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(54) A method and an apparatus for separating a first amount of liquid

(57) The invention relates to a method for separating a first amount of liquid into a plurality of second amounts of liquid, the method comprising the steps of bringing the first amount of liquid (210) into contact with at least one first fibre (110) being arranged substantially vertical, allowing the first amount of liquid to drain of the first fibre, thereby forming a coating film on the fibre, allowing the coating film to decompose, thereby forming a plurality of second amounts of liquid (220), and allowing the second amounts of liquid to drain of the first fibre and being captured at a crossing point (130) being constituted by the first fibre and at least one second fibre (120) being arranged substantially perpendicular to the first fibre and touching the first fibre. Furthermore, the invention relates to an apparatus for separating a first amount of liquid into a plurality of second amounts of liquid.

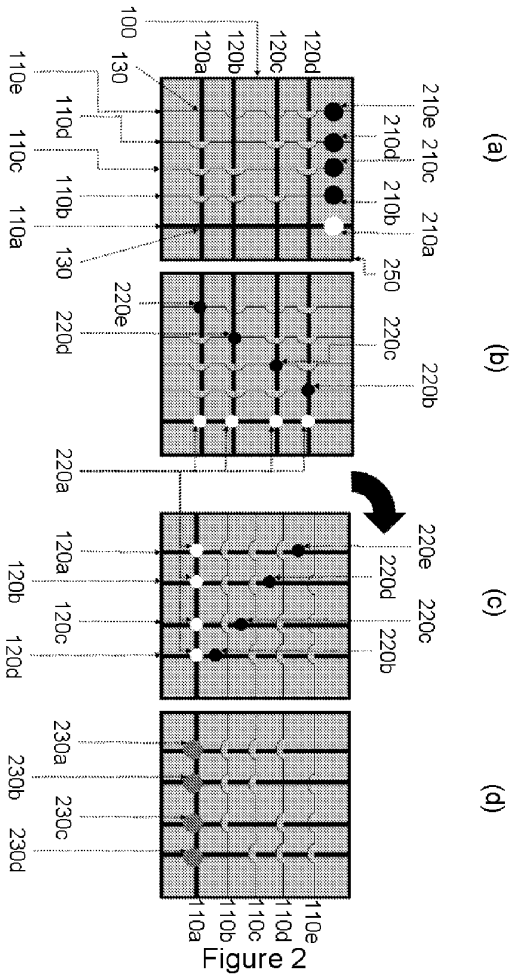

Figure 2

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Description

Field of the Invention

[0001] The invention relates to an apparatus and a method for separating a first amount of liquid into a plurality of second amounts of liquid. The method and the apparatus according to the present invention may be useful, in particular, for manipulating small amounts of liquids such as amounts of liquids comprising less than 1 ml of liquid. The separation of such a small amount of liquid into a plurality of even smaller amounts may be useful in order to perform a plurality of different chemical and/or biological reactions involving this liquid and a further reactant in solvent, solid or gaseous form.

Technical Background

[0002] Apparatus and methods for separating a first amount of liquid into a plurality of second amounts of liquid are known, e.g. by decanting from one vessel to another. However, the manipulation of small volumes of material, e.g. via a pipette can be time consuming. In microfluidics, very small amounts of liquids (typically less than 1~ml) are manipulated and these techniques are of considerable importance in many technological fields; such as microelectronics, biotechnology, analytical chemistry or medicine.

[0003] For example, in the medical field allergies are increasingly more common in everyday life. This worldwide health issue needs an efficient, systematic and low-cost tracking procedure. About 20 million children are asthmatic in developed countries, and this number is growing. Ideally, an allergy diagnostic should consist in an analysis of a small sample of physiologic liquid (tear, urine, sweat...) obtained as easily as possible. The analysis should be made with about 500 different allergens, for example. So an important problem, for example, is how to make 500 samples from a single volume of liquid as big as a tear to do 500 different biochemical reactions.

In the biological field, the generation of very small droplets will be useful for the spotting of micro-arrays on glass slides for DNA or protein analysis. Reducing the size of the droplets will increase the density of these micro-arrays and so increase the number of test for the same surface size.

[0004] Microelectronics is also confronted with the use of very small droplets. An example relates to very small components (e.g. a bare die) that must be glued (e.g. die attached) on a substrate. The dimensions of these components can go down to 200μm. There is a need to make a droplet of adhesive around these dimensions. Unfortunately, as no adequate system is available on the market, spotting is used and an important loss of adhesive material is resulted.

[0005] The food and pharmaceutical industries are also very interested in micro-encapsulation, which means wrapping one or several micro-droplets (the liquid of interest, i.e. a nutriment or a medicine), in a micro-shell. All those issues may be addressed by finding an efficient way to create a large number of micro-droplets starting from a small amount of liquid.

[0006] The splitting of a droplet into a huge amount of micro-droplets is easily done in air by atomization: the droplet is sprayed into the air via a Venturi effect. Nevertheless, this technique is not practical since the generated micro-droplets are not localized. It is thus impossible to make individual chemical reactions in each of those droplets. Micro-droplets can also be made by using a network of micro-channels filled with a carrying liquid, immiscible with the liquid of interest. This carrying liquid is set into motion by high-tech micro-pumps. This technology should correctly address the proposed issue. Nevertheless, the complex apparatus required to guarantee the perfect synchronization of micro-droplets in the carrying fluid is expensive, space-consuming and generally requires the expertise of a research laboratory. Moreover, the immiscibility constraint and the difficulty of cleaning/recycling the circuits make this technical solution relatively inappropriate and unattractive.

[0007] What is known as a lab-on-a-chip consists in a printed circuit on which droplets are placed. By applying a high voltage between the droplet and the substrate, it is possible to modify the droplet contact angle, and eventually to set it into motion. The main advantage of this process is that it is controlled electronically. Nowadays, it is not possible yet to divide a droplet into a large number of micro-droplets using this system. Moreover, the relatively high wettability of most of physiologic liquids leads to important liquid losses by coating during the droplet motion.

[0008] Therefore, current existing technologies are not suitable for the issue of interest.

Summary of the invention

[0009] It is therefore an object of the present invention to provide an apparatus and a method for separating a first amount of liquid into a plurality of second amounts of liquid. An advantage of the present invention is to be able to divide a first amount of liquid into at least one smaller second amount which is localized at a predefined position.

