

(43) International Publication Date
24 November 2016 (24.11.2016)

(51) International Patent Classification:

A61N 1/04 (2006.01) A61N 1/36 (2006.01)
A61N 1/05 (2006.01)

(21) International Application Number:

PCT/US2016/032994

(22) International Filing Date:

18 May 2016 (18.05.2016)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data:

62/162,891 18 May 2015 (18.05.2015) US

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

[Continued on next page]

(54) Title: CHIPLET BASED WIRELESS INTRANET FOR VERY LARGE SCALE RECORDING AND STIMULATION

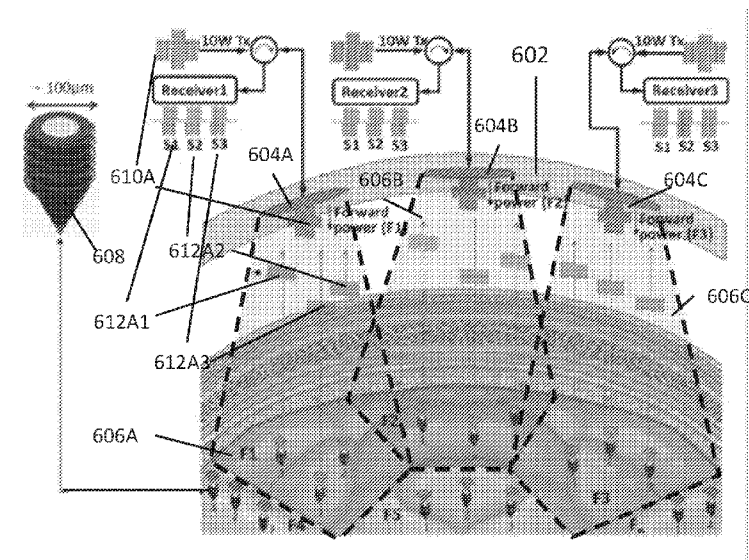


FIG. 6

(57) Abstract: The present disclosure is directed to systems, methods and apparatus for recording and/or stimulating a large number of sites within a subject's body. In some embodiments, the disclosed systems can include an external interface in wireless communication with a thousand or more chiplets implanted at different locations in a subject's body. The chiplets can comprise at least one probe configured to sense electrical and/or chemical properties of surrounding tissue, and to stimulate surrounding tissue using electrical, optical, or chemical means. The chiplets can be powered inductively by an electromagnetic signal transmitted transcutaneously by the external interface, can receive data from the external interface, and can send data back using backscatter modulation. A cell-based communications protocol can also be used to coordinate communications with the chiplets.



Published:

— with international search report (Art. 21(3))

— before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

CHIPLET BASED WIRELESS INTRANET FOR VERY LARGE SCALE RECORDING AND STIMULATION

CROSS REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Application No. 62/162,891 filed May 18, 2015 and entitled “Chiplet Based Wireless Intranet for Very Large Scale Recording and Stimulation,” the contents of which is incorporated herein in its entirety.

FIELD OF THE DISCLOSURE

[0002] This disclosure relates generally to systems, methods, and apparatus for recording and stimulation of a large number of sites within a subject's body.

BACKGROUND

[0003] There are major challenges in large scale recording from the cortex alone. A local region of $\sim 1\text{mm}$ contains a network of $\sim 10^4$ neurons. One brain area alone such as V_1 has about 10^8 neurons. Recording and stimulating brain circuits at a large scale is a challenging engineering problem. One current electrophysiological approach uses microelectrode arrays (MEA) in intracortical recording of neural population dynamics e.g. for human neuromotor prostheses applications, or for deep brain sensing/stimulation. Typically, the tissue penetrating probes are mechanically rigid platform devices with microscale Si-based electrodes for the electrical probe interface. These Si-based microelectrode arrays, coupled with bundles of microwires, are useful at the level of a hundred or so channels. However, extrapolating state-of-the art technology runs into major obstacles when required to record from and/or stimulate one thousand or more points (“nodes”) within the brain. Large scale brain mapping of functional neural circuits for in-vivo subjects requires entirely new types of engineering thinking. Challenges to scaling range from limits of microelectronic devices and wireless telecommunication to those posed by mechanically rigid neural sensor microelectrode arrays with interconnection wirings. Any scheme where physical wires are deployed is unlikely to be scalable to truly large scale neural recording and/or stimulation.

SUMMARY

[0004] The invention provides electronic access to a brain's microcircuits at

unprecedented level of scale and resolution using wireless means. This technology can deliver to the broader research community an entirely new set of tools for advancing fundamental and applied brain science that can allow untethered recording of large numbers of neurons across broad spatially distributed networks. Furthermore, this technology can fill in the gap between limited single cell sensing, which can be too narrow, and global brain imaging, which can be too broad.

BRIEF DESCRIPTION OF THE DRAWINGS

[0005] FIG. 1 shows a concept schematic whereby an ensemble of implanted, microscale electronic chiplets records and wirelessly transmits neural signals across different areas of the brain, according to some embodiments.

[0006] FIG. 2 shows an ensemble of clustered braindrops within brain tissue with wireless power and communication being transmitted through a subject's skull, according to some embodiments.

[0007] FIG. 3 shows the microcircuit design for an individual braindrop's components, according to some embodiments.

[0008] FIG. 4A shows a circuit diagram of our novel rectifier cell configured using only n-channel "zero V_t " MOSFETs, combining cross-connected and diode-connected FETs, according to some embodiments.

[0009] FIG. 4B shows a block diagram of an antenna, impedance matching network and multicell rectifier, along with modulation FET, according to some embodiments.

[0010] FIG. 4C shows a simulated conversion efficiency vs. available input power graph for the antenna, impedance matching network, and rectifier combination, according to some embodiments.

[0011] FIG. 5 shows an exemplary antenna configuration that splits up the antenna into segments that are smaller than the wavelength of the received signal, and terminating each segment with a lumped capacitor, according to some embodiments.

[0012] FIG. 6 shows an exemplary system for wirelessly communicating neural telemetry for brain sensing/stimulation using a plurality of transceivers and cells, according to some embodiments.

[0013] FIG. 7 shows a representative timing diagram for braindrop communication using

TDMA, according to some embodiments.

[0014] FIG. 8 shows a block diagram of a “helmet” braindrop electronic interface, including conceptual implementations of forward path and reverse path transmitters and receivers, according to some embodiments.

[0015] FIG. 9 shows examples of coated samples at Brown University.

[0016] FIG. 10 shows a concept schematic of placement of braindrops within a 6-layer cortex, according to some embodiments.

[0017] FIG. 11 shows an exemplary array of pneumatically or electromagnetically controlled “blow pipes” to specific targeted areas and tissue depths, according to some embodiments.

[0018] FIG. 12A shows an overview schematic of a planar array of braindrop chiplets embedded within a flexible polyimide film, with remote sensing and power provided by transcutaneous and transcranial RF radiation, according to some embodiments.

[0019] FIG. 12B shows an exemplary device process flow whereby arrayed chiplets are sealed within an insulating, biocompatible film using established microelectronic device processing techniques, according to some embodiments.

DESCRIPTION OF EXAMPLE EMBODIMENTS

[0020] This disclosure describes an entirely new neurotechnology that can allow access to circuits in the brain at unprecedented levels of large coverage yet with high spatial and temporal resolution. The disclosure can be further extended to medical and biomedical applications where physiological activity at a very large number (thousands) of points in-body and on-body (i.e., not necessarily in the brain or other internal organ) need to be sensed wirelessly for diagnostic purposes, or where corrective therapies by feedback delivered stimulation need to be delivered to a similarly large number of nodes. In some embodiments, the system in this disclosure can employ a large number of small devices that can be implanted in the body or placed on the body; each device can be capable of either (i) sensing an electrical, chemical, or other property of surrounding tissue or body parts and/or (ii) delivering stimulation to surrounding tissues or body parts using an electrical, optical or chemical signal. These devices are referred to herein as “microscale chiplets,” or “chiplets.” In the context of devices implanted in a subject’s brain, these devices can also be referred to as “braindrops.”

[0021] These microscale chiplets can be used to form an untethered network capable of monitoring, recording, stimulating and/or actuating a range of physiological activities conducted through-out the body or on the skin. In one or more embodiments, the technology enables general In-Body or On-Body physiological sensor/stimulator in a closed loop system.

[0022] In general, one thousand or more of these untethered microelectronic chiplets can be implanted into any body site to be monitored, either internal or external to the body. The chiplets integrate sensing microelectrodes with sophisticated microcircuits which are energized via externally delivered electromagnetic radiation in order to report on sensed neural activity in the vicinity of the chiplet and/or stimulate neural activity. In some embodiments, the sensing microelectrodes can be electrodes capable of detecting minute electrical currents, or chemical sensors that can detect chemical properties of surrounding tissue. Also in some embodiments, the microelectrodes can be used to stimulate the surrounding tissues, for example, by using an electric signal, using a light source, or using chemical reactions. The microelectronic chiplets can also be hermetically sealed by electromagnetically and optically transparent envelopes of materials, such as sapphire or glass or ceramics. The chiplet architecture and the hermetic sealing process can be configured to allow for a safe and implantable medical device.

[0023] The invention is described with particular attention to brain and neuronal applications; however, it is recognized that the disclosed innovations can be used for a range of sensing and stimulation applications throughout the body.

[0024] In one embodiment, the network is a neuro-network. Using the invention's application to neurotechnology as the concrete case example, it is contemplated to implant populations of untethered microelectronic chiplets as a network of individual nodes for active neural recording and electrical microstimulation. In some embodiments, one thousand or more of these untethered microelectronic chiplets can be implanted.

[0025] Communication between the chiplets and external devices can be accomplished using RF radiation, which in some embodiments can be at GHz frequencies. The RF radiation can be transmitted by an external interface and received transcutaneously by the chiplets or braindrops using special antenna structures. The chiplets can use microscale antennas, while external interfaces can use larger antenna arrays. In some embodiments, receiving electronics enable real-time read-out of neural activity via modulated backscattered

RF radiation from braindrops ensembles on a timescale of less than 1 msec. An estimate for outgoing neural data rates by 1000 chiplets, each capturing spikes, field potentials etc shows total neural data rates approaching 1 Gbit/sec, which approaches fundamental and practical limits on data rates that a conventional microelectrode array-based scheme employing physical wires can achieve. Here advanced RF telecommunication strategies are described to enable communication with the ensemble of chiplets to thousands of points. These thousands of points can be thought of as forming a “brain intranet.”

[0026] FIG. 1 shows a concept schematic whereby an ensemble of implanted, microscale electronic chiplets 104 (“braindrops”) records and wirelessly transmits neural signals across vast areas of the brain, according to some embodiments. Each chiplet can act as a node in a communication network 102, wherein each chiplet can access a few nearby neurons. The unique microelectronic chiplets (ASICs), together with innovative mobile telecommunication approaches also enable spatially and temporally controlled electrical microstimulation at single chiplet level. Thus the technology disclosed can provide read-out capability for targeted neural circuit information as well as imposing patterned micro-stimulation (“write-in”) on these circuits - thereby creating a closed-loop bidirectional electromagnetic interface between a subject brain and the external environment. Furthermore, by selectively activating and controlling a single chiplet out of the network of chiplets, wherein each chiplet can be configured to read and/or write from a single neuron or a small group of neurons, the presently disclosed system can read from and write into brain circuits at a single neuron level.

[0027] Current available technologies such as those based on wired microelectrode arrays have multiple challenges in scalability. By contrast, the development of an untethered wireless “brain intranet” is in principle, free of any such engineering scaling restrictions in terms of upper limits to the number and distribution of the braindrops.

[0028] External RF radiation has been used to sense and wirelessly transmit biophysical signals, though only from single or a handful of channels and low data rates. As described herein, provided is an entirely new platform technology that provides a synergy of bottom up (braindrop chiplets) and top-down (telecommunication systems) approaches to achieve very large scale neural recording and stimulation capability for research use in large animals and human clinical applications.

[0029] FIG. 2 shows an ensemble of clustered braindrops 202 implanted within brain

tissue 216 with wireless power and communication being transmitted through a subject's skull 204, according to some embodiments. The subject's skull can be protected by multiple protective layers, including 2 mm of skin 208, 2 mm of fat 210, 5mm of bone 212, and 1mm or more of cerebrospinal fluid (CSF) 214. Populations of braindrops 202 can be implanted within the subject's brain tissue 216 via guidetubes (such as hypodermic needles), by being propelled through the subject's protective layers and into the brain tissue 216 using electromagnetic or pneumatic force, or by other methods. In some embodiments, the braindrops 202 can be organized into one or more "clusters" as illustrated. The clusters can be a group of braindrops 202 that are grouped close in space to one another. External transceivers 206 located outside the subject's body can be used to communicate with braindrops 202, and also to transmit wireless power to braindrops 202 using electromagnetic radiation (e.g., RF waves). In some embodiments, one particular transceiver 206 can be configured to communicate with all the braindrops in a particular cluster, while another transceiver can be configured to communicate with another cluster. The way in which clusters can communicate with their corresponding transceivers is described in more detail in relation to FIG. 6, below.

