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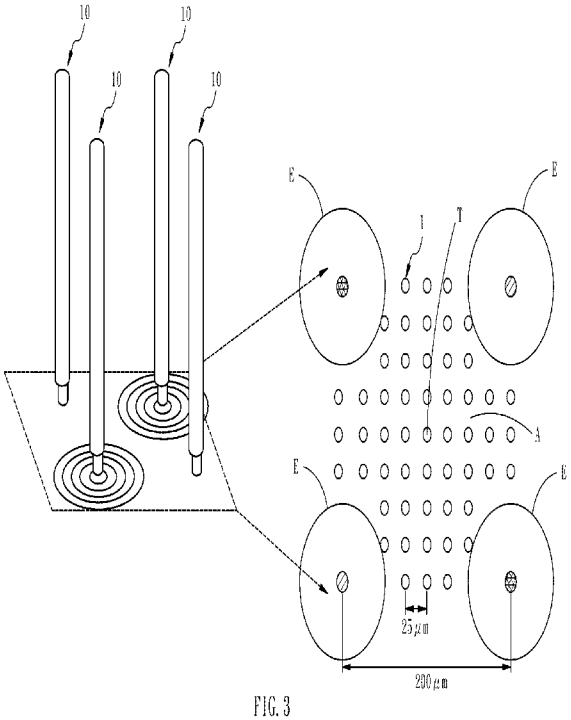


FIG. 3

(57) Abstract: A high-resolution microelectrode-based neural stimulation system includes at least two stimulating electrodes, a first control module, and a second control module. An overall periphery of the stimulating electrodes defines a stimulation area on the brain tissue. The first control module has a first signal source and at least two first switches. The first signal source provides a first current having a first frequency. The second control module has a second signal source and at least two second switches. The second signal source provides a second current having a second frequency. By controlling the current intensities of any of the two electrodes, stimulation can be selectively provided to a brain tissue on a target site in the stimulation area. The neural stimulation system benefits its user with decreased complexity of electrode installation and reduced setup costs while enabling high-precision stimulation to neurons.

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HIGH-RESOLUTION MICROELECTRODE-BASED NEURAL STIMULATION SYSTEM

BACKGROUND OF THE INVENTION

1. Field of the Invention:

The present invention relates to neural stimulation and, more particularly, to a high-spatiotemporal resolution microelectrode-based neural stimulation system.

2. Description of the Related Art:

Neurons play a crucial role in various brain functions, such as decision-making, motor control, and memory consolidation. Recent research has shown that neural stimulation has great potential in treating neurological conditions such as Parkinson's disease and in applications related to brain-machine interfaces for prosthesis control.

Stimulation with single-cell resolution can be achieved through microelectrode-based or two-photon optogenetic approaches. Microelectrode-based stimulation requires moving electrodes among neurons. However, since the brain operates

on a millisecond-level resolution, it is obviously impracticable to move electrodes one by one to stimulate the corresponding neurons. A high-density microelectrode array can deliver neural stimulation at multiple sites without moving electrodes in the tissue. However, the spatial resolution of the stimulation is limited by the density of the electrode, *i.e.,* the distance between the electrodes.

SUMMARY OF THE INVENTION

The primary objective of the present invention is to address the shortcomings of microelectrode-based stimulation in the prior art about being inferior in terms of spatial resolution and requiring a full-coverage microelectrode array.

To achieve the foregoing objective, one embodiment of the present invention provides a high-resolution microelectrode-based neural stimulation system, for providing electrical stimulation to a brain tissue, the microelectrode-based neural stimulation system comprising: at least two stimulating electrodes, being fixed to and contacting the brain tissue so that between two stimulating electrodes defines a stimulation area

on the brain tissue; a first control module, having a first signal source and at least two first switches, the first signal source providing a first current having a first frequency, each of the first switches corresponding to a respective one of the stimulating electrodes and being electrically connected to the first signal source, so as to respectively control each of the stimulating electrodes to form electric conduction with the first signal source; and a second control module, having a second signal source and at least two second switches, the second signal source providing a second current having a second frequency that is different from the first frequency, each of the second switches corresponding to a respective one of the stimulating electrodes and being electrically connected to the second signal source, so as to respectively control each of the stimulating electrodes to form electric conduction with the second signal source; whereby the first control module controls one of the first switches to form electric conduction between the corresponding stimulating electrode and the first signal source, so as to transmit the first current to the brain tissue, and the second control module controls one of the second

switches to form electric conduction between another of the stimulating electrodes and the second signal source, so as to transmit the second current to the brain tissue, in which the first control module and the second control module jointly form an electrical stimulation signal on a target site in the stimulation area by controlling current intensities of the first current and the second current so as to provide the electrical stimulation to the brain tissue.

Thereby, with the designed arrangement of those stimulating electrodes, the disclosed microelectrode-based neural stimulation system can use the first control module and the second control module to respectively control any two of the stimulating electrodes so as to form an electrical stimulation signal on a target site in a stimulation area and provide stimulation to a neuron on the target site, thereby accomplishing neural stimulation through electrodes with great operational freedom.

Additionally, with the first control module and the second control module respectively controlling the current intensities and frequencies of the first current and the second current, the

target site on which the neuron to receive stimulation is situated can be accurately located, thereby providing neural stimulation with high spatial resolution and high precision.

BRIEF DESCRIPTION OF THE DRAWINGS

Fig. 1 is an applied view of a microelectrode-based neural stimulation system according to a first embodiment of the present invention, showing stimulating electrodes attached to a brain.

Fig. 2A-2B is a schematic drawing illustrating an exemplary principle of stimulation according to the first embodiment of the present invention.

Fig. 3 is a schematic drawing illustrating an exemplary arrangement of the stimulating electrode according to the first embodiment of the present invention.

Fig. 4 is a circuit diagram of the microelectrode-based neural stimulation system according to the first embodiment of the present invention.

Fig. 5 is a schematic drawing illustrating the simulation of neural stimulation according to the first embodiment of the

present invention, showing that the stimulating electrodes activate a neuron on a target site.

Fig. 6 is another schematic drawing illustrating simulation of neural stimulation according to the first embodiment of the present invention, showing that the location of the target site can be configured by means of the setting of currents.

Fig. 7 is a schematic drawing illustrating an exemplary arrangement of the stimulating electrode according to a second embodiment of the present invention.

Fig. 8 is a schematic drawing illustrating an exemplary principle of stimulation according to the third embodiment of the present invention.

DETAILED DESCRIPTION OF THE INVENTION

The following preferred embodiments, when read with the accompanying drawings, are made to clearly exhibit the above-mentioned and other technical contents, features, and effects of the present invention. Through the exposition by means of the specific embodiments, people would further understand the technical means and effects the present invention adopts to

achieve the above-indicated objectives. However, the accompanying drawings are intended for reference and illustration, but not to limit the present invention, and are not made to scale.

Referring to **FIG. 1** through **FIG. 8**, the present invention provides a high-resolution microelectrode-based neural stimulation system **100**, for providing electrical stimulation to a brain tissue **B**. **FIG. 1** through **FIG. 6** depict a first embodiment of the present invention and **FIG. 7** illustrates a second embodiment of the present invention. In the present invention, the brain tissue **B** may be located inside a cranium of an animal or may be an acute brain slice obtained from a cranium of an animal.

In the first embodiment, the present invention provides a microelectrode-based neural stimulation system **100**, which comprises: four stimulating electrodes **10**, a first control module **20**, a second control module **30**, and a ground electrode **40**. Therein, the stimulating electrodes **10** and the ground electrode **40** are fixed to and in contact with the brain tissue **B**. The first control module **20** and the second control module **30**

are coupled to the stimulating electrode **10**.