[0010] The method and the apparatus according to the present invention may be useful, in particular, for manipulating small amounts of liquids such as amounts of liquids comprising less than 1 ml of liquid. The separation of such a small amount of liquid into a plurality of even smaller amounts may be useful in order to perform a plurality of different chemical and/or biological reactions involving this liquid and a further reactant in solvent, solid or gaseous form.

[0011] Furthermore, it is an advantage of the present invention to provide an apparatus and a method for a systematic division of a first amount of liquid into at least one smaller second amount of liquid which is characterized by a simple, economic and reliable construction.

[0012] The problem may be solved by an apparatus for separating a first amount of liquid into at least one second amount of liquid, comprising at least one first fibre being arranged substantially in a first direction, e.g. vertically, and at least one second fibre being arranged substantially perpendicular to the first fibre and touching (or being sufficiently close to) the first fibre at a crossing point, wherein said first and second fibres are comprising a surface energy being larger than the surface energy of the liquid being intended to form the first and second amount of liquid.

[0013] Furthermore, the problem may be solved by a method for separating a first amount of liquid into at least one second amount of liquid, the method comprising the steps of bringing the first amount of liquid into contact with at least one first fibre, optionally being arranged in a first direction, e.g. substantially vertical, allowing the first amount of liquid to drain over the first fibre by being subject to a force, thereby forming a coating film on the fibre, allowing the coating film to decompose, thereby forming a plurality of second amounts of liquid, and allowing the second amounts of liquid to drain along the first fibre by being subject to the force and being captured at a crossing point being constituted by the first fibre and at least one second fibre being arranged at an angle, e.g. substantially perpendicular to the first fibre and touching (or being sufficiently close to) the first fibre. The force may be gravity or any other force that can act upon the liquid (e.g. mechanical forces such as centrifugation, gravity, or electromagnetic or magnetic forces ...).

[0014] According to embodiments the present invention, a grid-like construction of a plurality of fibres is provided. Such a construction may be called a fibre network hereinafter. A location is called a crossing point hereinafter if two fibres arranged at angle to each other, e.g. substantially perpendicular, are sufficiently close to each other or touching each other at this location. By sufficiently close, it is meant 'with a spacing smaller than the characteristic size of the smallest amount of liquid that is required to be generated with the present apparatus'. A single fibre may have a diameter of less than 100 μm, less than 50 μm or even less than 25 μm. An aspect of the present invention relies on the fact that a relatively large amount of liquid slipping along, e.g. down a fibre under the influence of a force such as gravity is able to cross said crossing point and to continue its way along, e.g. down the fibre. However, a relatively small amount of liquid slipping along, e.g. down the fibre is caught by the crossing fibre and remains localized at the crossing point. Any of the first or the second fibres can have specific electrical, thermal, optical or chemical properties.

[0015] The liquid/fibre combination is preferably chosen so that the liquid wets the fibre. In order to form a plurality of second amounts of liquid being located at each crossing point from a single first amount of liquid, the surface tension of the liquid is chosen to be smaller than the surface energy of the fibres forming the fibre network. This will lead to a wetting of the fibre, i.e. a first amount of liquid slipping down on the fibre will coat this fibre with a thin liquid film. The thickness *h* of the coating film depends on the fibre radius *b*, the surface tension *s* and the mass *m* of the first amount of liquid slipping down the fibre:

$$\frac{h}{b} \propto \left(\frac{m \cdot g}{b \cdot s} \right)^{2/3} \qquad (1)$$

wherein g denotes the acceleration of gravity. An estimation of typical thicknesses *h* from equation (1) for typical liquids such as oil, soapy water or most biological liquids, leads to a thickness *h* of about 1 μm up to 10 μm.

[0016] Such coating films are able to spontaneously decompose into a plurality of small droplets of liquid. Usually, this decomposition is disadvantageous in technical processes such as lubrication or painting. According to the invention, the coating film is allowed to decompose into a plurality of droplets. These droplets will slip along, e.g. down the inclined fibre in the same way than the first amount of liquid. As these secondary droplets are below the critical size which is able to slip over a crossing point, the droplets will accumulate at the crossing points formed by two fibres. The size of the second amount of liquid forming at each crossing point may be controlled by the distance between two crossing points, the fibre radius, the mass of the first amount of liquid and the surface tension *s*.

[0017] In one embodiment, the fibre network may comprise fibres of any suitable material, including polymers, carbon, metal and glass. The fibres are preferably selected so that they can be wet by the relevant solution that will be used. For example, if aqueous solutions are to be used, then the fibres are preferably selected so that they can be wet by aqueous solutions. The surface of fibres may be altered by a treatment to make the surface more wettable, e.g. a corona or plasma treatment so as to allow wetting by aqueous solutions. Fibres may also be coated with a hydrophilic coating. Any suitable method of providing fibres that can be wet by aqueous solutions is included within the scope of the present invention. One suitable type of fibre is polyamide fibres. These fibres provide a surface tension *s* which will lead to a wetting surface for most of aqueous solutions which are common when handling biological liquids such as tears, sweat, urine or blood plasma. The present invention also includes fibres with optical, thermal, chemical or electrical properties,

such as optical fibres, electricity/heat conducting fibres, fibres coated with chemically active materials... Switching a property of the fibre to another provides a way to control the droplet behaviour in the network.

[0018] Nanofibres such as electrospun fibres are also suitable. Their small size allow a reduction in the size of the droplets.

[0019] In one embodiment of the invention, the fibre network may comprise at least one vertical fibre that does not form crossing points with all perpendicular fibres out of a plurality of perpendicular fibres, i.e. not all perpendicular fibres are touching the vertical fibre. This leads to secondary amounts of liquid being formed only on the crossing points, i.e. secondary amounts of liquid are formed only on selected fibres. This embodiment of the invention may advantageously be used when different chemical reactions are to be carried out on different secondary amounts of liquid being composed from the same first amount of liquid. The fibre network then plays the role of a chemical sampler where each small droplet at the junction can be considered as a microreactor.

[0020] In order to mix a first and a second droplet consisting of a first and a second liquid, the fibre network may be fixed on a pivot-mounted frame or rotatable frame. This provides the option of changing the inclination of the fibres depending on the angle of rotation of the frame. This feature may be useful to control the motion of amounts of liquid over the fibre network.

