that contains such analytes is discarded or not analyzed. Further, some events of interest may not end up being analyzed because of their location at the beginning or end of the fluid sample.

[0006] Careful sample line manufacturing methods are intended to provide consistent and reliable sample line volumes, as such careful manufacturing methods attempt to ensure that sample line volumes fall within a certain tolerance or range. This approach, however, often results in a higher cost of manufacturing and testing of sample lines. In addition, during analysis, sample arrival times must be calculated with larger margins of error to allow for variations in the line volume. This in turn results in waste of potentially valuable sample, and portions of both ends of the analysis period must be discarded (and with such discard, the potential loss of valuable information that could be critical for both research purposes as well as clinical purposes associated with diagnosing a patient).

[0007] Accordingly, there is a long-felt need in the art for improved methods and systems of line volume calibrations and sample measurements.

SUMMARY

[0008] In meeting the described challenges, the present disclosure first provides systems and methods for ~~measuring,~~ estimating~~, and/or determining~~ a volume ~~of~~ enclosed within a sample line. A method can comprise: disposing a calibration volume of a first fluid into the sample line such that the calibration volume completely fills the sample line, the completely filled sample line defining a volume SL therein; communicating into a sample zone the calibration volume of the first fluid and also a displacement volume of a second fluid, the calibration volume of the first fluid and the displacement volume of the second fluid defining a total volume; communicating the total volume from the sample zone to a sensor configured to identify a boundary between the first fluid and the second fluid; and from the boundary, estimating the volume SL of the sample line.

[0009] The present disclosure also provides systems and methods, the system comprising: a sample line enclosing a volume SL therein; a sample zone configured to receive a first fluid from the sample line; a fluid delivery train configured to (a) deliver a volume of the first fluid into the sample line, (b) deliver a calibration volume CV of the first fluid that completely fills the volume of the sample line from the sample line into the sample zone, and (c) deliver a displacement volume D of a second fluid into the sample zone such that the calibration volume CV of the first fluid and the displacement volume D of the second fluid define a total volume TV; a sensor region configured to receive the first fluid and the second fluid from the sample zone and to detect a boundary between the first fluid and the second fluid; a flow diverter train configured to (a) place the

sample line into fluid communication with the sample zone, (b) place the sample zone into fluid communication with the sensor, or both (a) and (b); and optionally, a processor configured to determine a volume enclosed by the ~~first~~ sample line based on at least a difference between the volume D of the displacement volume of the second fluid and the total volume TV.

[0010] Additionally provided are systems and methods for estimating a volume of a sample fluid, the method comprising: delivering an amount of a first fluid to a conduit; delivering an amount of a second fluid into the conduit so as to displace the first fluid within the conduit; estimating a total volume of the first fluid and the second fluid in the conduit; delivering the first fluid and the second fluid from the conduit to a sensor capable of determining a boundary between the first fluid and the second fluid; determining a volume of the second fluid in the total volume; and estimating a volume of the ~~sample~~ first fluid based on at least the volume of the first fluid and the estimated total volume of the ~~sample~~ first fluid and the ~~first~~ second fluid.

[0011] Also ~~provided~~ disclosed are systems for automatically determining the volume of a sample, the system comprising: a sensor region; a fluid delivery train configured to separately deliver a volume of a second fluid and a volume of a first fluid into the sensor region, the sensor region being configured to measure a signal through the sensor region, the signal differing based on the presence of the first fluid in the sensor region or the presence of the second fluid in the sensor region; and a processor configured to determine a volume of the sample based on the signal measured when the first fluid and the second fluid are communicated through the sensor region.

BRIEF DESCRIPTION OF THE DRAWINGS

[0012] The summary, as well as the following detailed description, is further understood when read in conjunction with the appended drawings. For the purpose of illustrating the disclosed subject matter, there are shown in the drawings exemplary embodiments of the disclosed subject matter; however, the disclosed subject matter is not limited to the specific methods, compositions, and devices disclosed. In addition, the drawings are not necessarily drawn to scale. In the drawings:

[0013] FIGs. 1A- 1I provide a depiction of an exemplary system and method according to the present disclosure;

[0014] FIG. 2 provides a depiction of an exemplary embodiment according to the present disclosure; and

[0015] FIG. 3 provides a flowchart of an embodiment of the disclosed technology.

