

Press release

High-density multi electrode array goes 3D: 3Brain and CSEM present the groundbreaking Khíron chip

Probing the grey matter

Zürich/Neuchâtel, 25 October 2018 - A new gold standard for electrical measurement in the emerging *in vitro* world of three dimensional models. That's what Swiss medtech 3Brain has established by partnering with CSEM. Its Khíron chip enables fast, accurate intra-tissue measurement and continuous nutrient and oxygen supply through all tissue layers for the first time. And it is set to unlock the potential of next-generation cell culture models in disease modeling and preclinical studies.

Modeling systems have become a highly promising tool for understanding the mysteries of the brain, one of the biggest scientific challenges of the century. Over the last decade, three dimensional *in vitro* biological models such as spheroids and brain organoids have emerged, proving to reliably mimic the microenvironment of living tissues and bridge the gap with *in vivo* animal models. As the spatial distribution of cells in tissue affects gene expression, signal transduction and several biological functions, this 3D approach enables far better disease modelling and preclinical pharmacokinetic studies than its 2D predecessor. Increasing use of this revolutionary technique has, however, revealed the limitations of existing methods for measuring the activity of neurons packed in a 3D environment.

Revolutionizing recording from complex 3D neuronal assemblies

The 'z-dimension' poses serious limits on optical measurements as well as on conventional planar micro electrode arrays (MEAs). Standard cell culture model measuring techniques can only monitor events on the surface of biological samples, thus missing the neuronal processing taking place in the three dimensions. 3Brain, the first company in the world to design and realize high resolution MEAs, has developed a solution that overcomes all these complex technological challenges. "With our new technology we aimed to get inside the tissue and replicate the right environment with continuous cell perfusion so that measurements are much more predictive of what will actually happen in clinical trials," says Mauro Gandolfo, CEO of 3Brain.

3Brain, a CSEM spin-off, developed its new MEA chip in partnership with CSEM within an [Innosuisse](#) project. Together, the partners have introduced several innovations. "These include microelectronic circuit design to interface a large neuronal network, post-CMOS MEMS processing to fabricate 3D electrodes and a packaging solution compatible with the culture of biological *in vitro* models," explains Michel Despont, Vice-President and Head of CSEM's microsystems program, whose team also carried out biological validation with relevant neuronal models. "CSEM's ability to bring together this wide variety of competencies, combined with its long successful relationship with 3Brain, were instrumental in getting the chip for 3D brain tissue modeling to market."

Improving disease understanding and drug development success

Named Khíron, the new application-specific integrated circuit (ASIC) provides a high density MEA specifically targeting intra-tissue measurement of a 3D structure *in vitro* models by integrating a micro-needle for each electrode for *in vitro* penetration of brain tissue. It also includes a microfluidic structure at the base of the chip for fluidic exchange even from the bottom layers, unlike most conventional MEA devices.

"The Khíron chip gives neuroscientists the tool they have been waiting for to solve their problems and acquire the information they want from 3D *in vitro* models" says Dr Gandolfo. "I think it will have a big impact in disease modeling for Alzheimer's and Parkinson's and also in the study of conditions like epilepsy and autism."

3Brain will present Khíron at the SfN Society for Neuroscience annual meeting 2018 (3-7 Nov). The company will introduce its innovation to the market in 2019, initially targeting laboratories and universities interested in undertaking validation studies. It will then be integrated into the next generation of its products for the pharmaceutical and biotechnology sectors. 3Brain expects its new technology to double sales in two years.

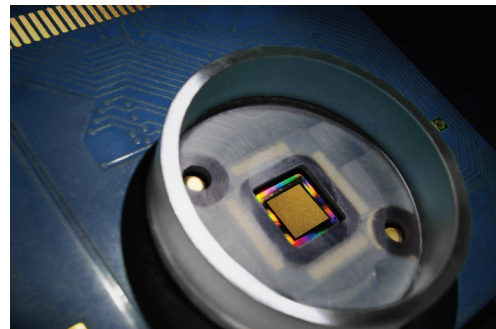
Khíron ID

The Khíron chip provides 4096 bi-directional recording and stimulating sensors in the shape of square micro-pillars, 20 μm wide, 80 μm high and spaced 40 μm apart, which penetrate brain tissue and organoids without causing damage.