[0021] In order to provide the first amount of liquid slipping along, e.g. down the first fibre, a liquid dosing apparatus may be provided. Such a dosing apparatus may comprise a spraying device, a syringe, an inkjet nozzle, a piezo-injector or any other device known in the art which is able to provide or dispense small amounts of liquid.

[0022] In a further aspect the present invention also provides the use of the fibre network as micro-sampler or as micro-dispensing device. In order to provide a micro-dispensing device, in one embodiment, the fibre network is assembled in a moving system such as a rotating system which monitors a position where dispensing will take place. Such a use is particularly helpful for dispensing equipment for the gluing of very small components (e.g. die attach). This system can also be automated and regulated in order to dispense droplets on demand or automatically (in production equipment for example).

[0023] These and other aspects of the invention will be apparent from and elucidated with reference to the embodiments described hereinafter.

Brief Description of the drawings

[0024] In the drawings:

Fig. 1 depicts a small amount of liquid being captured at a crossing point between two fibres and a large amount of the same liquid slipping over the crossing point.

Fig. 2 illustrates the separation of first amounts of liquid into a plurality of second amounts of liquid and the mixing of pairs of second amounts of liquid.

Fig. 3 illustrates the mixing of a pair of second amounts of liquid and their subsequent chemical reaction.

Detailed description of illustrative embodiments

[0025] The present invention will be described with respect to particular embodiments and with reference to certain drawings but the invention is not limited thereto but only by the claims. The drawings described are only schematic and are non-limiting. In the drawings, the size of some of the elements may be exaggerated and not drawn on scale for illustrative purposes. The dimensions and the relative dimensions do not correspond to actual reductions to practice of the invention.

[0026] Furthermore, the terms first, second, third and the like in the description and in the claims, are used for distinguishing between similar elements and not necessarily for describing a sequence, either temporally, spatially, in ranking or in any other manner. It is to be understood that the terms so used are interchangeable under appropriate circumstances and that the embodiments of the invention described herein are capable of operation in other sequences than described or illustrated herein.

[0027] Moreover, the terms top, bottom, over, under and the like in the description and the claims are used for descriptive purposes and not necessarily for describing relative positions. It is to be understood that the terms so used are interchangeable under appropriate circumstances and that the embodiments of the invention described herein are capable of operation in other orientations than described or illustrated herein.

[0028] It is to be noticed that the term "comprising", used in the claims, should not be interpreted as being restricted to the means listed thereafter; it does not exclude other elements or steps. It is thus to be interpreted as specifying the presence of the stated features, integers, steps or components as referred to, but does not preclude the presence or

addition of one or more other features, integers, steps or components, or groups thereof. Thus, the scope of the expression "a device comprising means A and B" should not be limited to devices consisting only of components A and B. It means that with respect to the present invention, the only relevant components of the device are A and B.

[0029] Similarly, it is to be noticed that the term "coupled", also used in the claims, should not be interpreted as being restricted to direct connections only. The terms "coupled" and "connected", along with their derivatives, may be used. It should be understood that these terms are not intended as synonyms for each other. Thus, the scope of the expression "a device A coupled to a device B" should not be limited to devices or systems wherein an output of device A is directly connected to an input of device B. It means that there exists a path between an output of A and an input of B which may be a path including other devices or means. "Coupled" may mean that two or more elements are either in direct physical or electrical contact, or that two or more elements are not in direct contact with each other but yet still co-operate or interact with each other.

[0030] Reference throughout this specification to "one embodiment" or "an embodiment" means that a particular feature, structure or characteristic described in connection with the embodiment is included in at least one embodiment of the present invention. Thus, appearances of the phrases "in one embodiment" or "in an embodiment" in various places throughout this specification are not necessarily all referring to the same embodiment, but may. Furthermore, the particular features, structures or characteristics may be combined in any suitable manner, as would be apparent to one of ordinary skill in the art from this disclosure, in one or more embodiments.

[0031] Similarly it should be appreciated that in the description of exemplary embodiments of the invention, various features of the invention are sometimes grouped together in a single embodiment, figure, or description thereof for the purpose of streamlining the disclosure and aiding in the understanding of one or more of the various inventive aspects. This method of disclosure, however, is not to be interpreted as reflecting an intention that the claimed invention requires more features than are expressly recited in each claim. Rather, as the following claims reflect, inventive aspects lie in less than all features of a single foregoing disclosed embodiment. Thus, the claims following the detailed description are hereby expressly incorporated into this detailed description, with each claim standing on its own as a separate embodiment of this invention.

[0032] Furthermore, while some embodiments described herein include some but not other features included in other embodiments, combinations of features of different embodiments are meant to be within the scope of the invention, and form different embodiments, as would be understood by those in the art. For example, in the following claims, any of the claimed embodiments can be used in any combination.

[0033] The present invention makes use of fibres at an angle to each other, e.g. perpendicular to each other, that touch or are sufficiently close to each other at at least one point. By sufficiently close, is meant 'with a spacing smaller than the characteristic size of the smallest amount of liquid that is required to be generated with the present apparatus'.

[0034] Fig. 1a shows a fibre 110 have a longitudinal direction, e.g. a substantially vertically arranged fibre 110. The present invention will be described with reference to a first and a second amount of liquid. The first amount of liquid is greater than the second amount of liquid. Fig. 1a shows a second amount of liquid 220 slipping down the substantially vertically arranged first fibre 110. A second amount of liquid in this context means an amount of liquid that is sufficiently small to get trapped at a crossing point, e.g. an amount of liquid that has been formed from a decomposed coating film. Fig. 1a details the motion of the second amount of liquid 220 at eight different points in time, wherein the earliest point in time is given on the most left patch of Fig. 1a.

[0035] Furthermore, Fig. 1a shows a second fibre 120 which is arranged at an angle, e.g. substantially perpendicular to the first fibre 110. The first fibre 110 and the second fibre 120 form a crossing point 130. The fibres may be tied together or taut in such a way that they touch each other or are sufficiently close to each other at the crossing point 130. The second amount of liquid 220 comprises a liquid that wets the first and second fibres, e.g. has a surface energy smaller than the surface energy of the first fibre 110 and the second fibre 120. In one embodiment, the first fibre 110 and the second fibre 120 may be made from any material, including a metal or an alloy or a polymer, e.g. polyamide. In other embodiments of the invention, either the first fibre 110 or the second fibre 120 may be made from any material, including another polymer, a metal or an alloy. Any of the first or the second fibre may be subjected to a treatment such as corona or plasma treatment or may comprise a coating in order to control the surface energy of the fibres 110 and/or the fibre 120. The coating may comprise an organic material, e.g. a polymer such as polytetrafluorethylene, or a resin or an inorganic compound such as an oxide, e.g. TiO, ZrO, or the like. The wetting may also be controlled by thermal or electrical effects induced in conducting fibres.

