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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,
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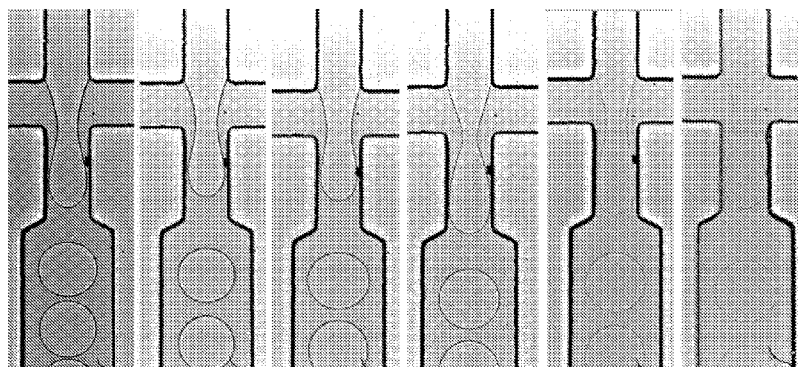


Figure 10

(57) **Abstract:** We describe a method of label-free cell and/or particle sorting in a microfluidic device, the method comprising; providing a stream of aqueous droplets in oil in a channel of said microfluidic device, wherein at least some of said droplets include cells and/or particles illuminating said stream from a first direction; detecting, for example, scattered light from cells and/or particles within said aqueous droplets in a second direction; determining, for example, a number of said cells and/or particles in each droplet from the scattered light; and sorting said aqueous droplets into one of a plurality of differentiated streams responsive to said determined number. The method further comprises modifying a refractive index of said oil to more closely match a refractive index of said aqueous droplets to reduce light scattered from boundaries of said droplets. Optionally a volume of the droplets is also controlled. In embodiments the oil is fluorinated oil. We describe examples of preferred refractive index modifying compounds.

INTERNATIONAL SEARCH REPORT

International application No
PCT/GB2014/052332

A. CLASSIFICATION OF SUBJECT MATTER
INV. B01L3/00
ADD.

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

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
B01L

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

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

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2008/053205 A1 (POLLACK MICHAEL G [US] ET AL) 6 March 2008 (2008-03-06) paragraphs [0395], [0396], [0407], [0550] - [0554] -----	1,18
A	DANIEL R GOSSETT ET AL: "Label-free cell separation and sorting in microfluidic systems", ANALYTICAL AND BIOANALYTICAL CHEMISTRY, SPRINGER, BERLIN, DE, vol. 397, no. 8, 25 April 2010 (2010-04-25), pages 3249-3267, XP019839258, ISSN: 1618-2650 page 3263 -----	1,2,18



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"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

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INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/GB2014/052332

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 2008053205 A1	06-03-2008	US 2008053205 A1	06-03-2008
		US 2011186433 A1	04-08-2011
		US 2015053562 A1	26-02-2015

INTERNATIONAL SEARCH REPORT

International application No.
PCT/GB2014/052332

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
1-12, 18-20(completely); 14-17(partially)

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: 1-12, 18-20(completely); 14-17(partially)

Claims 1-12 and claim 14 (first alternative: performing an assay by index matching of refractive indices of aqueous droplets and oil) and claims 15-17 dependent on this alternative relate to methods which are based on creating a stream of aqueous droplets in oil in a microfluidic channel. In these methods the refractive index of the oil is modified to more closely match the refractive index of said aqueous droplets in order to reduce light scattered from boundaries of the droplets . Claim 18 and dependent claims 19-20 are directed o a stream of microdroplets in an oil carrier fluid in which stream the refractive index of the oil phase is modified by a refractive index modifying compound to more closely match the refractive index of said aqueous droplets to the oil phase. In all these claims the problem that is solved amounts to reducing the refractive index mismatch between the aqueous droplets and the carrying oil phase.

2. claims: 13, 21(completely); 14-17(partially)

Claims 13, 14 (second alternative : controlling a volume of said droplets using said detected light), claims 15-17 dependent on said second alternative of claim 14, and claim 21 are directed to a method and system of regulating the volume of microdroplets flowing through a microfluidic channel by detecting light emitted from said microdroplets and determining so the flow rate of microdroplets. Here the problem of controlling the volume of the formed microdroplets is solved.
