Epilepsy Innovation Institute (Ei²)

MY SEIZURE GAUGE WORKSHOP

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EPILEPSY FOUNDATION | Ei 2

My Seizure Gauge Epilepsy Innovation Institute Workshop Notes

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We graciously thank the workshop attendees for their participation and discussions before, during and after the workshop. Please see appendix for the list of all Workshop Attendees.

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Executive Summary

On August 28th and 29th 2017, the Epilepsy Innovation Institute (Ei^2) hosted an innovation workshop to assess the state of the science on seizure forecasting and risk assessment algorithms. The workshop convened multiple stakeholders including people impacted by epilepsy, basic scientists, clinicians, data scientists, device manufacturers, regulators and industry within and outside the epilepsy space.

Conversations centered on what is currently possible, what are potential future directions, and what critical infrastructure is needed to move seizure forecasting forward. The notes from the workshop discussions are outlined below.

Overview

The nerve cells in our brain communicate through electrochemical mechanisms. When this communication is disrupted by uncontrolled, synchronous neural activity, a person experiences a seizure. Depending on where the disruption in communication occurs, the seizure manifests itself through a range of sensations, behaviors, movements, and/or loss of consciousness that differ in severity and frequency. Any one of us can be induced to have a seizure under a variety of conditions (e.g. through sleep deprivation, stress, high fever, or ingestion of toxins).

Epilepsy is a common neurological condition characterized by the occurrence of recurrent spontaneous seizures. The World Health Organization estimates that there are over 50 million people living with epilepsy worldwide ("WHO | Epilepsy," 2017). About a third of people living with epilepsy do not have seizure control, and those whose seizures are controlled are at risk of breakthrough seizures (Brodie, Barry, Bamagous, Norrie, & Kwan, 2012). This staggering number has not changed in decades, despite over 14 new therapies for epilepsy entering the market since the 1990s (Löscher & Schmidt, 2011).

In 2016, the Epilepsy Innovation Institute (Ei^2), a research program of the Epilepsy Foundation, released an online survey asking their community what aspects of epilepsy impact them the most. Over one thousand individuals responded from across the United States and abroad. An overwhelming majority of respondents, regardless of seizure frequency and type, selected unpredictability of seizures as a top issue ("Epilepsy Foundation | Ei^2 Community Survey, 2016). Many wrote about the fear of not knowing *when* a seizure will start and not knowing *what* triggers the seizure onset.

In response to this survey, Ei^2 hosted an innovation workshop to assess the state of the science on seizure forecasting and risk assessment algorithms. The workshop convened multiple stakeholders including people impacted by epilepsy, basic scientists, clinicians, data scientists, device manufacturers, regulators and industry within and outside the epilepsy space.

The following themes emerged when assessing the state of the science:

1. Seizures have multi-temporal patterns on ultradian, circadian, and multi-day time scales,
2. Multimodal analysis of seizure events coupling EEG with non-EEG measures may enhance seizure forecasting algorithms,
3. Individualization and personalization of a seizure forecasting algorithm is necessary

The following themes emerged when discussing practical considerations for implementation:

4. An open-source platform for multimodal data integration, analysis and collaboration agnostic of device will catalyze the field forward,
5. Engagement with all stakeholders early in the process is necessary, and
6. The timing is right to move forward with seizure forecasting.

Each of these themes is discussed in more detail below.

Assessing the State of the Science

SEIZURES HAVE MULTI-TEMPORAL PATTERNS

An overwhelming body of evidence indicates that seizures have non-random time specific patterns (Bercel, 2006; Griffiths & Fox, 1938; Langdon-Down & Russell Brain, 1929; Loddenkemper, Lockley, Kaleyias, & Kothare, 2011). Recently, these findings have been replicated in long-term ambulatory intracranial recordings from people implanted with the NeuroVista device (Cook et al 2013 and Karoly et al 2017), and more recently in the Neuropace RNS (Spencer et al., 2016; Baud et al., in press).

