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(74) Agent: VALEA AB; Lindholmpiren 5, S-417 56 Göteborg (SE).

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(71) Applicant (for all designated States except US): Q-SENSE AB [SE/SE]; Hångpilsgatan 7, S-426 77 Västra Frölunda (SE).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ROBINSON, Michael [US/US]; Omar Dr., Crownsville, Maryland 21032 (US). BJÖRN, Patrik [SE/SE]; Lådspikaregatan 12, S-GÖTEBORG 416 80 (SE).

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(54) Title: QUARTZ CRYSTAL MICROBALANCE MEMBRANE

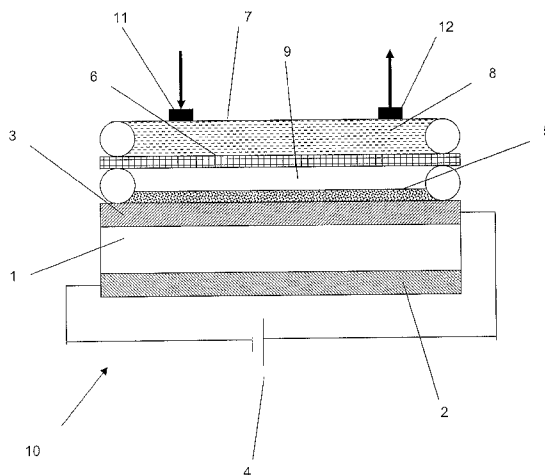


Fig. 1B

(57) Abstract: The present invention relates to a quartz crystal microbalance (QCM) detector device comprising a quartz crystal (1) sandwiched at least partly between a pair of electrodes (2) and (3) connected to a driving circuit to provide excitation of the crystal and detection of oscillations of the crystal, wherein the detector device further comprises a membrane (6) separating a first volume (7) arranged to hold a solution and an enclosed second volume (9) adjacent one side of the crystal (1) and that the membrane (6) is arranged to be vapor permeable providing a pre-determined vapor level in the second volume (9). The invention also relates to a method for controlling the relative humidity of an adsorbed sample layer at the QCM interface.

WO 2009/005452 A1

## QUARTZ CRYSTAL MICROBALANCE MEMBRANE

## TECHNICAL FIELD

The present invention relates to a quartz crystal microbalance (QCM) detector system and in particular to a QCM combined with a membrane suitable for controlling the relative  
5 humidity of the adsorbed sample layer at the QCM interface.

## BACKGROUND OF THE INVENTION

QCM is an electro acoustic method suitable for mass and viscoelastic characterization of thin films (in the nm range) of molecules such as proteins, polymers and cells at the solid/water interface.

10

A typical QCM sensor consists of a megahertz piezoelectric quartz crystal sandwiched between two gold electrodes. The crystal can be brought to resonant oscillation, and shear motions by means of A/C current between the electrodes. Since the resonant frequency ( $f$ ) can be determined with very high precision, usually less than 1 Hz, the  
15 adsorbed mass at the QCM-surface can be detected, or "balanced", down to a few  $\text{ng}/\text{cm}^2$ . It has also been shown that there is linear relation between the adsorbed rigid mass and the change in  $f$ , in an ideal air/solid situation.

In liquid, an adsorbed film may consist of a considerably high amount of water, which is  
20 sensed as a mass uptake by all QCMs. Molecules such as for example proteins at the water/QCM surface interface can also be quantified with  $f$  determination. However, adsorbed protein layers also have some degree of structural flexibility or viscoelasticity that are very difficult to interpret with simple  $f$  determination. Viscoelasticity can be visualised by measuring the energy loss, or dissipation ( $D$ ) of the shear movement of the  
25 crystal in water. A convenient principle of measuring  $D$  is to drive the crystal with A/C current at the resonant  $f$  followed by disconnection and analysis of the resulting damped sinusoidal curve. This invention of pulse assisted discrimination of  $f$  and  $D$  makes QCM measurements of adsorbed protein layers very simple and gives unique information about the hydrodynamic properties of the adsorbed protein layers and surrounding water. Very  
30 small structural and orientation changes of an adsorbed protein layer, including chemical cross-linking, can be monitored with high accuracy.