[0036] The liquid forming the second amount of liquid 220 may comprise an aqueous solution or an oil such as silicon oil.

[0037] The second amount of liquid 220 is slipping along, e.g. down the first fibre 110 due to the action of gravity. However, any other driving force such as a forced gas flow, inertial forces, mechanical forces such as centrifugation, vibration, thermal forces or chemical forces or electrostatic forces or magnetic forces may be applied in order to make the amount of liquid 220 travel alongside the first fibre 110. Hence the first fibre does not have to be vertical. It could be any angle depending for example on the direction of the driving force.

[0038] After having reached the crossing point 130, the amount of liquid 220 is caught by the second fibre 120. The

motion of the amount of liquid 220 on the first fibre 110 is stopped. This leads to the amount of liquid 220 being localized at the crossing point 130.

[0039] Fig. 1b details the same situation for a larger amount of liquid 210. Fig. 1b shows a first amount of liquid 210 slipping down the substantially vertically arranged first fibre 110. A first amount of liquid in this context means an amount of liquid that is sufficiently big not to get trapped at a crossing point 130, e.g. a larger amount of liquid that has been formed from the dosing apparatus.

[0040] Fig. 1b details the motion of the first amount of liquid 210 at eight different points in time, wherein the earliest point in time is given on the most left patch of Fig. 1b. As can be seen in Fig. 1b, the first amount of the same liquid slipping down the first fibre 110 by the same driving force is slowed down at the crossing point 130 by the action of the second fibre 120. However, the travelling speed of the first amount of liquid 210 does not stop completely. The first amount of liquid 210 will continue its way down the first fibre 110 without being caught at the crossing point 130.

[0041] Fig. 1 details a binary behaviour of first and second amounts of liquids respectively travelling along a first fibre 110 over a crossing point 130. Small amounts of liquids, i.e. amounts of liquids having less than a critical size, are blocked and remain localized at the crossing point 130. Amounts of liquids larger than the critical size are able to pass the crossing point 130, thereby wetting the whole length of first fibre 110. The critical size depends on the fibre radius *b*, the surface energy *s* and the mass *m* of the first and second amounts of liquid 210 and 220. It has been shown that the critical size may be calculated according to the following equation

$$m \cdot g \propto 4\pi \cdot s \cdot b \qquad (2)$$

[0042] In the embodiment detailed in Fig. 1, a first amount of liquid 210 made from silicon oil slipping down a first fibre 110 with a diameter of 80 μm will be able to travel over a crossing point 130 if this first amount of liquid 210 has a volume larger than 2 μl. A second amount of liquid 220 having less than 2 μl in volume will be caught at the crossing point 130 of the fibre network.

[0043] Fig. 2 illustrates an apparatus 100 for separating a first amount of liquid into a plurality of second amounts of liquid and its method of operation. The apparatus 100 according to Fig. 2 comprises a pivot-mounted frame 250. The frame 250 is adapted to accommodate a plurality of first fibres 110a, 110b, 110c, 110d and 110e. Furthermore, the frame accommodates a plurality of second fibres 120a, 120b, 120c and 120d. The second fibres 120 are arranged substantially perpendicular to the first fibres 110, thereby forming a fibre network. The first fibres 110 and the second fibres 120 are taut as such that crossing points 130 are formed at certain predefined locations only. In the embodiment detailed in Fig. 2, the first fibre 110a forms a crossing point 130 with any of the four second fibres 120a, 120b, 120c and 120d. The first fibre 110b is arranged as such that a crossing point 130 with the second fibre 120d is formed. The second fibres 120a, 120b and 120c do not touch the first fibre 110b. In the same manner, the first fibre 110c forms a crossing point with the second fibre 120c. The first fibre 110d forms a crossing point 130 with the second fibre 120b only. The second fibre 120a has a single crossing point 130 with the first fibre 110e. It should be clear to one skilled in the art that the arrangement of nine fibres described above is for illustrative purposes only and will not limit the scope of the invention. The fibre network may grow up to several hundred fibres 110 and/or 120.

[0044] In a first position of the pivot-mounted frame, the first fibres 110a, 110b, 110c, 110d and 110e are substantially vertical. A first amount 210a of liquid is brought into contact with the first fibre 110a. By way of example, this liquid may comprise a liquid under test such as blood or tears. The first amount 210b of a second liquid is brought into contact with the first fibre 110b. The second liquid which is used to form the first amount 210b may comprise a reactant which is able to react with the liquid of the first amount of liquid 210a. By way of example, this reaction may be used to determine a certain parameter being present in the amount of liquid 210a. This parameter may comprise a concentration of an electrolyte, a titre or the like. In the same manner, an amount of liquid 210c may be brought in contact with the first fibre 110c, an amount of liquid 210d may be brought into contact with the first fibre 110d and an amount of liquid 210e may be brought into contact with the first fibre 110e. It is clear to one skilled in the art that the amounts of liquids 210b, 210c, 210d and 210e must not necessarily comprise the same liquid. Furthermore, it should be clear to one skilled in the art that not any of the first fibres 110b, 110c, 110d and 110e must be brought in contact with a first amount of liquid 210b, 210c, 210d and 210e.

[0045] Fig. 2b details the situation after the first amounts of liquids 210a, 210b, 210c, 210d and 210e have slipped down the first fibres 110a, 110b, 110c, 110d and 110e by the action of gravity. As any of the second fibres 120a, 120b, 120c and 120d forms a crossing point 130 with the first fibre 110a, the amount of liquid 210a, which is large enough to travel across any of the crossing points 130, is split up into four amounts of liquids 220a which are located at any of the crossing points 130 of the first fibre 110a. As any of the second fibres 120a, 120b, 120c and 120d forms a single crossing point 130 with another first fibre 110b, 110c, 110d and 110e, the second fibres 120a, 120b, 120c and 120d accommodate

each one further second amount of liquid 220b, 220c, 220d, and 220e comprising a fraction of the first amounts of liquid 210b, 210c, 210d, and 210e, respectively.

