Title: EPILEPTIC EVENT DETECTION SYSTEMS

Abstract: Various systems and methods for predicting occurrence of a neurological event are disclosed. In certain embodiments, a neurological event detection system may comprise a sensor configured to be placed in the body of a patient, the sensor comprising a plurality of electrodes, at least one of the electrodes being configured to detect neurological signals emanating from a portion of the brain of the patient over a plurality of time periods. The system may also include a signal analyzer configured to analyze the signals to determine a number of spikes detected by each electrode during each time period. The system may also detect a number of instances where spikes associated with at least two neurons are detected at substantially the same time during each time period, and determine a correlation between the number of spikes and the number of instances for each time period.
EPILEPTIC EVENT DETECTION SYSTEMS

[001] This application claims the benefit of priority under 35 U.S.C. § 119(e) of U.S. Provisional Application No. 60/856,010, filed November 2, 2006, which is incorporated by reference herein in its entirety.

FIELD OF THE INVENTION

[002] The present disclosure relates to systems and methods for detecting, monitoring, and/or treating neurological events and, more particularly, to systems and methods for predicting neurological events based on electrical signals generated from the patient's body and generating a signal used to treat such event.

DESCRIPTION OF THE RELATED ART

[003] Recent advances in neurophysiology have allowed researchers to detect and study the electrical activity of highly localized groups of neurons located in a specific portion of the body with high temporal accuracy. The information in the sensed electrical activity may include a variety of information, including physiologic information and motor mapping information. These advances have created the possibility of extracting and processing that information and creating brain-machine interfaces (BMIs) that may allow treatment of certain neurological disorders.

[004] For example, epilepsy is a common neurological disorder, and brain-computer interfaces may be used to detect, diagnose and treat epileptic symptoms. Epilepsy may be characterized as electro-physiologic abnormalities causing sudden recurring seizures or motor, sensory, or psychic malfunctioning. While the majority of epileptic patients may be effectively treated with anti-epileptic drugs (AED), many patients continue to have symptoms or side effects that seriously impair their quality of life, and may have to rely on a surgical solution to reduce or eliminate their symptoms.

[005] While various surgical methods are currently available to treat the epileptic patients (e.g., resection of brain tissue to remove epileptic focus and/or stimulation of the Vagus nerve to suppress a seizure), the single most valuable information to an epileptic patient may be predictive information indicating, for
example, when a seizure might occur and with what probability. Such prediction capability may provide an epileptic patient with an opportunity to take appropriate responsive action to suppress the forthcoming seizure or transmit a warning signal to provide the patient with an opportunity to prepare for the seizure by, for example, lying down on a bed, pulling a car over to the side of a road, or getting out of a shower. The predictive information of the epileptic seizure may also provide useful information to a physician to enable development of enhanced therapeutic methods, such as biofeedback, drug delivery, and stimulation, to suppress or delay the seizure or otherwise dampen the severity of the seizure.

[006] Seizure prediction, however, requires detailed understanding of how individual cells behave as a population prior to the actual occurrence of the seizure. For instance, many researchers believe seizures to be a population phenomenon in which a seizure focus fires an initiation signal that synchronizes activity in the rest of the brain, thereby blocking its normal function. Therefore, in addition to the knowledge of precise localization of the epileptic focus, each individual cell activity may have to be detected to predict seizure occurrence.

[007] Various sensors have been used to detect electrical activity in a brain to identify the epileptic zone or focus. For example, noninvasive sensors, such as multi-channel electroencephalogram (EEG) sensors placed on the surface of a patient's scalp, have been used as simple BMI interfaces. EEG sensors, however, may not offer sufficient temporal or spatial resolution needed to fine grain the seizure focus or to detect single cell activity. Instead, EEG sensors detect mass fluctuations of averaged neuron activity and, therefore, provide much simpler, reduced forms of neuron activity information without providing information about the activity of single cells or their interactions.

[008] Therefore, there is a need for advanced epileptic detection systems and methods that may provide sufficient temporal or spatial resolution sufficient to accurately identify the location of a seizure focus and/or the temporal evolution of the shift from normal to seizure-like activity. This spatial and temporal resolution may require the monitoring of individual neuron activity, so as to detect and characterize various seizure-inducing conditions (e.g., specific firing patterns of the neuron spikes) that can be used to predict seizure occurrences. Moreover,
development of suitable algorithms or methods for use in connection with such advanced BMIs may be desirable to enhance the prediction capability and/or treatment of epileptic symptoms.

**SUMMARY**

[009] Therefore, various exemplary embodiments of the invention may provide a neurological event detection system that may include one or more sensors coupled to a signal analyzer for predicting the occurrence of a neurological event based on predetermined benchmark data derived from previously detected signals indicative of a neurological event. Upon predicting the occurrence of an upcoming neurological event, the system may generate warning signals and/or control signals for preventing or mitigating the effects of the neurological event.

[010] To attain the advantages and in accordance with the purpose of the invention, as embodied and broadly described herein, one exemplary aspect of the invention is a method for characterizing neurological activity. The method may comprise providing a plurality of electrodes configured to detect signals from a body of a patient and detecting signals indicative of neurological activity of the patient during a plurality of time periods. The signals may be analyzed to determine a number of individual neuron spikes detected by each electrode during each of the plurality of time periods. The method may also comprise detecting a number of instances where spikes associated with at least two neurons are detected during each of the plurality of time periods. The method may further include determining a correlation between the number of spikes and the number of instances for each of the plurality of time periods.

[011] According to another aspect, the present disclosure is directed toward a method for predicting occurrence of a neurological event. The method may comprise implanting a sensor comprising a plurality of electrodes in the body of a patient, at least one of the electrodes being configured to detect neurological signals emanating from a portion of the brain of the patient. The signals detected by each of the electrodes may be analyzed to determine a number of spikes over a time period. The method may also comprise detecting a number of instances over the time period where spikes associated with at least two neurons are detected at
substantially the same time. A correlation may be determined between the number of spikes and the number of instances during the time period. The correlation may then be compared with a predetermined correlation benchmark associated with a neurological event and the occurrence of the neurological event may be predicted based on the comparison.

[012] In accordance with yet another aspect, the present disclosure is directed toward a method for predicting occurrence of a neurological event based on a correlation between a physiological parameter and the number of spikes detected by one or more electrodes. The method may comprise providing a plurality of first electrodes configured to detect neurological signals emanating from a portion of the brain of a patient. The signals detected by each of the first electrodes may be analyzed to determine a number of spikes during each of a plurality of time periods. The method may also include providing at least one second electrode configured to detect signals indicative of physiological activity associated with the patient’s body to detect a change in the physiological activity during each of the plurality of time periods. The method may further include identifying a pattern between the number of spikes detected by each of the first electrodes and the change in the physiological activity. The pattern may subsequently be compared with a predetermined benchmark pattern associated with a neurological event to predict the occurrence of the neurological event.

[013] According to yet another aspect, the present disclosure is directed toward a method for predicting occurrence of a neurological event based on a correlation between a physiological parameter and the number of instances where spikes associated with at least two neurons are detected during a time period. The method may comprise providing a plurality of first electrodes configured to detect neurological signals emanating from a portion of the brain of a patient over a plurality of time periods and analyzing the signals detected by each of the first electrodes to determine a number of instances where spikes associated with at least two neurons are simultaneously detected during each time period. The method may also comprise providing at least one second electrode configured to detect signals indicative of physiological activity associated with the patient’s body and detecting a change in the physiological activity during each time period. A
pattern may then be identified between the number of instances and the change in the physiological activity during each time period and compared with a predetermined benchmark pattern associated with a neurological event. The occurrence of the neurological event may be predicted based on the comparison.

[014] In accordance with yet another aspect, the present disclosure is directed toward a system for characterizing neurological activity. The system may comprise a sensor comprising a plurality of electrodes, at least one of the electrodes being configured to detect neurological signals emanating from a portion of the brain of the patient over a plurality of time periods. The system may also comprise a signal analyzer configured to analyze the signals to determine a number of spikes detected by each electrode during each time period, detect a number of instances where spikes associated with at least two neurons are detected at substantially the same time during each time period, and determine a correlation between the number of spikes and the number of instances for each time period.

[015] Additional objects and advantages of the invention will be set forth in part in the description which follows, and in part will be obvious from the description, or may be learned by practice of the invention. The objects and advantages of the invention will be realized and attained by means of the elements and combinations particularly pointed out in the appended claims.

[016] It is to be understood that both the foregoing general description and the following detailed description are exemplary and explanatory only and are not restrictive of the invention, as claimed.

**BRIEF DESCRIPTION OF THE DRAWINGS**

[017] The accompanying drawings, which are incorporated in and constitute a part of this specification, illustrate several embodiments of the invention and together with the description, serve to explain the principles of the invention.

[018] In the drawings:

[019] Fig. 1 is a schematic illustration of a neurological event monitoring and therapy system, consistent with the disclosed embodiments;

[020] Fig. 2 is a schematic illustration of a remote brain implant system, in accordance with one exemplary embodiment;
Fig. 3 is a detailed perspective view of an exemplary multi-electrode array that may be implemented with the remote brain implant system shown in Fig. 2;

Fig. 4 is a schematic illustration of a remote brain implant system, in accordance with alternate exemplary embodiment;

Fig. 5 is a schematic illustration of a remote brain implant, in accordance with yet another exemplary embodiment;

Fig. 6 is a block diagram illustration of an epileptic event detection system that may be associated with the remote brain implant system, consistent with the disclosed embodiments;

Fig. 7 is a schematic illustration of another epileptic event detection system that may be associated with the remote brain implant system, in accordance with the disclosed embodiments;

Fig. 8 provides a flowchart depicting an exemplary method for establishing benchmark features indicative of a neurological event;

Figs. 9A-9F provide a plurality of graphs that illustrate frequency trend data indicative of neurological event activity collected by each electrode of a 10x10 multi-electrode array;

Fig. 10 is a series of charts representing segments of iEEG, LFP, and unit spike activity recorded by a plurality of channels three minutes prior to a seizure;

Fig. 11 is a series of charts representing segments of iEEG, LFP, and unit spike activity recorded by a plurality of channels 1 minute prior to a seizure;

Fig. 12 is a series of charts representing segments of iEEG, LFP, and unit spike activity recorded by a plurality of channels recorded at onset of a seizure;

Fig. 13 is a series of charts representing segments of iEEG, LFP, and unit spike activity recorded by a plurality of channels recorded during a seizure;

Fig. 14A-14L provide a plurality of graphs that illustrate a level of high-frequency neurological event activity monitored by each electrode of a 10x10 multi-electrode array, generated using exemplary methods consistent with the disclosed embodiments;
[033] Fig. 15 is a chart of spike activity rate and cluster density associated with a plurality of electrodes collected before, during, and after a neurological event; and

[034] Fig. 16 provides a flowchart depicting an exemplary method for predicting occurrence of a neurological event.

