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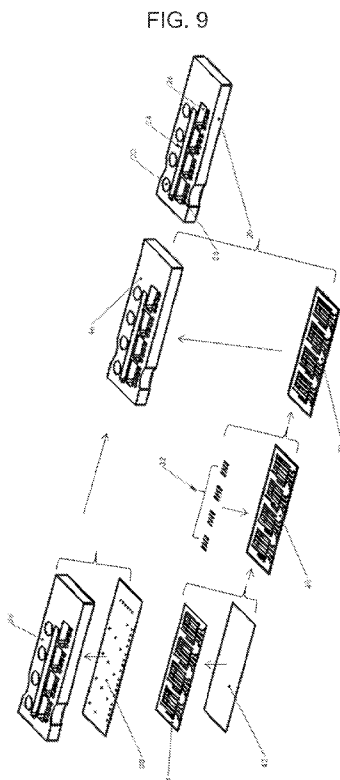
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(54) Title: MICROFLUIDIC DEVICES AND METHODS OF MANUFACTURE AND USE



(57) Abstract: Microfluidic devices are provided for conducting fluid assays, for example biological assays, that have the ability to move fluids through multiple channels and pathways in a compact, efficient, and low cost manner. Discrete flow detection elements, preferably extremely short hollow flow elements, with length preferably less than 700 micron, preferably less than 500 micron, and internal diameter preferably of between about 50 +/- 25 micron, are provided with capture agent, and are inserted into microfluidic channels by tweezer or vacuum pick-and-place motions at fixed positions in which they are efficiently exposed to fluids for conducting assays. Close-field electrostatic attraction is employed to define the position of the elements and enable ready withdrawal of the placing instruments. The microfluidic devices feature flow elements, channels, valves, and on-board pumps that are low cost to fabricate accurately, are minimally invasive to the fluid path and when implemented for the purpose, can produce multiplex assays on a single portable assay cartridge (chip) that have low coefficients of variation. Novel methods of construction, assembly and use of these features are presented, including co-valent bonding of selected regions of faces of surface-activatable bondable materials, such as PDMS to PDMS and PDMS to glass, while contiguous portions of one flexible sheet completes and seals flow channels, fixes the position of inserted analyte-detection elements in the channels, especially short hollow flow elements through which sample and reagent flow, and other portions form flexible valve membranes and diaphragms of pumps. A repeated make-and-break-contact manufacturing protocol prevents such bonding to interfere with moving the integral valve diaphragm portions from their valve seats defined by the opposed sheet member, which the flexible sheet material engages. Preparation of two subassemblies, each having a backing of relatively rigid material, followed by their assembly face-to-face in a permanent bond is shown. Hollow detection flow elements are shown fixed in channels, that provide by-pass flow paths of at least 50% of the flow capacity through the elements; in preferred implementations, as much as 100% or more. Metallized polyester film is shown to have numerous configurations and advantages in non-permanently bonded constructions. A method of preparing detection elements for an assay comprises batch coating detection elements, or hollow flow elements by mixing and picking and placing the ele-

ments in flow channels of a microfluidic device, capturing the flow elements by bonding two opposed layers while sealing the flow channels.





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PCT/US2012/030216**A. CLASSIFICATION OF SUBJECT MATTER***G01N 35/08(2006.01)i, G01N 21/64(2006.01)i, G01N 21/47(2006.01)i, G01N 33/53(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)

G01N 35/08; G01N 31/22; G01N 33/558; G01N 33/567; G01N 33/543; G01N 33/53; G01N 33/551; C12M 1/34

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: microfluidic, assay, flow, channel, detection, hollow, capture, agent

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2010-0081216 A1 (YAGER, PAUL et al.) 01 April 2010 See abstract; claims 1-2, 12; paragraphs [0012], [0078]; fig. 15A.	1-6, 40-44, 46-52, 55
A	US 6576478 B1 (WAGNER, PETER et al.) 10 June 2003 See abstract; claims 1, 3; column 7, lines 40-44; fig. 1.	1-6, 40-44, 46-52, 55
A	US 2005-0249633 A1 (BLATT, JOEL M. et al.) 10 November 2005 See abstract; claims 21, 52; paragraph [0101]; fig. 6A.	1-6, 40-44, 46-52, 55
A	US 2002-0102742 A1 (PARCE, JOHN WALLACE et al.) 01 August 2002 See abstract; claim 37; paragraphs [0041], [0049]; fig. 1.	1-6, 40-44, 46-52, 55
A	US 2009-0053732 A1 (VERMESH, OPHIR et al.) 26 February 2009 See abstract; claim 1; paragraphs [0049], [0053]; figs. 1-2.	1-6, 40-44, 46-52, 55

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

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