The Neurovista device was used in the first human trial for an implantable seizure warning system with the purpose of demonstrating the viability of seizure forecasting in long-term recordings for people with uncontrolled seizures (Cook et al., 2013). The Neurovista trial implanted an ambulatory intracranial EEG system in individuals with drug-resistant epilepsy and followed them for over 18 months with the purpose of creating a seizure advisory system. In addition to the intracranial EEG, participants had a microphone recorder that allowed the doctor to hear audio for any potential detected event and verify seizure occurrence. After a year's worth of EEG data, a seizure forecasting algorithm was developed using manual feature definition. The Neurovista trial established feasibility of seizure prediction using EEG data with sensitivities above 65% for all 11 individuals who completed the data collection period. However, the trial also demonstrated the limitations of the used algorithms. While the algorithm indicated feasibility of seizure prediction in a clinical framework it failed to generalize across all individuals. The prediction algorithm was applied to short periods of time (up to 2 months of EEG data per patient) thus not investigating algorithm performance over extended periods of device operation (Cook et al., 2013). Long term recordings from Neurovista participants also indicated clear time-specific electrographic patterns that were subject specific (Karoly et al., 2017). More importantly, seizure forecasting algorithms were significantly improved by incorporating subject specific patterns in seizure occurrence with respect to time of day (Karoly et al., 2017).

The Neuropace RNS system (NeuroPace, Inc., Mountain View, CA, USA) is an FDA approved intracranially implanted neurostimulator system that can record, detect and store epileptiform activity. The type of temporal pattern varied among individuals but 98% of people with an implanted Neuropace RNS device have clear circadian and/or ultradian patterns for electrographic seizures (Spencer et al., 2016). Another

Neuropace RNS study examined seizure counts over a longer time-period ranging up to a decade. In addition to the circadian patterns previously reported, these researchers also observed multi-day cycles of interictal epileptiform activity varying between 7 and 35 days across patients, but relatively stable within each patient (Baud et al., in press). These longer epilepsy rhythms modulated seizure likelihood and were present in both male and females. This suggests that there may be multiple time scales layered within a specific individual that contribute to seizure likelihood. Taken together, the studies suggest that seizure-forecasting algorithms could be enhanced by integrating multi-time scale patterns into the overall algorithm for assessing likelihood of seizure.

In some ways, these findings are not surprising. In 1938, Griffiths & Fox looked at over 110 males who lived at the Lingfield Colony and whose seizures had been recorded for up to 10 years. The researchers noted that the patterns were not just in 24-hour cycles, but also had longer time rhythms that could span days, weeks, or months (Griffiths & Fox, 1938). Interestingly, they also observed the complexity of detecting time patterns, highlighting that within the group of 110 there was a lot of variability, but within an individual, seizure time patterns could be very consistent. Understanding these brain rhythms, why they happen and how they can influence seizure occurrences may be key to understanding seizure susceptibility for the individual, and thus to developing a personalized therapeutic strategy.

Additionally, the recent studies with implanted devices in ambulatory humans have demonstrated the unreliability of patient diaries (Cook et al. 2013; Velez, Fisher, Bartlett, & Le, 2016) and localization variability of temporal lobe epilepsy (Spencer et al. 2011). Both these studies highlight the need for reliable “gold standard” assessment of seizures when evaluating new treatments.

MULTIMODAL ANALYSIS OF SEIZURE EVENTS COUPLING EEG WITH NON-EEG MEASURES MAY ENHANCE BREAKTHROUGH INNOVATIONS FOR SEIZURE FORECASTING

EEGS are critical to understanding seizures but there are more pieces to the puzzle that can potentially enhance the seizure forecasting algorithms. The temporal rhythm of seizures suggests that there may be several metabolic or biophysical measures that could be detected prior to a seizure event. For example, several biophysical parameters are suggested to change slowly during or preceding a seizure including extracellular levels of potassium, oxygen, pH, and intracellular NADH/FAD+ (Jirsa, Stacey, Quilichini, Ivanov, & Bernard, 2014). Very fast oscillations (VFOs) have also been observed to precede seizure onset, and a review of the literature suggests that their occurrence may be due to gap junctions that are brain pH dependent (Traub, Whittington, & Cunningham, 2010).

