

[0005] Due to the short interrogation time required for high analysis rates, high resolution imaging in flow cytometry has been limited. As opposed to collecting the integrated signal from the entire cell, an imaging detector such as a camera must detect light from much smaller locations on the cell on a pixel by pixel basis. The challenge of collecting high resolution images of single cells at high speeds is difficult because the photon count generated by each pixel is much lower than the integrated photon count. For this reason, imaging that is conducted in flow cytometers is generally done with much larger interrogation times to increase photon counts. The larger interrogation times, however, greatly reduce the event rate and therefore imaging flow cytometry is largely utilized in niche applications. Accordingly, there is a long-felt need in the art for apparatuses, systems and methods for imaging flow cytometry that are capable of operating so as to collect information at both comparatively slow and comparatively fast interrogation times.

SUMMARY

[0006] In one aspect, the present disclosure provides a system comprising: a flow channel, the flow channel having an inlet, and the flow channel defining a flow path for fluid communicated therethrough; a first optical train comprising a first illumination source and a first detection module, the first detection module being disposed so as to receive a signal related to illumination of a first region of the flow channel by the first illumination source, the first region being located at a first distance from the inlet of the flow channel; a second optical train comprising a second illumination source and a second detection module, the second detection module being disposed so as to receive a signal related to illumination of a second region of the flow channel by the second illumination source, the second region being located at a second distance from the inlet of the flow channel, the second distance being greater from the first distance, and (a) wherein the first region of the flow channel defines a first cross-sectional area, wherein the second region of the flow channel defines a second cross-sectional area, and wherein the first and second cross-sectional areas differ from one another in area, in shape, or in both area and shape.

[0006a] In another aspect, the present disclosure provides a system comprising: a flow channel, the flow channel having an inlet, and the flow channel defining a flow path for fluid communicated therethrough; a first optical train comprising a first illumination source and a first detection module, the first detection module being disposed so as to receive a signal related to illumination of a first region of the flow channel by the first illumination source, the first region being located at a first distance from the inlet of the flow channel; a second optical train comprising a second illumination source and a second detection module, the second detection module being disposed so as to receive a signal related to illumination of a second region of the flow channel by the second illumination source, the second region being located at a second distance from the inlet of the flow channel, the second distance being greater from the first distance, and wherein (i) the system comprises a conduit entering the flow channel between the inlet of the flow channel and the first region of the flow channel, (ii) the system comprises a conduit entering the flow channel between the first region and the second region of the flow channel, or both (i) and (ii).

[0006b] In another aspect, the present disclosure provides a system comprising: a flow channel, the flow channel having an inlet, and the flow channel defining a flow path for fluid communicated therethrough; a first optical train comprising a first illumination source and a first detection module, the first detection module being disposed so as to receive a signal related to illumination of a first region of the flow channel by the first illumination source, the first region being located at a first distance from the inlet of the flow channel; a second optical train comprising a second illumination source and a second detection module, the second detection module being disposed so as to receive a signal related to illumination of a second region of the flow channel by the second illumination source, the second region being located at a second distance from the inlet of the flow channel, the second distance being greater from the first distance, and wherein the system comprises a flowrate modulator configured to modulate a velocity of a particle in the flow path.

[0006c] In another aspect, the present disclosure provides a system comprising: a flow channel, the flow channel having an inlet, and the flow channel defining a flow path for fluid communicated therethrough; a first optical train comprising a first illumination source and a first detection module, the first detection module being disposed so as to receive a signal related to illumination of a first region of the flow channel by the first illumination source, the first region being located at a first distance from the inlet of the flow channel;

a second optical train comprising a second illumination source and a second detection module, the second detection module being disposed so as to receive a signal related to illumination of a second region of the flow channel by the second illumination source, the second region being located at a second distance from the inlet of the flow channel, the second distance being greater from the first distance, and the system further comprising a field module, the field module being configured to increase or reduce a field at a region of the flow channel so as to move at least some particles in a flow in the flow channel and sensitive to the field from a velocity streamline S_0 of particle velocity within the flow in the flow channel to a velocity streamline S_1 of particle velocity within the flow in the flow channel, wherein the particle velocity at S_0 during system operation differs from the particle velocity at S_1 , between the first and second regions of the flow channel.

