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Costanzo et al.

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(54) **OLFACTORY IMPLANT SYSTEM**

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A61N 1/05 (2006.01)
A61N 1/372 (2006.01)

(52) **U.S. Cl.**
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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

6,374,140 B1 * 4/2002 Rise A61N 1/36064 600/544
7,400,927 B1 * 7/2008 Litvin A61N 1/36025 128/898

(Continued)

OTHER PUBLICATIONS

Coelho DH, Costanzo RM. "Spatial Mapping in the Rat Olfactory Bulb by Odor and Direct Electrical Stimulation." Otolaryngol Head Neck Surg. May 10, 2016. pii: 0194599816646358.*

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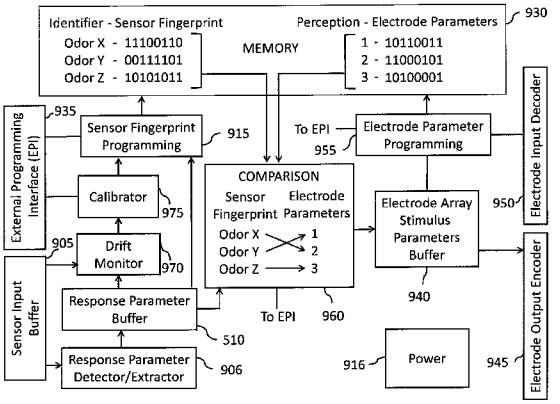
(57) **ABSTRACT**

The system includes five components: (1) a sensor array, (2) a processor, (3) a transmitter, (4) a receiver-stimulator, and (5) an implantable electrode array. The olfactory implant system generates odor fingerprints by detecting odors with an array of chemical sensors and then transmitting variable spatio-temporal stimulation patterns for an electrode array with electrode stimulating points positioned at different locations in the olfactory cortex (e.g., stimulating the olfactory bulb). Different patterns of activity in the olfactory cortex are thereby generated which mimic the sense of smell in a subject. Once trained the system should be usable by a subject to detect or correctly identify one or more odors.

18 Claims, 14 Drawing Sheets



(52) **U.S. Cl.**
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(56) **References Cited**

U.S. PATENT DOCUMENTS

2004/0152946	A1*	8/2004	Franck	A61N 1/08 600/25
2004/0229345	A1	11/2004	Oka et al.	
2006/0191319	A1	8/2006	Kurup	
2006/0206169	A1*	9/2006	Schuler	A61N 1/36007 607/58
2007/0179557	A1*	8/2007	Maschino	A61N 2/008 607/45
2008/0077192	A1*	3/2008	Harry	A61H 23/0263 607/48
2009/0044761	A1	2/2009	Chapin et al.	
2012/0197250	A1	8/2012	Ward	

* cited by examiner

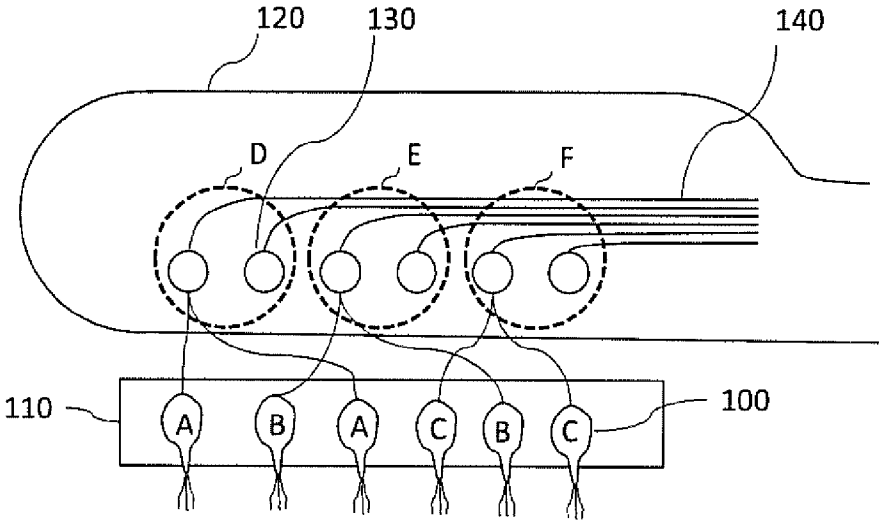

FIGURE 1

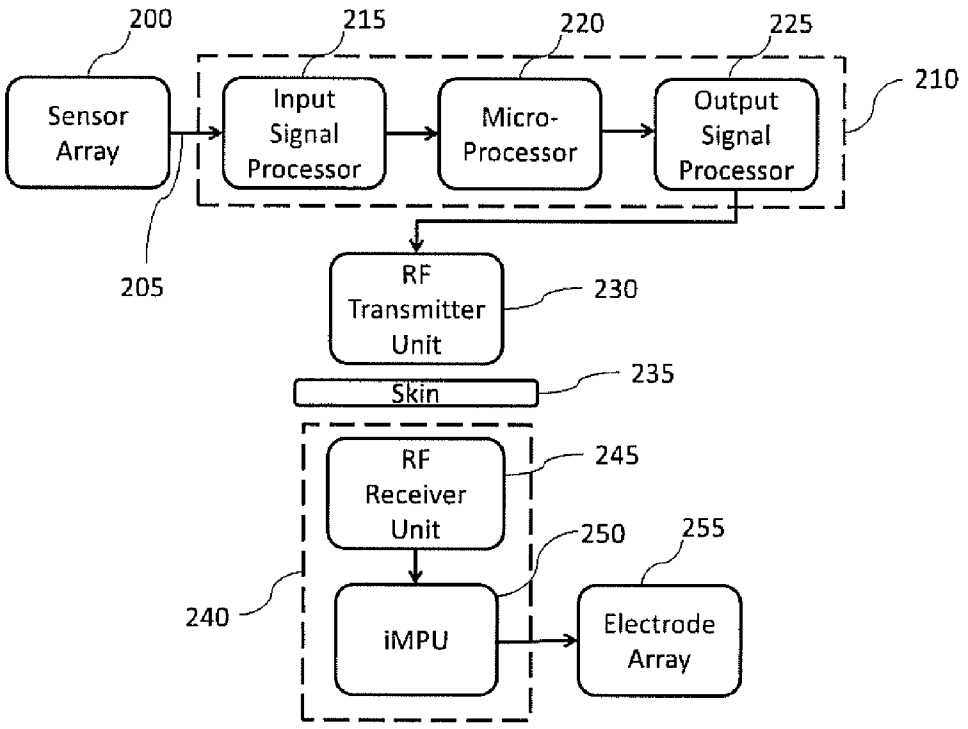
200
215
220
225
210
Sensor Array
Input Signal Processor
Micro-Processor
Output Signal Processor
205
RF Transmitter Unit
230
Skin
235
RF Receiver Unit
245
250
255
240
iMPU
Electrode Array