DESCRIPTION OF THE EMBODIMENTS

[035] Reference will now be made in detail to the exemplary embodiments of the invention, examples of which are illustrated in the accompanying drawings. Wherever possible, the same reference numbers will be used throughout the drawings to refer to the same or like parts.

[036] Systems and methods consistent with the invention may detect various neural, biological, or other physiological signals generated within a patient’s body, and process those signals to predict certain neurological events prior to their occurrence and/or to generate one or more control signals to suppress or control the neurological events. While the invention will be described in connection with a particular epileptic event, the invention may be applied to, or used in connection with, treatment of any other types of sensory or motor disorders, such as, for example, headaches, dizziness, and stroke, numerous neurological or neuropsychiatric disorders, such as, for example, depression, Parkinson's disease, or Alzheimer's disease; various biological conditions, such as, for example, cardiovascular disease, obesity, eating disorders, substance abuse or addiction, obsessive compulsive disorder, schizophrenia, mania, panic attacks, apnea, sleep apnea, other sleep disorders, movement disorders such as Tourette's syndrome, tics, cerebral palsy, or dystonia; or various biological or physiological activities.

[037] According to an exemplary embodiment of the invention, Fig. 1 illustrates a brain-machine interface (BMI) system 100 for monitoring epileptic activities in a patient's body. The system 100 may detect various signals generated from the body and process these signals to characterize various seizure-inducing conditions, differentiated from normal conditions, to accurately predict a future epileptic seizure or detect a current epileptic seizure. Upon predicting or detecting a seizure, the system 100 may be configured to generate one or more signals that
may be used, for example, to suppress or control the seizure. As will be described in detail herein, the prediction and/or detection capability may also provide a warning signal to the patient and/or another individual (e.g., physician or family members), so that the patient or other individual may take appropriate responsive action to suppress, dampen, or delay the seizure or to eliminate any possible harmful situation that may result from the seizure (e.g. by providing the patient with sufficient time to prepare for the seizure by, for example, lying down on a bed, pulling a car over to the side of a road, or getting out of a shower).

[038] As shown in Fig. 1, the system 100 may include a remote brain implant 200 placed in or on the brain 120 for detecting electrical signals indicative of spatial or temporal neural activities of the brain 120 and a central processing module 300 for processing the detected electrical signals and generating one or more signals for treating the epileptic seizure, such as suppressing, dampening, delaying, or otherwise treating. The system 100 may also include one or more sensors 150 for detecting other biological or physiological activities of the body, such as, for example, muscle movement including tremors, heartbeat rate, skin conductivity, pupil movement or dilation, perspiration, respiration, or levels of one or more blood constituents, such as dissolved oxygen or glucose, brain temperature, pressure, magnetic or electrical conductivity characteristic, which may be used in combination with the detected neural activities in the brain to predict or detect the epileptic seizure. In an exemplary embodiment, processing module 300 may include an event detector 320 for detecting certain conditions, which may be characterized as precursory conditions of a seizure, and a data recorder 380 for recording the detected electrical signals characterizing those seizure-inducing, precursory conditions. Moreover, processing module 300 may be configured to detect a current seizure and generate a control signal to suppress, dampen, delay, or control the seizure.

[039] The sensor 150 and the brain implant 200 may be connected to processing module 300 via suitable connections 130, which may be optical fibers, metallic wires, telemetry, combinations of such connectors, or wireless transceivers, or other conductors or data transceivers known in the art. As will be described further herein, the system 100 may include one or more external devices
400 for receiving, storing, and/or processing information, and/or providing biofeedback to the patient. For example, external devices 400 may generate a warning of a forthcoming seizure and/or information relating to the patient's condition, so that the patient can take appropriate responsive actions to suppress, control and/or prepare for the seizure. External device 400 may be one or more of visual indicators, auditory indicators, and tactile transducers, such as, for example, a computer, a cell phone, a beeper, or a PDA. Alternatively or additionally, this information may be supplied to a caretaker or clinician via a display device associated with a computer. The information may be sent to a local display device or any other suitable remote device known in the art.

[040] System 100 may be combined with an external device, such as, for example, a computer or prosthetic limb, movement or operation of which may be controlled by the system 100. Non-limiting examples of external devices may include a computer display, a mouse, a cursor, a joystick, a personal data assistant, a robot or robotic component, a computer controlled device, a teleoperated device, a communication system, a vehicular system such as a wheelchair or a car, an adjustable bed, an adjustable chair, a remote control device, a Functional Electrical Stimulator (FES) device, an artificial limb, a movement assist device, a medical therapeutic equipment such as a drug delivery apparatus, and a medical diagnostic equipment.

[041] Fig. 2 shows a brain implant 200 consistent with the disclosed embodiments. The brain implant 200 may include a subdural grid 210 having a plurality of rows of electrode contacts 220 configured to contact the cortical surface in the subdural or epidural space of the brain 120. Each electrode contact 220 may be individually connected to a connector 140 and the connector 140 may be connected to the central processing module 300 for processing of the detected electrical signals representative of the neural activity in the brain 120. Alternatively, subdural grid 210 and electrode contacts 220 may each have individual connectors (not shown). The large area of coverage in the brain 120 by the subdural grid 210 may enable monitoring of the overall neural activity in the brain 120 and may provide information relating to the precise localization of the epileptic focus. The shape or size of subdural grid 210, as well as the number of electrode contacts
220, or number of separate electrode sensor arrays, may vary depending upon, for example, the geometry and size of the implantation site in the brain 120. In various exemplary embodiments, the subdural grid 210 may include multiplexing circuitry (not shown), e.g. buried in a flex circuit in the subdural grid 210, which may be used to reduce the number of wires extending from brain implant 200 through the scalp or to a separate implant. For example, each wire extending from each of the contacts 220 in the subdural grid 210 may be connected to the multiplexing circuitry, which may then multiplex the detected signals in the wires into a reduced number of data lines connected to processing module 300. Appropriate demultiplexing circuitry may then be present at processing module 300 to demultiplex the received signals to appropriately process the neurological signals detected by the contacts 220. Alternatively or additionally, the multiplexing circuitry may include a preprocessor for preprocessing the detected signals (e.g., discriminating or discretizing the signals) to reduce the amount of information sent to processing module 300.

[042] Brain implant 200 may also include one or more multi-channel, high-density, micro-multi-electrode arrays 230, placed preferably at or near a suspected epileptic focus area or in such a way that seizure onset and spread can be electrically recorded by the array. Multi-electrode array 230 may penetrate the neural tissue of the brain 120 to allow each electrode to record electrical signals, light, and/or acoustic waves generated from one or more neurons in the cortex. In an exemplary embodiment, individual spiking signals may be detected from the cortical surface (i.e. without penetrating). In various exemplary embodiments of the invention, various exemplary arrays disclosed in U.S. Patent No. 5,215,088 to Normann et al., entitled "Three-Dimensional Electrode Device," U.S. Patent No. 6,171,239 to Humphrey, entitled "Systems, Methods, and Devices for Controlling External Devices by Signals Derived Directly from the Nervous System," and copending U.S. Patent Application No. 10/717,924, filed November 21, 2003, by Donoghue et al., entitled "Agent Delivery Systems and Related Methods Under Control of Biological Electrical Signals," the entire disclosures of which are incorporated by reference herein, may be used in connection with various systems and methods of this invention.
[043] As shown in Fig. 3, the multi-electrode array 230 may include a substrate 235 made of, for example, durable biocompatible material (e.g., silicon), and a plurality of sharpened projections 238 that may project from the substrate 235 and contact with or extend into the brain 120. Each projection 238 may have an active electrode distal tip 239 and may be electrically isolated from neighboring electrodes 239 by a suitable non-conducting material. In an exemplary embodiment, one or more projections 238 may include multiple electrodes 239 along its length. Also, multi-electrode array 230 may include different types of electrodes, such as, for example, recording electrodes, stimulating electrodes, photo sensors, acoustic transducers, or any combination thereof. Alternatively or additionally, the differences between electrode types may include different materials of construction, coatings, thicknesses, geometric shapes, etc. Each of the recording electrodes 239 may form a recording channel that may directly detect electrical signals generated from each of the neurons in the electrode’s vicinity. Further signal processing may isolate the individual neuron signals, each of which may comprise a series of electrical spikes, so as to precisely localize a seizure focus. Alternatively or additionally, while the electrodes 239 may detect multiple individual neuron signals, only a particular subset of the electrodes 239 may be selectively chosen for further processing. A suitable preprocessing method, such as, for example, a calibration process, may be used to selectively choose the subset of the electrodes 239.

[044] In an exemplary embodiment, multi-electrode array 230 may also include one or more electrodes with a fluid reservoir (not shown) for storage and delivery of therapeutic agents or drugs. For example, an exemplary array disclosed in the above-mentioned copending U.S. Patent Application No. 10/71 7,924 by Donoghue et al., the entire disclosure of which is incorporated by reference herein, may be used in connection with various systems and methods of this invention.

[045] In another exemplary embodiment, multi-electrode array 230 may be removably arranged with the subdural grid 210, so that multi-electrode array 230 may be easily repositioned to a different location within subdural grid 210 to facilitate detection and fine-tuning of the localization of epileptic focus. In an
alternative embodiment, multi-electrode array 230 may be placed or removed independent of the subdural grid 210.

[046] According to an exemplary embodiment of the invention, the combination of the subdural grid 210 and the multi-electrode array 230 provides a unique signal processing capability that may be used, for example: to predict an epileptic seizure prior to its occurrence; to confirm one or more epileptic focus prior to a surgical resection; to find multiple foci; and/or to diagnose or otherwise characterize an epileptic activity. While the subdural grid 210 may provide volume current or voltage potentials of the brain 120, the multi-electrode array 230 can measure each individual neuron's cellular activity and, as a whole, can measure local field potentials (LFPs) and other signals representing an integration of ranging from tens of neurons to millions of neurons.