What is claimed:

1. A method for estimating a volume enclosed within a sample line, comprising:

disposing a calibration volume of a first fluid into the sample line such that the calibration volume completely fills the sample line, the filled sample line defining a volume SL therein;

communicating into a sample zone the calibration volume of the first fluid and also a displacement volume **D** of a second fluid, the calibration volume of the first fluid and the displacement volume **D** of the second fluid defining a total volume;

communicating the total volume from the sample zone to a sensor configured to identify a boundary between the first fluid and the second fluid; and

from the boundary, estimating the volume SL of the sample line.

~~2. The method of claim 1, wherein the sensor detects a change in an electrical signal, a change in an acoustic signal, or any combination thereof.~~

~~3.~~2. The method of ~~any one of~~ claim~~s~~ 1~~-2~~, further comprising communicating into the sample line a volume of the first fluid that exceeds a volume that completely fills the sample line and removing first fluid that exceeds the volume that fills the sample line so as to leave the sample line completely filled.

~~4.~~3. The method of any one of claims 1-~~3~~2, further comprising measuring the volume of the second fluid based on a change in an electrical signal, a change in an acoustic signal, or any combination thereof.

~~5.~~4. The method of any one of claims 1-~~4~~3, wherein the first fluid and the second fluid are immiscible.

~~6. The method of any one of claims 1-5, wherein the method is performed in an automated fashion.~~

~~7. The method of any one of claims 1-6, wherein the second fluid comprises air.~~

~~8.~~5. The method of any one of claims 1-~~7~~4, further comprising operating the sample zone so as to analyze one or more fluid samples, each of the one or more fluid samples having a sample volume of the volume SL.

~~9.~~6. A system, comprising:

a sample line enclosing a volume therein;

a sample zone configured to receive a first fluid from the sample line;

a fluid delivery train configured to (a) deliver a volume of the first fluid into the sample line, (b) deliver a calibration volume CV of the first fluid that completely fills the volume of the sample line from the sample line into the sample zone, and (c) deliver a displacement volume **D** of a second fluid into the sample zone such that the calibration volume CV of the first fluid and the displacement volume **D** of the second fluid define a total volume TV;

a sensor region configured to receive the first fluid and the second fluid from the sample zone and to detect a boundary between the first fluid and the second fluid;

a flow diverter train configured to (a) place the sample line into fluid communication with the sample zone, (b) place the sample zone into fluid communication with the sensor, or both (a) and (b); and

optionally, a processor configured to determine a volume enclosed by the sample line based on at least a difference between the volume **D** of the displacement volume of the second fluid and the total volume TV.

~~10.~~7. The system of claim ~~9~~6, further comprising a vessel in fluid communication with an end of the sample line, the vessel being configured to receive fluid communicated through the sample line.

~~11.~~8. The system of claim ~~10~~7, wherein the fluid delivery train is further configured to remove fluid from the vessel while fluid is retained within the sample line such that the sample line is completely filled.

~~12.~~9. The system of any one of claims ~~9-11~~6-8, wherein the flow diverter train consists of a single valve.

~~13. The system of claim 12, wherein the single valve is characterized as a rotary valve.~~

~~14.~~10. The system of any one of claims ~~96~~-~~139~~, wherein the flow diverter train comprises a plurality of valves.

~~15.~~11. The system of any one of claims ~~96~~-~~1410~~, wherein the sensor region comprises a bubble sensor.

~~16.~~12. The system of any one of claims ~~96~~-~~1511~~, further comprising an instrument configured to analyze a sample disposed in first fluid received by the instrument from the sample zone.

~~17.~~13. The system of claim ~~1612~~, wherein the system is configured to operate the instrument based at least in part on a volume enclosed by the sample line.