The amount of water in an adsorbed film can be as high as 95% depending on the kind of molecule and the type of surface you are studying. If molecules are elongated and adsorb

flat on the surface, little water will be coupled to the molecules. However, if they adsorb standing up at the surface, lots of water will be coupled. With QCM-D the kinetics of *both* structural changes and mass changes are obtained simultaneously.

As many of the samples which are studied using the QCM or QCM-D technology have an  
5 intrinsic water content it is sometimes important to be able to control the humidity in the sample during the experimental set up in order to obtain correct information from the experiment.

Relative humidity is defined as the ratio of the partial pressure of water vapor in a gaseous mixture of air and water vapor to the saturated vapor pressure of water at a  
10 given temperature. Relative humidity is expressed as a percentage and is calculated in the following manner:

$$RH = \frac{P(H_2O)}{P^*(H_2O)} \times 100\%$$

where

$P(H_2O)$  is the partial pressure of water vapor in the gas mixture;

15  $P^*(H_2O)$  is the saturation vapor pressure of water at the temperature of the gas mixture;

and

$RH$  is the relative humidity of the gas mixture being considered

The thermophysical properties of water-air mixtures encountered at atmospheric conditions can be reasonably approximated by assuming that they behave like a mixture  
20 of ideal gases. For many practical purposes this assumption implies that both components (air and water) behave independently of each other and therefore the physical properties of the mixture can be estimated by considering the physical properties of each component separately. This is reflected in the definition of relative humidity - only the physical properties of water are considered when determining the relative humidity of a mixture.

25 The relative humidity of a system is dependent not only on the temperature but also on the absolute pressure of the system of interest. Therefore, a change in relative humidity can be explained by a change in system temperature, a change in the absolute pressure of the system, or change in both of these system properties.

Saturated (or unsaturated) salt solutions, and certain other chemicals, can be used to  
30 generate an environment of a particular relative humidity in an enclosed space. The value

of relative humidity obtained depends on the particular chemical salt, the concentration of the solution, and the temperature of use, among other things.

The water vapor concentration, and therefore the relative humidity over a salt solution is less than that over pure water. This is because water is present in both the gas and the liquid phase, whereas the scarcely volatile salt molecules are only present in the liquid. They dilute the water and hinder escape of water molecules into the air. The rate of return of water molecules to the liquid surface is proportional to their concentration in the gas, where there are no salt ions to interfere. The system therefore adjusts to equilibrium where there are fewer water molecules in the air than there would be over a pure water surface. The RH is therefore lower than 100%.

This argument applies to all salt solutions, saturated or not. The reason for using saturated solutions, in contact with an excess of salt, is that the concentration theoretically remains constant even if water enters or leaves the solution from the air. Each hydrated salt or saturated salt solution gives a discrete relative humidity at a given temperature. These have long been used as buffering devices to control the relative humidity of closed systems.

However open humidifying devices always represent a potential source of contamination of the samples. Contamination by salt solution spills must be absolutely prevented, since it can destroy samples or lead to false experimental results.

The present invention provides a method whereby the relative humidity surrounding the adsorbed sample layer at the QCM surface can be precisely controlled without risking contamination of the sample.

#### SUMMARY OF THE INVENTION

The present invention has advantages against known technology in that it is possible to provide a controlled level of vapour level for a surface and that this level may be changed continuously during an experiment. Furthermore, it is possible to provide a small volume of and small dimensions of the experimental chamber.

The invention relates particularly to a quartz crystal microbalance (QCM) detector device for characterization of material properties of a sample, comprising a quartz crystal (1) sandwiched at least partly between a pair of electrodes (2) and (3) connected to a driving circuit to provide excitation of the crystal and detection of oscillations of the crystal, wherein the detector device further comprises a membrane (6) separating a first volume

(7) arranged to hold a solution (8) and an enclosed second volume (9) adjacent one side of the crystal (1) and that the membrane (6) is arranged to be vapor permeable providing a pre-determined vapor level in the second volume (9).

5 In one embodiment of the invention the membrane (6) is water vapour-permeable.

In another embodiment of the invention the membrane (6) is microporous having pores with a diameter of less than 0.04 microns.

10 In yet another embodiment of the invention the membrane (6) is a Gore-Tex® membrane.

In one embodiment of the invention the solution (8) is a salt solution of one or more salts.