[047] Therefore, when the subdural grid 210 is used in combination with the multi-electrode array 230, a variety of new analytical information may become available when those measured values in the subdural grid 210 and the multi-electrode array 230 are combined and visualized at different signal levels. For example, the time/space interactions between the above-mentioned volume current potentials, individual cellular activity, and LFPs may present new computational and/or signal processing methods that may enable prediction of a particular epileptic event. For example, the following exemplary array of detected neuron potentials (shown only in part) may be generated at the single cell level:

\[
\begin{bmatrix}
1 & 0 & 1 & 1 & 1 \\
1 & 1 & 1 & 1 & 1 \\
1 & 1 & 0 & 1 & 1 \\
1 & 0 & 1 & 1 & 1 \\
1 & 0 & 1 & 1 & 1 \\
\end{bmatrix}
\]

where "1" represents a firing neuron. These values may be substituted with other measures of cell activity or a vector of activity. In an epileptic tissue, brain implant 200 may then observe and characterize a stereotyped, predictable pattern with a set of rules that may describe how neighboring neurons affect each other (i.e., cellular automata or correlation index). Based on these characterized patterns or models, it may be possible to predict epileptic events because, at the next signal
level (e.g., at LFP level), it may be possible to derive a partial differential equation that may describe the time and space evolution of the cellular activity. For example, certain epileptic events may be described using the following equation:

\[
\frac{\partial^n V(r, t)}{\partial r^n} = K \frac{\partial^m V(r, t)}{\partial t^m},
\]

where \( V(r, t) \) is the measured voltage at position \( r \) and time \( t \). The constant \( K \) may contain detailed information relating to, for example, evolution of firing patterns in time and space, which may be used to describe and characterize, for instance, how each of the neurons in the focus area interacts with its neighboring neurons and how its behavior evolves in time.

[048] Based on these characterized evolutional cellular behavior, it may be possible to predict a future occurrence of an epileptic event and the timing of that event. For example, with this new set of information, the detected and recorded electrical signals from large populations of neurons may be reanalyzed using various analytical methods to further characterize and define, for example, the epileptic focus and/or its behavior. Once sufficient information is gathered, which characterizes the epileptic focus and/or its behavior leading up to epileptic seizure, that information may be stored in a database, with which newly detected signals may be compared, to predict or detect occurrence of an epileptic seizure. For example, a suitable sensor may be placed in the vicinity of the focus to detect various signals. The detected signals may then be compared with those stored in the database to determine whether the detected signals include one of the signals characterizing occurrence of the epileptic seizure. Alternatively or additionally, the detected signals may be compared with any other suitable target signals, such as, for example, a target look-up table, neural nets, or a Bayesian probabilistic framework.

[049] In an alternative embodiment, the brain implant 200 may include one or more multi-electrode arrays 230 without the presence of a subdural grid, as shown in Figs. 4 and 5. The arrays 230 may be placed at, or in the vicinity of, the suspected epileptic focus or at a location where a neural activity having an
identifiable pattern of a seizure-inducing condition is likely to occur. In various exemplary embodiments, brain implant 200 may include three or more multi-electrode arrays 230 so that triangulation signal processing and signal location techniques, similar to that used in target positioning systems, may be used to locate, or otherwise characterize one or more epileptic foci.

[050] Prior to the placement of the arrays 230, a subdural grid and/or other suitable detection or imaging devices and methods may be used to identify a target location of the seizure focus. In an exemplary embodiment, a subdural grid may be initially used to localize the epileptic focus and then be removed from the brain 120, leaving or placing the multi-electrode arrays 230 in the brain 120 at the suspected epileptic focus. In this case, an ambulatory device or an implanted device may be attached to the arrays 230, so as to enable communication with, for example, an external device for two-way information transfer.

[051] According to another exemplary embodiment of the invention, brain implant 200 may include other suitable invasive or noninvasive sensors that may sense electrical signals from the brain 120. For instance, brain implant 200 may include non-penetrating or noninvasive sensors, such as one or more multi-channel electroencephalogram (EEG) sensors, placed on the surface of the scalp or in the subcutaneous tissue between the scalp and the skull, and/or any other invasive or noninvasive sensor, which may obtain information in the form of individual neuron spikes, local field potentials (LFPs), or electrocorticogram signals (ECoGs). In any event, brain implant 200 and/or the system 100 may be configured to sense or detect other forms of electrical information, or combinations of types of electrical information, depending on, among other things, the type and resolution of the desired information. For example, the system 100 may include other electrodes, such as, for example, scalp electrodes, subcutaneous electrodes, wire electrodes, and cuff electrodes, which may be placed throughout the central nervous system or various parts of the patient’s body. These electrodes (not shown) may be configured to interact with the brain implant 200 and the central processing module 300. In an exemplary embodiment, the system 100 may include a movement sensor (e.g., strain gauge) or a pressure monitoring device (e.g., a differential pressure transducer) placed in the brain 120 to detect contraction of the brain 120,
which may precede an epileptic seizure. The contraction of the brain 120 may cause a slight differential pressure within the brain 120 or movement of the brain 120, which may be detected by the movement sensor or the pressure monitoring device. In still another exemplary embodiment of the invention, the system 100 may include a spectrophotometer or any other suitable optical device to measure the change in optical density, which may precede an epileptic seizure, and the resulting signals may be characterized as a predictive parameter for predicting a seizure activity. Alternatively or additionally, brain implant 200 or any other sensor may be configured to monitor the changes in temperature, pH, or magnetic resonance intensity, which may precede an epileptic seizure.

[052] Processing module 300 may be implanted within or on a patient's body, such as, for example, the brain 120. In an exemplary embodiment, processing module 300 may be placed in, on or under the patient's skull 160, as shown in Fig. 5, but it may be placed on or in any other portion of the body, such as scalp 180, chest area, abdomen, or neck, or the device could be external and unattached to the body. In another exemplary embodiment, processing module 300 may be configured to be attachable to the patient's body or clothing. The central processing module 300 may process the detected electrical signals indicative of neural activities to perform various functions, including, but not limited to, receiving, recording, monitoring, displaying, and/or transmitting electrical signals, processing the electrical signals to create one or more control or biofeedback signals, transmitting the control signals, and/or sending or receiving power to or from brain implant 200 or other sensors 150, or one or more internal or external sensors or other devices.

[053] Processing module 300 may include a signal conditioner which preprocesses the received signals before analyzing the signals for extraction of neural information. The preprocessing may include, but is not limited to, measuring the background signals and calibrating the detected signal based on the measured background signals, noise filtering, impedance matching, rectifying, integrating, data reducing, analog to digital converting, digital to analog converting, differentiating, discretizing, and amplifying the signals. In addition, processing module 300 may characterize the obtained neural signals in comparison with the
other biological and/or physiological signals and differentiate abnormal neural signals from those resulting from normal activities, such as, moving a limb. Processing module 300 may employ a neuron separation algorithm to uniquely identify a single neuron's spikes ("spike sorting") and/or a spatial differentiation algorithm to spatially differentiate signals from the same multi-electrode array. For instance, in some situations multiple electrodes may each detect a single neuron spike. Processing module 300 may be configured with spike sorting identification capabilities that enable processing module 300 to determine when detection of activity of multiple electrodes is actually in response to a single neuron spike. This spike sorting algorithm enables processing module 300 to properly identify individual neuron spikes, while not "double-counting" single-neuron activity that may be detected simultaneously by multiple electrodes.

[054] Fig. 6 illustrates an exemplary neurological event detection system 100' that may be implemented as part of BMI system 100. As illustrated in Fig. 6, neurological event detection system 100' may comprise a sensor 500 for detecting multi-cellular activity, a signal conditioner 510, and a signal analyzer 520, each of which may cooperate to identify a feature 530 that may be indicative of onset of a neurological event. It is contemplated that one or more of sensor 500, signal conditioner 510, and signal analyzer 520 may be at least partially implanted within the body of a patient. For example, according to one embodiment, sensor 500 may be disposed in the skull of the patient, proximate the brain. Additionally, one or more of signal conditioner 510 and/or signal analyzer 520 may be configured for implantation in the patient's body. Alternatively, it is contemplated that signal conditioner 510 and/or signal analyzer 520 may be located external to the patient's body to allow for interface and/or maintenance by a user.

[055] Sensor 500 may include one or more monitoring devices adapted for detecting neurological, physiological, and/or biological signals generated by a patient's body. For example, sensor 500 may include a neurological monitoring device, such as subdural grid 210 of Fig. 2 and/or multi-electrode array 230 of Fig. 3. As explained, subdural grid 210 and/or multi-electrode array 230 may be configured to detect multicellular signals emanating from one or more living cells of a patient, such as neuron activity collected from the cortex of the brain.
Additionally, subdural grid 210 may include physiological and/or biological sensor electrodes for monitoring certain physiological or biological parameters of the brain and/or other portions of the body.

[056] Alternatively or additionally, sensor 500 may include one or more discrete monitoring devices, some of which may be implanted within the patient’s body such as, for example, subdural grid 210, multi-electrode array 230, and physiological sensors and some of which may be located external to the patient such as, for example, one or more EEG electrodes located on the patient's scalp. Sensor 500 may embody various types of multicellular signal sensors such as scalp electrodes, subcutaneous electrodes, EMG electrodes, depth electrodes, wire or wire bundle electrodes, and combinations thereof.

[057] In addition to detecting multicellular neurological activity, sensor 500 may be configured to monitor other types of biological or physiological parameters such as, for example, blood pressure, eye movement, respiration level, respiration content such as carbon monoxide content, pH, blood parameter information, glucose level, skin conductance, perspiration, and/or combinations thereof. Sensor 500 may also include sensors adapted to monitor non-physiologic parameters such as, for example, temperature, pressure, stress, strain, force, electromagnetic, magnetic, barometric pressure, light levels, time of day, and/or combinations thereof. In an alternative embodiment, sensor 500 may include a camera configured to monitor a portion of the patient’s body and display the image on a remote display device. Users may observe the patient to determine when the patient is experiencing the physical characteristics of the seizure during the ictal period of the neurological event. In another alternative embodiment, sensor 500 further includes a patient mounted sensor (e.g., a motion sensor attached to one or more appendages) configured to determine and/or confirm when a seizure is taking place.

