

14 may be in flow communication with inlet 10 and surround second outlet 22. The first outlet may be disposed a distance from outlet 18, of vesicle formation zone 16, greater than or equal to a distance of second outlet 22 from outlet 18. Vesicle formation zone 16 may be configured for a flow through of an organic stream, flowing from second outlet 22, at a volumetric flow rate less than or equal to a volumetric flow rate of an aqueous stream, flowing from the first outlet. The first outlet may be disposed about an outer perimeter second outlet 22. Device 300 may comprise a unitary outer sheath 12 extending throughout fluid introduction zone 14 and vesicle formation zone 16 and may be annular, for example outer sheath 12 may be a tube, or pipe.

[0043] In at least one aspect of the present disclosure, a device configured for the formation of vesicles comprises a longitudinally extending sheath 300 configured and disposed for the flowthrough of an aqueous stream and a parallel flowing organic stream. The sheath may comprise an aqueous stream inlet 10, configured and disposed to receive an aqueous stream into sheath 12, and organic stream inlet 11, configured and disposed to receive a parallel flowing organic stream centrally within the aqueous stream, and an outlet 18. The aqueous stream inlet 10 may be disposed at a distance greater than or equal to a distance of organic stream inlet 22, from outlet 18 of sheath 12. Aqueous stream inlet 10 may be configured for a first volumetric flow rate and organic stream inlet 22 may be configured for a second volumetric flow rate of an aqueous stream. The first volumetric flow rate may be greater than or equal to the second volumetric flow rate.

[0044] In at least one aspect of the present disclosure, a device for the formation of vesicles comprises an outer longitudinally extending sheath 12 having a fluid introduction zone 14, a vesicle formation zone 16, and a vesicle outlet 18. Sheath 12 is configured for a flow through of an aqueous stream. A longitudinally extending feed line 20 is disposed in outer longitudinally extending sheath 12 and is configured for a flow through of an organic stream. Sheath 12 has an inner diameter greater than an outer diameter of feed line 20. Feed line 20 and sheath 12 are configured and disposed for a parallel flow of an aqueous stream about an organic stream into vesicle formation zone 16. The device may be configured for a controlled and substantially uniform dispersion of an organic material in the organic stream at a plane perpendicular to vesicle formation zone 16.

[0045] Outer sheath 12 may be configured and disposed to create an aqueous flowing stream sheathing a parallel flowing organic flowing stream in at least a portion of vesicle formation zone 16, during the formation of vesicles. The device may comprise a plurality of longitudinally extending outer feed lines 24 disposed adjacent an inner surface of outer sheath 12, as shown in FIG. 1, and each having a terminating end, or outlet 27, in a plane substantially perpendicular to outer longitudinally extending sheath 12. Each longitudinally extending outer feed line 24 may be configured for a flow through of an aqueous stream. The device may comprise a terminating plane of each one of the plurality of feed lines, or outlets 27, at a distance from outlet 18 greater than or equal to a distance of a terminating end, or outlet 22, of central feed line 20, from outlet 18. The device may have vesicle formation zone 16 configured for a flow of an organic stream through central feed line 20 at a volumetric flow rate less than or equal to a volumetric flow rate of an aqueous stream flowing in parallel through sheath 12. Vesicle formation device

300 may have a smaller cross-sectional flow area of central feed line 20 than a cross-sectional flow area about central feed line 20.

[0046] FIG. 4 shows a process and mechanism of action for liposome formation using the parallel flow device for the formation of vesicles of the present disclosure. A process for the formation of vesicles may comprise flowing an aqueous stream into longitudinally extending sheath 12, via sheath inlet 10. An organic stream may then be centrally fed into longitudinally extending sheath 12 and parallel with the flow of the aqueous stream. The organic stream may be fed through central feed line 20, via inlet 11, and into the aqueous stream through outlet 22. A miscible organic material in the organic stream is then dispersed with the aqueous stream in vesicle formation zone 16 and vesicles may be expelled from outlet 18.

[0047] For example, an organic stream containing one or more organic molecules, such as amphiphilic molecules, or phospholipids and their derivatives, may be fed into vesicle formation zone 16 through vesicle introduction zone outlet, or vesicle formation zone inlet, 22. An aqueous stream may be fed into vesicle formation zone 16 through vesicle introduction zone inlet 10, or a vesicle formation zone inlet disposed about inlet 22. The organic molecules may then disperse throughout the co-flowing streams as lipid "rafts" depicted in (i). Liposomes may then be spontaneous self-assembled with the lipid mixture assembling into a spherical bilayer membrane in vesicle formation zone 16, as depicted in (ii), (iii), and (iv). Upon dispersion in water, the phospholipids may form closed vesicles called or liposomes, which may be characterized by lipid bilayers substantially encapsulating an aqueous core or form a spherical bilayer membrane. The outer sheathing of the organic stream with the aqueous stream may create physicochemical conditions in the aggregate co-flowing streams that are substantially symmetric about a cross-section of the co-flowing streams. As the mutually miscible aqueous and organic streams disperse or diffusively mix, as shown in (i), the amphiphilic molecules may self-assemble into liposomal vesicles, as shown in (ii)-(iv).

[0048] FIG. 5 shows the mutual dispersion of miscible fluids in vesicle formation zone 16 of the parallel flow device for the formation of vesicles of the present disclosure. Outer annular longitudinally extending sheath 12 has aqueous solution 25 flowing about a perimeter of central feed line 20 to sheath line outlet 18. Central feed line 20 is parallel feeding an organic containing solution 23 into a central portion of flowing aqueous solution 25. This parallel flow of organic stream 23 with aqueous stream 25, into vesicle formation zone 16, may provide for feeding an intra-annular organic stream into a parallel flowing annular sheathing aqueous stream. This may result in a device configured for controlled and substantially uniform dispersion of an organic material in the co-flowing streams, at a plane perpendicular to vesicle formation zone 16.

[0049] FIG. 5 shows a numerical model of an alcohol/water, stream 23 flowing through central feed line 20, mixing, diffusing, or dispersing, just post exit 22 from an inner PEEK tube 20. In this gray scale model it is shown that alcohol, represented by the dark gray central longitudinal portion extending from central feed line 20, is distributed along a channel diameter of outer sheath 12. The aqueous flow is represented by the dark gray outer flow portion adjacent the inner wall of outer sheath 12. As can be seen with the controlled reduction of alcohol in the central stream, a controlled