In another embodiment of the invention the salt solution (8) is a saturated salt solution.

15

In yet another embodiment of the invention the salt solution (8) is modified with a soluble non-electrolyte.

In one embodiment of the invention the first volume (7) is fitted with an inlet (11) and  
20 outlet (12) system.

In another embodiment of the invention the inlet (11) or outlet (12) of the first volume (7) is provided with a pumping device.

25 In yet another embodiment of the invention the first volume (7) is fitted with a temperature control device.

The invention also relates to a method for measuring the material characteristics of an adsorbed sample on a quartz crystal (1) of a QCM using the device described above,

30 wherein the method is

providing a solution (8) of known characteristics in a first volume (7);  
allowing vapour from the solution (8) diffusing through a vapour porous membrane (6) into a second volume (9) adjacent to a quartz crystal (1);  
obtaining a determined vapour level in the second volume;

adsorbing molecules from the vapour directly or indirectly on the quartz crystal (1) surface; and  
detecting changes of mechanical characteristics of the quartz crystal (1);

- 5 In one embodiment of the invention solutions (8) providing different relative humidities are continuously pumped into and out from the first volume (7) so as to create a gradient of increasing or decreasing relative humidity during the measurement.

In another embodiment of the invention the solution (8) is thermostatically controlled so as  
10 to create a gradient of increasing or decreasing relative humidity during which the measurements can be obtained.

#### BRIEF DESCRIPTION OF THE DRAWINGS

In the following the invention will be described in a non-limiting way and in more detail  
15 with reference to exemplary embodiments illustrated in the enclosed drawings, in which:

Fig. 1A illustrates schematically an embodiment of the QCM solution according to the present invention; and

Fig. 1B illustrates schematically a further embodiment of the QCM solution according to  
20 the present invention; and

Fig. 2 illustrates schematically a QCM system according to the present invention.

#### DETAILED DESCRIPTION OF PREFERRED EMBODIMENTS

25 The quartz crystal microbalance (QCM) has been used for a long time to monitor thin film deposition in vacuum or gas. After it was shown that the QCM may be used in the liquid phase, the number of applications for the QCM has increased dramatically.

With reference to Fig. 1A wherein the 1 reference numeral 10 generally refers to a quartz crystal microbalance (QCM) setup. A QCM consists of a thin quartz crystal 1 sandwiched  
30 between a pair of electrodes 2 and 3. Due to the piezoelectric properties of quartz, it is possible to excite the crystal to oscillation by applying an AC voltage 4 across its electrodes. The resonance frequency ( $f$ ) of the crystal depends on the total oscillating mass, including the water coupled to the oscillation. When a thin film 5 of a sample is attached to the sensor crystal, the frequency decreases. If the film 5 is thin and rigid the

decrease in frequency is proportional to the mass of the film. Thus, the QCM operates as a very sensitive balance. However, details about the QCM measurement principle are well published in the literature and will not be elaborated upon here.

The QCM system according to the present invention may be equipped to measure other  
5 physical parameters using optional add on equipment, for instance it may further comprise a light source for generating a beam of light and a light detector for detecting the light from the light source (not shown) allowing for measuring optical properties of the sample in question.

A chamber (a first volume) 7 containing a solution 8 of one or more salts is arranged to  
10 provide an atmosphere of predetermined or known humidity around the adsorbed film 5. The type of chamber used is at the option of the user, but the chamber 7 should preferably be sealed in order to avoid excessive water evaporation from the solution to the environment.

As discussed above, it is well known that saturated salt solutions have well-defined  
15 equilibrium vapor pressures, supporting well-defined equilibrium relative humidities. Such solutions are sometimes referred to as constant humidity solutions. The saturated salt solution, made up as a slushy mixture with distilled water and chemically pure salt is enclosed in the chamber. At any temperature the concentration of a saturated solution is fixed and by providing excess solute the solution will remain saturated even in the  
20 presence of modest moisture sources and sinks. When part of the solute is a solid in the pure liquid phase, it is easy to determine that the solution is saturated. The chamber 7 is fitted with an inlet 11 and outlet 12 system providing means for filling and emptying the chamber of the salt solution. Optionally the inlet 11 and outlet 12 of the chamber 7 can be fitted with a pumping device (not shown) which continuously or intermittently pumps salt  
25 solutions containing different salts providing different relative humidity levels (see table 1 below) into the chamber in order to provide a gradient of increasing or decreasing relative humidity during which the measurements can be obtained.

