

DROPLET-BASED SELECTION

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Patent Application Ser. No. 60/959,358, filed Jul. 13, 2007, entitled "Droplet-Based Selection," by Weitz, et al., and U.S. Provisional Patent Application Ser. No. 61/048,304, filed Apr. 28, 2008, entitled "Microfluidic Storage and Arrangement of Drops," by Schmitz, et al. Each of these is incorporated herein by reference.

GOVERNMENT FUNDING

[0002] Research leading to various aspects of the present invention were sponsored, at least in part, by the National Science Foundation, Grant Nos. DMR-0213805, DMR-0602684, and DBI-0649865. The U.S. Government has certain rights in the invention.

FIELD OF INVENTION

[0003] The present invention generally relates to fluidic droplets, and techniques for screening or sorting such fluidic droplets. In some embodiments, the fluidic droplets may contain cells that can secrete various species, such as antibodies, for example, hybridoma cells.

BACKGROUND

[0004] The manipulation of fluids to form fluid streams of desired configuration, discontinuous fluid streams, droplets, particles, dispersions, etc., for purposes of fluid delivery, product manufacture, analysis, and the like, is a relatively well-studied art. For example, highly monodisperse gas bubbles, less than 100 microns in diameter, have been produced using a technique referred to as capillary flow focusing. In this technique, gas is forced out of a capillary tube into a bath of liquid, the tube is positioned above a small orifice, and the contraction flow of the external liquid through this orifice focuses the gas into a thin jet which subsequently breaks into roughly equal-sized bubbles via capillary instability. In a related technique, a similar arrangement can be used to produce liquid droplets in air.

SUMMARY OF THE INVENTION

[0005] The present invention generally relates to fluidic droplets, and techniques for screening or sorting such fluidic droplets. The subject matter of the present invention involves, in some cases, interrelated products, alternative solutions to a particular problem, and/or a plurality of different uses of one or more systems and/or articles.

[0006] In one aspect, the invention is directed to a screening method. In one set of embodiments, the method comprises an act of determining a characteristic of a species expressed by a hybridoma contained within a fluidic droplet. In some cases, the fluidic droplet may be one of a plurality of fluidic droplets contained within a liquid, where the droplets have an average dimension of less than about 500 micrometers and a distribution of dimensions such that no more than about 5% of the droplets have a dimension greater than about 10% of the average dimension.

[0007] In another set of embodiments, the method includes an act of determining a characteristic of a species present within a fluidic droplet using a signaling entity comprising a microparticle and an agent, immobilized relative to the

microparticle, able to bind the species. In some cases, the fluidic droplet may be one of a plurality of fluidic droplets contained within a liquid, where the droplets have an average dimension of less than about 500 micrometers and a distribution of dimensions such that no more than about 5% of the droplets have a dimension greater than about 10% of the average dimension.

[0008] In another aspect, the invention is a method. According to a first set of embodiments, the method includes acts of providing a plurality of fluidic droplets contained within a liquid, where at least some of the fluidic droplets contain antibody-producing cells, and culturing the antibody-producing cells to secrete antibodies or portions thereof. In another set of embodiments, the method includes acts of providing a plurality of fluidic droplets contained within a liquid, where at least some of the fluidic droplets contain cells able to secrete a species, and culturing the cells to secrete the species. The method, in yet another set of embodiments, includes acts of providing a plurality of fluidic droplets contained within a liquid, where at least some of the fluidic droplets contain non-immortal cells, and determining a characteristic of a species secreted by the non-immortal cells within the fluidic droplets. The method, in still another set of embodiments, includes acts of providing a plurality of fluidic droplets contained within a liquid, where at least some of the fluidic droplets contain non-immortal cells, and determining a characteristic of a species secreted by the non-immortal cells within the fluidic droplets.

[0009] In one set of embodiments, the method includes acts of providing a plurality of fluidic droplets contained within a liquid, where some of the fluidic droplets contain cells able to secrete an species and some of the fluidic droplets contain cells not able to secrete the species, and at least partially separating the fluidic droplets containing the cells able to secrete the species from the fluidic droplets containing the cells not able to secrete the species.

[0010] The method, according to another set of embodiments, includes acts of providing a fluidic droplet contained within a liquid, the droplet containing an antibody-producing cell and a target, culturing the antibody-producing cell to secrete antibodies able to recognize the target, and determining association of the antibodies to the target. In still another set of embodiments, the method includes acts of providing a fluidic droplet contained within a liquid, the droplet containing an antibody-producing cell, a first target, an a second target, culturing the antibody-producing cell to secrete antibodies able to recognize at least one of the first target and the second target, and determining a difference in binding between the antibodies and the first and second targets.

[0011] The method, in one set of embodiments, includes acts of providing a plurality of fluidic droplets contained within a liquid, at least some of the fluidic droplets containing an antibody-producing cell and a target, where the antibody-producing cells contained within the plurality of fluidic droplets are able to secrete a plurality of distinguishable antibodies and the antibody-producing cells do not all produce the same antibodies, culturing the antibody-producing cell to secrete antibodies within the droplets, and determining, for at least some of the fluidic droplets, association of antibodies contained within the droplet and the target. In another set of embodiments, the method includes acts of providing a plurality of fluidic droplets contained within a liquid, at least some of the fluidic droplets containing an antibody-producing cell, a first target, and a second target, where the antibody-