Each of the stimulating electrodes **10** has a columnar shape in the present embodiment and a diameter smaller than 100 μm. In a preferred embodiment, the diameter ranges between 5 and 200 μm. A smaller diameter will be easier to maintain the integrity of the brain tissue **B**. It should be noted that the stimulating area **A** can be formed between any two stimulating electrodes **10** if there are more than two stimulating electrodes **10**. In some cases, those stimulating electrodes 10 can be arranged in a circular, semicircular, straight or almost straight manner. Moreover, these electrodes 10 do not necessarily need to be arranged in the same plane. Depending on the pattern of brain tissue B, they can be arranged on a curved surface or, if brain tissue B has a three-dimensional structure, those stimulating electrodes 10 can be set at different positions on the same probe to stimulate different depths of brain tissue B, creating a three-dimensional stimulating area **A**.

As shown in **FIG. 2A**, the target position **T** can be stimulated by controlling the frequencies and current intensities of the two stimulating electrodes **10**. For example, when the

current intensity of the two stimulating electrodes **10** is the same, the target position **T** will be located in the middle of the two stimulating electrodes **10**. Please refer to **FIG. 2B**, when the current intensity of the two stimulating electrodes **10** is different, the target position **T** will move to the side of the stimulating electrode **10** with the lower current intensity. In this way, the user is able to select the desired stimulating target position **T** by adjusting the current intensity of the stimulating electrode **10**.

As shown in **FIG. 3**, this embodiment is illustrated by taking four stimulating electrodes **10** as an example. An overall periphery of all of the four stimulating electrodes **10** as a whole defines a stimulation area **A** on the brain tissue **B**. The stimulation area **A** includes a target site **T** and an excluded area **E**. The target site **T** is a region in which at least two of the stimulating electrodes **10** have resonance with each other. In the drawing, circles in the stimulation area each represent a target site **T**. In practical use, the distances between and the number of the target sites **T** may be set and adjusted without limitation. The stimulating electrodes **10** are configured to apply electrical

signals, such as currents or voltages, to the brain tissue **B** for stimulation. However, the intensity and the frequency of the electrical signal tends to be too high around the stimulating electrodes **10** to prevent proper stimulation on the brain tissue **B** and desired high-frequency oscillation around the stimulating electrodes **10**, the areas around the stimulating electrode **10** are each defined as an excluded area **E** in the present invention. In other words, neural stimulation is impossible for the brain tissue **B** located in any excluded area **E**. In the present embodiment, an excluded area **E** is a region covering a radius of 50μm around a stimulating electrode **10**. The covering radius of the excluded area **E** should depend on the intensity of the current and neuronal type. More specifically, a preferred radius of the excluded area **E** ranges between one-fourth to one-third of the distance between the stimulating electrodes **10**. Two or more stimulating electrodes **10** can affect a neuron **1** on a target site **T** with temporal interference (TI) by generating high-frequency wave currents of different intensities. In the present embodiment, the spatial resolution of the target site **T** is 25μm. Stated differently, in the stimulation area **A**, at least one site

can be selected for neural stimulation every 25μm.

Also referring to **FIG. 4**, in the present embodiment, the first control module **20** has a first signal source **21**, a first signal amplifier **22**, and four first switches **23**. The first signal source **21** provides a first current having a first frequency through the first signal amplifier **22**. Each of the first switches **23** corresponds to a respective stimulating electrode **10** and is electrically connected to the first signal source **21**, so as to independently control whether a stimulating electrode **10** is in electric conduction with the first signal source **21**.

The second control module **30** has a second signal source **31**, a second signal amplifier **32**, and four-second switches **33**. The second signal source **31** provides a second current having a second frequency through the second signal amplifier **32**. Each of the second switches **33** corresponds to a respective stimulating electrode **10** and is electrically connected to second signal source **31**, so as to independently control whether a stimulating electrode **10** is in electric conduction with the second signal source **31**. Therein, every stimulating electrode **10** is connected to both a first switch **23** and a second switch

33, wherein the first switch **23** and the second switch **33** connected to the same stimulating electrode 10 will not be on at the same time so as to prevent abnormal output of the stimulating electrode **10**.

In the present embodiment, the first signal source **21** and the second signal source **31** are each an Analog Discovery 2™ arbitrary waveform generator (Diligent Corporation), and the first signal amplifier **22** and the second signal amplifier **32** are each a power amplifier from BioPro Scientific Corporation.

To provide stimulation to a neuron **1**, the first control module **20** controls one of the first switches **23** to establish electric conduction between the corresponding stimulating electrode **10** and the first signal source **21**, so as to transmit the first current to the brain tissue **B**. The second control module **30** controls one of the second switches **33** to establish electric conduction between another stimulating electrode **10** and the second signal source **31**, so as to transmit the second current to the brain tissue **B**.

By controlling the intensities and the frequencies of the first current and the second current, the first control module **20**

and the second control module **30** jointly form an electrical stimulation signal on the target site **T** in stimulation area A so as to provide electrical stimulation to the brain tissue **B**. In the present embodiment, the electrical stimulation signal may have sine waves or a PWM (Pulse-Width Modulation) waveform, with the sine wave more preferable.

It is to be noted that, in the present embodiment, for preventing mutual interference among the stimulating electrodes **10**, only two stimulating electrodes **10** are operated to output electrical stimulation signals to stimulate the neuron **1** at the same time. In other words, the first control module **20** turns on only one of the first switches **23** at one time, and the second control module **30** turns on only one of the second switches **33** at one time, and the stimulating electrode **10** corresponding to the first switch **23** is different from the stimulating electrode **10** corresponding to the second switch **33**. Of course, it is feasible to activate plural stimulating electrodes **10** at the same time despite possible temporal interference among the current stimulation signals that may bring about additional complexity.

To be more specific, the second frequency is different from the first frequency. Therein, each of the first frequency and the second frequency is in the range between 800 and 10000 Hz, preferably between 2000 and 4000 Hz. Additionally, the frequency difference between the first frequency and the second frequency ranges between 1 and 500 Hz. An excessively large frequency difference between the first frequency and the second frequency can prevent stimulation from acting on the neurons **1**. In the present embodiment, the first frequency is 2000 Hz, and the second frequency is 2040 Hz. In other words, a base frequency of the first frequency and the second frequency is 2000 Hz, and a modulation frequency is the differences between the two frequencies, which is 40 Hz.

Also, the values of the first current and the second current have to be within a defined range because a current of an excessively large or small value may fail to interact with the neurons **1** and prevent the neurons **1** from being stimulated and generating an action potential. Moreover, an excessively high current can lead to water electrolysis, which may break or damage the brain tissue **B**. In the present embodiment, each of

the first current and the second current ranges between 100 and 500 μA.

Furthermore, the first current and the second current have to gradually boost the currents acting on the neuron **1** for stimulation through a period of 50 ms. Such a current ramping process effectively inhibits the onset action potential. In the present embodiment, the ramping rate of the first current and the second current is up to 5 μA/ms.

As shown in **FIG. 5**, in the present embodiment, the four stimulating electrodes **10** are arranged into a two-by-two two-dimensional array, which is composed of, from left to right, a first column **C1** and a second column **C2**, and from the bottom to the top, a first row **R1** and a second row **R2**. Any two adjacent stimulating electrodes **10** are separated. Specifically, the first column **C1** and the second column **C2** are separated by a first distance **d1**, and the first row **R1** and the second column **R2** are separated by a second distance **d2**. Each of the first distance **d1** and the second distance **d2** ranges between 50 and 1000μm. In the present embodiment, each of the first distance **d1** and the second distance **d2** is 200μm.

