



US009012390B2

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

(10) **Patent No.:** **US 9,012,390 B2**  
(45) **Date of Patent:** **Apr. 21, 2015**

(54) **FLUOROCARBON EMULSION STABILIZING SURFACTANTS**

(75) Inventors: **Christian Holtze**, Medford, MA (US);  
**David A. Weitz**, Cambridge, MA (US);  
**John Brian Hutchison**, Medford, MA (US)

4,022,575 A 5/1977 Hansen et al.  
4,034,966 A 7/1977 Suh et al.  
4,059,552 A 11/1977 Zweigle et al.  
4,091,042 A 5/1978 Alexanderson et al.  
4,117,550 A 9/1978 Folland et al.  
4,130,394 A 12/1978 Negersmith  
4,210,809 A 7/1980 Pelavin

(Continued)

(73) Assignee: **Raindance Technologies, Inc.**, Billerica, MA (US)

FOREIGN PATENT DOCUMENTS

(\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 1251 days.

AU 2004225691 B2 6/2010  
CA 2520548 A1 10/2004

(Continued)

(21) Appl. No.: **12/310,048**

(22) PCT Filed: **Aug. 7, 2007**

(86) PCT No.: **PCT/US2007/017617**

§ 371 (c)(1),  
(2), (4) Date: **Dec. 10, 2009**

(87) PCT Pub. No.: **WO2008/021123**

PCT Pub. Date: **Feb. 21, 2008**

(65) **Prior Publication Data**

US 2010/0105112 A1 Apr. 29, 2010

**Related U.S. Application Data**

(60) Provisional application No. 60/836,455, filed on Aug. 7, 2006.

(51) **Int. Cl.**  
**C12P 17/14** (2006.01)  
**B01F 17/00** (2006.01)  
**C08G 65/00** (2006.01)

(52) **U.S. Cl.**  
CPC ..... **B01F 17/0035** (2013.01); **C08G 65/007** (2013.01)

(58) **Field of Classification Search**  
USPC ..... 510/417; 435/212, 41  
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  
2,656,508 A 10/1953 Coulter  
2,692,800 A 10/1954 Nichols et al.  
2,797,149 A 6/1957 Skeggs  
2,879,141 A 3/1959 Skeggs  
2,971,700 A 2/1961 Peeps  
3,479,141 A 11/1969 Smythe et al.  
3,608,821 A 9/1971 Simm et al.  
3,698,635 A 10/1972 Sickles  
3,784,471 A \* 1/1974 Kaiser ..... 508/138  
3,816,331 A 6/1974 Brown, Jr. et al.  
3,930,061 A 12/1975 Scharfenberger  
3,960,187 A 6/1976 Stock et al.  
3,980,541 A 9/1976 Aine  
3,982,541 A 9/1976 L'Esperance, Jr.  
4,014,469 A 3/1977 Sato

OTHER PUBLICATIONS

Holtze et al. (surfactants for water-in-fluorocarbon emulsions Lab Chip, 2008, 8, 1632-1639).  
Tonelli et al. (Journal of fluorine Chemistry, 118 (2002) 107-121).  
International Preliminary Report on Patentability & Written Opinion for PCT/US2007/017617, mailed on Feb. 19, 2009.  
International Search Report for PCT/US2007/017617, mailed on Jan. 11, 2008.

(Continued)

*Primary Examiner* — Mark Eashoo

*Assistant Examiner* — M. Reza Asdjodi

(74) *Attorney, Agent, or Firm* — Thomas C. Meyers; Brown Rudnick LLP

(57) **ABSTRACT**

Surfactants (e.g., fluorosurfactants) for stabilizing aqueous or hydrocarbon droplets in a fluorophilic continuous phase are presented. In some embodiments, fluorosurfactants include a fluorophilic tail soluble in a fluorophilic (e.g., fluorocarbon) continuous phase, and a headgroup soluble in either an aqueous phase or a lipophilic (e.g., hydrocarbon) phase. The combination of a fluorophilic tail and a headgroup may be chosen so as to create a surfactant with a suitable geometry for forming stabilized reverse emulsion droplets having a disperse aqueous or lipophilic phase in a continuous, fluorophilic phase. In some embodiments, the headgroup is preferably non-ionic and can prevent or limit the adsorption of molecules at the interface between the surfactant and the discontinuous phase. This configuration can allow the droplet to serve, for example, as a reaction site for certain chemical and/or biological reactions. In another embodiment, aqueous droplets are stabilized in a fluorocarbon phase at least in part by the electrostatic attraction of two oppositely charged or polar components, one of which is at least partially soluble in the dispersed phase, the other at least partially soluble in the continuous phase. One component may provide colloidal stability of the emulsion, and the other may prevent the adsorption of biomolecules at the interface between a component and the discontinuous phase. Advantageously, surfactants and surfactant combinations of the invention may provide sufficient stabilization against coalescence of droplets, without interfering with processes that can be carried out inside the droplets.