FIGURE 2

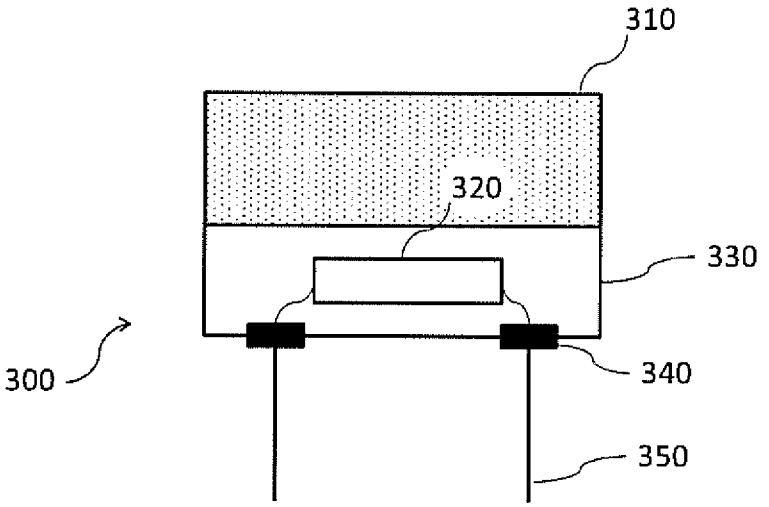

FIGURE 3

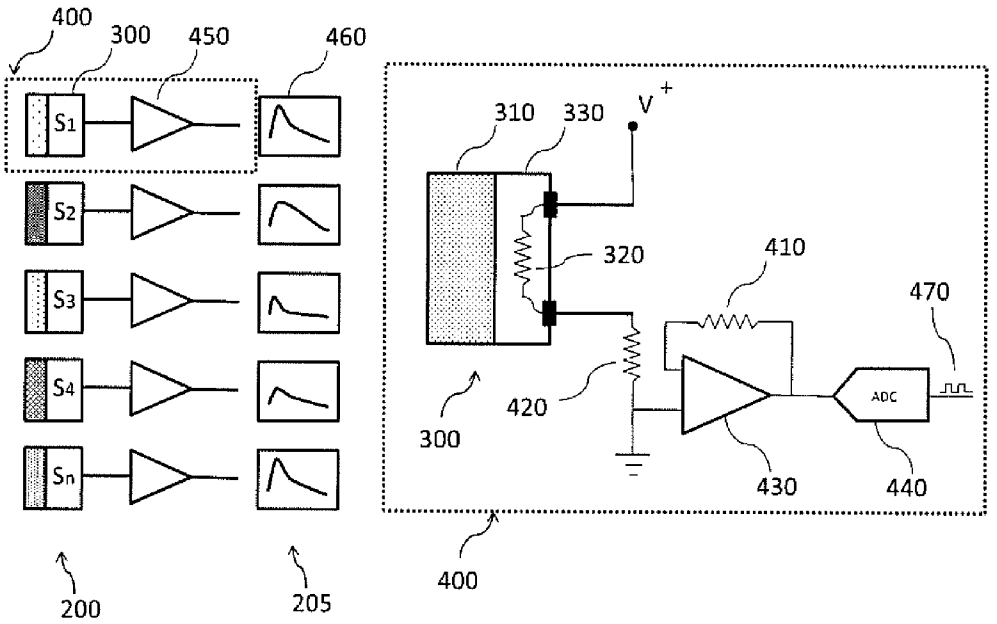
400
300
450
460
S1
S2
S3
S4
Sn
200
205
310
330
V+
320
410
470
420
300
ADC
430
440
400

FIGURE 4

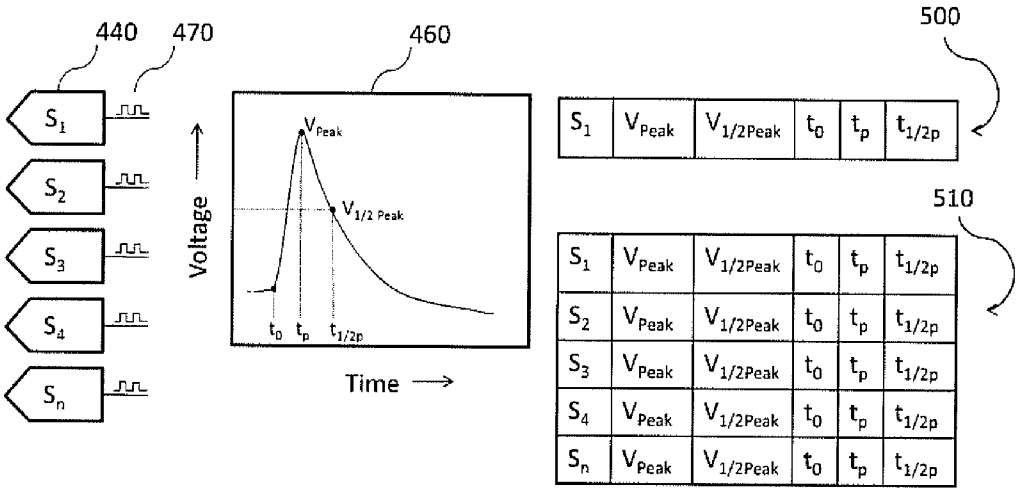
440
470
460
500
510
S1
S2
S3
S4
Sn
Voltage
Time
VPeak
V1/2 Peak
t0
tp
t1/2p
V1/2Peak

FIGURE 5

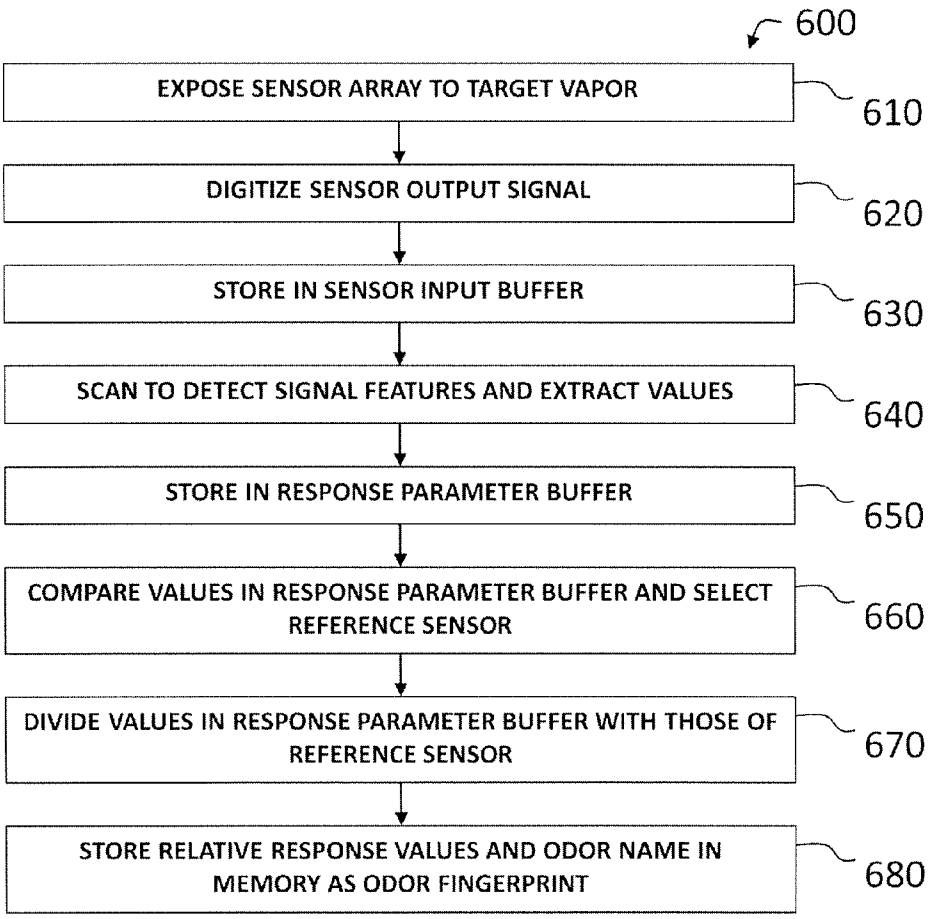
600
EXPOSE SENSOR ARRAY TO TARGET VAPOR
610
DIGITIZE SENSOR OUTPUT SIGNAL
620
STORE IN SENSOR INPUT BUFFER
630
SCAN TO DETECT SIGNAL FEATURES AND EXTRACT VALUES
640
STORE IN RESPONSE PARAMETER BUFFER
650
COMPARE VALUES IN RESPONSE PARAMETER BUFFER AND SELECT REFERENCE SENSOR
660
DIVIDE VALUES IN RESPONSE PARAMETER BUFFER WITH THOSE OF REFERENCE SENSOR
670
STORE RELATIVE RESPONSE VALUES AND ODOR NAME IN MEMORY AS ODOR FINGERPRINT
680

FIGURE 6

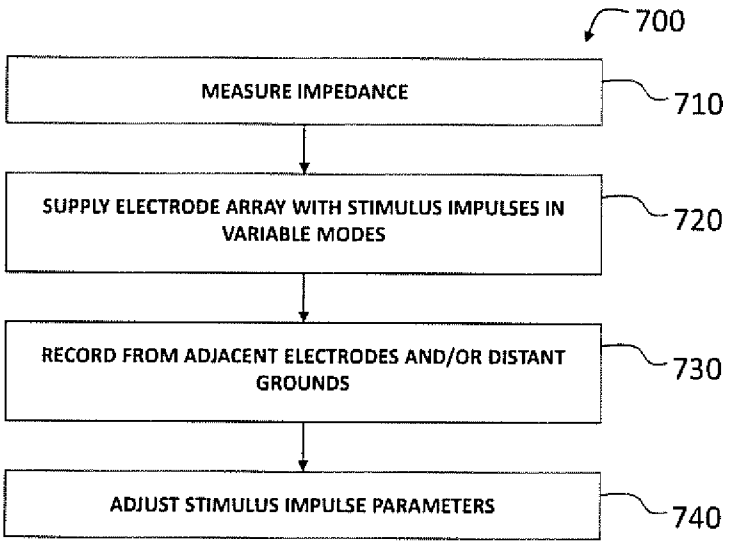
700
MEASURE IMPEDANCE
710
SUPPLY ELECTRODE ARRAY WITH STIMULUS IMPULSES IN VARIABLE MODES
720
RECORD FROM ADJACENT ELECTRODES AND/OR DISTANT GROUNDS
730
ADJUST STIMULUS IMPULSE PARAMETERS
740

