

[0005] The present invention may further comprise a system for unclogging and sealing a nozzle in a flow cytometer comprising: a nozzle system comprising a nozzle that creates a stream of sheath fluid that flows through a nozzle tip; a sheath supply port that provides a supply of pressurized sheath fluid to the nozzle; a sheath supply valve that opens and closes the sheath supply port to the nozzle; a waste disposal port that provides access to a disposal of waste fluids; a waste valve that opens and closes the waste disposal port; a docking station comprising: a rinse fluid supply that has a predetermined pressure; a tip sealing cup coupled to the rinse fluid supply; a nozzle mover coupled to the nozzle system that moves the nozzle system from an operating position to a docking position where the nozzle tip is inserted into the tip sealing cup so that the rinse fluid supply can be flushed through the nozzle to the waste disposal port when the waste valve is closed.

[0006] In one aspect, the present disclosure provides methods of unclogging a flow cytometer, comprising: converting the flow cytometer from an operating state to a docking state such that in the docking state, a nozzle system of the flow cytometer is aligned with a docking station, the converting being effected by relative motion between the nozzle system and the docking station, the docking state being such that a nozzle tip of the nozzle system engages with a tip sealing cup of the docking station so as to form a seal between the tip sealing cup and the nozzle tip, the nozzle tip being in fluid communication with at least one fluid pathway of the nozzle system; with a rinse fluid pump, communicating a rinse fluid from said docking station to the nozzle tip so as to flush the nozzle tip and at least a portion of the at least one fluid pathway.

[0007] Also provided are flow cytometer systems, comprising: a nozzle system comprising a nozzle tip and a sheath fluid conduit, the nozzle tip configured to communicate a sheath fluid therethrough and the nozzle tip being in communication with the sheath fluid conduit; a sheath supply valve configured to interrupt fluid communication between the nozzle tip and a supply of sheath fluid; a waste disposal port in fluid communication with the nozzle tip; a waste valve configured to interrupt fluid communication between the nozzle tip and the waste disposal port; a docking station, comprising: a rinse fluid conduit; a tip sealing cup, and a rinse fluid pump configured to exert rinse fluid into the rinse fluid conduit, the tip sealing cup configured to sealably engage with the nozzle tip so as to form a seal between the tip sealing cup and the nozzle tip; and a nozzle mover configured to move the nozzle system from an operating position to a docking position, in which docking position the nozzle tip engages with the tip sealing cup such that said rinse fluid can be communicated through the

obtained from the sheath supply port 116 that is mixed with living cells or other material under analysis.

[0025] Sheath fluid can be, e.g., saline or other solution that protects the viability of the living cells that are mixed with the sheath fluid. The sheath fluid can be jetted out of the small nozzle orifice of the nozzle tip 108. Typically, the orifices range from 50 to 200 microns. For example, nozzle tip 108 can have an opening of, e.g., 50, 70, 100, 120, 150 and 200 microns.

[0026] Because nozzle tips are relatively small orifices that communicate a mixture of salt water and cells, cells can clump together to clog the orifice, and the flow cytometer's operator may have to expend significant amount time and effort to unclog the nozzle tip 108. In addition to clogging that can occur as a result of flow cytometer operation, if the nozzle system 102 is left to sit for several hours (e.g., overnight) sheath fluid can evaporate, leaving behind salt crystals in the nozzle tip 108 and/or in other locations within nozzle body 110, and this crystallization can also cause clogs or partial clogs that affect the operation of the nozzle system 102.

[0027] As described here, in the disclosure technology provides an automated way of preventing crystal formation and removing or dislodging clogs resulting from clumps of cells. As disclosed, this can be achieved by effecting relative motion between nozzle system 102 (in FIG. 1) and docking station 126 so that the nozzle tip 108 is inserted into a tip sealing cup 130. This can be accomplished by, e.g., moving nozzle system 102 such that nozzle tip 108 engages with tip sealing cup 130.

