US010816536B2

(12) **United States Patent**
Mitsunaka et al.

(10) **Patent No.: US 10,816,536 B2**
(45) **Date of Patent: Oct. 27, 2020**

(54) **BIOPARTICLE OBSERVATION APPARATUS AND BIOPARTICLE OBSERVATION METHOD**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **16/436,338**

(22) Filed: **Jun. 10, 2019**

(65) **Prior Publication Data**

US 2019/0376947 A1 Dec. 12, 2019

(30) **Foreign Application Priority Data**

Jun. 11, 2018 (JP) 2018-111342

(51) **Int. Cl.**
G01N 33/00 (2006.01)
G01N 33/483 (2006.01)
G01N 21/01 (2006.01)

(52) **U.S. Cl.**
CPC ***G01N 33/4833*** (2013.01); ***G01N 21/01*** (2013.01)

(58) **Field of Classification Search**
CPC G01N 33/4833; G01N 21/01; G01N 15/1484; G01N 15/1031; G01N 2015/1006; B03C 5/026; B03C 5/005; B03C 2201/26; G01B 7/14
USPC 250/492.1, 251, 281, 282; 204/450, 452
See application file for complete search history.

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(57) **ABSTRACT**

A bioparticle observation apparatus includes a dielectrophoresis electrode that outputs a first signal causing a dielectrophoresis force to act on a bioparticle, a sensor electrode that detects an impedance difference between the bioparticle and the liquid, and a control circuit that controls the first signal so that the detected impedance difference is fixed.