The ground electrode **40** is located far away from the stimulating electrodes **10** (as shown in **FIG. 1**), so as to prevent electric leakage. In the present embodiment, the ground electrode **40** is separated from any of the stimulating electrodes **10** by a distance that is eight to fifteen times as large as the first distance **d1**.

Referring to **FIG. 5** and **FIG. 6**, to evaluate the stimulation effect of the disclosed neural stimulation system **100**, simulation waveforms were generated using PYTHON in an electric field in an actual brain, with the simulation environment simplified using LFPY and NEURON.

For the simulation, the first frequency of the first signal source **21** was set as 2040 Hz, and the second frequency of the second signal source **31** was set as 2000 Hz. The stimulating electrodes **10** so obtained were arranged into a two-by-two two-dimensional array to define the stimulation area **A**, with the first distance **d1** and the second distance **d2** each set as 200μm.

While only simulation results in the central part of the stimulation area **A** are shown, neural stimulation can actually be performed on any target site **T** located on any straight line

linking the stimulating electrodes **10**. In the present embodiment, the area for simulation was divided into 49 (7 by 7) equal-size neurons arranged in grid. After the variation and inorganization of neurons **1** were removed, the 49 neurons **1** (ball-and-stick neurons) were distributed across the grid, so that any two adjacent neurons **1** were separated by 25μm.

As shown in **FIG. 5**, the electrodes **10** for stimulation were the one at the position **(C1, R1)**, and the one at the position **(C2, R2)**, while the center of the stimulation area **A** was set as a target site **T**.

By conducting the stimulating electrode **10** at the position **(C1, R1)** with the first signal source **21**, and conducting the stimulating electrode **10** at the position **(C2, R2)** with the second signal source **31**, while having the first current and the second current set as 220μA, the stimulating electrode **10** at the position **(C1, R1)** outputted sinusoidal waves of 2040Hz, 220μA, and the stimulating electrode **10** at the position **(C2, R2)** outputted sinusoidal waves of 2000Hz, 220μA.

As indicated by the membrane potentials of the neurons **1** in the 49 neurons arranged in grid, the neuron **1** on the target

site **T** was stimulated and fluctuated obviously (with pulses). The neurons **1** near the stimulating electrode **10** at the position **(C1, R2)** and the stimulating electrode **10** at the position **(C2, R1)** that did not output any current had their membrane potentials remaining low and relatively stable. The neurons **1** near the stimulating electrode **10** at the position **(C1, R1)** and the stimulating electrode **10** at the position **(C2, R2)** that were conducted stimulation showed membrane potentials that were relatively high but relatively stable. As demonstrated, the stimulating electrodes **10** can perform stimulation accurately on a neuron **1** on a target site **T**, without affecting non-target neurons **1**.

A further simulation was conducted in an electric field in an actual brain for evaluating control of target sites **T**. As shown in **FIG. 6**, the stimulating electrode **10** at the position **(C1, R1)**, and the stimulating electrode **10** at the position **(C2, R2)** were again selected for stimulation in this simulation.

When the first current was changed to 125μA, and the second current was changed to 375μA, the stimulating electrode **10** at the position **(C1, R1)** outputted sinusoidal waves of

2040Hz, 125μA, and the stimulating electrode 10 at the position **(C2, R2)** outputted sinusoidal waves of 2000Hz, 375μA. As indicated by the membrane potentials of the neurons **1** in the 49 neurons arranged in grid, the target site **T** fluctuating obviously had moved from the center toward the stimulating electrode **10** at the position **(C1, R1)** that had a relatively small output current. This demonstrated that the stimulating electrode **10** can select the location of the target site **T** according to the location of the neuron **1** to receive stimulation by controlling the current intensities of the first current and the second current. It is also to be noted that since the attenuation of the current intensity with respect to the distance is not linear, the intensity ratio between the first current and the second current is not necessarily equal to the distance ratio between the distances from the target site **T** to each of the two stimulating electrodes **10**.

In a second embodiment, the present invention provides another microelectrode-based neural stimulation system **100**, which is similar to its counterpart as described in the first embodiment except that the number of the stimulating

electrodes **10** is nine. Therefore, the first control module **20** has nine first switches **23**, and the second control module **30** has nine second switches **33**. Therein, every stimulating electrode **10** is connected to a first switch **23** and a second switch **33**.

Referring to **FIG. 7**, in the present embodiment, the nine stimulating electrodes **10** are arranged into a three-by-three two-dimensional array composed of, from left to right, a first column **C1**, a second column **C2**, and a third row **C3**, and, from the bottom to the top, a first row **R1**, a second row **R2**, and a third column **R3**. the first column **C1** and the second column **C2** are separated by a first distance **d1**. The first row **R1** and the second row **R2** are separated by a second distance **d2**. The second column **C2** and the third row **C3** are separated by a third distance **d3**. The second row **R2** and the third column **R3** are separated by a fourth distance **d4**. Each of the first distance **d1**, the second distance **d2**, the third distance **d3**, and the fourth distance **d4** ranges between 50 and 1000μm. Therein, the first distance **d1** is greater than the third distance **d3**. The first distance **d1** is equal to the second distance **d2**. The third distance **d3** is equal to the fourth distance **d4**. In the present

embodiment, the first distance **d1** and the second distance **d2** are each 200μm, while the third distance **d3** and the fourth distance **d4** are each 100μm.

It is to be noted that since the target site **T** is determined by the locations of the stimulating electrodes **10** and the current intensities, and in the present embodiment, there are two stimulating electrodes **10** providing currents at the same time, the target site **T** is on the straight line linking the two stimulating electrodes **10** providing currents. In the present embodiment, with the increased number of the stimulating electrodes **10**, which is now nine, the arbitrariness of selecting the target site in the stimulation area **A** can be significantly increased. Thus, with the increased number of the stimulating electrodes **10** and the selected distances between the stimulating electrodes **10**, the scope of the stimulation area **A** can be expanded and more combinations of the stimulating electrodes **10** can be provided, thereby significantly increasing possible locations of the target site **T** in the stimulation area **A**.

Referring to **FIG. 8**, these stimulating electrodes **10** can simultaneously stimulate different locations through frequency

control. In the present embodiment, stimulating electrode **10a** and stimulating electrode **10b** can be considered as a first pair of electrodes, with the frequency of stimulating electrode **10a** set to 1005Hz and the frequency of stimulating electrode **10b** set to 1040Hz to stimulate neurons at target position **T1**. Similarly, stimulating electrode **10a** and stimulating electrode **10c** can be considered as a second pair of electrodes, with the frequency of stimulating electrode **10a** set to 2005Hz and the frequency of stimulating electrode **10c** set to 2040Hz to stimulate neurons at target position **T2**. Stimulating electrode **10a** can emit current signals with frequencies of 1005Hz and 2005Hz during different time periods, corresponding to stimulating electrode **10b** and stimulating electrode **10c**, respectively, to stimulate neurons at target position **T1** and target position **T2**, respectively. Since the frequency difference between stimulating electrode **10b** and stimulating electrode **10c** is more than 500Hz, there is no interference between the first pair of electrodes and the second pair of electrodes. Similarly, stimulating electrode **10b** and stimulating electrode **10d** can also stimulate neurons and may be combined with other

stimulating electrodes **10a** and **10c** for superimposed stimulation at the same neuron location.To sum up, the present invention at least provides the following beneficial effects:

1. With the designed arrangement of the at least four stimulating electrodes **10**, the disclosed microelectrode-based neural stimulation system can use the first control module **20** and the second control module **30** to respectively control any two of the stimulating electrodes **10**, so as to form an electrical stimulation signal on a target site **T** in a stimulation area **A** and perform stimulation on a neuron on the target site **T**, thereby accomplishing neural stimulation through electrodes with great operational freedom.

