



- (51) International Patent Classification:
B01L 3/00 (2006.01) *B01L 9/00* (2006.01)
- (21) International Application Number:
PCT/US2016/025321
- (22) International Filing Date:
31 March 2016 (31.03.2016)
- (25) Filing Language: English
- (26) Publication Language: English
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- (81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.
- (84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

— with international search report (Art. 21(3))

(54) Title: MONOLITHIC CARRIER STRUCTURE FOR DIGITAL DISPENSING

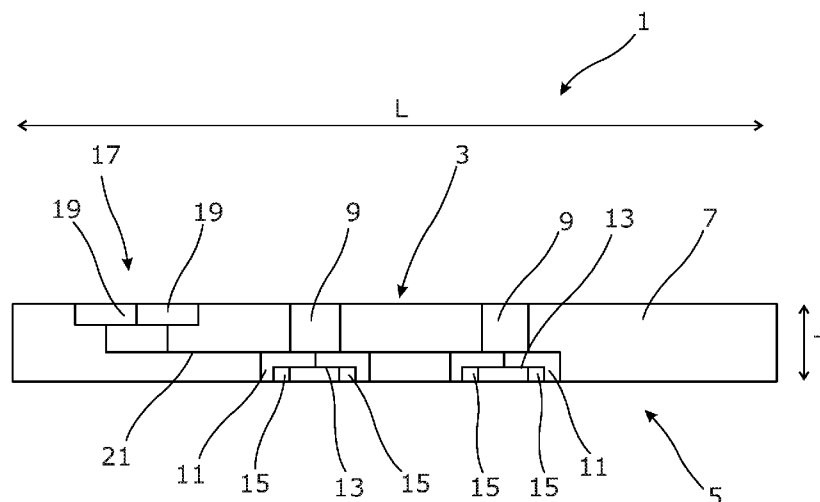


Fig. 1

(57) Abstract: A digital dispense apparatus comprising a plurality of fluid dispense devices, at least one reservoir connected to the plurality of fluid dispense devices to deliver fluid to the plurality of fluid dispense devices, at least one contact pad array, and a single monolithic carrier structure.

MONOLITHIC CARRIER STRUCTURE FOR DIGITAL DISPENSING

BACKGROUND

[0001] In the field of titration, digital titration is replacing manual or analogue titration because of its efficiency and precision. High precision digital titration apparatuses include replaceable, digital titration cassettes that are to be placed and replaced in a digital dispense host apparatus.

[0002] Digital titration cassettes are provided with a row of fluid dispense dies on a bottom side and an equal number of reservoirs on a top side. The fluid dispense dies can be discrete MEMSs (Micro-Electro-Mechanical Systems), wherein each die dispenses drops of between 11 pico-liters and 10 microliters in volume. The reservoirs are open at the top to receive fluid, for example from a pipette, and may have a narrower opening at the bottom to deliver the fluid to respective fluid dispensers at the bottom.

[0003] In operation, the dispensing dies dispense the fluid drops in wells of a well plate, e.g. micro- or multi-well plate, positioned below the cassette. For example each well may contain reagent for later analysis wherein the reagent components are at least partially determined by the digital titration host apparatus. Typically a digital titration host apparatus holds the cassette and the well plate. The host apparatus controls fluid ejection from the dies, to eject fluid into the wells. The host apparatus may properly position the cassette with respect to the well plate to dispense desired quantities of fluid in each predetermined well of the plate, for example by moving the dispensing cassette and well plate with respect to each other after each dispense action.

DRAWINGS

[0004] Fig. 1 illustrates a diagram of a cross sectional front view of an example dispense apparatus;

[0005] Fig. 2 illustrates a bottom view of another example dispense apparatus;

[0006] Fig. 3A-3C illustrate a diagrams of an example digital titration cassette in a front view, bottom view and top view, respectively;

[0007] Fig. 4 illustrates an example of a monolithic carrier structure including fluid dispense devices and electrical routing;

[0008] Fig. 5A - 5C illustrate diagrammatic examples of different fluid dispense die arrays, and Fig. 5D illustrates a corresponding reservoir array.

[0009] Fig. 6 illustrates an example of a monolithic carrier structure including contact pad arrays and a large array of reservoirs, in a perspective view onto a top side of the structure;

[0010] Fig. 7 illustrates the example monolithic carrier structure of Fig. 6 in a perspective view on a bottom side;

[0011] Fig. 8 illustrates a detail of the example monolithic carrier structure of Fig. 6 and 7, in an enlarged, perspective view on a portion of the bottom side;

[0012] Fig. 9 illustrates an example of a monolithic carrier structure in top view including a row of fluid dispense devices, electrical routing and contact pad arrays;

[0013] Fig. 10 illustrates an example of a digital titration cassette in top view, including the monolithic carrier structure of Fig. 9 and a row of reservoirs;

[0014] Fig. 11 illustrates a perspective view onto a bottom side of an example of a digital titration cassette;

[0015] Fig. 12 illustrates a perspective view onto a top side of the example digital titration cassette of Fig. 11;

[0016] Fig. 13 illustrates a perspective view onto a top side of an example of a digital titration cassette;

[0017] Fig. 14 illustrates a perspective view onto a bottom side of the example digital titration cassette of Fig. 13;

[0018] Fig. 15 illustrates another example of a dispense assembly in a cross sectional side view;

[0019] Fig. 16 illustrates an example of a method of manufacturing a digital titration cassette;

[0020] Fig. 17 illustrates another example of a method of manufacturing a digital titration cassette; and

[0021] Fig. 18 illustrates another example of a method of manufacturing a digital titration cassette.

DESCRIPTION

[0022] Fig. 1 illustrates an example of a digital dispense apparatus 1 in a diagrammatic cross sectional front view. In one example the digital dispense apparatus 1 is a digital titration cassette. The digital titration cassette may be intended for insertion into a digital titration host apparatus, and for replacement by another cassette after usage. The digital titration cassette may dispense fluids into micro- or multi-well plates or the like that extend below the digital titration cassette during dispensing, for receiving the fluids. In an example, the well plates are to hold separate reagents of similar or different compositions in separate containers. In different examples the wells are to hold several picoliters to several microliters of fluid. Although one example of the digital dispense apparatus is a digital titration cassette that includes digitally actuable fluid dispense devices, the principles described in this disclosure may also apply to other application areas that involve high precision, digitally driven, fluid dispensing.

[0023] The illustrated dispense apparatus 1 has a top side 3 and a bottom side 5. Although this disclosure refers to “top” and “bottom”, these words should be considered as relative to each other. The dispense apparatus 1 can have any orientation, wherein what is called a top side may in practice extend on a bottom and vice versa. In one example, the top and bottom refer to orientation of the apparatus 1 during dispensing.

[0024] The digital dispense apparatus 1 includes at least one monolithic carrier structure 7. The carrier structure 7 is cast as a single piece. Example monolithic carrier structures 7 may include epoxy mold compound, glass, FR4, or any suitable molded plastics or PCB. In the illustrated example, the digital dispense apparatus 1 is of a relatively planar shape, wherein “planar” may refer to a thickness T of at least three times less than a length L or width (the width extending into the page) of the apparatus 1, or at least five times less its length L or width.

[0025] The at least one carrier structure 7 carries reservoirs 9 that are to receive fluid. Each reservoir 9 may be to receive fluid from an external source

such as a pipette and deliver that fluid to a fluid dispense device 11 downstream of the reservoir 9. The reservoirs 9 may extend at the top side 3 of the carrier structure 7. The reservoirs 9 can be pre-molded cut outs in the carrier structure 7 or separately attached cups that fluidically connect to the fluid dispense devices 11.

[0026] The at least one carrier structure 7 carries fluid dispense devices 11 at its bottom side 5. Each fluid dispense device 11 may be provide with an array of drop generators 15 to dispense fluid drops into a well of a well plate. The fluid dispense devices 11 can be embedded in the carrier structure 7 or adhered to it, either directly or indirectly through another carrier structure. In one example the apparatus 1 includes at least one row and at least two columns of fluid dispense devices 11. An example dispense apparatus 1 had more columns than rows in the array of dispense devices 11. A length of a row may extend parallel to the length L of the apparatus 1.

[0027] For example, the reservoirs 9 may be partly cup shaped, i.e. open at the top, to receive fluid, and also open at a bottom or side to deliver fluid towards the fluid dispense devices. The reservoir 9 may be wider at the top and narrower at the bottom, for example tapering or curving in the direction of flow. The reservoirs 9 may fluidically connect to fluid feed slots in the fluid dispense devices 11. In one example, additional fluid routing is provided between the reservoirs 9 and fluid dispense devices. In one example, fluid routing is provided to deliver fluid from one reservoir 9 to a plurality of fluid dispense devices 11. The fluid dispense devices 11 may include at least one feed slot and micro channels 13 downstream of the feed slot, for example in a fan out manner, to receive the fluid from the reservoirs 9 and guide the fluid towards nozzle arrays.

[0028] Each fluid dispense device 11 may be part of a MEMS die. In one example each one fluid dispense device 11 is formed by one separate die. In another example, a single die includes a plurality of fluid dispense devices 11. The die may include processed silicon and thin film layers. A fluid feed slot may extend through a silicon substrate of the die. Drop generators 15 and micro channels 13 may extend in the thin film layers. In this disclosure, each drop generator 15 may include a nozzle chamber, at least one drop ejection

actuators in the nozzle chamber and at least one corresponding nozzle. The nozzle chambers receive fluid from the microchannels. The drop ejection actuators dispense the fluid out of the nozzle chamber through the nozzles. The nozzles extend through a nozzle plate of the fluid dispense device 11. For example, the actuators can be thermal resistors or piezo actuators. Each fluid dispense device 11 includes at least one drop generator array. The drop generators may function similar to drop generators used in thermal inkjet or piezo inkjet printheads. Each fluid dispense device 11 may have any number of drop generators 15, varying from 1 to approximately 1000, for example. Each fluid dispense device 11 may facilitate dispensing a single drop out of a single nozzle at a time, allowing for very low volumes of fluid to be ejected, for example 11 picoliters or less.

[0029] The digital dispense apparatus 1 includes an array 17 of contact pads 19. The contact pad array 17 is to interface with electrodes of a host apparatus to allow the host apparatus to control the drop generators 15 of the fluid dispense devices 11. The dispense apparatus 1 further includes electrical routing 21 that connects said contact pad array 17 with the plurality of fluid dispense devices 11. In one example, one contact pad 19 of an array 17 can connect to a plurality of fluid dispense devices 11. Each other contact pad 19 in the array 17 may also connect to a plurality of fluid dispense devices 11. Hence, rather than using a separate contact pad array 17 for each fluid dispense device 11, a single contact pad array 17 can be used to drive a plurality of fluid dispense devices 11.

[0030] In operation, at least one contact pad 19 and associated electrical routing 21 may connect to a ground circuit of the host apparatus. The grounded contact pad may be connected to the plurality of fluid dispense devices 11 through associated electrical routing 21. Another one or more contact pads 19 may connect to signaling circuitry of the host apparatus. Each signaling contact pad 19 may also be connected to a plurality of fluid dispense devices 11, through associated electrical routing 21, to signal drop generators 15 of the plurality of fluid dispense devices 11 to dispense fluid. In an example each signaling contact pad may be at least one of a supply voltage (Vdd), data, clock,

etc. Also dummy pads may be provided in the contact pad array 17, that do not connect to the fluid dispense devices 11. In certain examples, certain pads may have a different function than facilitating dispensing, for example authentication

[0031] In an example, one functional contact pad is connected to a plurality of fluid dispense devices 11. Each functional contact pad 19 may be to conduct one of ground signals, supply voltage, data and clock to/from the plurality of fluid dispense devices 11. In this disclosure, a functional contact pad array 17 includes not more than the contact pads 19 that are needed to actuate the fluid dispense device 11 to dispense fluid. One single functional contact pad array 17 wherein each functional contact pad 19 has a separate function can connect to a plurality of fluid dispense devices 11.

[0032] In one example, the dispense apparatus 1 is provided with a plurality of reservoirs 9 in a single monolithic carrier structure 7. In another example, the dispense apparatus 1 is provided with a plurality of fluid dispense devices 11 carried by a single monolithic carrier structure 7. In a further example, one or each contact pad 19 of a functional contact pad array 17 is connected to the plurality of fluid dispense devices 11.