FIGURE 7

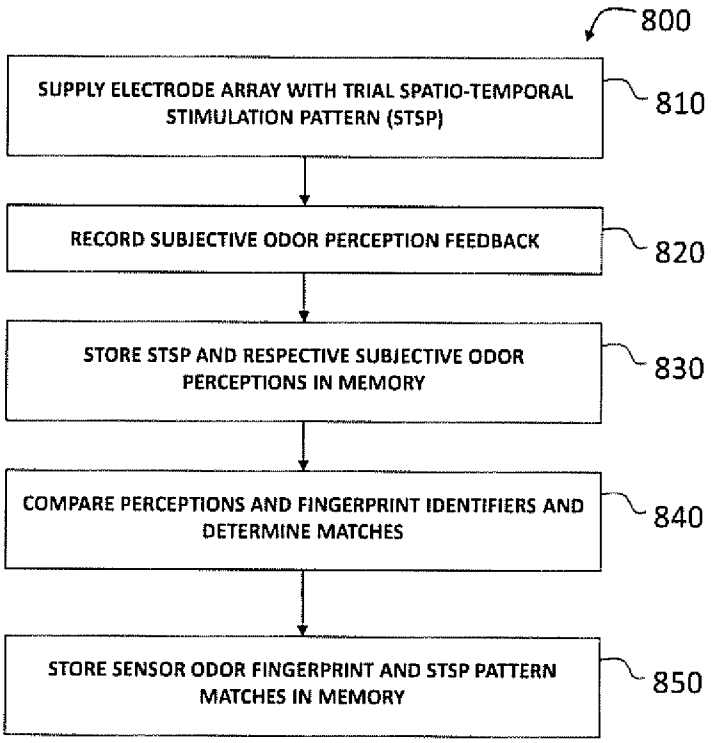
800
SUPPLY ELECTRODE ARRAY WITH TRIAL SPATIO-TEMPORAL STIMULATION PATTERN (STSP)
810
RECORD SUBJECTIVE ODOR PERCEPTION FEEDBACK
820
STORE STSP AND RESPECTIVE SUBJECTIVE ODOR PERCEPTIONS IN MEMORY
830
COMPARE PERCEPTIONS AND FINGERPRINT IDENTIFIERS AND DETERMINE MATCHES
840
STORE SENSOR ODOR FINGERPRINT AND STSP PATTERN MATCHES IN MEMORY
850

FIGURE 8

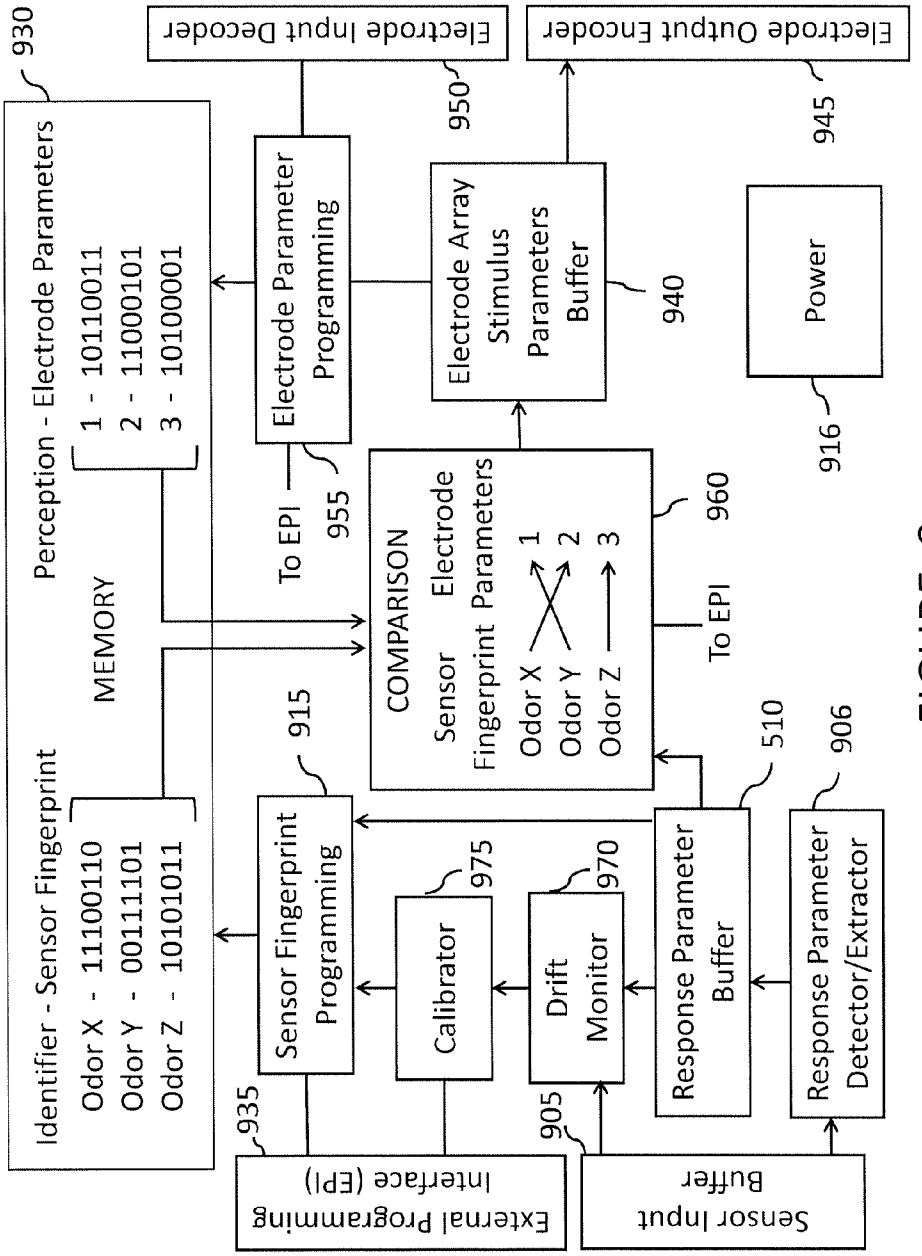
930
Perception - Electrode Parameters
1 - 10110011
2 - 11000101
3 - 10100001
MEMORY
Identifier - Sensor Fingerprint
Odor X - 11100110
Odor Y - 00111101
Odor Z - 10101011
Electrode Input Decoder
950
Electrode Output Encoder
945
Electrode Parameter Programming
To EPI
955
Electrode Array Stimulus Parameters Buffer
940
Power
916
COMPARISON
Sensor Fingerprint
Electrode Parameters
Odor X
Odor Y
Odor Z
1
2
3
960
To EPI
915
Sensor Fingerprint Programming
Calibrator
975
Drift Monitor
970
Response Parameter Buffer
510
Response Parameter Detector/Extractor
906
935
External Programming Interface (EPI)
905
Sensor Input Buffer

FIGURE 9

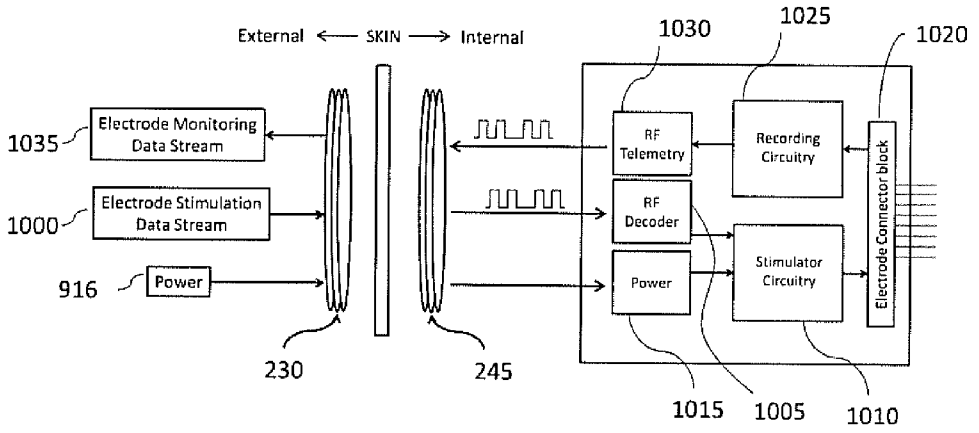
External
SKIN
Internal
1030
1025
1020
1035
Electrode Monitoring Data Stream
1000
Electrode Stimulation Data Stream
916
Power
230
245
RF Telemetry
RF Decoder
Power
Recording Circuitry
Stimulator Circuitry
Electrode Connector block
1015
1005
1010