16 Claims, 4 Drawing Sheets

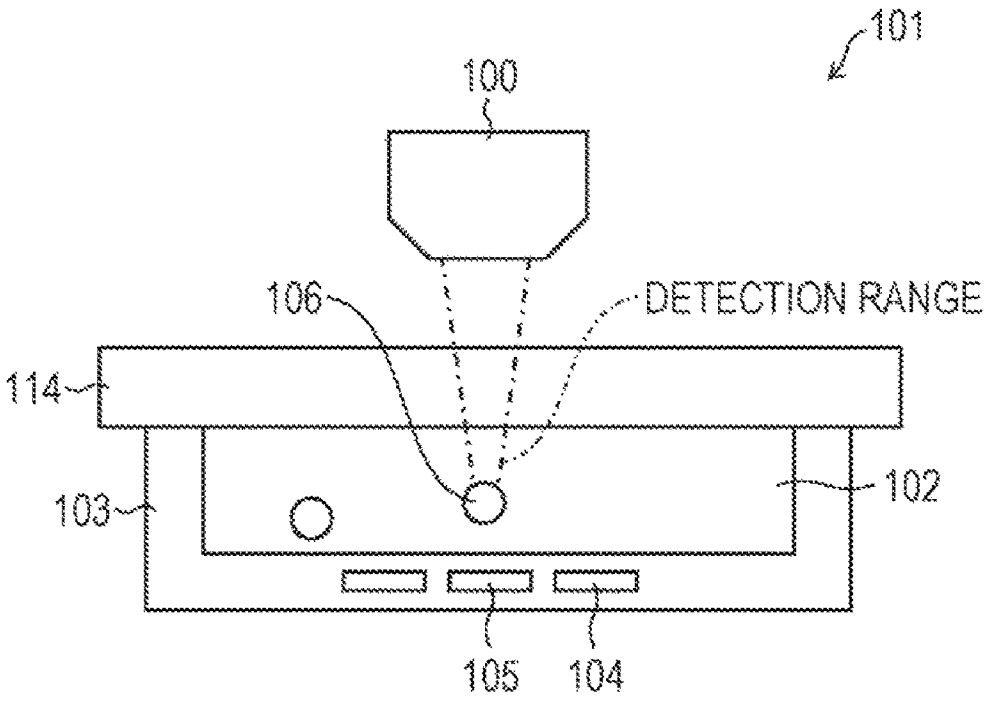


FIG. 1

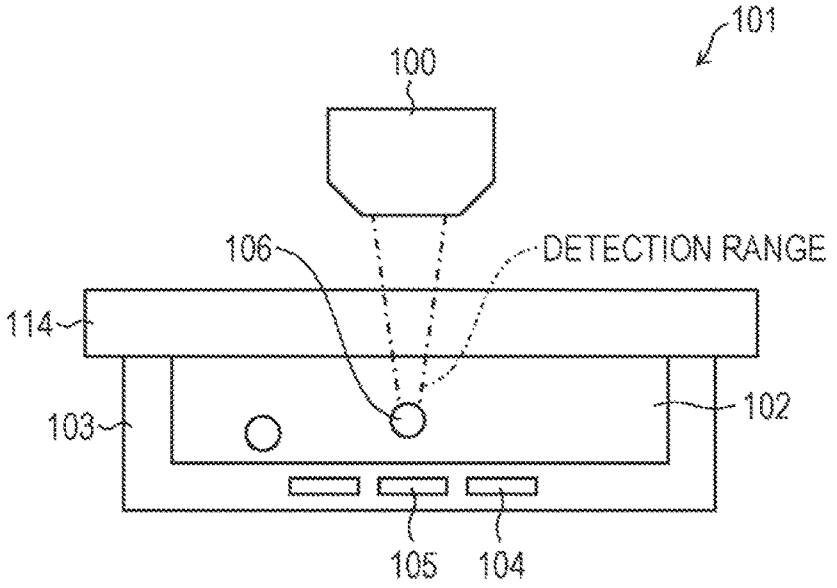


FIG. 2A

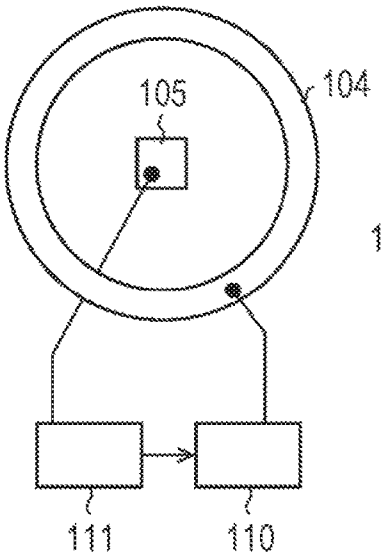


FIG. 2B

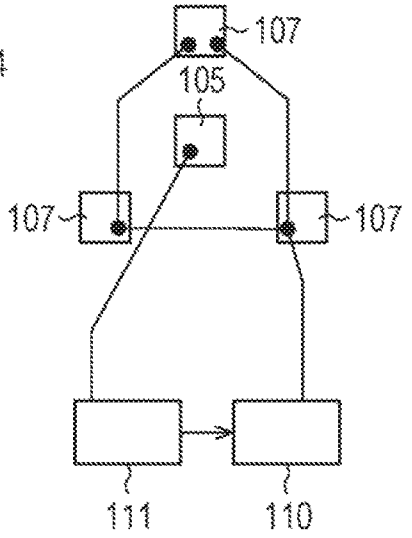


FIG. 2C

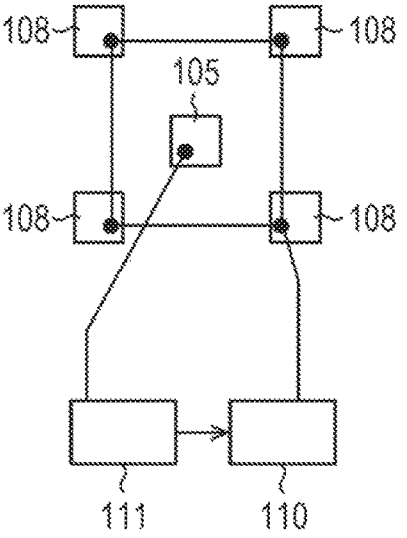


FIG. 3

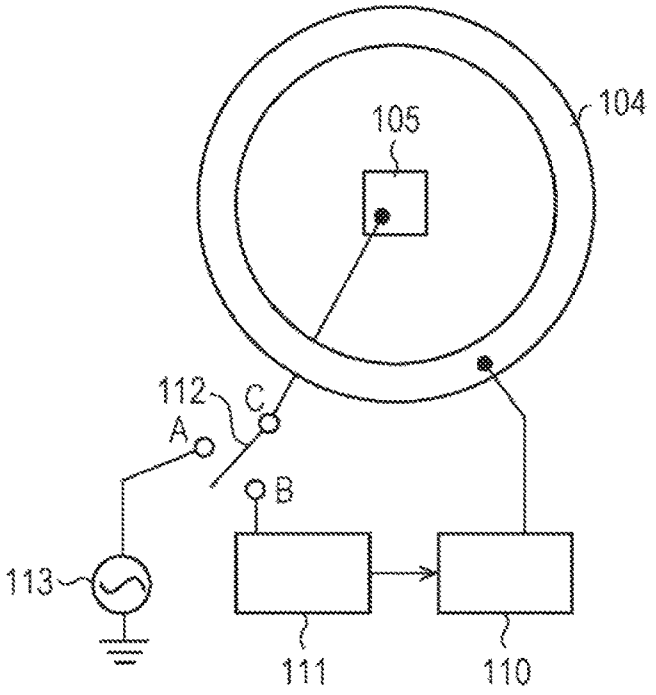

104
105
112
C
A
B
113
111
110