[0033] Placing arrays of dispense components in a single, planar monolithic carrier structure 7, and allowing them to be triggered via a single functional contact pad array 17, wherein each functional contact pad 19 is connected to the plurality of fluid dispense devices 11, may facilitate (i) denser arrays of fluid dispense devices, for example of more than eight fluid dispense devices 11, (ii) flexibility in fluid dispense device array arrangements, and/or (iii) cost efficient manufacturing of the dispense apparatus 1. This may allow for optimizing digital titration cassettes to well plates of any dimension or type.

[0034] Fig. 2 illustrates a diagram of an example of a digital dispense apparatus 101 that includes a monolithic carrier structure 103 and two rows of fluid dispense dies 131. Each die 131 provides for a separate fluid dispense device 111. The fluid dispense dies 131 have nozzle arrays 123, each nozzle being part of a drop generator. In different examples, the plurality of fluid dispense dies 131 can be adhered to the carrier structure 103, directly overmolded in the carrier structure 103, or adhered to a single PCB (printed

circuit board) that is subsequently overmolded in the carrier structure 103. In an example, the plurality of fluid dispense dies 131 is adhered to a single PCB without subsequently overmolding wherein the PCB is the carrier structure 103.

[0035] The digital titration cassette 101 includes a single functional contact pad array 117. Each single functional contact pad 119 may be electrically connected to the plurality of fluid dispense dies 131. Each singular functional contact pad 119 may be connected to the plurality of dies 131 through electrical routing that extends in or along the monolithic carrier structure 103. For example, the electrical routing can be formed using MID (molded interconnect device) and/or LDS (laser direct structuring) technology. For example, all fluid dispense dies 131 in the apparatus 101 are connected to the same functional contact pads 119 of the contact pad array 117.

[0036] Figs. 3A-3C illustrates a diagram of another example digital titration cassette 201 in a front view, bottom view and top view, respectively. The digital titration cassette 201 is generally planar as illustrated by Fig. 3A. The digital titration cassette 201 includes at least one rigid, monolithic carrier structure 203 that carries reservoirs 209, fluid dispense devices 211, electric routing 221, contact pad arrays 217, etc.

[0037] Fig. 3B illustrates a bottom view of the example cassette 201. The cassette 201 includes an array 225 of fluid dispense devices 211. Each fluid dispense device 211 may be formed of a discrete, thin sliver, fluid dispense die that includes drop generator circuitry provided in thin film layers. In this disclosure a thin sliver die may include a silicon substrate with at least one thin film layer on top, wherein the die is to be provided with additional support to obtain structural stability. The monolithic carrier structure may provide such structural support. In different examples a thin sliver die has a thickness (extending into the page of the drawing) of less than approximately 500 micron, for example less than approximately 300 micron, for example less than approximately 200 micron or for example less than approximately 150 micron. In one example, the rigid monolithic carrier structure 203 may provide for mechanical support to the thin die.

[0038] Electrical routing 221 may electrically connect the fluid dispense devices 211 to the contact pad array 217. In the illustrated example, most of the electrical routing 221 is disposed on a surface of the rigid monolithic carrier structure 203, for example on the bottom surface. In different examples, the electrical routing 221 can be disposed using MID technology, LDS technology and/or flexible circuitry adhered to or embedded in the carrier structure 203. In another example the electrical routing 221 is provided on a separate PCB (printed circuit board) adhered to or embedded in the carrier structure 203. Part of the electrical routing 221 may extend through the carrier structure 203. To that end, the electrical routing 221 may include bond pads, vias or contact points 227 that connect the fluid dispense devices 211 on the bottom surface to the contact pad array 217 on the top surface. Suitable techniques such as soldering and/or wire bonding may be applied between the contact points or vias 227 and the rest of the electrical routing 221. Similarly soldering or wire bonding may be applied to connect the electrical routing 221 to the fluid devices 211 and the contact pad array 217.

[0039] Fig. 3C illustrates a top side of the example cassette 201. A contact pad array 217 that includes multiple contact pads can be provided on the top side, to interface with host apparatus circuitry. In one example singular contact pads within the contact pad array 217 are connected to a plurality of fluid dispense devices 211.

[0040] The top side of the cassette 201 further includes an array of reservoirs 209. In an example the reservoirs 209 are an integral part of the monolithic carrier structure 203. For example, the reservoirs 209 are directly molded or cut out as openings in the carrier structure 203. Each reservoir 209 may fluidically connect to a different fluid dispense device 211, for example to be able to hold and dispense different fluids, as indicated by symbols A – H. In an example, each reservoir 209 is shaped to hold approximately 100 microliter or less, approximately 50 microliter or less or approximately 20 microliter or less, in an operational position in the host apparatus.

[0041] Fig. 4 illustrates another example of a digital titration cassette 301 including a monolithic carrier structure 303, fluid dispense devices 311 and

electrical routing 321. The cassette 301 may have similar features as explained above with Figs. 3A – 3C. The cassette 301 of Fig. 4 has a plurality of rows and a plurality of columns of fluid dispense devices 311. In the illustration, the cassette 301 has two rows and eight columns of fluid dispense devices 311. Furthermore, the cassette 301 may have two separate electrical routing assemblies 321 wherein each routing assembly 321 includes bond pads, contact points and/or vias 327 to connect the electrical routing to corresponding contact pad arrays and fluid dispense dies. Routing and contact technologies may be similar as addressed previously for Figs. 3A – 3C, for example including flex circuitry, PCB circuitry, LDS, MID, etc. Each electrical routing assembly 321 may connect to a corresponding contact pad array, so that one contact pad array may be provided per row.

[0042] Figs. 5A – 5C illustrate different examples of fluid dispense device arrays 425 and Fig. 5D illustrates an example of a corresponding reservoir array 429 that delivers fluid to the fluid dispense device arrays 425. As indicated with dotted axes in Figs. 5A – 5D, the fluid dispense devices 411 in each fluid dispense array 425 are provided at the same pitch P as reservoirs 409 in each reservoir array 429. In one example the pitch P is approximately 9 millimeters. In other examples, the pitch P can be a multitude of 0.5 or 0.75 millimeters. The pitch P of each fluid dispense device can be chosen based on a well pitch of a well plate.

[0043] Each example fluid dispense array 425 in Figs. 5A – 5C has the same amount of fluid dispense devices 411. Each example fluid dispense array 425 in Figs. 5A – 5C has a different amount of fluid dispense dies 431. Fig. 5A illustrates an example wherein each fluid dispense device 411 is formed by a separate, single die 431. Fig. 5B illustrates an example wherein a single die 431 includes two fluid dispense devices 411. Fig. 5C illustrates an example wherein each single die 431 includes four fluid dispense devices 411. Each die 431 of Figs. 5B and 5C is fluidically connected to multiple reservoirs 409 so that different fluids can be dispensed from a single die into different corresponding wells. In other examples, different numbers of fluid dispense devices 411 can be included in a single die 431.

[0044] In Figs. 5A - C, each fluid dispense die 431 has a thickness, width and length wherein the thickness extends into the page, the width extends parallel to the pitch axes A, and the length extends perpendicular to the pitch axes A. The fluid dispense die 431 can be a thin sliver die, for example having a thickness of approximately 0.9 millimeters or less, approximately 0.5 millimeters or less, 300 micron or less, 200 micron or less or 150 micron or less. The width of each die 431 can be approximately 1 millimeter or less, 0.5 millimeters or less, for example approximately 0.3 millimeters or less. The length of each die 431 may depend on the pitch P and the chosen number of fluid dispense devices 411 that the die 431 incorporates. Where the pitch P is 9 millimeters, the length of each die 431 of Fig. 5A is approximately 1.5 millimeters, the length of each die 431 of Fig. 5B is approximately 10 millimeters, and the length of each die 431 of Fig. 5C is approximately 30 millimeters. For example the length of the die can be captured in a formula such as $L_s = (n * P) + m$, wherein L_s is the die length, n is the chosen number of fluid dispense devices that the die incorporates, P is the fluid dispense device pitch (that may be based on a well plate well pitch), and m may be depend on a chosen length of each fluid dispense device. For example, m can be between 0,2 and 3 millimeters. In turn the chosen length m of the fluid dispense device can depend on the desired length of a nozzle array.

[0045] As said, a plurality of fluid dispense devices 411 can be included in one die 431. A fluid dispense device is defined by being configured to dispense fluid in a separate well. The contact pad array 417 and electrical routing 421 can be configured to drive each fluid dispense device 411 separately on the same die 431. In one example, a nozzle plate includes regions with nozzle arrays spaced by regions with without nozzles, wherein the nozzle array regions define the fluid dispense devices 411 in the die 431. In another example a nozzle array may extend uninterruptedly over the length of the die, wherein the electrical routing, software and/or firmware may be configured to activate separate nozzle groups within the larger array for dispensing into separate wells, wherein each nozzle group may define a separate fluid dispense device 411. In other

examples, dummy nozzles may be provided between zones of active nozzles wherein active nozzle regions define the fluid dispense devices.

[0046] Figs. 6 – 8 illustrate an example of a monolithic carrier structure 503 in perspective views. The monolithic carrier structure 503 includes a relatively dense reservoir array 529. The illustrated monolithic carrier structure 503 may be an intermediate product without fluid dispense device array. The fluid dispense device array can be manufactured and connected separately. Fig. 6 illustrates a top side of the monolithic carrier structure 503 while Figs. 7 and 8 illustrate a bottom side of the carrier structure 503.

[0047] In the illustrated example, the carrier structure 503 includes a grip 545 that may extend in the main plane of the carrier structure 503, protruding from an edge of the structure 503. The grip is integrally molded in the carrier structure 203.

[0048] In the illustrated example, the reservoirs 509 are integrally molded in the carrier structure 503 in multiple rows and columns. For example, the reservoirs 509 are directly defined by surfaces of the monolithic carrier structure 503 so that when filled the carrier structure 503 is in direct contact with the fluid to receive the fluid from an external source and guide the fluid to the fluid dispense devices. In the illustrated example, the rows are labeled A – D and the columns are labeled 1 – 12. In the illustrated example, forty-eight reservoirs 509 are pre-molded in the carrier structure 503. In other examples, less reservoirs 509 or more reservoirs 509 can be incorporated in the carrier structure 503, for example also in a matrix arrangement.

[0049] The carrier structure 503 may carry at least one contact pad array 517 to connect to the plurality of fluid dispense devices. As illustrated by Fig. 6, the carrier structure 503 can include a plurality of discrete contact pad arrays 517 such as four discrete contact pad arrays 517, distanced from each other, wherein single functional contact pads 519 within each array 517 are to be connected to a plurality of fluid dispense devices. One fluid dispense device can be positioned under each reservoir 509. Hence, in the illustrate example each discrete contact pad array 517 connects to one row A - D of fluid dispense devices.

[0050] The contact vias 527 route through the carrier structure 503, from the top side to the bottom side, using appropriate via techniques such as mentioned earlier. As illustrated in Figs. 7 and 8, separate electrical routing groups 521A - 521D are provided on the bottom, wherein each separate electrical routing group 521A - 521D connects to a discrete contact pad array 517 on the top side. At the opposite end of the routing with respect to the contact pad arrays 517, each electrical routing group 521A - 521D is to connect to one row A - D of fluid dispense devices, for example by wire bonding each routing 521 to the appropriate die. In the illustrated example each electrical wire within each group 521A - 521D ends near a reservoir 509 from where it will connect to a corresponding fluid dispense device. Again, electrical routing 521A - 521D can be applied to the carrier structure 503 using MID and/or LDS technology

[0051] In one example, a second monolithic carrier structure such as a PCB that carries the fluid dispense devices can be readily bonded to the bottom of the illustrated monolithic carrier structure 503. The fluid dispense dies can be molded in or adhered to the second carrier structure. For example, such second monolithic carrier structure can be placed in a rectangular pre-molded cut out 551 in the bottom of the carrier structure 503. For example, bond pads of such second monolithic carrier structure can be connected to end points of the electrical routing 521A - 521D. In different examples, the first monolithic carrier structure 503 can be made of FR4, glass, molded plastics, etc. The second monolithic carrier structure can for example be made of FR4, glass, molded plastics, PCB board material, etc.