[0030] In some embodiments, a transceiver 206 can comprise an oscillator 222 configured to generate a wireless signal to be transmitted to the braindrops 202. The oscillator 222 can be coupled to a power amplifier 224 configured to amplify the signal from the oscillator, and to relay the amplified signal to a transmit antenna 220. The transmit antenna can then generate wireless signals that are sent to the braindrops 202. These signals can be used to provide power to the braindrops 202, as well as to send both data and commands to the braindrops. The transmit antenna can also be used to receive signals sent from the braindrops using backscatter modulation. The transmit antenna can process the received signals through a low noise amplifier (LNA) 228. The output of LNA 228 can be passed to an analog-to-digital converter (ADC) 226, which can be configured to convert the analog signal from the LNA 228 into a digital signal. The digital signal can then be passed on to a computer (PC) 230, which can perform analysis on the signal received from the braindrops 202, as well as store the signals and data from braindrops 202 in memory for later analysis and communication. In FIG. 2, the only subcutaneous, subcranial and subdural implants are the microelectronic chiplets – no physical wires for providing power or relaying data are necessary for connecting the chiplets either to each other or to any external interface. For further detail on the components of transceivers 206, please refer to FIG. 8 and its

corresponding discussion below. Such a network of RF accessible braindrops require a number of innovations across a intertwined range of technical problems as are presented herein:

[0031] • Design of microelectrodes with a small footprint that provides sensing of neural transmembrane currents by chiplets of 100 μm size or smaller (for anatomical reasons).

[0032] • Design of microelectronic fabrication techniques for the design, integration, and fabrication of similarly sized dedicated ultralow-power integrated circuits (ASICs). These circuits can amplify and digitize the detected neural signals on the chip which modulate the electromagnetic cross-section of the specially designed and integrated microwave microantenna element enveloping each braindrop. The ASICs can also incorporate a microscale energy conversion circuit for converting incident microwave energy into power for chip operations/processing and for neural stimulation. Furthermore, the ASICs can also store in memory an individual RF identification code that uniquely identifies each chiplet.

[0033] • Design of RF telecommunication system and protocols that can provide parallel access to the braindrops population for extracting neural signals using external (to head) transmit/receive microwave electronics 206 is implemented for real-time communication with the brain.

[0034] • Balancing of safety and efficacy considerations regarding microwave radiation exposure for use in dynamic brain mapping of primates.

[0035] • Design of hermetic sealing of braindrops designed for chronic use. Braindrops can be hermetically sealed by an electrochemically robust thin film barrier which can be applied via a high-throughput batch process to large numbers (thousands) of chiplets per unit time. The barrier materials can be chemically prepared to mitigate tissue reaction when in the brain.

[0036] • Design of methods of implanting the chiplets that minimize any tissue damage, while delivering chiplets to specific target locations (e.g., specific layers of the cortex) with high accuracy and precision. These methods can be informed by knowledge of the neuroanatomic and functional architecture of a given brain region.

[0037] Certain features of exemplary embodiments are described below.

A. Microelectrode Geometry and Mixed Signal Microelectronics:

[0038] Neural recordings are traditionally done with transient differential voltage measurements between microscale recording electrodes and a macro reference electrode. In one embodiment, braindrop chiplets do not have access to a global reference, and thus recordings are of local potential gradients. Numerical simulations of electrostatics of membrane potential gradients for model neurons show that microelectrode separation of less than 100 μm is adequate for single-unit neural spike recordings with signal amplitudes comparable to established techniques without the use of a global reference.

[0039] In certain embodiments, the electrode materials utilized in the braindrop chiplet for planar, bio- and CMOS-process compatible fabrication can be thin films of Pt and Pt/Ir in a disk-shape geometry, with areas on a sub-100 μm scale tailored for targeted (electrode/tissue) impedance in the 10 k Ω -100 k Ω range. Thin films of TiN (also CMOS process compatible), especially for electrochemically stable stimulation can also be used.

i. Braindrop ASIC Configuration:

[0040] FIG. 3 shows the microcircuit design for an individual braindrop's components, according to some embodiments. The upper left of FIG. 3 shows a block diagram 300 of the main microelectronic components of a braindrop. The upper right shows a schematic 320 of physical structure in a planar ASIC implementation. The lower left of FIG. 3 shows a schematic 340 depicting how the neural recording electrode and RF antenna terminal can be placed on a chiplet. The lower right shows a cross-sectional illustration 360 an arrangement of the mixed signal and RF sub-ASIC circuits and their integration. In some embodiments, the ASIC planar chip can be a 90nm IBM CMOS process with silicon-on-insulator base. In certain embodiments, the chip is designed to maintain high performance while consuming ultra-low dc power. Also, in certain embodiments, the entire braindrop can be hermetically sealed by one or more envelopes comprising electromagnetically and optically transparent materials (e.g., sapphire, glass, or ceramics).

[0041] With reference to the upper left portion of FIG. 3, block diagram 300 includes three functional blocks: a RF and power functional block 300a, a digital functional block 300b, and an analog functional block 300c. The RF and power functional block 300a includes a low voltage RF rectifier 301, a matching and backscatter modulator 303, and a receiver and clock recovery module 304. Coupled to the RF and power functional block 300a is an antenna 302. The digital functional block 300b includes a unique ID memory module 305, a data buffer 306, control logic module 307, and an analog to digital converter (ADC) 308. The

analog functional block 300c includes an op amp 309, a biphasic stimulation module 310, a Pt-Ir positive electrode 311, and a Pt-IR negative electrode 312.

[0042] With regard to the RF receiving and power functions of the chiplet, antenna 302 can be configured to receive electromagnetic signals (e.g., RF signals) from an external transceiver. The received signals can be passed to low voltage RF rectifier 301 to convert the signal into a DC signal to power the chiplet. The received signals can also be passed to the receiver and clock recovery module 304 to determine a clock signal associated with the received signal, and with the external transceiver. Control logic module 307 can be a microprocessor, ASIC, processor, or other logic processing module, and can utilize the DC power provided by RF rectifier 301 and the clock signal recovered by receiver and clock recovery module 304 to control the operations of the chiplet.

[0043] Turning now to the sensing and stimulation functions of the chiplet, biphasic stimulation module 310 can control positive electrode 311 and negative electrode 312, which can extend through the one or more hermetically sealing envelopes, to deliver a stimulating signal to neurons within the brain. When a chiplet is implanted in some other part of the body, the electrodes 311 and 312 can be used to stimulate other types of body tissue or body parts. Electrodes 311 and 312 can also be used to sense electrical signals passing through surrounding neurons or other types of body tissue. Where the chiplet is configured to sense other types of signals (e.g., chemical signals), other types of sensors can also be used. The electrodes 311 and 312 can also be coated with carbon-based materials such as graphene and carbon nanotube thin films to enable electrochemical sensing of nerve chemicals such as dopamine, serotonin and related metabolically important neurochemicals. The sensed signals from electrodes 311 and 312 can be passed to op amp 309, which can then be passed to analog to digital converter (ADC) 308. ADC 308 can convert the sensed analog signals into digital signals which can be stored, interpreted and processed by control logic 307. In some embodiments, a data buffer 306 can be provided to store the converted digital signals.

[0044] Chiplets can also transmit their sensed data to an external transceiver via backscatter modulation. In some embodiments, a unique ID can be stored in a unique ID module 305, which identifies the chiplet. The unique ID can be sent along with data sensed by electrodes 311 and 312, as well as other data – this other data can be stored in data buffer 306 in some embodiments. The data to be transmitted can be sent to matching and backscatter modulator 303, which can then send the data to the external transceiver by modulating the

RF signal transmitted by the external transceiver. By sending the unique ID of the chiplet along with the sensed physiological data, an external transceiver can differentiate between signals originating from different parts of the subject's body.

[0045] Referring now to the upper right of FIG. 3, the physical structure 320 of an exemplary chiplet is shown. In some embodiments, the electrodes 311 and 312 can be located at opposite ends of the chiplet to detect differences in electrical potential. Furthermore, an exemplary chiplet can be shaped like a bullet with a tapered end such that the chiplet can be easily inserted into the subject's body with minimal damage to surrounding tissue (e.g., brain tissue). The reference electrode 311 can be positioned at the base of the bullet (i.e., the flat end of the bullet) while the sensing electrode 312 can be positioned at the tip of the bullet. Both electrodes can be exposed, with no protective covering, to enable the electrodes to come into direct contact with surrounding tissue (e.g., neurons).

[0046] Referring now to the bottom left of FIG. 3, the schematic 340 illustrates how the chiplet can be built using multiple substrate layers encapsulated within an antenna coil. At the bottom right of FIG. 3, cross-sectional diagram 360 shows how each of the functional blocks, i.e., the RF and power functional block 300a, the digital functional block 300b, and the analog functional block 300c can be built on separate substrate layers which are stacked on top of each other. Each of these functional blocks can be arranged in the fashion depicted in cross-sectional diagram 360, with the digital functional block 300b disposed on top of analog functional block 300c, which is in turn disposed on top of an interposer 362. The interposer 362 can provide a substantially rigid chassis for providing structural support and power and data connections between different functional blocks. On the opposite end of interposer 362, the RF and power functional block 300a can be disposed. Other arrangements of the functional blocks (e.g., wherein the functional blocks are stacked on top of each other in a different order) are also possible. Antenna 302 can be arranged around the entire structure. Configuring the antenna 302 in this fashion maximizes the surface area of the antenna to enable it to better receive power and signals from an external transceiver. By breaking each of the functional block 300a, 300b and 300c into separate substrate layers, stacking the substrate layers on top of one another, and surrounding the substrate layers with an antenna, the overall dimensions of the chiplet can be minimized while maximizing the chiplet's ability to receive wireless RF power and commands.

[0047] For the neural recording preamplifiers, the small amplitude and fine timescale of

neural potential fluctuations makes noise and bandwidth a primary concern. However, noise performance should be balanced with the low power requirements of the energy harvesting system. The achievable input noise (v_n), bandwidth (BW), and power consumption (P) can be related through a metric called the Noise Efficiency Factor (NEF), by:

$$P = V_{DD} \times \frac{NEF^2}{V_{n-rms}^2} \times BW \times 2\pi\phi_t kT$$

where ϕ_t is the thermal voltage, k is Boltzmann's constant, and T is the absolute temperature. The NEF compares the power and noise performance to an ideal bipolar transistor, and sets a lower bound of $NEF > 1$. For a targeted amplifier performance of $5\mu V_{rms}$, $V_{DD}=1V$, $BW=5kHz$, $T=309^\circ K$, and $NEF=2.5$, this implies a total power consumption of $1\mu W$. An NEF of 2.5 represents the state-of-the-art in low power amplifiers today.

ii. Digitization and Sample Buffering:

[0048] The amplified neuro-potentials can be digitized at 10kS/s at 8-10bit resolution, using a power-and-area-efficient analog-to-digital converter (ADC). The converter can implement a charge-redistribution successive-approximation algorithm; 10-bit resolution with a 0.5V full-scale range corresponds to an equivalent input-referred noise of $141\mu V_{RMS}$, which can be achieved using sub-pF sampling capacitors in a small active area. An energy budget of 100fJ per conversion step enables ADC power consumption of at levels below $1\mu W$ in a chiplet. Digitized samples can be collected in a small local memory buffer until the chiplet's assigned RF timeslot, during which the accumulated data can be read out serially in a burst transfer to the external RF detector array (referred to below as the "helmet", see also FIG. 6).

iii. Electrical Microstimulation:

[0049] In addition to the function of recording neuron activity, the braindrops can be used for producing, under external command, waveforms for the stimulation of neurons in their vicinity. When chiplets are implanted in other areas of the body, the chiplets can be used to stimulate other body parts under external command. Programmable biphasic μA -scale current stimulation can be multiplexed onto the recording electrodes, to allow interactive interrogation of adjacent neurons. In some embodiments, this stimulation can be implemented by biphasic stimulation module 310 in conjunction with electrodes 311 and 312, illustrated in

FIG. 3. The biphasic stimulation module 310 can contain a programmable state machine that shares timing circuits with the communications infrastructure; frequency and stimulation intervals can be programmable via wireless means and each braindrop can be individually addressable for stimulus. Stimulation can be enabled by a switched capacitor bank transferring charge from the RF rectifier 301 to the electrodes 311 and 312; charge can be transferred to the electrodes sequentially and with opposite polarity for charge-balanced stimulation. The overall stimulation charge that can be delivered can be constrained both by the energy harvesting output and by the area of the necessary charge storage. Maximizing charge storage for stimulation can have tradeoffs with the active area of the chiplet. The voltage levels that can be achieved in the on-board rectifier can be in the range 0.8-1V. The braindrop can be provided with a switching matrix to allow connecting this voltage to external electrodes, with alternating polarity to minimize electrochemical corrosion reactions. Target current levels for the external stimuli can be on the order of 1 -10 uA in bipolar bursts of duration (e.g., 10-100µsec), supplied from a capacitor charged from the rectifier. Timing control on longer time scales can be handled off-chip (in the control electronics associated with the external RF “helmet”).

iv. Other Supporting Hardware:

[0050] Each braindrop can host a unique digital ID, which is written into a one-time-programmable e-Fuse register on the chiplet at the time of manufacture (e.g., unique ID module 305 in FIG. 3). The system clock can be recovered from the RF input together with frame synchronization pulses and timeslot assignments from the external “helmet”. In some embodiments, this can be accomplished by receiver and clock recovery module 304. Clock generation circuits and distribution networks can be optimized for minimum power consumption.