FIG. 4

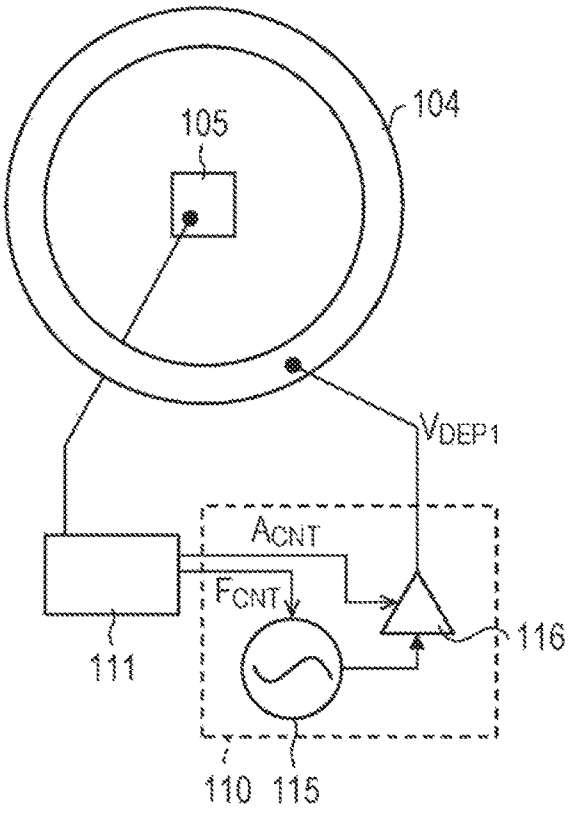

104
105
VDEP1
ACNT
FCNT
116
111
110
115

FIG. 5

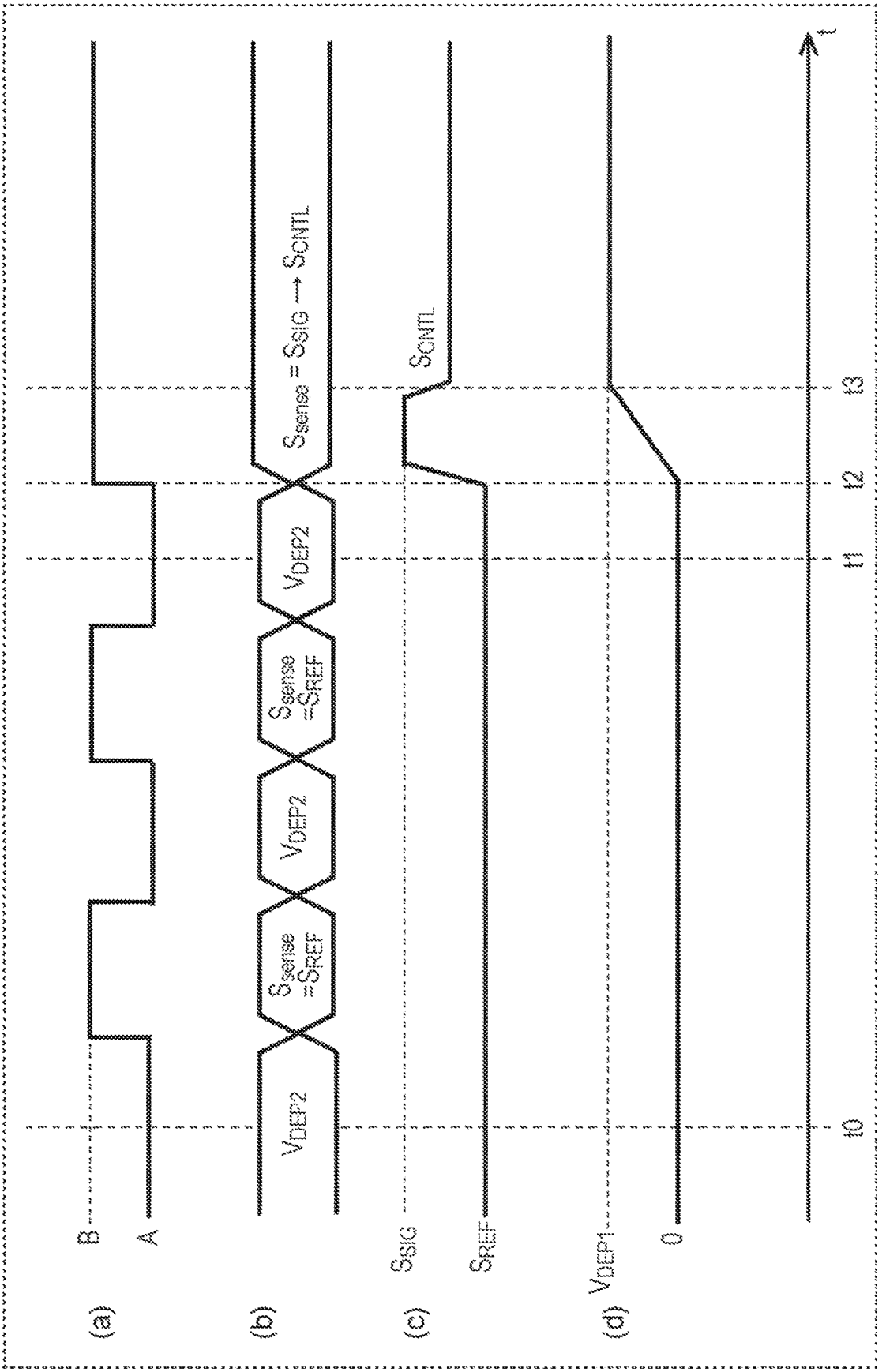

(a)
B
A
(b)
VDEP2
Ssense =SREF
VDEP2
Ssense =SREF
VDEP2
Ssense = SSIG → SCNTL
(c)
SSIG
SREF
SCNTL
(d) VDEP1
0
t
t0
t1
t2
t3

FIG. 6

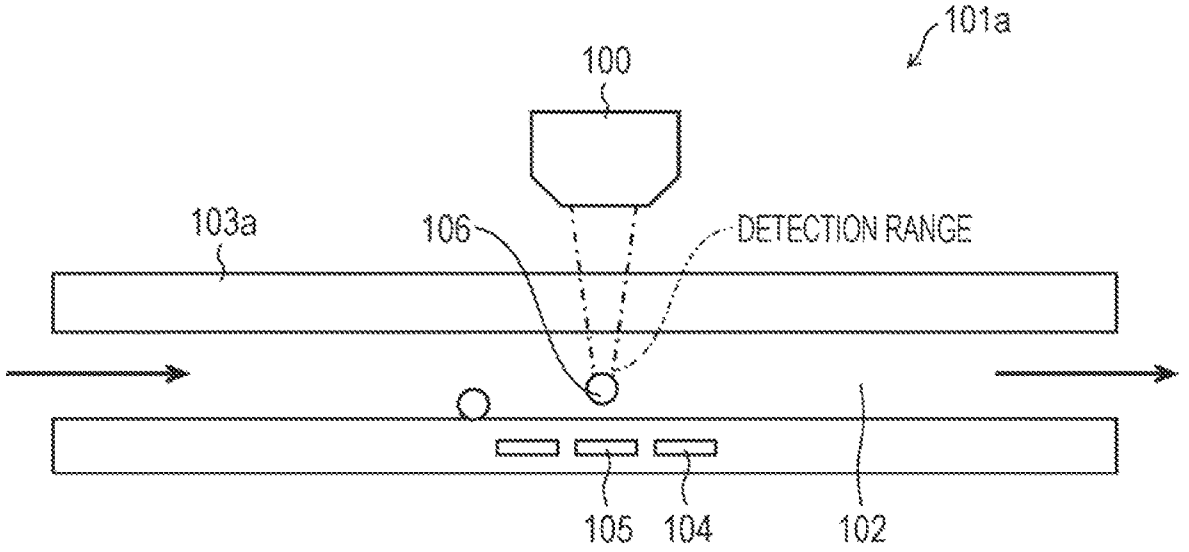
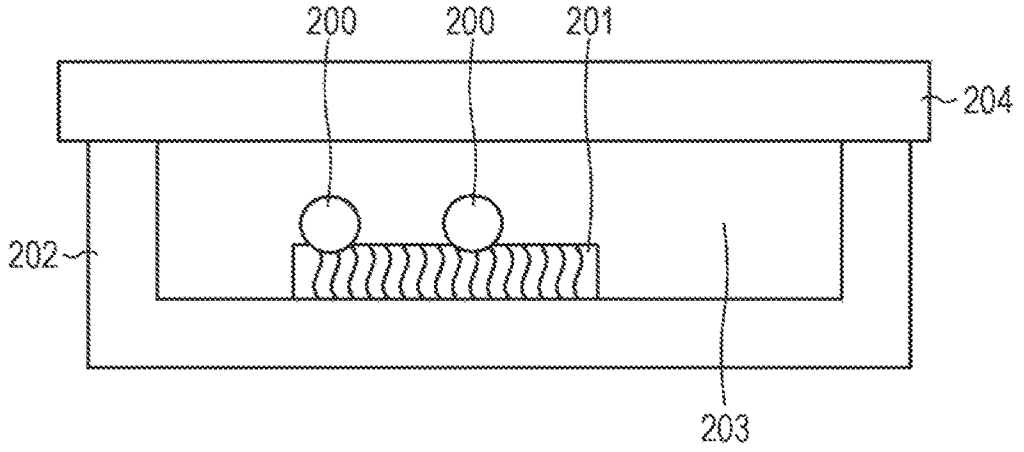