[0052] Fig. 9 illustrates a top view of an example of an assembly of a monolithic carrier structure 603 with fluid dispense dies 631 attached to it. The illustrated example monolithic carrier structure 603 includes eight through holes 635. A single row of eight fluid dispense dies 631 is attached in or over the holes 635, to the monolithic carrier structure 603. In the illustrated example, top sides of the fluid dispense die 631 are visible through the holes 635.

[0053] The carrier structure 603 may be a PCB. Contact pad arrays 19 and electrical routing 621 are provided on the carrier structure 603. For example, printed circuit layers of the PCB are used to form the electrical routing 621. The

fluid dispense dies 631 are attached to the PCB and to the electrical routing 621. For example such attaching is performed using (i) screen printed solder paste, (ii) needle or jet dispensing adhesive, (iii) stamp transferring adhesive or (iv) die attach film. Bond pads of the fluid dispense die 631 can be wire bonded to the routing 621 or the fluid dispense die 631 can be attached through heated screen printed solder paste for electrical connection. In the illustrated example, each routing group 621 of each die 631 connects to a separate contact pads array 617. A row of eight discrete contact pad arrays 617 extends along the row of fluid dispense dies 631, for connection to host apparatus electrodes to drive the fluid dispense dies 631.

[0054] Fig. 10 illustrates a digital titration cassette 601 including the assembly of Fig. 9. The assembly of Fig. 9 is assembled to a second monolithic carrier, in this example referred to as a support frame 603B. The support frame 603B may serve to slide into a host digital titration apparatus so as to be held in position. The support frame 603B may include a grip 645 to facilitate gripping and manual placement in the host apparatus. The first monolithic carrier structure 603 may be adhered to the frame 603B. The frame 603B may further support a memory device 637. For example, the memory device 637 may include product identification data, authentication data, etc. The memory device 637 may be at least one of a read-only memory, a read-write memory, a micro-controller, integrated circuitry, etc.

[0055] In the illustrated example, discrete reservoir cups 609 are adhered to the single PCB assembly on top of the through holes 635, to deliver fluids to each fluid dispense die. In another example a single monolithic reservoir cup array that contains molded reservoirs may be adhered over the PCB assembly.

[0056] Fig. 11 illustrates an example of a digital titration cassette 701, including first monolithic carrier structure 703A having embedded therein a plurality of thin sliver fluid dispensing dies 731, in such a manner that at least its nozzles are exposed. The dies 731 may be overmolded into the first molded carrier structure 703A, for example by compression molding. For example, electrical routing 721 may electrically connect to ends of the dies 731. The electrical routing 721 may be encapsulated by encapsulation material 739. The

electrical routing 721 may extend through the first monolithic carrier structure 703A to a top side of the first monolithic carrier structure 703A. Electrical traces may extend through the monolithic carrier structure 703A for example in the form of TMV (through mold vias) to route electrical wiring to the dies 731. The dies 731 may be wirebonded to the electrical routing 721. Electrical routing 721 may be provided on a second monolithic carrier structure 703B on a top side of the first monolithic carrier structure 703A.

[0057] Fig. 12 illustrates a the digital titration cassette 701 of Fig. 11 on a top side, with a view on a second monolithic carrier structure 703B on top of the first monolithic carrier structure 703A and a third monolithic carrier structure 703C on top of the second monolithic carrier structure 703B. The second monolithic carrier structure 703B may be a PCB assembly. The second monolithic carrier structure 703B may be assembled to the top of the first monolithic carrier structure 703A, for example using adhesive such as PSA (pressure sensitive adhesive). The second monolithic carrier structure 703B includes electrical routing connected to TMVs or bond pads of the first monolithic carrier structure 703A, to connect to the fluid dispense dies 731. The second monolithic carrier structure 703C further includes at least one contact pad array 717 for interfacing with a host apparatus. The at least one contact pad array 717 may extend along an edge of the second monolithic carrier structure 703B, for example between the edge and a reservoir array.

[0058] The third monolithic carrier structure 703C may be a molded, relatively rigid array of cups that form reservoirs 709 for delivering fluid to each of the fluid dispense dies 731. As illustrated by the combination of Figs. 11 and 12, a length of a single die 731 can span a column of multiple cup-shaped reservoirs 709. For example the die 731 includes a plurality of fluid dispense devices wherein each device fluidically connects to a separate reservoir 709, so that one die 731 can dispense different fluids into different corresponding wells. Similar structures were explained with reference to Figs. 5A – 5D. The pitch of the reservoirs 709 may be the same as the pitch of the intra-die fluid dispense devices.

[0059] Figs. 13 and 14 illustrate an example of a digital titration cassette 801 having only one monolithic carrier structure 803. Fig. 13 illustrates a perspective view on a top side and Fig. 14 a perspective view on a bottom side. As illustrated in Fig. 13, the monolithic carrier structure 803 includes an array of pre-molded reservoirs 809. The illustrated carrier structure 803 includes one row of reservoirs 809. Discrete contact pad arrays 817 are provided along the row of reservoirs 809. Electrical routing 821 is provided on the top side, between electrical routing 821 and electrical vias 827, such as TMVs. The electrical routing 821 can be formed by MID, for example by directly plating wires onto the carrier structure 803. The electrical vias 827 extend through the carrier structure 803 to the bottom side, to connect to fluid dispense dies 831. As illustrated in the view on the bottom in Fig. 14, further electrical routing 821 may extend from each via 827 to each fluid dispense die 801, for example again using TMV and/or MID technologies.

[0060] The fluid dispense dies 831 may be embedded in the carrier structure 803, in the bottom portion. The dies 831 may be thin sliver dies. In one example the dies 831 are overmolded using compression molding techniques. At least one fluid slot in the top of the die 831 may fluidically connect to the reservoir 809. For example wire bonding can be applied to connect the dies 831 to the routing 821 at the bottom side.

[0061] Fig. 15 illustrates a cross section of a digital titration cassette 901 having a single molded monolithic carrier structure 903. The cassette 901 is illustrated bottom up. A reservoir 909 is integrally molded in the carrier structure 903, opening into a molded fluidic passage 941. The carrier structure 903 may include molded pockets 943 in the bottom side to receive and adhere fluid dispense dies 931. Stamp transferring adhesive may be used to adhere the die 931 to the bottom surface, for example in the pocket 943. TMVs 927 may be formed in the carrier structure 903 that connect to electrical routing 921 on both sides of the carrier structure 903. The die 931 may be wire bonded to the electrical routing 921. The wire bond wires 921B and/or TMVs 927 may be encapsulating using encapsulation material 939, such as adhesive, epoxy-

based compound, etc. The encapsulation material 939 may extend in the pocket 943, between the die 931 and pocket walls.

[0062] Fig. 16 illustrates a method of manufacturing a digital titration cassette. The method includes molding a monolithic carrier structure having a reservoir array (block 100). In an example the carrier structure is planar and the reservoirs are holes through the planar carrier structure, for example having tapered or curved portions to receive and guide fluid. The method further includes providing electrical routing on the carrier structure (block 110). In different examples, the electrical routing can be provided using MID and/or LDS techniques, as well as by creating through hole vias such as TMVs. The method further includes attaching fluid dispense devices to the monolithic carrier structure (block 120). The fluid dispense devices may include or be part of fluid dispense dies that are fluidically connected to the reservoirs. Different adhesion techniques may include (i) screen printed solder paste, (ii) needle or jet dispensing adhesive, (iii) stamp transferring adhesive or (iv) die attach film, to facilitate attaching the dies to the carrier structure. The electrical routing is electrically bonded to the dies, for example through wire bonding (block 130).

[0063] Fig. 17 illustrates another example of a method of manufacturing a digital titration cassette. The method includes molding an array of fluid dispense devices into a single monolithic carrier structure near one side of the monolithic carrier structure (block 200). In one example the fluid dispense devices are thin sliver fluid dispense dies and the dies are compression molded in a plastic compound such as epoxy mold compound. The method further includes providing a fluid passage in the monolithic carrier structure (block 210). For example an array of through holes is molded in the carrier structure that connects to the die, or cut outs serving as fluid routing are molded in the carrier structure. The method further includes providing an array of reservoirs on the opposite side of the monolithic carrier structure (block 220). In one example at least one reservoir is molded into the side of the monolithic carrier structure that is opposite to the side of the fluid dispense dies, so as to connect to the earlier mentioned fluid passage or fluid routing. In another example at least one

reservoir cup is adhered to the side of the monolithic carrier structure that is opposite to the side of the fluid dispense dies.

[0064] Fig. 18 illustrates yet another example of a method of manufacturing a digital titration cassette. The method includes molding a monolithic carrier structure with an array of through holes that are to form reservoir cups for receiving and delivering fluid (block 300). The method further includes forming TMVs next to the through holes (block 310). In one example the TMVs connect to electrical routing that is applied to both sides of the monolithic carrier structure in order to electrically connect fluid dispense devices on one side with contact pad arrays on the other side. The electrical routing may be applied using MID and/or LDS techniques and/or other techniques such as patterning printed circuit layers in PCBs or by using flexible circuits. The method further includes attaching fluid dispense devices to the monolithic carrier structure over the through holes, opposite to the cupped holes, so that the holes fluidically connect to the fluid dispense devices (block 320). The method further includes connecting the TMVs with the fluid ejection devices (block 330), for example through wire bonding and/or solder paste. In a further example the bond wires and/or TMVs may be encapsulated.

[0065] As illustrated in the examples of Figs. 3B, 4, 6 – 10, and 14, most of the length of the electrical routings extends along the planar monolithic carrier structure, parallel to the monolithic carrier structure, except where it passes through the carrier structure by means of vias. Also, the contact pad arrays may generally extend on the surface of a planar monolithic carrier structure, parallel to the monolithic carrier structure. In addition, nozzles of nozzle arrays may extend through a plane that is parallel to the main surfaces of the monolithic carrier structure. Herein, the plane can be defined by the plane of the view of Figs. 2, 3B, 3C, 4, 5A – 5D, 9, 10, or the length direction L that is illustrated in Fig. 1.

[0066] In certain examples of this disclosure the pitch of the fluid dispense devices is aligned with a pitch of wells in existing well plates. For example, certain well pitches of existing well plates are 750 micron and 9 millimeters. Accordingly, the pitch of fluid dispense devices can be 9 millimeters or a

multitude of 750 micron. In the examples of this disclosure, the pitch of reservoirs in one row of reservoirs can be a discrete number times the pitch of fluid dispense devices in one row. For example where the pitch of the fluid dispense devices is 750 micron or a multitude thereof, for example 1.5 or 3 millimeter, the pitch of the reservoirs may be a discrete number times that pitch, for example 0.75, 1.5, 3, 6, 12 millimeters, etc. Fluid routing can be provided to route fluid from one reservoir to a plurality of fluid dispense devices.

[0067] The different dispense apparatus described in this disclosure may be relatively planar or planar. With “planar” it may be understood that the array 1 has a thickness T (e.g. see Fig. 1) that is at least three times or at least five times less than a width of the dispense apparatus. In Fig. 1 the width extends into the page. The length L of the dispense apparatus may be more than the width wherein the length and width of the array may form a main plane along which the monolithic carrier structure extends. For example, a total length of the cassette may be between approximately 50 and 300 millimeters, for example approximately 100 millimeters, and a total width may be between approximately 15 and approximately 200 millimeters, for example approximately 35 millimeters, not counting a protruding grip (where present), or for example approximately 20 millimeters longer including the grip. A maximum thickness of such dispense apparatus, between a top side and a bottom side, could be less than 10 millimeters, for example less than 6 millimeters, for example less than 5 millimeters, for example approximately 4 millimeters. For example the dispense apparatus can be similarly shaped as the examples of Figs. 6, 7, 10, 13 and 14.

[0068] One of the aspects of this disclosure is about using one monolithic carrier structure or a plurality of parallel monolithic carrier structures that each carry relatively large arrays of components such as reservoirs, fluid passages, fluid devices, electrical routing, etc. Also, the monolithic carrier structure may include cut out fluid routing to rout the fluid from the reservoir to the die. In one example the fluid flows directly from the reservoir to the die.