2. With the first control module **20** and the second control module **30,** respectively controlling the current intensities of the first current and the second current, the target site on which the neuron **1** to receive stimulation is situated can be accurately located, thereby providing neural stimulation with high spatial resolution and high precision.

3. By setting the ramping rate of the first current and the second current up to 5 μA/ms, the onset action potential can be

effectively prevented if not eliminated.

4. By increasing the number of the stimulating electrodes **10** to nine and arranging them as described in Embodiment 2, the arbitrariness of selecting the target site in the stimulation area **A** can be significantly increased.

5. By separating the ground electrode **40** away from the stimulating electrodes **10**, the distance between the ground electrode **40** and any of the stimulating electrodes **10** is eight to fifteen times as large as the first distance **d1**, so as to prevent electric leakage.

6. Since the arrangement of first distance **d1** is not equal to the third distance **d3**, and the second distance **d2** is not equal to the fourth distance **d4**, the flexibility of target site selection can be increased.

The present invention has been described with reference to the preferred embodiments and it is understood that the embodiments are not intended to limit the scope of the present invention. Moreover, as the contents disclosed herein should be readily understood and can be implemented by a person skilled in the art, all equivalent changes or modifications which do not

depart from the concept of the present invention should be encompassed by the appended claims.

What is claimed is:

1. A high-resolution microelectrode-based neural stimulation system for providing electrical stimulation to a brain tissue, the microelectrode-based neural stimulation system comprising:

at least two stimulating electrodes, being fixed to and contacting the brain tissue so that between two stimulating electrodes defines a stimulation area on the brain tissue;

a first control module, having a first signal source and at least two first switches, the first signal source providing a first current having a first frequency, each of the first switches corresponding to a respective one of the stimulating electrodes and being electrically connected to the first signal source, so as to respectively control each of the stimulating electrodes to form electric conduction with the first signal source; and

a second control module, having a second signal source and at least two second switches, the second signal source providing a second current having a second frequency that is different from the first frequency, each of the second switches corresponding to a respective one of the stimulating electrodes

and being electrically connected to the second signal source, so as to respectively control each of the stimulating electrodes to form electric conduction with the second signal source;

whereby the first control module controls one of the first switches to form electric conduction between the corresponding stimulating electrode and the first signal source, so as to transmit the first current to the brain tissue, and the second control module controls one of the second switches to form electric conduction between another of the stimulating electrodes and the second signal source, so as to transmit the second current to the brain tissue, in which the first control module and the second control module jointly form an electrical stimulation signal on a target site in the stimulation area by controlling current intensities of the first current and the second current so as to provide the electrical stimulation to the brain tissue.

2. The microelectrode-based neural stimulation system of claim 1, wherein each of the first frequency and the second frequency is in a frequency range between 800 and 10000 Hz.

3. The microelectrode-based neural stimulation system of

claim 2, wherein each of the first frequency and the second frequency is in the frequency range between 2000 and 4000Hz.

4. The microelectrode-based neural stimulation system of claim 1, wherein a frequency difference between the first frequency and the second frequency ranges between 1 and 500 Hz.

5. The microelectrode-based neural stimulation system of claim 1, wherein each of the first current and the second current is in a current range between 100 and 500 μA.

6. The microelectrode-based neural stimulation system of claim 1, wherein each of the first current and the second current has a current ramping rate up to 5 μA/ms.

7. The microelectrode-based neural stimulation system of claim 1, wherein those stimulating electrodes are four stimulating electrodes arranged into a two-by-two two-dimensional array that is composed of a first column, a second column, a first row, and a the second row that the first column and the second column are separated by a first distance while the first row and the second row are separated by a second distance, in which each of the first distance and the second

distance ranges between 50 and 1000μm.

8. The microelectrode-based neural stimulation system of claim 7, wherein each of the first distance and the second distance is 200 μm.

9. The microelectrode-based neural stimulation system of claim 7, further comprising a ground electrode, which is separated from any of the stimulating electrodes by a distance that is eight to fifteen times as large as the first distance.

10. The microelectrode-based neural stimulation system of claim 1, wherein those stimulating electrodes are nine stimulating electrodes arranged into a three-by-three two-dimensional array that is composed of a first column, a second column, a third column, a first row, the second row, and a third row that the first column and the second column are separated by a first distance, the first row and the second row are separated by a second distance, the second column and the third row are separated by a third distance, and the second row and the third column are separated by a fourth distance.

11. The microelectrode-based neural stimulation system of claim 10, wherein each of the first distance, the second

distance, the third distance, and the fourth distance ranges between 50 and 1000 μm.

12. The microelectrode-based neural stimulation system of claim 11, wherein the first distance is greater than the third distance, the first distance is equal to the second distance, and the third distance is equal to the fourth distance.

13. The microelectrode-based neural stimulation system of claim 12, wherein each of the first distance and the second distance is 200 μm, and each of the third distance and the fourth distance is 100 μm.

14. The microelectrode-based neural stimulation system of claim 1, wherein each of the stimulating electrodes has a columnar shape, and a diameter ranging between 5 and 200 μm.

15. The microelectrode-based neural stimulation system of claim 1, wherein an excluded area is defined in the stimulation area and is located in a radius of 50 μm around each of the stimulating electrodes.

16. The microelectrode-based neural stimulation system of claim 1, wherein the brain tissue is located inside a cranium of an animal or is an acute brain slice obtained from a cranium

of an animal.