~~18.~~14. The system of claim ~~1713~~, further comprising an autosampler, wherein the autosampler is located at a distance from the instrument.~~.~~

~~19. The system of claim 18, wherein the autosampler is located at a distance from the instrument.~~

~~20.~~15. The system of claim ~~1914~~, wherein the sample line places the autosampler into fluid communication with the instrument.

~~21. The system of any one of claims 9-20, wherein the system comprises a region configured to contact a sample and the first fluid.~~

~~22. The system of claim 21, wherein the sample comprises cells, cellular components, or both.~~

~~23.~~16. The system of any one of claims ~~96~~-~~2215~~, wherein the volume enclosed by the sample line is in the range of from about 30 microliters to about 2.5 milliliters.

~~24.~~17. A method for estimating a volume of a first fluid, the method comprising:

delivering an amount of a first fluid to a conduit;

delivering an amount of a second fluid into the conduit so as to displace the first fluid within the conduit;

estimating a total volume of the first fluid and the second fluid in the conduit;

delivering the first fluid and the second fluid from the conduit to a sensor capable of determining a boundary between the first fluid and the second fluid;

determining a volume of the second fluid in the total volume; and

estimating a volume of the first fluid based on at least the volume of the first fluid and the estimated total volume of the first fluid and the second fluid.

~~25. The method of claim 21, wherein the first fluid comprises air.~~

~~26.~~18. The method ~~of any one of~~ claim ~~s 21-22~~17, further comprising operating an instrument based at least in part on the estimated volume of the first fluid, the instrument optionally being configured for fluid communication with the conduit.

~~27.~~19. The method of claim ~~23~~18, wherein the instrument is a flow cytometer.

~~28.~~20. The method of any one of claims ~~26-27~~18-19, wherein the first fluid is communicated to the instrument from a sample line.

~~29.~~21. The method of claim ~~28~~20, wherein the volume of the first fluid delivered to the instrument is a volume enclosed by the sample line.

~~30.~~22. The method of any one of claims ~~28-29~~20-21, wherein the sample line is disposed so as to place an autosampler in fluid communication with an instrument.

~~31.~~23. The method of claim ~~30~~22, wherein the autosampler is located at a distance from the instrument.

~~32.~~24. The method of any one of claims ~~21-31~~17-23, wherein ~~the~~ determining the volume of the second fluid in the total volume is based, at least in part, on detecting the boundary between the first fluid and the second fluid.

~~33. A system for automatically determining the volume of a sample, the system comprising:~~

~~a sensor regio~~n;

~~a fluid delivery train configured to separately deliver a volume of a second fluid and a volume of a first fluid into the sensor region,~~

~~the sensor region being configured to measure a signal through the sensor region, the signal differing based on the presence of the first fluid in the sensor region or the presence of the second fluid in the sensor region; and~~

~~a processor configured to determine a volume of the sample based on the signal~~

measured when the first fluid and the second fluid are communicated through the sensor region.

34. The system of claim 33, wherein the second fluid comprises air.

35. The system of any one of claims 33-34, further comprising an instrument and optionally a flow modulator, the system being configured to place the instrument into fluid communication with the sensor region.

36. The system of claim 35, wherein the instrument comprises a flow cytometer, the flow cytometer optionally being characterized as an acoustic flow cytometer.

37. The system of any one of claims 35-36, further comprising a sample line, the system being configured to place the sample line into fluid communication with the instrument.

38. The system of claim 37, wherein the instrument is operable based on an estimated volume of the sample line.

39. The system of any one of claims 37-38, further comprising a collection train configured to collect excess fluid from the sample line so as to leave the sample line completely filled.

40. The system of any one of claims 37-38, further comprising a source of the first fluid, the system being configured to place the source of first fluid into fluid communication with the sample line.

41. The system of any one of claims 33-40, wherein the system is configured to contact the first fluid with a sample.

42. The system of claim 41, wherein the sample comprises cells, cellular components, or both.