[0046] As detailed in Fig. 2c, the pivot-mounted frame 250 is turned through an angle such as 90 degrees clockwise. This leads to the second fibres 120a, 120b, 120c and 120d being arranged substantially vertical and the first fibres 110a, 110b, 110c, 110d and 110e being arranged substantially horizontally. Due to the action of gravity, the second amounts of liquids 220b, 220c, 220d and 220e are slipping down the second fibres 120a, 120b, 120c, and 120d respectively towards the first fibre 110a and the second amounts of liquid 220a located there.

[0047] Fig. 2d shows the situation after one of the second amounts of liquid 220a and the second amount of liquid 220e has been mixed to a third amount of liquid 230a. In the same way, one of the second amounts of liquid 220a and the second amount of liquid 220d has been mixed to a third amount of liquid 230b. The third amount of liquid 230c comprises one of the first amounts of liquid 220a and the second amount of liquid 220c. The fourth amount of liquid 230d comprises one of the first amounts of liquid 220a and the second amount of liquid 220b. The four second amounts of fluid 220a and the respective second amounts of liquid 220b, 220c, 220d, and 220e may now chemically react. Such a reaction may comprise a plurality of analytical reactions revealing characteristics of the liquid forming the first amount of liquid 210a. For example, determination of allergens in a tear is provided by the present invention by sampling one tear without need of dilution and local reaction in each smaller formed droplet with a specific detection reactant. Coupling it with on-line analytical devices (colorimetric, spectroscopic detections) makes the chemical identification fast and costless.

[0048] The widely spread combinatorial approach in chemical synthesis is another application that benefits from the present invention. Testing a multi-step synthesis sequence on related products that allows the handling of only tiny quantities of materials (e.g. ng scale of a drug or radiolabelled compounds) in such a combinatorial approach is also speeded up by the quick sampling of the reactants in well-defined microreactors that can easily be coupled with spectroscopic analytical techniques.

[0049] In another embodiment of the invention, an encapsulation of the liquid provided by the first amount of liquid 210a may be performed. Such an encapsulation means a first amount of liquid 210a being split into a plurality of second amounts of fluid 220a, wherein each of these second amounts 220a is enclosed by a relatively hard shell. In order to form the shell, the second amounts 230a are brought into contact with a cross-linkable polymer which may be solidified by electromagnetic radiation such as ultraviolet light. The cross-linkable polymer may be at least a fraction of the second amounts of liquid 210b, 210c, 210d and 210e. As the second amounts of liquid 220a, 220b, 220c, 220d, and 220e have a volume which is controllable with high precision by the distance of two neighboured second fibres 120a, 120b, 120c, and 120d and the film thickness formed on the first fibres 110a, 110b, 110c, 110d and 110e, the volume of the encapsulated second amounts of liquid 220a may be controlled with high precision as well. For example encapsulation of a drug in a polycyanoacrylate or any other type of solid shell (polymer, silica) can be provided by percolation of the drug solution followed by a non miscible monomer solution followed by photo-, thermo-, induced polymerization. As an example, the formation of insulin reservoir coated with a glucose responsive shell that can trigger the release of insulin in respect to the glucose concentration is highly valuable in diabetic treatment.

[0050] Fig. 3 shows in greater detail the mixing process of a first amount of liquid 220a and second amount of liquid 220b and the formation of a third amount of liquid 230. Fig. 3 details this mixing process and a subsequent chemical reaction at five different points in time, wherein the earliest point in time is given by Fig. 3a on the left-hand side of the Figure.

[0051] Fig. 3a shows a first fibre 110 and a second fibre 120 as explained in greater detail with respect to Fig. 1 and 2. A second amount of liquid 220a has been generated at the crossing point 130 between the fibres 110 and 120 as explained with respect to Fig. 2. In order to clarify the basic principle of the invention, the second amount of liquid 220a comprises H_2SO_4. However, one skilled in the art will realise that the invention is not limited to this example. A second amount of liquid 220b slips down the second fibre 120. By way of an example, this second amount of liquid 220b may comprise NaOH.

[0052] Fig. 3b shows the point in time where the second amount of liquid 220b has reached the first amount of liquid 220a.

[0053] Fig. 3c shows the mixing of the two second amounts of liquid 220b and 220a to form a third amount of liquid 230. As the volume of this amount of liquid 230 is chosen to be well below the critical size where an amount of liquid is able to leave the crossing point 130 and to travel down the second fibre 120, the third amount of liquid 230 persists at the crossing point 130.

[0054] As detailed in Figs. 3d and 3e, a mixing zone 240 develops inside the third amount of liquid 230. At this mixing zone, the H_2SO_4 and the NaOH react and an acid-base chemical reaction is performed inside the third amount of liquid. This reaction is a simple exemplary model of any reaction that occurs upon mixing two or more reactants. Local heating, or light irradiation or addition of catalyst is also possible by using the network inducing more complex reactions at the level of the microdroplet. Combination of the network with anaytical tool (e.g. by using optical fibres for spectroscopy) leads directly to detection of the reaction progress. As mentioned above this might be helpful in detection of analytes (microassay detection) or for combinatorial chemistry on restricted amounts of materials (e.g. radiolabeled com-

pounds,...).

[0055] This present invention has numerous advantages. Firstly, a small amount of liquid, e.g. a few tears will be sufficient to make the 500 allergic tests. The separation into small drops of liquid can be done very rapidly, the main droplet is spontaneously divided into tens of micro-droplets in less than one second. Moreover, the device is robust and transportable (microdroplets are displaced from the intersections only with extreme inertial forcing), cleanable, zero-energy consuming and a recycling procedure of damaged parts is possible. Finally, the technique is overly simple and low-cost to produce. It does not need neither any high-tech device nor any expertise from a research lab.

[0056] The range of applications of the present invention is not limited to the above mentioned applications. A large variety of chemical and biochemical reactions requiring multiplexing can be processed according to the present invention : enzymatic analysis, DNA analysis, proteomics, analytical chemistry ... More generally, this new and powerful technique and apparatus is of interest for current applications of microfluidics and microreactor arrays. The present invention also provides systematic and low-cost tracking devices, e.g. for diagnostic analysis of a small sample of physiologic liquid (tear, urine, sweat...). The present invention also provides microreactors for chemical reactions in droplets. Micro-droplets can be made by using the fibre network. The fibre network may also be used as a creator / dispenser of tiny amounts of liquid. This comprises the creation of micro-droplets of glue to be applied on electro-mechanical micro-systems, including micro-electronic devices. The crossings 130, where the glue droplets 220 are collected, are put into contact with the specific points that may be covered by glue. The invention may also be applied as a controlled way of dispensing tiny amounts of liquid to lubricate electro-mechanical micro-systems.