101a
100
103a
106
DETECTION RANGE
105
104
102

FIG. 7


200
200
201
204
202
203

BIOPARTICLE OBSERVATION APPARATUS AND BIOPARTICLE OBSERVATION METHOD

BACKGROUND

1. Field

The present disclosure relates to a bioparticle observation apparatus and a bioparticle observation method that are used to observe fine bioparticles in liquid.

2. Description of the Related Art

In accordance with an existence form in cell culture, cells, which are one kind of bioparticle, are roughly classified into one kind called adherent cells, which adhere to a culture container and grow, and another kind called suspended cells, which grow in a state of being suspended in a medium.

When observing a suspended cell such as a hematopoietic cell by using a microscope to trace a growth pattern, an observation target is to be fixed at a predetermined position. For observing the suspended cell under the microscope, a method of setting aside the suspended cell, which is in a medium, in a dish or the like for observation is considered, but when culture and observation using the microscope are performed for a long time, a suspended state is not maintained and the cells are thus greatly damaged.

On the other hand, as a proposal for fixing the suspended cells, as illustrated in FIG. **7**, a method of forming a fixing agent **201**, such as a protein or a polymer, that has excellent compatibility with a surface of a cell **200** in solution **203** and thereby fixing the cell surface to a dish **202** or the like is known. Since a cell wall of the cell **200** is not directly bonded to a bottom surface of the dish **202** or the like, a suspended state is maintained, even after culture and observation are performed for a long time. The observation is performed through a lid **204** such as a cover glass. According to the aforementioned configuration, less damage to the cell is expected. For example, Japanese Unexamined Patent Application Publication No. 2005-80579 (published on Mar. 31, 2005) proposes a method in which the fixing agent **201** has a phosphorylcholine-like group and a hydrazide group. With the method, a protein that fixes the suspended cell to the dish or the like is modified in advance and is bonded and mixed with the surface of the suspended cell for fixation. This makes it possible to fix the surface of the cell **200** to the dish **202** or the like.

However, with the method of fixing the suspended cell according to the related art disclosed in Japanese Unexamined Patent Application Publication No. 2005-80579 described above, it is difficult to selectively fix a type of cell among a plurality of types of cell by using protein to be modified or to fix only a single cell, which poses a problem of fixing a plurality of cells at the same time in many cases. The method of fixing the suspended cell according to the related art also has problems in which it is difficult to observe behavior of a single cell under the microscope and in which there is a concern about damage to the cells because a plurality of cells are intensively fixed.

An aspect of the disclosure is made in view of the problems of the related art described above and provides a bioparticle observation apparatus and the like that are able to reduce damage to bioparticles and facilitate observation of a single bioparticle.

SUMMARY

A bioparticle observation apparatus according to an aspect of the disclosure is a bioparticle observation apparatus usable for observing a bioparticle in liquid, and includes: a dielectrophoresis electrode that outputs a first signal causing a dielectrophoresis force to act on the bioparticle; a sensor electrode that detects an impedance difference between the bioparticle and the liquid; and a control circuit that controls the first signal so that the detected impedance difference is fixed.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. **1** is a schematic view illustrating an outline configuration of a bioparticle observation apparatus according to Embodiment 1 of the disclosure;

FIGS. **2**A to **2**C are schematic views illustrating variations in arrangement of a dielectrophoresis electrode in the bioparticle observation apparatus;

FIG. **3** is a schematic view illustrating an example of a configuration to capture a bioparticle in the bioparticle observation apparatus;

FIG. **4** is a schematic view illustrating an example of a configuration to capture the bioparticle;

FIG. **5** is a timing chart when the bioparticle is captured by a sensor electrode in the bioparticle observation apparatus;

FIG. **6** is a schematic view illustrating an outline configuration of a bioparticle observation apparatus according to Embodiment 2 of the disclosure; and

FIG. **7** is a schematic view for explaining a method of observing a bioparticle according to the related art.

DESCRIPTION OF THE EMBODIMENTS

Embodiment 1

A bioparticle observation apparatus **101** according to Embodiment 1 of the disclosure will be described below with reference to FIG. **1**. The bioparticle observation apparatus **101** of the present embodiment relates to an apparatus that observes, by using a microscope **100** or the like, a bioparticle **106**, such as a cell or a bacterium, which is suspended in a solution such as a medium. The bioparticle observation apparatus **101** is used mainly for research, clinical testing, and the like in biology and medicine.

More specifically, the bioparticle observation apparatus **101** observes, by using the microscope **100**, the bioparticle **106** suspended in a solution (liquid) **102** in a container **103**. A lid **114** such as a cover glass may be provided on the top of the container **103**.

Moreover, the bioparticle observation apparatus **101** of the present embodiment includes at least a dielectrophoresis electrode **104** and a sensor electrode **105** in a bottom surface of the container **103** in which the solution **102** such as the medium is storing. The dielectrophoresis electrode **104** is an electrode that outputs a signal (first signal) V_{DEP1} which causes a dielectrophoresis force to act on the bioparticle **106**. The sensor electrode **105** is an electrode for detecting an impedance difference between the bioparticle **106** and the solution **102**. Note that, the sensor electrode **105** may be a single electrode as illustrated in FIGS. **2**A to **2**C or may be a differential electrode (not illustrated).