[0069] In an example, each reservoir of this disclosure is shaped to hold fluid volumes of approximately 200 microliter or less, approximately 100 microliter or less, approximately 50 microliter or less or approximately 20 microliter or less.

[0070] Each fluid dispense device of this disclosure can be composed of, or part of, a thin sliver die. A thin sliver die may have a thickness of approximately 0.9 millimeters or less, 0.5 millimeters or less, 300 micron or less, 200 micron or less or 150 micron or less. The width of each die can be approximately 1 millimeter or less, 0.5 millimeters or less, for example approximately 0.3 millimeters. The length of each die may depend on the pitch and the chosen number of fluid dispense devices it incorporates. For example the length of the die can be between approximately 1 and 80 millimeters.

[0071] The fluid dispense die technology may be leveraged from inkjet printhead technology, for example piezo or thermal inkjet technology. In different examples of this disclosure, a number of fluid dispensing nozzles per fluid dispense device may vary from 1 nozzle to approximately 1000 nozzles, for example between 5 and 600 nozzles, for example approximately 100 nozzles, not counting dummy nozzles or sensing nozzles, if any.

[0072] In the examples of this disclosures, fluid flow actuators may include thermal actuators or piezo actuators. These actuators may form part of the die. The dispense apparatus may be void of other fluid flow actuators outside of the die. For example, fluid flow may be established by at least one of fluid actuators, gravity, and capillary forces. No further proactive backpressure regulation needs to be provided. For example, no filter, no capillary media, etc.

[0073] Although this disclosure has mostly addressed digital titration cassettes, the disclosed features can apply to any digital dispense apparatus having similar features and should not be interpreted as limiting to titration applications only.

CLAIMS

What is claimed is:

1. A digital dispense apparatus, comprising
a plurality of fluid dispense devices, each device including at least one nozzle,
at least one reservoir fluidically connected to the plurality of fluid dispense
devices to deliver fluid to the plurality of fluid dispense devices,
a contact pad array wherein each contact pad is electrically connected to the
plurality of fluid dispense devices to drive the plurality of fluid dispense devices, and
a single monolithic carrier structure carrying at least one of said plurality of
fluid dispense devices, at least one reservoir and contact pad array.
2. The digital dispense apparatus of claim 1 wherein all of its fluid dispense
devices are carried by the single monolithic carrier structure.
3. The digital dispense apparatus of claim 1 wherein interconnect traces connect
each single functional contact pad to the plurality of fluid dispense devices, and the
interconnect traces are provided on the monolithic single carrier structure.
4. The digital dispense apparatus of claim 1 wherein the monolithic carrier
structure is at least one monolithic carrier structure, planar and carries at least two of
all the fluid dispense devices, all reservoirs, and all contact pad arrays.
5. A generally planar digital dispense apparatus of claim 4 wherein
the contact pads extend in one plane,
the nozzle arrays of the plurality of fluid dispense devices extend in one plane,
the at least one reservoir extends through one plane,
most of the lengths of the electrical traces extend in one plane, and
said planes extend parallel to each other.
6. The digital dispense apparatus of claim 1 wherein the fluid dispense devices
are embedded in a single monolithic carrier structure.

7. The digital dispense apparatus of claim 1 wherein the at least one reservoir is defined by surfaces of the monolithic carrier structure so that when filled the carrier structure is in direct contact with the fluid to receive the fluid from an external source and guide the fluid to the fluid dispense devices.
8. The digital dispense apparatus of claim 1 wherein
a first monolithic carrier structure has embedded therein the plurality of fluid dispense devices,
electrical traces extend through the single monolithic carrier to connected to the plurality of fluid dispense devices, and
a second monolithic carrier includes at least one of (i) a contact pad array, and (ii) a plurality of reservoirs.
9. The digital dispense apparatus of claim 8 wherein the second monolithic carrier includes the at least one contact pad array and comprising a third monolithic carrier that defines the plurality of reservoirs.
10. The digital dispense apparatus of claim 1 comprising a single monolithic carrier structure that includes
at least one cut out that defines the at least one reservoir,
the contact pad array, and
electrical routing connected to the contact pad array and fluid dispense devices.
11. The digital dispense apparatus of claim 1, comprising
at least one die that defines the plurality of fluid dispense devices, wherein the die is provided at a side of the carrier structure that is opposite to the reservoir,
interconnect traces are provided through the carrier structure to connect the contact pad array to the plurality of fluid dispense devices.

12. The digital dispense apparatus of claim 11 wherein the monolithic carrier forms fluid routing between the reservoir and the die so that in operation fluid routing walls, downstream of the reservoir, are in contact with fluid to guide fluid from the reservoir to the die.
13. A digital titration cassette, comprising
 - a single monolithic carrier structure that carries
 - a plurality of fluid dispense devices, and
 - interconnect traces connected to the plurality of fluid dispense devices;
 - at least one reservoir fluidically connected to the plurality of fluid dispense devices to deliver fluid to the plurality of fluid dispense devices; and
 - at least one contact pad array electrically connected to the plurality of fluid dispense devices, to connect to host device electrodes to drive the fluid dispense devices.
14. A method of manufacturing a digital titration cassette, comprising
 - molding a monolithic carrier structure having a reservoir array,
 - providing for at least one contact pad array and electrical routing on the monolithic carrier structure,
 - attaching a plurality of fluid dispense devices to the monolithic carrier structure, and
 - wire bond electrical routing to dies.
15. A method of manufacturing a digital titration cassette, comprising
 - overmolding a plurality of fluid dispense devices into a monolithic compound carrier structure at one side of the monolithic compound carrier structure,
 - providing fluid routing in the monolithic compound carrier structure, and
 - providing for reservoirs and contact pad arrays on an opposite side of the monolithic carrier structure.
16. A method of manufacturing a digital titration cassette, comprising

molding a monolithic carrier structure with an array of through holes that are to form reservoir cups,
forming at least one contact pad array and electrical routing on the monolithic carrier structure,
forming TMVs (through mold vias) next to the holes,
attaching fluid dispense devices to the holes, opposite to the cups, to fluidically connect to the holes, and
connecting the TMVs and fluid dispense devices.

17. A planar digital titration cassette, comprising
a plurality of fluid dispense dies having thicknesses of less than approximately 0.9 millimeters and including fluid actuators to dispense fluid,
a single monolithic carrier structure that carries
the plurality of fluid dispense dies, and
electrical routing connected to the plurality of fluid dispense dies;
a reservoir array wherein the reservoirs are open at the top to receive fluid and fluidically connected to the plurality of fluid dispense dies to deliver the fluid to the plurality of fluid dispense dies, wherein part of the fluid routing is formed by the carrier structure; and
a contact pad array connected to the plurality of fluid dispense dies, to connect to host device electrodes to drive the plurality of fluid dispense dies, wherein the fluid dispense dies provide for more than eight fluid dispense devices.

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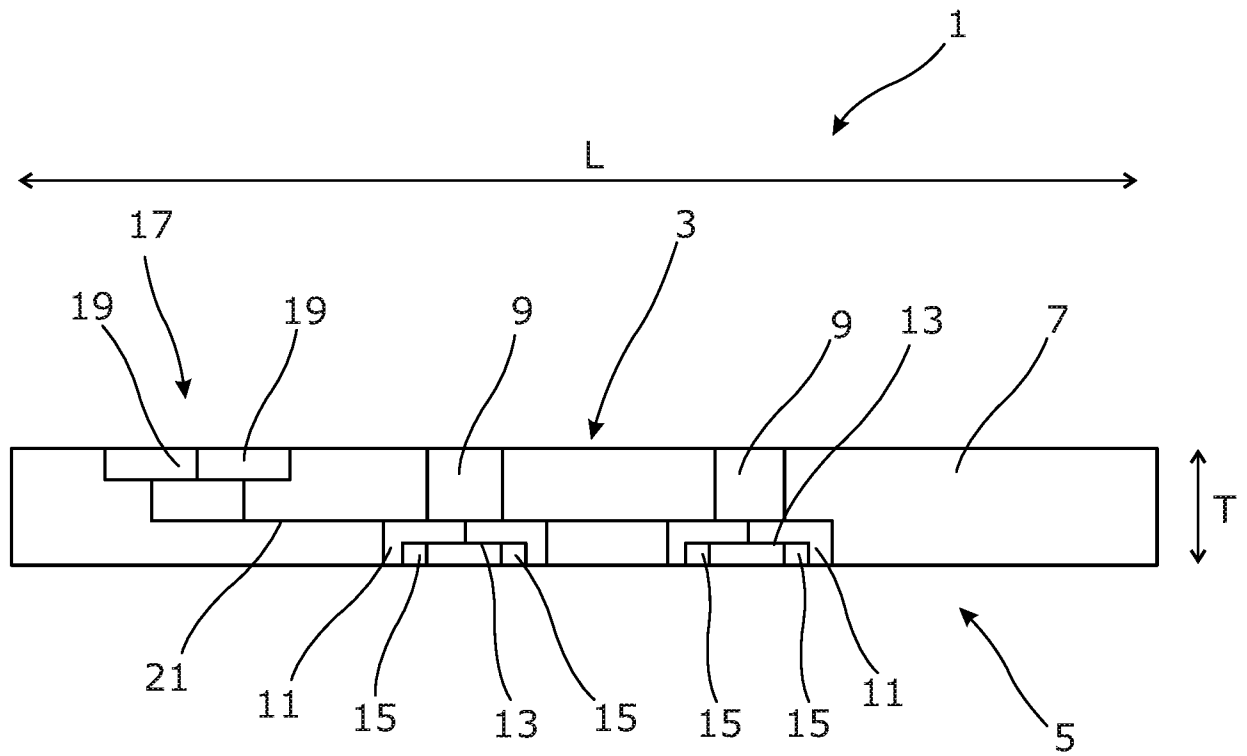


