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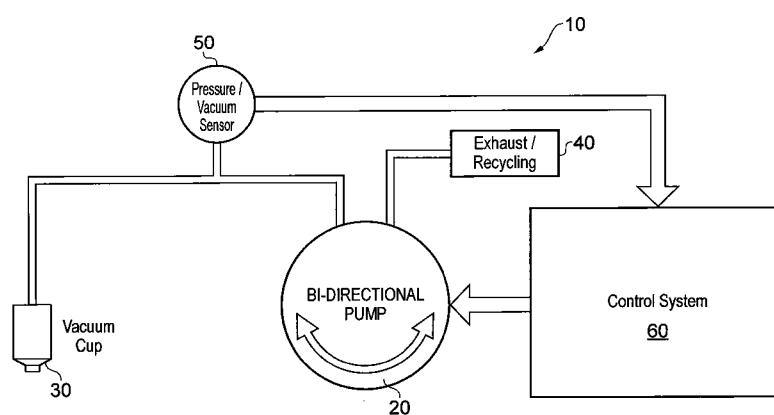


FIG. 1

(57) Abstract: An object handling device, a method of handling an object and a computer program product operable to perform the method of handling an object. The object handling device comprises: a source of variable suction; a suction cup operable to receive an object to be handled and coupled, via a conduit, to the source of variable suction; a sensor operable to determine an operational parameter of fluid in the conduit; and a controller operable to receive an indication of the determined operational parameter and adjust the variable suction source in dependence upon the received indication. Aspects and embodiments described herein provide a means by which a pick and place device may be operable to handle delicate objects, for example, delicate sectioned biological tissue. The delicate objects may be moveable by a device in accordance with aspects and embodiments by direct engagement with a delicate object itself or by gripping a surrounding support material.



SPECIMEN HANDLING DEVICE

FIELD OF THE INVENTION

An object handling device, a method of handling an object and a computer program
5 product operable to perform the method of handling an object.

BACKGROUND

Automatic object handling devices are known. In general, when an object is to be
transported, a vacuum “pick and place” device can be provided. That pick and place
10 device may operate to lift an object of interest. A pick and place nozzle, connected to a
vacuum, or suction source, is used to engage an object of interest. A vacuum cup
having an air suction port forms a pick and place nozzle. Air is sucked in from the air
suction port by a vacuum generated by a vacuum generator such as an ejector or
vacuum pump and an object can be lifted by the vacuum cup of the pick and place
15 nozzle.

Use of a conventional pick and place system may be incompatible with transportation
of some objects. It is desired to provide an alternative handling device.

20 SUMMARY

Accordingly, a first aspect provides an object handling device comprising: a source of
variable suction; a suction cup operable to receive an object to be handled and coupled,
via a conduit, to the source of variable suction; a sensor operable to determine an
operational parameter of fluid in said conduit; and a controller operable to receive an
25 indication of the determined operational parameter and adjust the variable suction
source in dependence upon the received indication.

As described above, automatic object handling devices are known. Suction gripper
devices are known and can be used to move an object in air and/or within a fluid, for
30 example, water. According to such arrangements, a suction cup is connected to a
vacuum, or suction source. The suction cup can be engaged with the object to be
handled. Fluid (gas or air) may be sucked through the suction cup by means of a pump
or vacuum source. Operation of such a device is such that the suction cup is typically
moved to contact the object to be handled. On contact, a partial vacuum is formed,
35 enabling the object to be transported by the suction cup. The level of suction applied
typically comprises a pre-set value. Release of the object is typically achieved by
opening a vacuum conduit to, for example, atmospheric pressure. Alternatively, some

arrangements may implement application of a positive pressure to achieve a faster release of an object to be handled. Known suction gripper devices are typically binary in operation and suction is either “off” or “on”.

5 The first aspect recognises that in a typical vacuum pick and place device application of a suction force is substantially binary. That is to say, a vacuum generator or suction source may be set to operate at a particular flow rate. A motor, for example, may be provided to move fluid by running at a substantially constant rotation to support the particular selected fluid flow rate. Such an approach may cause damage to an object to
10 be lifted, particularly if the object is delicate. This may be of particular relevance where an object to be handled comprises, for example, a delicate ultra-thin biological or material section. Such materials may be damaged by binary pressure transients. Binary pressure transients may also be inadequate to achieve successful delicate object manipulation.

15 Provision of a sensor to monitor an operational parameter in a conduit between a pick and place vacuum cup and a suction source may allow for finer control of a force being exerted by a vacuum cup on an object to be moved. Although it may be known to provide sensors to monitor operational parameters experienced in a conduit linking a
20 vacuum cup with a suction source, it is typically the presence or absence of an object on a vacuum cup which is determined. In other words, a sensor may be provided to assess whether or not an object has been lifted or whether or not an object has dropped from the vacuum cup as the object is transported to a final position. If an object has not been lifted, a re-pick and place operation may be performed.

25 The first aspect recognises that rather than simply detecting the presence or absence of an object on a vacuum cup, in some embodiments, monitoring an operational parameter in the conduit linking a vacuum cup to a suction source, for example, pneumatic pressure, may allow that operational parameter to be used as a control
30 input. In particular, the first aspect recognises that a variable suction source can be controlled on the basis of a detected change in, for example, a pressure or flow value measured by an appropriate sensor provided in a conduit linking the vacuum cup and the suction source.

35 The first aspect recognises that when an object is brought into contact with a pick and place device vacuum cup, the fluid which can be drawn through an input port in the vacuum cup decreases because the port becomes at least partially occluded and the

pressure and/or flow of fluid in the suction passage changes compared to a case in which no object is in contact with the vacuum cup. In order to handle delicate objects the force exerted by a vacuum cup, and in particular, a suction source exerted on an object through the vacuum cup, may be monitored and the suction source adjusted.

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In some embodiments, the object to be handled comprises a specimen. A device in accordance with the first aspect may be of use as a sectioned sample handling device.

Recent biological tissue processing technologies combine advanced imaging and brain tissue sectioning into a single commercially available system. Typically sectioned

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tissue, once cut, falls away from a tissue / agar block and a cut surface can be imaged.

For example, a mouse brain can be sectioned up to 500 times, each section slice having a thickness of between 50 and 100 microns.

A system which enables sectioning and imaging together with organised storage

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allowing correlative tissue analysis may be of use in the field of biological tissue

analysis. A pick and place device which can be configured to handle delicate objects

may have significant commercial applications in such a field. A suitable pick and place device may be used as an add-on module to commercial high-value sample sectioning

systems, microtomes and similar and may provide opportunities for automated post-

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processing processes.

It will be appreciated that similarly delicate samples may be produced in the materials field, for example, thin mineral slices, and the handling of those objects may also be suited to a device in accordance with aspects and embodiments described herein.

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In one embodiment, the operation of the variable suction source is controlled to obtain a target value of the operational parameter, that target value being selected to prevent

damage to the object to be handled. Accordingly, the handling of various delicate

samples may be accommodated by the handling device. It will be appreciated that the

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target value may be selected such that an object can be lifted and held in position of a

suction cup, but such that damage, including surface damage, to the object can be

mitigated. The target value may be adjusted in dependence upon a type of object to be

lifted. Repeated lifting and handling of an object of a single type may allow a device

controller to learn or adjust a target value in relation to that type of object, or a

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particular handling configuration.

In one embodiment, the operation of the variable suction source is controlled by a closed loop controller, in dependence upon the determined operational parameter and the target value of the operational parameter. In one embodiment, the operation of the variable suction source is controlled by a proportional integral derivative controller, in dependence upon the determined operational parameter and the target value of the operational parameter. Accordingly, a control loop feedback mechanism may be implemented. The controller may, for example, be operable to calculate a difference between a measured or determined value and a target value and attempt to minimise that difference by adjusting operation of the variable suction source. The controller may be operable to consider an instantaneous measurement of an operational parameter, and/or a rate of change of the measured parameter and/or likely future change to the operational parameter to provide a control output signal to the variable suction source to meet the target operational parameter.

In one embodiment, the controller is operable to control the variable suction source in real time in dependence upon a real time received indication from the sensor. Accordingly, dynamic handling of objects may be achieved such that the likelihood of damage to delicate objects can be mitigated.

In one embodiment, the fluid in the conduit comprises a liquid. Accordingly, hysteresis and lag in responsiveness to a suction source may be less than that which can be achieved if the fluid is gaseous. As a result, the likelihood of object damage may be mitigated. In one embodiment, the fluid in the conduit comprises gas. In one embodiment, the fluid in the conduit comprises air.

In one embodiment, the source of variable suction comprises a bidirectional pump. Accordingly, a device may be operable to both lift and release an object on the suction cup. Furthermore, if it is determined that a force being exerted on an object being handled is too great, a negative suction may be applied, allowing a holding force to be adjusted.

In one embodiment, the operational parameter comprises pressure of the fluid in the conduit. In one embodiment, the operational parameter comprises flow rate of the fluid in the conduit. Accordingly, a force being exerted on an object being handled may be related to fluid condition in the conduit.

In one embodiment, the device comprises a plurality of suction cups. Accordingly, a plurality of suction cups may be arranged or configured to be suited to an object to be handled. The number of cups provided and/or the form of the suction cups provided may be selected to prevent damage, including surface damage, to an object to be
5 handled. Furthermore the configuration of the plurality of suction cups may be selected in dependence upon the type of object to be handled.

In one embodiment, the plurality of suction cups are coupled to the variable source of suction via a common conduit. Accordingly, the operation of the plurality of suction
10 cups may be synchronous. That is to say, the same suction source may be used for all suction cups and the variance of the suction may be uniformly applied across some or all suction cups provided.

In one embodiment, each of the plurality of suction cups is coupled to a variable source
15 of suction via an independent conduit. Accordingly, the operation of the plurality of suction cups may be asynchronous. That is to say, a different suction source may be used for each suction cup, or a sub set of suction cups and the variance of the suction may be independently applied across some or all suction cups provided.

20 In one embodiment, the device further comprises an object housing, configured to receive and store an object handled by said suction cup. Accordingly, a device may be used to support a catalogue function.

In one embodiment, the object housing is configured to receive a plurality of objects
25 handled by the suction cup. In one embodiment, the device is arranged to place a sequence of the plurality of objects handled by the suction cup into the object housing in a preselected order. Accordingly, cataloguing for future identification of objects handled by the device may be supported.

30 A second aspect provides a method of handling an object, the handling method comprising: providing a source of variable suction; arranging a suction cup operable to receive an object to be handled and coupling the suction cup via a conduit to the source of variable suction; providing a sensor operable to determine an operational parameter of fluid in the conduit; and controlling the variable suction source in dependence upon
35 an indication of the determined operational parameter.

In one embodiment, the operation of the variable suction source is controlled to obtain a target value of the operational parameter, that target value being selected to prevent damage to the object to be handled.

- 5 In one embodiment, the operation of the variable suction source is controlled by a proportional integral derivative controller, in dependence upon the determined operational parameter and the target value of the operational parameter.

10 In one embodiment, adjustment of the variable suction source occurs in real time in dependence upon a real time received indication from the sensor.

In one embodiment, the fluid in the conduit comprises a liquid.

15 In one embodiment, the source of variable suction comprises a bidirectional pump.

In one embodiment, the operational parameter comprises pressure of the fluid in the conduit.

20 In one embodiment, the operational parameter comprises flow rate of the fluid in the conduit.

In one embodiment, the method comprises providing a plurality of suction cups.

25 In one embodiment, the plurality of suction cups are coupled to the variable source of suction via a common conduit.

In one embodiment, each of the plurality of suction cups are coupled to a variable source of suction via an independent conduit.

30 In one embodiment, the method further comprises providing an object housing, configured to receive and store an object handled by said suction cup.

In one embodiment, the object housing is configured to receive a plurality of objects handled by the suction cup.

35 In one embodiment, the method further comprises placing a sequence of the plurality of objects handled by the suction cup into the object housing in a preselected order.

A third aspect provides a computer program product operable, when executed on a computer, to perform the method of the second aspect. Aspects and embodiments described herein may overcome some issues associated with a 'binary' on/off suction
5 system. According to some embodiments, the device may comprise: adaptive proportional control logic. The control logic may be operable to provide real-time adaptive proportional control. The device may comprise a variable flow bi-directional pump. The device may comprise: a pressure sensor. The device may comprise: a vacuum cup connected via a conduit to the variable flow bi-directional pump. The
10 device may comprise a vacuum cup assembly. The vacuum cup assembly may be mounted to a manipulator.

It will be appreciated that provision of adaptive pumping in accordance with some embodiments may offer some advantages. That adaptive pumping may comprise
15 proportional pumping. The adaptive proportional pumping may be performed, according to some embodiments, in real-time. Logic may be provided within a device to implement appropriate adaptive pumping, proportional adaptive pumping and/or real-time adaptive proportional pumping.

20 Provision of an adaptive real-time proportional control method and device may provide a means by which to allow for manipulation of ultra-thin, delicate objects without damage.

According to some embodiments, a device operable to provide dynamic control of
25 suction pressure is provided. According to some embodiments, control logic is provided which is operable to control the rate of change of suction pressure to alleviate potential specimen rupture damage.

According to some embodiments, a device operable to provide dynamic control of
30 object release pressure is provided. According to some embodiments, control logic is provided which is operable to control the rate of change of suction pressure and implement controlled object release. Such a controlled release is implemented to prevent rapid fluid flow transients, thus alleviating potential specimen damage and/or loss of object orientation.

35 Some aspects and embodiments may provide a method and device in which a plurality of operational modes are implemented. Accordingly, each operating mode may have

operational parameters selected such that object damage may be minimised and such that optical handling of each object is maximised, thereby allowing, for example, an optimal specimen collection yield.