[0028] Rinse fluid (e.g., pressurized deionized water) 128 is then exerted backwards through the nozzle tip 108, which fluid in turn flushes any clogs in nozzle tip 108 out through waste disposal port 118. Other rinse fluids (e.g., ethanol, methanol, acetone) besides deionized water can be used. The nozzle tip 108 can stay in its docked position until again placed in use; in this way, fluid around the nozzle tip 108 cannot evaporate and cause salt crystals to form.

[0029] As illustrated in FIG. 1, the nozzle system 102 can be placed in an operating position (or first state) so that cell sorting or cell analysis can occur. As shown, sheath supply port 116 can be connected to nozzle body 110 and nozzle tip 108 such that with sheath supply valve 112 in the open position, stream 122 of sheath fluid can be pumped through nozzle 106. Nozzle mover 104 can be a five-axis mover configured to move nozzle tip 108 in a forward and back direction, in a side to side direction, in a vertical direction and is capable of tilting the nozzle tip 108 in two axes. This in turn allows the stream 122 that is jetted from the

[0043] FIG. 3 provides an illustration of a fluid monitoring train. As shown, a droplet camera 300 can be used to view stream 302 and droplet 304 that breaks off from stream 302. Droplet camera 300 can use strobed infrared light in sync with the droplet formation to monitor the breakoff point. As shown, the train can include a column of infrared LEDs 308 (supported by support 310), which infrared LEDs can have a diffuser 306 in front of them that is directly opposite the stream from the camera. In this arrangement, camera 302 is thus really looking at stream 302 as stream 302 is back-lit. In this way, camera 300 can be used to monitor droplet formation, which droplet formation can be used to assess whether a clog has developed within the fluid flow system, e.g., at the nozzle tip (not shown).

[0044] An additional train is shown in FIG. 4. This train can be placed further downstream from the train shown in FIG. 3, and can be used to observe droplets as the droplets are deflected by an electrostatic deflection for sorting. The additional train's location at a downstream distance from the nozzle tip provides a useful point to observe the exit angle. As shown in FIG. 4 (left panel is a side view; right panel is a top view), the additional train can use infrared LEDs (408, supported by support 410) to illuminate stream 402 (and, when present, droplets 404) from the back with a camera (400) on the same side as the LEDs so as to visualize the illuminated stream and deflected droplets. A blocking background 414 can be used to keep stray light from reaching camera 400. Mirror 412 can be added to part of the background at, e.g., a 45-degree angle, such that stream 402 (and droplets 402) can be observed in the front-back angle. In this manner, camera 400 can be used to observe fluid both side-to-side and front-to-back and can detect the exit angle of the stream.

[0045] The foregoing description of the invention has been presented for purposes of illustration and description. It is not intended to be exhaustive or to limit the invention to the precise form disclosed, and other modifications and variations may be possible in light of the above teachings. The embodiment was chosen and described in order to best explain the principles of the invention and its practical application to thereby enable others skilled in the art to best utilize the invention in various embodiments and various modifications as are suited to the particular use contemplated. It is intended that the appended claims be construed to include other alternative embodiments of the invention except insofar as limited by the prior art.

[0046] Aspects

[0047] The following Aspects are illustrative only and do not limit the scope of the present disclosure or the appended claims.

What is Claimed:

1. A method of unclogging a flow cytometer, comprising:

converting the flow cytometer from an operating state to a docking state such that in the docking state, a nozzle system of the flow cytometer is aligned with a docking station,

the converting being effected by relative motion between the nozzle system and the docking station,

the docking state being such that a nozzle tip of the nozzle system engages with a tip sealing cup of the docking station so as to form a seal between the tip sealing cup and the nozzle tip,

the nozzle tip being in fluid communication with at least one fluid pathway of the nozzle system;

with a rinse fluid pump, communicating a rinse fluid from said docking station to the nozzle tip so as to flush the nozzle tip and at least a portion of the at least one fluid pathway.
2. The method of claim 1, further comprising maintaining said nozzle system in said docking state until operation of said flow cytometer is initiated.
3. The method of any one of claims 1-2, further comprising converting the flow cytometer from the docking state to the operating state.
4. The method of claim 3, wherein the converting is effected in an automated fashion.
5. The method of any one of claims 1-4, further comprising collecting at least one signal related to a fluid exiting the nozzle tip of the nozzle system when the flow cytometer is in the operating state.