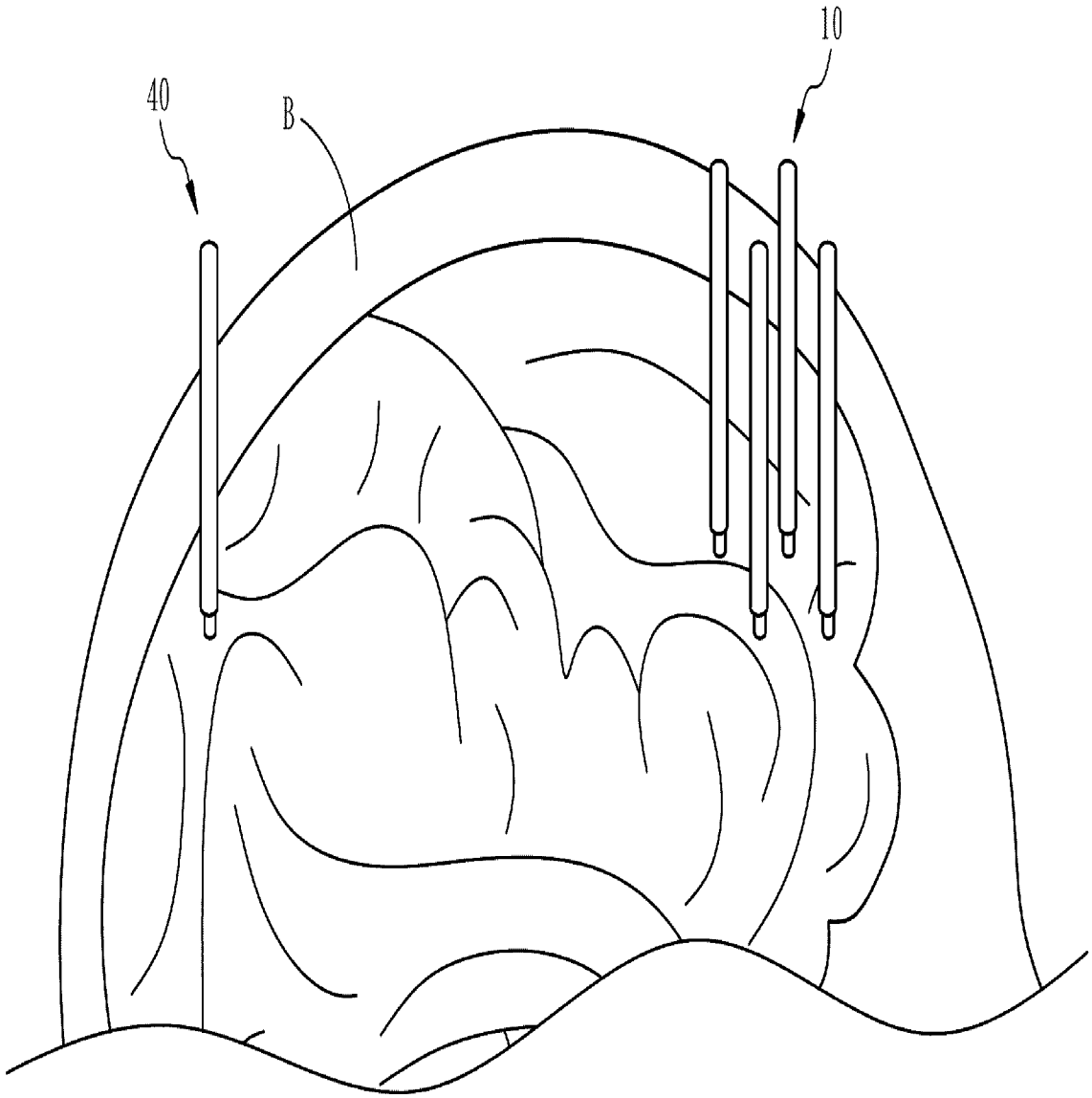


FIG. 1

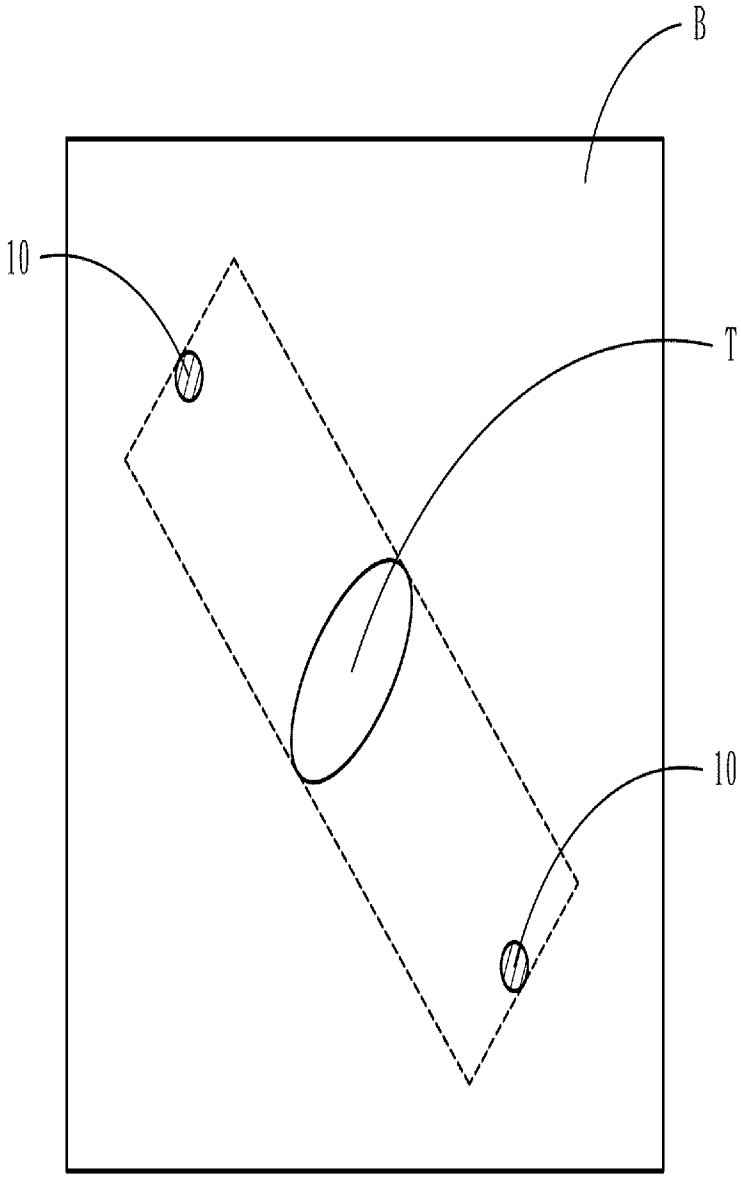


FIG. 2A

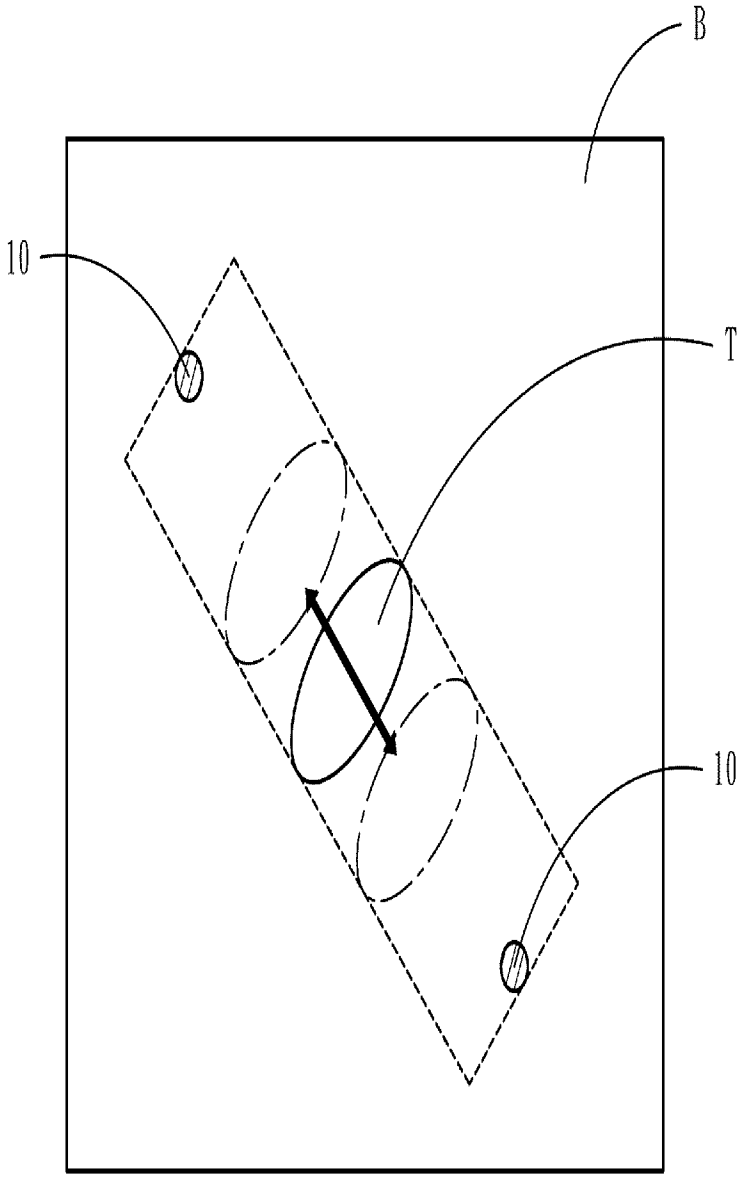


FIG. 2B