These pillars have a larger pedestal which forms a matrix of 15 μm high microchannels at the base of the chip. This microfluidic structure enables nutrients and oxygen exchange for tissues such as

acute brain slices and brain organoids and means they can be kept under observation for longer.

Based on a third generation version of 3Brain's CMOS chip, the Khíron chip has enhanced signal sensitivity at both low and high frequency of the biological signal spectrum (0.1Hz to 2kHz) and significantly improved noise performance. Combining enhanced circuit robustness with an innovative light-shielding active and passive dual mechanism opens up the opportunity to use of optogenetic stimulation, an increasingly important modeling technique.



Khíron embedded in its substrate, ready to be used with cells.

Additional information

3Brain AG

Mauro Gandolfo

CEO

Tel: +41 813227086

Email: mauro.gandolfo@3brain.com

CSEM

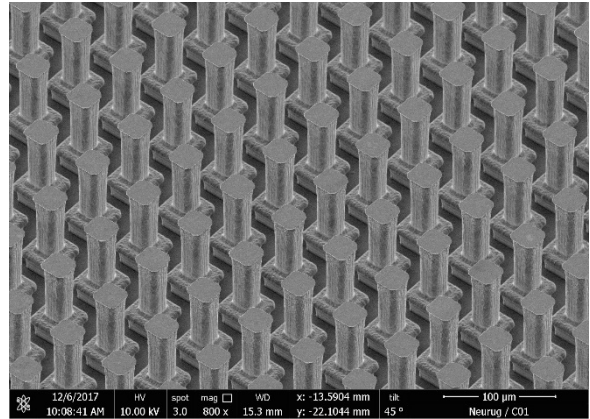
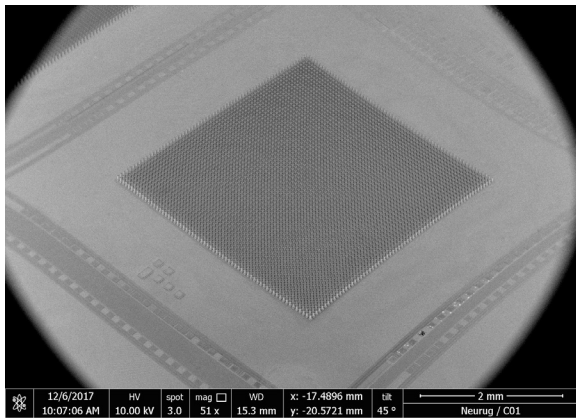
Michel Despont

VP, Head of microsystems

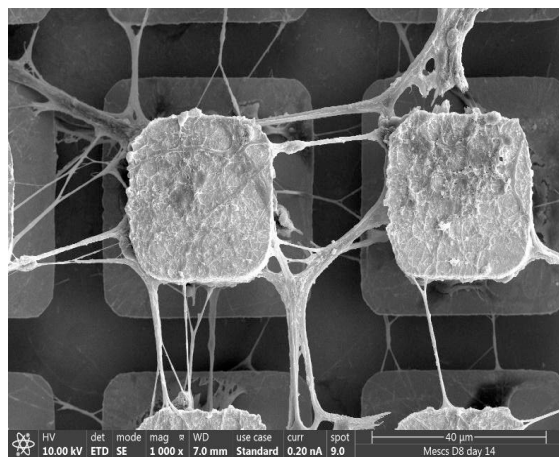
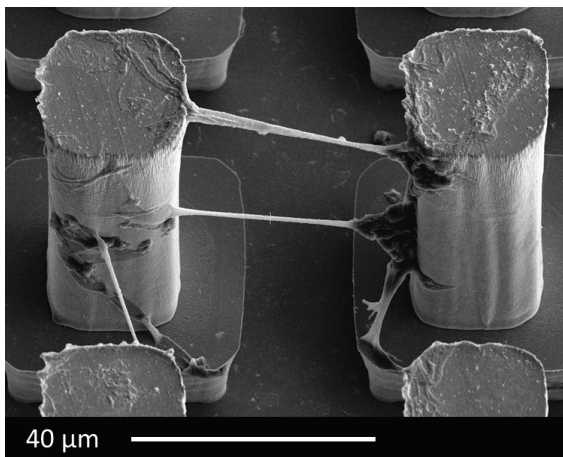
Tel. +41 32 7205478