[0057] Encapsulation may also be performed on this fibre network. The present invention provides droplet devices for the food and pharmaceutical industries, e.g. for micro-encapsulation. The liquid of interest (generally aqueous) is placed on the nodes by using the liquid division technique. Then, another immiscible liquid, made from cross-linkable polymers, is provided and wraps these micro-droplets before being solidified, e.g. by UV light. The liquid of interest is thus encapsulated. The junctions confine and control the encapsulations. This latter method is particularly interesting for the food and pharmaceutical industries, for the production of micro-capsules with controlled volume.

[0058] Finally, the fibre junction can be the equivalent in microfluidics of the diode in electronics: the fundamental logic component. Therefore, it is possible to make complex logical fluidic operations on a fibre network.

[0059] While the invention has been illustrated and described in detail in the drawings and the foregoing description, such illustration and description are to be considered illustrative or exemplary and not restrictive; the invention is not limited to the disclosed embodiments. Other variations to the disclosed embodiments can be understood and effected by those skilled in the art in practicing the claimed invention, from a study of the drawings, the disclosure, and the appended claims. In the claims, the indefinite article "a" or "an" does not exclude a plurality. The mere fact that certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage. Any reference signs in the claims should not be construed as limiting the scope.

Claims

1. An apparatus (100) for separating a first amount (210) of liquid into a plurality of second amounts (220) of liquid comprising:

   - at least one first fibre (110),
   - at least one second fibre (120) being arranged at an angle to the first fibre (110) and touching or being sufficiently close to the first fibre at a crossing point (130) to trap a droplet of the liquid ,
   - said first and second fibres (110, 120) having a surface property so that they are wettable by the liquid, and
   - at least one dosing apparatus which is adapted to provide the first amount (210) of liquid so that it can travel along the at least one first fibre as the droplet.

2. The apparatus according to claim 1, said first and second fibres (110, 120) having a surface energy larger than the surface energy of the liquid being intended to form the first and second amount (210, 220) of liquid, and/or wherein the first and second fibre (110, 120) have a diameter of less than 500 μm and/or wherein the first and second fibres (110, 120) are made from a polymer.

3. The apparatus according to claim 1 or 2, further comprising a plurality of first and second fibres (110, 120) being arranged at a distance from 2 mm up to 70 mm with respect to each other.

4. The apparatus according claim 3, wherein a group of first fibres (110) is arranged substantially perpendicular to a plurality of second fibres (120) and any of the first fibres (110) touches only one respective second fibre (120) at a crossing point (130).

5. The apparatus according to any previous claim, wherein the surfaces of any of the first or the second fibres (110, 120) are covered by a layer in order to modify the surface energy.

6. The use of the apparatus according to any of claims 1 to 8 for chemical or biochemical reactions, including multiplexing operations or not.

7. The use of the apparatus according to any of claims 1 to 6 as a droplet dispenser

8. A method for separating a first amount (210) of liquid into a plurality of second amounts (220) of liquid, the method comprising the following steps:

- bringing the first amount (210) of liquid into contact with at least one first fibre (110),
- allowing the first amount (210) of liquid to drain along the first fibre (110) by being subject to a force, thereby forming a coating film on the fibre,
- allowing the coating film to decompose, thereby forming a plurality of second amounts (220) of liquid,
- allowing the second amounts (220) of liquid to drain along the first fibre (110) by being subject to the force and be captured at a crossing point (130) being constituted by the first fibre (110) and at least one second fibre (120) being arranged at an angle to the first fibre (110) and touching the first fibre.

9. The method according to claim 8, wherein the first and second fibres (110, 120) are selected as such that their surface energy is larger than the surface energy of the liquid forming the first and second amount (210, 220) of liquid.

10. The method according to any of claims 8 or 9, wherein a first amount (210) of a first liquid is brought into contact with a first fibre (110a) which forms a plurality of crossing points (130) with a plurality of second fibres (120a, 120b, 120c, 120d), a plurality of first amounts (210b, 210c, 210d, 210e) of a second liquid is brought into contact with respective first fibres (110b, 110c, 110d, 110e), each of which forms a single crossing point (130) with a single second fibre (120a, 120b, 120c, 120d) out of the plurality of second fibres (120a, 120b, 120c, 120d), rotating the relative directions of the force and the arrangement of first (110a, 110b, 110c, 110d, 110e) and second (120a, 120b, 120c, 120d) fibres, and allowing the second amounts of the first (220a) and/or the second (220b, 220c, 220d, 220e) liquid to drain along the second fibres (120a, 120b, 120c, 120d) and to mix (230a, 230b, 230c, 230d).

11. The method according to any of claims 8 to 10, wherein the first (110a, 110b, 110c, 110d, 110e) and second (120a, 120b, 120c, 120d) fibres are chosen to have a diameter of less than 500 μm.

12. The method according to any of claims 8 to 11, wherein the first amount of liquid comprises an aqueous liquid.

13. The method according any of claims 8 to 12, wherein the first amount of a second liquid comprises a liquid which is immiscible with the aqueous liquid and comprises at least one cross-linkable polymer.

14. The method according to claim 13, comprising further the step of curing the cross-linkable polymer by means of electromagnetic radiation.

15. The method according any of claims 8 to 114, wherein a biochemical reaction between the second amounts of the first liquid and the second liquid is carried out.