Fig. 1

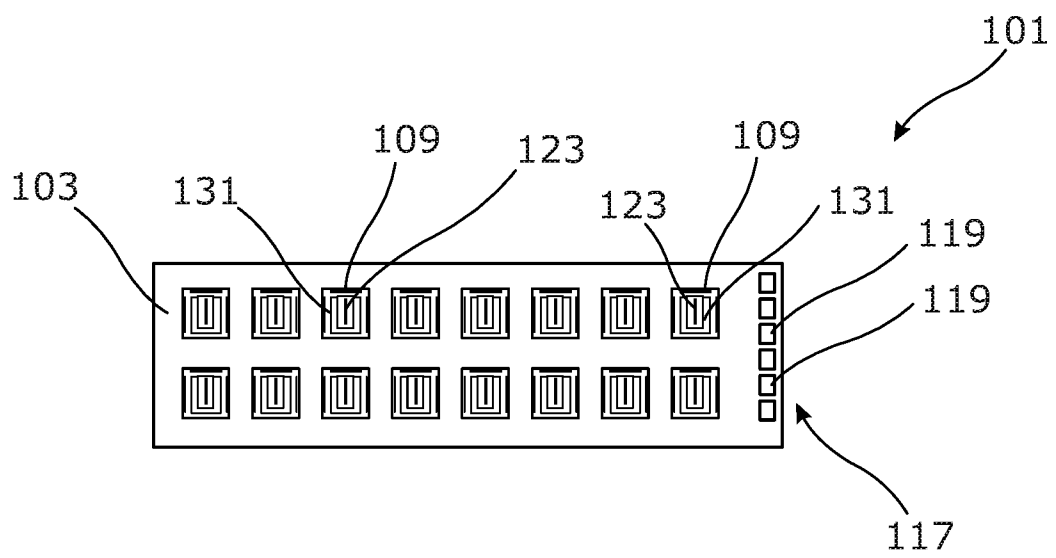


Fig. 2

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Fig. 3A

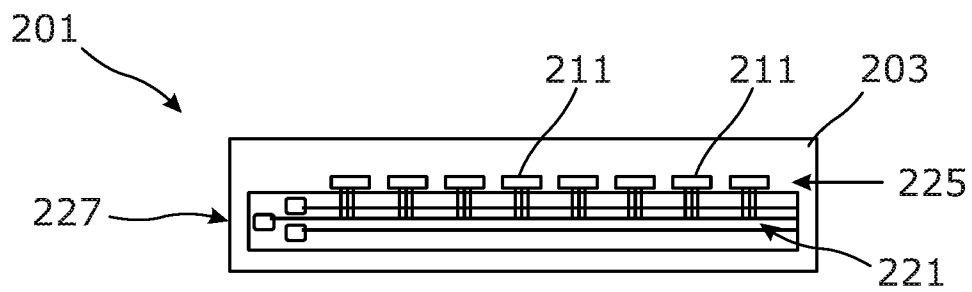


Fig. 3B

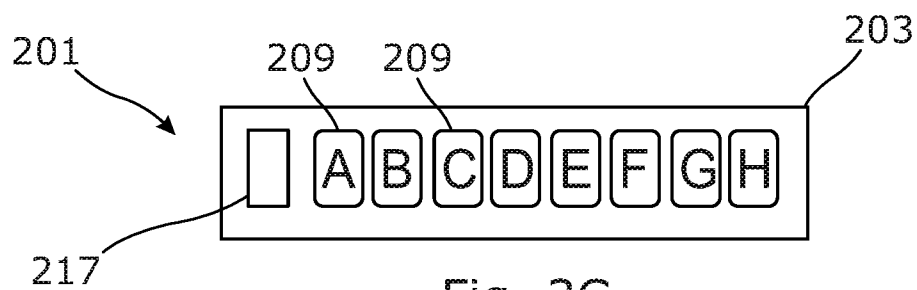


Fig. 3C

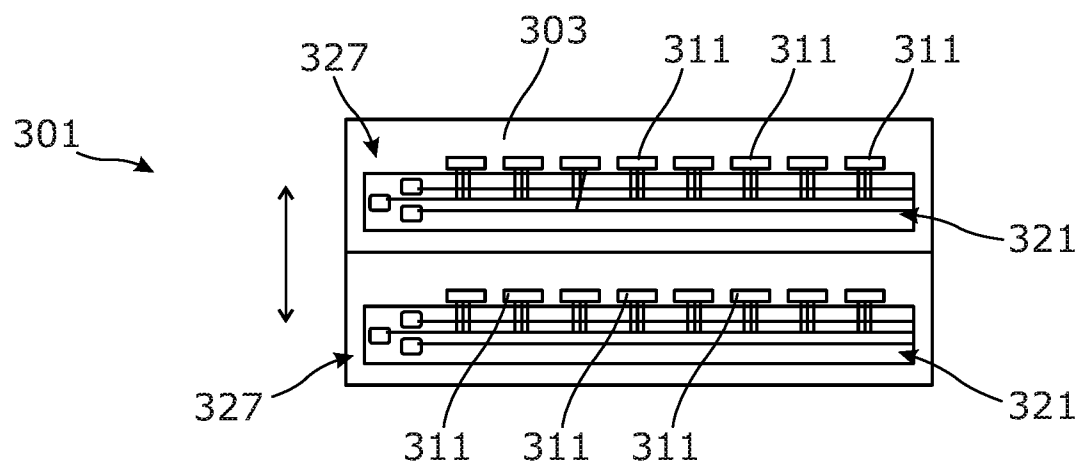
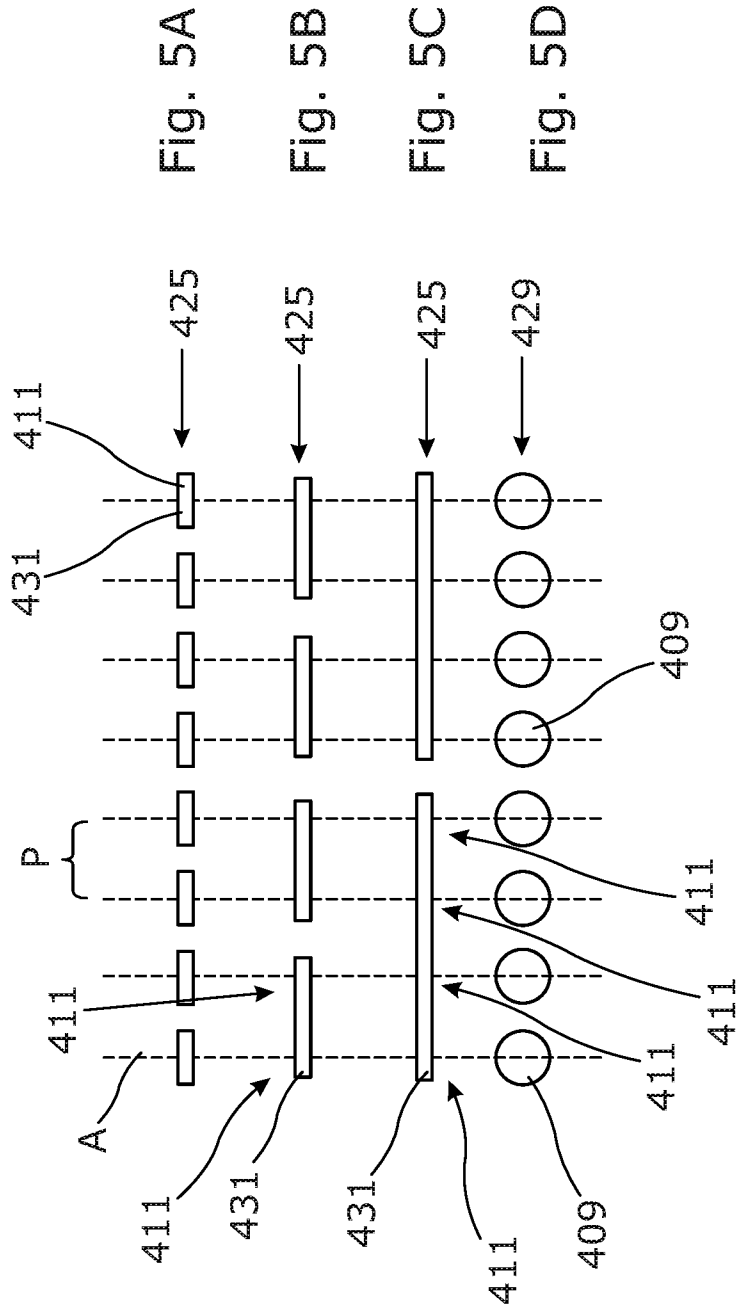


Fig. 4



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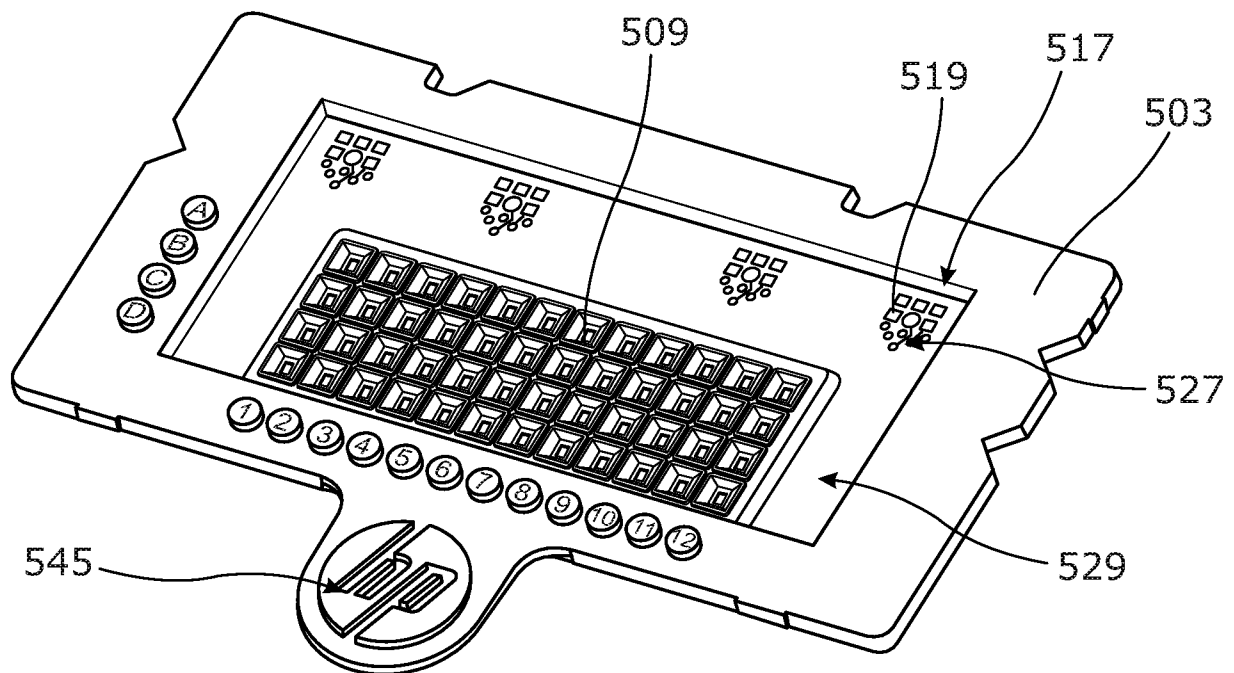