B. RF Energy Harvesting and Electromagnetics:

i. RF-to-DC Energy Conversion:

[0051] Maximizing the efficiency of conversion of RF power delivered to the antenna into DC power available for circuit operation is provided to achieve at least the following objectives. One is the desire for the rectifier to respond to the very small voltages that are transmitted to the braindrop’s antenna; another is to achieve impedance matching so that the power available from the antenna is delivered to the rectifier without reflection. To address the low voltage objective, a novel circuit is described that employs transistors whose

threshold voltages are near zero, in order to eliminate the voltage “dead zone” that affects the majority of rectifier designs.

[0052] FIG. 4A shows a circuit diagram of the novel rectifier cell configured using only n-channel “zero V_t ” MOSFETs, combining cross-connected and diode-connected FETs, according to some embodiments. FIG. 4B shows a block diagram of an antenna, impedance matching network and multicell rectifier, along with modulation FET, according to some embodiments. FIG. 4C shows a simulated conversion efficiency vs. available input power graph for the antenna, impedance matching network, and rectifier combination, according to some embodiments.

[0053] The circuit in FIG. 4A is configured to use only the n-channel FETs 402 with “zero” threshold voltage (V_t) provided in 90nm CMOS foundry processes (avoiding p-FETs, which are obtainable with very low V_t only in boutique processes that cannot support the remaining circuitry). Under ideally matched conditions, simulations show that power conversion efficiency (PCE) above 60% is obtainable at μW input power levels. In order to optimize the impedance matching between rectifier and antenna, a resonant LC network can be employed, and the rectifier can be partitioned into multiple units driven in parallel by the RF, whose DC output voltages sum together. For N stages, the input impedance of the rectifier decreases in principle by N^2 as in the block diagram of Fig. 4b. Detailed simulations based on the IBM 90nm CMOS node indicate that overall efficiency (ratio of dc output power to available RF power at the antenna) reaches $>15\%$ in the baseline design, as shown in Fig.4C. The resulting DC power available is ample to drive the CMOS circuits. “Integrated passive device” technology can be used, which allows $5\ \mu m$ thick metallizations and features a high resistivity silicon substrate to further reduce losses. Such technology can be used to provide advanced means for converting low-power incident RF power to useful electrical energy for the chiplet active microelectronic circuits.

ii. Electromagnetics of Braindrop Powering:

[0054] Anatomical constraints of neurological tissue suggest the volume of an individual braindrop to be less than the wavelength of RF radiation at frequencies (up to few GHz) where tissue remains reasonably transparent. Even if current state-of-the-art solid-state batteries with energy densities of $30\ J/cm^3$ could be miniaturized to sub-mm scale they would only provide sufficient power for < 1 minute of operational time at $1\ \mu W$ before needing to be re-charged. Energy harvesting through a glucose biofuel cell yields at most $3.4\ \mu W/cm^2$ of

continuous power density, or 1.4 nW when utilizing the entire braindrop surface as biofuel cell electrodes. Thus in one or more embodiment, the braindrops include a wireless/transcutaneous power delivery .

[0055] There are at least two approaches to deliver power transcutaneously: through electromagnetic or acoustic energy. While acoustic energy at ultrasonic frequencies has desirable path loss properties through neurological tissue, it has not been widely adopted as a mechanism for transcutaneous power delivery due to the high attenuation through bone, necessitating an invasive three-layered approach (electromagnetic coupling to a subdural receiver, which then delivers energy acoustically to a deeper implant). In addition, state-of-the-art piezoelectric crystals have orientation-induced losses, and have not yet been proven at microsize scales.

[0056] In one or more embodiments, the system is capable of inductively powering neural devices using electromagnetic energy transmitted transcutaneously from an antenna external to the subject's body to the neural devices implanted in the subject's body. Reliable powering of mm-sized implants at frequencies into the GHz regime is contemplated. GHz frequencies can be used for small-scale implanted antennas, as a trade-off between increasing tissue losses and increasing antenna efficiency.

[0057] Electromagnetic simulations were performed for sub-mm-sized antennas. In some embodiments, the system can feature a single external antenna that delivers transcutaneous power to and receives recording information from a network of up to 1000 braindrops within a $\approx 1 \times 1 \text{ cm}^2$ cortical area spanning several mm of human cortical depth (see FIG. 2 above). Multiple external antennas can be used to interrogate spatially-separated networks of braindrops, for tens of thousands of parallel channels. At the frequencies of interest, the transmit power is limited by tissue heating and should not exceed IEEE specific absorption rate (SAR) specifications of 2 W/kg averaged over 10 g for chronic human use, or 10 W/kg for persons in controlled environments. These limits can, however, be exceeded in non-chronic animal models; for example, when taking blood perfusion into account. Simulations show that 10 W of power delivered to a 300 ml brain can increase the temperature of the brain tissue by as little as 0.7°C after two minutes of exposure, setting a rough upper bound in terms of delivered power and duty cycle for animal models, in certain embodiments.

[0058] To validate and optimize transcutaneous power delivery, a simulation model was constructed that incorporates the frequency-dependent dielectric properties of tissues, based

on measurement data. The size of the external antenna was not constrained, but instead was constrained to be 5 mm away from skin due to packaging considerations. Then, 2 mm of skin, 2 mm of fat, 5 mm of bone, and 1 mm of cortex was modeled. The optimal frequency for power transmission was determined by performing a parametric analysis of varying external (TX) and implant (RX) antenna sizes when employing single-loop antennae, choosing the frequency with the best Maximum Available Gain (MAG), which takes into account optimal matching, as optimal for each data point. As shown in FIG.5, the optimal frequency is primarily dependent on the TX antenna size, while MAG is primarily dependent on the RX antenna size. At an RX size of 200 μm , the optimal TX size lies between 10-20 mm, with an un-optimized MAG of approximately -60 dB at an optimal frequency around 1 GHz.

[0059] Next, both MAG and the amount of deliverable power were maximized under SAR constraints. While both of these properties can be maximized through TX and RX optimizations, the latter can be optimized only through TX optimizations. Standard loop antennas suffer from electric field concentrations at the antenna feed point, thereby setting the limit of deliverable power under SAR constraints. By splitting up the antenna into segments that are much smaller than the wavelength, and terminating each segment with a lumped capacitor to maintain resonance, the electric field concentration can be reduced by up to 3 dB, as shown in Fig. 5, thereby improving deliverable power by the same amount. The solenoid antenna better concentrates the magnetic field, providing an additional increase in MAG. At 13 mm in diameter and operating at 1 GHz, IEEE SAR constraints can be satisfied while delivering up to 0.8 W of power into the TX antenna for persons in controlled environments with an MAG approaching -50 dB along the central axis of the TX antenna. At these numbers, approximately -21 dBm (on the order of 10 μW) can be delivered to the implanted antenna.

[0060] A network of multiple braindrops can be powered directly from a single TX antenna. Braindrops were simulated to reside within a 1 cm^2 (or 2.6 cm^2) area of the central axis of the TX antenna while receiving within 3 dB (or 5 dB) of the power delivered to an antenna located on the central axis. This configuration maximizes the net power transfer efficiency from the external antenna to the braindrop network by utilizing a larger fraction of the magnetic field energy along the plane formed by the network. This configuration can support more than 1000 braindrops at a time with a pitch of 300 μm between braindrops.

C. High RF Data Rate Telecommunication System and Protocol:

[0061] The communication link from the external antenna to the braindrop (the forward link) and communication from the braindrop back to the external antenna (the reverse link) is one of the most important aspects of the system. As such, it represents a unique opportunity to apply traditional telecommunications network concepts to the human body itself. In this case, the disclosed network is able to capture the *full range* of neural data sampled by hundreds or thousands (or tens of thousands) of brain drops. The network itself is robust against channel impairments and naturally and easily capable of scaling to eventually tens of thousands of braindrop nodes, for an aggregated data rate in the Gb/sec range at the “helmet”.

[0062] The braindrop concept enables all of the nodes to independently sample and digitize local neural data, which is then transmitted back to the helmet. These individual braindrops should not interfere with each other during transmission, and they each function with the absolute minimum of DC power supplied by the RF-DC converter. In some embodiments, a combination of time-division multiple access (TDMA) and frequency division multiple access (FDMA) cellular techniques can be used for the deployment of the braindrop system. This network design can allow thousands of braindrop nodes to communicate back to the helmet independently and without interfering with each other.

[0063] FIG. 6 shows an exemplary system for wirelessly communicating neural telemetry for brain sensing/stimulation, according to some embodiments. Wireless RF backscatter telemetry of high fidelity broadband neural data being transmitted transcranially / transcutaneously from thousands of nodes implies very large data rates. In some embodiments, a combination of time-division multiple access (TDMA) and frequency division multiple access (FDMA) cellular techniques can be used to handle these data rates and to deploy the braindrop network.

[0064] FIG. 6 includes a “helmet” 602, which serves as platform for mounting multiple transceivers 604A-C which are in communication with multiple chiplets 608. In some embodiments, the helmet 602 can be shaped like a helmet and can be configured to be worn on the subject’s head. Transceivers 604A-C are capable of both transmitting electromagnetic signals and power to chiplets 608 as well as receiving messages from chiplets 608 via backscatter-modulation. Each transceiver 604A-C can communicate with chiplets within a cell 606A-C (i.e., transceiver 604A can communicate with chiplets within cell 606A, transceiver 604B can communicate with chiplets within cell 604B, and transceiver 604C can communicate with chiplets within cell 606C). Each cell illustrated in FIG. 6 can correspond

to a “cluster” of braindrops illustrated in FIG. 2.

[0065] An antenna in each transceiver 604A-C can transmit sufficient RF power in the forward link to provide at least 100 μ W of RF power to antennas embedded in each chiplet 608, and thus roughly 5 μ W of DC power is available for the braindrop system for each chiplet 608. On the reverse link, the backscattered forward-link power from the braindrop back to the transceivers 604A-C provides adequate received power to minimize the bit-error-rate (BER) of the received signal.

[0066] The distributed braindrops can be organized as a time-shared (TDMA) wireless network supporting bidirectional communications between the chiplets and its corresponding transceiver in the helmet 602. Each braindrop can have a unique hardware ID that is known at the time of implant, and the hardware IDs are consecutive (1,2,3,...) within a given cell 606A-C. For example, the hardware IDs within cell 606A can be numbered 1, 2, 3 and so on in ascending order. Each cell 604A-C is set to operate at a different frequency so that communications between chiplets and transceivers in one cell will not interfere with communications in a neighboring cell. While chiplets within a given cell are all set to operate at one frequency, communications with individual chiplets within a cell are time-multiplexed. That is, each chiplet 608 within a cell is given a different time slot in which to communicate with its corresponding transceiver.

[0067] Each chiplet 608 can transmit its accumulated neural data back to the helmet during its designated time slot. Communications between chiplets 608 and its transceiver can be organized in time according to frames. A synchronization pulse 610A superimposed on the RF signal sent from the transceiver 604A at the beginning of each frame initializes each braindrop's internal counter to “zero,” insuring that all the braindrops in a given cell are beginning data transmission at the appropriate time slot determined by their pre-assigned ID.

[0068] In some embodiments, the transceiver 604A (in the helmet) receives time interleaved digitized recordings 612A1, 612A2 and 612A3 transmitted from each of the braindrops in its corresponding cell, with no data loss. (See FIG. 12 for additional disclosure regarding an exemplary messaging structure). The transceivers 604B and 604C can receive similar time interleaved digital recordings from the braindrops in their corresponding cells. When the chiplets are not transmitting, they are measuring/accumulating neural data for later retransmission using DC power supplied by the incoming RF signal from the transceivers 604A-C. The requirement for accumulated clock jitter between two different braindrop

oscillators at the end of the frame is minimized by the short time window for transmission and the long set-up time.

[0069] The braindrop nodes can be configured to have no long-term energy storage. Thus when the “helmet” power from the transceivers 604A-C is disabled, the braindrops can become inactive. The system can initialize with application of RF power by the helmet, upon which the implanted braindrops can power on. With approximately 100 μW of received power per braindrop, 5 μW of dc power can be available for operation.

[0070] While only three cells are illustrated in FIG. 6, and only three chiplets 608 are illustrated per cell, it is understood that the present system can be scaled up to include an arbitrarily large number of cells, with an arbitrarily large number of chiplets in each cell. In some embodiments, a thousand or more chiplets (indeed, tens or even hundreds of thousands of chiplets) can be powered and communicated with using the methods and schemes described above. Also in some embodiments, frequencies can be re-used between cells that are separated in space by at least a certain number of cells to minimize interference between cells.

[0071] Also, while the transceivers in FIG. 6 are described as both providing power to the chiplets as well as receiving data from the chiplets, these two functions need not be provided by the same component(s), as other embodiments are possible. For example, a single antenna can provide RF power for all the chiplets embedded in a subject's brain or body, while multiple receivers can be positioned to receive data from different chiplets.

[0072] Furthermore, while FIG. 6 illustrates transceivers disposed within a “helmet” that can be worn by the subject's head, the present disclosure is not limited to external interfaces that are shaped like helmets, nor is it limited to chiplets that are implanted in a subject's brain. Chiplets may be implanted in any part of the subject's body, including the subject's skin, internal organs (e.g., heart, lungs, digestive tract) or bones, and the external interface that functions as a platform for the transceivers need not conform to any particular shape or size. The external interface can be configured to be worn by the subject, or it can simply be a handheld or non-mobile device that is positioned close to the subject.