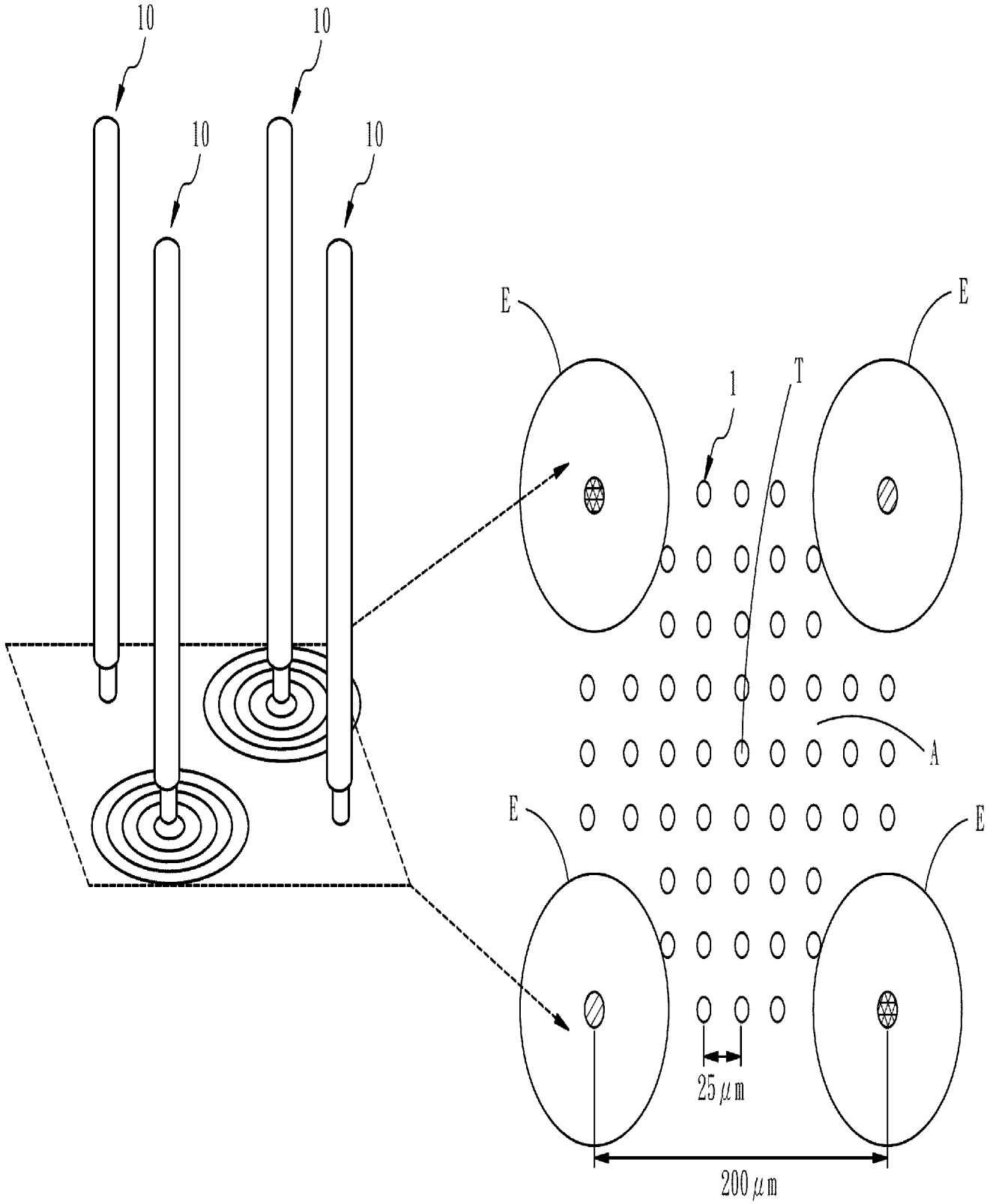


FIG. 3

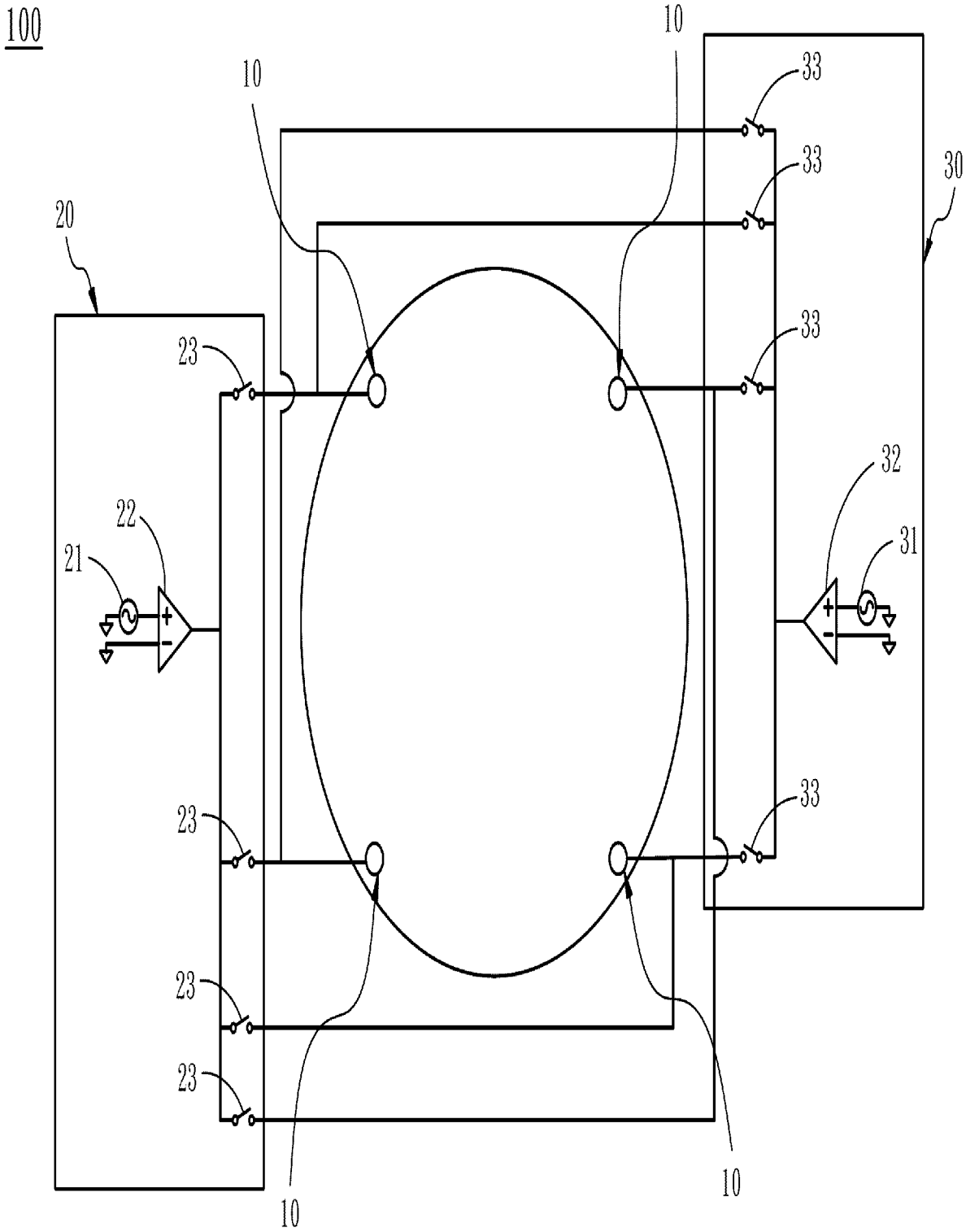


FIG. 4

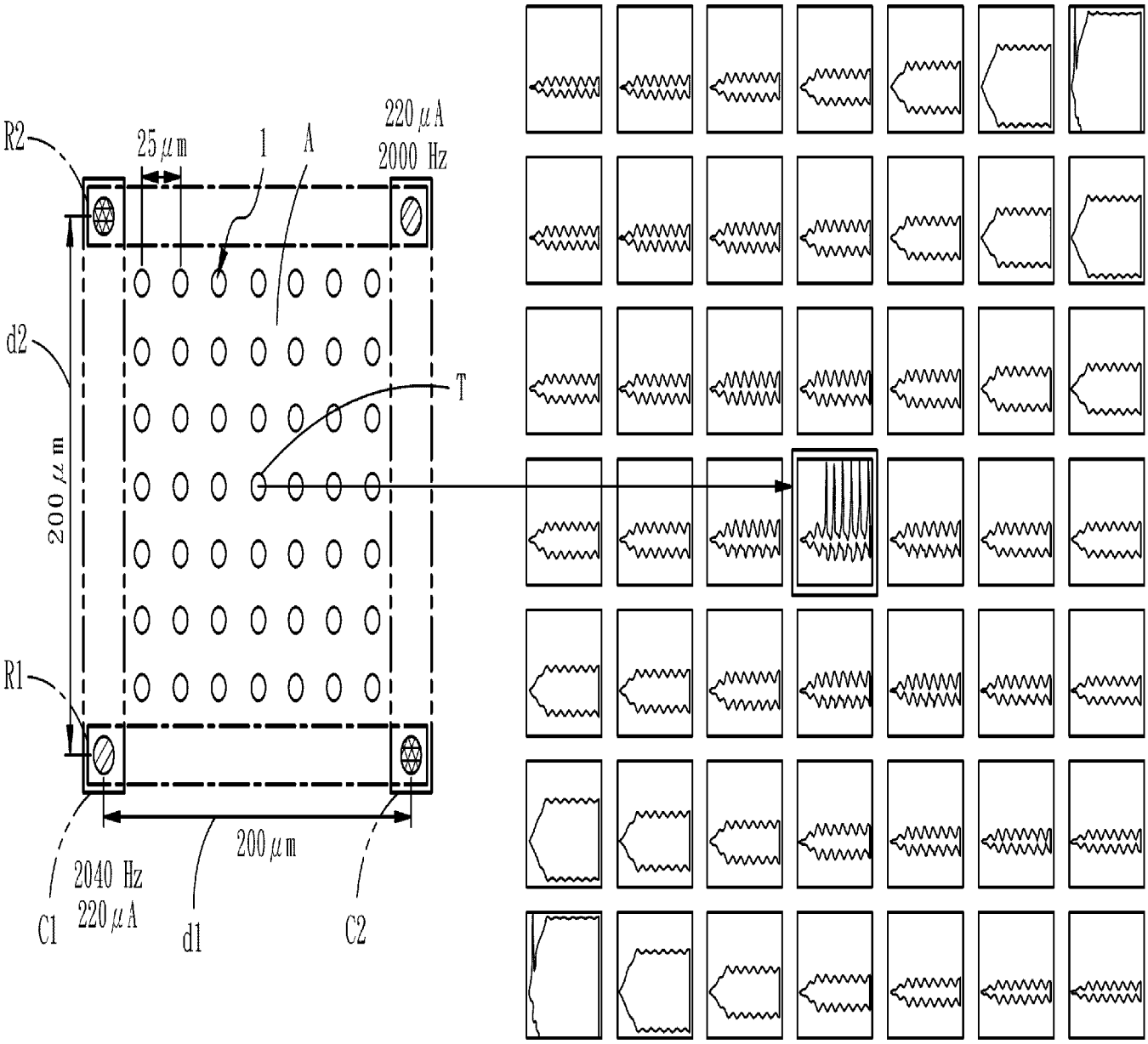

R2