- 5 Some aspects and embodiments may provide a method and device in which a plurality of operational modes are implemented and in which different control methods, for example, open-loop or closed-loop control techniques, are applied to the plurality of operating modes.
- 10 Some aspects and embodiments may provide a method and device in which lifting or pulling of the object to the vacuum cup is enabled. Such an implementation may be operable to prevent damage that could otherwise be caused to an object by sandwiching that object between the vacuum cup and a pick-up surface.
- 15 Some aspects and embodiments may provide a method and device in which detection of 'object connection' to the vacuum cup is provided. Detection of the object connection event may be a threshold or trigger which enables the method and device to move to implementation of another operating mode.
- 20 Some aspects and embodiments may provide a method and device in which detection of pressure loss when the object is in transit is provided. Such provision may allow for control logic to take steps to implement automatic pressure compensation to be applied, with the aim of preventing specimen detachment from the suction cup.
- 25 Some aspects and embodiments may provide a method and device in which detection of failed suction events is enabled. Such event detection based on, for example, monitoring of one or more operational parameters, can enable appropriate action to be taken if a threshold or target value is not reached. Appropriate actions may, for example, include: putting a vacuum cup of a device into "standby" mode. In, for
30 example, a sub-aqueous implementation, the "standby" mode may be one in which the control logic is operable to prevent air entering the conduit associated with the "standby" vacuum cup. That functionality may, for example, be beneficial when there is a need to dispense measured fluid volumes.
- 35 Some aspects and embodiments may provide a method and device in which event detection features may be provided. Accordingly one or more operational parameters may be monitored and when one or more criteria are met, control logic may be

operable to recognise an event, for example: 'object connected' or 'set-point reached'. Failure to detect an expected event may indicate that part of a handling process has failed. This information may be used to determine a best handling action. For example, if three of the four suction grippers are determined to be successfully
5 connected, a "timeout" or "standby" event may be implemented in relation to the fourth suction gripper into standby. Further object manipulation and handling may then be attempted with three suction grippers.

Some aspects and embodiments may provide a method and device in which a plurality
10 of vacuum cups with independent measurement and control are provided. The plurality of vacuum cups may be master-controlled according to a handling sequence selected to be appropriate to an object handling application. Accordingly, independently controllable suction cups may provide an ability to anchor part of an object. Anchoring part of an object before it is totally free to move may prevent
15 potential subsequent loss of the object.

Some aspects and embodiments may provide a method and device in which detection of conduit blockages is enabled. Detection of such a blockage by monitoring operational parameters may enable the system to attempt automatic clearing of a
20 conduits suction cup.

Some aspects and embodiments may provide a method and device in which data-logging of events, measurement and/or control parameters is enabled. Such data logging, using for example, a memory logic unit, may allow for the tuning of a device
25 and method forming part of a system as applied to a specific implementation. Data-logging of one or more monitored operational parameters may also be useful in relation to maintenance of a device.

Some aspects and embodiments may provide a method and device in which the ability
30 to lift or pull a sample to the vacuum cup is provided. Accordingly, objects may be lifted from a vibrating surface such as, for example, a microtome blade.

Some aspects and embodiments may provide a method and device in which proportional flow/vacuum or suction control, performed in real-time, may enable an
35 object to be successfully manipulated across fluid medium boundaries such as, for example, a transition from water to air.

Some aspects and embodiments may provide a method and device in which a plurality of vacuum or suction cups are provided, those suction cups being configured to suit, for example, geometry of the object or objects to be handled. The configuration of the plurality of suction cups may enable both rotational and face orientation of an object being handled to be maintained. This may be advantageous for down-stream processes according to which orientation of an object is of importance.

Some aspects and embodiments may provide a method and device in which a suction cup and bidirectional pump are configured, in sub-aqueous (or other fluid) applications, to dispense a measured quantity of fluid on release of the object being handled. Accordingly, fluid may be transferred, with an object, to an object destination container.

Some aspects and embodiments may provide a method and device which operates to recirculate 'exhaust' fluid. Recirculation of exhaust fluid may enable object bath solution height to be maintained.

Some aspects and embodiments may provide a method and device configured to dispense fluid. In some embodiments, the device is arranged to enable the dispensing of fluid from a separate reservoir. Accordingly, in arrangements where no top-up of a bath in which the objects to be handled are housed is possible, it may be possible to ensure that fluid height in the specimen bath is maintained by provision of a separate reservoir of fluid.

It will therefore be understood that embodiments may provide: an object handling device controlled to provide adaptive real-time proportional object handling. Accordingly, such proportional object handling may be performed in relation to at least one determined threshold or criteria associated with said operational parameter of fluid in said conduit. Control may be performed in dependence upon a value of the determined operational parameter and the target threshold or criteria.

It will therefore be understood that aspects and embodiments may provide: an object handling device and a method of controlling the object handling device. Aspects and embodiments may also provide a computer program product operable, when executed on a computer to execute the control method.

According to some embodiments, the operational parameter of interest in relation to

the fluid in the conduit comprises fluid pressure. Accordingly, the sensor provided may comprise a pressure sensor operable to measure pressure within the conduit between the suction cup and source of variable suction.

- 5 According to some embodiments, the source of variable suction comprises: a proportionally controllable bi-directional pump.

According to some embodiments, the suction cup is connected via a conduit to the source of variable suction.

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According to some embodiments, there is provided at least one suction cup movement actuator. Accordingly, aspects and embodiments may also provide method of manipulating the suction cup in three dimensions.

- 15 In some embodiments, the object handling device and method of handling an object are configured to allow multiple operating modes in relation to each phase of object handling. Such object handling phases may comprise, for example: object location, object pick-up, object movement, and/or object release.

- 20 In some embodiments, the object handling device and method of handling an object are configured to provide open-loop and/or closed-loop control modes.

In some embodiments, the object handling device and method of handling an object are configured to enable pressure loss detection.

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In some embodiments, the object handling device and method of handling an object are configured to enable failed suction event detection.

- 30 In some embodiments, the object handling device and method of handling an object are configured to enable conduit blockage detection.

In some embodiments, the object handling device and method of handling an object are configured to enable synchronised control of multiple asynchronous suction channels.

- 35 In some embodiments, the object handling device and method of handling an object are configured to enable fluidic priming of the conduit between the suction cup and the variable suction source.

In some embodiments, the object handling device and method of handling an object are configured to enable dispensing of a measured fluid quantity from the suction cup.

5 In some embodiments, the object handling device and method of handling an object are configured to actuate use of an external reservoir for dispensing of fluid from the suction cup. Accordingly, the object handling device may comprise an external fluid reservoir. The device may comprise a reservoir valve. The reservoir valve may be controlled in accordance with the method of handling and object. The external
10 reservoir may be connected to the conduit and/or variable source of suction via a reservoir conduit. The reservoir valve may be moved between a first position in which fluid is drawn from the external reservoir and a second position in which fluid is not drawn from the external reservoir. In some embodiments, the external reservoir may comprise a reservoir of specimen hydration fluid.

15 In some embodiments, the object handling device and method of handling an object are configured such that each suction cup has a dedicated variable suction source.

In some embodiments, the object handling device and method of handling an object are
20 configured such that each suction cup has a dedicated sensor. That sensor may comprise a pressure sensor.

In some embodiments, the object handling device and method of handling an object are configured such that each suction cup is independently controlled.

25 In some embodiments, the object handling device and method of handling an object are configured such that each variable suction source is bi-directional, thus allowing fluid to be inhaled (object suction) and aspired (object release). According to some embodiments, the variable suction source comprises a pump. The pump may comprise
30 a peristaltic type pump. It will be appreciated, however, that any pump or combination of two pumps could be configured to operate in this manner, for example, the combination of two diaphragm pumps.

In some embodiments, the object handling device and method of handling an object are
35 configured such that the variable suction source is operable to maintain pressure in a closed-fluid system without continuous actuation. It may be possible to operate a peristaltic type pump in such a manner. It is possible to achieve constant pressure with

continuous variable speed rotation of a pump such as a gear pump or rotary vane pump.

5 In some embodiments, the object handling device and method of handling an object are configured to operate using a variable suction source which may be driven by a motor that is suited to speed control. Examples of such motors include, for example, a brushed DC motor, a stepper motor or a brushless dc motor.

10 In some embodiments, the object handling device comprises: a plurality of suction cups, configured to suit object geometry.

In some embodiments, the object handling device comprises: a suction cup housing.

15 In some embodiments, the object handling device comprises a suction cup housing and said suction cup housing is configured to be connectable to an object manipulation device, for example, a robotic hand. In some embodiments, said suction cup housing is configured to be connectable to a manual manipulator tool.

20 In some embodiments, the suction cup housing is configured to be spatially manipulated by a manipulation device, for example, a robot. In some embodiments, the suction cup housing is configured to be spatially manipulated manually.

25 In some embodiments, the object handling device conduit is integrally formed with the object manipulation tool or robotic hand.

Further particular and preferred aspects are set out in the accompanying independent and dependent claims. Features of the dependent claims may be combined with features of the independent claims as appropriate, and in combinations other than those explicitly set out in the claims.

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Where an apparatus feature is described as being operable to provide a function, it will be appreciated that this includes an apparatus feature which provides that function or which is adapted or configured to provide that function.

35 BRIEF DESCRIPTION OF THE DRAWINGS

Embodiments of the present invention will now be described further, with reference to the accompanying drawings, in which:

Figure 1 illustrates schematically main components of a device according to one embodiment;

Figures 2a to 2c illustrate schematically a sample pick and place method according to one embodiment;

5 Figure 3 illustrates schematically operation of a device control unit according to one embodiment;

Figure 4 illustrates schematically a device according to a further embodiment;

Figure 5 illustrates schematically a device according to a further embodiment;

Figure 6 illustrates schematically a device according to one embodiment;

10 Figure 7 illustrates schematically a method of control according to one embodiment;

Figures 8a to 8g illustrate schematically an object handling method according to one embodiment;

Figure 9 illustrates schematically a device according to a further embodiment;

Figure 10 illustrates schematically a device according to a further embodiment; and

15 Figure 11 illustrates schematically, by block diagram, one embodiment of a device controller.

DESCRIPTION OF THE EMBODIMENTS

Overview

20 Before discussing the embodiments in any more detail, first an overview will be provided. Industrial processes commonly utilize a vacuum or a suction device in 'pick and place' systems. Aspects and embodiments described herein provide a means by which a pick and place device may be operable to handle delicate objects, for example, delicate sectioned biological tissue. The delicate objects may be moveable by a device
25 in accordance with aspects and embodiments by direct engagement with a delicate object itself or by gripping a surrounding support material.

Typically industrial systems use an air driven vacuum generator to lift and move packaging or goods. Delicate objects, for example, biological tissue, requires more
30 controlled application of a vacuum to prevent damage.

Some aspects and embodiments utilise a miniature pump with pressure feedback to generate a desired lifting force. In some embodiments, the pump may be bi-directional, and include appropriate valve or non-return mechanisms thereby enabling
35 finely controlled pick-and-place operations.

Figure 1 illustrates schematically main components of a device according to one embodiment. The delicate object handling device 10 shown in Figure 1 comprises a suction device 20, coupled to a sample engaging element, in this case, a vacuum cup 30. The suction device of the embodiment shown in Figure 1 comprises a bidirectional
5 pump operable to move a fluid between the vacuum cup 30 and a fluid exhaust 40 and vice versa. The coupling between the suction device 20 and the vacuum cup 30 is monitored by a sensor 50. In the embodiment shown in Figure 1, the sensor comprises a pressure sensor operable to monitor the pressure of fluid within the coupling. The handling device 10 further comprises a control system 60 operable to communicate
10 with sensor 50 and control operation of suction device 20 in dependence on a monitoring signal generated by sensor 50. According to aspects and embodiments the control system 60 may be operable, by means of a typical feedback loop, to maintain pressure in the coupling at a desired value, that value being selected to hold, but not damage, a delicate object.

15 Recent biological tissue processing technologies combine advanced imaging and brain tissue sectioning into a single commercially available system. Typically sectioned tissue, once cut, falls away from a tissue/agar block and a cut surface can be imaged. For example, a mouse brain can be sectioned up to 500 times, each section slice having
20 a thickness of between 50 and 100 microns.

A system which enables sectioning and imaging together with organised storage allowing correlative tissue analysis may be of use in the field of biological tissue analysis. A pick and place device which can be configured to handle delicate objects
25 may have significant commercial applications in such a field. A suitable pick and place device may be used as an add-on module to commercial high-value sample sectioning systems, microtomes and similar and may provide opportunities for automated post-processing histology processes.

30 Figure 2 illustrates schematically an application of a device according to one embodiment in the field of biological tissue sectioning. In the example shown an experimental brain is encapsulated within a support material, in this case an agar block. Typically an 'agar cube' is bonded to the base of bath subsequently filled with saline. During sectioning, the tissue typically falls away from a microtome cutting
35 blade rendering the tissue difficult to recover, particularly in the case where up to 500 slices taken over 48 hours. The handling device described herein may enable collection and handling of each tissue section as it is cut.