The temperature of the salt solution 8 can be controlled in a number of ways. For example  
30 the chamber 7 with the salt solution 8 can be fitted with a thermostat or the chamber can be submerged in a thermostatically controlled external water bath. Alternatively the chamber can also be fitted with a pump system with a heating coil through which the salt solution can circulate (not shown). This will also provide a system with a gradually changing relative humidity as an increase or decrease of the temperature of the salt  
35 solution will gradually change the relative humidity in the closed chamber 7 together with

the experimental conditions. The invention is however not limited to these described examples but can be realized in any suitable manner which will bring the salt solution to the required temperature.

- 5 Salts which can be used to provide specifically defined equilibrium water pressures can be found in the literature. Table 1 lists some well known salts suitable for this purpose. The table also includes the range of relative humidity (RH) each salt will provide and at which temperature ranges they can be obtained.

10 Table 1

Saturated Salt Solution	Relative Humidity (RH) (%)	Temperature range used for the RH (°C)
Lithium Chloride (LiCl)	11.23±0.54 - 9.90±0.77	0 to 100
Potassium Acetate (KC <sub>2</sub> H <sub>3</sub> O <sub>2</sub> )	23.28±0.53 - 21.61±0.53	10 to 30
Magnesium Chloride (MgCl <sub>2</sub> )	33.66±0.33 - 21.97±0.60	0 to 100
Potassium Carbonate (K <sub>2</sub> CO <sub>3</sub> )	43.13±0.66 - 43.17±0.50	0 to 30
Magnesium Nitrate (Mg(NO <sub>3</sub> ) <sub>2</sub> )	60.35±0.55 - 45.44±0.60	0 to 50
Sodium Chloride (NaCl)	75.51±0.34 - 76.29±0.65	0 to 80
Potassium Chloride (KCl)	88.61±0.53 - 78.50±1.0	0 to 90
Potassium Nitrate (KNO <sub>3</sub> )	95.33±2.9 - 84.78±2.5	0 to 50
Potassium Sulphate (K <sub>2</sub> SO <sub>4</sub> )	98.77±1.1 - 95.82±0.45	0 to 50

The salt 8 is thus chosen to provide the desired relative humidity. If no saturated salt solution gives precisely the relative humidity desired, the solution can be modified by adding another component. Addition of a soluble non-electrolyte always lowers the equilibrium relative humidity over the solution. A non-electrolyte is a substance with molecules that do not in solution dissociate to ions, and, therefore do not carry an electric current. Ethanol (ethyl alcohol) is an example of a non-electrolyte. Therefore, if one cannot find a salt that supports the desired relative humidity, one selects a salt that supports a slightly higher relative humidity, and then adds a soluble non-electrolyte in such quantity as to lower the relative humidity to the desired level. While it would be possible to add a judiciously chosen second salt to a saturated salt solution, it is better to use a soluble non-electrolyte. When mixed salt solutions are generated, the effects are complex, and differ depending on exactly which salts are involved. The situation is much simpler and more easily controlled when a soluble non-electrolyte is added. The

equilibrium relative humidity of the modified solution may be calculated to a first approximation as the product of the equilibrium relative humidity (as a decimal fraction) of the unmodified saturated salt solution and that of a solution of the soluble non-electrolyte in the concentration it is to be used.

5

Between the surface of the adsorbed film 5 and the saturated salt solution 8 is provided a membrane 6. The membrane 6 can either be inherently water vapour-permeable, i.e., water molecules pass directly through the material of the membrane, or it can be impermeable to the solution but microporous, i.e., it has microscopic pores in it through which water molecules can pass. Any microporous film which allows the transmission of water vapour without allowing the solution itself to pass through the film could be used. Microporous membranes 6 have pores with a diameter of about 0.02 microns to allow water vapour to pass through it. The pore diameter should be less than 0.04 microns because of the possibility of wicking of moisture through larger pores, thus risking the contamination of the adsorbed film 5, but any film or membrane with sufficiently high water vapour permeability can be used. A particularly preferred film of this type is the Gore-Tex® membrane.