Fig. 6

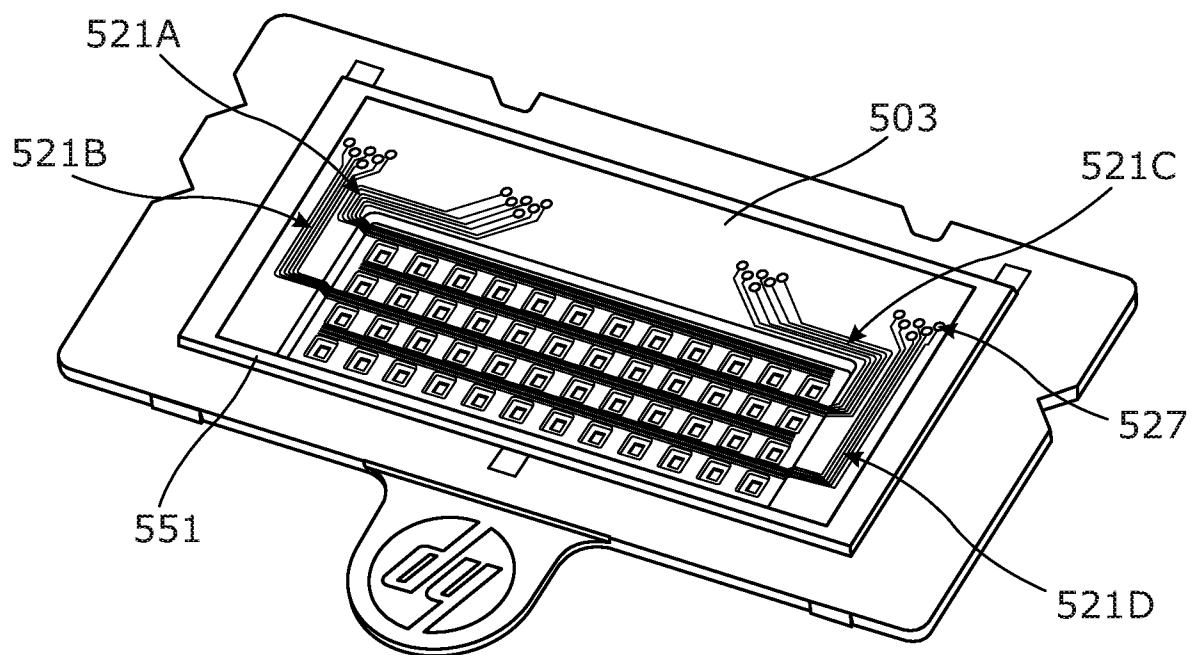


Fig. 7

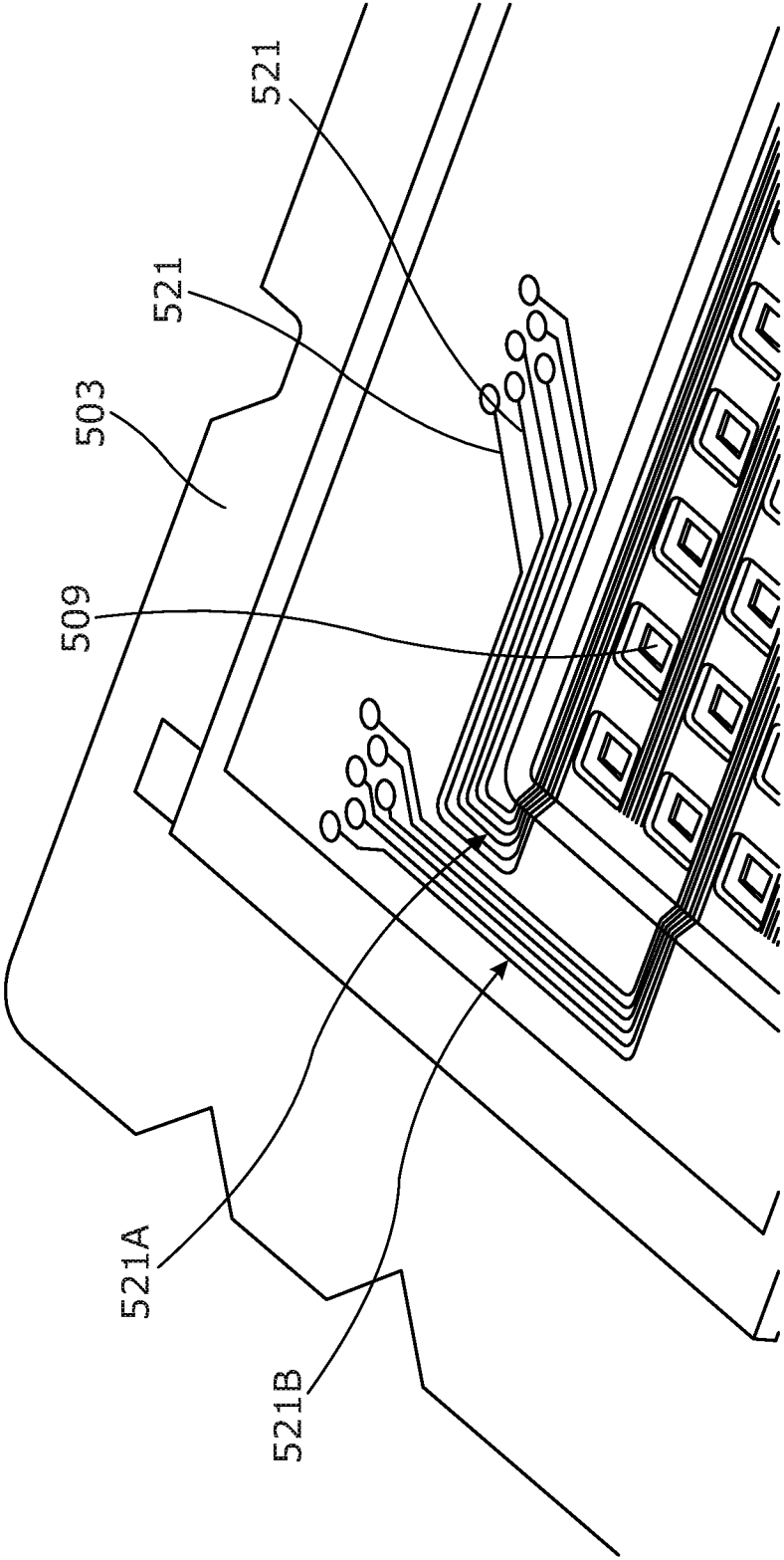


Fig. 8

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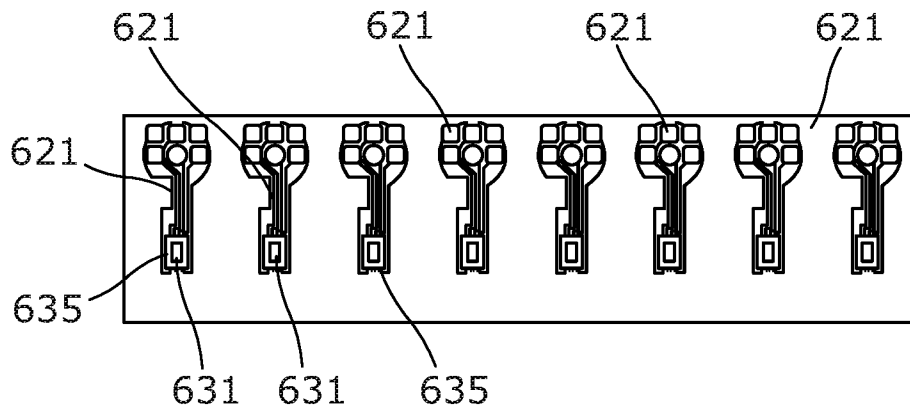


Fig. 9

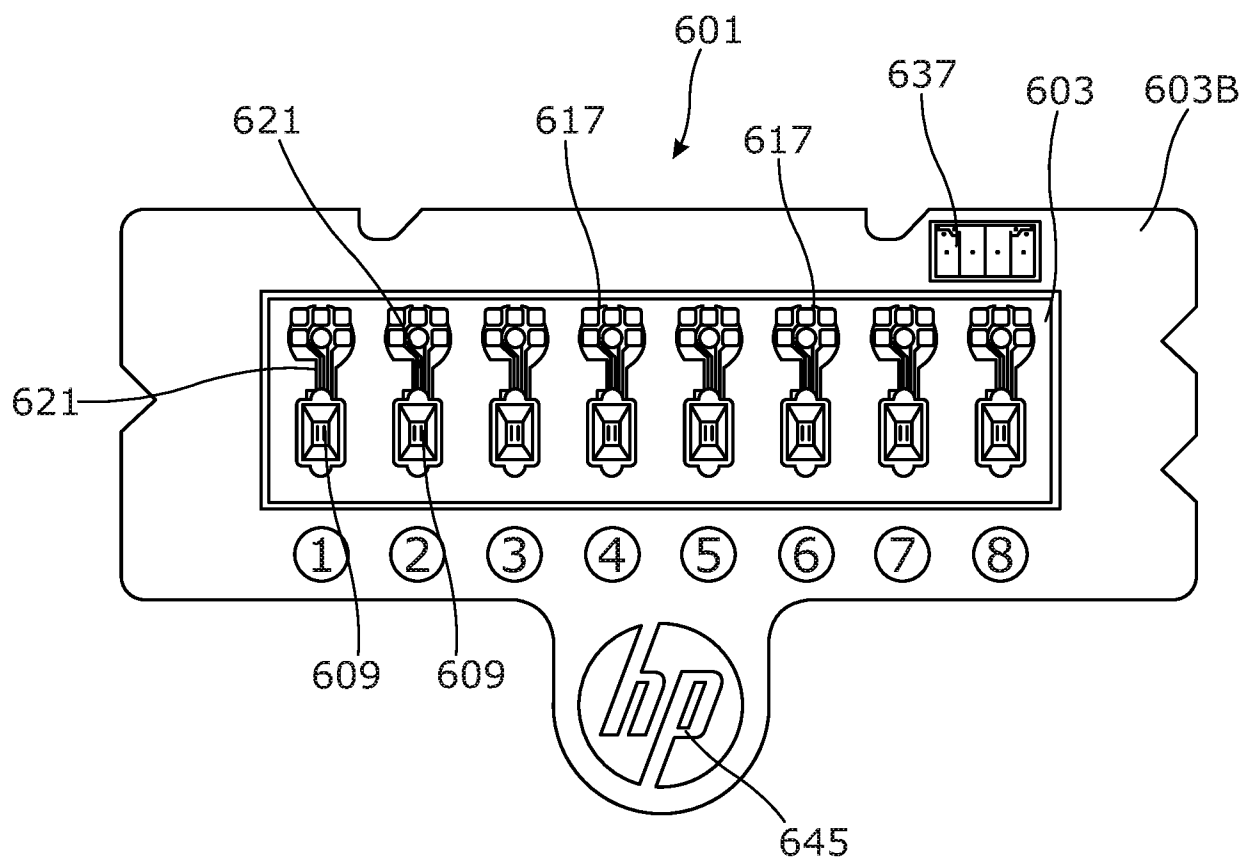


Fig. 10

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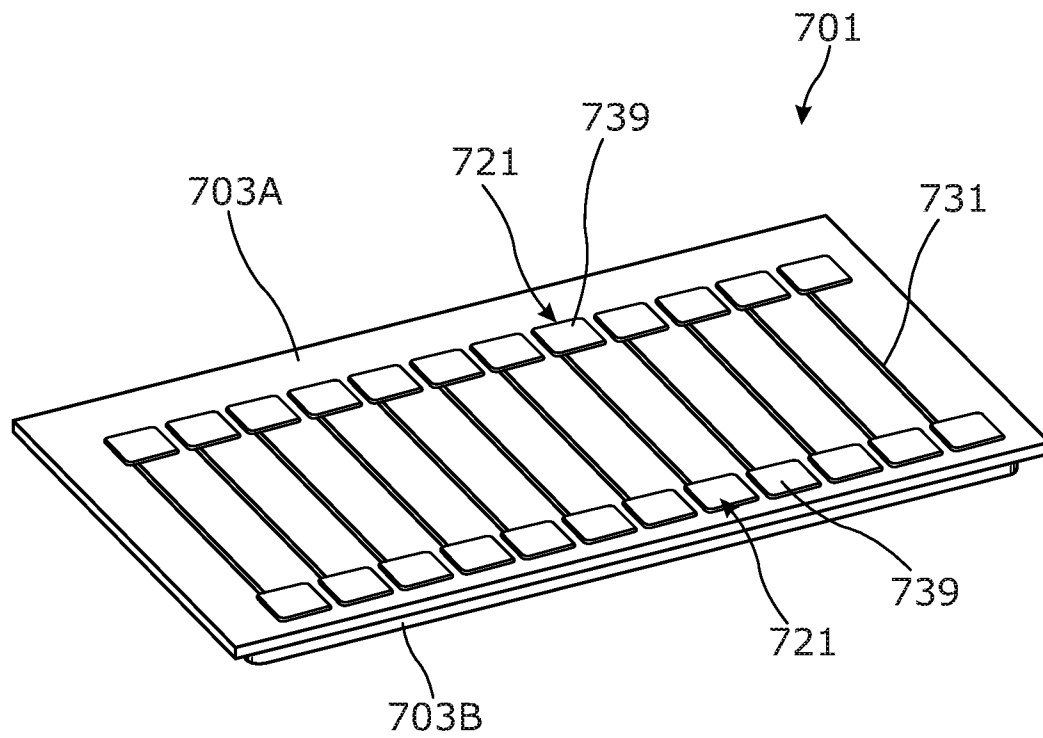