Figures 2a to 2c illustrate schematically a sample pick and place method according to one embodiment. In the example method shown in Figure 2, a device according to one embodiment is used to collect, hold and move a biological tissue sample section. A biological tissue sample is encapsulated in an agar block 200. That block is supported in a fluid sectioning bath 210. A microtome 220 is aligned to cut a sample section from the block 200. In the example shown, the exhaust from the pump 20 is recycled to the sectioning bath, thus maintaining solution height. As the tissue is sectioned by the microtome 220, the delicate object handling device 10 slowly primes with fluid. That is to say, fluid from the sectioning bath is drawn through the vacuum cup 30 into the coupling by pump 20 and passed through to the pump exhaust 40. The free flow of fluid through the vacuum cup into the coupling is such that pressure sensor detects no increase in pressure in the coupling and the pressure signal sent to control unit is such that the control unit maintains a substantially constant flow of fluid through the bidirectional pump.

Figure 2b illustrates schematically an instance in which sectioning of a sample by a microtome is almost complete and, as a result of positioning of the vacuum cup 30 and/or appropriate selection of a flow rate of fluid through the bidirectional pump, the device 10 is operable to pull the tissue section sample to the vacuum cup. As the sample begins to engage with the vacuum cup 30 and impede fluid entry into the vacuum cup, the negative pressure in the coupling between the cup and the pump begins to rise and the pressure signal sent to the control unit by the pressure sensor 50 changes (increases). As the pressure indicated by the signal generated by the pressure sensor increases, a control signal sent by the control unit 60 to the pump 20 may be such that the fluid pump rate or pump motor rotation is reduced as the pressure in the coupling reaches, but does not exceed, a value selected to hold, but not damage, the sectioned sample 240.

Figure 2c illustrates schematically an instance in which sectioning is complete and the sectioned sample slice 240 is held in place on vacuum cup 30. If there is no leakage from the bidirectional pump system, the control system 60 may operate such that the pump motor is turned off when a desired pressure in the coupling between the vacuum cup 30 and the pump 20 is determined by the pressure sensor 50 to be reached.

Figure 3 illustrates schematically general operation of a device control unit 60 according to one embodiment. In the arrangement shown schematically in Figure 3

control unit 60 comprises control logic 300 operable to receive a signal from pressure sensor 50 and apply a proportional integral derivative control algorithm (PID control) to the received signal in order to generate a control signal to be transmitted to a motor driver 310 of the pump 20. PID controller is typically used in a control loop feedback mechanism and is operable to calculate a difference between a measured (pressure) value and a desired (pressure) set point. The control logic is operable to try to minimise the difference by generating an appropriate signal to be fed to the motor driver. In the implementation shown, if a pressure value received is determined to be below a desired value, the motor may be sent a signal to increase motor speed and thus increase flow rate of fluid being sucked through the vacuum system. If the pressure is determined to be above a desired value, the motor driver may be instructed to stop the motor or reduce the rotation rate of the motor to reduce fluid flow through the vacuum system and/or change the direction of the motor to reduce the pressure in the vacuum system. It will be appreciated that use of the pressure sensor can provide a dynamic or real-time input signal, and appropriate real time motor driver control signals may be generated.

Devices in accordance with aspects and embodiments described may take a range of forms and, for example, may include any number of vacuum cups enabling manipulation of larger sections. In some embodiments, vacuum measurement and control may be shared between vacuum ports or each vacuum port may be independently controlled.

Figure 4 illustrates schematically a device according to a further embodiment in which there are multiple vacuum cups coupled with a single pump and single control unit.

Figure 5 illustrates schematically a device according to a further embodiment in which there are multiple vacuum cups each having independent pumps and pressure control.

Various alternative implementations may be envisaged. For example, although described in relation to submerged aqueous sample handling applications; principles of aspects and embodiments may, for example, be applied to dry sectioning sample techniques.

In the example described in relation to Figure 2, a tissue samples is encapsulated in a moulded agar cube. The agar perimeter provides a vacuum cup of a device according to

some embodiments with an attachment surface. It will be appreciated that the agar cube may be substituted by any appropriate alternative sample embedding medium.

5 According to some aspects and embodiments it may be possible to grip or hold a biological tissue sample directly. Aspects and embodiments may allow for controlled pressure to be exerted on a sample. That pressure may be selected to ameliorate sample surface damage.

10 The 'vacuum cup' of a device according to embodiments may take various forms. The form of the vacuum cup may be selected, arranged or configured to provide a suitable contact surface for the object being manipulated.

15 According to further aspects, a biological sample sectioning system may be configured to include a device operable to detect positioning of a sample cutter, thus enabling synchronisation of a sample pick and place device and, for example, delicate sample cutting and preparation by a microtome.

20 It will be appreciated that whilst a system according to one embodiment is described utilizes a pressure or vacuum suction sensor to detect successful contact with a delicate object to be moved, an alternative embodiment may use a flow sensor to detect contact with a delicate object.

25 A system in accordance with a described embodiment utilises a bi-directional pump, but it will be appreciated that any method of fluid transfer can be utilised, for example, a uni-directional pump with an appropriate release valve or a vacuum pump.

A device in accordance with some aspects and embodiments may be used for automatic handling of biological samples including tissue samples, but also to handle other delicate objects including other materials cut by microtomes such as minerals.

30

A further aspect allows for a pick and place device to be paired with a microtome. Such an arrangement may be further coupled with an additional storage or catalogue system or a sample analysis or processing device arranged to use the cut material.

35 Figure 6 illustrates schematically a device according to one embodiment. The embodiment shown in Figure 6 comprises an object handling device in which four

suction cups are provided, though only two fluid channels, associated with suction cups “a” and “b” are shown in detail.

5 The adaptive real-time control processes shown schematically in Figure 6 recognise that handling an ultra-thin specimen may requires a device controller (shown as “master control” in Figure 6) to adapt operation of a variable suction source (bidirectional pump a or bidirectional pump b as shown in Figure 6) to match a device operating mode. At each stage of the handling of an object, for example, in each of the: object capture, object move and/or object release phases of object handling, a control
10 method may be implemented to minimise damage to an object and maximise specimen collection yield during that phase or “operating mode”.

The control process implemented by the master controller in relation to an object handling device may be altered to suit a particular object handling scenario. Variables
15 may be adjusted to provide, for example, an operating pressure an/or rate-of-change of pressure suited to a particular object or object capture and move environment. Operating modes implemented by an object handling device controller may be matched to a selected handling process.

20 Figure 7 illustrates schematically an embodiment of an adaptive real-time control process. The process shown in Figure 7 may be applied to a device such as that illustrated in Figure 6.

Figure 7 illustrates schematically the relative timing of a set of distinct ‘operating
25 modes’ in relation to a set of key events (M1 to M12) associated with the handling of an object. In relation to each key event, Figure 7 shows a proportional or relative pressure signal as might be measured in a conduit between the suction cup and the variable suction source, together with a graphical representation of proportional control of pump speed, that pump forming the basis of the variable suction source.

30 Operating modes M1 to M12 as illustrated schematically in Figure 7 are described in more detail below:

Operating mode (M1) comprises a ‘standby’ mode. When in a standby mode, the
35 control system of the object handling device operates to prevent active operation of the suction pumps.

Operating mode (M2) comprises a 'system priming' operating mode. When in system priming mode, the control system of the object handling device operates to manipulate the suction cup(s) so that, for example, in a sub-aqueous object handling environment, the suction cup(s) become submerged in a fluid bath surrounding the object to be
5 handled. The pump or pumps forming the variable suction source are instructed by the control system according to an open-loop control method and operate such that fluid in the bath is pulled in to the suction cup(s), thus filling the conduit and pumps with the same liquid as the fluid bath. The pump rate can be very low to prevent disturbance to the object to be handled located within the fluid bath. The duration of the system
10 priming mode may be substantially static. On completion of system priming, the pump may be switched off by the control system. As can be seen from Figure 7, during system priming, the pressure sensor reports an indication of a negative detected pressure. A threshold or trigger pressure value may be set such that if the control system receives an indication of a measurement of pressure which exceeds the threshold, the control
15 system may report detection of conduit or suction cup obstruction.

Operating mode (M3) comprises a 'move suction cup over object' mode. According to such a mode the suction cup is manipulated so that it is located in the immediate vicinity of the object to be handled. The suction cup may, for example, be located
20 directly above an intended suction application position. There may be a defined clearance between the suction cup and object to be handled.

Operating mode (M4) comprises a 'pull / lift object to vacuum cup' mode. According to such a mode of operation the control system is operable to instruct the pump or pumps
25 forming the variable suction source to accelerate their rate of flow (or rotation) quickly in an open-loop control mode to thereby lift or pull the object towards the suction cup.

Operating mode (M5) comprises an 'object connected to vacuum cup' mode. According to such a mode, the control system may operate to implement a closed-loop control
30 method. Accordingly. The control system operates to decelerate the rate of rotation (rate of fluid flow through) the pump or pumps to apply controlled suction to the object.

Operating mode (M6) comprises an 'apply controlled suction at controlled rate' mode.
35 According to such a mode of operation a closed-loop control method operates to compare a predetermined set-point (or target) value with a measured input variable, if the control system determines that there is a difference between the measured value

and the target value then the controller is operable to output an appropriate corrective proportional command to a proportional actuator. As the measured value indicates that the target value is being reached, the pump speed is reduced to prevent pressure overshoot. A further control process feature recognises that an ultra-thin specimen
5 may be damaged by rapid pressure transients. The controller may be operable to regulate the rate-of-change of suction pressure to alleviate damage to an object.

Operating mode (M7) comprises a 'pressure set-point reached' mode. Such a mode is entered when the target value of operating mode M6 is reached. When the target value
10 is reached, pressure is maintained in the conduit by fine control of the pump. Where a pump such as a peristaltic type is used, the pump may be substantially stationary on reaching the target value in accordance with mode M6. In the event of pressure target value overshoot, the controller may operate to reverse the rotation of the pump or pumps to ensure the target value is reached.

15 Operating mode (M8) comprises a 'transport object' mode. According to such a mode the object is attached to the suction cup(s) and transport of the object can be initiated.

Operating mode (M9) comprises a 'pressure loss detection and correction' mode.
20 According to some arrangements, a further control process feature is provided which recognises that handling an ultra-thin specimen can require close monitoring throughout object transport, especially when crossing medium boundaries such as liquid to air or vice-versa. Monitoring of one or more operational parameters of the handling device can enable corrective action to be taken as the object is moved, thus
25 preventing loss of an object from a suction cup.

Operating mode (M10) comprises a 'release object at a controlled rate' mode.
According to such a mode, the controller operates to ensure controlled release of an object. Such a mode may be of particular use when handling ultra-delicate specimens.
30 Accordingly, a device controller may be operable to implement a closed-loop control method which ensures a dynamically controlled release of pressure in the conduit thus preventing rapid fluid flow transient and mitigating chances of potential object damage and/or loss of object orientation.

35 Operating mode (M11) comprises an 'object released from vacuum cup' mode. Such a mode of operation recognises that delicate specimens tend to have a low mass and may not fall away from a suction cup when the pressure in the conduit is reduced. The

device controller may operate to monitor one or more operational parameters and detect object release. Only when object release is detected can the next operating mode commence.

- 5 Operating mode (M12) comprises a 'dispense medium to container' mode. According to such a mode the device controller system may be operable to enable dispensing of fluid to a specimen container to which an object has been moved and into which it has been released. One embodiment of an object handling device may include an external fluid reservoir and change-over valve as illustrated further in Figure 9.

10

Figures 8a to 8g illustrate schematically operating modes M1, M2, M3-M5, M6-M7, M8-M9, M10-M11 and M12 respectively.

15

In the particular application shown schematically in Figures 8a to 8g, the object to be handled by the device according to one arrangement is a biological specimen. The specimen comprises a mouse brain encapsulated within support material, in this case, an agar block. Typically an 'agar' cube is bonded to the base of a bath. The bath is subsequently filled with saline solution. The mouse brain can be sectioned up to 500 times. Each section is typically 50 microns thick. During sectioning, the tissue may fall away from a microtome cutting blade rendering the tissue difficult to recover, particularly in the case where up to 500 slices are taken over the period of 48 hours. The handling device described herein may enable collection and handling of each tissue section as it is cut.

20

- 25 The vacuum cup assembly in the arrangement illustrated comprises four independent suction cups with associated independent conduits and variable suction sources (pumps). For reasons of clarity, a single suction gripper arrangement is illustrated in Figures 8a to 8g. The suction cup housing in the illustrated example is manipulated by a robotic end effector. The purpose of the specimen handling system in this example is to transport the sectioned specimen from the microtome blade through the aqueous-air boundary to a specimen container. Following specimen release, the specimen container is partially filled with saline to prevent dehydration of the specimen.
- 30

Figure 8a illustrates schematically operation of the object handling device when in standby mode (M1). As shown in Figure 8a, the microtome is sectioning the specimen.

35

Figure 8b illustrates schematically operation of the object handling device when in priming mode (M2).

5 Figure 8c illustrates schematically operation of the object handling device when in modes M3, M4 and M5.

Figure 8d illustrates schematically operation of the object handling device when applying suction to the specimen to reach a target pressure value at a controlled rate according to operating modes M6 and M7.

10

Figure 8e illustrates schematically operation of the object handling device as the suction cups are controlled to manipulate the specimen through a liquid – air boundary according to modes M8 and M9.

15 Figure 8f illustrates schematically operation of the object handling device as the suction cups are controlled to release the specimen into an external specimen container in accordance with operating modes M10 and M11.

20 Figure 8g illustrates schematically operation of the object handling device when as the suction cups are controlled to dispense fluid into the specimen container to maintain specimen hydration in accordance with operating mode M12.

25 Figure 9 illustrates schematically a device according to a further embodiment. The device shown in Figure 9 further comprises an external fluid reservoir and a valve to prevent or allow suction of fluid from that external reservoir by the variable suction source in accordance with a signal issued by the device controller.