FIGURE 10

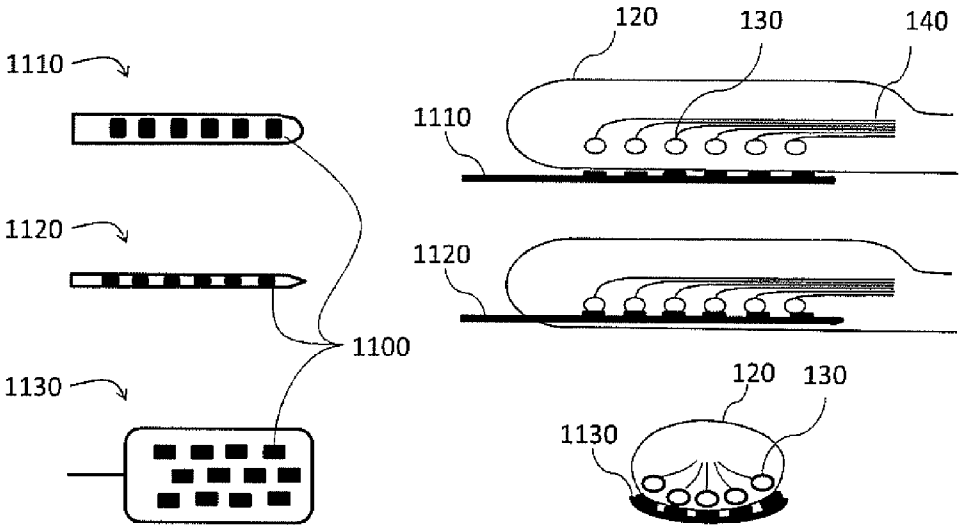

FIGURE 11

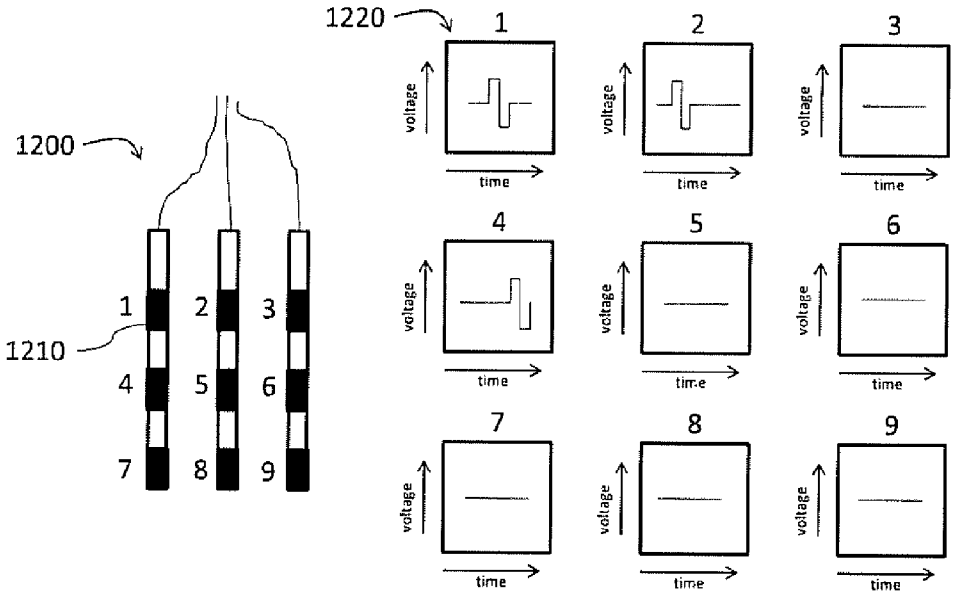

FIGURE 12

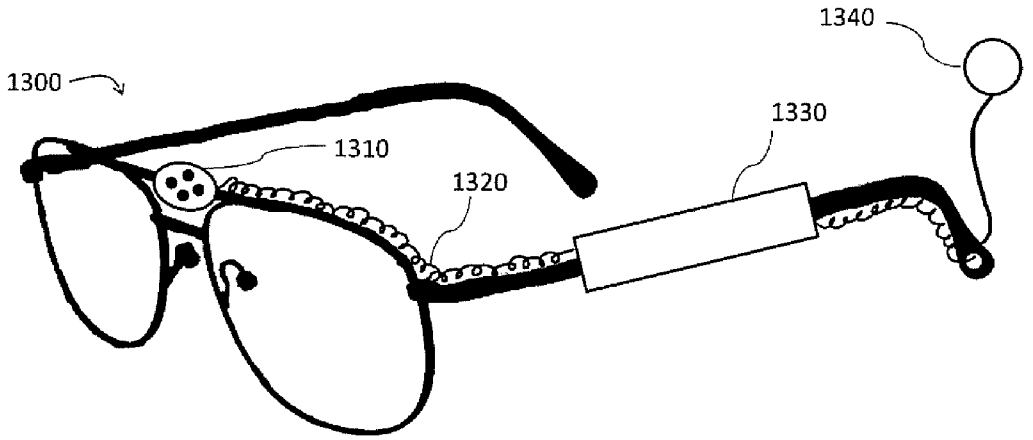

FIGURE 13A

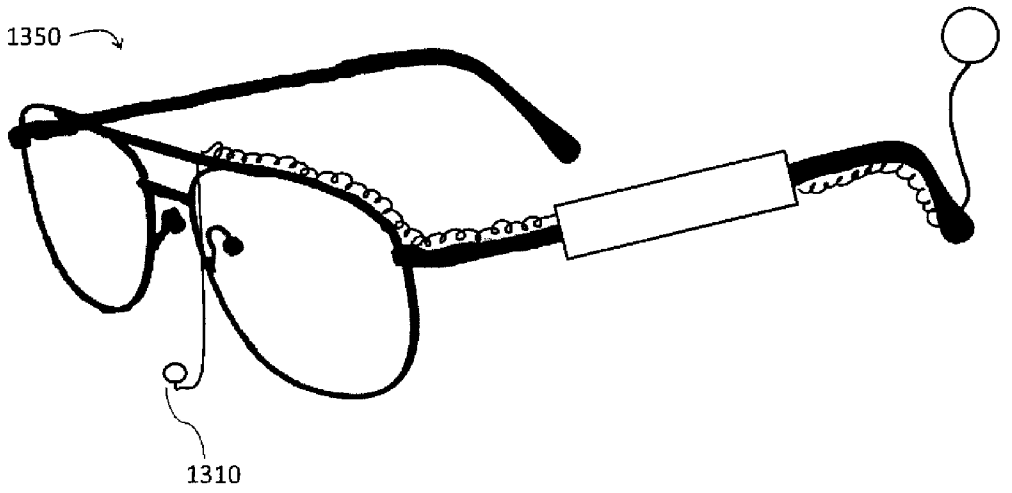

FIGURE 13B

OLFACTORY IMPLANT SYSTEM

BACKGROUND OF THE INVENTION

Field of the Invention

The present invention generally relates to prosthetic devices and, more particularly, to an olfactory implant system for individuals who have an impaired or lost sense of smell.

Background Description

Information is transmitted in the human body by the nervous system. Electrical pulses, or propagating action potentials, travel along the extensions (axons) of a nerve cell, from one nerve to another (or between many nerves) to create a functional network of communication. Electric pulses begin when the organs of sensation are stimulated. Olfaction, or the sense of smell, is controlled by the olfactory system comprising olfactory nerves. In humans, the odorant-detecting portions of the olfactory nerves are within the nasal cavity where they have exposure and therefore access to odor molecules which are inhaled by the subject. The nerves pass from the nasal cavity through the cribiform plate of the anterior skull base and synapse with 2nd order neurons in the olfactory bulb. In cases where a subject has a damaged or lost sense of smell, it is most commonly due to destruction or interruption of the olfactory nerves. The olfactory bulb in these circumstances usually remains intact and healthy.

Sensors and sensor arrays for the detection and identification of some airborne molecules are known and used to detect odor molecules which stimulate the human olfaction system as well as vapor molecules which humans may not have the ability to smell. Sensors of this kind, which are sometimes referred to as "electronic noses", are found in food, industrial, and environmental applications, for example. US Patent Publication No. 2006/0191319 to Kurup describes detecting soil born contaminants or volatile organic compounds in soil. This may be useful in areas where industry operations such as hydrocarbon extraction (e.g. hydraulic fracturing, or "fracking") are performed. Odor detection may be used by a food processing plant to help detect spoiled goods. Carbon monoxide detectors are commonly found in both commercial and residential environments as a safety precaution since humans cannot sense carbon monoxide, which can be lethal if large amounts are inhaled.

Stimulating devices and techniques for electrical stimulation of particular tissues of the human body are also known. U.S. Pat. No. 3,236,240 to Bradley is a very early US patent pointing to stimulation of muscle tissue, in this case the muscles controlling the bladder. Many modern stimulatory applications have been directed to interacting more closely with the central nervous system. Deep brain stimulation, for example, may involve a small linear array of stimulating electrodes which are implanted to provide small low power electrical fields in selected regions of the brain. This has been successfully used for maladies from Parkinson's Disease to depression.