[058] Signal conditioner 510 may include hardware devices and/or software applications configured to perform signal processing techniques to prepare collected signals for analysis by signal analyzer 520. For example, signal conditioner 510 may include hardware and/or software for removing noise from the neurological signals detected by sensor 500. For example, signal conditioner 510
may be configured to remove DC and low frequency (e.g., 60 Hz) noise that may be introduced by power supply devices. Signal conditioner 520 may also include spike sorting software configured to identify individual neuron's spikes present in the neurological signals collected by sensor 500. Accordingly, signal conditioner 510 may be configured to classify cellular signals into individual neuron spikes, using one or more spike sorting algorithms.

[059] According to one exemplary embodiment, signal conditioner 510 may condition EEG and/or LFP signals using a variety of signal processing techniques such as, for example, analog or digital filtration schemes, Fourier and fast Fourier transforms, wavelet transformations, and/or combinations thereof. Additionally, it is contemplated that signal conditioner 510 may be configured to perform any signal conditioning function including, but not limited to: amplification, analog and/or digital filtration, data reduction or correction, conditioning, combining, multiplexing, analog to digital conversion, digital to analog conversion, and other suitable signal conditioning function.

[060] Signal analyzer 520 may include hardware devices and/or software modules that may be configured to analyze the conditioned signals generated by signal conditioner 510, identify one or more characteristics of the conditioned signals, compare the characteristics of the conditioned signals with characteristics indicative of a previously detected neurological event, and predict the occurrence of a neurological event or feature associated therewith.

[061] As illustrated in Fig. 6, signal analyzer 520 may receive one or more signals from signal conditioner 510. Alternatively and/or additionally, signal analyzer 520 may receive signals from additional and/or different devices such as, for example, one or more signal analyzers from other event detection systems located in or on the patient's body.

[062] Signal analyzer 520 may be configured to identify one or more features 530 that may be indicative of a neurological event of a patient. Feature, as the term is used herein, refers to characteristics of neurological signals associated with a neuron and/or a group of neurons that may be indicative of the onset of a neurological event. Features may also refer to interactions between single neurons or groups of neurons that may be indicative of onset of a neurological event.
Features may include, for example, increases in action potential frequency (i.e., spike frequency) associated with a neuron or group of neurons, a number of neurons that are generating neurological activity (i.e., "participating" neurons), a synchronicity of neuron activity between adjacent cells or cells located in a particular area (also referred to as inter-neuron synchronization), the presence of high-frequency bursts associated with one or more neurons, and a rate of occurrence of the high frequency bursts. Features may also include a correlation between a physiological parameter that may accompany a neurological event or may otherwise be linked to the timing of a seizure (e.g., changes in heart rate, involuntary brain movement(s), involuntary body or eye movements, changes in intercranial pressure, temperature, blood pressure, blood sugar level, respiration rate, respiration content, and/or pH) and neurological signals associated with a cell or a cluster of cells and/or the frequency of the neurological signals generated by one or more cells.

[063] According to one embodiment, the feature(s) 530 may include a geometrical pattern associated with neuron activity, as detected by multiple electrodes of the multi-electrode array 230. For example, using signal processing techniques, the signal analyzer 520 may be configured to geometrically "map" the layout of the multi-electrode array. The signal analyzer 520 may then monitor particular geometrical patterns characteristic of the neurological activity. For example, the signal analyzer 520 may be configured to detect patterns in propagation of neurological activity based on a geometrical pattern of detection by the electrodes. More specifically, over time neurological signals may propagate across the brain, resulting in a corresponding migration in the detection of electrical signals across the multi-electrode array. The signal analyzer 520 may identify these geometrical and/or migration patterns and establish a correlation between geometrical firing pattern of one or more neurons and a neurological event.

[064] In addition to geometrical pattern "migration" of dynamic signals, the signal analyzer 520 may also be configured to identify particular geometrical pattern of static signals. For example, if a particular neuron firing pattern produces a corresponding geometry as detected by one or more electrodes or electrode clusters that, although stationary with respect to a position of the multi-electrode
array, exhibits a change in frequency, the signal analyzer 520 may be configured to identify the pattern and/or a frequency associated therewith. Changes in the pattern and/or changes in the frequency of the pattern, may be indicative of increased neurological activity associated with a seizure or other neurological event.

[065] According to one exemplary embodiment, geometrical pattern recognition may be performed either automatically (e.g., by a computer system or diagnostic tool) or manually (e.g., by a laboratory technician). According to one embodiment, the signal analyzer 520 may be adapted with pattern recognition software for determining changes in neuron firing geometry, as detected by the multi-electrode array 230. The signal analyzer 520 may automatically identify changes in the neuron firing geometries and identify any particular patterns associated therewith. These patterns may be compared with neurological event data to determine if the pattern is consistent with activity preceding the neurological event.

[066] Alternatively or additionally, a laboratory technician or medical professional may manually identify geometrical firing patterns associated with the neurons. For example, a computer display may be connected as an output to the multi-electrode array 230. A grid corresponding to the geometrical layout of the multi-electrode array 230 may be provided on the display. During real-time event analysis, neuron firing activity detected by each individual electrode may be displayed. In some cases, colors on the display may be used to differentiate particular aspects of the detected signals (e.g., amplitude of the spike(s), frequency of the spikes, etc.) The laboratory technician or medical professional may be configured to manually identify geometrical features and/or patterns exhibited by signals detected by the electrodes. In some cases, these features and patterns may be flagged, recorded, and used by the signal analyzer 520 as part of a learning process to detect neurological events.

[067] Signal analyzer 520 may be configured to identify spike firing patterns by using one or more pattern recognition techniques. Pattern recognition techniques may include frequency component analysis based on one or more spike waveform values or properties such as, for example, the rate-of-change of the
amplitude of spike (i.e., slopes), a peak amplitude (i.e., maximum and minimum or highs and lows), a number of spike oscillations, or any other suitable waveform characteristics. Signal analyzer may also utilize data collected from one or more manual data analysis techniques. For example, according to one embodiment, the technician may visually "find" a spike on a display, and identify one or more spike characteristics (e.g., where the signal crosses zero, inflection points, etc.) by flagging the characteristics (e.g., by drawings a "hoop" or ring around the desired characteristic. When the spike sorter recognizes a signal passing through each of the flagged characteristics (e.g., passing through all of the hoops) within a predetermined time limit, a spike may be detected. It is contemplated that one or more manual and automatic (e.g., computerized) pattern recognition analysis techniques may be employed during signal analysis processes.

[068] Signal analyzer 520 may be configured to identify features and characteristics indicative of a neurological event using various supervised or unsupervised classification algorithms. Such classification algorithms may analyze one or more of the conditioned signals or combinations of the conditioned signals. In supervised classification, training data is used. Training data may include conditioned signals that represent a feature indicative of a neurological event of the patient (i.e., data that has already been identified as containing a neurological event). Training data may also include, for example, one or more of neurological data of at least one of the patient undergoing testing, neurological data of previous patients that have undergone testing, simulated data based on ideal or empirical data models, and/or combinations thereof. The training data may be presented to a learning mechanism, which learns one or more sets of relationships that may define particular benchmark features and characteristics indicative of a neurological event. New data that is being recorded in real-time may then be passed through the learning mechanism, which subsequently classifies the new data using the learned relationships.

[069] Some of the learning algorithms that may be employed are linear regression algorithms and processes (e.g., multiple linear regression (MLR), partial least squares (PLS) regression and principal components regression (PCR)), binary decision trees (e.g., recursive partitioning processes such as CART-classification
and regression trees), artificial neural networks such as back-propagation networks, discriminant analyses (e.g., Bayesian classifier or Fischer analysis), logistic classifiers, and support vector classifiers (support vector machines), among others.

[070] Signal analyzer 520 may also employ classification models that are created and formed using unsupervised learning methods. Unsupervised classification attempts to learn classifications based on similarities within the data set of conditioned signals or between multiple conditioned signals that represent a feature indicative of a neurological event of the patient. Unsupervised methods do not require pre-classification of the features. Unsupervised learning methods may include, for example, statistical cluster analysis. A statistical cluster analysis attempts to divide the neurological data into groups that have members that are very similar to each other (e.g., clusters of electrodes of multi-electrode array that are located in close proximity to one another), and very dissimilar to members of other groups. Similarity is determined using a distance metric, which measures the distance between data items and groups certain data items together if the distance between the data items are within the predefined data metric of one another. Statistical clustering techniques include k-means method, nearest neighbor method, furthest neighbor method, quality threshold method, fuzzy c-means method, group average method, centroid method, median method, ward method, flexible method, etc. Cluster distance metrics may include Pearson's correlation coefficient, squared Euclidean distance, standardized squared Euclidean distance, Mahalanobis' distance, Minkowsky distance and self-organizing map algorithm, among others.

[071] Signal analyzer 520 may also identify characteristics and features indicative of a neurological event using artificial neural network learning systems such as back-propagation networks, discriminant analyses (e.g., Bayesian classifier or Fischer analysis), logistic classifiers, and support vector classifiers (support vector machines).

[072] According to one embodiment, signal analyzer 520 may isolate particular neurons or groups of neurons for analysis. For example, over time, certain neurons or groups of neurons may be identified as not containing valid neurological activity data for predicting neurological events. Signal analyzer 520
may ignore sensor or data channels that monitor neurological activity associated with these "inactive" neurons, thus ensuring that feature identification is not influenced by neurons that may not contain relevant data associated with a particular feature.

[073] For example, signal analyzer 520 may select particular neurons for inclusion in feature detection by establishing a minimum firing rate and selectively removing data associated with neurons that do not conform to the minimum firing rate requirements. Because neurons with lower firing rates may convey less useful information about the features indicative of a neurological event than do neurons with higher firing rates, removal of activity associated with neurons with firing rates below the minimum threshold ensures that only relevant neuronal activity is included in feature analysis. According to one embodiment, the firing rate threshold may be global (i.e., applies to all neurological signals collected by sensor 500) or local (applies only to neurological activity associated with a particular neuron or group of neurons). Moreover, because certain locations of the brain are known to produce relevant neurological activity (e.g., epileptic focus), data collected from data channels and/or electrodes located in or around these areas may be included in feature analysis processes, regardless of any minimum firing rate criteria that may be imposed by signal analyzer 520.

[074] It is contemplated that neurological activity associated with a particular neuron may be useful in identifying certain features, but may not be relevant in the identification of certain other features. Accordingly, signal analyzer 520 may include neurological activity for a particular neuron during identification of one or more specific features, while disqualifying neurological activity associated with this neuron during identification of other features.