[0073] Finally, while FIG. 6 and the above description disclose an exemplary embodiment that distinguishes between cells using Frequency Division Multiple Access (FDMA) (i.e., cells use different frequencies to prevent interference), and distinguishes between chiplets within a cell using Time Division Multiple Access (TDMA) (i.e., chiplets

are assigned unique time slots to communicate with its transceiver), the disclosure is not so limited. Other ways of preventing interference and cross-talk between (i) cells and (ii) chiplets within a cell are contemplated, including using code division multiple access (CDMA), orthogonal frequency-division multiple access (OFDMA), orthogonal frequency division multiplexing (OFDM), and spread spectrum techniques. In some embodiments, transceivers may communicate with more than one cell.

[0074] FIG. 7 shows a representative timing diagram for braindrop communication using TDMA with an exemplary system having 100 chiplets within one cell, according to some embodiments. The braindrops can digitize and accumulate neural data at a slow clock rate (e.g., 1 kHz) and then transmit the neural data in serial fashion at a fast clock rate (e.g., 4 MHz). So for example, braindrop 1 can transmit its data at a rate of 4 MHz during a first period of the slow clock rate, labeled #1. Braindrop 2 can transmit its data at the same rate during a second period of the slow clock rate, labeled #2. Each successive braindrop can transmit its data during its corresponding time slot, until braindrop 100 can transmit its data at the fast clock rate of 4 MHz during the one-hundredth period of the slow clock rate, labeled #100. The transmit period can be 500 μ s, and a total of 2000 bits can be transmitted with each transmission at a rate of 4 MB/sec. In some embodiments, Manchester coding can be used to transmit this data.

[0075] FIG. 8 shows a block diagram of an external chiplet electronic interface (e.g., a “helmet”) in communication with an individual chiplet. FIG. 8 includes conceptual implementations of forward path and reverse path transmitters and receivers, according to some embodiments. As discussed above, the chiplet or braindrop can utilize RF backscattering to transmit accumulated data. FIG. 8 includes an exemplary transceiver 802 in the helmet and an exemplary braindrop 850. The transceiver 802 can comprise a controller 804, an oscillator 806, a microwave circulator 808, an antenna 810, and a passive mixer 812. The braindrop 850 can comprise an antenna 852, RF-DC power source 854, a controller 856, and neural probes 858. One or more neural probes 858 can be used to sense electrical or chemical signals from nearby neurons. For example, the neural probes can be coated with carbon-based materials such as graphene and carbon nanotube thin films to enable electrochemical sensing of nerve chemicals such as dopamine, serotonin and related metabolically important neurochemicals. In some embodiments, neural probes 858 can also be used to stimulate nearby neurons using electrical, optical or chemical signals. For example, spectroscopically targeted optical stimulation, and/or specifically targeted electrical

stimulation, can be used to induce a neurochemical response. Neural data recorded by the braindrop 850 for transmission to the transceiver 802 is denoted 860, and can be sent via a reverse link 840. Neural data received, demodulated and recovered by the transceiver 802 is denoted 814. The transceiver 802 can send power and signals to the braindrop 850 via a forward link 830.

[0076] As depicted in FIG. 8, both the forward link 830 and reverse link 840 suffer from signal loss due to passage through the skin, bone, dura and cortex of the subject. The forward link 830 can suffer a 50 dB loss, while the reverse link 840 can suffer a 50 dB loss or less. In some implementations, the loss can be as little as 10 dB. The performance of the reverse link communications link 840 from the braindrop to the external antenna is ultimately determined by the bit-error rate (BER) performance of the received signal. For example, if a maximum BER limit of 10^{-3} is set, then the minimum *Signal-to-Noise Ratio* (SNR) of the received backscattered signal is approximately 10 dB.

[0077] In some embodiments, the braindrop 850 and the transceiver 802 can employ two-level Amplitude-Shift Keying (ASK), where the incident RF power transmitted from the antenna 810 of the transceiver 802 can be reflected from the braindrop antenna 852, and where the amplitude of the reflection is modulated by the digital information to be transmitted (e.g., neural data 860). Because the system employs direct detection the incoming and outgoing frequencies are the same. This can cause problems with self-interference, wherein the signal 830 transmitted from the transceiver 802 interferes with the signal 840 received at the transceiver 802. The problem of self-interference can be mitigated by Manchester-encoding the digitized neural data, which removes the DC component of the transmitted data and allows for simple recovery of the braindrop clock at the helmet transceiver 802. The Manchester encoding eases demodulation of the signal in the presence of strong interference, but doubles the bandwidth of the transmitted signal, increasing the background noise by 3dB.

[0078] The *noise* power of the received signal can be determined by the system bandwidth, which is approximately double the bit rate in this case, thanks to the Manchester encoding, and the receiver Noise Figure, which can be designed to be less than 5 dB. The *signal* power in this case is the backscattered signal from the braindrop node. In this case, there is a 3dB loss due to the “on-off” keying of the signal, another 3dB loss due to the fact that only 50% of the signal is backscattered (the rest can be absorbed by the braindrop to

supply the transmit DC power) and a 50 dB path loss from the braindrop back to the helmet.

[0079] As FIG. 8 shows, with parameters described, the communications link can in fact be very robust at the 100 node level. In some embodiments, the received signal power can be 0.1 nW (-70 dBm) and the received noise power can be $FkTB$ or roughly -100 dBm. So the SNR in this embodiment is approximately 30 dB, well within the 10 dB SNR requirement for a BER of less than 10^{-3} . Even at the thousand node level, the link stays robust with a 10X increase in the number of links and hence the noise power; the resulting SNR is roughly 20 dB, still well in excess of the 10 dB requirement. Since the helmet resides outside the head, it can consume considerably more DC power and space than the braindrops. As a result, it can employ state-of-the-art microwave antenna, receiver and transmitter technology, with high performance. The link budget for the system is determined by the RF performance of the helmet.

[0080] The performance challenges of the receiver originate from two aspects of the system. First, the external source/receiver ("Helmet") receiver has an intrinsic *self-jamming* problem, caused by the fact that the helmet is transmitting (to the braindrop) and receiving (from the braindrop) at the same time, and at the same frequency. To mitigate this problem, the transmit and receive signals can be separated by a microwave circulator 808, i.e., a non-reciprocal microwave device that separates incident waves at different ports. A high performance circulator can achieve roughly 30 dB of isolation, reducing the 10W (40 dBm) of transmitted power to 10 mW (10 dBm) at the receiver input. This is a vast improvement, but the system can still require separation of the leaked transmit signal from the received signal which is roughly -70 dBm. Therefore, the helmet receiver needs to have at least an 80 dB dynamic range. This separation is achieved by using a small portion (roughly 100 mW) of the transmitted signal to serve as the local oscillator (LO) for the passive mixer 812 in the helmet receiver. In some embodiments, the passive mixer can comprise a signal multiplier that multiplies the received signal with a local signal that is 90° out of phase with the leaked transmit signal, so as to cancel out the leaked transmit signal component of the received signal. Then the leaked transmit signal mixes with itself, and becomes simply a DC output of the mixer, which can be removed with a high-pass capacitor (an important benefit of Manchester coding).

[0081] The second aspect of the helmet receiver design is that the Noise Figure should be as low as possible (e.g., under 3 dB), in order to achieve the best possible link margin. The

dynamic range can be at least 80 dB. In other embodiments, multiple antennas can also be used. Each doubling of the number of antennas roughly doubles the number of braindrops that can be deployed. The antennas can be configured not to interfere with each other, as interference can potentially increase the bit error rate of the received signal.

[0082] The issue of frequency reuse among different cells is now described. As discussed above with reference to FIG. 6, each individual cell 606A-C operates at a distinct frequency. Assume that there are N different cells within a *group*, wherein a group constitutes a plurality of cells which all utilize distinct frequencies. A typical cellular reuse pattern (like in a traditional cellular network) corresponds to $N=7$, but many other values are possible as long as they satisfy the well-known constraint of $N=i^2+iq+q^2$ (for integer values of i and q). As the value of N grows, the distance between cells (D) sharing the same frequency (increasing this distance reduces co-channel interference) grows modestly as $D=R(3N)^{1/2}$ where R is the cell radius. The value of D should be as *large* as possible to minimize co-channel interference, but the value of D should also be as *small* as possible to maximize the number of braindrops that can be deployed. The values of D and R must therefore be optimized to balance these competing considerations. In some embodiments, a value of $D=5\text{mm}$ and $R=1\text{mm}$ can provide the best result (i.e., highest density of braindrops and most feasible frequency reuse pattern), resulting in an N of 9, and a braindrop density of 100 mm^{-3} . Also in some embodiments, each data bit could be multiplied by a Walsh code, which can orthogonalize each of the interfering bits and allow recovery of the original data even in the presence of modest co-channel interference.

D. Hermetic Sealing and Packaging of Braindrops: High Throughput Photopolymerization in Microfluidic Channels:

[0083] A high-throughput, micro-fluidic based photopolymerization technique can be used to hermetically insulate the braindrop chiplets for chronic implant in animal models. The hermetic sealing can be accomplished by enveloping chiplets in at least one layer of electromagnetically and optically transparent material, such as sapphire, glass, or ceramics.

[0084] For sealing, the chiplets can be completely protected from the brain's cerebrospinal fluid (CSF) environment. Of special concern are ions, such as Cl^- , which are known to accelerate localized corrosion in occluded regions where oxygen in the solution is easily depleted. In order to achieve the required level of hermeticity, special attention can be given to coatings of corners and edges and the boundary between an exposed electrode and

the rest of the chiplet. In addition to examining possible corrosive attack of the chiplet, the response of the tissue around the implanted chip should be considered. A number of studies have shown that the insertion of an electrode in the brain leads to the formation of scar tissue that is primarily composed of reactive astrocytes and activated microglia and that this scar tissue can deteriorate electrode performance.

[0085] Optofluidic maskless lithography (OFML) technique can be used to encapsulate microchips of small footprint and thickness with photocurable materials. OFML is immune to variations in size, shape and orientation of microchips thanks to its automated image processing based dynamic mask generation capabilities. FIG. 9 shows examples of coated samples at Brown University. The left picture shows an empty “bullet shape” chiplet; the right picture shows a coated micro-RFID tag. In the OFML based chiplet encapsulation approach, the chiplets are mixed with a photocurable resin, such as polyethylene (glycol) diacrylate (PEGDA) and flowed through a PDMS-based optofluidic microchannel. The PEGDA resin around the chiplet is selectively cured by UV light with a pattern transferred from a digital micromirror device (DMD). The light pattern can be dynamically generated by using a digital image of the chiplet, acquired prior to curing. This is an important asset of OFML, due to the random nature of chiplets’ movement in the fluid environment. In OFML, spatial selectivity and control on the microscale of the coating profile can be obtained to, for instance, coat only the areas of interest. PEGDA is known to be biocompatible and its electrical and mechanical properties are tunable (e.g. a substantial increase in the conductivity can be obtained by mixing graphene oxide flakes with a 2 % weight ratio). Other possible coatings include those with tunable mechanical properties, to pave the way for reduced scar formation in tissues.

E. Insertion:

[0086] Implanting the braindrop chiplets with targeted precision into the brain (or other parts of the body) requires special techniques. For example, a typical goal could be to implant 1,000 or more braindrops (e.g., tens of thousands, or hundreds of thousands) into the specific layers of the non-human primate or human cortex to focus on recording spiking activity in ensembles of single neurons and high-spatiotemporal resolution LFPs. FIG. 10 shows a concept schematic of placement of braindrops within a 6-layer cortex according to some embodiments – the image of the cortex is obtained from an actual Nissl stain.

[0087] Whether the active electronic chiplets are aimed at the use in brain

sensing/stimulation, or elsewhere in the body as a distributed network of implanted microscale “points” of physiological sensing and stimulation, specific targeting and implant methods are required. One approach is to deliver the braindrops by injection through guidetubes (such as small size hypodermic needles). Another approach uses ballistic delivery of the chiplets in parallel by an array of pneumatically or electromagnetically driven microbarrels.

[0088] FIG. 11 shows an exemplary array of pneumatically or electromagnetically controlled “blow pipes” 1102 to specific targeted areas and tissue depths, according to some embodiments. FIG. 11 includes an inert gas chamber 1104, an acceleration chamber 1106, a cartridge holder 1108, and braindrops 1110. In some embodiments, braindrops 1110 can initially be disposed within cartridge holder 1108. Cartridge holder can then be coupled with inert gas chamber 1104 and acceleration channel 1106. By forcing pressurized gas through acceleration channel 1106 and into cartridge holder 1108, braindrops 1110 can be driven along braindrop guide tube 1102 at high speed. When braindrops 1110 emerge from braindrop guide tube 1102, they can possess sufficient velocity and kinetic energy to penetrate into brain or other tissue to pre-determined depths. Here, the “bullet” shape of the chiplet envelope is an asset to minimize tissue damage. The penetration of the chiplets into specific depths of brain or other tissue is determined by their incident velocity and kinetic energy. Also as illustrated in FIG. 11, the acceleration channels 1106 and guide tubes 1102 can be configured as an array, wherein the array is configured to conform to a contour of a subject’s body. For example, where the “blow pipes” are used to implant braindrops into a subject’s brain, the acceleration channels 1106 and guide tubes 1102 can form an array that is configured to conform to a surface of the subject’s head.