The air space in the chamber 7, immediately above a saturated salt solution will after a certain time reach an equilibrium relative humidity. Preferably this space is as small as possible so that the time it takes to reach the equilibrium is short (Fig 1A). With a good membrane, such as the Gore-Tex® membrane, it is possible to turn the chamber up-side down so that there is no air space between the surface of the solution 8 and the membrane 6 (Fig. 1B). Water molecules evaporate from the salt solution until the characteristic relative humidity of the air above the saturated salt solution at the given temperature is attained. As the water vapour reaches the membrane 6, water molecules will pass through the membrane and fill up the space 9 between the quartz crystal with the adsorbed sample layer 5 and the membrane 6. Again it is advantageous if this space 9 is as small as possible in order to quickly reach equilibrium relative humidity. A benefit of having a membrane 6 is that it will prevent any contact between the adsorbed sample 5 and the salt solution 9, while at the same time providing an evenly distributed relative humidity around the adsorbed sample 5.

In another alternative use of the present invention, different membranes may be evaluated using the above experimental set-up. If a known film with a known behaviour is adsorbed

on the surface of the crystal, its response can be compared when using different membranes, having differing pore size, thickness or surface coatings.

Fig. 2 illustrates a QCM system 200. The QCM setup 10 may be located in a casing 201 comprising the QCM sensor crystal (i.e. quartz crystal and electrodes) together with signal source and electronics for driving the signal source, for signal treatment (e.g. pre amplification and noise elimination or reduction), and/or interface electronics for interfacing 204 to a signal analysis setup 202. The signal analysis setup 202 in turn may be connected 205 to a computer terminal 203 for further analysis. The signal analysis setup 202 may be provided for amplification, averaging, and/or filtering of signals and for digitization of signals prior to being connected to the computer terminal. It should be appreciated that the casing 201 is provided only for protective purposes and that all electronics may be located in the signal analysis setup 202 which also may be provided inside the casing 201.

15

The present invention finds applicability in testing how certain materials react to vapour, e.g. how paint films react to water molecules.

It should be noted that the word "comprising" does not exclude the presence of other elements or steps than those listed and the words "a" or "an" preceding an element do not exclude the presence of a plurality of such elements. It should further be noted that any reference signs do not limit the scope of the claims, and that several "means", "units" or "devices" may be represented by the same item of hardware.

25 The above mentioned and described embodiments are only given as examples and should not be limiting to the present invention. Other solutions, uses, objectives, and functions within the scope of the invention as claimed in the below described patent claims should be apparent for the person skilled in the art.

30

## CLAIMS

1. A quartz crystal microbalance (QCM) detector device for characterization of material properties of a sample, comprising a quartz crystal (1) sandwiched at least partly between a pair of electrodes (2) and (3) connected to a driving circuit to provide excitation of the crystal and detection of oscillations of the crystal, characterized in that the detector device further comprises a membrane (6) separating a first volume (7) arranged to hold a solution (8) and an enclosed second volume (9) adjacent one side of the crystal (1) and that the membrane (6) is arranged to be vapor permeable providing a pre-determined vapor level in the second volume (9).
2. The QCM device according to claim 1, characterized in that the membrane (6) is water vapour-permeable.
3. The QCM device according to claim 1, characterized in that the membrane (6) is microporous having pores with a diameter of less than 0.04 microns.
4. The QCM device according to claim 1, characterized in that the membrane (6) is a Gore-Tex® membrane.
5. The QCM device according to claim 1, characterized in that the solution (8) is a salt solution of one or more salts.
6. The QCM device according to claim 5, characterized in that the salt solution (8) is a saturated salt solution.
7. The QCM device according to claim 5, characterized in that the salt solution (8) is modified with a soluble non-electrolyte.
8. The QCM device according to claim 1, characterized in that the first volume (7) is fitted with an inlet (11) and outlet (12) system.
9. The QCM device according to claim 1, characterized in that the inlet (11) or outlet (12) of the first volume (7) is provided with a pumping device.