[075] Other methods that can be used by signal analyzer 520 to identify features indicative of neurological events of the patient include inter-neuron synchronization or the synchronization of any of the conditioned signals recorded. Synchronization may be calculated by examining the spike frequency or the frequency of spike bursts of a neuron as compared to itself, other neurons, groups of neurons, or of groups of neurons to other groups of neurons. These rates may be compared to any other conditioned signals such as EEG, LFP, or other
physiological or environmental data. Synchronicity may be observed though entrainment of one of these variables with another one or by using cross-correlation techniques or other techniques for measuring changes in features associated with the conditioned signals such as, for example, the periodicity of the time-series data, a periodicity of the FFT-derived frequency domain representation of the data, or a rate of change of the frequency of the time series or power in a given frequency range, or other measure of correlation. In addition, features may be characterized by geometrical patterns associated with the neuron firing characteristics (as explained above).

[076] Other, more generalized techniques may be used to investigate features. For example signal analyzer 520 may be configured to monitor correlation between spikes of individual neurons and/or groups of neurons using one or more of the clustering techniques described above. The clustering of the data can be developed to represent the features apparent during a neurological event, by, for example, training the clustering algorithm with data that is thought to represent a feature that is indicative of neurological events of the patient, and subsequently running data through a real-time model of the cluster to determine the similarity between the current data and the feature-specific data used to train the clustering algorithm. When the real-time data falls within a certain distance from the cluster (measured using a distance metric), then it may be considered to represent the feature indicative of a neurological event of the patient.

[077] Signal analyzer 520 may also be configured to perform time-domain-based analyses of features. For example, signal analyzer 520 may perform waveform-feature analysis, such as the Gotman algorithm. In the Gotman system, EEG waveforms are filtered and decomposed into "features" representing characteristics of interest in the waveforms. One such feature is characterized by the regular occurrence (i.e., density) of half-waves exceeding a threshold amplitude in a specified frequency band between approximately 3 Hz and 20 Hz, especially in comparison to background (non-ictal) activity. Signal analyzer 520 may associate a feature indicative of neurological activity with the detection of these half-waves. The Gotman system is described in greater detail in H. Qu and J. Gotman, A Seizure Warning System for Long Term Epilepsy Monitoring, Neurology 1995; 45:

[078] A more computationally demanding approach is to transform EEG or LFP signals into the frequency domain for rigorous spectrum analysis. See, for example, U.S. Pat. No. 5,995,868 to Dorfineister et al., which is herein incorporated by reference.

[079] Features 530 may also include parameters that are indicative of the timing of a seizure. For example, signal analyzer 520 may detect a particular pattern of cellular firing that has been previously identified as characteristic activity that occurs 30 seconds before a neurological event. According to another example, signal analyzer 520 may detect a particular synchronicity of neurological activity in clusters of neurons that has been previously identified as activity that occurs 2 minutes prior to the onset of a seizure.

[080] Features 530 may also be indicative of a surrogate to a seizure, such as, for example, a change in heart rate associated with a seizure or other physiologic event which is a precursor to or otherwise linked to the timing of a seizure.

[081] Fig. 7 illustrates an alternate embodiment of a neurological event detection system 100" that may be implemented as part of BMI system 100. Similar in structure and function to neurological event detection system 100' of Fig. 6, neurological event detection system 100" includes a plurality of sensors associated with sensor 500, a signal conditioner 510 for conditioning data collected by each of the sensors associated with sensor 500, and a plurality of signal analyzers 520 for identifying a plurality of event features 531 and 532.

[082] Sensor 500 may include a penetrating electrode array (PEA) sensor 501, a subdural grid 502, a physiologic sensor 503, and a non-physiologic sensor, such as environmental sensor 504. The signals detected by the various components of sensor 500 are received by signal conditioner 510, which performs one or more signal conditioning functions such as noise elimination, neural spike classification, filtering, and other signal conditioning functions. The signals
processed by signal conditioner 510 are delivered to signal analyzer 520, for further analysis and classification.

[083] Signal analyzer 520 may include multiple analyzers, such as signal analyzer 1, signal analyzer 2, signal analyzer 3, and signal analyzer 4. Each of the signal analyzers receives input signals from one or more of sensor 500 (via signal conditioner 510) or a different signal analyzer. In certain embodiments, one or more signal analyzers may receive input signals from one or more devices external to neurological event detection system 100" (not shown), such as from sensors or signal analyzers associated with other event detection systems that may be disposed within the patient's body.

[084] In the embodiment shown in Fig. 7, signal analyzer 2 receives an output from signal analyzer 1, so as to modify the analyses performed by signal analyzer 2 based on an analysis of signal analyzer 1. For example, signal analyzer 1 may be configured to perform a first signal analysis function (e.g., clustering of neuron spike activity). In contrast, signal analyzer 2 may be configured to perform a correlation between neurological spike activity associated with a single neuron and neurological spike activity associated with the cluster of neurons identified by signal analyzer 1. Signal analyzer 2 may then determine the strength of a relationship between data associated with a single neuron and a cluster of active neurons. Numerous iterations of how one analysis can modify one or more parameters of a second analysis can be made without departing from the scope of this disclosure. The results of signal analyzer 1, signal analyzer 2, and signal analyzer 3 are received by signal analyzer 4. Signal analyzer 4 may be configured to identify correlations between the output of signal analyzer 1, signal analyzer 2, and signal analyzer 3 in order to identify features 531 and 532 indicative of the a future neurological event.

[085] It is contemplated that neurological event detection system 100" (and/or 100") may comprise additional and/or different components and subsystems than those illustrated in Fig. 7. For example, system 100" may include a data recorder (not shown) configured to record one or more of signals received from the sensor, conditioned signals produced by the signal conditioner, and/or signals
produced by the signal analyzer. The data recorder may include a memory device which may be located internal or external to the patient's body.

[086] Alternatively or additionally, system 100" may include a neurological event alert device (not shown) configured to alert the patient of the identification of one or more features indicative of a neurological event. According to one embodiment, neurological event alert device may embody a tactile, audio and/or visual transducer that is activated when one or more of the features are identified.

[087] According to another embodiment, system 100" may include a therapeutic element (not shown) configured to deliver therapeutic treatments for preventing the onset of a predicted neurological event and/or delaying or limiting the effects of an upcoming neurological event. The therapeutic element may include one or more of: an implanted drug delivery device, an external drug delivery device, a stimulating device including, for example, a device for delivering energy to the patient's brain via the multi-electrode array 230.

[088] In accordance with yet another embodiment, system 100" may include a visual recording device (not shown), such as a camera configured to provide visual information to signal analyzer 520. Alternatively or additionally, system 100" may include an audio recording device (not shown), such as a miniaturized audio recorder configured to provide audio information to signal analyzer 520. Alternatively or additionally, system 100" may include a manual input device (not shown), such as a handheld device configured to allow an operator, such as the patient, a family member, or healthcare provider to enter information into system 100". The information may categorize the patient state (e.g., a psychiatric state or neurological state).

[089] In another embodiment, system 100" may include a GPS module (not shown) to provide patient location information. Signal analyzer 520 may collect patient location information and provide this information to a health care provider or doctor upon detection of an upcoming neurological event. According to one embodiment, system 100" may include a GPS-enabled wireless transmitter such as a cell phone transmitter configured to transmit the patient's location such as when signal analyzer 520 has identified one or more features indicative of activity of a neurological event.
System 100" and/or one or more components associated therewith may include an integral configuration routine or integral permission routine. A calibration or other configuration routine may be performed at one or more times after sensor 500 has been implanted, and may need to be re-performed on a routine basis. Changes to one or more system parameters, such as a parameter involved in the analysis performed by signal analyzer 520 may be modified in a system configuration routine. A permission routine (which requires an operator such as a clinician to enter a proper code and/or utilize a mechanical or electromechanical key which "mates" with a component of system 100") may be invoked to ensure that the system parameter modification be performed only by an authorized operator.

Fig. 8 provides a flowchart 800 depicting an exemplary method for identifying features and characteristics indicative of a neurological event. These features and characteristics may be stored in memory associated with neurological event detection system 100' (or 100"). During real-time operations of neurological event monitoring system, these features and characteristics may be used as benchmarks for comparison with real-time neurological data to predict whether the real-time neurological data is indicative of a neurological event.

As illustrated in Fig. 8, neurological event detection system 100' may monitor neurological activity associated with a patient (Step 810) during a plurality of neurological events to gather sample data before, during, and after the neurological event. For example, sensor 500 may include a multi-electrode array 230 disposed within the skull of the patient proximate the brain. Sensor 500 may collect neurological signals and store the neurological signals in memory. Upon detection of a plurality of neurological events, the data may be retrieved from memory and analyzed to create characteristics of a neurological event at a plurality of time periods before, during, and after the neurological event. These characteristics may be stored and subsequently used as benchmarks for predicting neurological events during real-time monitoring of neurological activity.

Once sufficient neurological activity data has been gathered, signal analyzer 520 may extract signals indicative of neurological events (Step 820) before, during, and after the event. Signal analyzer 520 may analyze these signals
to identify certain characteristics and features of a neurological event over a plurality of different time periods (Step 830). Because sensor 500 may include a multi-electrode array that comprises a plurality of data channels, each of which may be associated with one or more particular neurons, signal analyzer 520 may employ a plurality of classification techniques (described above) to analyze and determine trends in data collected from individual data channels and identify relationships between or among different data channels.

[094] Signal analyzer 520 may be configured to determine benchmark features indicative of neurological events at predetermined time intervals relative to the neurological event (Step 840). For example, signal analyzer 520 may analyze a plurality of data samples collected 120 seconds prior to onset of a neurological event. Consequently, signal analyzer 520 may identify one or more common features that may be characteristic of neurological signals 120 seconds prior to the onset of the neurological event. According to one embodiment, features may include a frequency of spikes generated by one or more neurons, a number of single neurons generating spikes, a number of clusters of neurons generating spikes, a synchronization of spikes generated by a plurality of neurons, and a rate of occurrence of high-frequency bursts of spikes.

[095] Signal analyzer 520 may be configured to determine spike frequencies of single neurons and/or groups of neurons. Spike frequencies may be identified as discrete timing of each spike (inter-spike-interval) and/or calculated as an average of spike frequencies across a sliding time window. Signal analyzer 520 may estimate a spike frequency based on similarity to a pre-designated statistical model (e.g., Bayesian-based spike rate estimator) that predicts the instantaneous frequency using Poisson or other statistical model in conjunction with historical spike rate data. The frequency of the spikes of a group of neurons may be determined as a weighted combination of the firing rates of the single-neuron spikes or multi-neuron activity that make up the group. Signal analyzer 520 may be configured to identify patterns and/or trends associated with the identified features and store these trends in memory, for future analysis (Step 850).