Next, FIG. **2**A illustrates a vicinity of a region where the dielectrophoresis electrode **104** and the sensor electrode **105** are arranged when the bottom surface of the container **103** is seen from above.

In the bioparticle observation apparatus **101**, the dielectrophoresis electrode **104** surrounds the sensor electrode **105**. FIG. **2**A illustrates the dielectrophoresis electrode **104**

formed to surround, in a circular shape, a periphery of the sensor electrode **105** with the sensor electrode **105** located at a center, but the dielectrophoresis electrode **104** may be formed to surround, in a polygonal shape, the periphery of the sensor electrode **105** with the sensor electrode **105** located at the center.

Though the container **103** is filled with the solution **102** such as the medium, the bioparticle **106** such as a cell or a bacterium that is suspended is a suspended cell.

A dielectrophoresis force F_{DEP} that the dielectrophoresis electrode **104** applies to the bioparticle **106** is represented by, in general, the following formula (1).

$$F_{DEP} = 2\pi\left(\frac{d}{2}\right)^3 \varepsilon_m \mathrm{Re}\left[\frac{\varepsilon_p^* - \varepsilon_m^*}{\varepsilon_p^* - 2\varepsilon_m^*}\right] \nabla E^2 \quad (1)$$

where d is a diameter of a single bioparticle **106**, ε_p* and ε_m* are complex dielectric constants of the bioparticle **106** and the solution **102**, respectively and E is an electric field applied by the dielectrophoresis electrode **104**.

In accordance with a positive or negative sign of a real number component of

$$\frac{\varepsilon_p^* - \varepsilon_m^*}{\varepsilon_p^* - 2\varepsilon_m^*},$$

which is a CM factor, it is possible to calculate whether the dielectrophoresis force of the dielectrophoresis electrode **104** attracts or repels the bioparticle **106**.

In the present embodiment, a force (a negative dielectrophoresis force) repelling the bioparticle **106** from the dielectrophoresis electrode **104** is used. Since the bioparticle **106** represented by a cell generally has a higher density than the solution **102** such as the medium, the bioparticle **106** sinks in the liquid due to gravity. Here, when the signal (first signal) V_{DEP1} that provides the negative dielectrophoresis force is applied to the dielectrophoresis electrode **104**, the bioparticle **106** does not sink but remains suspended in the liquid.

The dielectrophoresis electrode **104** is configured to surround the sensor electrode **105** concentrically. The electric field generated by the dielectrophoresis electrode **104** is strongest at the dielectrophoresis electrode **104** and weakens in line with distance from the dielectrophoresis electrode **104**. In a vicinity of the sensor electrode **105** surrounded by the dielectrophoresis electrode **104**, the dielectrophoresis force acts in a direction to enable attraction to the sensor electrode **105** or in a direction to enable repulsion from the sensor electrode **105** in accordance with a size or a frequency of the electric field provided by the dielectrophoresis electrode **104**, and thus the bioparticle **106** is retained in a part surrounded by the dielectrophoresis electrode **104** as viewed with the microscope **100** (i.e., from above the container **103**).

A detection circuit **111** determines a distance between the sensor electrode **105** and the bioparticle **106** and causes a control circuit **110** to adjust a signal amplitude or a signal frequency of the signal V_{DEP1}. Note that, the direction of the dielectrophoresis force changes depending on the signal frequency. This is able to be determined in accordance with a positive or negative sign of a real part of the CM factor (mathematical formula 2). Moreover, when the signal amplitude varies, a repulsion force or an attraction force increases or decreases (refer to ∇E^2 of mathematical formula 1). Since the direction and size of the repulsion force or attraction force vary depending on the dielectric constants (ε_p*, ε_m*) of a target cell and the suspending solution **102**, the dielectrophoresis force depends on the environment.

The control circuit **110** outputs the signal amplitude or the signal frequency of the signal V_{DEP1} so that the impedance difference detected by the sensor electrode **105** is fixed. For example, as illustrated in FIG. **4**, the control circuit **110** performs control by outputting a signal F_{CNT} with respect to a frequency of an oscillator **115** constituted by a ring oscillator or the like on the basis of a detection signal of the detection circuit **111**. Regarding the frequency with which the bioparticle **106** is suspended in the solution **102**, an upper limit and a lower limit of the frequency in the attraction direction and the repulsion direction are determined in advance and the frequency is adjusted by the signal F_{CNT} in a range of the upper limit and the lower limit. An output amplitude of a buffer circuit **116** in the output of the oscillator **115** is controlled by outputting a signal A_{CNT} from the detection circuit **111**. The signal V_{DEP1} is output from the control circuit **110** by using an external signal source (not illustrated).

According to the aforementioned configuration, with the signal amplitude or the signal frequency of the signal V_{DEF1}, the bioparticle **106** is suspended in the liquid without sinking due to gravity and by the negative dielectrophoresis force while keeping a certain fixed distance from the sensor electrode **105**.

When determining the distance between the sensor electrode **105** and the bioparticle **106**, the impedance difference between the solution **102** and the bioparticle **106** is measured by performing sensing using a dielectric constant difference between the solution **102** and the bioparticle **106**. In this case, it is desirable to perform the sensing with a sensing frequency in the sensor electrode **105** higher than the frequency of the signal V_{DEP1} used for dielectrophoresis. By measuring the dielectric constant difference between the solution **102** and the bioparticle **106** at the measurement frequency of the sensor electrode **105**, the impedance is able to be measured without affecting the dielectrophoresis force F_{DEP}.

