



US008772046B2

(12) **United States Patent**
Fraden et al.

(10) **Patent No.:** **US 8,772,046 B2**
(45) **Date of Patent:** **Jul. 8, 2014**

(54) **MANIPULATION OF FLUIDS AND REACTIONS IN MICROFLUIDIC SYSTEMS**

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(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1092 days.

(21) Appl. No.: **12/525,749**

(22) PCT Filed: **Feb. 6, 2008**

(86) PCT No.: **PCT/US2008/001544**

§ 371 (c)(1),
(2), (4) Date: **Mar. 9, 2010**

(87) PCT Pub. No.: **WO2008/097559**

PCT Pub. Date: **Aug. 14, 2008**

(65) **Prior Publication Data**

US 2010/0163109 A1 Jul. 1, 2010

Related U.S. Application Data

(60) Provisional application No. 60/899,849, filed on Feb. 6, 2007.

(51) **Int. Cl.**

G01N 1/38 (2006.01)

B01L 3/00 (2006.01)

(52) **U.S. Cl.**

CPC **G01N 1/38** (2013.01); **B01L 3/5027** (2013.01); **G01N 2001/386** (2013.01)

USPC **436/180**; 422/502

(58) **Field of Classification Search**

CPC ... **G01N 1/38**; **G01N 2001/386**; **B01L 3/5027**

USPC **422/502, 503; 137/2, 14; 436/180**

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2,097,692 A 11/1937 Fiegel
2,164,172 A 6/1939 Dalton

(Continued)

FOREIGN PATENT DOCUMENTS

AU 2004225691 B2 10/2004
CA 2520548 A1 9/2004

(Continued)

OTHER PUBLICATIONS

Adang, A.E. et al., The contribution of combinatorial chemistry to lead generation: an interim analysis, *Curr Med Chem* 8: 985-998 (2001).

(Continued)

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(57) **ABSTRACT**

Microfluidic structures and methods for manipulating fluids and reactions are provided. Such structures and methods may involve positioning fluid samples, e.g., in the form of droplets, in a carrier fluid (e.g., an oil, which may be immiscible with the fluid sample) in predetermined regions in a microfluidic network. In some embodiments, positioning of the droplets can take place in the order in which they are introduced into the microfluidic network (e.g., sequentially) without significant physical contact between the droplets. Because of the little or no contact between the droplets, there may be little or no coalescence between the droplets. Accordingly, in some such embodiments, surfactants are not required in either the fluid sample or the carrier fluid to prevent coalescence of the droplets. Structures and methods described herein also enable droplets to be removed sequentially from the predetermined regions.

25 Claims, 18 Drawing Sheets