Figure 10 illustrates schematically a device according to a further embodiment. The device shown in Figure 10 comprises two suction cups which share a variable suction device and are controlled synchronously by a device controller.

30

Figure 11 illustrates schematically, by block diagram, one embodiment of a device controller.

35 A person of skill in the art would readily recognize that steps of various above-described methods can be performed by programmed computers. Herein, some embodiments are also intended to cover program storage devices, e.g., digital data storage media, which are machine or computer readable and encode machine-

executable or computer-executable programs of instructions, wherein said instructions perform some or all of the steps of said above-described methods. The program storage devices may be, e.g., digital memories, magnetic storage media such as a magnetic disks and magnetic tapes, hard drives, or optically readable digital data storage media. The
5 embodiments are also intended to cover computers programmed to perform said steps of the above-described methods.

The functions of the various elements shown in the Figures, including any functional blocks labelled as “processors” or “logic”, may be provided through the use of dedicated
10 hardware as well as hardware capable of executing software in association with appropriate software. When provided by a processor, the functions may be provided by a single dedicated processor, by a single shared processor, or by a plurality of individual processors, some of which may be shared. Moreover, explicit use of the term
15 “processor” or “controller” or “logic” should not be construed to refer exclusively to hardware capable of executing software, and may implicitly include, without limitation, digital signal processor (DSP) hardware, network processor, application specific integrated circuit (ASIC), field programmable gate array (FPGA), read only memory (ROM) for storing software, random access memory (RAM), and non volatile storage. Other hardware, conventional and/or custom, may also be included. Similarly, any
20 switches shown in the Figures are conceptual only. Their function may be carried out through the operation of program logic, through dedicated logic, through the interaction of program control and dedicated logic, or even manually, the particular technique being selectable by the implementer as more specifically understood from the context.

25 It should be appreciated by those skilled in the art that any block diagrams herein represent conceptual views of illustrative circuitry embodying the principles of the invention. Similarly, it will be appreciated that any flow charts, flow diagrams, state transition diagrams, pseudo code, and the like represent various processes which may
30 be substantially represented in computer readable medium and so executed by a computer or processor, whether or not such computer or processor is explicitly shown.

The description and drawings merely illustrate the principles of the invention. It will thus be appreciated that those skilled in the art will be able to devise various
35 arrangements that, although not explicitly described or shown herein, embody the principles of the invention and are included within its spirit and scope. Furthermore, all examples recited herein are principally intended expressly to be only for pedagogical

purposes to aid the reader in understanding the principles of the invention and the concepts contributed by the inventor(s) to furthering the art, and are to be construed as being without limitation to such specifically recited examples and conditions.

Moreover, all statements herein reciting principles, aspects, and embodiments of the
5 invention, as well as specific examples thereof, are intended to encompass equivalents thereof.

CLAIMS

1. An object handling device comprising:
a source of variable suction;
5 a suction cup operable to receive an object to be handled and coupled, via a conduit, to said source of variable suction;
a sensor operable to determine an operational parameter of fluid in said conduit; and
a controller operable to receive an indication of said determined operational parameter
and adjust said variable suction source in dependence upon said received indication.
10
2. A device according to claim 1, wherein operation of said variable suction source
is controlled to obtain a target value of said operational parameter, that target value
being selected to prevent damage to said object to be handled.
- 15 3. A device according to claim 2, wherein operation of said variable suction source
is controlled by a closed loop controller, in dependence upon said determined
operational parameter and said target value of said operational parameter.
4. A device according to any preceding claim, wherein said controller is operable
20 to control said variable suction source in real time in dependence upon a real time
received indication from said sensor.
5. A device according to any preceding claim, wherein said fluid in said conduit
comprises a liquid.
25
6. A device according to any preceding claim, wherein said source of variable
suction comprises a bidirectional pump.
7. A device according to any preceding claim, wherein said operational parameter
30 comprises pressure of said fluid in said conduit.
8. A device according to any one of claims 1 to 6, wherein said operational
parameter comprises flow rate of said fluid in said conduit.
- 35 9. A device according to any preceding claim, wherein said device comprises a
plurality of suction cups.

10. A device according to claim 9, wherein said plurality of suction cups are coupled to said variable source of suction via a common conduit.
11. A device according to claim 9, wherein each of said plurality of suction cups are
5 coupled to a variable source of suction via an independent conduit.
12. A device according to any preceding claim, wherein said device further comprises an object housing, configured to receive and store an object handled by said suction cup.
- 10 13. A device according to claim 12, wherein said object housing is configured to receive a plurality of objects handled by said suction cup.
14. A device according to claim 13, wherein said device is arranged to place a
15 sequence of said plurality of objects handled by said suction cup into said object housing in a preselected order.
15. A device according to any preceding claim, wherein said object to be handled comprises a sectioned biological specimen.
- 20 16. A method of handling an object, said handling method comprising:
providing a source of variable suction;
arranging a suction cup operable to receive an object to be handled and coupling said suction cup via a conduit, to said source of variable suction;
25 providing a sensor operable to determine an operational parameter of fluid in said conduit; and
controlling said variable suction source in dependence upon an indication of said determined operational parameter.
- 30 17. A computer program product operable, when executed on a computer, to perform the method of claim 16.

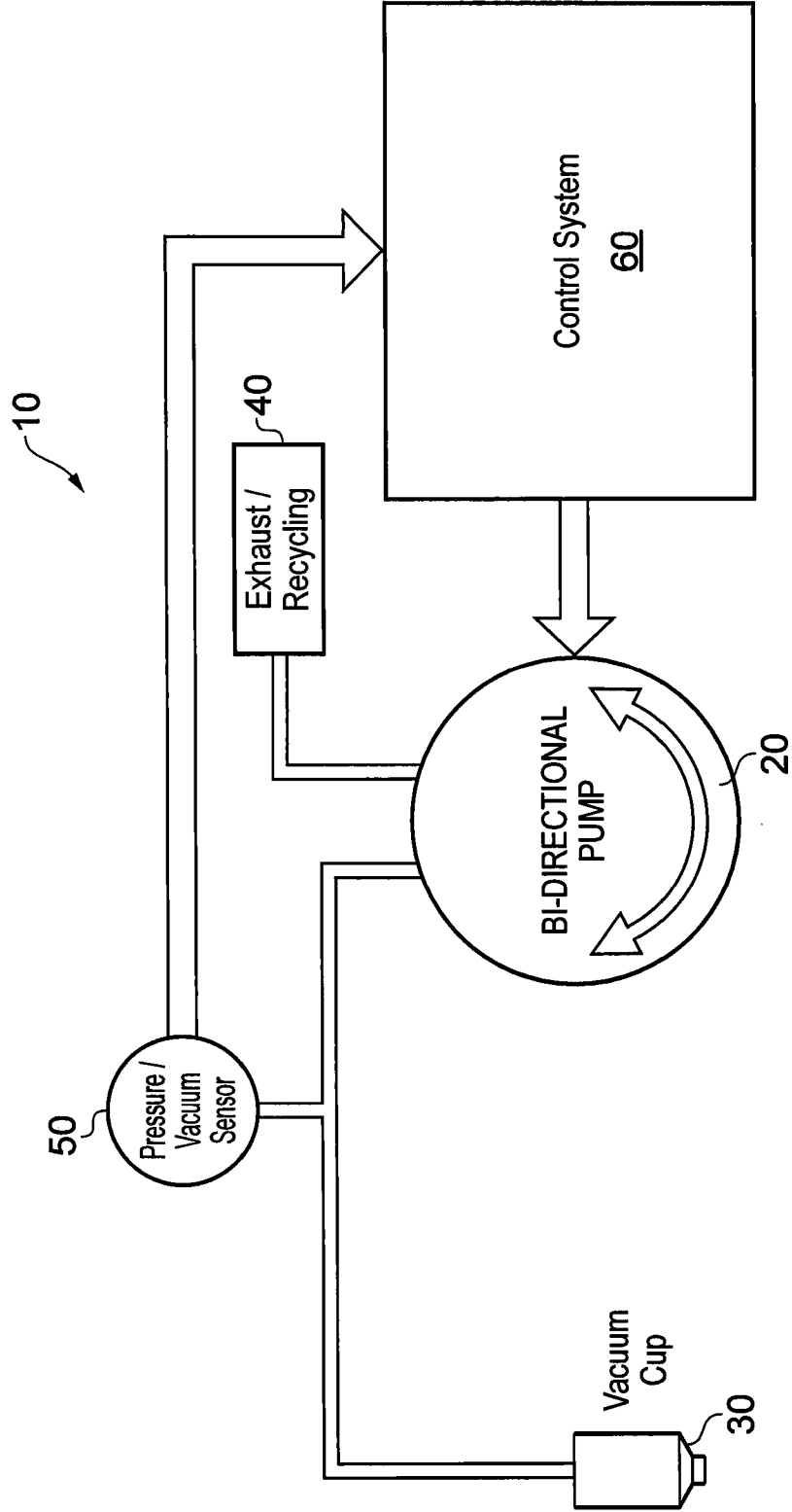


FIG. 1

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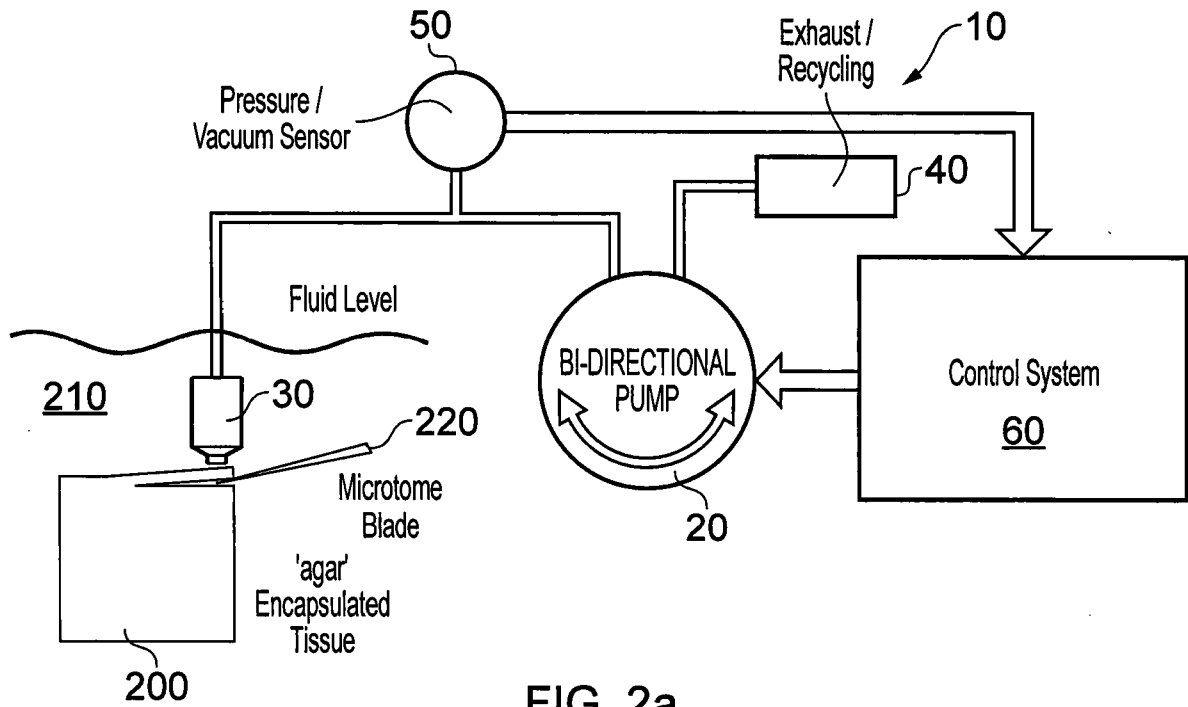


