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- with international search report (Art. 21(3))
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments (Rule 48.2(h))

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(54) Title: COALESCENCE OF DROPLETS

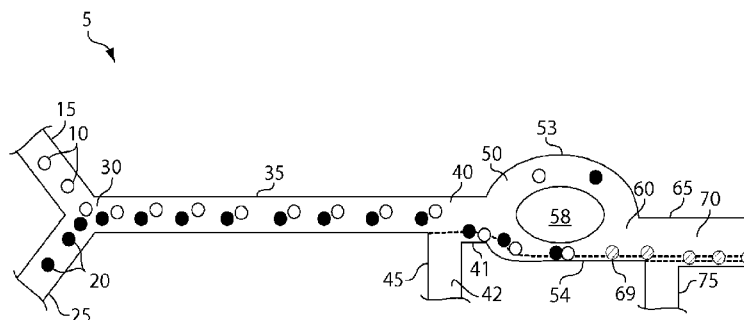


Fig. 4A

(57) **Abstract:** The present invention generally relates to microfluidics, and, in particular, to systems and methods for coalescing or fusing droplets. In certain aspects, two or more droplets within a microfluidic channel are brought together and caused to coalesce without using electric fields or charges. For example, in certain embodiments, droplets stabilized with a surfactant may be disrupted, e.g., by exposing the droplets to a solvent able to alter the surfactant, which may partially destabilize the droplets and allow them to coalesce. In some instances, the droplets may also be physically disrupted to facilitate coalesce. In addition, in some cases, the positions of one or more droplets may be controlled within a channel using a groove in a wall of the channel. For example, a droplet may at least partially enter the groove such that the position of the droplet is at least partially controlled by the groove.

A. CLASSIFICATION OF SUBJECT MATTER

IPC(8) - B01L 3/00 (2014.01)

CPC - B01L 2300/0816; B01L 3/502715

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)

CPC (B01L2300/0816; B01L3/502715; G01N2021/0353; B01L2300/0877; B01L2200/143; B01L3/0241; B01L2200/0673; B01L2200/061; F17D3/01; B01L3/502784; B01J19/0046; B01J2219/00653; B01J2219/00675; B01J2219/00378; B01J2219/00621; B82Y30/00; B01L3/50)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC (422/502; 137/561.00R; 506/16; 536/25.3; 506/30; 424/424; 424/93.7; 435/325; 424/93.71; 424/93.72; 977/894; 424/93.73)

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

PatBase, Google Patents/Scholar - Terms: microfluidics droplet bubble first second stabilize solvent surface-tension interfacial alter surfactant merge pair disrupt flow electrification change modify decrease increase lower raise reduce coalescence combine contact field

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2011/0000560 A1 (MILLER et al.) 06 January 2011 (06.01.2011) para [0007], [0039], [0040], [0050], [0120]; figure 1	1-3 and 38
A	US 2012/0220497 A1 (JACOBSON et al.) 30 August 2012 (30.08.2012) -- the entire patent	1 and 38
A	US 2010/0255059 A1 (MARQUEZ et al.) 07 August 2010 (07.08.2010) -- the entire patent	1 and 38

☐ Further documents are listed in the continuation of Box C.

* 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

21 November 2014 (21.11.2014)

Date of mailing of the international search report

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Name and mailing address of the ISA/US

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Continuation of BOX NO 3. Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-3 and 38, directed to a method, comprising flowing a first fluidic droplet and a second fluidic droplet in a liquid within a microfluidic channel

Group II: Claims 39-41, directed to an article, comprising: a first, second, third, fourth and fifth microfluidic channels

Group III: Claims 53-55 and 75-77, directed to an article/method, comprising microfluidic channel containing a groove defined in a wall of the channel, wherein the groove comprises at least one wall that is not substantially parallel to a wall of the microfluidic channel.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features

Group I requires a method, comprising: flowing a first fluidic droplet and a second fluidic droplet in a liquid within a microfluidic channel, the first fluidic droplet and the second fluidic droplet each stabilized in the liquid using a surfactant, not required by groups II and III

Group II requires an article, comprising: a first, second, third, fourth and fifth microfluidic channels, not required by groups I and III

Group III requires an article/method, comprising microfluidic channel containing a groove defined in a wall of the channel, wherein the groove comprises at least one wall that is not substantially parallel to a wall of the microfluidic channel, not required by I and II

Common Technical Features

Groups I-III share the common feature of a flowing a fluidic droplet in a liquid in a microfluidic channel. However, this technical feature, does not represent a contribution over prior art, as being anticipated by US 2011/0000560 A1 to Miller et al. (hereinafter Miller). Miller teaches a method, comprising: flowing a first fluidic droplet and a second fluidic droplet in a liquid within a microfluidic channel (para [0007] --providing a microfluidic system comprising at least one microfluidic channel; producing a first plurality of fluidic droplets within said microfluidic channel at a first frequency; producing a second plurality of fluidic droplets within said microfluidic channel at a second frequency, wherein at least one fluidic droplet from said first plurality and at least one fluidic droplet from said second plurality are paired).

Therefore, Groups I-III lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Note: Claims 4-37, 42-52, 56-74 and 78-83 determined unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

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.: 4-37, 42-52, 56-74 and 78-83
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:

---please see continuation in supplemental box ---

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 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.:
1-3 and 38

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.

Continuation of BOX NO 3. Observations where unity of invention is lacking

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I: Claims 1-3 and 38, directed to a method, comprising flowing a first fluidic droplet and a second fluidic droplet in a liquid within a microfluidic channel

Group II: Claims 39-41, directed to an article, comprising: a first, second, third, fourth and fifth microfluidic channels

Group III: Claims 53-55 and 75-77, directed to an article/method, comprising microfluidic channel containing a groove defined in a wall of the channel, wherein the groove comprises at least one wall that is not substantially parallel to a wall of the microfluidic channel.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Special Technical Features

Group I requires a method, comprising: flowing a first fluidic droplet and a second fluidic droplet in a liquid within a microfluidic channel, the first fluidic droplet and the second fluidic droplet each stabilized in the liquid using a surfactant, not required by groups II and III

Group II requires an article, comprising: a first, second, third, fourth and fifth microfluidic channels, not required by groups I and III

Group III requires an article/method, comprising microfluidic channel containing a groove defined in a wall of the channel, wherein the groove comprises at least one wall that is not substantially parallel to a wall of the microfluidic channel, not required by I and II

Common Technical Features

Groups I-III share the common feature of a flowing a fluidic droplet in a liquid in a microfluidic channel. However, this technical feature, does not represent a contribution over prior art, as being anticipated by US 2011/0000560 A1 to Miller et al. (hereinafter Miller). Miller teaches a method, comprising: flowing a first fluidic droplet and a second fluidic droplet in a liquid within a microfluidic channel (para [0007] --providing a microfluidic system comprising at least one microfluidic channel; producing a first plurality of fluidic droplets within said microfluidic channel at a first frequency; producing a second plurality of fluidic droplets within said microfluidic channel at a second frequency, wherein at least one fluidic droplet from said first plurality and at least one fluidic droplet from said second plurality are paired).

Therefore, Groups I-III lack unity under PCT Rule 13 because they do not share a same or corresponding special technical feature.

Note: Claims 4-37, 42-52, 56-74 and 78-83 determined unsearchable because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).