

[0058] As mentioned, the fluid may be present within the liquid as one or more droplets. In some cases, the droplets may be formed in a device (e.g., a microfluidic device), which allows for the formation of fluidic droplets having a controlled size and/or size distribution. The device may be free of moving parts in some cases. That is, at the location or locations at which fluidic droplets of desired shape and/or size are formed, the device is free of components that move relative to the device as a whole to affect fluidic droplet formation. For example, where fluidic droplets of controlled shape and/or size are formed, the droplets are formed without parts that move relative to other parts of the device that define a channel within which the fluidic droplets flow. This can be referred to as “passive control” or “passive breakup.”

[0059] In one example of a passive system, fluid may be urged through a dimensionally-restricted section of a channel of a fluidic device, which can cause the fluid to break up into a series of droplets within the channel. The dimensionally-restricted section can take any of a variety of forms. For example, it can be an annular orifice, elongate, ovoid, square, or the like. Preferably, it is shaped in any way that causes the surrounding liquid to surround and constrict the cross-sectional shape of the fluid being surrounded. The dimensionally-restricted section is non-valved in certain embodiments. That is, it is an orifice that cannot be switched between an open state and a closed state, and typically is of fixed size. One or more intermediate fluid channels can also be provided in some cases to provide an encapsulating fluid surrounding discontinuous portions of fluid being surrounded. Thus, in one embodiment, two intermediate fluid channels are provided, one on each side of a central fluid channel, each with an outlet near the central fluid channel. Control of the fluid flow rate, and ratio between the flow rates of the various fluids within the device, can be used to control the shape and/or size of the fluidic droplets, and/or the monodispersity of the fluidic droplets. The microfluidic devices of the present invention, coupled with the flow rate and ratio control as taught herein, thus may allow significantly improved control and range.

[0060] Some embodiments of the present invention involve formation of fluidic droplets in a liquid where the fluidic droplets have a mean cross-sectional dimension no smaller than the mean cross-sectional dimension of the dimensionally-restricted section. The invention, in such embodiments, may involve control over these mean cross-sectional dimensions by control of the flow rate of the fluid, liquid, or both, and/or control of the ratios of these flow rates. In other embodiments, the fluidic droplets have a mean cross-sectional dimension no smaller than about 90% of the mean cross-sectional dimension of the dimensionally-restricted section, and in still other embodiments, no smaller than about 80%, about 70%, about 60%, about 50%, about 40%, or about 30% of the mean cross-sectional dimension of the dimensionally-restricted section.

[0061] In another set of embodiments, droplets of fluid can be created in a channel from a fluid surrounded by a liquid by altering the channel dimensions in a manner that is able to induce the fluid to form individual droplets. The channel may, for example, be a channel that expands relative to the direction of flow, e.g., such that the fluid does not adhere to the channel walls and forms individual droplets instead, or a channel that narrows relative to the direction of flow, e.g., such that the fluid is forced to coalesce into individual droplets. In some embodiments, internal obstructions may also be used to cause droplet formation to occur. For instance, baffles,

ridges, posts, or the like may be used to disrupt liquid flow in a manner that causes the fluid to coalesce into fluidic droplets. In some cases, the channel dimensions may be altered with respect to time (for example, mechanically, electromechanically, pneumatically, etc.) in such a manner as to cause the formation of individual fluidic droplets to occur. For example, the channel may be mechanically contracted (“squeezed”) to cause droplet formation, or a fluid stream may be mechanically disrupted to cause droplet formation, for example, through the use of moving baffles, rotating blades, or the like.

[0062] As a non-limiting example of droplet production, a schematic diagram of a device able to produce fluidic droplets is illustrated in FIG. 1. Briefly, a continuous liquid phase **12** is supplied from side channels **11** of the device, and a liquid stream **15** (e.g., containing one or more cells, signaling entities, etc.) is supplied from a center channel **14**. In this geometry, the continuous liquid phase **12** surrounded the inner liquid stream **15**; of course, in other embodiments, other arrangements are also possible. The resulting inner liquid stream has an unstable cylindrical morphology, and may break up within dimensional restriction **13** in a generally periodic manner to release fluidic droplets **19** contained within continuous liquid phase **12** into outlet channel **18**.

[0063] Other techniques of producing droplets of fluid surrounded by a liquid are described in U.S. patent application Ser. No. 11/024,228, filed Dec. 28, 2004, entitled “Method and Apparatus for Fluid Dispersion,” published as U.S. Patent Application Publication No. 2005/0172476 on Aug. 11, 2005; U.S. patent application Ser. No. 11/360,845, filed Feb. 23, 2006, entitled “Electronic Control of Fluidic Species,” published as U.S. Patent Application Publication No. 2007/000342 on Jan. 4, 2007; or U.S. patent application Ser. No. 11/368,263, filed Mar. 3, 2006, entitled “Systems and Methods of Forming Particles,” published as U.S. Patent Application Publication No. 2007/0054119 on Mar. 8, 2007, each incorporated herein by reference. For example, in some embodiments, an electric charge may be created on a fluid surrounded by a liquid, which may cause the fluid to separate into individual droplets within the liquid.

[0064] In certain embodiments of the invention, the droplets may be produced at relatively high frequencies. For example, the droplets may be formed at frequencies between approximately 100 Hz and 5000 Hz. In some cases, the rate of production may be at least about 200 Hz, at least about 300 Hz, at least about 500 Hz, at least about 750 Hz, at least about 1,000 Hz, at least about 2,000 Hz, at least about 3,000 Hz, at least about 4,000 Hz, or at least about 5,000 Hz. In other embodiments, at least about 10 droplets per second may be produced in some cases, and in other cases, at least about 20 droplets per second, at least about 30 droplets per second, at least about 100 droplets per second, at least about 200 droplets per second, at least about 300 droplets per second, at least about 500 droplets per second, at least about 750 droplets per second, at least about 1000 droplets per second, at least about 1500 droplets per second, at least about 2000 droplets per second, at least about 3000 droplets per second, at least about 5000 droplets per second, at least about 7500 droplets per second, at least about 10,000 droplets per second, at least about 15,000 droplets per second, at least about 20,000 droplets per second, at least about 30,000 droplets per second, at least about 50,000 droplets per second, at least about 75,000 droplets per second, at least about 100,000 droplets per second, at least about 150,000 droplets per second, at least about 200,000 droplets per second, at least about 300,000 droplets