Cochlear implants are another well-known biostimulatory application. A stimulating electrode array is implanted into the human cochlea to artificially trigger action potentials in the human auditory nerves for persons who have impaired or lost capacity for hearing. Electrode arrays have been used with the central nervous system; at the end organs (cochlea, eye, brain, kidney, liver, stomach, muscle or other tissue, for example); and along the nerve pathways, both afferent and efferent, of the peripheral nervous system which bridge the central nervous system with the end organs. Unfortunately not all five human senses are treatable by bioelectrical stimulation means or otherwise in the case of lost or impaired function. For anosmics, or persons who have lost their sense of smell due to injury or disease, there is currently no known means for recreating this important sense.

SUMMARY OF THE INVENTION

An exemplary embodiment of the present invention is to provide a system and method to recreate, simulate, and/or mimic a sense of smell in a subject.

It is another exemplary embodiment of the present invention to provide a system that permits direct implantation and interfacing with the olfactory centers of the brain, the olfactory bulb as a particular example, for a renewed or improved perception of smell.

According to the present invention, these and other embodiments and advantages are achieved in an olfactory implant system including: (1) a sensor array, (2) a processor, (3) a transmitter, (4) a receiver-stimulator, and (5) an implantable electrode array. The olfactory implant system generates odor maps by detecting odors with an array of chemical sensors and then transmitting variable spatio-temporal stimulation patterns by an electrode array with electrode stimulating points positioned at different locations about the olfactory bulb or other part of the olfactory cortex. Different patterns of activity in the olfactory cortex are thereby generated which mimic the sense of smell in a subject. Once trained the system should be usable by a subject to detect or correctly identify one or more odors.

BRIEF DESCRIPTION OF THE DRAWINGS

The foregoing and other objects, aspects and advantages will be better understood from the following detailed description of a preferred embodiment of the invention with reference to the drawings, in which:

FIG. **1** shows basic neurophysiology of an olfactory system;

FIG. **2** is a schematic of an olfactory implant system;

FIG. **3** is a schematic of a single odor sensor;

FIG. **4** shows a sensor array comprising a plurality of odor sensors, analog output signals therefrom, and control circuitry;

FIG. **5** shows response parameters usable for generation of odor fingerprints;

FIG. **6** is a flow diagram of a process for generating a lookup table of odor fingerprints;

FIG. **7** is a flow diagram of a process for testing an electrode array;

FIG. **8** is a flow diagram of a process for stimulation programming for training an olfactory implant system;

FIG. **9** is a schematic diagram of an exemplary embodiment of a processor or processor system which may be used in the olfactory implant system;

FIG. **10** shows diagrams of exemplary embodiments of a transmitter and a receiver-stimulator;

FIG. **11** are schematic diagrams of electrode arrays;

FIG. **12** shows a spatio-temporal stimulation pattern; and

FIGS. **13**A and **13**B are diagrams of wearable devices.

DETAILED DESCRIPTION

Referring now to the drawings, and more particularly to FIG. **1**, there is shown a schematic of basic neurophysiology of the human or animal olfactory system.

Olfactory receptors **100** located in the olfactory epithelium **110** line the nasal cavity. When volatile or airborne substances bind to olfactory receptors **100** capable of receiving one or more particular airborne ligands, olfactory information from the activated odorant receptors **100** is passed to localized regions in the olfactory bulb **120**. In particular, the projecting nerve fibers have dendrites which synapse onto particular well-defined microregions of the olfactory bulb **120** called glomeruli **130**. Although the receptors **100** for a given ligand or family of ligands appear dispersed with little spatial organization across the olfactory epithelium, the nerve endings from the same receptors **100** converge on the same glomerulus. Different receptor subtypes (e.g. A, B, and C) connect to or associate with specific glomeruli **130** within localized regions (e.g. D, E, and F) of the olfactory bulb **120**. The information from the receptors creates unique spatial neurological activity patterns of neural activity for different odors. These patterns are called odor maps. Different chemicals generate different patterns of neural activity. As stimulation of the receptors occurs in continuous time, the odor maps are spatio-temporal patterns in the olfactory bulb **120** which provide the olfactory system means to reproducibly discriminate between different odors. The neural activity patterns in the olfactory bulb **120** are transmitted to higher levels of the brain via second order mitral cell nerve fibers that make up the olfactory tract **140**. Unique spatial neurological activity patterns of neural activity for different odors (i.e. odor maps) are not limited to the olfactory bulb **120**. Odor maps of nervous system structures additional to the olfactory bulb, in particular regions and parts of the olfactory cortex, may be utilized in accordance with the invention. As used herein, "olfactory cortex" is meant to include, but is not limited to, one or more of olfactory bulb, amygdala, pyriform cortex, orbitofrontal cortex, olfactory turbercle, and the entorhinal cortex. While some exemplary embodiments herein discuss stimulation of the olfactory bulb in particular, these are but illustrative examples, and one or more other parts of the olfactory cortex may alternatively or additionally be stimulated as described for simulation or mimicking an odor.

Referring now to FIG. **2**, an olfactory implant system for use with a human or animal olfactory system such as that which is illustrated in FIG. **1** includes one or more sensors or a sensor array **200**, one or more processors **210**, one or more transmitters **230**, one or more receiver-stimulators **240**, and one or more implantable electrode arrays **255**. One or more vapors from a subject's surrounding environment is detected with sensor array **200**. Sensor array **200** produces sensor output signals **205** in response to detecting one or more vapors of a possible plurality of vapors. Processor **210** processes the sensor output signals **205** into digital encoded information. Processor **210** can include an input signal processor **215** which digitizes the analog sensor output signals, one or more microprocessors **220**, and an output signal processor **225** which provides digital encoded information. Transmitter **230**, which may be an RF or other wireless transmitter, transcutaneously transmits the digital encoded information across the skin **235** of the subject to a receiver-stimulator **240**. Receiver-stimulator **240** can include receiver **245**, which may be an RF or other wireless receiver to communicate with transmitter **230**, and one or more implant processors or internal microprocessing units (iMPUs) **250** which generates electrical impulses as a function of the digital encoded information. Implanted electrode array **255** includes at least one stimulating electrode for stimulating the olfactory bulb in the subject with the electrical impulses. The electrical impulses may be associated with spatio-temporal electrical stimulation patterns which mimic the effect of the naturally occurring spatio-temporal electrical stimulation patterns of the olfactory system. Unless otherwise noted, 'simulate', 'mimic', 'recreate', and 'restore' (with reference to the sense of smell) are treated herein as functionally equivalent and may be used interchangeably herein.

Referring now to FIGS. **3** and **4**, odor stimuli are detected by sensor(s) **300** or sensor array **200** having a plurality of individual sensors (S_1, S_3, S_4, . . . , S_n). Each sensor **300** is configured to detect and respond to at least one molecule or group of molecules sharing certain chemical properties in vapor form, hereafter referred to as a 'target vapor' or 'target molecules'. 'Odor' and 'vapor' are used equivalently herein, as are 'odor molecule', 'chemical', and 'vapor molecule', unless noted otherwise. 'Vapor' as used herein is meant to indicate any collection of airborne molecules or particles which evoke/cause a particular response by the olfactory implant system. The opposite, a 'nontarget vapor', is therefore any collection of airborne molecules or particles which have no significant effect upon the response or behavior of the sensor array. As such, a 'target vapor' may be a pure vapor comprising a plurality of molecules all having the same chemical formula, or it may be a mixed vapor comprising a plurality of molecules of different chemical formulae the combination of which produces a sensor array response which is different from the sensor array response to one or more of the chemical formulae provided individually. A group of target molecules may share, for example, similar binding/ligand properties or rates of diffusion through a filter. When target molecules interact with the surface of a sensor **300** they change the conductivity of the sensor and alter the amount of current that is detected. In some embodiments filters **310** that impede the access of chemicals may be used to modify the selectivity of different sensors so that different chemicals produce different sensor array outputs **205**.

Each sensor **300** or grouping of sensors of a sensor array **200** may be configured to be sensitive only to a particular target vapor. In an embodiment, a sensor array **200** comprises a plurality of groupings of one or more sensors, where each grouping is configured to detect a different vapor. Alternatively, each sensor **300** may have sensitivity to a plurality or range of vapors. Still as a further alternative, a sensor array of identical sensors can be modified to include a different filter on each sensor to distinguish different vapors. FIG. **3** shows an exemplary embodiment of an odor sensor **300** which includes a filter **310**, a conducting element **320** that changes its resistance to current flow when exposed to target molecules, lead wire attachment sites **340**, and pin connectors **350**. Conducting element **320** is within sensor compartment **330**.