Below is a table of potential markers to enhance future seizure forecasting algorithms that were discussed at the workshop. Most likely, we will need an array of variables to optimize our seizure forecasting algorithms. This array panel could be akin to cytokine inflammatory panels, where often one cytokine measurement without the other cytokine values does not explain what is happening in the system.

*Table 1 These measures could be collected in numerous ways: *indicates those that could be captured by patient diary, others could be measured through smartphone, biosensors or through sweat collection*

• Mood* • Cortisol • Orexin • Patient self-prediction* • Electrical Dermal Activity • Heart rate • Temperature / Weather • Respiration • Sleep cycle changes (sleep/wake staging) • Sleep quality	• Stress* • Fatigue* • Irritability* • Sex hormones • pH (brain) • Time of day* • Antiepileptic Drug levels • Blood oxygen • Inflammatory markers • Glucose • External environment	• Compliance • Illness* • Food/alcohol intake • Orientation (cognitive) • Gait • Finer movements • Ketones • Speech • Body Temperature

With advances in bioengineering, we have the capabilities to measure ionic changes *in vivo* coupled with intracranial EEG recordings. A recent study demonstrated that changes in the extracellular composition of potassium, calcium and magnesium independent of local electrical activity could distinguish which rodents were in a sleep brain state versus an awake brain state (Ding et al., 2016). This study highlights how measuring brain ionic changes *in vivo* could enhance our understanding of seizure vulnerable brain states.

There may also be multiple ways to capture information about an individual noninvasively that were previously impossible. In 2017, Mike Snyder's group provided the proof of principle for how commercially wearable biosensors could identify early signs of Lyme disease and inflammatory responses (Li et al., 2017)**.** With video and 3D imaging analysis, we are also now capable of mapping sub-second unites of movement that are indiscernible to the human eye to analyze behavior (Wiltschko et al., 2015). These tools could be used to analyze potential physiological and behavioral changes occurring hours prior to a seizure event. Sheryl Haut's group has reported that a subset of people living with epilepsy are very good at predicting their seizures up to 6 hours before the seizure event occurs (Haut, Hall, Borkowski, Tennen, & Lipton, 2013). These individuals kept a diary and reported premonitory features associated with accurate predicted seizure occurrence. The top ten features included blurred vision, light sensitivity, dizziness, feeling emotional, concentration difficulty, hunger/food cravings, noise sensitivity, tiredness/weariness, thirst, and difficulty with thoughts. This all suggests that there may be alterations in body chemistry, associated behaviors and symptoms that could improve seizure forecasting. Some of these body changes could be picked up through existing biosensors, mobile devices, or video monitoring. There are also preliminary findings reported by Dean Freestone, University of Melbourne, that atmospheric change such as humidity and pressure may be a variable in seizure likelihood for people with epilepsy. This intriguing finding suggests that the surround environments may also play a role in the analysis.

EEG is the gold standard for seizure detection, and any current seizure forecasting algorithm will need EEG validation of the seizure event. As seizures may cause altered awareness, patient seizure diaries are often unreliable (Fisher et al., 2012). Therefore, the goal in the short-term is to not exclude EEG, but to enhance our analysis capabilities by incorporating a whole host of other biophysical measures that could be coupled with EEG analysis to push the field forward in understanding seizure vulnerable states in the brain.

Seizure forecasting may be analogous to weather forecasting. Weather prediction has dramatically improved since the 1980's. Much of this improvement is due to the advances in satellite imaging that would allow additional variables from outside local regions to be included in the forecasting analysis (Wallace, Wallace, & Hobbs, 2006). New York City does not live in a silo, and therefore forecasting New York weather depends on changes in weather patterns around the world not just locally in the city. The brain, like New York City, does not live in a silo. The brain is a dynamic organ reacting to internal and external inputs. Similar to weather forecasting, we should be thinking about including additional measurements around the body and external environment in addition to EEG to enhance our understanding of seizure likelihood.