[0089] While FIG. 11 is directed at a system that uses pressurized inert gas to propel the chiplets into a subject’s body, other embodiments are possible. For example, instead of an inert gas chamber 1104, electromagnetic coils can be arranged in and around the guide tubes 1102. By varying current applied to these electromagnetic coils, shifting electrical and magnetic fields can be induced within the guide tubes 1102, and the chiplets can be propelled along the guide tubes using electromagnetic force.

F. A Planar Device for wireless 1000-channel neural or other body area electronic interface: Chiplets within a Flexible Sheet.

[0090] FIG. 12A shows an alternative embodiment in which a planar array of braindrop

chiplets 1204 can be embedded within a flexible polyimide film 1202. As with previously described embodiments, remote sensing and power can be provided by RF radiation transmitted transcutaneously and transcranially from an external transceiver. In some embodiments, 1,000 or more wireless chiplets 1204 can be embedded into a flexible sheet 1202 for application to the brain or other body areas. The flexible sheet can, in some embodiments, provide for electrical connections between each of the wireless chiplets such that the chiplets can share a common reference electrical ground. This specific planar embodiment of the above chiplet platform can enable creation of a generalized biomedical device system of potential significance for broad research and clinical use. For example, in the field of neurotechnology, the use of electrocorticography is widespread in basic primate neuroscience and human clinical diagnostics, the latter especially in context of refractory epilepsy. Further, for neuromotor prostheses use, recent work has shown how ECoG derived signals can be decoded to usefully infer movement intent in monkeys. Issues of spatial resolution and access to neural populations with improved focus are being pursued by reduction of the individual electrode size to sub-mm scale (“micro-ECoG”). Recent epilepsy research in seizure detection and prediction has raised the issue of improving the technology of subdural ECoG techniques to improve the temporal and spatial resolution. Thus reducing the individual electrode size while maintaining a large area coverage is needed to overcome limitations of current ECoG based recording.

[0091] In some embodiments, access to the individual chiplets as well as to the entire planar array can be accomplished entirely wirelessly and externally by RF means using a plurality of channels (e.g., 1,000+ channels). This is unlike prior known systems which use wired configurations. The wireless configuration of these embodiments leads to several advantages. First, this enables an ECoG device to be subdurally implanted at least subchronically (> 1 month) as a standalone unit, provided that the dielectric insulation has adequate hermeticity (see below). Second, this enables the subject to retain its mobility, and not be hampered by wired tethering.

[0092] In some embodiments, flexible, wireless, subdural micro-ECoG array “sheet” concepts can be implemented in which planar chiplets (200-300 μm diameter) are hermetically embedded within thin (<100 μm) biocompatible (polyimide) planar polymer sheets for mechanical flexibility conforming to cortical contours.

[0093] FIG. 12B shows an exemplary device process flow whereby arrayed chiplets are

sealed within an insulating, biocompatible film using established microelectronic device processing techniques. Polyimide can be used as the principal material substrate within which the chiplets are embedded. Platinum/iridium planar disk shape electrodes with their local references can also be used.

[0094] Step 1: Polyimide spin-casting/patterning on substrate with sacrificial layer:

In a first step of the exemplary device process flow, a polyimide layer 1202a can be deposited on a sacrificial substrate layer 1208 using spin-casting / patterning techniques. This polyimide layer can be deposited in such a way that a hole is formed, exposing the underlying sacrificial substrate layer 1208.

[0095] Step 2: Au trace patterning by lift-off for reference or common ground:

In a second step of the exemplary device process flow, Au (gold) trace patterning can be performed on the polyimide layer 1202a. This Au trace patterning can later be used to connect different chiplets 1204 together so that they can have a common reference ground (i.e., zero electrical potential).

[0096] Step 3: Flip chip bonding of wireless ECoG chip: In a third step of the exemplary device process flow, a chiplet 1204 can be bonded on top of the polyimide layer 1202a using flip chip bonding techniques. The chiplet 1204 can be bonded in such a way that its recording electrode can be positioned on top of the hole formed in the polyimide layer 1202a, and the reference electrode can be positioned in contact with the Au (gold) trace patterning laid down in step 2, such that the reference electrode can be put in electrical contact with the reference electrodes of other chiplets 1204.

[0097] Step 4: Spin casting top polyimide layer and releasing ECoG sheet by removing sacrificial layer: In a fourth step of the exemplary device process flow, a second polyimide layer 1202b can be deposited on top of the polyimide layer 1202a and the top surface of the chiplet 1204. By sandwiching the chiplet 1204 between the polyimide layer 1202a and 1202b, the chiplet 1204 can be hermetically sealed from exposure for long-term implantation. Then, the polyimide layer 1202a, chiplet 1204, and polyimide layer 1202b can all be peeled off (removed) from the sacrificial layer 1208. The sacrificial layer 1208 can then be discarded. By removing the sacrificial layer 1208, the sensing electrode disposed on top of the hole formed in the polyimide layer 1202a can be exposed, such that the sensing electrode can come into contact with surrounding tissue when implanted.

[0098] The braindrops described above can have approximate heights of $<100\ \mu\text{m}$ with

the on-board ASICs and antenna structure. A multilayer spin-casting deposition technique of polyimide can be used to sandwich the chiplets whereby the use of sacrificial materials layers during processing enables the neural sensing (Pt) electrode surfaces be left exposed for contact with the cortical surface. The absence of physical wires simplifies the processing considerably, including maximizing hermetic reliability and minimizing the stiffness to the native polyimide which internal metallization interconnect wiring typically adds in ribbon-type cables.

[0099] The time-and-frequency domain communication protocols described above (FIGS. 6-8) can also be used to enable recording of epicortical neural signals including high frequency components up to several hundred Hz.

CLAIMS

1. A system for sensing or stimulating a large number of points within a subject's body, the system comprising:
 - an external interface comprising a wireless transceiver, the external interface configured to be located outside of the subject's body; and
 - at least one thousand chiplets configured to be implanted within the subject's body, each chiplet comprising at least one probe configured to perform at least one of the following functions: sense a property of tissue within the subject's body and stimulate surrounding tissue within the subject's body;
 - wherein each chiplet is configured to be powered inductively by electromagnetic signals transmitted through the subject's body by the transceiver, to receive data transmitted wirelessly by the transceiver via a forward link signal, and to send data to the transceiver using backscatter modulation via a reverse link signal.
2. The system of claim 1, wherein the transceiver further comprises:
 - an oscillator configured to generate the forward link signal to the chiplets; and
 - a mixer configured to remove a leaked forward link signal component from the reverse link signal received from the chiplets.
3. The system of claim 1, wherein the at least one probe of each chiplet is configured to sense at least one of an electrical and a chemical property of tissue within the subject's body.
4. The system of claim 1, wherein the at least one probe of each chiplet is configured to stimulate surrounding tissue using at least one of an electrical signal, an optical signal, and a chemical signal.
5. The system of claim 1, wherein the external interface comprises a plurality of transceivers, wherein the at least one thousand chiplets are divided into a plurality of cells corresponding to different locations of the subject's body, and wherein each transceiver is configured to communicate with at least one cell of chiplets.
6. The system of claim 1, wherein the chiplets have a flat end and a tapered end opposite to the flat end, and wherein one electrode is arranged on the flat end and another electrode is arranged on the tapered end.
7. The system of claim 1, wherein the external interface is shaped like a helmet, and the chiplets are configured to be implanted within the subject's brain.

8. The system of claim 1, wherein each of the at least one thousand chiplets is hermetically sealed by at least one envelope of electromagnetically and optically transparent material.
9. A system for performing at least one of sensing and stimulating a large number of points within a subject's body, the system comprising:
 - a plurality of transceivers configured to be located outside of the subject's body; and
 - at least one thousand chiplets divided into a plurality of cells, each chiplet being configured to be implanted within the subject's body and each cell corresponding to a different location in the subject's body, each chiplet comprising at least one probe configured to perform at least one of the following functions: sense an electrical or chemical property of surrounding tissue within the subject's body and stimulate surrounding tissue;
 - wherein each transceiver is configured to communicate wirelessly with a cell of chiplets using a frequency that is different from frequencies used by transceivers in communication with adjacent cells.
10. The system of claim 9, wherein each transceiver is configured to communicate wirelessly with the chiplets in its corresponding cell using time-division multiple access (TDMA).
11. The system of claim 10, wherein each chiplet in a cell is assigned a different time slot in which to communicate with its corresponding transceiver.
12. The system of claim 11, wherein each transceiver is configured to transmit a synchronization pulse to the chiplets in its corresponding cell.
13. The system of claim 9, wherein each chiplet comprises a memory containing a unique ID code.
14. The system of claim 9, wherein transceivers positioned 5mm or more apart from each other use the same frequency.
15. The system of claim 9, wherein each of the at least one thousand chiplets is hermetically sealed by at least one envelope of electromagnetically and optically transparent material.
16. A chiplet for performing at least one of sensing and stimulating surrounding tissue within a subject's body, the chiplet comprising:
 - a planar RF and power substrate layer configured to convert energy received via a RF signal into DC power;
 - a planar digital substrate layer comprising a controller;
 - a planar analog substrate layer comprising electrodes configured to perform at

least one of the following functions: sense a property of tissue within the subject's body and stimulate surrounding tissue within the subject's body; and

an antenna;

wherein the RF and power substrate layer, the digital substrate layer, and the analog substrate layer are stacked on top of one another, and wherein the antenna is configured to surround the stacked layers.

17. The chiplet of claim 16, wherein the chiplet is hermetically sealed by at least one envelope of electromagnetically and optically transparent material.
18. An apparatus for sensing or stimulating a large number of points within a subject's body, the apparatus comprising:
 - a flexible, planar substrate sheet; and
 - a plurality of chiplets disposed on the flexible substrate sheet, each chiplet comprising at least one probe configured to perform at least one of the following functions: sense a property of tissue within the subject's body and stimulate surrounding tissue within the subject's body,
 - wherein each chiplet is configured to be powered inductively by electromagnetic signals transmitted through the subject's body by an external transceiver, to receive data transmitted wirelessly by the transceiver via a forward link, and to send data to the transceiver using backscatter modulation via a reverse link.
19. A method for manufacturing an apparatus for sensing or stimulating a large number of points within a subject's body, the method comprising:
 - forming a first substrate layer on top of a sacrificial layer, wherein the first substrate layer forms a hole;
 - bonding a chiplet on top of the first substrate layer, the chiplet comprising at least one probe configured to perform at least one of the following functions: sense a property of tissue within the subject's body and stimulate surrounding tissue within the subject's body, wherein the at least one probe is positioned within the hole formed in the sacrificial layer;
 - forming a second substrate layer on top of the first substrate layer and the chiplet such that the chiplet is hermetically sealed; and
 - removing the sacrificial layer such that the at least one probe of the chiplet is exposed through the hole formed in the first substrate layer.

20. An apparatus for implanting a plurality of chiplets into the body of a subject, wherein each chiplet comprises at least one probe configured to perform at least one of the following functions: sense a property of tissue within the subject's body and stimulate surrounding tissue within the subject's body, the apparatus comprising:

an array of guidetubes, the array configured to conform to a surface of a subject's body, wherein each guidetube includes at least one chiplet disposed therein;

a gas chamber configured to inject pressurized gas into the array of guidetubes, such that the chiplets can be expelled from the guidetubes at a velocity sufficient to penetrate into the subject's body.