A sensor array **200** shown in FIG. **4** illustrates an embodiment which has a plurality of identical sensors **300**, but with each sensor having a different filter **310**. In some embodiments each filter differentially affects the passage or flow of different molecules across the filter. For example, this could be a form of active regulation or alternatively could be a form passive regulation, such as absorption or diffusion at different rates for different vapor molecules. Each sensor therefore has a different reaction/sensitivity to the different vapor molecules. As a result, one or more sensors may give a different response profile for a given vapor which can be associated with a unique odor fingerprint.

Filter **310**, which may also be referred to as a selectivity filter, may be fixedly attached to the sensor or integrally formed thereon. In an embodiment the filter may selectively

absorb a target vapor, such that the target molecules have a different (e.g. faster) rate of diffusion through the filter than do non-target molecules. A filter-sensor pair is preferentially sensitive or tuned to a particular odor molecule or group of odor molecules. The number of sensors and the number of target vapors which the sensor array detects may be variable, for instance as low as 1 or as high as numbering in the thousands, depending on the desired resolution of the system. In an alternative embodiment, the filter for each sensor could selectively block some molecules while permitting one or more other molecules to pass. One skilled in the art would recognize a variety of considerations may be made in selecting the resolution of the sensor array, such as cost of materials, size of the device, and complexity of the device. Furthermore, while FIGS. **3** and **4** show the use of filters, a sensor array without filters could be employed in the practice of the invention.

Target vapors to which the sensor array is sensitive can vary depending on the intended use of the olfactory implant system. For improving quality of life to an anosmic, target vapors may include molecules commonly associated with forms of pleasure or gratification, including molecules associated with food or fragrances, such as amyl acetate (banana), ethyl butyrate (fruity,pineapple), ethyl valerate (apple), citral (lemon), d-limonene (orange), and phenyl ethyl acetate (rose), or molecules associated with the outdoors, such as decyl methyl ether (fresh air), hexyl benzoate (woody, pine), and iso propyl quinolone (earthy, woody). Personal safety may be improved with target vapors including t-butyl mercaptan (rotten egg smell added to natural gas) or burnt wood or plastics (smoky), for example. Detection of these vapors may alert a user to the presence of harmful or dangerous substances in the environment, such as smoke or fire. Sensitivity to methane, for instance, could alert a user to the presence of a gas leak. In some embodiments target vapors may include vapors for which humans naturally have no sensitivity. That is to say, the sensor array is not limited to detection of odors which the natural human olfactory system is capable of detecting. It may include sensitivity to carbon-monoxide, for instance, to provide awareness of the presence of this harmful vapor in the surrounding air.

FIG. **4** shows a sensor array **200** having multiple sensors **300** and operational amplifiers circuits **450**, where the analog waveforms generated or produced from each of the sensors are provided as sensor output signals. An exemplary sensor module **400** including sensor **300** shows filter **310**, sensor compartment **330**, conducting element **320**, feedback gain resistor **410** for operational amplifier **430**, load resistor **420** and analog to digital converter **440** that may digitize the waveform (see ADC output **470**).

One of ordinary skill in the art will recognize that known sensor arrays and even processing for existing sensor arrays may be used in the practice of the invention. In an alternative embodiment, a commercially-available sensor array for detecting vapor molecules may be adapted for use with the present invention. An exemplary sensor array for this purpose would be Cyranose Electronic Nose manufactured and sold by Intelligent Optical Solutions (California, USA). The Cyranose Electronic Nose is a handheld package which may use different types of sensor (e.g. for CO_2, H_2S, O_2, or VOCs) and can include a database of digital images or "smellprints" for known vapors and perform best match comparisons between existing "smellprints" and unknown vapors.

One additional example of a sensor array which could be adapted for use with the present invention is an "electronic nose" being developed by the National Institute of Standards and Technology (NIST) having 16 microheater elements and eight types of sensors coupled with a pattern-recognition module. A description of the NIST "electronic nose" is available online at the institute's website in an article titled 'Sniffing Out a Better Chemical Sensor'.

FIG. **5** shows a schematic illustrating response parameter detection and extraction for generation of odor fingerprints. FIG. **6** shows a process for generating a look-up table of odor fingerprints. After the sensor array is exposed/subjected to a target vapor (see step **610** of process **600**) sensor output signals **205** from the sensors (S_1 to S_n, any one of which may be generically identified as S_x) in sensor array **200** are digitized (see step **620**) into digitized waveforms and stored as data in one or more sensor input buffers in processor **210** (see step **630**). Digitization may be performed individually by an analog-to-digital converter **440** associated with an individual sensor, as shown in sensor module **400** which produces digitized waveforms **470** as output. Alternatively, digitization may be performed by one or more input signal processors **215** associated with processor **210**. Digitized waveforms **460** are scanned to detect specific response parameters **500**, for example (but not limited to) peak voltage (V_{Peak}), half peak voltage ($V_{1/2Peak}$), time to peak voltage ($t_p - t_o$), slope, rise time, area under the curve, and time to half peak voltage ($t_{1/2p} - t_o$), the values of which are extracted (see step **640**) and stored in a response parameter buffer **510** (see step **650**). Values for the response parameters of each of the sensors are compared and the sensor with the largest peak voltage (V_{Peak}) is selected as a reference sensor (S_{ref}) (see step **660**). A sensor in the sensor array may be arranged without a filter. It could therefore have the largest peak voltage and be used as a common reference sensor for most or all iterations of process **600**. Values for response parameters **500** stored in the response parameter buffer **510** are divided by the corresponding response parameter values associated with the reference sensor (S_{ref}) to obtain final relative response values (S_x/S_{ref}) for sensors **1** to n (see step **670**). All relative response values associated with the same sensor (S_x) are stored in memory together with an identifier (e.g. a name, label, or chemical formula) which identifies the target vapor to which the sensor array was exposed (see step **680**). This data set for the target vapor is referred to as an odor fingerprint. A plurality of odor fingerprints are generated and stored for a plurality of target vapors which the olfactory implant system is configured to detect.

Preferably, a receiver-stimulator **240** and electrode array **255** may be implanted in the subject. The receiver-stimulator may include receiver **245** and an internal micro-processor unit (iMPU) **250**. The receiver-stimulator **240** may be implanted or positioned anywhere in the body, including both intracranial and extracranial locations. Examples include but are not limited to behind the subject's ear, in the chest (such as done with pacemakers), and in subcutaneous tissues of the scalp. In some embodiments, a receiver-stimulator **240** may be adjacent to or even incorporated with the electrode array. In still other embodiments, a receiver-stimulator **240** may be percutaneous and not require transcutaneous signal transmission by a transmitter **230**. A receiver-stimulator **240** may be connected by direct electrical wiring or by wireless communications to an electrode array **255** which is implanted next to the olfactory bulb or another part of the olfactory cortex.

FIG. **7** shows an exemplary process **700** for testing of the electrode array to ensure proper functionality and performance. Electrode integrity is tested by measuring impedance (see step **710**). In a single iteration of what can be an iterative testing process, the electrode array is supplied with

stimulus impulses of one of a plurality of variable modes (see step **720**), the effects of which are measured and recorded from either adjacent recording electrodes and/or distant grounds (see step **730**). The stimulus impulse parameters are adjusted to a different mode (see step **740**) and some or all of the steps of process **700** may be repeated. The variable modes of step **720** may be variations on stimulation variables/parameters such as timing, amplitude (e.g. 0-500 μA), pulse duration (e.g. 5-1000 ns), frequency (e.g. up to 5000 Hz), and stimulation mode (e.g. bipolar). Each electrode in the electrode array is preferably individually controllable/programmable. Alternatively, electrodes may be grouped into units which are controlled together.

The electrode array may have recording electrodes in addition to stimulatory electrodes, or it may have electrodes which can serve either purpose depending on their configuration settings. For feedback, at least one recording electrode may be provided for recording one or more bioelectric properties (e.g. electric field properties) at the olfactory bulb in the subject. The recording electrode or electrodes may be separate from or an integral part of the stimulating electrode array. The recordings from the recording electrodes may be used to adjust stimulus impulse parameters as a function of the bioelectric properties.

One or more ground or reference electrodes for the electrode array may be arranged within a casing of a receiver-stimulator, for example, and/or placed in any other soft tissue location of the body, in which case the electrode may be provided with a conducting wire from the receiver-stimulator separate from conducting wires of the main electrode array positioned at the target stimulation site (e.g. the olfactory bulb). The use of a distant ground electrode is comparable to the use of distant ground electrodes with some cochlear implants.

