US009409173B2

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

(10) **Patent No.: US 9,409,173 B2**
(45) **Date of Patent: Aug. 9, 2016**

(54) **METHOD AND DEVICE FOR GENERATING A TUNABLE ARRAY OF FLUID GRADIENTS**

(71) Applicant: **The Arizona Board of Regents on behalf of The University of Arizona**, Tucson, AZ (US)

(72) Inventors: **Matthew D Estes**, Phoenix, AZ (US); **Cedric M Hurth**, Tempe, AZ (US); **Frederic Zenhausern**, Fountain Hills, AZ (US)

(73) Assignee: **The Arizona Board of Regents on Behalf of The University of Arizona**, Tucson, AZ (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

(21) Appl. No.: **14/092,239**

(22) Filed: **Nov. 27, 2013**

(65) **Prior Publication Data**

US 2014/0162262 A1 Jun. 12, 2014

Related U.S. Application Data

(60) Provisional application No. 61/797,139, filed on Nov. 30, 2012.

(51) **Int. Cl.**

B01L 3/00	(2006.01)
G01N 33/53	(2006.01)
B01F 13/00	(2006.01)

(Continued)

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

CPC ***B01L 3/502776*** (2013.01); ***B01F 13/0059*** (2013.01); ***B01F 15/0404*** (2013.01); ***G01N 33/5304*** (2013.01); *B01L 7/52* (2013.01); *B01L 2200/0636* (2013.01); *B01L 2200/0694* (2013.01); *B01L 2300/0816* (2013.01); *B01L 2400/0472* (2013.01);

(Continued)

(58) **Field of Classification Search**

CPC B01F 13/0059; B01F 15/0404; B01L 2200/0636; B01L 2200/0694; B01L 2300/0816; B01L 2400/0472; B01L 3/502776; G01N 33/5304

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

7,112,444 B2 9/2006 Beebe et al.
7,314,070 B2 1/2008 Jeon et al.

(Continued)

OTHER PUBLICATIONS

Abhyankar et al. (2006) "Characterization of a Membrane-Based Gradient Generator for Use in Cell-Signaling Studies," *Lab Chip.* 6:389-393.

(Continued)

Primary Examiner — Jennifer Wecker
(74) *Attorney, Agent, or Firm* — Lathrop & Gage LLP

(57) **ABSTRACT**

Provided herein are devices and methods for generating microfluidic gradients, including an array of unique microfluidic gradients within an array of microchannels. Fluids within conduits are mixed in an intersection region to generate a mixed flow stream in a source reservoir channel that provides a gradient that varies with axial distance from the intersection region. Microchannels having an inlet connected to the source reservoir channel are configured to provide a microfluidic gradient in the microchannel. An outlet end of the microchannel is connected to a sink reservoir channel. By varying the ratio of fluid flow rates from the fluid conduits, the microchannel gradients are tuned. In this manner, a large number of unique gradients or array of microfluidic gradients is provided, wherein the gradient can be any number of physical or chemical parameters, including concentrations and physical fluid properties.

18 Claims, 8 Drawing Sheets