Though the dielectrophoresis electrode **104** may be formed to surround, in a circular shape, the sensor electrode **105** with the sensor electrode **105** located at the center as illustrated in FIG. **2**A, a structure may be provided in which three dielectrophoresis electrodes **107** are arranged at intervals of 120 degrees with the sensor electrode **105** located at the center as illustrated in FIG. **2**B. Further, a structure may be provided in which four dielectrophoresis electrodes **108** are arranged at intervals of 90 degrees with the sensor electrode **105** located at the center as illustrated in FIG. **2**C. It is sufficient that the periphery of the sensor electrode **105** is surrounded with a dielectrophoresis electrode with the sensor electrode **105** located at the center.

[Capturing of Bioparticle]

When the bioparticle **106** suspended in the solution **102** is captured in the center of the dielectrophoresis electrode **104**, a positive dielectrophoresis signal V_{DEP2} to capture the bioparticle **106** is applied to the sensor electrode **105**. FIG. **3** illustrates an example of a configuration to capture the bioparticle **106**. A terminal connected to the sensor electrode **105** includes a switch **112**, and connection destinations of the switch **112** are a point A and a point B starting from a point C.

The point A is connected to a signal source **113**. When the switch **112** is connected to the point A, the signal source **113**

applies, through the switch **112** to the sensor electrode **105**, the positive dielectrophoresis signal (second signal) V_{DEP2} to capture the bioparticle **106**. At this time, the detection circuit **111** and the control circuit **110** in which the switch **112** is switched off do not operate and in addition the dielectrophoresis electrode **104** does not operate, and as a result the bioparticle **106** is not affected by the dielectrophoresis electrode **104**. When the switch **112** is connected to the point B, the signal obtained from the sensor electrode **105** is detected by the detection circuit **111** as illustrated in FIGS. **2**A to **2**C.

Next, a timing chart for capturing the bioparticle **106** in the sensor electrode **105** will be described with reference to FIG. **5**. (a) of FIG. **5** illustrates an operation timing of the point C of the switch **112**, and the switch **112** is alternately connected to the point A and the point B for a fixed period t_0 to t_1. As illustrated in (b) of FIG. **5**, as a signal handled at the point C of the switch **112**, the positive dielectrophoresis signal V_{DEP2} is applied to the sensor electrode **105** or S_{sense} is acquired by operating the detection circuit **111**, and the application of the positive dielectrophoresis signal V_{DEP2} and the acquisition of S_{sense} are alternately performed through the operation of the switch **112** of (a) of FIG. **5**.

The period t_0 to t_1 indicates an example of a state where the bioparticle **106** is not captured, and when the switch **112** is connected to the point B, the signal S_{sense} detected by the sensor electrode **105** is $S_{sense}=S_{REF}$ as a signal calculated using the dielectric constant of the solution **102**.

A value of the signal S_{REF} calculated using the dielectric constant of the solution **102** is stored in a memory (not illustrated) or the like attached to the detection circuit **111**. Since the switch **112** is connected to the point A or the point B for a fixed period as illustrated in (a) of FIG. **5**, when the switch **112** is connected to the point A, the positive dielectrophoresis signal V_{DEP2} is applied to the sensor electrode **105**.

Here, it is assumed that the sensor electrode **105** attracts the bioparticle **106** at a certain timing (t_1). Subsequently, when the switch **112** is connected to the point B (t_2), the sensor electrode **105** detects a signal S_{SIG} calculated using the dielectric constant of the bioparticle **106**. When it is determined that there is a difference between the values of S_{SIG} and S_{REF} because S_{SIG} and S_{REF} have different values as illustrated in (c) of FIG. **5**, the switch **112** remains connected to only the point B.

At the same time, as illustrated in (d) of FIG. **5**, the signal V_{DEP1} by which the negative dielectrophoresis force acts on the dielectrophoresis electrode **104** is provided. At this time, the dielectrophoresis force that enables attraction to the sensor electrode **105** does not act on the bioparticle **106** but the dielectrophoresis force that enables repulsion is applied to the bioparticle **106** by the dielectrophoresis electrode **104** which surrounds the periphery of the sensor electrode **105**, and as a result the bioparticle **106** moves (floats) in a direction (upper direction) away from the sensor electrode **105**.

Since the bioparticle **106** is generally denser than the solution **102**, when the solution **102** does not flow or flows very slowly, the bioparticle **106** sinks (is attracted to the sensor electrode **105**), but at the time t_3 and thereafter, by providing the signal V_{DEP1} of the appropriate negative dielectrophoresis force that enables repulsion via the dielectrophoresis electrode **104**, the bioparticle **106** remains suspended above the sensor electrode **105** in the solution **102**.

The signal V_{DEP1} is a signal by which a position of the bioparticle **106** is adjusted so that a value ($=S_{CNTL}$) between S_{SIG} and S_{REF} illustrated in (c) of FIG. **5** is obtained from the sensor electrode **105**. For example, control is performed in such a manner that, when S_{CNTL} has a value larger than an appropriate value, the bioparticle **106** approaches the sensor electrode **105**, and as a result, for example, the amplitude of the signal V_{DEP1} is increased, and when S_{CNTL} has a value smaller than the appropriate value, the bioparticle **106** moves away from the sensor electrode **105**, and as a result the amplitude of the signal V_{DEP1} is reduced.

According to the aforementioned configuration, when the dielectrophoresis force acts on the bioparticle **106**, a single bioparticle **106** is able to be fixed at a predetermined position in a suspended state. Thereby, the bioparticle **106** is not fixed by protein or the like, and there is no physical contact with a surface of the bioparticle **106**, thus making it possible to reduce damage to the bioparticle **106** and facilitate observation of the single bioparticle **106**.

Embodiment 2

Another embodiment of the disclosure will be described below. Note that, for convenience of description, members having the same functions as those of the members described in the aforementioned embodiment will be given the same reference signs and description thereof will not be repeated.

In the aforementioned embodiment, an embodiment in which the container **103** is a container such as a Petri dish whose top surface is opened has been described. However, as in a bioparticle observation apparatus **101***a* of the present embodiment, a structure that causes the solution **102** to flow from upstream to downstream like a microfluidic channel **103***a* may be adopted (refer to FIG. **6**) instead of the container **103**. The bioparticle **106** flows in the microfluidic channel **103***a*.

