pharmaceutical compounds are ineffective in 30-40% of the cases and, often, the ultimate route is resective neurosurgery with obvious serious risks.

Epilepsy is one of the major brain disorders, affecting more than 50M of people worldwide, and with a broad spectrum of underlying causes. The repeated nature of seizures exposes patients to physical and psychological harm, with a major negative impact on their overall quality of life.
Today's most ambitious neurotechnologies have hinted at future clinical approaches involving electrical stimulations or the advanced manipulation of nerve cells by means of light, magnetic, or ultrasound fields, requiring no systemic drug administration. They appear very promising and uniquely positioned for effectively tackling seizure suppression. And yet, all those techniques require invasive interventions, with necessary gene manipulation or "augmentation" whose long-term effects are unknown.

The IN-FET project explores a breakthrough microtechnological route to neuro-modulation, as an alternative to traditional electrical brain pacemakers and genetic engineering. It aims at controlling the pathological "excess" of electrical activity in nerve cells altering the local concentration of ions, key to neuronal activity, such as potassium and calcium. IN-FET focuses on three objectives:
• fabricating silicon microdevices, capable of advanced sensing of nerve cells activity;
• demonstrating how electrochemical modulation of ion concentration regulates cell excitability;
• combine cell sensing and actuation to suppress pathological electrical rhythms in vitro.

These objectives will be achieved under controlled in vitro conditions, laying the foundations for a subsequent exploitation of the technology in implantable devices for preclinical applications.

Lavoro eseguito dall'inizio del progetto fino alla fine del periodo coperto dalla relazione e principali risultati finora ottenuti

Despite heavily affected by COVID-19 containment measures, IN-FET's initial progress and results have been successful to pave the way to its most ambitious goals. The microfabrication processes, already selected and successfully validated to maximize the biocompatibility, have been first demonstrated in the design and fabrication of arrays of microtransducers and initially tested with nerve cells in vitro.

The consortium is implementing a contingency plan to accelerate the availability of a prototype further and dramatically for a complete system, based on CMOS arrays of microtransducers, an electronic amplifier, and an acquisition software.

Guiding the entire design process, there are in-depth studies of the combined nerve cell biophysics and silicon device performances, based on mathematical modelling and computer simulations. The core of IN-FET's proposed technological breakthrough has progressed despite the heavy initial lockdown restrictions, enabling first experiments with electro-activated polymers. Indeed, this was made possible by the contingency plan adoption of an existing platform based on substrate-integrated glass microelectrode arrays, as an intermediate technological step.

Wet lab activity restarted and proceeded at full speed, generating three "disease models in a dish" which may be immediately used for the proof of concept of both sensing and ionic actuation.

Dissemination and outreach activities progressed, through scientific publications, press-releases, and online/in person conferences or events, aimed at the scientific community as well as at the general public.

Progressi oltre lo stato dell’arte e potenziale impatto previsto (incluso l’impatto socioeconomico e le implicazioni sociali più ampie del progetto fino ad ora)

Our major progress beyond the state-of-the-art is represented by the established modelling and simulation workflow addressing, from first physical principles, the phenomena at the interface between the biological membrane of a nerve cell and a silicon-based sensing, or polymer-based actuating elements.

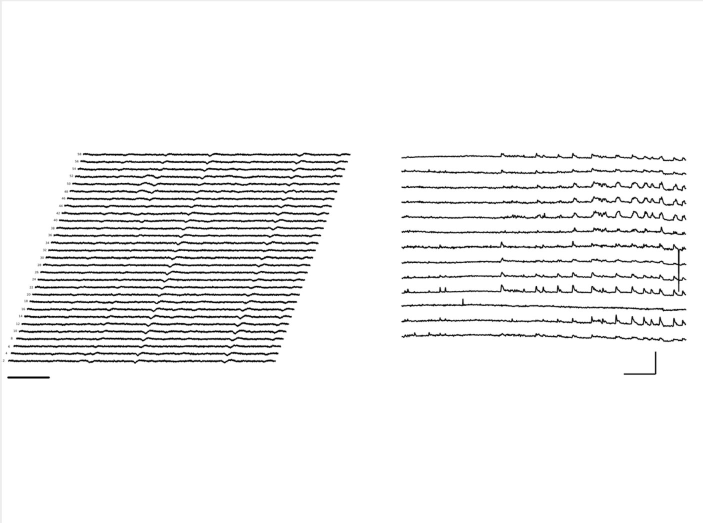
Another breakthrough is the generation of novel “in vitro disease models” of aberrant electrical activity, serving as an imminent benchmark and case study for the integrated IN-FET forthcoming technological platform.