Fig. 11

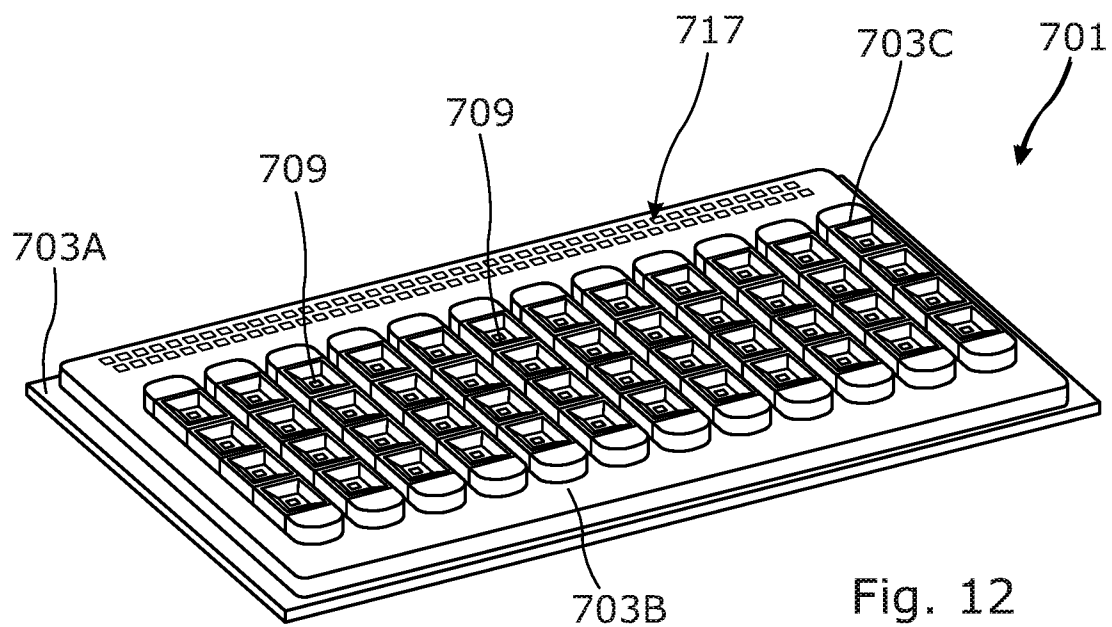


Fig. 12

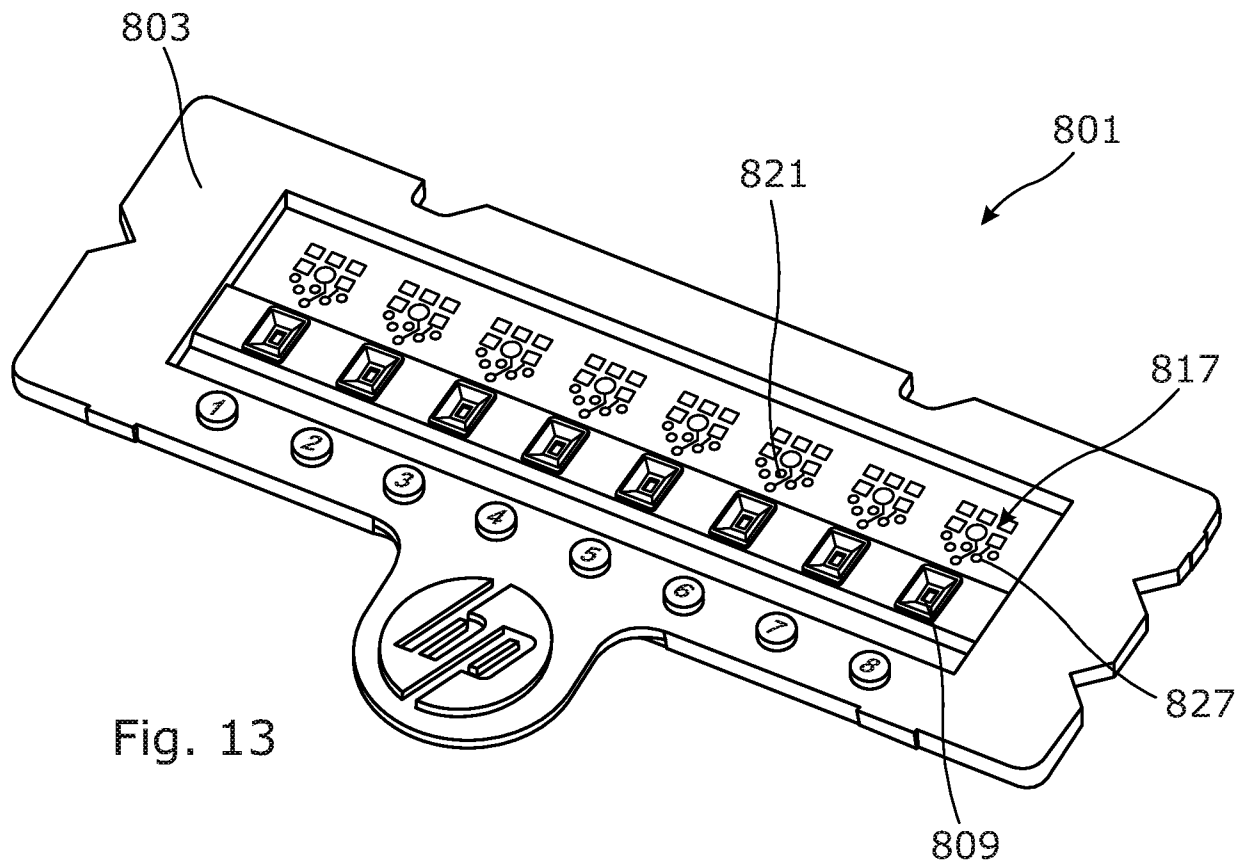


Fig. 13

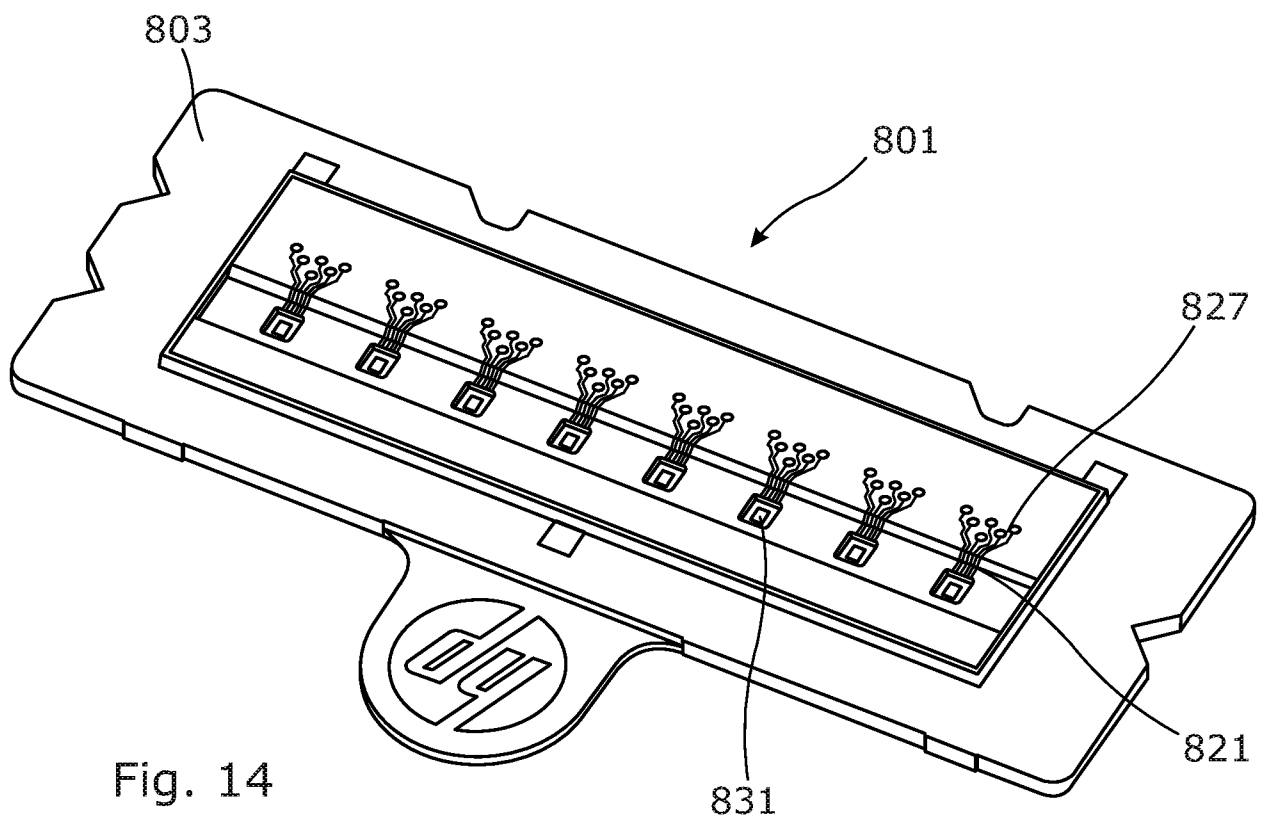


Fig. 14

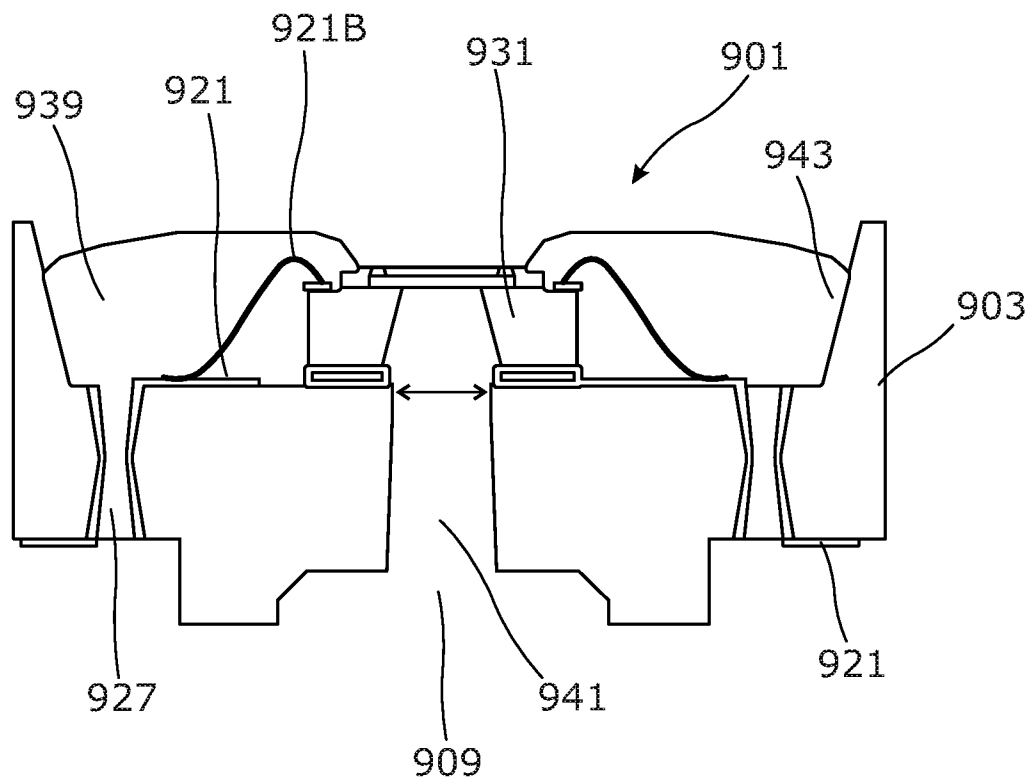


Fig. 15

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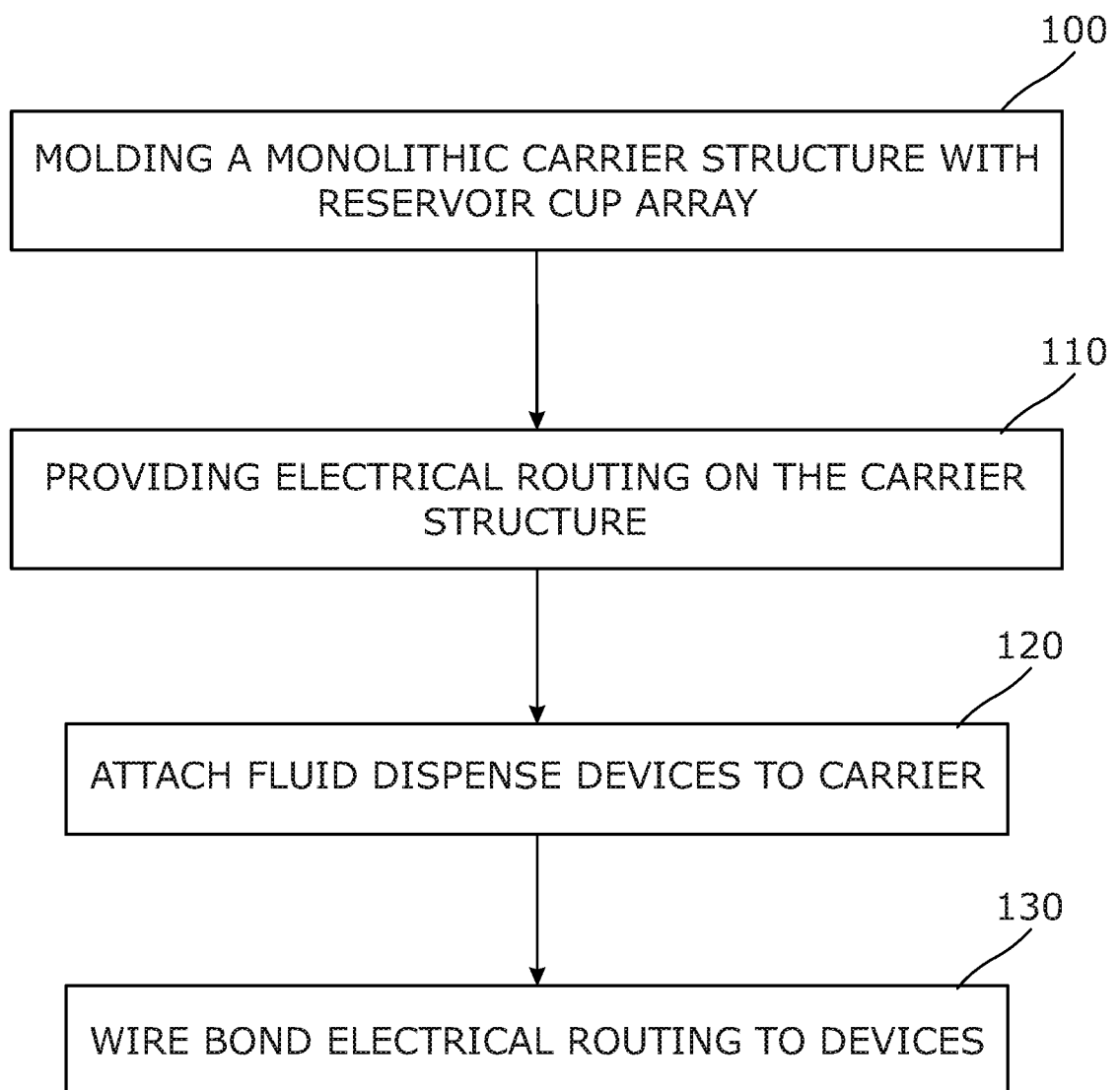