In this case, it is desirable that a top surface of the sensor electrode **105** be made of a transparent material that enables check by the microscope **100**. The flow of the solution **102** may be controlled so that a flow rate of the solution **102** changes, for example, by stopping the flow of the solution **102** or causing the solution **102** to flow slowly to such an extent that the bioparticle **106** does not move away from above the sensor electrode **105** in the center of the dielectrophoresis electrode **104**, after the time t_1 when the bioparticle **106** is captured as described in FIG. **5**.

CONCLUSION

A bioparticle observation apparatus according to an aspect 1 of the disclosure is a bioparticle observation apparatus usable for observation of a bioparticle in liquid, and includes: a dielectrophoresis electrode that outputs a first signal causing a dielectrophoresis force to act on the bioparticle; a sensor electrode that detects an impedance difference between the bioparticle and the liquid; and a control circuit that controls the first signal so that the detected impedance difference is fixed.

According to the aforementioned configuration, when the dielectrophoresis force is caused to act on the bioparticle, the single bioparticle is able to be fixed at a predetermined position in a suspended state. Thereby, the bioparticle is not fixed by protein or the like and there is no physical contact with a surface of the bioparticle, thus making it possible to reduce damage to the bioparticle and facilitate observation of the single bioparticle.

In the bioparticle observation apparatus according to an aspect 2 of the disclosure, it is desirable that the control circuit controls an amplitude or a frequency of the first signal

in the aspect 1. According to the aforementioned configuration, when the control circuit controls the amplitude or the frequency of the first signal output from the dielectrophoresis electrode, the bioparticle floats in the liquid without sinking due to gravity and a negative dielectrophoresis force while keeping a certain fixed distance away from the sensor electrode.

In the bioparticle observation apparatus according to an aspect 3 of the disclosure, the dielectrophoresis electrode may have a circular shape or a polygonal shape to surround a periphery of the sensor electrode with the sensor electrode located at a center and output a signal, which provides a negative dielectrophoresis force, as the first signal to the bioparticle, in the aspect 1 or 2. According to the aforementioned configuration, since the dielectrophoresis force near the sensor electrode acts in a direction to enable attraction to the sensor electrode or in a direction to enable repulsion from the sensor electrode in accordance with a size of an electric field provided by the dielectrophoresis electrode, and therefore it is possible to cause the bioparticle to stay in a part surrounded by the dielectrophoresis electrode.

In the bioparticle observation apparatus according to an aspect 4 of the disclosure, the dielectrophoresis electrode may include a plurality of electrodes arranged to surround a periphery of the sensor electrode with the sensor electrode located at a center and may output a signal, which provides a negative dielectrophoresis force, as the first signal to the bioparticle, in the aspect 1 or 2. According to the aforementioned configuration, it is possible to cause the bioparticle to stay in a part surrounded by the dielectrophoresis electrode.

In the bioparticle observation apparatus according to an aspect 5 of the disclosure, the sensor electrode may be a single electrode or a differential electrode, in any one of the aspect 1 to the aspect 4.

In the bioparticle observation apparatus according to an aspect 6 of the disclosure, it is desirable that the sensor electrode is connected to a switch and is able to switch, through the switch, between a function of detecting the impedance difference and a function of outputting a signal, which provides a positive dielectrophoresis force, to the bioparticle, in any one of the aspect 1 to the aspect 5. According to the aforementioned configuration, it is possible to capture the bioparticle, which floats in the liquid, in the center of the dielectrophoresis electrode.

In the bioparticle observation apparatus according to an aspect 7 of the disclosure, it is desirable that a second signal that provides a positive dielectrophoresis force is output from the sensor electrode, in any one of the aspect 1 to the aspect 6. According to the aforementioned configuration, it is possible to capture the bioparticle.

It is desirable that the bioparticle observation apparatus according to an aspect 8 of the disclosure further includes a microscope that enables observation from outside of a state where the bioparticle stays at a predetermined position, in any one of the aspect 1 to the aspect 7. According to the aforementioned configuration, it is possible to reduce damage to the bioparticle and facilitate observation of the single bioparticle.

The bioparticle observation apparatus according to an aspect 9 of the disclosure may further include a microfluidic channel in which the bioparticle flows, in any one of the aspect 1 to the aspect 8.

A bioparticle observation method according to an aspect 10 of the disclosure includes causing a bioparticle to stay at a predetermined position in liquid by using the bioparticle observation apparatus according to any one of the aspect 1 to the aspect 9, and observing a state where the bioparticle stays at the predetermined position from outside by using a microscope. According to the aforementioned method, it is possible to reduce damage to the bioparticle and facilitate observation of the single bioparticle.

[Other Expression of Disclosure]

The disclosure may be expressed as below. That is, a bioparticle observation apparatus according to an aspect of the disclosure is a bioparticle observation apparatus that causes a single fine bioparticle to stay at a predetermined position in liquid, includes a dielectrophoresis electrode and a sensor electrode, and has a configuration in which an impedance difference between the bioparticle and the liquid existing around the bioparticle is detected and a signal output from the dielectrophoresis electrode is controlled by a control circuit so that the bioparticle stays at the predetermined position in the liquid.

Moreover, in the bioparticle observation apparatus according to an aspect of the disclosure, it is desirable that the control circuit controls an amplitude or a frequency of the signal output from the dielectrophoresis electrode.

Moreover, in the bioparticle observation apparatus according to an aspect of the disclosure, it is desirable that the dielectrophoresis electrode has a circular shape or a polygonal shape to surround the sensor electrode with the sensor electrode located at a center and outputs a signal, which provides a negative dielectrophoresis force, to the bioparticle.

Moreover, in the bioparticle observation apparatus according to an aspect of the disclosure, it is desirable that the dielectrophoresis electrode includes a plurality of electrodes arranged to surround the sensor electrode with the sensor electrode located at a center and outputs a signal, which provides a negative dielectrophoresis force, to the bioparticle.