INDIVIDUALIZATION AND PERSONALIZATION TO A SEIZURE FORECASTING ALGORITHM IS NECCESSARY

There are many paths to a seizure and multiple causes for epilepsy. The International League Against Epilepsy (ILAE) has stratified the underlying causes for epilepsy into 6 categories: genetics, brain structure abnormalities, metabolism changes, immune system abnormalities, infectious disease, and unknown causes (Berg & Millichap, 2013). Not only are there multiple causes for a seizure, there are also varying responses to those causes. For example, in 1987, there was an outbreak of food poisoning from mussels. Over 100 people became ill from eating mussels containing domoic acid, but only 12 of them had to be hospitalized due to seizures (Perl et al., 1990)**.** This case study highlights the increasing complexity of the seizure susceptibility question. Not only are there multiple paths (causes) to a seizure, there also may be multiple thresholds within an individual that could lead to a seizure vulnerable brain state.

This complexity and heterogeneity suggest that pooling data across all people living with epilepsy is suboptimal. Data from the NeuroVista trial underscored that forecasting algorithms needed to be at the level of the individual (for review, see: Freestone, Karoly, & Cook, 2017). The periods of seizure likelihood varied greatly between individuals but remained consistent for an individual over many years (Karoly et al., 2016). The need for individualization also underscores the need for longitudinal data. Seizures are episodic events, and there needs to be enough seizures for the algorithms to be optimized over time.

In addition to individualization, personalization of the algorithm is critical. There are different utilities for knowing when someone is at risk for seizures. For example, some individuals may want to know when they are likely to have a subclinical seizure (an electrographical seizure without any outward symptoms) while others may only want to know when they are likely to be experiencing a tonic-clonic seizures (convulsions) or loss of consciousness. Some are troubled more than others by false positive warnings, which can elevate anxiety levels. There should also be considerations about what forecasting ranges are useful and what forecasting probabilities would be meaningful. Lessons learned from the Neurovista trial were that, although it was a mathematically sound way to characterize performance, a patient might have a different assessment of what a good performance algorithm means. Therefore, for any algorithm, a patient feedback loop is critical to ensuring specificity of the algorithm, successful adoption and good performance. One of the workshop participants likened it to a Pandora Music algorithm, where the user would hit like or don't like to the forecasting to ensure that the forecasting algorithm could be optimized and fine-tuned to the individual.

Deep learning has proven to be highly successful at automated complicated pattern recognition tasks in EEG (Nurse and Mashford et. Al, 2016; I. Kiral-Kornek et al., 2017) and multimodal data, and therefore constitutes a generalisable technique for a seizure prediction system that can be tuned to an individual's unique seizure data signature.

Practical Considerations for Implementation

AN OPEN-SOURCE PLATFORM FOR MULTIMODAL DATA INTEGRATION, ANALYSIS AND COLLABORATION AGNOSTIC OF DEVICE WILL CATALYZE THE FIELD FORWARD

For integration of longitudinal data to be possible on a multi-temporal, multi-modal time scale, there needs to be the ability to aggregate, harmonize and standardize multiple data sets. Longitudinal data is critical to this process as seizures are episodic events and the heterogeneity of seizures argues against pooling the data across individuals. Additionally, we need to have remote data mining capabilities that can use integrated bioinformatics tools to facilitate analysis.

Such a data system needs to be part of an Application Program Interface (API) ecosystem that would allow a plug and play approach for different cohorts of individuals using different sensors to be housed in the same database. Another key consideration for the platform is to ensure time synchrony of all the inputs enabling seamless data exploration across multiple parameters.

Currently, there are too few available data sets, which has subsequently led to overtraining for seizure forecasting algorithms. The overtraining may result in finding irrelevant patterns from the limited samples. Ideally, we would have a platform that would then allow researchers to test and train algorithms on data before moving forward to validate their proposed algorithms on a separate data set. The power of using these long-term data sets also allows for crowd-sourcing, which was extremely

successful in the Kaggle competitions which improved existing seizure detection and forecasting algorithms at relatively low cost (Brinkmann et al., 2016).