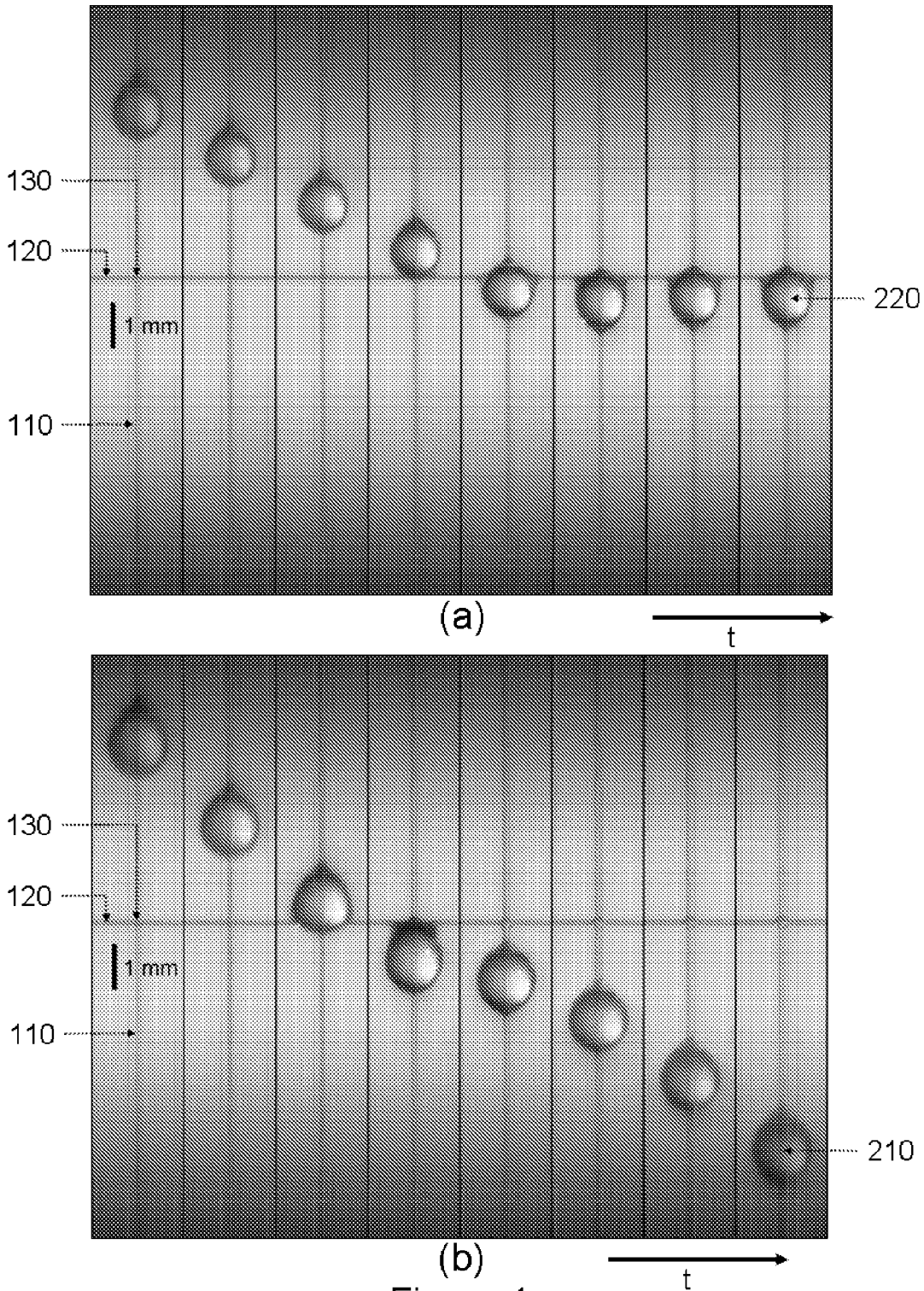

Figure 1

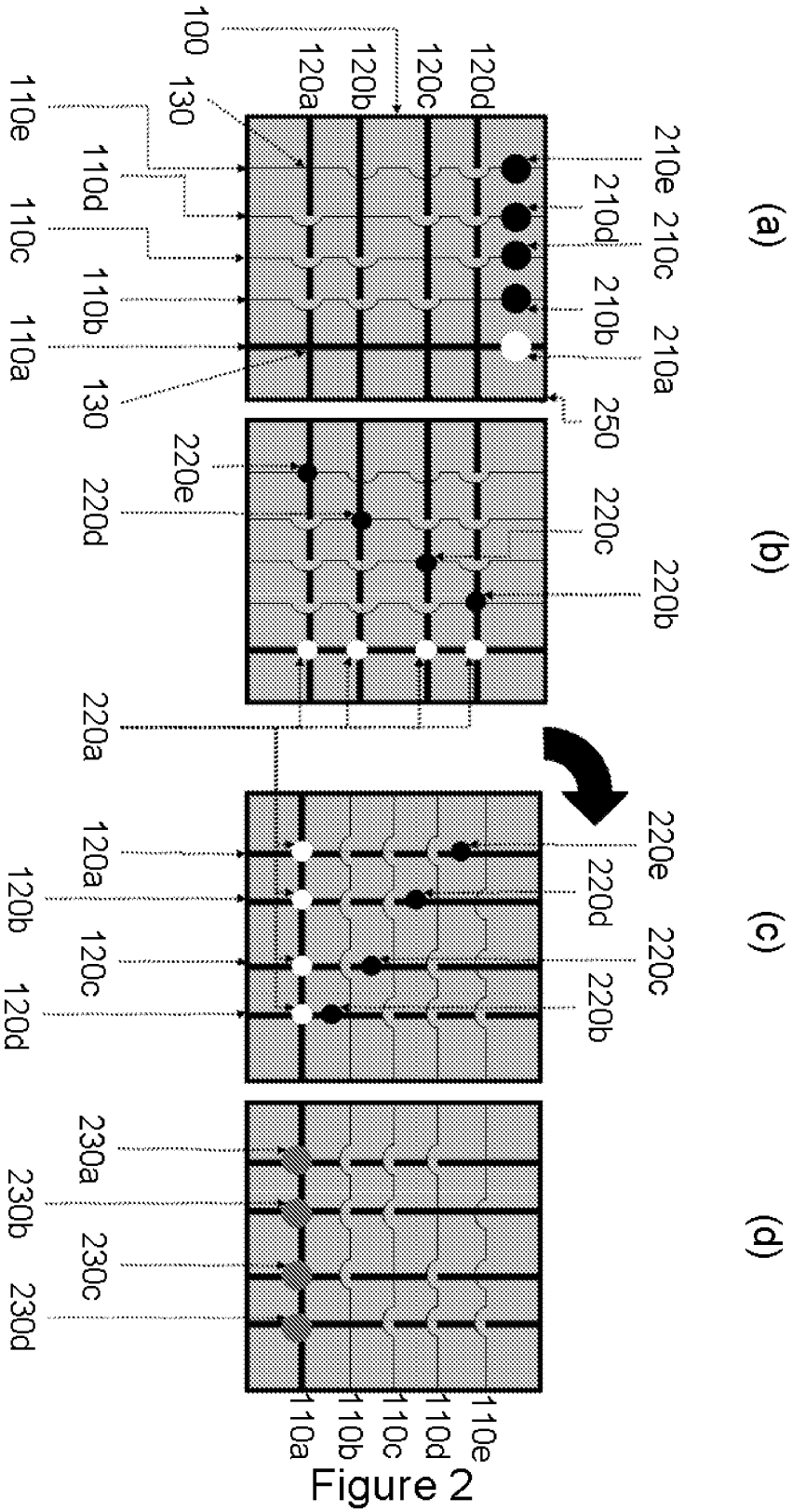
(a)
(b)
(c)
(d)
100
130
110e
110d
110c
110b
110a
120a
120b
120c
120d
210e
210d
210c
210b
210a
250
220e
220d
220c
220b
220a
230a
230b
230c
230d