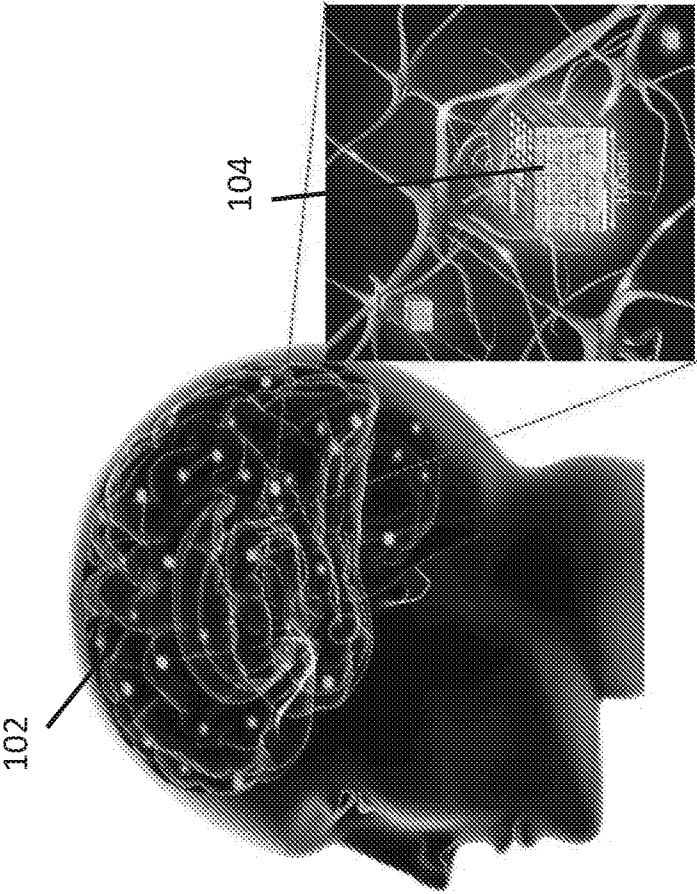
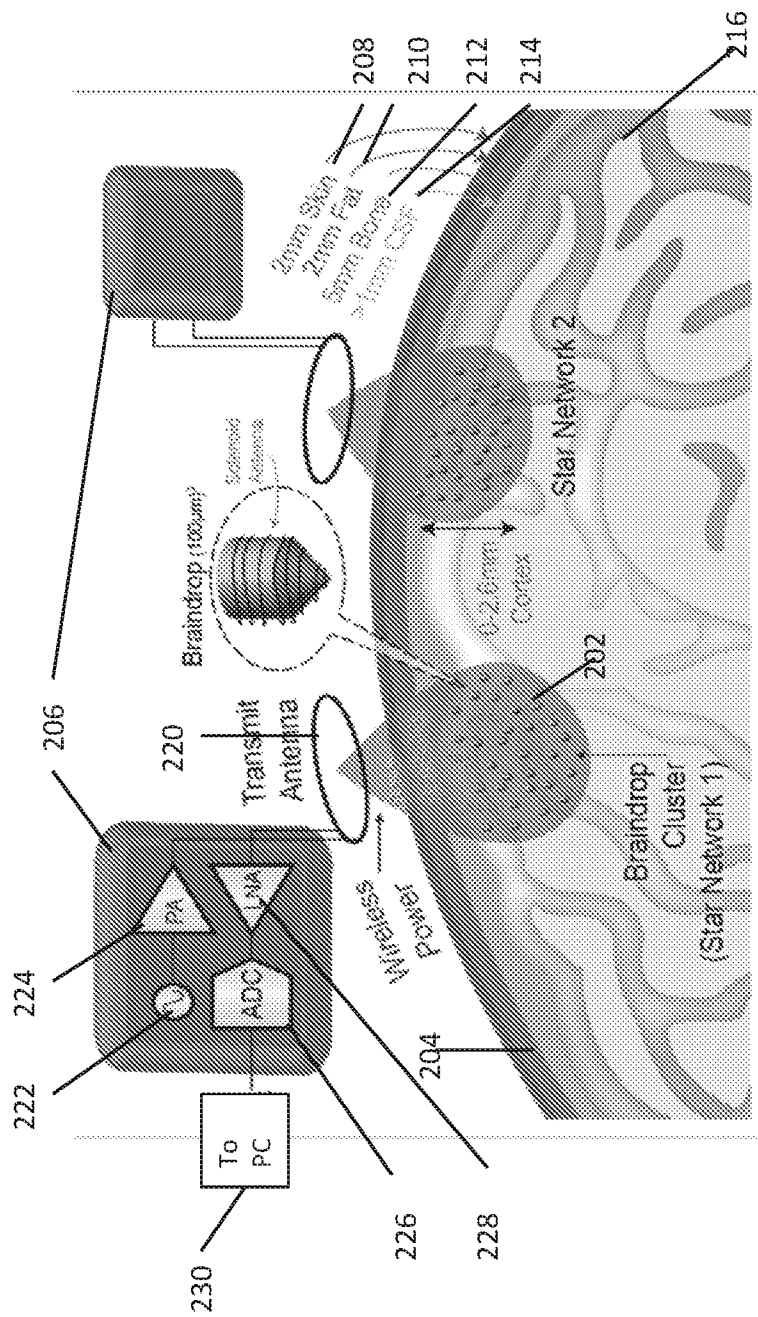


FIG. 1



2GFL

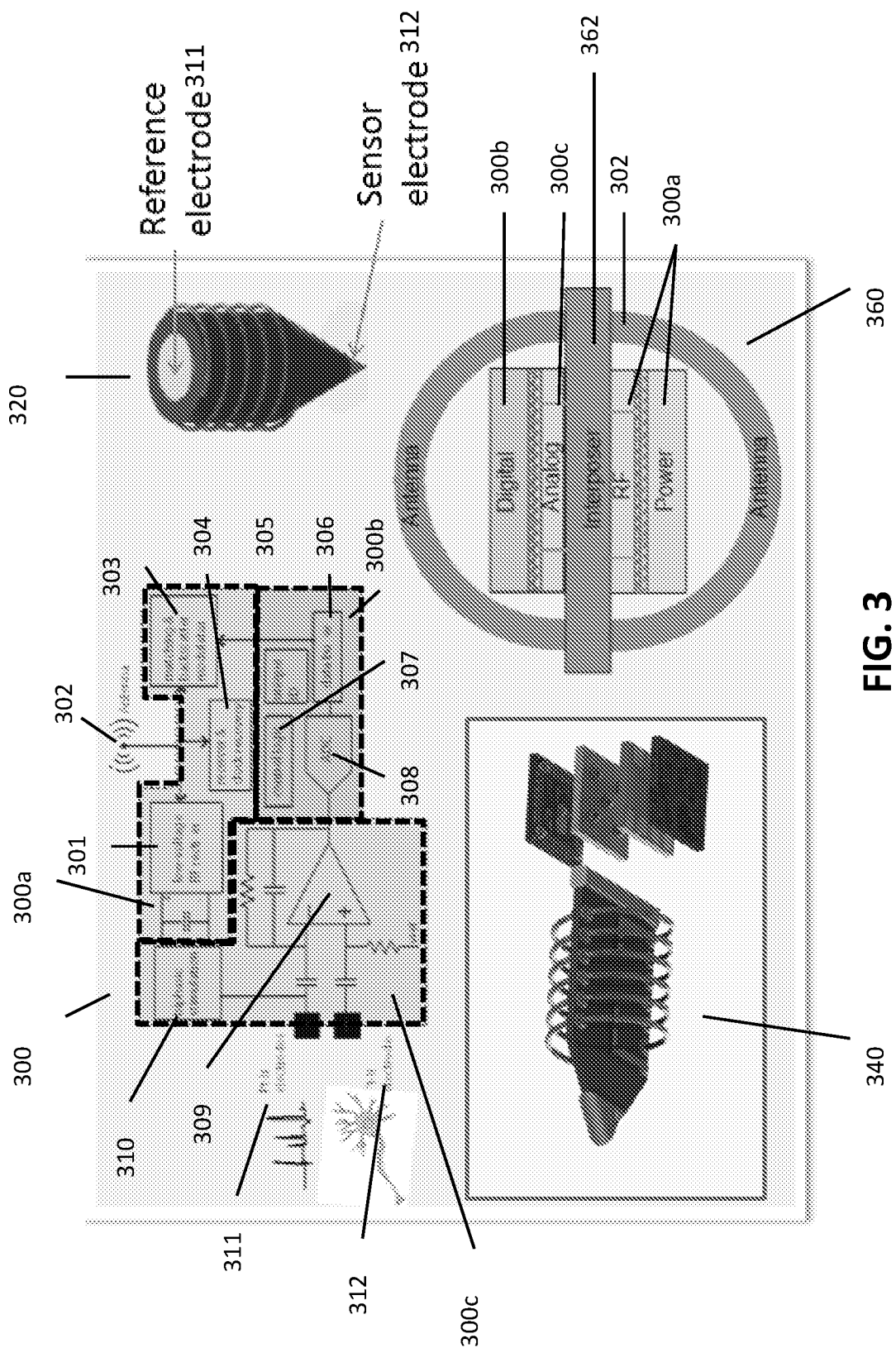
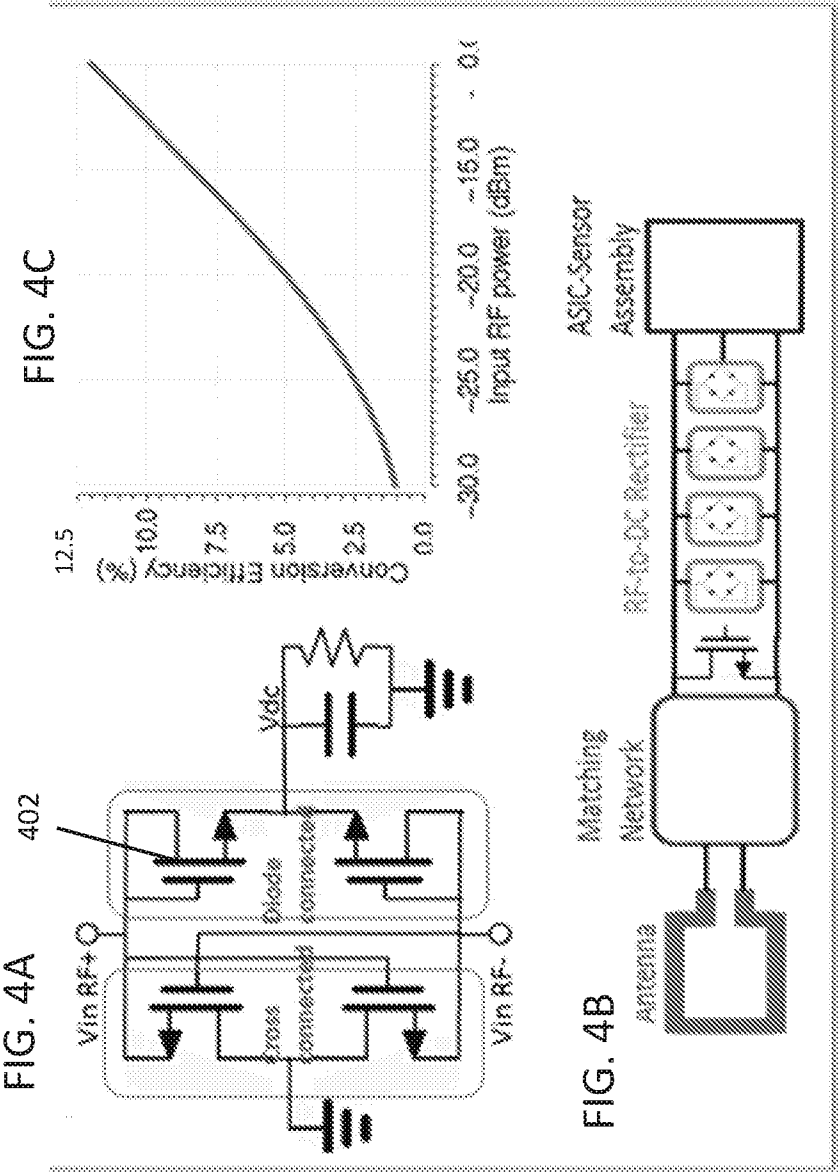


FIG. 3



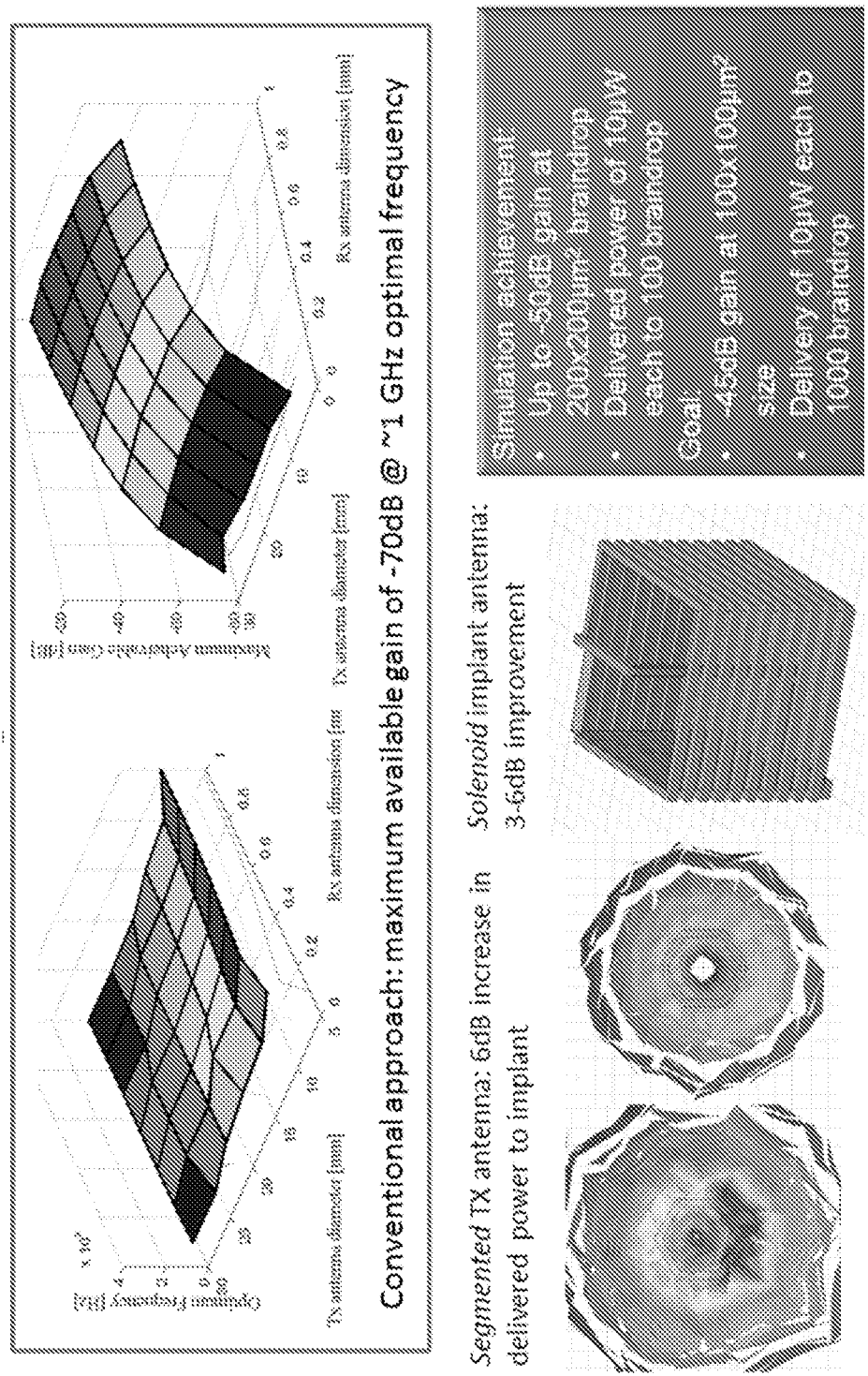


Figure 5: Concept of solenoid antenna wrapped around each braindrop for enhancement of the RF energy harvesting and signal backscattering