[096] Figs. 9A-15 illustrate exemplary benchmark features that are derived based on previously-detected neurological event data collected, for example,
during a learning session. For instance, during a learning session, subdural grid 210 and microelectrode array 230 may each be implanted proximate the brain of a patient. Subdural grid 210 may collect iEEG signals, while multi-electrode array may collect local field potential (LFP) data and individual neuron spike activity (action potentials). The LFPs may be band-passed between 0.5 Hz and 1 KHz band and may be characteristics of the summed synaptic potentials near the electrode tips and representative of mean dendritic activity within a cortical volume (comprising afferent input and local interneuronal processing). The neuron spike activity may be band-passed between 500 Hz and 30 KHz and may be derived by classifying waveform morphologies into putative single-neuron unit activity, which may be biased toward larger cells and represent output to other brain areas. Each of Figs. 9A-14L illustrates data collected and sampled over a 10 second window (e.g., at 50 samples/s). However, it is contemplated that this time period and the data sampling rate associated therewith may be adjusted without departing from the scope of the present disclosure.

[097] It should be noted that the spatial and temporal resolution of intracranial electroencephalography (iEEG), while superior to scalp EEG, may not possess sufficient resolution to observe ictogenesis (i.e., the onset of seizure activity) at a cellular level. Penetrating multi-electrode arrays, such as multi-electrode array 230, may permit analysis of neurological signals at the requisite resolution to enable (in conjunction with signal processing, cluster analysis, and pattern recognition algorithms) to predict the onset of a neurological event. Data illustrated in Figs. 9A-15 was collected with a multi-electrode array with 96 subpial contacts arranged in a 10x10 grid and represents analysis of six (6) neurological events. The array was implanted in a patient undergoing iEEG for localization of extratemporal partial epilepsy. Signal conditioning included LFP data sampling at 30 KHz/channel and spike classifying using a waveform analysis and clustering algorithm.

[098] Figs. 9A-9F provide graphs depicting an exemplary benchmark feature indicative of neurological activity at a plurality of time periods associated with a neurological event which was generated using the method described in Fig. 8. Figs. 9A-9F depict frequency characteristics corresponding to each electrode in
a 10-by-10 multi-electrode array. Specifically, Figs. 9A-9F shows the percentage of 200-millisecond segments over a 10-second period in which each electrode measured neurological activity.

[099] Figs. 9A-9F illustrates a benchmark trend in frequency of spike activity associated with each electrode that may be used in the analysis of real-time neurological signals to predict occurrence of a neurological event. As illustrated in Fig. 9A, at 300 seconds prior to seizure onset, a small cluster (which is circled in Fig. 9B) of electrodes detects neurological activity (i.e., middle clusters located in the brown and orange rows of clusters). However, as shown in Fig. 9B, at 120 seconds prior to seizure onset, a larger cluster of electrodes in the same region detects neurological activity, with increasing frequency than illustrated in Fig. 9A. Similarly, Fig. 9C illustrates that continuation of the trend in Fig. 9B, with the same cluster of electrodes measuring neurological activity at 30 seconds prior to seizure onset, with greater frequency than illustrated Fig. 9B. Furthermore, it appears that a small amount of activity is beginning to become noticeable in other portions of the electrode array (illustrated by the arrows in Fig. 9C). These trends in cluster data increases at 10 seconds prior to seizure onset (Fig. 9D), at seizure onset (Fig. 9E), and at 60 seconds after seizure onset (Fig. 9F). At seizure onset, another small amount of isolated activity is detected by yet another portion of the electrode array (illustrated by the arrow of Fig. 9E), which becomes substantially more active after the onset of the seizure, as illustrated in Fig. 9F.

[0100] The trend data illustrated in Figs. 9A-9F may be stored in memory and used during analysis of real-time neurological signals. Accordingly, real-time neurological event data associated with one or more single neurons or neuron clusters may be analyzed based on the stored neurological event data at a corresponding time interval. If there is high correlation between the real-time signals and the stored neurological event trend data, system analyzer 520 may predict the occurrence of a neurological event, such as a prediction made at least 60 seconds, preferably 120 seconds or more prior to the seizure. It is contemplated that the amount of correlation required to make a prediction may be based on high-single instance correlation (e.g., correlation at one time interval) or somewhat lower correlations over multiple instances (e.g., correlation over two multiple time
intervals). Accordingly, a neurological event may be predicted with very low correlation between real-time data and stored feature data, if the correlation is persistent over multiple time periods.

[0101] In addition to establishing frequency trend benchmarks in individual neurons or clusters of neurons, signal analyzer 520 may be configured to identify patterns in single-neuron spike activity, as well as establish patterns in synchronicity between spike activities in multiple neurons.

[0102] For example, Figs. 10-13 illustrate exemplary iEEG data collected from subdural grid 210, LFP data collected from multi-electrode array 230, and unit activity (i.e., single-neuron activity) derived from one or more of the iEEG data and LFP data. The unit activity may be determined based on one or more of the signal analysis techniques (e.g., clustering, spike sorting, etc.) performed by signal analyzer 520. Each vertical trace of Figs. 10-13 shows data associated with a single channel (e.g., electrode) of subdural grid 210 and multi-electrode array 230.

[0103] As illustrated in Figs. 10-13, raw iEEG and LFP data may not exhibit visible trends in neurological activity until the onset of a seizure. As a result, it may be difficult to compare real-time iEEG signals and LFP signals with iEEG signals and LFP signals indicative of a neurological event, since there are very few discernible features prior to onset of a neurological event. In contrast with the iEEG and LFP data, single-neuron spike activity exhibits measurable trends that may be used to predict occurrence of a neurological event.

[0104] For example, in comparing unit activity data of Figs. 10-13, the number of neurons exhibiting neurological activity progressively increases as a neurological event approaches. Accordingly, signal analyzer 520 may store information associated with these increases at particular time intervals. As such, real-time data exhibiting increases in the number of "participating" neurons that are consistent with corresponding increases associated with the previously-detected neurological event data may be flagged as indicative of a neurological event.

[0105] Signal analyzer 520 may also identify the frequency of spike activity associated with a single neuron. As illustrated in Figs. 10-13 individual channels exhibit significant increases in frequency of spike activity as the neurological event approaches. Accordingly, signal analyzer 520 may identify trends in frequency
changes associated with these channels and store these trends as indicative of neurological event activity.

[0106] The unit activity illustrated in Figs. 10-13 also illustrates synchronicity between individual neurons (illustrated by the circled vertical samples). For example, as illustrated in Fig. 10, at 3 minutes prior to seizure onset there are only 3 instances during the analysis time period when at least 5 channels detected spikes simultaneously. In contrast, as illustrated in Fig. 11, at one minute prior to seizure onset, there are at least 10 instances during the analysis time period when at least 5 channels detected spikes simultaneously. Similarly, as illustrated in Fig. 12, at seizure onset, there are at least 14 instances during the analysis time period when at least 5 channels detected spikes simultaneously. As expected, as illustrated in Fig. 12, during the seizure, a majority of data channels synchronously detected spikes.

[0107] Signal analyzer 520 may store the trends in synchronicity between multiple data channels (e.g. single or group neuron activity, or activity detected by a single electrode or group of electrodes) and use this data in real-time monitoring of neurological activity. Consequently, if trends in synchronicity between channels during real-time neurological activity correlates with synchronicity between channels associated with a previously-detected neurological event, signal analyzer 520 may predict the occurrence of a neurological event.

[0108] According to another exemplary embodiment, signal analyzer 520 may be configured to identify patterns of high-frequency (>200 Hz) bursts in previously detected neurological event data. Signal analyzer 520 may store the identified patterns as benchmarks for comparison with real-time neurological event data to predict occurrence of a neurological event. Figs. 14A-14L illustrate high frequency activity detected by each electrode of electrode array at various time periods associated with a neurological event.

[0109] For example, Figs. 14A-14F illustrate high-frequency content detected before onset of a seizure, while Figs. 14G-14L illustrate high-frequency content detected during and after seizure onset. As illustrated in Figs. 14A-14F, high-frequency power is very low 120 seconds prior to seizure onset and
progressively increases until seizure onset. As illustrated in Figs. 14G-14L, high frequency power continues to increase well after onset and during the seizure.

[01 10] Signal analyzer 520 may identify patterns or trends in the increases in power associated with these high-frequency bursts such as, for example, a percentage increase in single-neuron high-frequency power at each time interval or percentage increases in high-frequency power associated with particular groups of neurons. Signal analyzer 520 may store this data in memory as benchmark data associated with high-frequency bursts. Accordingly, signal analyzer 520 may compare real-time high-frequency burst data with the high-frequency benchmark data and predict occurrence of a neurological event if the real-time high-frequency burst data exhibits strong correlation with the high-frequency benchmark data.

[01 11] As illustrated in Fig. 15, signal analyzer 520 may also be configured to establish benchmarks based on monitored trends in the number of individual neuron spikes, the cluster density of neuron firings, and/or a correlation therebetween. Cluster density, a measure of simultaneity of spike discharges determined with a k-means clustering technique (pruned to eliminate clusters of less than 5 spikes in a 70 ms period), increases earlier than overall spike rate.

[01 12] In Fig. 15, both the number of individual neuron spikes over a predetermined time window and the cluster density exhibit an increasing trend well before onset of a seizure. Signal analyzer 520 may record trend data for each of the single-neuron activity and cluster density. Signal analyzer 520 may subsequently analyze real-time neurological activity to determine real-time single neuron activity and cluster density. Signal analyzer 520 may subsequently correlate one or more of real-time single-neuron data activity data and cluster density with the trend data associated with each of these characteristics. Strong correlation indicates the likelihood that the current neurological activity is indicative of a neurological event.

[01 13] In addition to determining correlation between each of single-neuron activity and cluster density with their corresponding predetermined benchmark, signal analyzer 520 may be configured to determine a relationship between single neuron activity and cluster density, and correlate this relationship with a relationship
benchmark derived from the recorded trend data associated with actual neurological events.

[01 14] Once a plurality of analysis benchmarks associated with one or more neurological event features have been identified by signal analyzer 520, neurological event detection system 100" (or 100") may be configured to analyze real-time data collected by sensor 500 and predict occurrence of a neurological event. Fig. 16 provides a flowchart 900 depicting an exemplary method for predicting occurrence of a neurological event.