FIG. **8** shows an exemplary process **800** for stimulation programming for training an olfactory implant system of the present invention for optimized performance customized for the individual user. The electrode array is supplied with a first trial spatio-temporal stimulation pattern (STSP) (see step **810**) with settings such as those stated above for testing of the array. The subjective odor perception from the subject's feedback is recorded (see step **820**), and the subjective odor perception feedback is recorded together with the STSP parameters in memory (see step **830**). This process is repeated with different STSP parameters multiple times to generate a library of subject odor perceptions and the electrical stimulation features which may be used to reproduce the perceptions. In an exemplary embodiment, stimulating the olfactory bulb, olfactory tract, or other part of the olfactory cortex in the subject with a first spatio-temporal electrical stimulation pattern simulates or mimics a first odor in the olfactory bulb, olfactory tract, or other part of the olfactory cortex in the subject, while stimulating the olfactory bulb, olfactory tract, or other part of the olfactory cortex with a second spatio-temporal electrical stimulation pattern which is different from the first spatio-temporal electrical stimulation pattern simulates or mimics a second odor in the olfactory bulb, olfactory tract, or other part of the olfactory cortex in the subject which is different from the first odor. That is to say, each spatio-temporal electrical stimulation pattern may simulate or mimic a unique odor/perception of an odor. Perceptions as reported by the subject can be compared with the identifiers of stored odor fingerprints and matches determined (see step **840**). Matches may be stored in a non-volatile, computer-readable memory/storage medium (see step **850**).

FIG. **9** shows an external micro-processor unit (eMPU), which is equivalent to processor **210** shown in FIG. **2**. The eMPU **210** preferably performs several functions. These functions may be a subset of or all of the steps of processes **600**, **700**, and **800**. It processes the sensor output data digitized and temporarily stored in one or more sensor input buffers **905**. Detection and extraction of response parameters **500** may be performed by a response parameter/extractor circuit **906** and temporarily stored in response parameter buffer **510**. The eMPU **210** may use the data temporarily stored in response parameter buffer **510** to perform sensor fingerprint programming **915** according to process **600**. The eMPU may also or alternatively use the stored response parameters for comparison to stored subject perceptions in order to determine an electrode stimulus suitable for mimicking the detected vapor. Odor identifiers and their respective odor fingerprints are programmed into memory **930** after exposing the sensory array to a target vapor/odorant and then storing the odor fingerprint in memory along with one or more identifiers keyed in from an external programming interface **935**, such as a computer. The eMPU and data stored in memory **930** may be programmed and accessed by an external programming interface (EPI) **935**. Power may be supplied to components of the system by a power source **916** such as one or more commercially available batteries such as hearing aid batteries or rechargeable batteries.

A comparison circuit **960** associated with microprocessor **220** compares odor fingerprint identifiers stored in memory **930** with the subjective odor perceptions also stored in memory and determines matches (see step **840** of process **800**). For each match, the comparison circuit **960** links the odor fingerprint with the corresponding STSP parameters which will generate an intended odor perception. During stimulation programming, matches are stored in memory **930** (see step **850** of process **800**). During regular use of the system, a best match is used to determine the electrode array stimulus parameters which may be temporarily stored in a buffer **940** before being sent to an electrode output encoder **945** which supplies the electrode array with the stimulatory impulses which can be used to generate a sensation in the olfactory bulb.

Recording electrode signals from recording electrodes can arrive at the processor at electrode input decoder **950** and the data used for electrode parameter programming **955** according to process **700** as described above.

In some embodiments, one or more matches between odor fingerprints and corresponding STSP parameters/odor perceptions may be manually determined or overridden (such as by a user) in order for a given odor fingerprint to yield a different odor perception than might otherwise be expected. This allows a user to choose a matching at his/her discretion. As an example, a system may be arranged in which, under normal conditions, detection of a potato odor generates a stimulatory pattern which simulates or mimics a first odor. Detection of an apple odor, on the other hand, generates a stimulatory pattern which simulates or mimics a second odor which is different from the first odor. A user or authorized administrator (e.g. a doctor) may configure the system (at, for example, a processor or receiver-stimulator) such that detection of a potato odor generates a stimulatory pattern which simulates or mimics the second odor (that which was matched with apple) instead of a stimulatory pattern which simulates or mimics the first odor (that which was matched with the potato). Thus, the user would have the perception normally associated with apple odor now associated with both apple odor and potato odor. In effect, one or more matchings between odor fingerprints and stimulatory pat-

terns providing particular odor perceptions may be adjusted or changed, either permanently or temporarily.

In some embodiments, a stimulatory pattern may be generated in response to entry of a command or instruction from a user (received at, e.g., an external programming interface) with or without detection of an odor fingerprint regularly associated with that stimulatory pattern. For example, despite an odor from an apple not being present and therefore not being detected by the sensor array, a user may command or instruct the implant system to nevertheless stimulate the olfactory cortex (e.g. the olfactory bulb) with the STSP parameters which simulate or mimic the perception of apple. This feature may be desirable if, for example, a user is consuming a bland food and selective simulation or enhancement of a food aroma is desired. An input from the user can be received by the implant device which prompts stimulation such that one or more aromas not appreciably present from the food are perceived by the user. A user may choose which aroma or aromas are simulated.

As with all measuring instruments, fluctuations and deviations of signal readings (i.e. "sensor drift") are to be expected over time, especially as the sensors age. As such, processor **210** may include a drift monitor **970** to monitor and identify fluctuations or gradual changes in the behavior/signal outputs of the sensors over time, as shown in FIG. **9**. The monitor can compare one or more of the analog sensor output signals, the digitized sensor output signals stored in sensor input buffer **905**, and the response parameter values stored in response parameter buffer **510** for a target vapor with the odor fingerprint stored in memory. Processor **210** may furthermore comprise a calibrator **975** which accounts for fluctuations or gradual changes in the electrical characteristics and/or sensitivity of the sensors of the sensor array. One skilled in the art will recognize that this may be done in a variety of ways. Calibrator **975** may adjust the fingerprint database in memory **930** by sensor fingerprint programming **915**. Alternatively, calibrator **975** may store a quantitative record of sensor drift in memory which could be used as an additional variable by comparison circuit **960**. The drift monitor **970** may be configured to communicate with the calibrator **975** to automatically adjust for fluctuations or changes. The drift monitor and calibrator may also be integral with one another and/or integral with sensor fingerprint programming **915**. In some embodiments, the drift monitor and/or calibrator may be in communication with an external programming interface **935** which allows user access and/or configuration of the drift monitor and calibrator.

Processing of sensor output signals may include the steps of detecting a first electrical profile from the sensor output signals, extracting one or more values describing that electrical profile, comparing one or more of the extracted values with one or more values of at least one other electrical profile of a known vapor, and generating digital encoded information associated with at least one of the other electrical profiles of known vapors which the processor has matched with the detected electrical profile. Electrical profiles may be of current, resistance, voltage, or impedance over time, for example.

FIG. **10** illustrates how data is transferred between eMPU **210** and iMPU **250** by wireless signals across the skin (e.g. radio frequencies). An output of processor **210**, which is an electrode stimulation data stream **1000** representing the STSP parameters for an odor perception, is sent to transmitter **230** and converted to radiofrequency (RF). The data stream **1000** can be encoded (including, for example, digital to analog conversion) by an electrode output encoder **945** before wireless transmission. The RF signal is fed to an amplifier. RF decoder **1005** associated with iMPU **250** decodes the digital data stream into instructions for electrode stimulation. Stimulation variables (e.g. onset, current intensity, pulse duration, interpulse interval, number of pulses) at each electrode in the array are set by the iMPU **250** according to electrode array stimulus parameters for the different odor perceptions experienced by the subject. Current level is controlled by a digital to analog convertor which is a part of stimulator circuitry **1010**. The stimulator circuitry is comprised of amplifiers and timing circuits that control both the stimulus intensity (current levels) and the pulse parameters (duration, inter pulse intervals, and number of pulses) that is sent to each of the electrodes.

A primary (external) inductor associated with transmitter **230** transmits energy wirelessly to a secondary (internal) inductor associated with receiver **245**. The two inductors may be kept in alignment by magnets within the center of each. A capacitor can be used to create resonance. The generated power at the secondary inductor can be rectified using a full wave rectifier and the energy stored in power module **1015**. This power is used to operate the receiver-stimulator and to provide current needed to send stimulus pulses to the electrodes at an electrode connector block **1020** output of the iMPU **250**. Power is preferably supplied to power module **1015** by power source **916**. Power is also used for recording circuitry **1025** which may send electrode monitoring data encoded by the iMPU back to the eMPU by RF telemetry **1030**. The recording circuitry is comprised of amplifiers and analogue to digital converters (ADCs) that processes the voltage changes detected at each of the electrodes and sends them to the RF telemetry circuits. Transmitter **230** sends an electrode monitoring feedback data stream **1035** to processor **210** where it can be decoded (including, for example, analog to digital conversion) by electrode input decoder **950**.