10. The QCM device according to claim 1, characterized in that the first volume (7) is fitted with a temperature control device.
11. A method for measuring the material characteristics of an adsorbed sample on a quartz crystal (1) of a QCM using the device of claim 1, characterized in that
- providing a solution (8) of known characteristics in a first volume (7);
  - allowing vapour from the solution (8) diffusing through a vapour porous membrane (6) into a second volume (9) adjacent to a quartz crystal (1);
  - obtaining a determined vapour level in the second volume;
  - adsorbing molecules from the vapour directly or indirectly on the quartz crystal (1) surface; and
  - detecting changes of mechanical characteristics of the quartz crystal (1);
12. The method according to claim 11, characterized in that solutions (8) providing different relative humidities are continuously pumped into and out from the first volume (7) so as to create a gradient of increasing or decreasing relative humidity during the measurement.
13. The method according to claim 11, characterized in that the solution (8) is thermostatically controlled so as to create a gradient of increasing or decreasing relative humidity during which the measurements can be obtained.

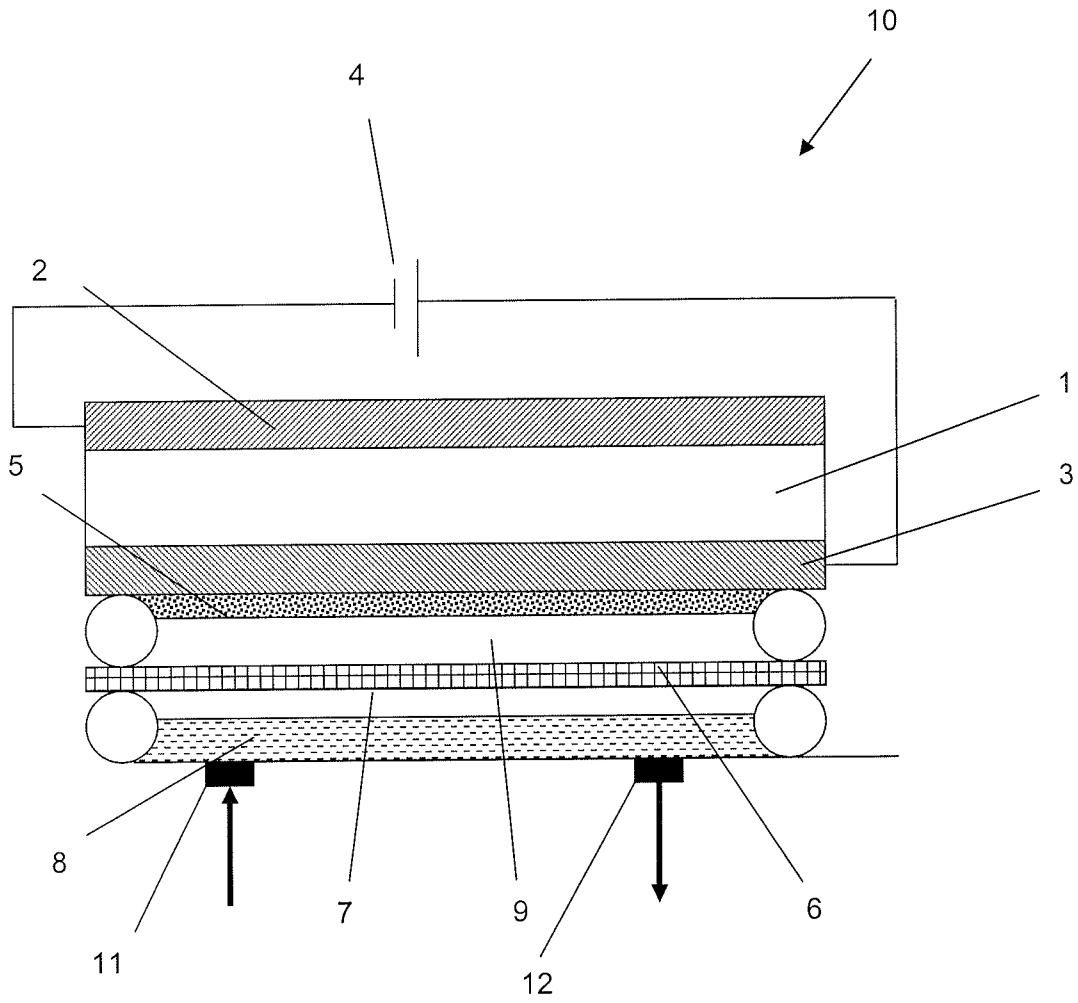


Fig. 1A

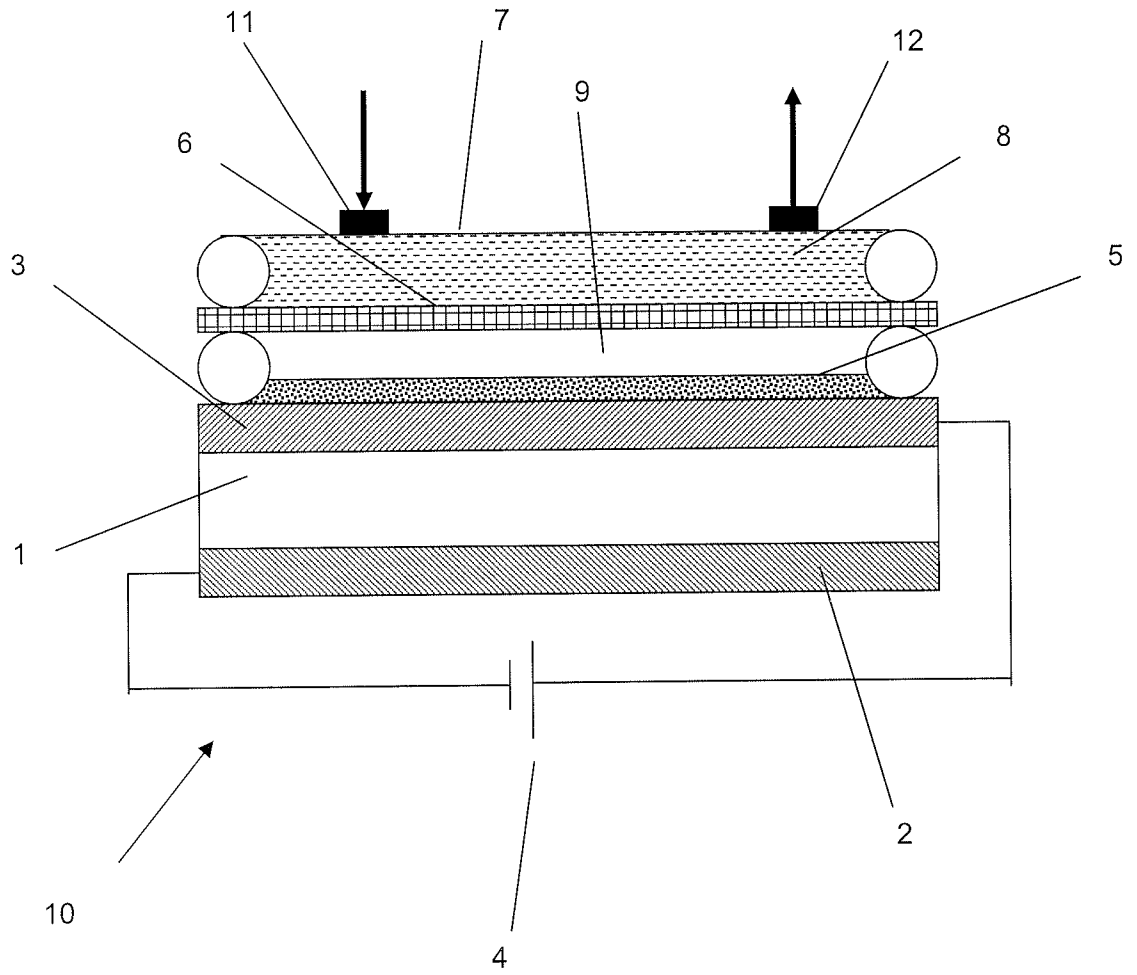