25 μm
1
A
220 μA
2000 Hz
d2
T
200 μm
R1
200 μm
2040 Hz
220 μA
C1
d1
C2

FIG. 5

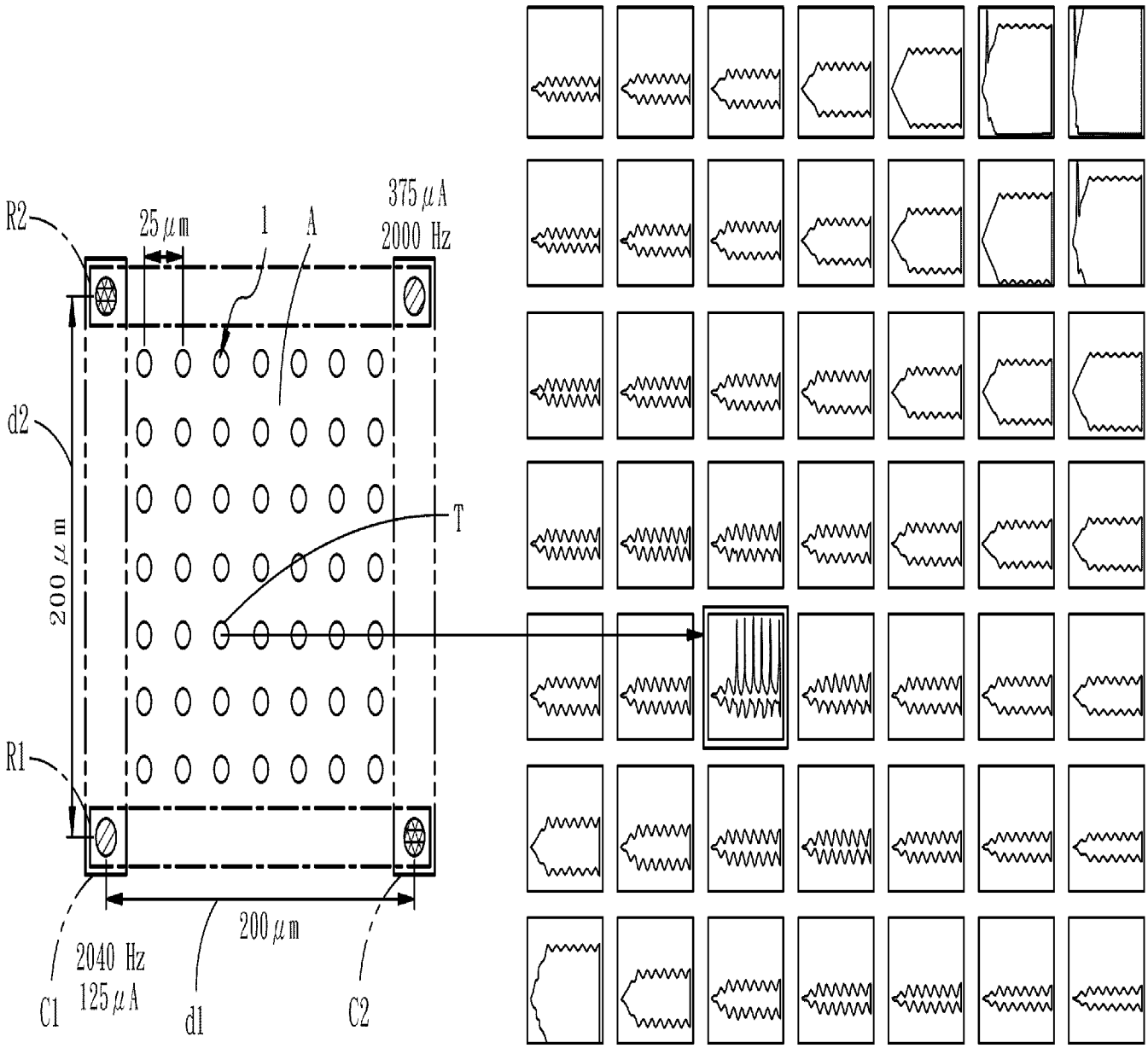

R2
25 μm
1
A
375 μA
2000 Hz
d2