Email: michel.despont@csem.ch

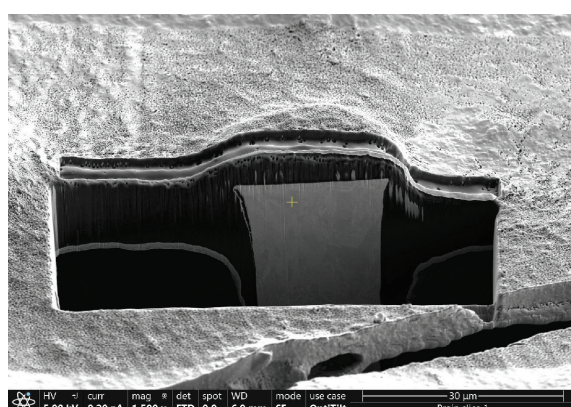
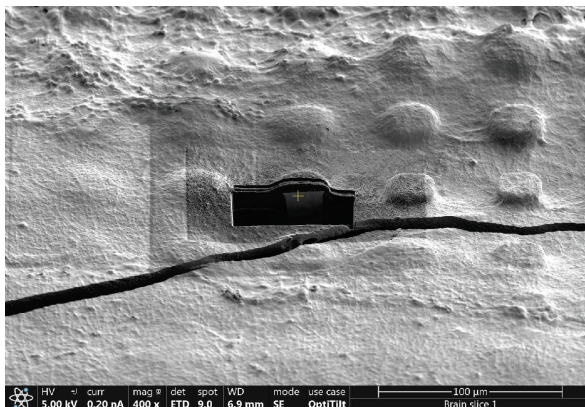
Illustrations ([HD pictures](#) (at the end of the web page))



The Khiron chip with 4096 3D electrodes (64 X 64 matrix forming a 4 mm X 4 mm sensing area)



Close-up of human neurons grown on 3D electrodes for 12 days



Close-up of a brain slice penetrated by a pillar

About 3Brain

3Brain strives to provide researchers with the latest breakthrough technologies to improve understanding of organs such as the brain and heart and their related illnesses. It is leading the development, manufacture, marketing and distribution of analytical equipment and sensor chips for research and development laboratories in the field of cell biology. Based in Zurich, it has already developed the first commercially available Active Pixel Sensor Multi Electrode Array (APS-MEA) whose ability to simultaneously record a huge volume of electrical signals has opened up new perspectives on neuronal network activity and the orchestrated complex signal processing that underpins high-level mechanisms such as learning and memory.

Further information is available at www.3brain.com

About CSEM

CSEM—technologies that make the difference

CSEM, founded in 1984, is a Swiss research and development center (public-private partnership) specializing in microtechnology, nanotechnology, microelectronics, system engineering, photovoltaics and communications technologies. Around 450 highly qualified specialists from various scientific and technical disciplines work for CSEM in Neuchâtel, Zurich, Muttenz, Alpnach, and Landquart.

Further information is available at www.csem.ch

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Media contact

CSEM

Aline Bassin Di Iullo

Strategic Communication Manager

Tel. +41 32 720 5226 Mobile: +41 76 577 4489

Email: aline.bassin@csem.ch

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