The project progresses leveraged on the in-depth theoretical studies and are now focusing on the fabrication of novel CMOS-based high-density arrays of microtransducers with 3-dimensional cell-to-electrode interfaces, as well as to a voltage-controlled polymeric release of potassium ions in the extracellular medium.

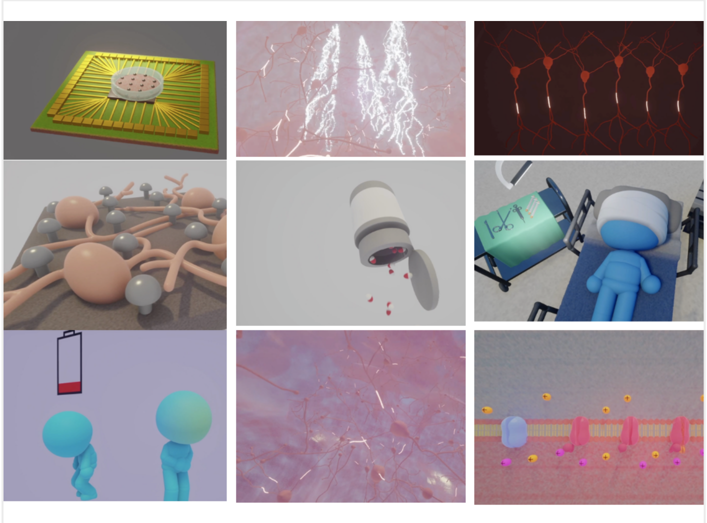
Even if only partially successful, the further development of all these directions (i.e. microtechnological, in vitro experimental, and theoretical/simulation) will advance neuromodulation technologies. The benefit, from a societal and economic point of view will be large as
• our proof-of-concept will offer immediately a novel platform for in vitro drug screening and studying of biological neuronal network activity, in in vitro models of functional and dysfunctional brain circuits;
• our proof-of-concept will offer an electroceutical alternative to pharmacological treatment of epilepsy;
• our breakthrough technological concept will immediately complement existing designs of neuropixel-like integrated arrays of microelectrodes, mainly used today as recording devices only;
• our novel neuronal modulation technology will compare more favorably for biocompatibility than genetic manipulations (e.g. as in optogenetics);
• our new type of microsystem will enable a new generation of future neuroprostheses, capable of neuron-selective high-resolution signal transduction in clinical therapies;
• our technology will boost the current understanding of neuronal information processing, complementing existing techniques, at single-cell levels.

Thanks to the presence of key industrial players in the market, IN-FET’s expected results will also have an important impact on miniaturized biomedical technologies, drug-screening platforms and microsystems that today already employ automated array systems and ad hoc microfluidics. It will immediately strengthen the global competitiveness of the EU industry in applications involving the screening of neuroactive compounds and drug-discovery, which today employ quite expensive automated patching platforms, one-cell at a time.

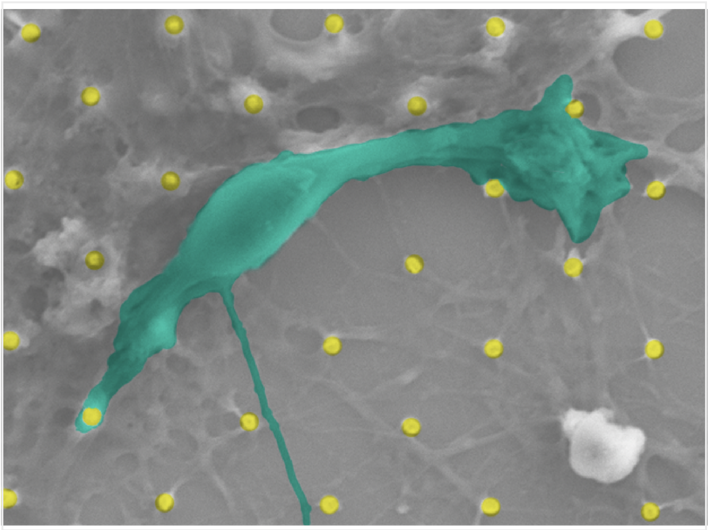
Ultimately, the high degree of collaboration at the level of junior scientists, co-supervised by different senior investigators will contribute to the next generation of innovators at the boundary between biology and ICT, keeping EU at the forefront of future emerging technologies.



First recording of neuronal activity via IN-FET technology, compared to conventional Calcium imaging



Rendering of IN-FET technology concept by a digital artist.



Scanning electron microscopy photograph of a rat nerve cell onto a micro fabricated Silicon chip

Ultimo aggiornamento: 1 Aprile 2024

Permalink: https://cordis.europa.eu/project/id/862882/reporting/it