200 μm
T
R1
200 μm
2040 Hz
125 μA
C1
d1
C2

FIG. 6

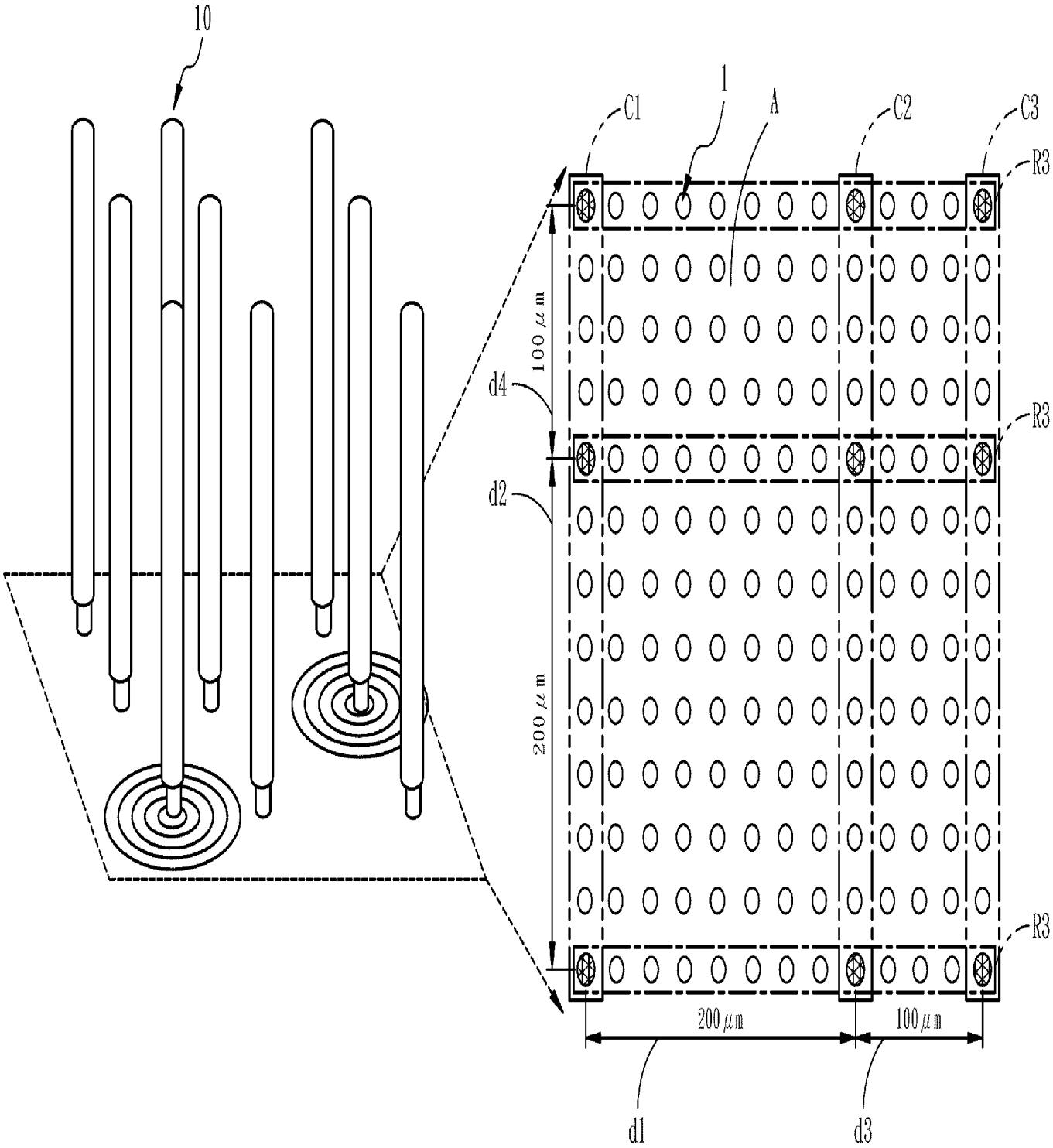


FIG. 7

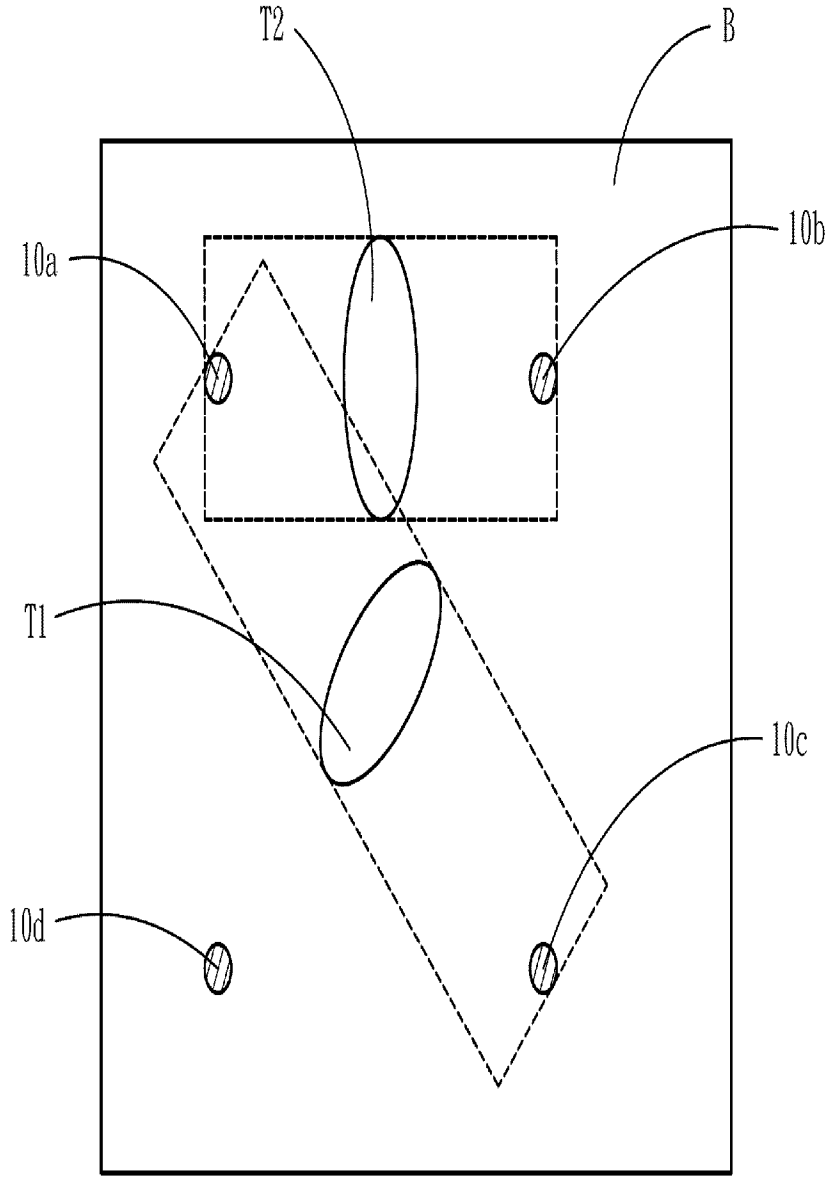


FIG. 8