FIG. 2a

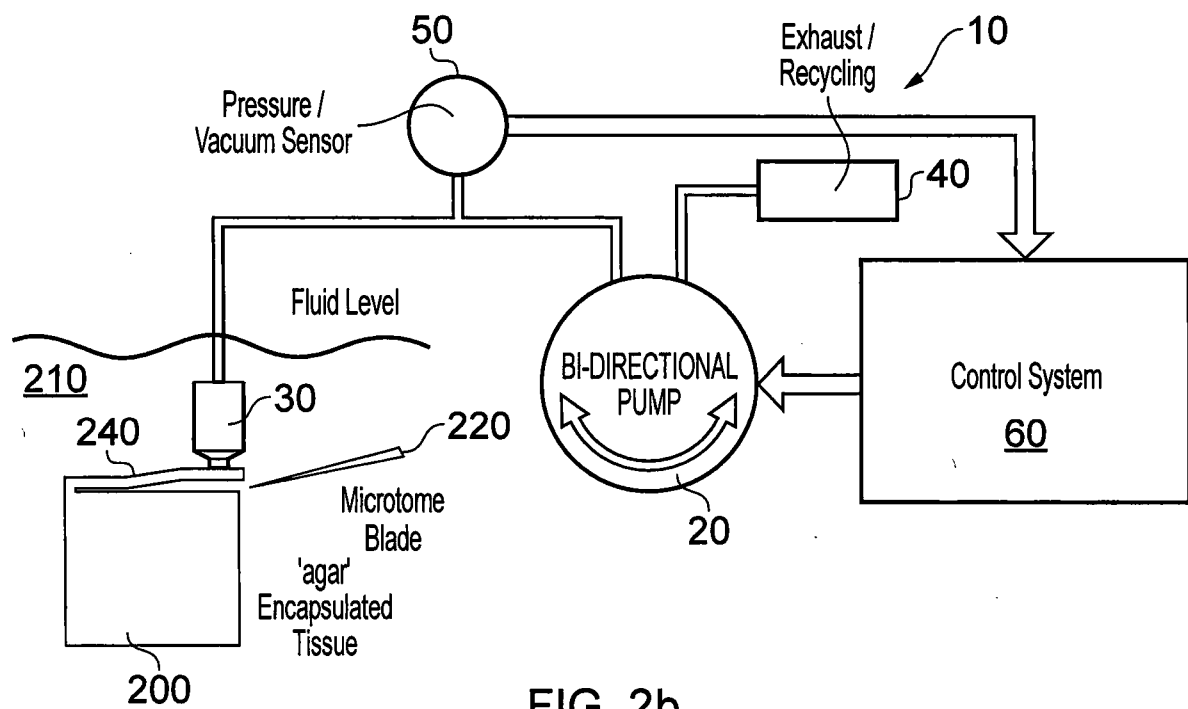


FIG. 2b

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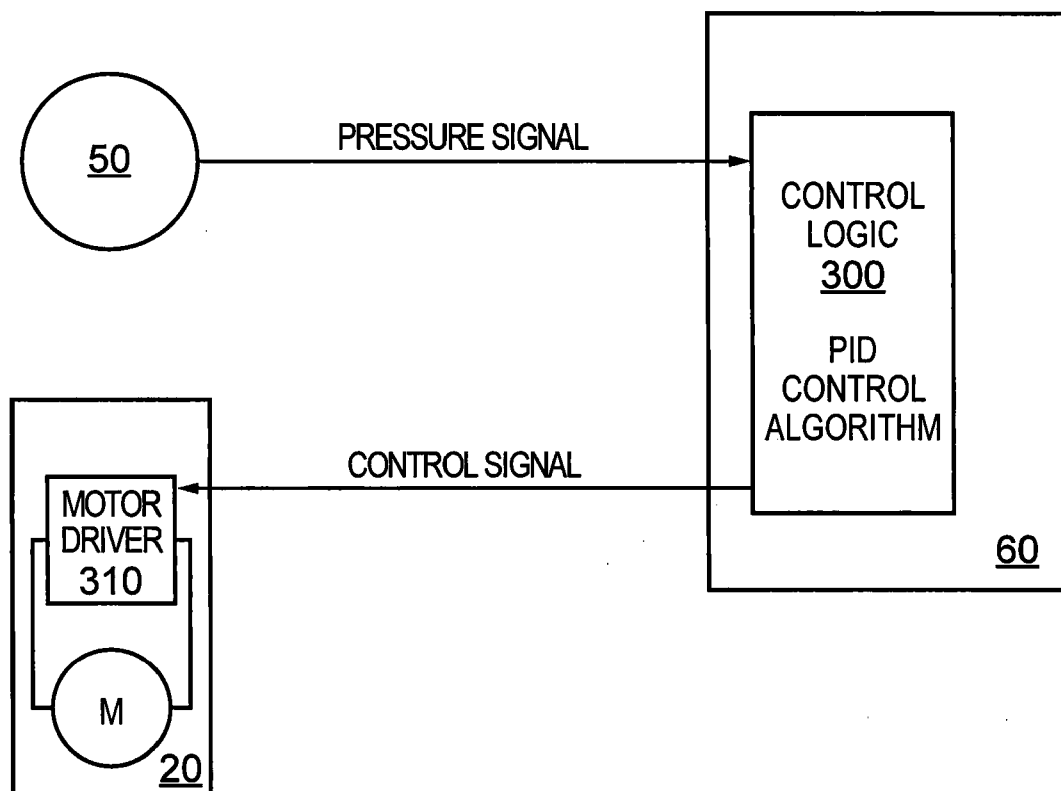


FIG. 3

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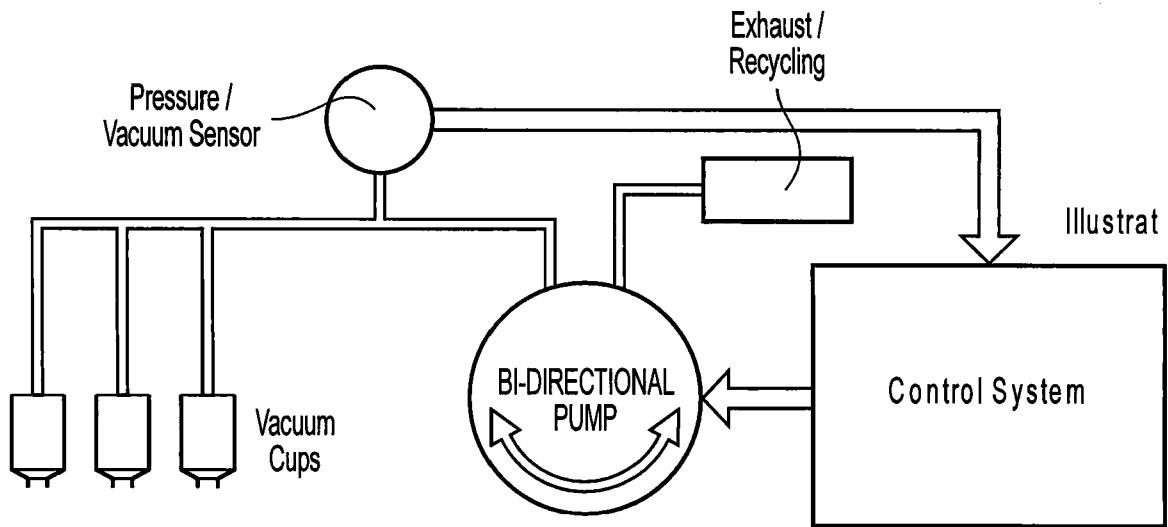


FIG. 4

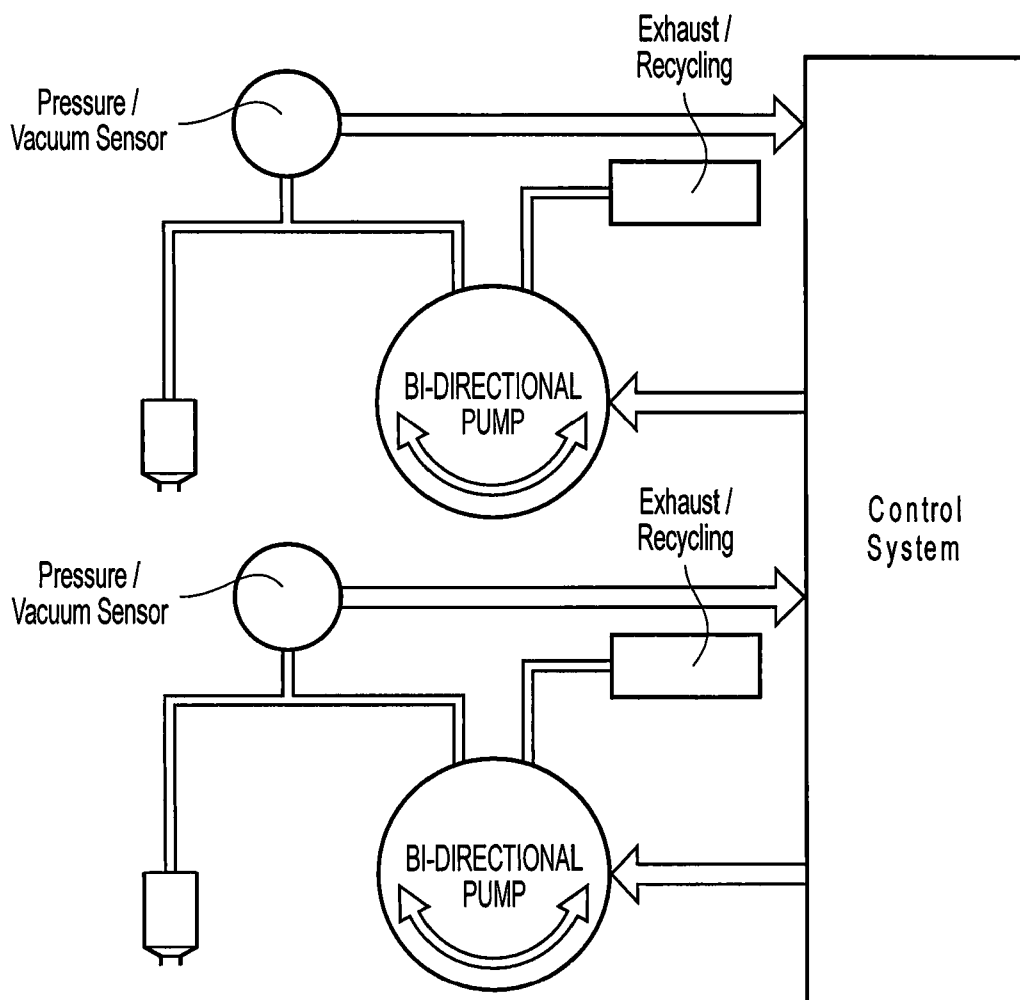


FIG. 5

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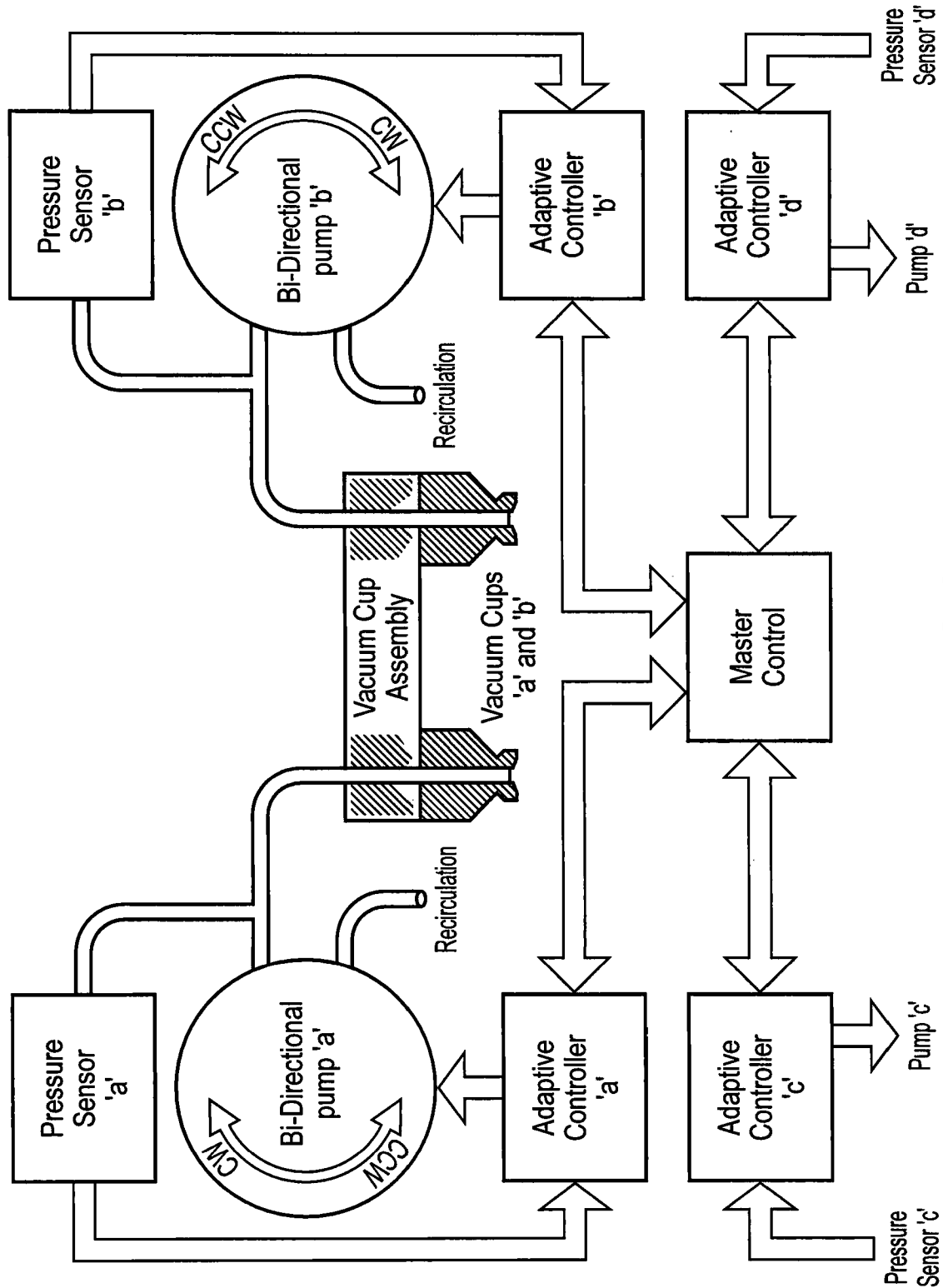


