Patent Application Publication No. 2007/000342 on Jan. 4, 2007, incorporated herein by reference.

[0111] In the embodiments illustrated in FIG. **4**, a microfluidic system takes as one input an aqueous suspensions of cells and as another input an aqueous suspension of beads to be used as part of a signaling entity. In addition, controlled fusion of a droplet containing one bead and a droplet containing one cell is performed in the microfluidic system to make a suspension or stream of droplets containing exactly one cell and one bead. In some cases, the system can produce droplets with any number of cells and/or beads. In some embodiments, such a system could prepare controlled mixtures of cell types.

[0112] As another example, illustrated in FIG. **5**, a droplet comprising a cell and a signaling entity may be fused with another droplet comprising a second signaling entity. In some instances, this step may be performed after a preparation step similar to that illustrated in FIG. **4**. In the set of embodiments illustrated in FIG. **5**, the prepared cells may be incubated for an appropriate period according to their nature (since, for instance, different cell types may need different incubation times). In some embodiments, controlled fusion may be performed to merge a droplet comprising a cell and a signaling entity with a droplet comprising other reagents, signaling entities, cells, etc. In some cases, analysis of the fused droplet may be used to select and/or sort desired droplets, which can be used, for example, to isolate one or more cells, such as antibody-producing cells.

[0113] One of ordinary skill in the art will understand that FIGS. **4** and **5** offer a representative example schematic for a broad class of similar operations, and accordingly should not be considered to be limiting. In some cases, pre-incubation reporters will not be required. In some instances, analysis may be performed without post-incubation, for example.

[0114] In one set of embodiments, two or more fluidic droplets, such as those described above, may be fused or coalesced into one droplet. For example, in one set of embodiments, systems and methods are provided that are able to cause two or more droplets (e.g., arising from discontinuous streams of fluid) to fuse or coalesce into one droplet. In some cases, the two or more droplets ordinarily are unable to fuse or coalesce due to, for example, composition, surface tension, droplet size, the presence or absence of surfactants, etc. In certain microfluidic systems, the surface tension of the droplets, relative to the size of the droplets, may also prevent fusion or coalescence of the droplets from occurring in some cases.

[0115] In one embodiment, two fluidic droplets may be given opposite electric charges (i.e., positive and negative charges, not necessarily of the same magnitude), which may increase the electrical interaction of the two droplets such that fusion or coalescence of the droplets can occur due to their opposite electric charges, e.g., using the techniques described herein. For instance, an electric field may be applied to the droplets, the droplets may be passed through a capacitor, a chemical reaction may cause the droplets to become charged, etc. As an example, as is shown schematically in FIG. **17**A, uncharged droplets **651** and **652**, carried by a liquid **654** contained within a microfluidic channel **653**, are brought into contact with each other, but the droplets are not able to fuse or coalesce, for instance, due to their size and/or surface tension. The droplets, in some cases, may not be able to fuse even if a surfactant is applied to lower the surface tension of the droplets. However, if the fluidic droplets are electrically charged with opposite charges (which can be, but are not necessarily of, the same magnitude), the droplets may be able to fuse or coalesce. For instance, in FIG. **17**B, positively charged droplets **655** and negatively charged droplets **656** are directed generally towards each other such that the electrical interaction of the oppositely charged droplets causes the droplets to fuse into fused droplets **657**.

[0116] In another embodiment, the fluidic droplets may not necessarily be given opposite electric charges (and, in some cases, may not be given any electric charge), and are fused through the use of dipoles induced in the fluidic droplets that causes the fluidic droplets to coalesce. In the example illustrated in FIG. **17**C, droplets **660** and **661** (which may each independently be electrically charged or neutral), surrounded by liquid **665** in channel **670**, move through the channel such that they are the affected by an applied electric field **675**. Electric field **675** may be an AC field, a DC field, etc., and may be created, for instance, using electrodes **676** and **677**, as shown here. The induced dipoles in each of the fluidic droplets, as shown in FIG. **17**C, may cause the fluidic droplets to become electrically attracted towards each other due to their local opposite charges, thus causing droplets **660** and **661** to fuse to produce droplet **663**. In FIG. **17**D, droplets **660** and **661** approach each other from opposite directions. Droplets **660** and **661** are affected by an applied electric field, and dipoles are induced in each of the fluidic droplets. As shown in FIG. **17**D, droplets **651** and **652** meet at point **699** and are fused to create droplet **663**.

[0117] It should be noted that, in various embodiments, the two or more droplets allowed to coalesce are not necessarily required to meet "head-on." Any angle of contact, so long as at least some fusion of the droplets initially occurs, is sufficient. As an example, in FIG. **16**A, droplets **73** and **74** each are traveling in substantially the same direction (e.g., at different velocities), and are able to meet and fuse. As another example, in FIG. **16**B, droplets **73** and **74** meet at an angle and fuse. In FIG. **16**C, three fluidic droplets **73**, **74** and **68** meet and fuse to produce droplet **79**.

[0118] It should be noted that when two or more droplets "coalesce," perfect mixing of the fluids from each droplet in the resulting droplet does not instantaneously occur. In some cases, the fluids may not mix, react, or otherwise interact, thus resulting in a fluid droplet where each fluid remains separate or at least partially separate. In other cases, the fluids may each be allowed to mix, react, or otherwise interact with each other, thus resulting in a mixed or a partially mixed fluid droplet. In some cases, the coalesced droplets may be contained within a carrying fluid, for example, an oil in the case of aqueous droplets.

[0119] Other examples of fusing or coalescing fluidic droplets are described in International Patent Application Serial No. PCT/US2004/010903, filed Apr. 9, 2004 by Link, et al. and International Patent Application Serial No. PCT/US2004/027912, filed Aug. 27, 2004 by Link, et al., incorporated herein by reference.

[0120] A variety of materials and methods, according to certain aspects of the invention, can be used to form the fluidic or microfluidic system. For example, various components of the invention can be formed from solid materials, in which the channels can be formed via micromachining, film deposition processes such as spin coating and chemical vapor deposition, laser fabrication, photolithographic techniques, etching methods including wet chemical or plasma processes, and the like. See, for example, *Scientific American,* 248:44-55, 1983 (Angell, et al).