REGULAR ENGAGEMENT WILL FACILITATE SUCCESS

The Neurovista trial showed that seizure forecasting could be done, which led some to argue that seizure forecasting is now an engineering problem. The questions should be geared towards optimization and reducing the invasiveness of the procedure. As we begin to examine this question and think about the end product, all the stakeholders (from people impacted by epilepsy, scientists, clinicians, and industry, to regulators and payers) should be brought to the table to ensure usefulness and success of the product under consideration, that is being brought to market.

Too often, a researcher may have expertise on how to conduct research but not have training in other areas to advance healthcare solutions such as clinical operations, regulatory, and/or business expertise. Researchers may mistakenly assume that commercial issues are not important until later on in the process, which can contribute to unforeseen delays of bringing a product to market. However, if those considerations are addressed earlier on in the process, it helps improve the efficiency of the health care cycle.

A key stakeholder that is often missing from the conversation is the patient. People impacted by epilepsy can be willing partners of the research process and can provide invaluable insights to the product design and the usefulness of the algorithm. They have the most at stake for a seizure-forecasting algorithm. As discussed in the individualization and personalization section, having a patient feedback loop incorporated in the training of a seizure will ensure that it can be a sustainable, viable and meaningful product.

As we begin to explore uncharted therapies for potential devices, there are also opportunities to obtain FDA feedback on pre-marketing submissions early on in the research process and ensure that studies are designed to address FDA concerns. For example, learning algorithms *can* be incorporated into FDA approved devices, as long as they are for a fixed interval and correctly indicated for their intended usage during that time. Therefore, as one considers a seizure susceptibility assessment algorithm and potential device prototype, one should also have the end-goal (a product for people living with epilepsy) in mind and reach out to the regulators early on in the process.

Moreover, as developers consider biosensors, or smartphone capabilities to be part of the seizure forecasting algorithms, one should be aware of the regulatory guidance that may be beneficial. For example, the Food and Drug Administration (FDA) issued guidance on medical mobile applications (https://www.fda.gov/downloads/MedicalDevices/.../UCM263366.pdf), general wellness guidance products (http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/uc

m429674.pdf), and benefit risk considerations (https://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm506679.pdf) for devices.

What was not discussed at the workshop but should also be considered is the return of results to the individual. What is our ethical obligation to the participants in letting them know their seizure forecasting results while the algorithm is in beta testing and accuracy has not been verified?

THE TIMING IS RIGHT TO MOVE FORWARD WITH SEIZURE FORECASTING

The Holy Grail for seizure prediction has been sought after for decades. Why would this time be any different? There are a couple of existing factors that were not around decades ago that could enhance our chance for success.

1. Previously, we only had short-term intracranial EEG data (typically up to 1 week) for analysis from pre-surgical monitoring units (Mormann, Andrzejak, Elger, & Lehnertz, 2007). The short-term recordings are too limited of a time span with limited interictal and ictal data to build patient-specific models for seizure likelihood. There are now over a thousand individuals who have ambulatory intracranial EEG systems through the FDA approved Neuropace RNS system or through the Activa PC system by Medtronic in clinical trials. This allows us to have access to real-time longitudinal data (on the magnitude of years) of EEG recordings. We need EEG to ensure that real world seizure events can be validated against the current EEG gold standard in this patient population. Moreover, there are now several companies starting to develop less invasive long-term EEG recording devices.

