# MASSIVELY PARALLEL CELL ANALYSIS AND SORTING APPARATUS AND METHODS

## CROSS REFERENCE TO RELATED APPLICATIONS

**[0001]** The present application claims the benefit of U.S. Provisional Patent Application No. 63/419,852, filed on October 27, 2022, which is incorporated herein by reference in its entirety.

## BACKGROUND

**[0002]** Microfluidic devices have been used to analyze populations of particles and sort particles according to the results of the analysis. This is conventionally accomplished by flowing the particles through a region where analysis occurs such as a region where optical interrogation and detection are performed.

## SUMMARY

**[0002a]** In one aspect, the present disclosure relates to a microfluidic chip, comprising:

a plurality of sections that are stacked or layered in a stacking direction to form a plurality of microchannels at least partially oriented to flow along a stacking direction, the plurality of sections including:

a transfer section for introduction of sample fluid including particles;

and

a second section including a measurement section or the measurement section and an actuation section including a plurality of interrogation regions, each of the plurality of interrogation regions is associated with at least one microchannel in the plurality of microchannels.

**[0003]** A microfluidic chip is disclosed. In some examples, the microfluidic chip includes a plurality of sections that are stacked or layered in a stacking direction to form a plurality of microchannels at least partially oriented to flow along the stacking direction. The plurality of sections includes a transfer section for introduction of sample fluid including particles. The plurality of sections includes a particle focusing section configured to focus the particles in the sample fluid. The plurality of sections includes an actuation section including a plurality of interrogation regions and a plurality of actuators. Each of the plurality of

interrogation regions and each of the plurality of actuators is associated with at least one microchannel in the plurality of microchannels.

**[0003a]** In another aspect, the present disclosure relates to a particle processing system, comprising

a microfluidic chip including a plurality of sections that are stacked or layered in a stacking direction to form a plurality of microchannels at least partially oriented to flow along the stacking direction, the plurality of sections including:

a transfer section for introduction of sample fluid including particles,

and

a second section including a measurement section or the measurement section and an actuation section including a plurality of interrogation regions, each of the plurality of interrogation regions is associated with at least one microchannel in the plurality of microchannels;

an electromagnetic source system to illuminate the plurality of interrogation regions;

a detection system to receive light from the plurality of interrogation regions; and

a computing system operably connected to the detection system and the actuation section of the microfluidic chip, the computing system configured to control actuation of the plurality of particle deflectors based upon signals received from the detection system.

**[0004]** A particle processing system is disclosed. In some examples, the particle processing system includes a microfluidic chip having a plurality of sections that are stacked or layered in a stacking direction to form a plurality of microchannels at least partially oriented to flow along the stacking direction. The plurality of sections include a transfer section for introduction of sample fluid including particles. The plurality of sections include a particle focusing section configured to focus the particles in the sample fluid. The plurality of sections include an actuation section including a plurality of interrogation regions and a plurality of actuators. Each of the plurality of interrogation regions and each of the plurality of actuators is associated with at least one microchannel in the plurality of microchannels. In some examples, the particle processing system includes an electromagnetic source system

to illuminate the plurality of interrogation regions. In some examples, the particle processing system includes a detection system to receive light from the plurality of interrogation regions. In some examples, the particle processing system includes a computing system operably connected to the detection system and the actuation section of the microfluidic chip. In some examples, the computing system is configured to control actuation of the plurality of particle deflectors based upon signals received from the detection system.

**[0004a]** In yet another aspect, the present disclosure relates to a method of assembling a microfluidic chip, comprising:

aligning a transfer section with a plurality of alignment holes in a focusing section using a plurality of alignment posts;

bonding the transfer section to the focusing section;

aligning a second section including a measurement section, or the measurement section and an actuation section, to the focusing section by aligning a plurality of alignment holes in the actuation section to the alignment posts; and

bonding the second section to the focusing section.

**[0005]** A method of assembling a microfluidic chip is disclosed. In some examples, the method includes aligning a transfer section with a plurality of alignment holes in a focusing section using a plurality of alignment posts. The method includes bonding the transfer section to the focusing section. The method includes aligning an actuation section to the focusing section by aligning a plurality of alignment holes in the actuation section to the alignment posts. The method includes bonding the actuation section to the focusing section.

**[0005a]** In yet another aspect, the present disclosure relates to a method of sorting particles using a microfluidic chip, comprising:

flowing a sample stream including particles through a plurality of microchannels formed by a plurality of sections that are stacked or layered in a stacking direction to form the microfluidic chip, the plurality of microchannels at least partially oriented to flow along the stacking direction;

focusing particles in each of the plurality of microchannels using a focusing section of the plurality of sections;

detecting particle characteristics of particles flowing through a plurality of interrogation regions in an actuation section of the plurality of sections, each interrogation region associated with a microchannel; and

in response to the detected particle characteristics, sorting the particles using an actuator associated with each microchannel

**[0006]** In some examples, a method of sorting particles using a microfluidic chip is disclosed. The method includes flowing a sample stream including particles through a plurality of microchannels formed by a plurality of sections that are stacked or layered in a stacking direction to form the microfluidic chip. The plurality of microchannels are at least partially oriented to flow along the stacking direction. The method includes focusing particles in each of the plurality of microchannels using a focusing section of the plurality of sections. The method includes detecting particle characteristics of particles flowing through a plurality of interrogation regions in an actuation section of the plurality of sections. Each interrogation region is associated with a microchannel. The method includes sorting the particles using an actuator associated with each microchannel in response to the detected particle characteristics.

## BRIEF DESCRIPTION OF THE DRAWINGS

**[0007]** It is to be noted that the various features and combinations of features described below and illustrated in the figures can be arranged and/organized differently to result in embodiments which are still within the spirit and scope of the present disclosure. Further, components in the drawings are not necessarily to scale nor are they necessarily rendered proportionally, emphasis instead being placed upon clearly illustrating the relevant principles. Even further, various features may not be shown in certain figures in order to simplify the illustrations. Additionally, for the purposes of describing or showing items between layers or