FIG. 6

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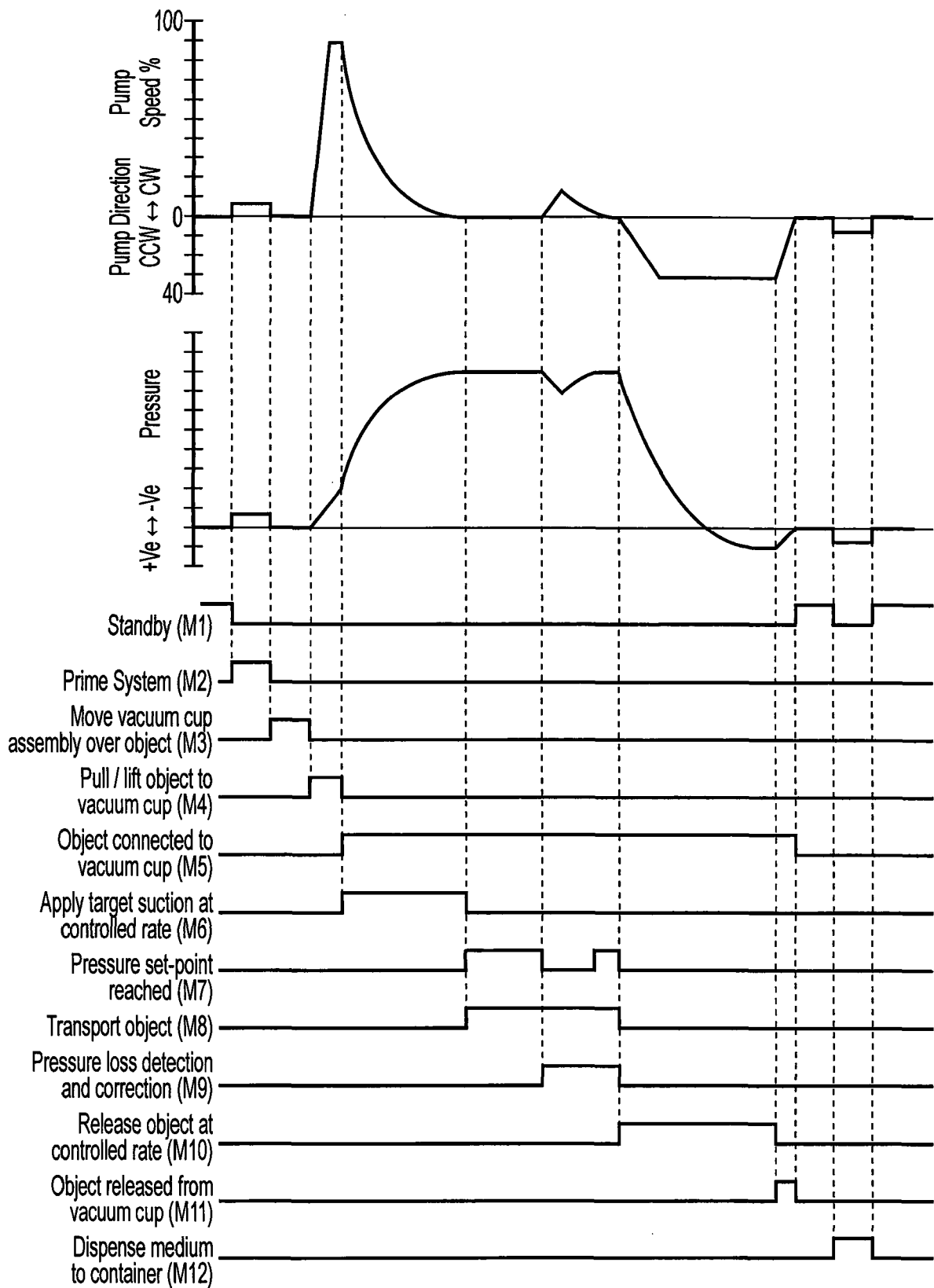


FIG. 7

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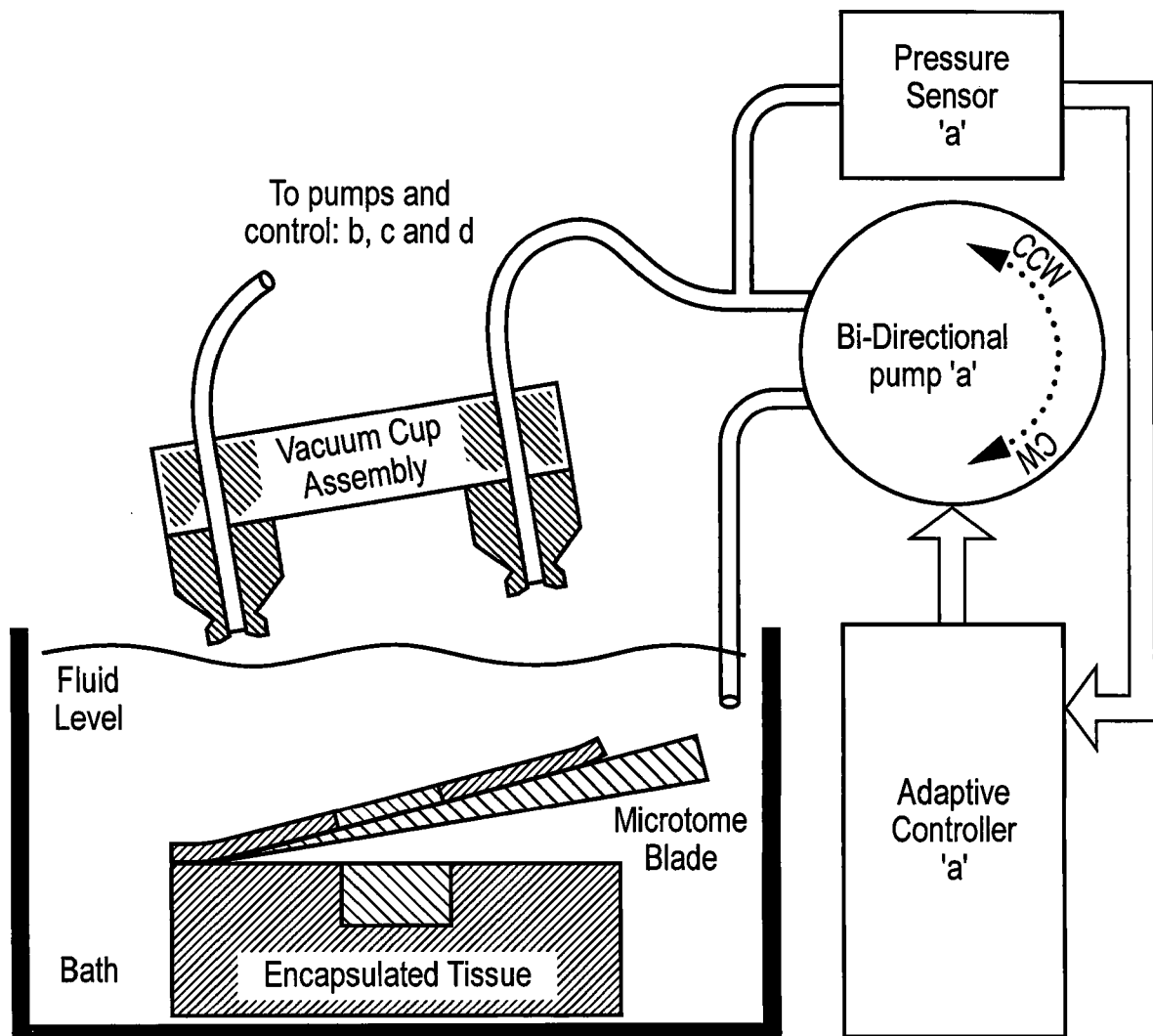


FIG. 8a

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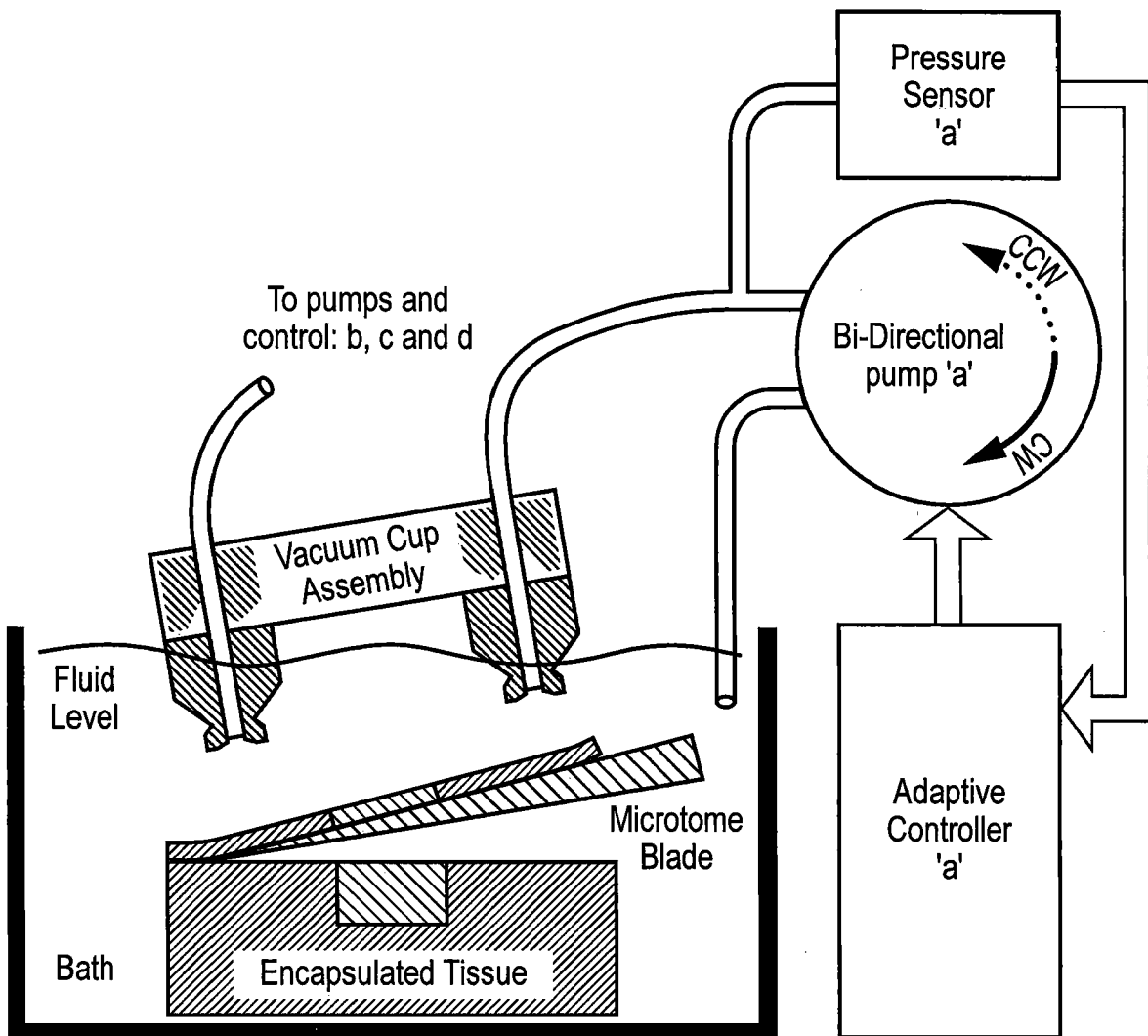


FIG. 8b

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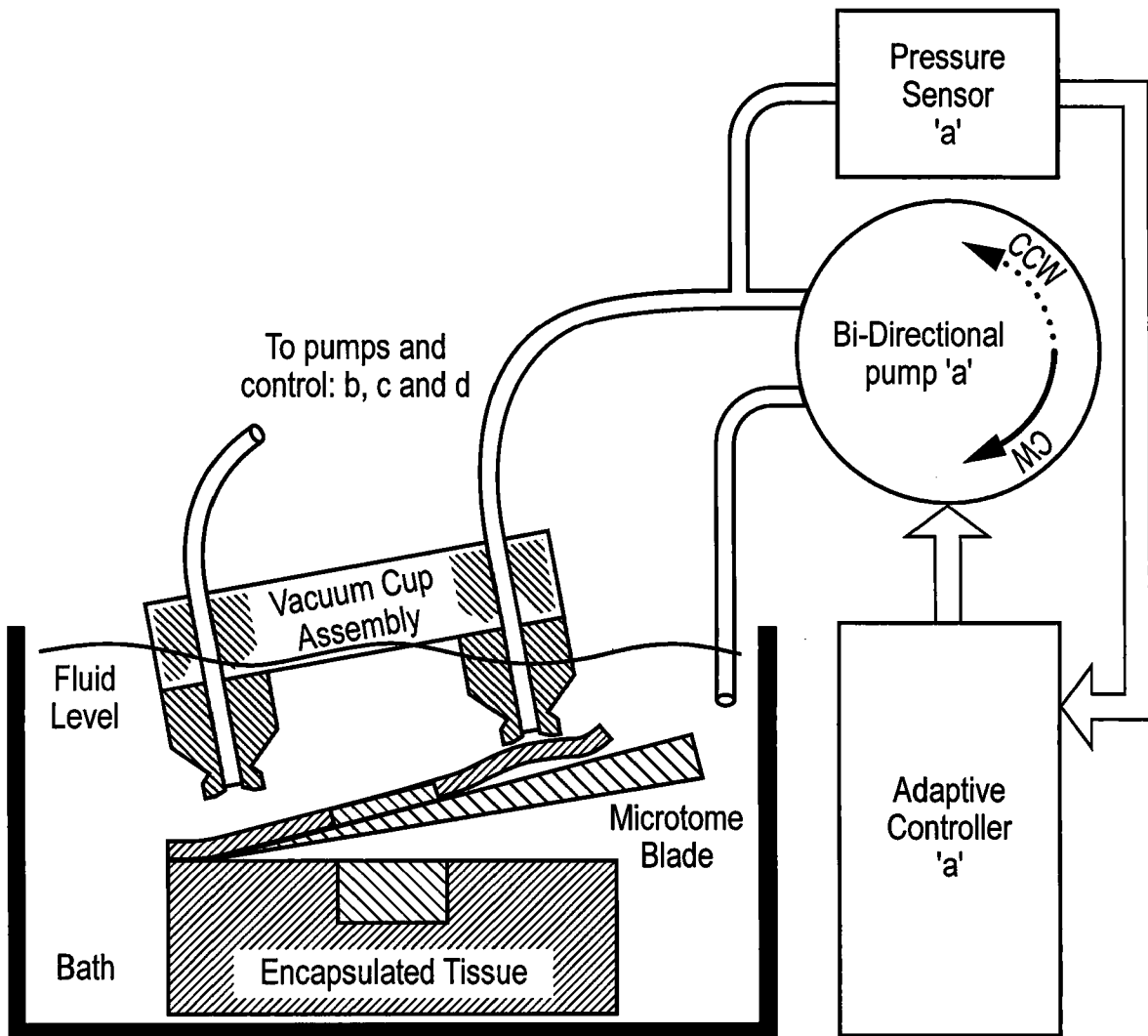