[01 15] As illustrated in Fig. 16, system 100" may collect/monitor real-time neurological activity associated with a patient (Step 910). For example, sensor 500 may collect neurological data from subdural grid 210 and/or multi-electrode array 230. In addition to collecting/monitoring neurological activity, sensor 500 may also receive other physiological and/or biological data associated with the patient.

[01 16] System 100" may analyze the collected neurological, physiological, and/or biological data to determine one or more characteristics or features associated with the collected data (Step 920). As explained, signal analyzer 520 may be configured to analyze, using one or more of a plurality of data analysis techniques (cluster analysis, learning algorithms, neural network, etc.) one or more of a frequency of spikes generated by one or more neurons, a number of single neurons generating spikes, a number of clusters of neurons generating spikes, a synchronization of spikes generated by a plurality of neurons, and a rate of occurrence of high-frequency bursts of spikes.

[01 17] Once one or more features associated with the collected neurological activity has been determined, system 100" may compare the current features with previously-determined benchmark features that have been derived from neurological event data, such as those illustrated in Figs. 9A-15 (Step 930). According to one embodiment, the comparison between the current features and the previously determined benchmarks involves determining a correlation or cross-correlation factor to statistically quantify the relationship between the current features and the corresponding predetermined benchmark.

[01 18] For example, signal analyzer 520 may compare a current feature, such as cluster density, a trend in frequency of spikes generated by one or more
neurons, and/or a trend in high-frequency burst activity, with a corresponding benchmark derived from analysis of a neurological event. If the current feature does not correlate with a benchmark (Step 940: No), which may indicate little or no relationship between the current activity and data indicative of a neurological event, system 100” may simply continue to monitor real-time neurological activity.

[0119] If, on the other hand, the current feature corresponds with its corresponding benchmark (Step 940: Yes), which may indicate the existence of a relationship between the real-time activity and data indicative of a neurological event, system 100” may predict the occurrence of a neurological event (Step 950). According to one embodiment, signal analyzer 520 may determine a correlation factor between a feature or characteristic associated with current neurological activity and a previously determined benchmark indicative of a neurological event. If the correlation factor exceeds a predetermined correlation threshold (which may be set by a user or determined by signal analyzer 520 based on empirical data gathered from correlations between actual neurological events), signal analyzer 520 may predict a neurological event.

[0120] Upon prediction of a neurological event, system 100” may generate an event alert (Step 960). Event alert may include, among other things, an audible alarm, a visual signal (illumination of a warning lamp or strobe), a combination audio-visual alarm, a text message to a mobile electronic device (e.g., associated with a caregiver, technician, nurse, lab assistant, medical professional), or any other type of alarm. Furthermore, upon detection of a neurological event, system 100” may also be configured to generate one or more control signals for controlling a device for mitigating, treating, preventing, or otherwise reacting to the upcoming neurological event. For example, system 100” may be coupled to a therapeutic delivery device for administering therapeutic treatment (e.g., anti-seizure medication, electrical or physical stimulation, etc.) to a particular portion of the body in order to mitigate or prevent negative effects of a seizure.

[0121] In addition to monitoring neurological activity and determining relationships between neurological characteristics, system 100” may also be configured to determine relationships between neurological activity and physiological and/or biological data. For example, systems analyzer 520 may be
configured to monitor and compare relationships between physiological characteristics and neurological features associated with actual neurological events and establish these relationships as benchmarks for predicting occurrence of a neurological event.

[0122] Other embodiments of the invention will be apparent to those skilled in the art from consideration of the specification and practice of the invention disclosed herein. It is intended that the specification and examples be considered as exemplary only, with a true scope and spirit of the invention being indicated by the following claims.
WHAT IS CLAIMED IS:

1. A method for characterizing neurological activity, comprising:
   providing a plurality of electrodes configured to detect signals from a body of a patient;
   detecting signals indicative of neurological activity of the patient during a plurality of time periods;
   analyzing the signals to determine a number of spikes detected by one or more electrodes during each of the plurality of time periods;
   detecting a number of instances where spikes associated with at least two neurons are detected during each of the plurality of time periods; and
   determining a correlation between the number of spikes and the number of instances for each of the plurality of time periods.

2. The method of claim 1, further comprising identifying a trend in the correlation between the number of spikes and the number of instances over the plurality of time periods.

3. The method of claim 1, wherein determining the number of spikes comprises:
   establishing a spike firing pattern; and
   counting the number of spikes detected by each electrode that correlate with the spike firing pattern.

4. The method of claim 3, wherein the spike firing pattern comprises one or more of a pattern associated with a spike frequency component.

5. The method of claim 4, wherein the spike frequency component includes at least one of a peak spike amplitude associated with the plurality of time periods, a minimum spike amplitude associated with the plurality of time periods, a number of oscillations, and a rate-of-change of the spike amplitude.
6. The method of claim 1, wherein the signals indicative of neurological activity comprise signals indicative of a neurological event.

7. The method of claim 6, further comprising establishing a benchmark correlation factor for predicting occurrence of a future neurological event.

8. The method of claim 7, wherein the benchmark correlation factor is determined based previously detected data collected from at least one of the patient, one or more different patients, or a combination of the patient and the one or more different patients.

9. The method of claim 1, wherein determining the number of spikes comprises determining a trend in the number of spikes over the plurality of time periods.

10. The method of claim 9, further comprising determining a trend in the number of instances over the plurality of time periods.

11. The method of claim 10, further comprising identifying a pattern between the trend in the number of spikes and the trend in the number of instances.

12. The method of claim 11, further comprising:
   comparing the pattern with a benchmark pattern derived from previously-detected signals indicative of a neurological event; and
   predicting occurrence of the neurological event based on the comparison.

13. The method of claim 12, further comprising generating a control signal for controlling at least one device in response to the prediction.
14. The method of claim 13, wherein the at least one device comprises a therapy delivery device.

15. The method of claim 14, wherein the therapy delivery device comprises a drug delivery device.

16. The method of claim 14, wherein the therapy delivery device comprises a device for delivering electric stimulation.

17. The method of claim 1, further comprising detecting signals indicative of physiological activity of the patient during the plurality of time periods.

18. The method of claim 17, further comprising:
   identifying a pattern between the number of spikes detected and a change in the physiological activity during each of the plurality of time periods; and
   determining a correlation between the number of spikes and the change in the physiological activity.

19. The method of claim 17, further comprising:
   identifying a pattern between the number of instances and a change in the physiological activity during each of the plurality of time periods; and
   determining a correlation between the number of spikes and the change in the physiological activity.

20. The method of claim 17, wherein the physiological activity comprises at least one of heart rate, blood pressure, blood glucose level, eye movement, respiration rate, respiration content, pH, and intercranial pressure.

21. The method of claim 1, further comprising:
   establishing a benchmark pattern derived from previously-detected signals indicative of a neurological event;
determining a pattern in the correlation between the number of spikes and the number of instances for each of the plurality of time periods; and predicting occurrence of the neurological event based on a comparison between the determined pattern and the benchmark pattern.

22. The method of claim 21, further comprising generating a control signal for controlling at least one device in response to the prediction.

23. The method of claim 22, wherein the at least one device comprises a therapy delivery device.

24. A method for predicting occurrence of a neurological event, comprising:
   implanting a sensor comprising a plurality of electrodes in the body of a patient, at least one of the electrodes being configured to detect neurological signals emanating from a portion of the brain of the patient;
   analyzing the signals detected by each of the electrodes to determine a number of spikes over a time period;
   detecting a number of instances over the time period where spikes associated with at least two neurons are detected at substantially the same time;
   determining a correlation between the number of spikes and the number of instances during the time period;
   comparing the correlation with a predetermined correlation benchmark associated with a neurological event; and
   predicting the occurrence of the neurological event based on the comparison.

25. The method of claim 24, wherein predicting the occurrence of the neurological event comprises generating a warning signal when the correlation matches the predetermined correlation benchmark within a threshold value.
26. The method of claim 25, wherein the warning signal comprises one or more of an audible alarm, a visual signal, and an electronic message.

27. The method of claim 24, further comprising generating a control signal for controlling at least one device in response to the prediction.

28. The method of claim 27, wherein the at least one device comprises a therapy delivery device.

29. The method of claim 28, wherein the therapy delivery device comprises a drug delivery device.

30. The method of claim 28, wherein the therapy delivery device comprises a device for delivering electric stimulation.

31. The method of claim 24, wherein at least one of the plurality of electrodes is configured to detect signals indicative of physiological activity associated with the patient's body.

32. The method of claim 31, wherein the physiological activity comprises at least one of heart rate, blood pressure, blood glucose level, eye movement, respiration rate, respiration content, pH, and intercranial pressure.

33. The method of claim 31, further comprising identifying a pattern between the number of spikes and a change in the physiological activity during each of the plurality of time periods.

34. The method of claim 33, further comprising:
   comparing the pattern with a benchmark pattern between the number of spikes and the change in the physiological activity, which is indicative of the neurological event; and
predicting the occurrence of the neurological event based on the comparison between the identified pattern and the benchmark pattern.

35. The method of claim 31, further comprising identifying a pattern between the number of instances and a change in the physiological activity during each of the plurality of time periods.

36. The method of claim 35, further comprising:
   comparing the pattern with a benchmark pattern between the number of instances and the change in the physiological activity, which is indicative of the neurological event; and
   predicting the occurrence of the neurological event based on the comparison between the identified pattern and the benchmark pattern.

37. The method of claim 24, wherein the sensor comprises one or more of a subdural grid, a multi-electrode array, a physiological sensor, and a biological sensor.

38. The method of claim 37, wherein the sensor comprises the subdural grid and the multi-electrode array.

39. A method for predicting occurrence of a neurological event, comprising:
   providing a plurality of first electrodes configured to detect neurological signals emanating from a portion of the brain of a patient;
   analyzing the signals detected by each of the first electrodes to determine a number of spikes during each of a plurality of time periods;
   providing at least one second electrode configured to detect signals indicative of physiological activity associated with the patient's body;
   detecting a change in the physiological activity during each of the plurality of time periods;
identifying a pattern between the number of spikes detected by each of the
first electrodes and the change in the physiological activity;
comparing the pattern with a predetermined benchmark pattern associated
with a neurological event; and
predicting the occurrence of the neurological event based on the
comparison.

40. The method of claim 39, wherein predicting the occurrence of the
neurological event comprises generating a warning signal when the correlation
matches the predetermined correlation benchmark within a threshold value.