Fig. 16

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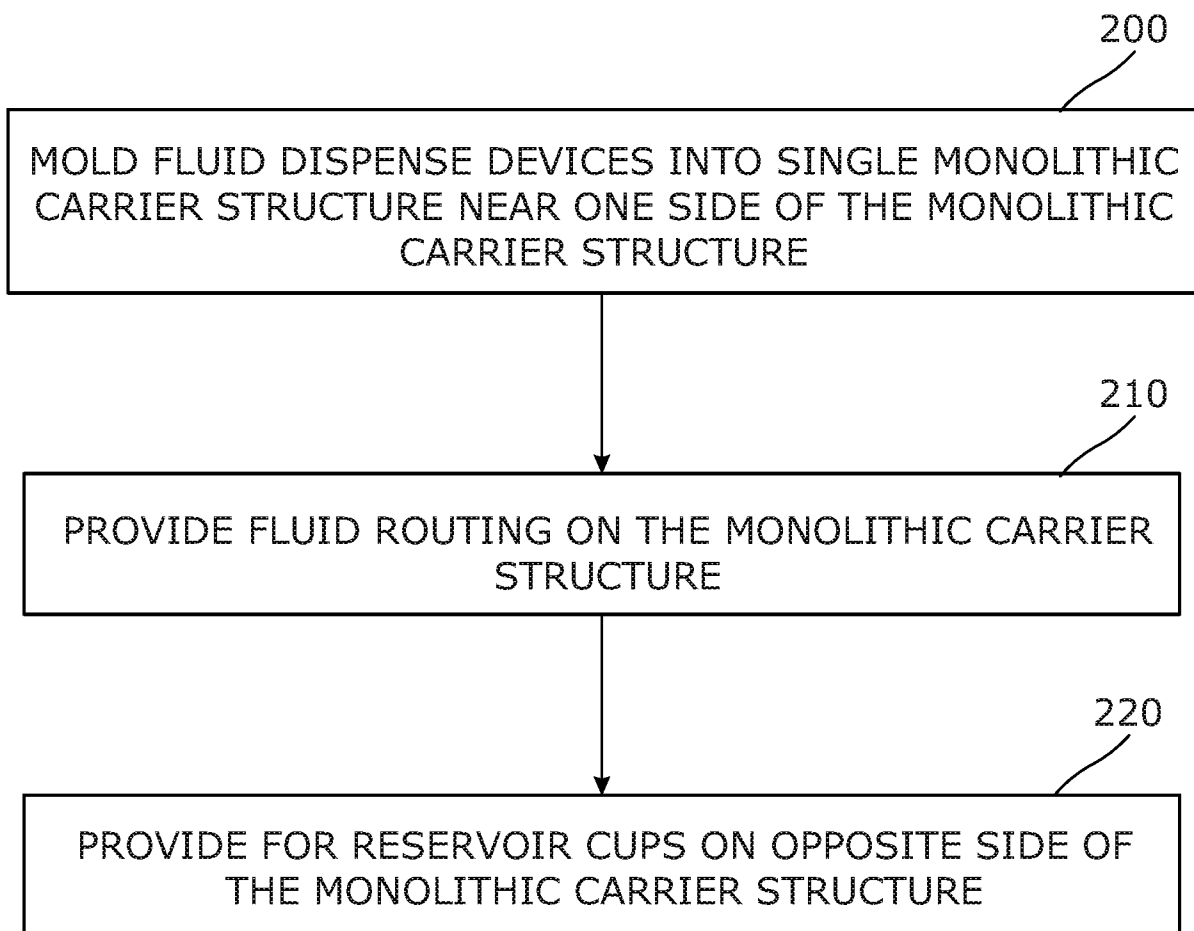


Fig. 17

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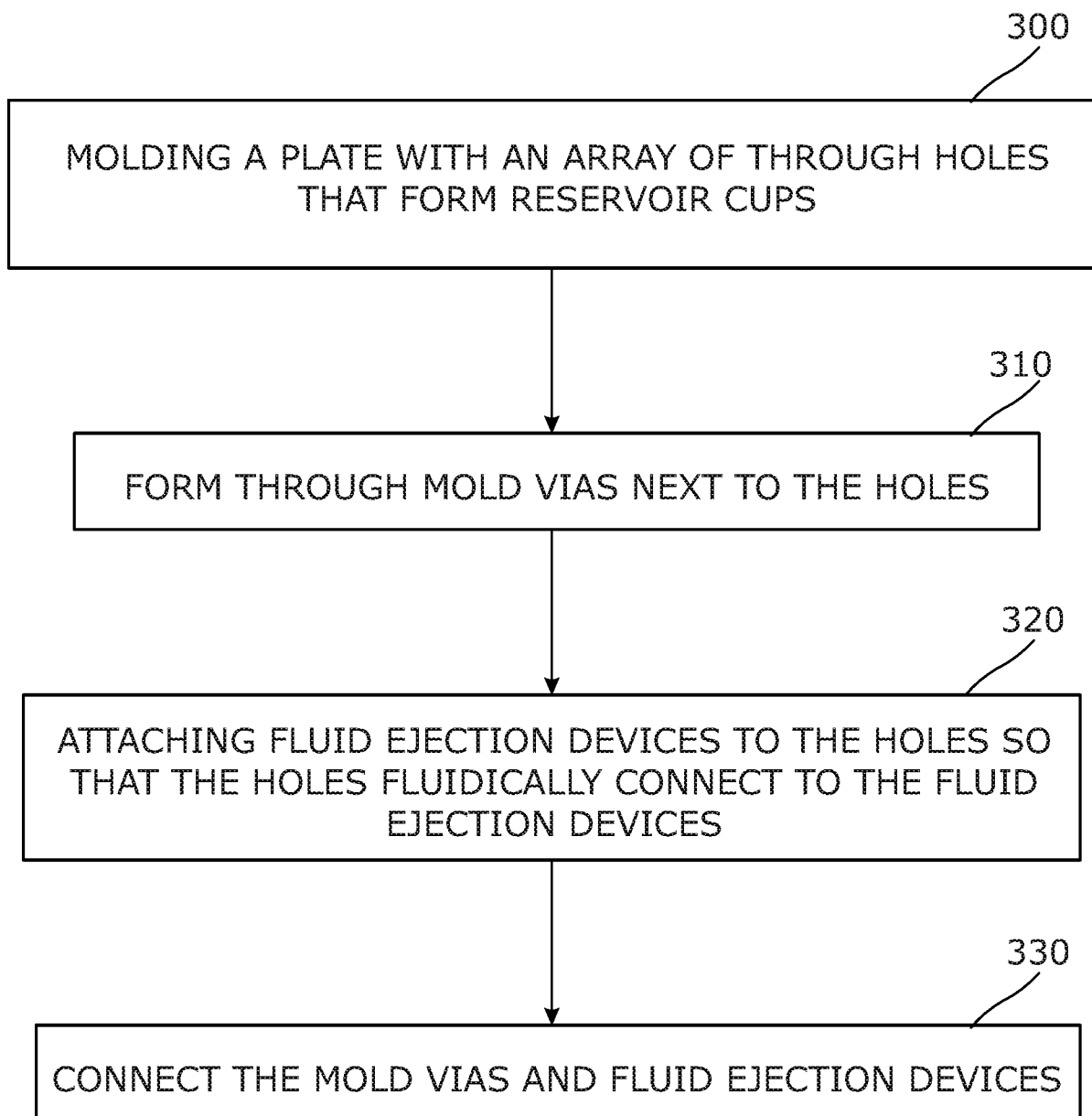


Fig. 18

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2016/025321**A. CLASSIFICATION OF SUBJECT MATTER****B01L 3/00(2006.01)i, B01L 9/00(2006.01)i**

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)

B01L 3/00; B01L 302; G05B 15/02; B41J 2/155; G01N 21/47; G01N 110; B01L 9/00

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

Korean utility models and applications for utility models

Japanese utility models and applications for utility models

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

eKOMPASS(KIPO internal) & Keywords: digital titration, fluid dispense, reservoir, nozzle, contact pad, cassette, carrier, die, electrical routing**C. DOCUMENTS CONSIDERED TO BE RELEVANT**

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2014-0193309 A1 (HEWLETT-PACKARD DEVELOPMENT COMPANY, L.P.) 10 July 2014 See paragraphs [0025], [0027]-[0029], [0031], [0033], [0047], [0048]; claims 1, 12, 13; and figures 8-10, 15.	1-13, 17
A		14-16
A	US 2014-0297029 A1 (PETERS, K. F.) 02 October 2014 See paragraph [0025]; and figure 1C.	1-17
A	US 2012-0051984 A1 (DUDENHOEFER, C. et al.) 01 March 2012 See paragraphs [0024]-[0036]; claim 1; and figures 1-10.	1-17
A	US 6068367 A (FABBRI, F.) 30 May 2000 See claim 1; and figures 1-3.	1-17
A	US 6833112 B2 (HOUMMADY, M.) 21 December 2004 See claim 1; and figures 1-18.	1-17

☐ Further documents are listed in the continuation of Box C.☒ See patent family annex.

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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

22 December 2016 (22.12.2016)

Date of mailing of the international search report

22 December 2016 (22.12.2016)

Name and mailing address of the ISA/KR

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/US2016/025321

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2014-0193309 A1	10/07/2014	US 9050592 B2	09/06/2015
US 2014-0297029 A1	02/10/2014	CN 103998144 A	20/08/2014
		EP 2771128 A1	03/09/2014
		EP 2771128 A4	30/09/2015
		WO 2013-062580 A1	02/05/2013
US 2012-0051984 A1	01/03/2012	US 9433939 B2	06/09/2016
US 6068367 A	30/05/2000	DE 69417990 T2	14/10/1999
		EP 0652107 A2	10/05/1995
		EP 0652107 A3	20/03/1996
		EP 0652107 B1	21/04/1999
		IT 1272050 B	11/06/1997
		IT T0930852 A1	10/05/1995
		JP 07-186386 A	25/07/1995
		JP 3542389 B2	14/07/2004
US 6833112 B2	21/12/2004	AT 317299 T	15/02/2006
		AU 2001-267673 B2	25/05/2006
		AU 6767301 A	24/12/2001
		CA 2311622 A1	15/12/2001
		CA 2411748 A1	20/12/2001
		CN 1436099 A	13/08/2003
		CN 1436099 C	28/03/2007
		DE 60117146 T2	19/10/2006
		DK 1289660 T3	12/06/2006
		EP 1289660 A1	12/03/2003
		EP 1289660 B1	08/02/2006
		ES 2258533 T3	01/09/2006
		IL 153216 A	11/02/2007
		JP 2004-503389 A	05/02/2004
		KR 10-0780971 B1	29/11/2007
		KR 10-2003-0016286 A	26/02/2003
		US 2002-0121529 A1	05/09/2002
		WO 01-96019 A1	20/12/2001