Figure 2

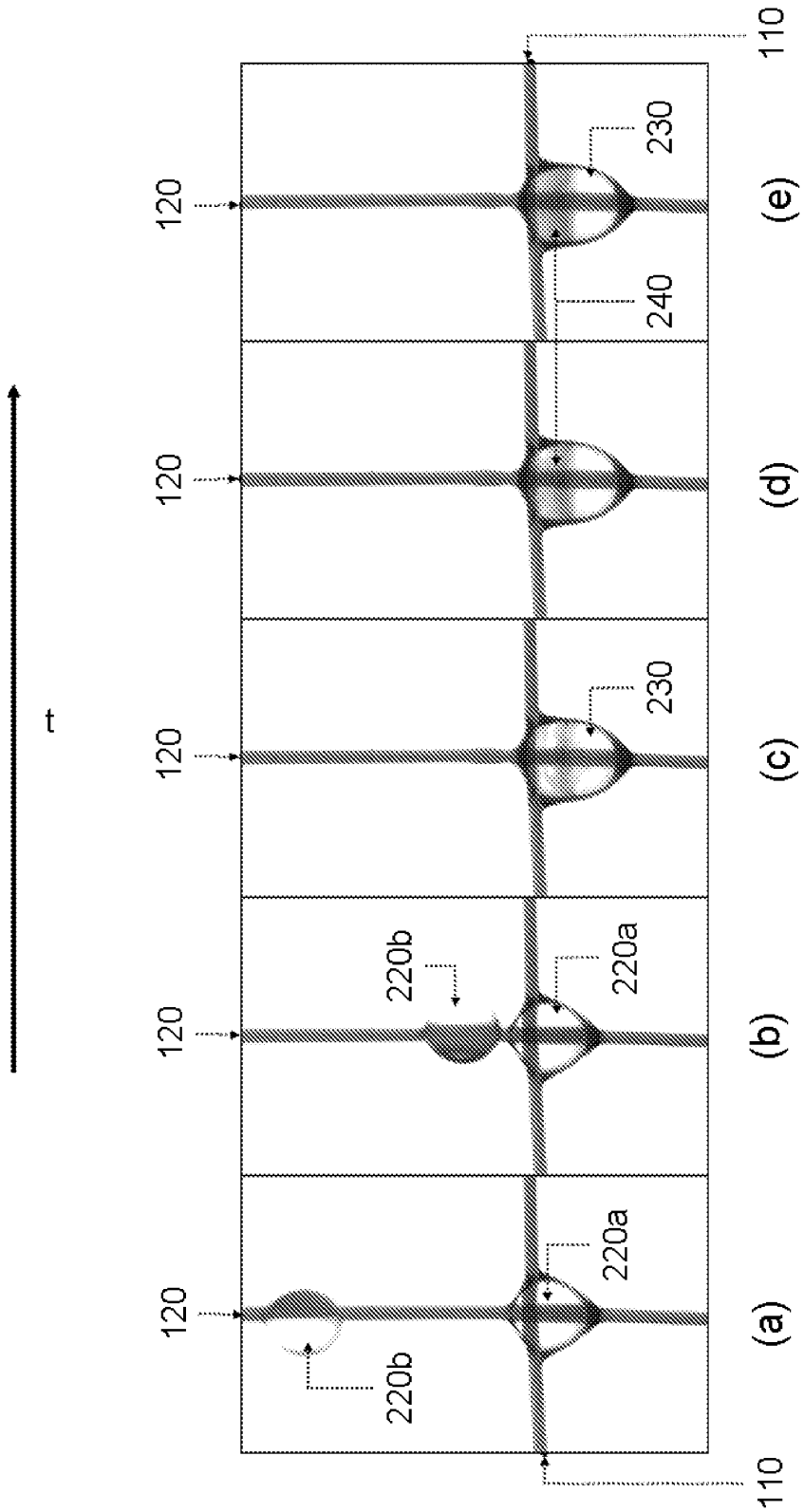

Figure 3

Europäisches Patentamt
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EUROPEAN SEARCH REPORT

Application Number
EP 09 15 4128

DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (IPC)
X	US 6 309 600 B1 (HUNTER IAN W [US]) 30 October 2001 (2001-10-30) * figures 1a-1c,2a-2d,4,6 * * column 3, lines 53-67 * * column 4, lines 3-17 * * column 5, lines 15-38 * * column 7, lines 12-34 * -----	1-3,5-7	INV. B01L3/00

TECHNICAL FIELDS SEARCHED (IPC)

B01L

The present search report has been drawn up for all claims

1

Place of search	Date of completion of the search	Examiner
Munich	5 August 2009	Hoyal, Barnaby

CATEGORY OF CITED DOCUMENTS

X : particularly relevant if taken alone
Y : particularly relevant if combined with another document of the same category
A : technological background
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T : theory or principle underlying the invention
E : earlier patent document, but published on, or after the filing date
D : document cited in the application
L : document cited for other reasons

& : member of the same patent family, corresponding document

EPO FORM 1503 03.82 (P04C01)

ANNEX TO THE EUROPEAN SEARCH REPORT ON EUROPEAN PATENT APPLICATION NO. EP 09 15 4128

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
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05-08-2009

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 6309600 B1	30-10-2001	US 2002001544 A1	03-01-2002

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82