FIG. 5

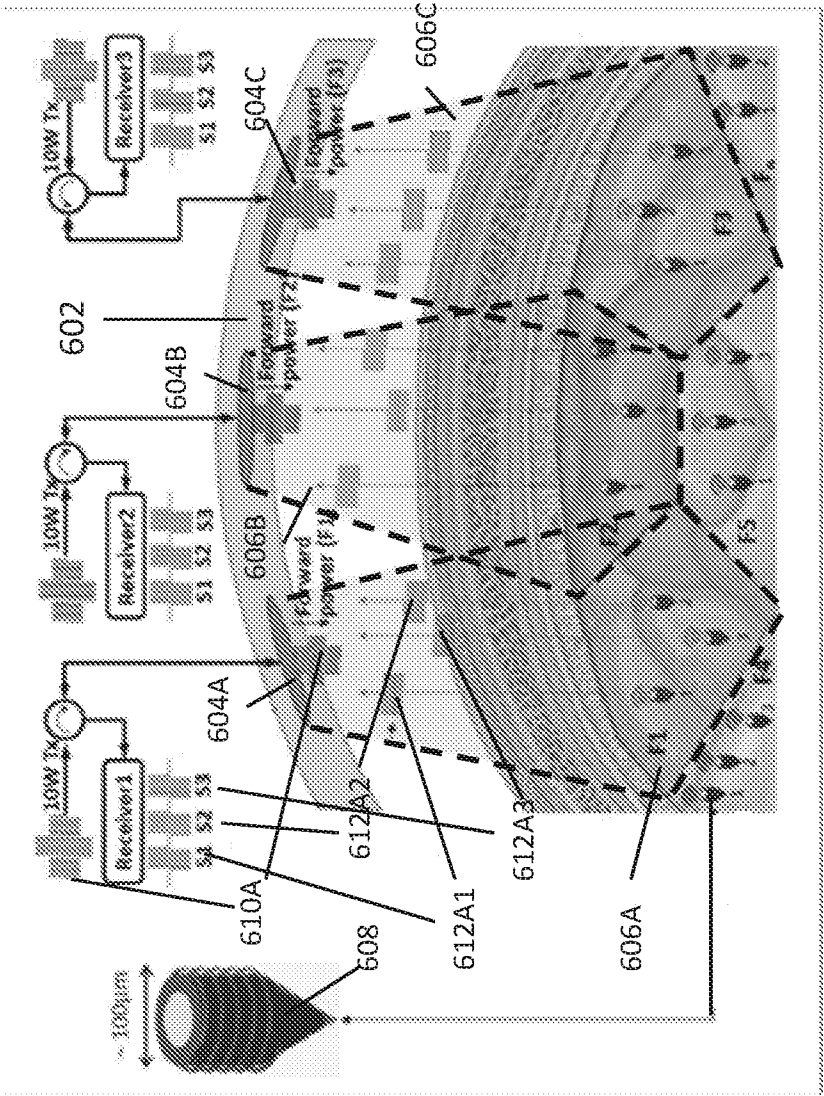


FIG. 6

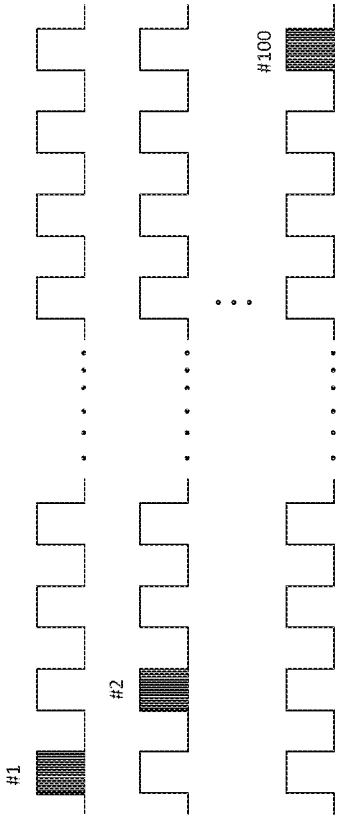


FIG. 7

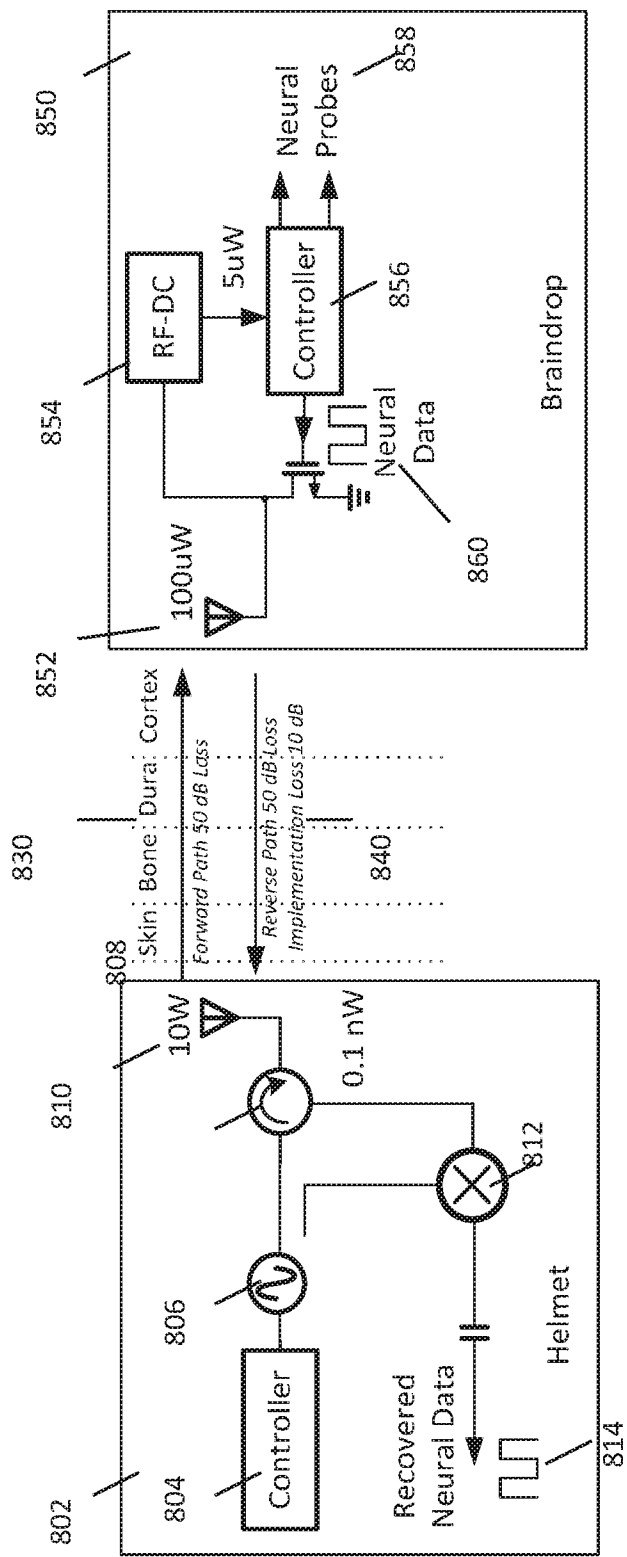


FIG. 8

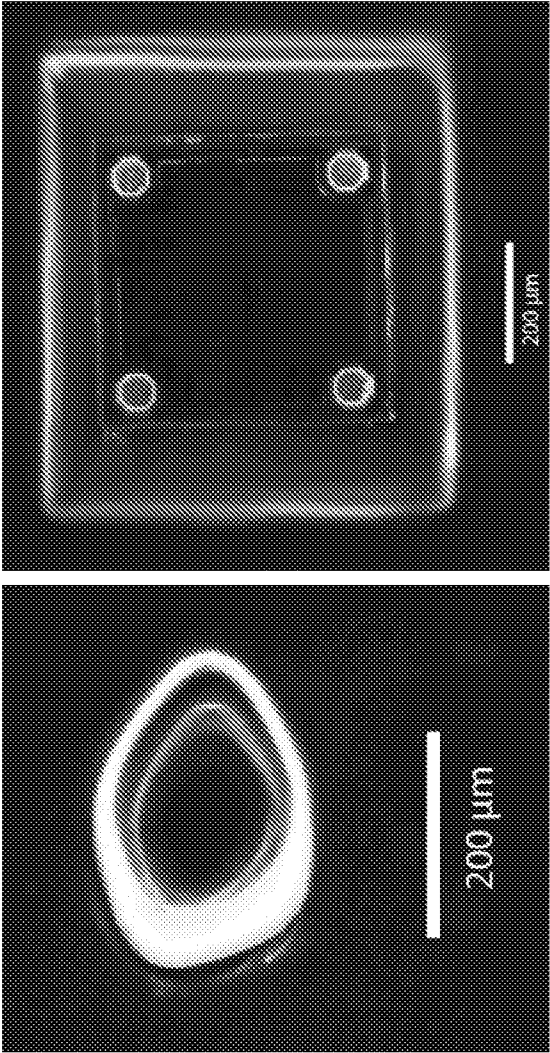


FIG. 9

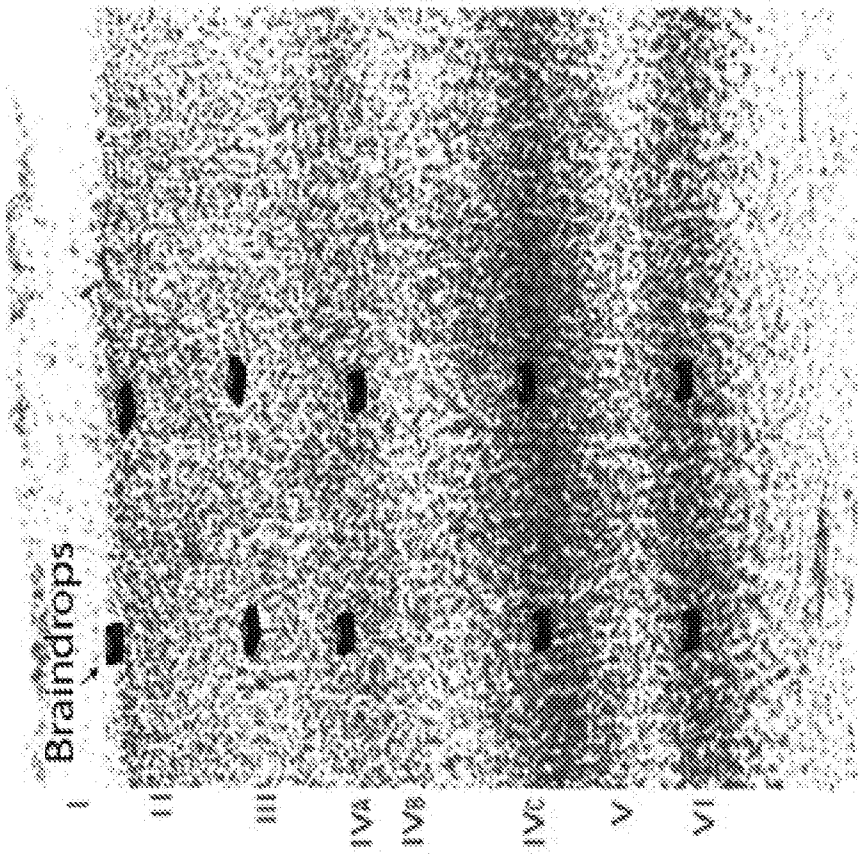


FIG. 10

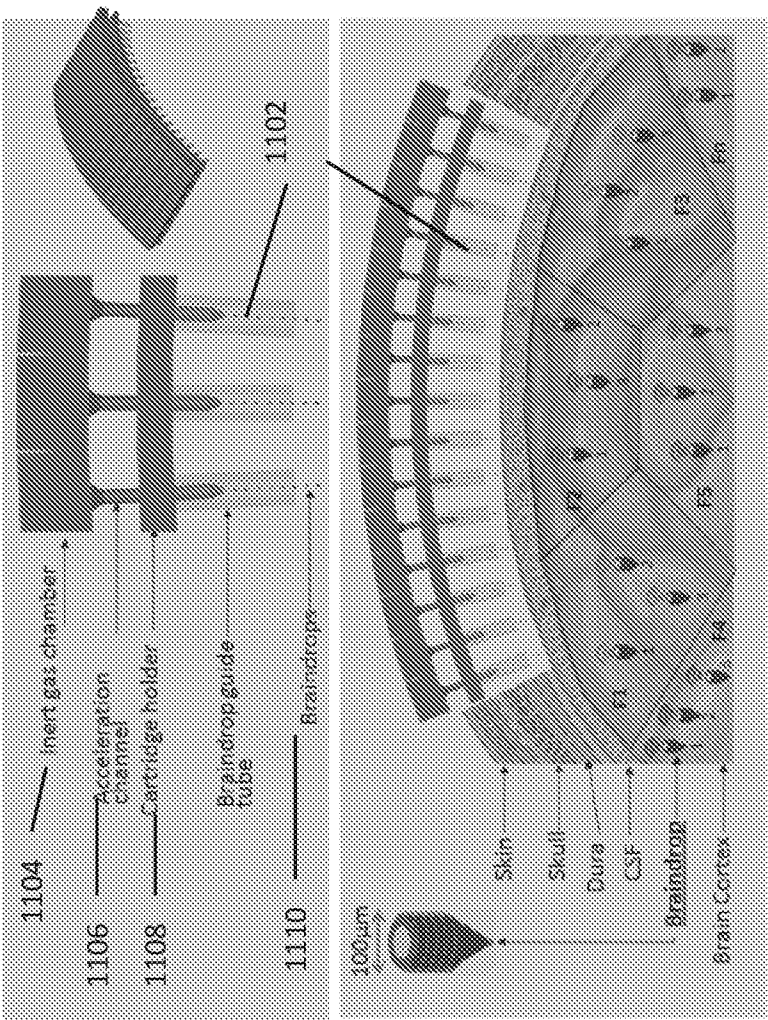


FIG. 11

FIG. 12A

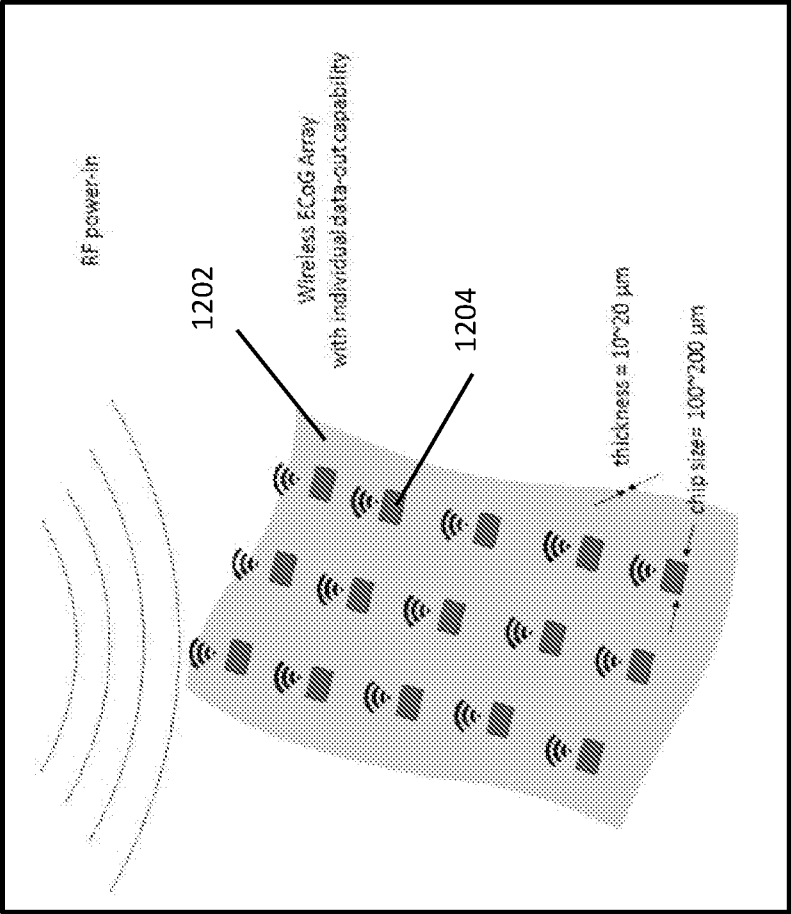
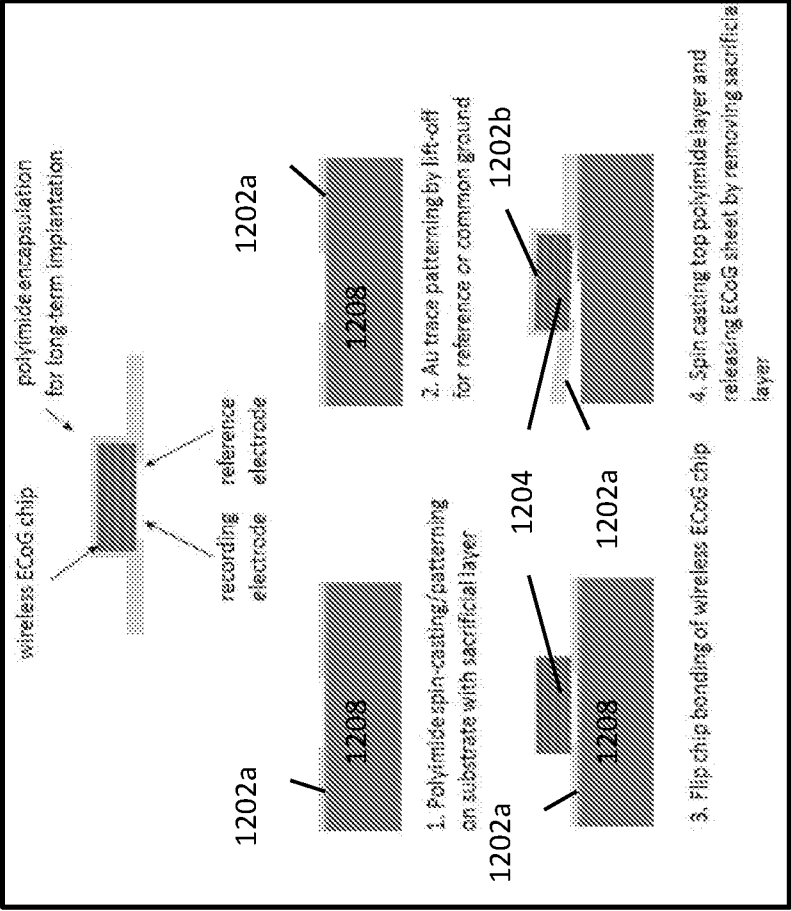


FIG. 12B



INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2016/032994

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - A61N 1/04; A61N 1/05; A61N 1/36 (2016.01)

CPC - A61N 1/0456; A61N 1/0504; A61N 1/18; A61N 1/32; A61N 1/36007; A61N 1/36017 (2016.08)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC - A61N 1/04; A61N 1/05; A61N 1/36

CPC - A61N 1/0456; A61N 1/0504; A61N 1/18; A61N 1/32; A61N 1/36007; A61N 1/36017; A61N 1/36021

A61N 1/3605; A61N 1/36125; A61N 1/36128; A61N 1/36146; A61N 1/36153

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

607/40; 607/41; 607/57; 607/59; 607/65; 607/66; 607/70; 607/72; 607/74 (keyword delimited)

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

Orbit, Proquest, Google

Search terms used: brain, cranial, cortex, intercranial, electrocortical, electroencephalograph, nerves, cardiac, transceiver, array, electrodes, stimulator, stimulating, hermetically, backscatter, modulation, TDMA, FDMA

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2014/0194944 A1 (ROMANELLI et al) 10 July 2014 (10.07.2014) entire document	1-15, 18
Y	US 2014/0128932 A1 (UNIVERSITY OF NORTH DAKOTA et al) 08 May 2014 (08.05.2014) entire document	1-8, 18
Y	US 9,031,658 B2 (CHIAO et al) 12 May 2015 (12.05.2015) entire document	2, 9-15
Y	US 2007/0250119 A1 (TYLER et al) 25 October 2007 (25.10.2007) entire document	5-8, 11, 12, 14, 15

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

14 September 2016

Date of mailing of the international search report

05 OCT 2016

Name and mailing address of the ISA/

Mail Stop PCT, Attn: ISA/US, Commissioner for Patents

P.O. Box 1450, Alexandria, VA 22313-1450

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Authorized officer

Blaine R. Copenheaver

PCT Helpdesk: 571-272-4300

PCT Q3P: 571-272-7774

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US2016/032994

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

See supplemental page

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-15, 18

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

Continued from Box No. III Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claims 1-15 and 18, are drawn to a system for performing at least one of sensing and stimulating a large number of points within a subject's body.

Group II, claims 16 and 17, are drawn to a chiplet.

Group III, claim 19 are drawn to a method for manufacturing an apparatus.

Group IV, claim 20, is drawn to an apparatus for implanting a plurality of chiplets into the body of a subject.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

The special technical features of Group I, a system, the system comprising: an external interface comprising a wireless transceiver; and a plurality of chiplets configured to be implanted within the subject's body, each chiplet comprising at least one probe; wherein each chiplet is configured to communicate wirelessly by electromagnetic signals transmitted through the subject's body by the transceiver, are not present in Groups II-IV; the special technical features of Group II, a chiplet, the chiplet comprising: a planar RF and power substrate layer configured to convert energy received via a RE signal into DC power; a planar digital substrate layer comprising a controller; a planar analog substrate layer comprising electrodes; and an antenna; wherein the RF and power substrate layer, the digital substrate layer, and the analog substrate layer are stacked on top of one another, and wherein the antenna is configured to surround the stacked layers, are not present in Groups I and III-IV; the special technical features of Group III, a method, the method comprising: forming a first substrate layer on top of a sacrificial layer, wherein the first substrate layer forms a hole; bonding a chiplet on top of the first substrate layer, the chiplet comprising at least one probe, wherein the at least one probe is positioned within the hole formed in the sacrificial layer; forming a second