FIG. 8c

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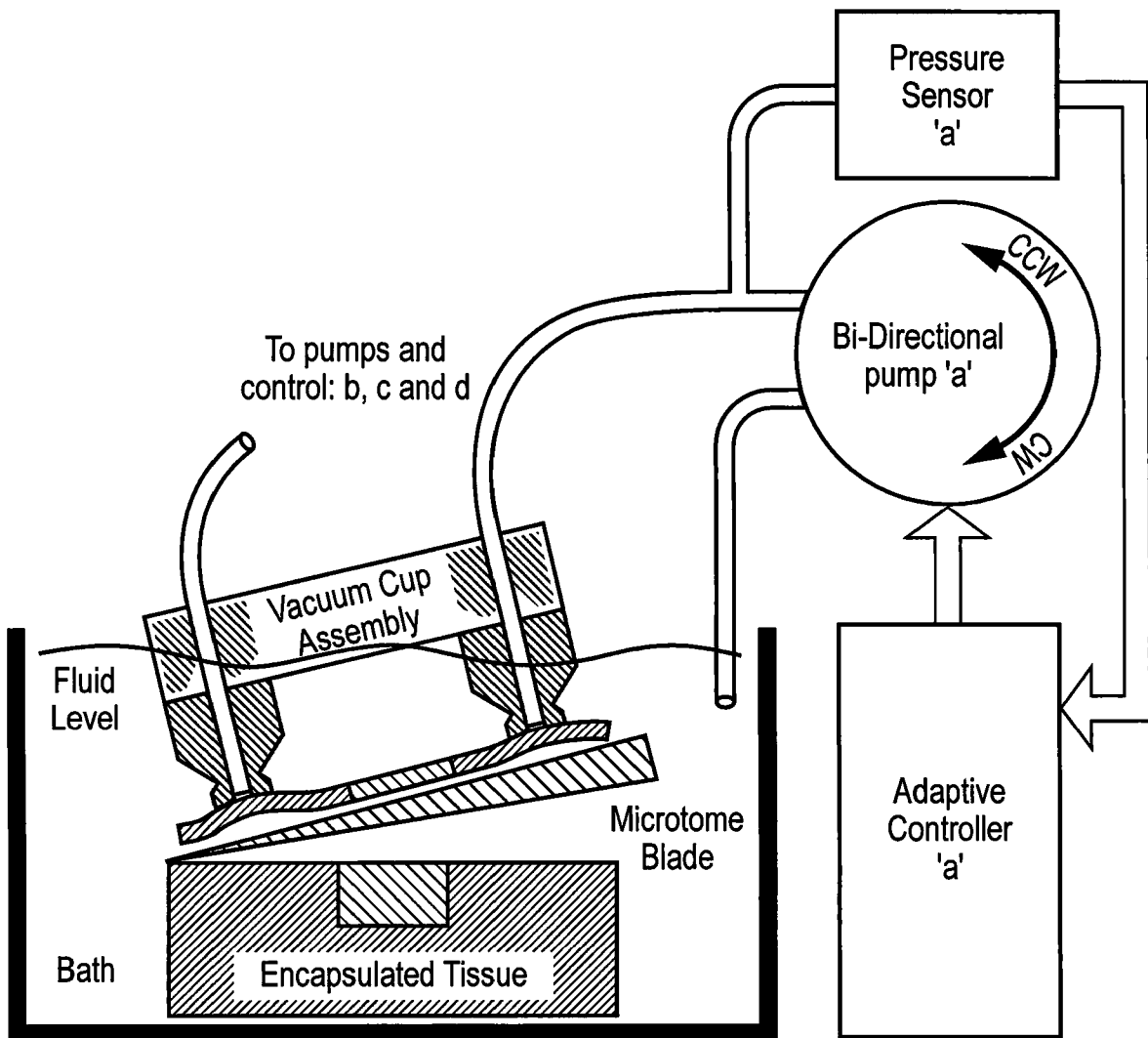


FIG. 8d

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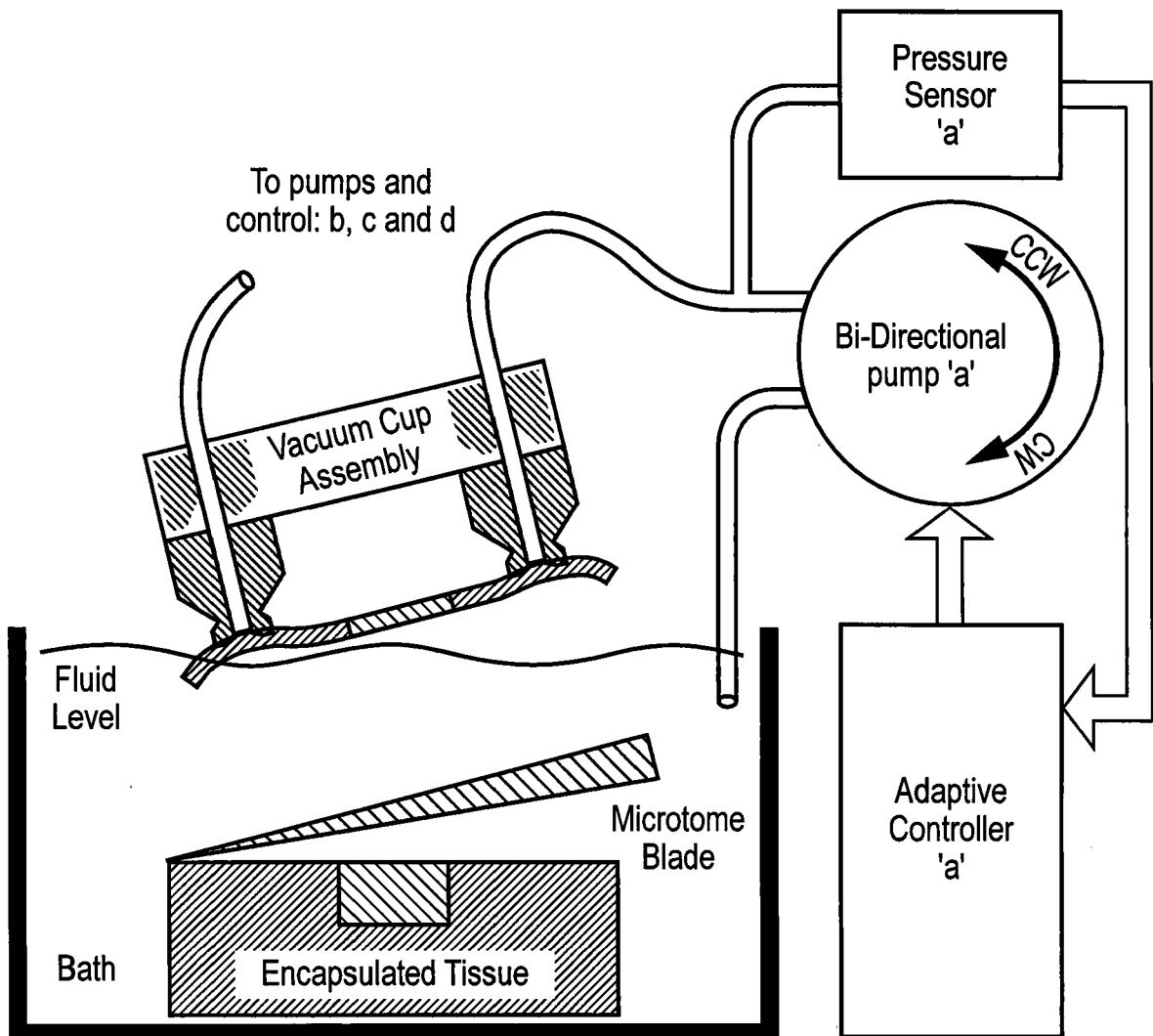


FIG. 8e

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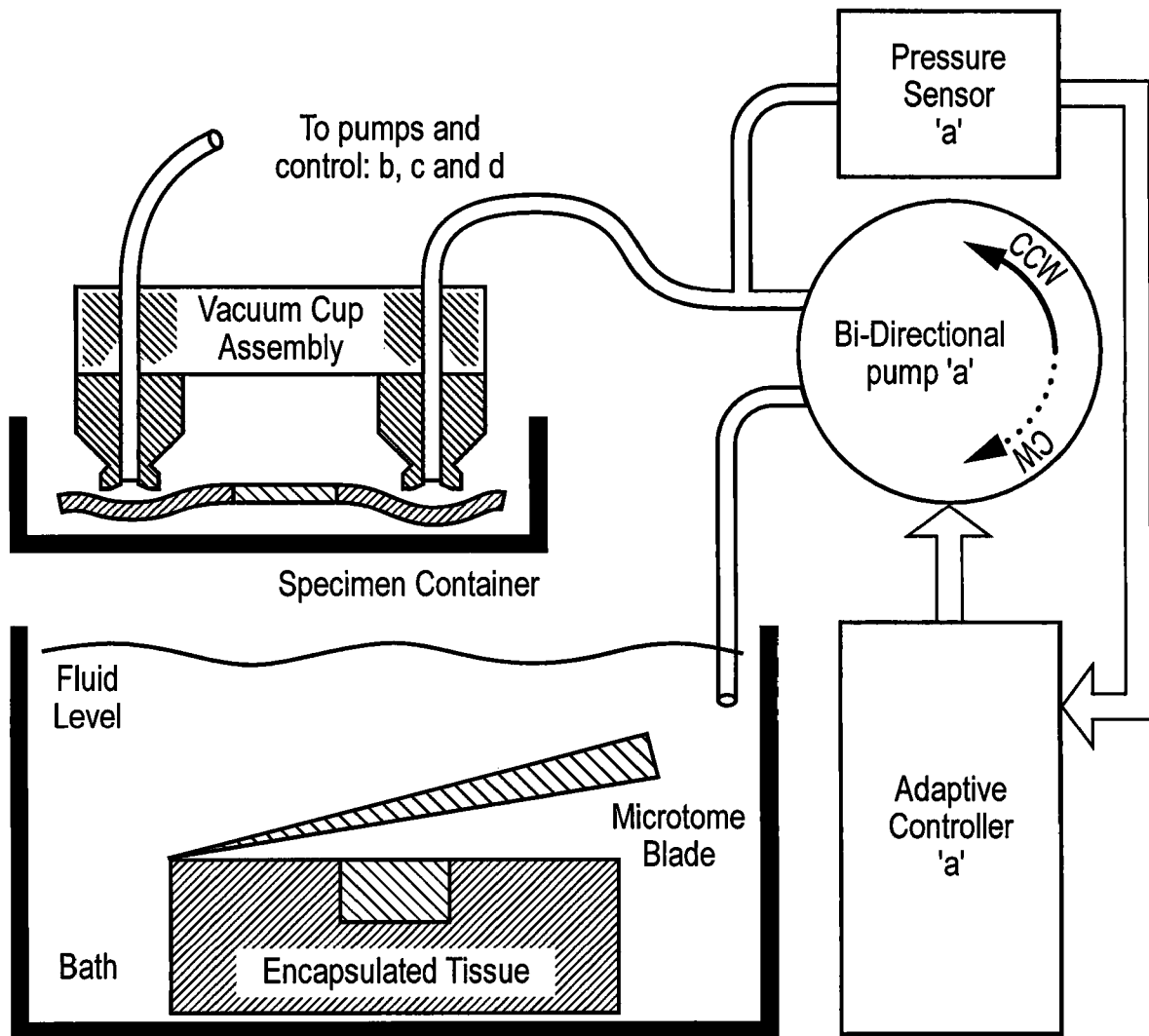