2. With the advances in bioengineering and biosensors, we have the capability to acquire noninvasive multimodal data that allow us to identify potential lead candidate signals that inform about seizure probability to circle back and test. Indeed, sweat sensing technologies have advanced rapidly in the past 5 years. It will soon be possible to have noninvasive continuous monitoring of various metabolites such as cortisol, something that was not possible previously (Bandodkar & Wang, 2014; Rose et al., 2015; Sonner et al., 2015). There are also optical measures of motion and stress that can recognize heart rate and respiration at a distance (Nam et al., 2016). Furthermore, the emergence of brain-inspired – so called neuromorphic - processors capable of running advanced machine learning models at ultra-low power consumption allows real-time analysis of biomedical data at the point of sensing in always-on mode which is a prerequisite for developing wearable or implantable seizure prediction systems. (Nurse and Mashford et al., 2017; Harrer et al. 2016; I. Kiral-Kornek et al., 2017)

3. Large-scale machine learning capabilities have advanced. Machine learning is not the answer for all problems, but it works well with unstructured data. However, for such an approach to be meaningful, subject matter expertise is critical to ensure accurate classifications of the data and

interpretable results. For example, mathematical modeling of electrophysiological signatures of seizures conserved across species from flies to humans has yielded 16 different seizure categories (Jirsa et al., 2014). This new taxonomy may spur potential new insights into seizure mechanism that could help interpret the data findings and find correlations in body chemistry associated with these different seizure classifications. Moreover, insights into seizure onset mechanisms from a dynamical systems perspective may help identify useful data features (Meisel & Kuehn, 2012) to integrate into machine learning algorithms.

Next steps

The overarching goal of Ei^2 is to lead an effort that would create an individualized seizure gauge that will allow a person with epilepsy to monitor the likelihood of a seizure on a daily basis. From the Innovation Workshop, it is clear that Ei^2 should focus on identifying and better understanding the changes in the body that may precede the onset of a seizure, at a time course that may be hours or days before the clinical (observable) seizure. For this effort, following a cohort of individuals with already implanted intracranial EEGs such as the Neuropace device and measuring a host of non-EEG based methods from emerging biosensors and wearable device technology on a longitudinal time scale would help advance the seizure forecasting field forward. Specifically, it can help us begin to think about what the array of parameters should be for calculating seizure likelihood. As companies begin to develop less invasive EEG approaches (such as the UNEEG device), it will also be important to assess the validity of these less invasive methods and whether they could be substituted for intracranial EEG monitoring moving forward. This effort although initially focused on implantable EEGs could then expand to other cohorts to test the generalizability of results.

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Appendix: Workshop Attendees