41. The method of claim 40, wherein the warning signal comprises one or
more of an audible alarm, a visual signal, and an electronic message.

42. The method of claim 39, further comprising generating a control signal
for controlling at least one device in response to the prediction.

43. The method of claim 42, wherein the at least one device comprises a
therapy delivery device.

44. The method of claim 43, wherein the therapy delivery device
comprises a drug delivery device.

45. The method of claim 43, wherein the therapy delivery device
comprises a device for delivering electric stimulation.

46. The method of claim 39, wherein the physiological activity comprises
at least one of heart rate, blood pressure, blood glucose level, eye movement,
respiration rate, respiration content, pH, and intercranial pressure.
47. The method of claim 39, further comprising identifying a pattern between the number of instances and the change in the physiological activity during each of the plurality of time periods.

48. The method of claim 47, further comprising:
   comparing the pattern with a benchmark pattern between the number of instances and the change in the physiological activity, which is indicative of the neurological event; and
   predicting the occurrence of the neurological event based on the comparison between the identified pattern and the benchmark pattern.

49. A method for predicting occurrence of a neurological event, comprising:
   providing a plurality of first electrodes configured to detect neurological signals emanating from a portion of the brain of a patient over a plurality of time periods;
   analyzing the signals detected by each of the first electrodes to determine a number of instances where spikes associated with at least two neurons are simultaneously detected during each time period;
   providing at least one second electrode configured to detect signals indicative of physiological activity associated with the patient's body;
   detecting a change in the physiological activity during each time period;
   identifying a pattern between the number of instances and the change in the physiological activity during each time period;
   comparing the pattern with a predetermined benchmark pattern associated with a neurological event; and
   predicting the occurrence of the neurological event based on the comparison.

50. The method of claim 49, wherein predicting the occurrence of the neurological event comprises generating a warning signal when the correlation matches the predetermined correlation benchmark within a threshold value.
51. The method of claim 50, wherein the warning signal comprises one or more of an audible alarm, a visual signal, and an electronic message.

52. The method of claim 49, further comprising generating a control signal for controlling at least one device in response to the prediction.

53. The method of claim 52, wherein the at least one device comprises a therapy delivery device.

54. The method of claim 53, wherein the therapy delivery device comprises a drug delivery device.

55. The method of claim 53, wherein the therapy delivery device comprises a device for delivering electric stimulation.

56. The method of claim 49, wherein the physiological activity comprises at least one of heart rate, blood pressure, blood glucose level, eye movement, respiration rate, respiration content, pH, and intercranial pressure.

57. The method of claim 49, further comprising identifying a pattern between the number of spikes and the change in the physiological activity during each of the plurality of time periods.

58. The method of claim 57, further comprising:
   comparing the pattern with a benchmark pattern between the number of spikes and the change in the physiological activity, which is indicative of the neurological event; and
   predicting the occurrence of the neurological event based on the comparison between the identified pattern and the benchmark pattern.

59. A system for characterizing neurological activity, comprising:
a sensor comprising a plurality of electrodes, at least one of the electrodes being configured to detect neurological signals emanating from a portion of the brain of the patient over a plurality of time periods;

a signal analyzer configured to:

analyze the signals to determine a number of spikes detected by each electrode during each time period;

detect a number of instances where spikes associated with at least two neurons are detected at substantially the same time during each time period; and

determine a correlation between the number of spikes and the number of instances for each time period.

60. The system of claim 59, wherein the signal analyzer is further configured to identify a trend in the correlation between the number of spikes and the number of instances over the plurality of time periods.

61. The system of claim 59, wherein determining the number of spikes comprises:

establishing a spike firing pattern; and

counting the number of spikes detected by each electrode that correlate with the spike firing pattern.

62. The system of claim 59, wherein the signals indicative of neurological activity comprise signals indicative of a neurological event.

63. The system of claim 62, wherein the signal analyzer is further configured to establish a benchmark correlation factor for predicting occurrence of a future neurological event.

64. The system of claim 59, wherein determining the number of spikes comprises determining a trend in the number of spikes over the plurality of time periods.
65. The system of claim 64, wherein detecting the number of instances comprises determining a trend in the number of instances over the plurality of time periods.

66. The system of claim 65, wherein the signal analyzer is further configured to identify a pattern between the trend in the number of spikes and the trend in the number of instances.

67. The system of claim 66, wherein the signal analyzer is further configured to:
   compare the pattern with a benchmark pattern derived from previously-detected signals indicative of a neurological event; and
   predict occurrence of the neurological event based on the comparison.

68. The system of claim 59, wherein at least one of the plurality of electrodes is further configured to detect signals indicative of physiological activity of the patient during each of the plurality of time periods.

69. The system of claim 68, wherein the physiological activity comprises at least one of heart rate, blood pressure, blood glucose level, eye movement, respiration rate, respiration content, pH, and intercranial pressure.

70. The system of claim 69, wherein the signal analyzer is further configured to identify a pattern between the number of spikes and a change in the physiological activity during each of the plurality of time periods.

71. The system of claim 69, wherein the signal analyzer is further configured to identify a pattern between the number of instances and a change in the physiological activity during each of the plurality of time periods.
72. The system of claim 59, wherein the signal analyzer is further configured to:
   compare the correlation with a predetermined correlation benchmark associated with the neurological event; and
   predict the occurrence of the neurological event based on the comparison.

73. The system of claim 72, wherein the signal analyzer is further configured to generate a warning signal when the correlation matches the predetermined correlation benchmark within a threshold value.

74. The system of claim 73, wherein the warning signal comprises one or more of an audible alarm, a visual signal, and an electronic message.

75. The system of claim 73, wherein the signal analyzer is further configured to generate a control signal for controlling at least one device in response to the prediction.

76. The system of claim 75, wherein the at least one device comprises a therapy delivery device.

77. The system of claim 76, wherein the therapy delivery device comprises a drug delivery device.

78. The system of claim 76, wherein the therapy delivery device comprises a device for delivering electric stimulation.

79. The system of claim 59, wherein the sensor includes a subdural grid configured to be placed proximate the brain of the patient.

80. The system of claim 79, wherein the subdural grid comprises at least one multi-electrode array.
81. The system of claim 79, wherein the subdural grid includes at least one physiological sensor.

82. The system of claim 59, wherein the sensor includes a subdural grid configured to monitor iEEG signals and a multi-electrode array configured to monitor LFP signals.

83. The system of claim 59, wherein the signal analyzer is at least partially implanted within the body of the patient.

84. The system of claim 59, wherein the signal analyzer is located external the body of the patient.

85. The system of claim 59, further including a signal conditioner communicatively coupled to the sensor and configured to condition one or more of the signals for processing by the signal analyzer.

86. The system of claim 85, wherein the signal conditioner is further configured to filter noise from signals detected by the sensor.

87. The system of claim 86, wherein the signal conditioner is further configured to classify neurological signals into one or more individual neuron spikes.

88. The system of claim 86, wherein the signal conditioner is at least partially implanted within the body of the patient.

89. The system of claim 86, wherein the signal conditioner is located external to the body of the patient.

90. A method for predicting occurrence of a neurological event, comprising:
providing a plurality of electrodes configured to detect signals from a body of a patient;
detecting signals indicative of neurological activity of the patient during a plurality of time periods;
analyzing the signals to determine a geometrical pattern associated with neuron spikes detected by one or more electrodes during each of the plurality of time periods; and
determining a correlation between the geometrical pattern and a benchmark geometrical pattern indicative of a neurological event.

91. The method of claim 90, wherein predicting the occurrence of the neurological event comprises generating a warning signal when the correlation matches the predetermined correlation benchmark within a threshold value.

92. The method of claim 91, wherein the warning signal comprises one or more of an audible alarm, a visual signal, and an electronic message.

93. The method of claim 90, further comprising generating a control signal for controlling at least one device in response to the prediction.

94. The method of claim 93, wherein the at least one device comprises a therapy delivery device.

95. The method of claim 94, wherein the therapy delivery device comprises a drug delivery device.

96. The method of claim 94, wherein the therapy delivery device comprises a device for delivering electric stimulation.

97. The method of claim 90, wherein at least one of the plurality of electrodes is configured to detect signals indicative of physiological activity associated with the patient's body.
98. The method of claim 97, wherein the physiological activity comprises at least one of heart rate, blood pressure, blood glucose level, eye movement, respiration rate, respiration content, pH, and intercranial pressure.

99. The method of claim 97, further comprising identifying a trend between the geometrical pattern and a change in the physiological activity during each of the plurality of time periods.

100. The method of claim 99, further comprising:
    comparing the pattern with a benchmark trend between the geometrical pattern and the change in the physiological activity, which is indicative of the neurological event; and
    predicting the occurrence of the neurological event based on the comparison between the identified trend and the benchmark pattern.

101. The method of claim 90, wherein the sensor comprises one or more of a subdural grid, a multi-electrode array, a physiological sensor, and a biological sensor.

102. The method of claim 101, wherein the sensor comprises the subdural grid and the multi-electrode array.
FIG. 6

FIG. 7
MONITOR NEUROLOGICAL ACTIVITY

EXTRACT SIGNALS INDICATIVE OF NEUROLOGICAL EVENTS

ANALYZE SIGNALS INDICATIVE OF NEUROLOGICAL EVENTS

DETERMINE CHARACTERISTICS ASSOCIATED WITH THE NEUROLOGICAL EVENT SIGNALS AT PREDETERMINED TIME INTERVALS

STORE NEUROLOGICAL EVENT CHARACTERISTICS IN MEMORY FOR FUTURE ANALYSIS

FIG. 8
THREE MINUTES PRIOR TO SEIZURE ONSET

FIG. 10
FIG. 11

ONE MINUTE PRIOR TO SEIZURE ONSET
FIG. 12
FIG. 13
MONITOR REAL-TIME NEUROLOGICAL ACTIVITY

ANALYZE NEUROLOGICAL ACTIVITY; DETERMINE CURRENT CHARACTERISTICS

COMPARE CURRENT CHARACTERISTICS WITH CHARACTERISTICS INDICATIVE OF NEUROLOGICAL EVENTS

DO CURRENT CHARACTERISTICS CORRELATE WITH BENCHMARK CHARACTERISTICS INDICATIVE OF NEUROLOGICAL EVENT(S)?

YES

PREDICT OCCURRENCE OF NEUROLOGICAL EVENT

NO

GENERATE EVENT ALERT

FIG. 16