FIG. **11** shows three different electrode arrays used to stimulate the olfactory cortex in different ways. One or more olfactory bulbs **120**, one more olfactory glomeruli **130**, and/or one or more olfactory tract nerve fibers **140** may all be stimulated by varying the shape of electrode contact region **1100**. This may be accomplished with a straight electrode array **1110**, a penetrating electrode array **1120**, and/or a pad/panel electrode array **1130**. Other regions or parts of the olfactory cortex may likewise be stimulated with an electrode array. Such other parts of the olfactory cortex include, but are not limited to, the amygdala, the pyriform cortex, the orbitofrontal cortex, the olfactory turbercle, and the entorhinal cortex. A particular stimulation target of the olfactory cortex may be selected for various reasons. For example, some regions are more accessible by known surgical implant methods and may therefore involve less complicated medical procedures. One or more particular stimulation targets may also be selected according to the desired resolution of the physiological response. The amygdala, pyriform cortex, and orbitofrontal cortex may, for example, be particularly well suited for stimulation by an electrode array according to their respective spatial neurological activity patterns of neural activity for different odors (odor maps). As was previously indicated, the olfactory bulb is just one exemplary target for stimulation.

An exemplary electrode array is a flexible pad electrode array. This allows for the array to be configured about the three-dimensional surface of an olfactory bulb **120** with each electrode **1100** touching or immediately adjacent to the surface of the bulb. The size of the array is dependent on the size of the olfactory bulb of the subject. In humans, an adult

olfactory bulb measures about 10 mm by 2 mm. Glomeruli are about 0.1 mm in diameter. The array may contain as many as 64 electrodes. However, fewer electrodes may be chosen to reduce cost or for other considerations and in some cases even improve performance of the device. The electrode array stimulates the olfactory bulb according to a particular spatio-temporal stimulation pattern which mimics a sense of smell of a particular odor in the central nervous system of the subject.

The electrode array may be a custom array designed specifically for the present invention. Alternatively, the electrode array may be commercially acquired from an existing manufacturer for stimulatory devices such as cochlear implants. One example of a commercial source for an electrode array which may be used in accordance with the present invention is NeuroNexis (the home website of which is neuronexistech.com as of Apr. 1, 2013). NeuroNexis offers catalog surface electrode arrays and penetrating electrodes, for example, in addition to customized electrode arrays.

FIG. **12** is an example visual representation of a spatio-temporal stimulation pattern for a 3×3 electrode array. An electrode array **1200** is another embodiment of an electrode array which may be used in the practice of the invention. Electrode Array **1200** comprises three groups of three electrodes wherein each of the nine electrodes **1210** are preferably independently controllable. The nine voltage-time plots **1220** show the stimulation parameters for each electrode **1210**. In this example, electrodes **1**, **2**, and **4** each are supplied a biphasic single stimulatory pulse of approximately equal magnitude and duration but having start times offset from one another. The remaining six electrodes are not supplied a stimulatory pulse. Each stimulatory electrode **1210** may be exclusively utilized for stimulation of a single glomerulus. Alternatively, one or more may be positioned to stimulate more than one glomerulus with equal or different intensity.

FIGS. **13**A and **13**B show diagrams of wearable modules which may be used for a subject to carry the external components of the present invention, including the sensor array, eMPU, and transmitter. In an exemplary embodiment as shown in FIG. **13**A, sensor array **1310** may be attached to a pair of eyeglasses **1300** or safety glasses, such as on the bridge of the glasses. Sensor array **1310** may also be formed integrally therewith to improve the cosmetic appearance of the device, for example. As another alternative, FIG. **13**B shows a sensor array **1310** which can be positioned under the external naris (nostril) of the nose. In this position vapors would pass across the sensors when the subject sniffs or inhales through the nose. Processor **1330** may likewise be fixedly or removably attached to the eyeglasses, such as on the temple or earpiece, or formed integrally therewith. Sensor array **1310** and processor **1330** may be connected such that the sensor array is in communication with the processor. When both components are disposed on a pair of eyeglasses they can be connected by wiring **1320**. Alternatively, the sensor array and processor may be positioned at some distance to one another. The sensor array and/or processor could be attachable to a hat, for instance, or to a belt similar to a pager or a cell phone, in which case the sensor array may communicate wirelessly with the processor. Processor **1330** is shown connected to transmitter **1340** for transcutaneously transmitting digital encoded information to the implanted stimulator-receiver in the subject. In some embodiments, percutaneous transmission may also be used. This may be especially useful in research applications, for example.

While processing as described in FIGS. **5-9** has been disclosed as mostly or entirely taking place on board a processor **240**, this represents only one exemplary embodiment of the current invention. Processing steps may be divided over a plurality of separate processors which may be external or internal (i.e. implanted in the subject). Processing steps may also be performed remotely, with the sensor array and/or receiver-stimulator in wireless communication with a processor which is not carried or worn by the subject. Furthermore, one of ordinary skill in the art will recognize that all necessary processing (for example, that which is performed by comparison circuit **960**) may be performed by hardware, software (e.g. computer programs), firmware, or a wide range of combinations thereof and is not limited to the exemplary processor shown in FIG. **9**.

The subjects which are the end-users of the methods and devices of the invention are generally mammals, and are usually humans. Veterinary applications of this technology are also contemplated.

While the invention has been described in terms of preferred embodiments, those skilled in the art will recognize that the invention can be practiced with modification within the spirit and scope of the appended claims.

Having thus described our invention, what we claim as new and desire to secure by Letters Patent is as follows:

1. A method for mimicking a sense of smell in a subject, comprising the steps of:

detecting one or more vapors with a sensor array, said sensor array producing sensor output signals in response to detecting said one or more vapors;

processing said sensor output signals into digital encoded information;

transmitting said digital encoded information transcutaneously into said subject;

generating electrical impulses as a function of said digital encoded information, wherein said electrical impulses are determined according to training conducted by a user; and

stimulating the olfactory cortex in said subject with said electrical impulses with an implantable electrode array comprising at least one stimulating electrode.

2. The method as claimed in claim **1**, wherein said electrical impulses are associated with spatio-temporal electrical stimulation patterns.

3. The method as claimed in claim **2**, wherein stimulating the olfactory cortex in said subject with a first spatio-temporal electrical stimulation pattern simulates or mimics a first odor and stimulating the olfactory cortex with a second spatio-temporal electrical stimulation pattern which is different from said first spatio-temporal electrical stimulation pattern simulates or mimics a second odor which is different from said first odor.

4. The method as claimed in claim **1**, wherein said processing step comprises the steps of:

detecting a first electrical profile from said sensor output signals;

extracting one or more values describing said first electrical profile;

comparing said one or more values of said first electrical profile with one or more values of at least one other electrical profile of a known vapor; and

generating digital encoded information associated with one of said at least one other electrical profile of a known vapor which matches said detected electrical profile.

5. The method as claim in claim **4**, wherein said electrical profile is a voltage profile.

6. The method as claimed in claim 1, wherein said sensor array comprises a plurality of groupings of one or more sensors, each grouping configured to detect a different vapor.

7. The method as claimed in claim 1, wherein said sensor array comprises a plurality of the same sensor, wherein a different filter is associated with each sensor of said plurality of the same sensor which differentially affects the passage or flow of different molecules across the filter.

8. The method as claimed in claim 1, further comprising the step of recording one or more bioelectric properties of the olfactory cortex in said subject with at least one recording electrode.

9. The method as claimed in claim 8, wherein said at least one recording electrode is an integral part of said implantable electrode array.

10. The method as claimed in claim 1 wherein said stimulating step stimulates the olfactory bulb.

11. A system for mimicking a sense of smell in a subject, comprising:

a sensor array comprising a plurality of sensors for detecting one or more vapors, said sensor array producing sensor output signals in response to detecting said one or more vapors;

a processor for processing said sensor output signals into digital encoded information;

a transmitter for transmitting said digital encoded information transcutaneously into said subject;

a receiver-stimulator configured to receive said transcutaneously transmitted digital encoded information and generate electrical impulses as a function thereof, wherein said electrical impulses are determined according to training conducted by a user; and

an implantable electrode array comprising at least one stimulating electrode configured to stimulate the olfactory cortex in said subject with said electrical impulses.

12. The system as claimed in claim 11, wherein said electrical impulses are associated with spatio-temporal electrical stimulation patterns.

13. The system as claimed in claim 11, wherein each of said at least one stimulating electrode of said implantable electrode array is individually controllable.

14. The system as claimed in claim 11, wherein said sensor array comprises a plurality of groupings of one or more sensors, each grouping configured to detect a different vapor.

15. The system as claimed in claim 11, wherein said sensor array comprises a plurality of the same sensor, wherein a different filter is associated with each sensor of said plurality of the same sensor which differentially affects the passage or flow of different molecules across the filter.

16. The system as claimed in claim 11, further comprising at least one recording electrode for recording one or more bioelectric properties of the olfactory cortex in said subject.

17. The system as claimed in claim 16, wherein said at least one recording electrode is an integral part of said implantable electrode array.

18. The system as claimed in claim 11 wherein the implantable electrode array is configured for stimulating the olfactory bulb.

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