[0007] In another aspect, the present disclosure provides methods, comprising: flowing a population of particles through a flow channel; with a first optical train, illuminating at least some of the population of particles at a first region of the flow channel and collecting a first signal related to said illuminating; with a second optical train, illuminating at least some of the population of particles at a second region of the flow channel and collecting a second signal related to said illuminating, a particle velocity at the first region of the flow channel differing from a particle velocity at the second region of the flow channel, and the first signal differing from the second signal.

[0008] Further provided are methods, comprising: communicating a population of particles through a flow channel, in a direction from a first region of the flow channel toward a second region of the flow channel; with a first optical train, illuminating at least some of the population of particles at the first region of the flow channel and collecting a first signal related to said illuminating; with a second optical train, illuminating at least some of the population of particles at the second region of the flow channel and collecting a second signal related to said illuminating, increasing or reducing a field on a subset of the particles between the first and second regions of the flow channel, the field being increased or reduced so as to move the subset of particles from a velocity streamline S_0 of particle velocity within the flow channel to a velocity streamline S_1 of particle velocity within the flow channel, wherein the particle velocity at S_0 differs from the particle velocity at S_1 .

BRIEF DESCRIPTION OF THE DRAWINGS

[0009] 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 technology, there are shown in the drawings exemplary and preferred embodiments of the invention; however, the disclosure is not limited to the specific methods, compositions, and devices disclosed. In addition, the drawings are not necessarily drawn to scale, and the text labels on the various parts of the drawings are illustrative only and are not limiting of the disclosed technology. In the drawings:

What is Claimed:

1. A system, comprising:

a flow channel,

the flow channel having an inlet, and

the flow channel defining a flow path for fluid communicated therethrough;

a first optical train comprising a first illumination source and a first detection module,

the first detection module being disposed so as to receive a signal related to illumination of a first region of the flow channel by the first illumination source, the first region being located at a first distance from the inlet of the flow channel;

a second optical train comprising a second illumination source and a second detection module,

the second detection module being disposed so as to receive a signal related to illumination of a second region of the flow channel by the second illumination source, the second region being located at a second distance from the inlet of the flow channel,

the second distance being greater from the first distance, and

wherein the first region of the flow channel defines a first cross-sectional area, wherein the second region of the flow channel defines a second cross-sectional area, and wherein the first and second cross-sectional areas differ from one another in area, in shape, or in both area and shape.

2. The system of claim 1, wherein the first and second cross-sectional areas differ from one another in area and the ratio of the first cross-sectional area to the second cross-sectional area is from about 100:1 to about 1:100, excluding 1:1.

3. The system of any of claims 1-2, wherein the flow channel defines a major axis, and wherein at least one of the first and second illumination sources is configured to provide illumination essentially parallel to the major axis of the flow channel.
4. The system of any of claims 1-3, wherein the flow path is at least partially nonlinear.
5. The system of any of claims 1-4, further comprising a particle separator in fluid communication with the flow channel, wherein the separator is configured to divert particles based upon particle size, particle shape, particle mass, a signal associated with one or more particles, or any combination thereof.
6. The system of claim 5, wherein the separator is configured to divert particles within the flow channel based upon the signal associated with one or more particles.
7. The system of any of claims 5-6, wherein the system is configured to collect one or more images of separated particles.
8. The system of any of claims 1-7, wherein at least one of the first or second detection modules comprises a plurality of detectors.
9. The system of any of claims 1-8, further comprising a light reflector, a light splitter, or both in optical communication with at least one detection module.
10. The system of any of claims 1-9, wherein one or both of the first or second optical trains is configured to effect imaging at two or more planes within the flow channel.
11. The system of claim 10, wherein one or both of the first or second optical trains is configured to collect an image at two or more focal planes.
12. The system of any of claims 10-11, wherein at least one of the first or second optical trains is configured to focus illumination at two or more planes.
13. The system of any of claims 1-10, wherein the first optical train is configured such that an illumination axis from the first illumination source is offset by an angle from the first detection module, wherein the second optical train is configured such that an