FIG. 8f

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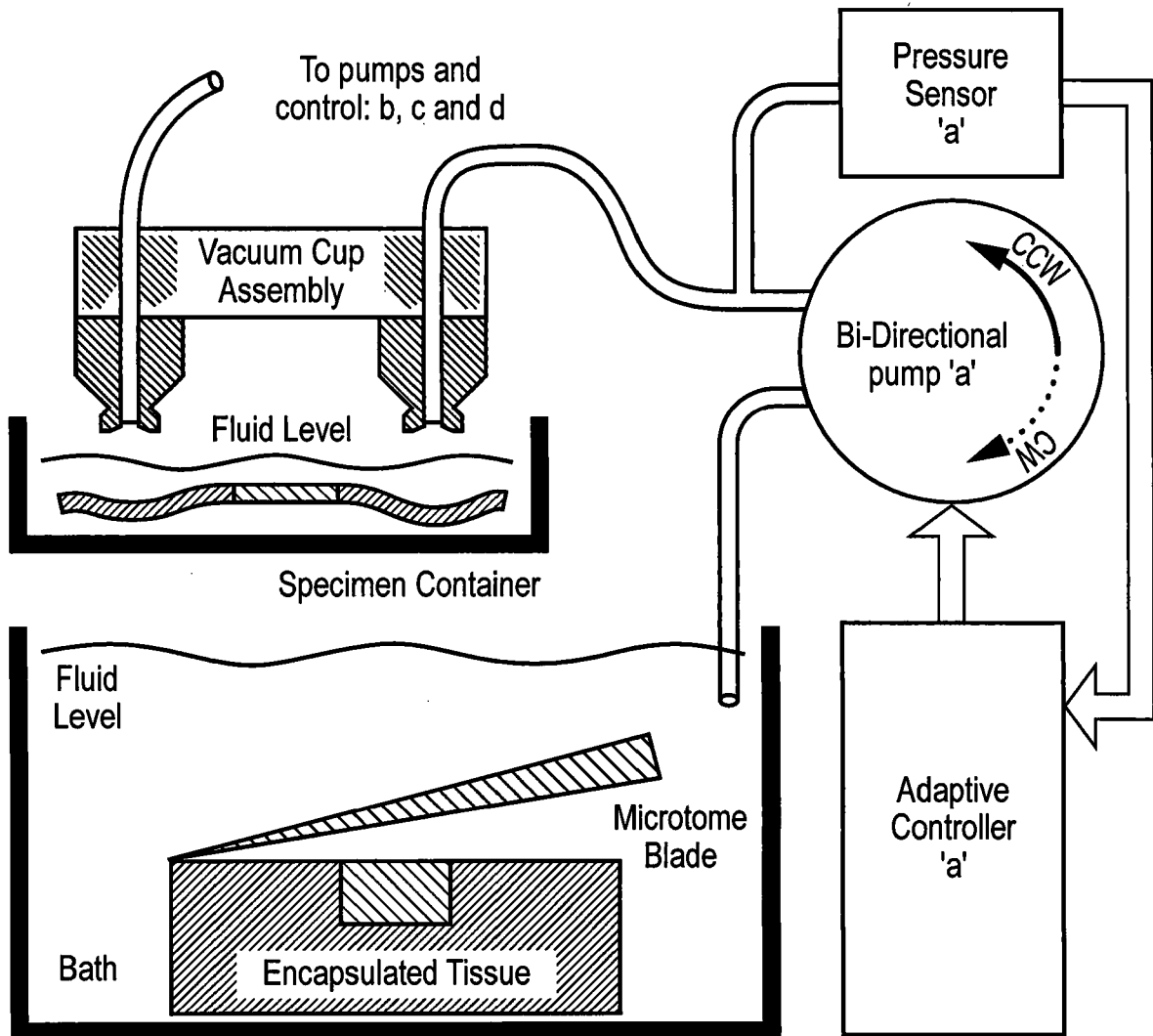


FIG. 8g

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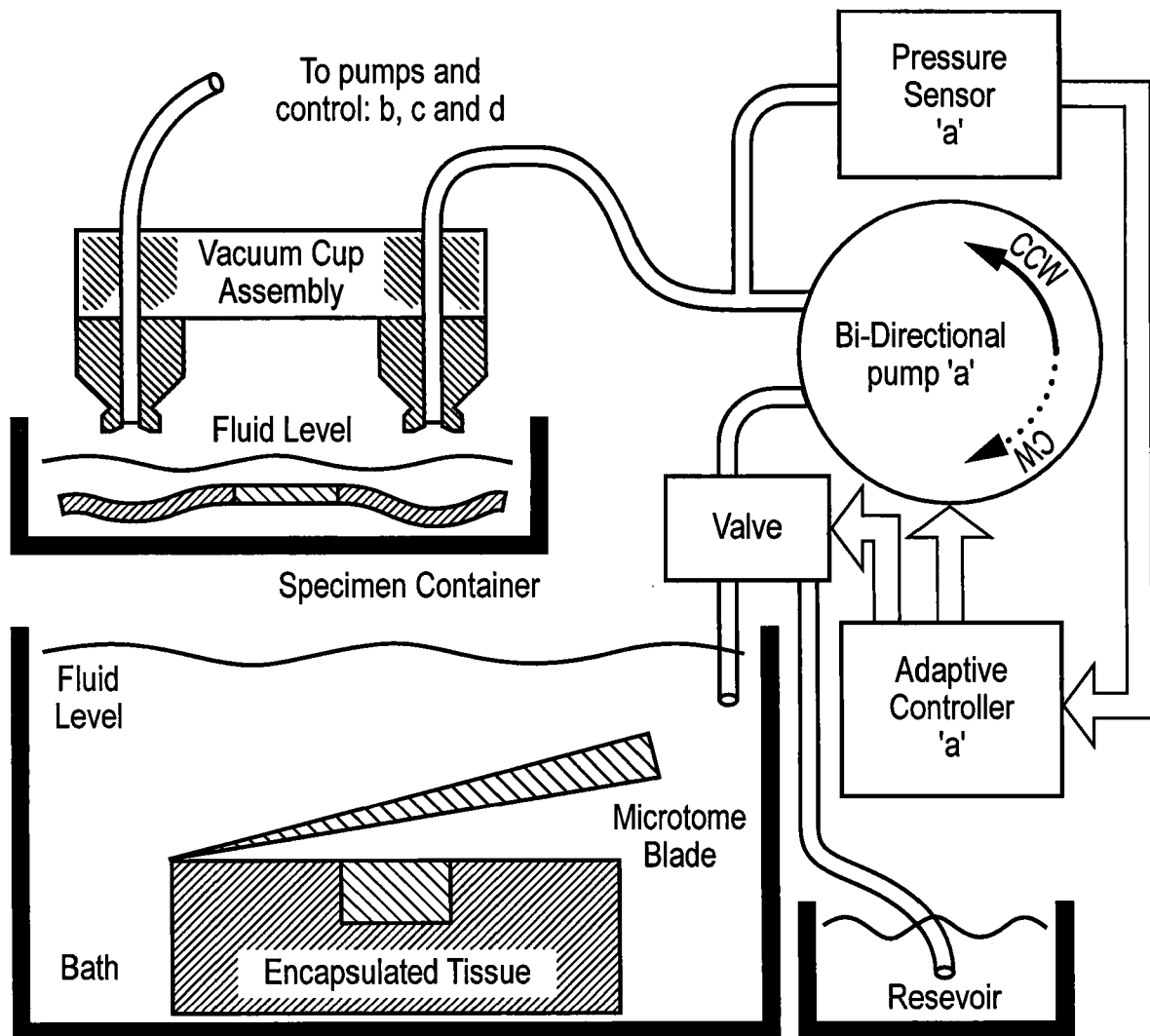


FIG. 9

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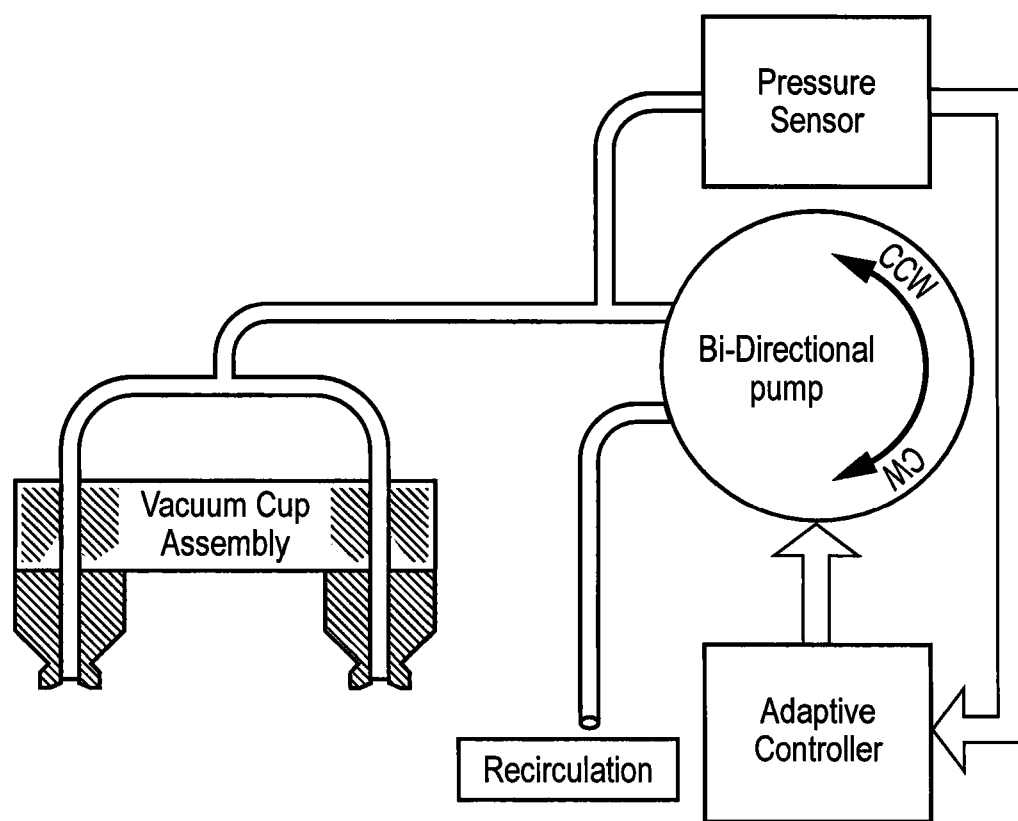


FIG. 10

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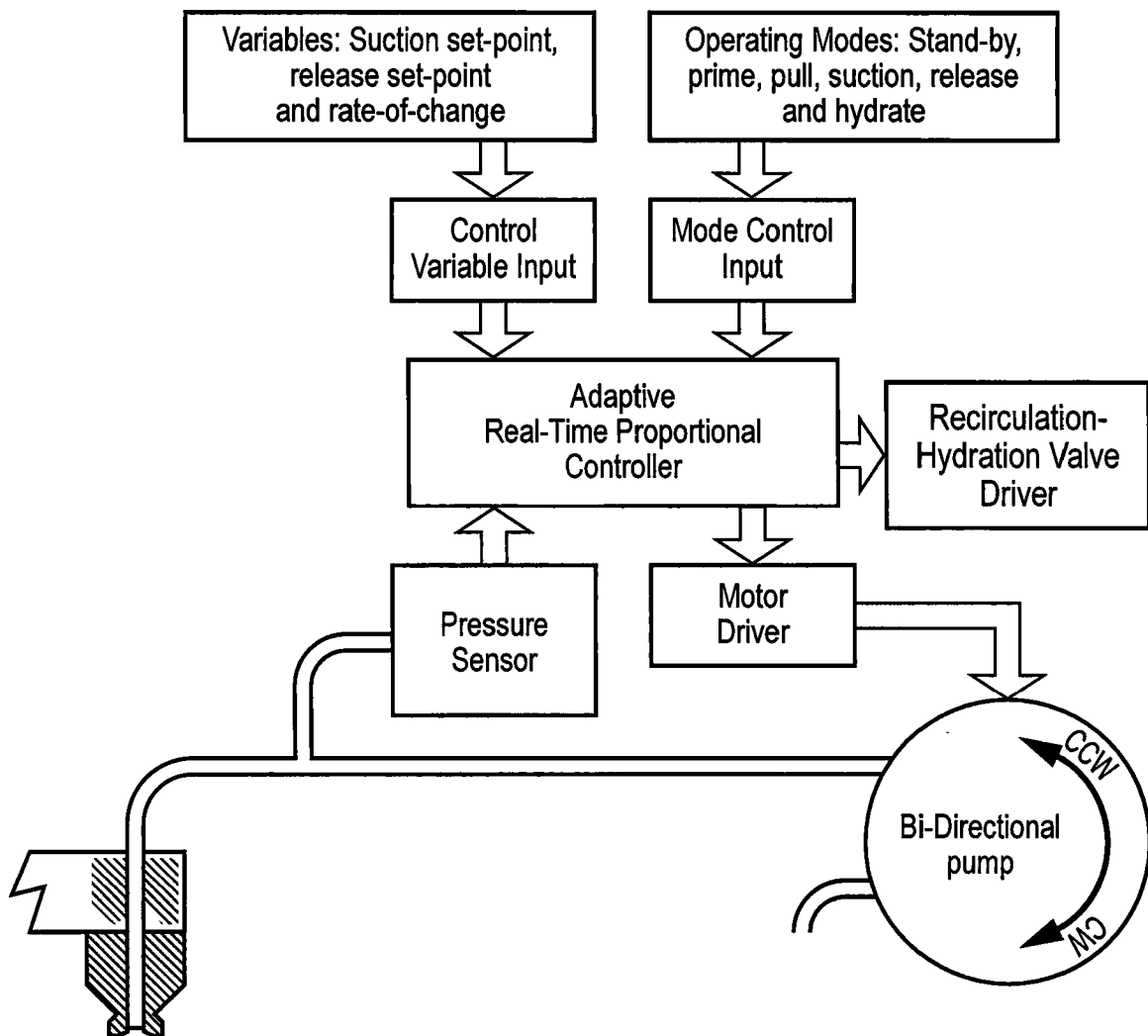


FIG. 11

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2014/051899

A. CLASSIFICATION OF SUBJECT MATTER

INV. G01N1/06

ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

G01N B25J B65G

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

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

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
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X	EP 1 733 853 A1 (KOGANEI LTD [JP]) 20 December 2006 (2006-12-20) paragraph [0042] figure 1	1,3,4,8, 16

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

☒ See patent family annex.

* Special categories of cited documents :

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

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search

16 September 2014

Date of mailing of the international search report

24/09/2014

Name and mailing address of the ISA/

European Patent Office, P.B. 5818 Patentlaan 2
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Authorized officer

Schrauwen, Annelore

INTERNATIONAL SEARCH REPORT

International application No

PCT/GB2014/051899

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

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Information on patent family members

International application No

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