substrate layer on top of the first substrate layer and the chiplet such that the chiplet is hermetically sealed; and removing the sacrificial layer such that the at least one probe of the chiplet is exposed through the hole formed in the first substrate layer, are not present in Groups I-II and IV; and the special technical features of Group IV, an apparatus for implanting a plurality of chiplets into the body of a subject, wherein each chiplet comprises at least one probe, the apparatus comprising: an array of guidetubes, the array configured to conform to a surface of a subject's body, wherein each guidetube includes at least one chiplet disposed therein; a gas chamber configured to inject pressurized gas into the array of guidetubes, such that the chiplets can be expelled from the guidetubes at a velocity sufficient to penetrate into the subject's body, are not present in Groups I-III.

Groups I through IV all share the technical feature of an apparatus for performing at least one of sensing and stimulating surrounding tissue within a subject's body, comprising a chiplet comprising at least one probe configured to perform at least one of the following functions: sense a property of tissue within the subject's body and stimulate surrounding tissue within the subject's body. However this shared technical feature does not represent a contribution over the prior art. Specifically US 2014/0194944 A1 to Romanelli et al. discloses an apparatus for performing at least one of sensing and stimulating surrounding tissue within a subject's body (para. [0072] "the implantable device 150 may be used not only for the acquisition of bioelectrical signals from the cortical surface, but also for its electrical stimulation, for example to prevent the epileptic seizures at their onset"), comprising a chiplet comprising at least one probe (FIGS. 3-4; para. [0048] "the implantable device 150 comprises a plurality of active electrodes 1100 arranged on the grid 1000 according to a predefined pattern"; it is noted that an electrode is capable of acting as a probe) configured to perform at least one of the following functions: sense a property of tissue within the subject's body (para. [0059] "the active electrodes 1100 are individually connected to the electronic module 200 so as to allow the acquisition of bioelectrical signals in parallel in the whole area of the portion of the cortical surface on which the active electrodes 1100 of the implantable device 150 are arranged") and stimulate surrounding tissue within the subject's body (para. [0072] "the implantable device 150 may be used not only for the acquisition of bioelectrical signals from the cortical surface, but also for its electrical stimulation, for example to prevent the epileptic seizures at their onset").

Groups I and III also share the technical feature of a chiplet disposed on a flexible substrate sheet. However this shared technical feature does not represent a contribution over the prior art. Specifically US 2014/0194944 A1 to Romanelli et al. discloses a chiplet disposed on a flexible substrate sheet (FIGS. 3-4; paras. [0048]-[0049] "the implantable device 150 comprises a plurality of active electrodes 1100 arranged on the grid 1000 according to a predefined pattern... grid 1000 is preferably made on a flexible printed circuit 900, which is elastically deformable by a force of a limited extent, allowing ease of adaptation of the implantable device 150 to the shape, in particular the curvature, of the portion of the cortical surface onto which it is applied").

Groups I and IV also share the technical feature of a plurality of chiplets. However this shared technical feature does not represent a contribution over the prior art. Specifically US 2014/0194944 A1 to Romanelli et al. discloses a plurality of chiplets (para. [0058] "The number of active electrodes 1100 on the grid 1000 may vary depending on the size of the surface area of the cortical surface to be monitored, as well as on the desired mapping resolution, and may for example be equal to one hundred twenty eight, two hundred fifty six, one thousand twenty four and two thousand forty eight. In the illustrated embodiment one hundred twenty eight active electrodes 1100 are shown").

Since none of the special technical features of the Group I-IV inventions are found in more than one of the inventions, unity of invention is lacking.