illumination axis from the second illumination source is offset by an angle from the second detection module, or both.

14. The system of any of claims 1-13, wherein the first illumination source, the second illumination source, or both comprises a laser, a lamp, a light-emitting diode, or any combination thereof.
15. The system of any of claims 1-14, wherein the first detection module, the second detection module, or both comprises a photomultiplier tube, an avalanche photodiode, a camera, a silicon photomultiplier, or any combination thereof.
16. The system of any of claims 1-15, wherein the system is configured such that (a) operation of the second optical train, (b) operation of the separator, if present, or both (a) and (b), are related to a signal collected by the first optical train.
17. The system of any of claims 1-16, wherein the field module comprises a source of magnetic field, an electric field, an acoustic field, or any combination thereof.
18. A system, comprising:
 - a flow channel,
 - the flow channel having an inlet, and
 - the flow channel defining a flow path for fluid communicated therethrough;
 - a first optical train comprising a first illumination source and a first detection module,
 - the first detection module being disposed so as to receive a signal related to illumination of a first region of the flow channel by the first illumination source, the first region being located at a first distance from the inlet of the flow channel;
 - a second optical train comprising a second illumination source and a second detection module,
 - the second detection module being disposed so as to receive a signal related to illumination of a second region of the flow channel by the second illumination source,

the second region being located at a second distance from the inlet of the flow channel,

the second distance being greater from the first distance, and

wherein (i) the system comprises a conduit entering the flow channel between the inlet of the flow channel and the first region of the flow channel, (ii) the system comprises a conduit entering the flow channel between the first region and the second region of the flow channel, or both (i) and (ii).

19. A system, comprising:

a flow channel,

the flow channel having an inlet, and

the flow channel defining a flow path for fluid communicated therethrough;

a first optical train comprising a first illumination source and a first detection module,

the first detection module being disposed so as to receive a signal related to illumination of a first region of the flow channel by the first illumination source, the first region being located at a first distance from the inlet of the flow channel;

a second optical train comprising a second illumination source and a second detection module,

the second detection module being disposed so as to receive a signal related to illumination of a second region of the flow channel by the second illumination source, the second region being located at a second distance from the inlet of the flow channel,

the second distance being greater from the first distance, and

wherein the system comprises a flowrate modulator configured to modulate a velocity of a particle in the flow path.

20. A system, comprising:

a flow channel,

the flow channel having an inlet, and

the flow channel defining a flow path for fluid communicated therethrough;

a first optical train comprising a first illumination source and a first detection module,

the first detection module being disposed so as to receive a signal related to illumination of a first region of the flow channel by the first illumination source, the first region being located at a first distance from the inlet of the flow channel;

a second optical train comprising a second illumination source and a second detection module,

the second detection module being disposed so as to receive a signal related to illumination of a second region of the flow channel by the second illumination source, the second region being located at a second distance from the inlet of the flow channel,

the second distance being greater from the first distance, and

the system further comprising a field module,

the field module being configured to increase or reduce a field at a region of the flow channel so as to move at least some particles in a flow in the flow channel and sensitive to the field from a velocity streamline S_0 of particle velocity within the flow in the flow channel to a velocity streamline S_1 of particle velocity within the flow in the flow channel, wherein the particle velocity at S_0 during system operation differs from the particle velocity at S_1 , between the first and second regions of the flow channel.