Moreover, in the bioparticle observation apparatus according to an aspect of the disclosure, the sensor electrode may be a single electrode or a differential electrode.

Moreover, in the bioparticle observation apparatus according to an aspect of the disclosure, the sensor electrode may include a switch circuit to have a function of detecting the impedance difference between the bioparticle and the liquid existing around the bioparticle and a function of outputting a signal, which provides a positive dielectrophoresis force, to the bioparticle.

Moreover, in the bioparticle observation apparatus according to an aspect of the disclosure, after a reference signal is detected from an impedance value in a state where the bioparticle is not captured in the sensor electrode and stored in a memory circuit, the switch circuit may be switched, and the bioparticle may be captured by outputting a signal, which provides a positive dielectrophoresis force, from the sensor electrode, and while keeping the capturing of the bioparticle by outputting a signal, which provides a negative dielectrophoresis force, from the dielectrophoresis electrode, a capturing signal may be detected from the impedance value of the bioparticle captured in the sensor electrode, and on the basis of the reference signal stored in the memory circuit and a setting signal set from the capturing signal, the signal which provides the negative dielectrophoresis force may be output from the dielectrophoresis electrode by controlling an amplitude or a frequency thereof so that the bioparticle stays at a predetermined position in the liquid, and thereby the bioparticle may stay at the predetermined position.

Moreover, the bioparticle observation apparatus according to an aspect of the disclosure may further include a

microscope that enables observation from outside of a state where the bioparticle stays at a predetermined position.

APPENDIX

The disclosure is not limited to the respective embodiments described above and may be modified in various manners within the scope of the claim, and an embodiment achieved by appropriately combining techniques disclosed in each of different embodiments is also encompassed in the technical scope of the disclosure. Further, by combining the techniques disclosed in each of the different embodiments, a new technical feature may be formed.

The present disclosure contains subject matter related to that disclosed in Japanese Priority Patent Application JP 2018-111342 filed in the Japan Patent Office on Jun. 11, 2018, the entire contents of which are hereby incorporated by reference.

It should be understood by those skilled in the art that various modifications, combinations, sub-combinations and alterations may occur depending on design requirements and other factors insofar as they are within the scope of the appended claims or the equivalents thereof.

What is claimed is:

1. A bioparticle observation apparatus usable for observation of a bioparticle in liquid, the bioparticle observation apparatus comprising:

a dielectrophoresis electrode that outputs a first signal causing a dielectrophoresis force to act on the bioparticle;

a sensor electrode that detects an impedance difference between the bioparticle and the liquid; and

a control circuit that controls the first signal so that the detected impedance difference is fixed,

a second signal that provides a positive dielectrophoresis force being output from the sensor electrode.

2. The bioparticle observation apparatus according to claim **1**, wherein

the control circuit controls an amplitude or a frequency of the first signal.

3. The bioparticle observation apparatus according to claim **1**, wherein

the dielectrophoresis electrode has a circular shape or a polygonal shape to surround a periphery of the sensor electrode with the sensor electrode located at a center and outputs a signal, which provides a negative dielectrophoresis force, as the first signal to the bioparticle.

4. The bioparticle observation apparatus according to claim **1**, wherein

the dielectrophoresis electrode includes a plurality of electrodes arranged to surround a periphery of the sensor electrode with the sensor electrode located at a center and outputs a signal, which provides a negative dielectrophoresis force, as the first signal to the bioparticle.

5. The bioparticle observation apparatus according to claim **1**, wherein

the sensor electrode is a single electrode or a differential electrode.

6. A bioparticle observation apparatus for observation of a bioparticle in liquid, the bioparticle observation apparatus comprising:

a dielectrophoresis electrode that outputs a first signal causing a dielectrophoresis force to act on the bioparticle;

a sensor electrode that detects an impedance difference between the bioparticle and the liquid; and

a control circuit that controls the first signal so that the detected impedance difference is fixed,

the sensor electrode being connected to a switch and being able to switch, through the switch, between a function of detecting the impedance difference and a function of outputting a signal, which provides a positive dielectrophoresis force, to the bioparticle.

7. The bioparticle observation apparatus according to claim **1**, further comprising

a microscope that enables observation from outside of a state where the bioparticle stays at a predetermined position.

8. The bioparticle observation apparatus according to claim **1**, further comprising

a microfluidic channel in which the bioparticle flows.

9. A bioparticle observation method, comprising:

causing a bioparticle to stay at a predetermined position in liquid by using the bioparticle observation apparatus according to claim **1**, and

observing a state where the bioparticle stays at the predetermined position from outside by using a microscope.

10. The bioparticle observation apparatus according to claim **6**, wherein

the control circuit controls an amplitude or a frequency of the first signal.

11. The bioparticle observation apparatus according to claim **6**, wherein

the dielectrophoresis electrode has a circular shape or a polygonal shape to surround a periphery of the sensor electrode with the sensor electrode located at a center and outputs a signal, which provides a negative dielectrophoresis force, as the first signal to the bioparticle.

12. The bioparticle observation apparatus according to claim **6**, wherein

the dielectrophoresis electrode includes a plurality of electrodes arranged to surround a periphery of the sensor electrode with the sensor electrode located at a center and outputs a signal, which provides a negative dielectrophoresis force, as the first signal to the bioparticle.

13. The bioparticle observation apparatus according to claim **6**, wherein

the sensor electrode is a single electrode or a differential electrode.

14. The bioparticle observation apparatus according to claim **6**, further comprising

a microscope that enables observation from outside of a state where the bioparticle stays at a predetermined position.

15. The bioparticle observation apparatus according to claim **6**, further comprising

a microfluidic channel in which the bioparticle flows.

16. A bioparticle observation method, comprising:

causing a bioparticle to stay at a predetermined position in liquid by using the bioparticle observation apparatus according to claim **6**, and

observing a state where the bioparticle stays at the predetermined position from outside by using a microscope.

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