Fig. 1B

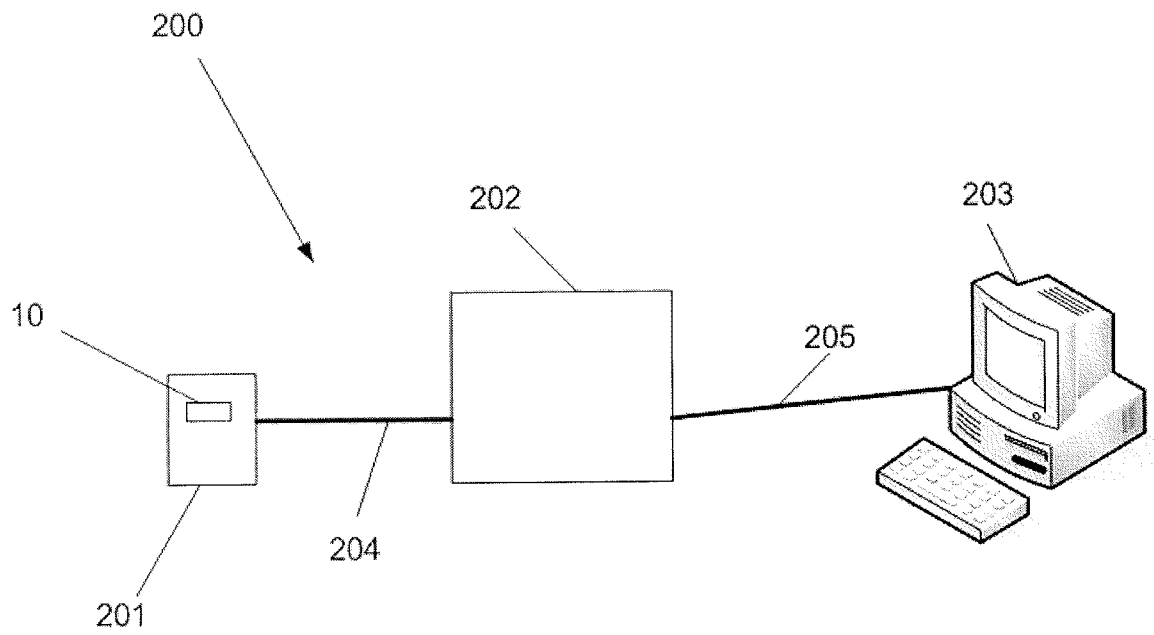


Fig. 2

**INTERNATIONAL SEARCH REPORT**

International application No.

**PCT/SE2008/050764**

**A. CLASSIFICATION OF SUBJECT MATTER**

**IPC: see extra sheet**

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

**B. FIELDS SEARCHED**

Minimum documentation searched (classification system followed by classification symbols)

**IPC: G01G, G01N**

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

**SE,DK,FI,NO classes as above**

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

**EPO-INTERNAL, WPI DATA, PAJ**

**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 20050028593 A1 (RODIER, DANIEL), 10 February 2005 (10.02.2005), figure 2B, paragraphs [0027], [0052]  --	1-13
Y	US 6251344 B1 (GOLDSTEIN, MARK K.), 26 June 2001 (26.06.2001), column 4, line 5 - line 37; column 5, line 9 - line 18; column 12, line 1 - line 11, column 13, line 28 - line 35, figure 9  --	1-13
A	GB 2255190 A (GREAVES, PETER), 28 October 1992 (28.10.1992), abstract  --	1-13

Further documents are listed in the continuation of Box C.

See patent family annex.

\* Special categories of cited documents:

- "A" document defining the general state of the art which is not considered to be of particular relevance
- "E" earlier application or patent but published on or after the international filing date
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- "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
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Date of the actual completion of the international search

**13 October 2008**

Date of mailing of the international search report

**16-10-2008**

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## INTERNATIONAL SEARCH REPORT

International application No.

PCT/SE2008/050764

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	EP 0363194 A2 (PHILIP MORIS PRODUCTS INC.), 11 April 1990 (11.04.1990), page 5, line 25 - line 40, abstract  --	1-13
A	DE 2247505 A1 (VEB KOMBINAT LUFT- UND KÄLTETECHNIK), 3 May 1973 (03.05.1973), page 2, figures 1-3  -- -----	1-13

**International patent classification (IPC)****G01G 3/13** (2006.01)**G01N 17/00** (2006.01)**G01N 19/10** (2006.01)**Download your patent documents at [www.prv.se](http://www.prv.se)**

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Use the application number as username.

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Paper copies can be ordered at a cost of 50 SEK per copy from PRV InterPat (telephone number 08-782 28 85).

Cited literature, if any, will be enclosed in paper form.

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

30/08/2008

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