6. The method of claim 5, wherein the signal is indicative of an amplitude of fluid droplets, a direction of fluid flow, or any combination thereof.
7. The method of any one of claims 5-6, wherein the converting the system from the operating state to the docking state is in response to the at least one signal.
8. The method of claim 1, further comprising (a) closing a sheath fluid supply valve in fluid communication with the nozzle tip, (b) closing a waste valve in fluid communication with the nozzle tip, the waste valve being configured to permit passage therethrough of rinse fluid communicated from the docking station to the nozzle tip, or (c) both (a) and (b); and

determining whether rinse fluid communicated from the docking station is leaking from the seal between the tip sealing cup and the nozzle tip.
9. The method of claim 8, wherein the determining comprises detecting whether the rinse fluid pump pumps the rinse fluid.
10. The method of any one of claims 8-9, wherein the determining comprises detecting a pressure of said rinse fluid.
11. The method of any one of claims 8-10, further comprising opening the waste valve after determining that no leak exists at the seal between the tip sealing cup and the nozzle tip.
12. The method of any one of claims 1-11, wherein the relative motion comprises movement of the nozzle system.
13. The method of claim 12, wherein the movement of the nozzle system is effected by a five-axis mover.
14. The method of any one of claims 1-13, wherein at least one resilient member maintains engagement between the nozzle tip and the tip sealing cup.

15. The method of any one of claims 1-14, wherein the tip sealing cup comprises a resilient material.

16. A flow cytometer system, comprising:

a nozzle system comprising a nozzle tip and a sheath fluid conduit, the nozzle tip configured to communicate a sheath fluid therethrough and the nozzle tip being in communication with the sheath fluid conduit;

a sheath supply valve configured to interrupt fluid communication between the nozzle tip and a supply of sheath fluid;

a waste disposal port in fluid communication with the nozzle tip;

a waste valve configured to interrupt fluid communication between the nozzle tip and the waste disposal port;

a docking station, comprising:

a rinse fluid conduit;

a tip sealing cup, and

a rinse fluid pump configured to exert rinse fluid into the rinse fluid conduit,

the tip sealing cup configured to sealably engage with the nozzle tip so as to form a seal between the tip sealing cup and the nozzle tip; and

a nozzle mover configured to move the nozzle system from an operating position to a docking position, in which docking position the nozzle tip engages with the tip sealing cup such that said rinse fluid can be communicated through the nozzle tip to the waste disposal port when said waste valve is open and said sheath supply valve is closed.

17. The system of claim 16, wherein at least one of the sheath supply valve and the waste valve are electronically operated manifold valves.

18. The system of any one of claims 16-17, wherein the nozzle mover is a five-axis mover.
19. The system of any one of claims 16-18, further comprising a pressure transducer configured to monitor a pressure of rinse fluid pumped by the pump.
20. The system of any one of claims 16-19, further comprising an optical train configured to collect at least one signal related to a fluid exiting the nozzle tip system when the nozzle tip is in the operating position.
21. The system of claim 20, wherein the signal is indicative of an amplitude of fluid droplets, a direction of fluid flow, or any combination thereof.
22. The system of any one of claims 20-21, wherein the nozzle mover is configured to move the nozzle system from the operating position to the docking position in response to the at least one signal.
23. The system of any one of claims 16-22, wherein the system is configured such that the nozzle mover (a) moves the nozzle system from the operating position to the docking position according to a predetermined schedule, (b) moves the nozzle system from the docking position to the operating position according to a predetermined schedule, or (c) both (a) and (b).
24. The system of any one of claims 16-23, further comprising a resilient member configured to maintain engagement between the nozzle tip and the tip sealing cup.
25. The system of any one of claims 16-24, wherein the pump is configured to deliver the rinse fluid at a predetermined pressure sufficient to remove obstructions in the nozzle tip, the conduit, or both the nozzle tip and the conduit.
26. A method, comprising: operating a system according to any one of claims 16-25.