Adam Willamson, PhD Head, Neuroengineering Subgroup ERC Research Fellow Institut de Neurosciences des Systemes (INSERM)	**Daniel Friedman, MD** Neurologist New York University Langone Medical Center	**Jay Gupta** Branch Chief, Neurological Devices Center for Devices and Radiological Health Food and Drug Administration
Amanda Christini, MD President Blackfynn, Inc	**Dean Freestone, PhD** Senior Research Fellow University of Melbourne	**John Murphy, PhD** Vice President of Research & Development LivaNova (unable to attend in person due to Hurrican Harvey
Anna Belle, PhD Postdoctoral Researcher Center for Micro and Nano Technology Materials Engineering Division Lawrence Livermore National Laboratory	**Doug Sheffield, VMD, PhD** Chief Scientific Officer Cadence Neuroscience	**Kent Leyde** Owner Cascade Medical Devices, LLC
Barbara Jobst, MD, PhD Professor of Neurology Dartmouth University	**Edmund (Ned) Talley, PhD** Program Director Channels, Synapses and Circuits Cluster & Brain Initiative National Institute of Neurological Disorders and Stroke (NINDS) National Institutes of Health (NIH)	**Kathleen Farrell, MB BCh BAO** Senior Clinical Program Manager Epilepsy Foundation
Ben Brinkmann, PhD Assistant Professor of Neurology and Biomedical Engineering Mayo Clinic	**Gardiner Lapham** Research and Health Care Advocate	**Liz Higgins** Manager, Research Administration Citizens United for Research in Epilepsy (CURE)
Brandy Fureman, PhD Vice President of Research & New Therapies Epilepsy Foundation	**Gregory Bergey, MD** Professor Neurology Director, Johns Hopkins Epilepsy Center Johns Hopkins University	**Lynn Kramer, MD** Corporate Officer Eisai Company Ltd
Brian Litt, MD Director of the The Center for Neuroengineering and Therapeutics (CNT) Perelman School of Medicine University of Pennsylvania	**Gregory (Greg) Worrell, MD, PhD** Associate Professor of Neurology Div. of Epilepsy & Electroencephalography Mayo Clinic	**Mark Lehmkuhle, PhD** Research Assistant Professor Department of Neurosurgery University of Utah Chief Executive Officer and Chief Technology Officer Epitel, Inc.
Carlos Pena, PhD Division Director Center for Devices and Radiological Health Food and Drug Administration	**Ingo Helbig, MD** Assistant Professor of Neurology & Pediatrics, Perelman School of Medicine University of Pennsylvania, Division of Neurology, Department of Biomedical and Health Informatics, The Children's Hospital of Philadelphia	**Martha (Marty) Morrell, MD** Chief Medical Officer NeuroPace, Inc.
Christian Meisel, MD Neurologist Research Group Leader University of Dresden, Germany	**Ivan Soltesz, PhD** James R. Doty Professor of Neurosurgery and Neurosciences Stanford University	**Maxime Baud, MD, PhD** Staff Clinical Specialist Wyss Center University of Geneva
Christophe Bernard, PhD Head, Physiology & Physiopathology of Brain Networks Group Institut de Neurosciences des Systemes (INSERM)	**Jackie French, MD** Neurologist, NYU Langone Medical Center Chief Scientific Officer, Epilepsy Foundation	**Michael Privitera, MD** Director, Epilepsy Center UC Neuroscience Institute
Daniel Fischer, MBA Director, Epilepsy Therapy Project Epilepsy Foundation Caregiver Representative	**Jason Heikenfeld, PhD** Professor & Assistant Vice President Commercialization University of Cincinnati	**Patty Shafer, RN, MN** Epilepsy Clinical Nurse Specialist Comprehensive Epilepsy Center Beth Israel Deaconess Medical Center

Penny Dacks, PhD Senior Manager, Research American Epilepsy Society	**Sonya Dumanis, PhD** Director, Epilepsy Innovation Institute Epilepsy Foundation	**Tobias Loddenkemper, MD** Associate Professor in Neurology Harvard Medical School Physician, Department of Neurobiology Children's Hospital Boston
Ray Dingledine, PhD Chair, Department of Pharmacology Emory School of Medicine	**Stefan Harrer, PhD** Head of Brain Inspired Computing Research Program and Team of IBM Research – Australia	**Roger Traub, MD** Research Staff Member Department of Physical Sciences IBM TJ Watson Center
Robert (Bob) Fisher, MD, PhD Maslah Saul Professor, Department of Neurology Professor, Neurosurgery Stanford University Medical Center	**Robert (Bob) Smith** Chair, Board of Directors Epilepsy Foundation	**Vicky Whittemore, PhD** Program Director, Synapses, Channels and Neural Circuits Cluster National Institute of Neurological Diseases and Stroke (NINDS) National Institutes of Health (NIH)
Robert (Rob) Moss Co-Founder Seizure Tracker	**Stephanie Christopher** Program Director Medical Device Innovation Consortium (MDIC)	**Warren Lammert** Board of Directors Epilepsy Foundation Caregiver Representative
Rosalind Picard, SCD FEEE Director of Affective Computing Research MIT Media Lab Chief Scientist, Empatica	**Steve Schachter, MD** Chief Academic Officer and Program Leader of Neurotechnology, Consortia for Improving Medicine with Innovation & Technology (CIMIT) Professor of Neurology Harvard Medical School	**William (Bill) Heetderks, MD** Neurostimulation Devices Psychiatry Branch Division of Neurological and Physical Medicine Devices Food and Drug Administration
Shivkumar (Shiv) Sabesan, PhD Staff Hardware Engineer Verily Life Sciences LLC	**Tim Denison, PhD** Vice President of Research and Core Technology Technical Fellow Medtronic	**William (Bill) Stacey, MD, PhD** Assistant Professor of Neurology University of Michigan