about the cancer. Furthermore, other CTC technologies are limited in their ability to efficiently capture an adequate number of CTCs from whole blood and from various types of cancer. Thus, currently available technologies do not solve the challenge of providing physicians and drug development companies conducting clinical trials in oncology with a broadly applicable, efficient, and economical method which allows fast analysis of predictive markers on CTCs for diagnosis, prognosis and therapy.

[0015] Accordingly, there remains a need for new instruments and methods that will enable and improve the quick and efficient identification of target particles. More particularly, there is a need for new instruments and methods that will enable and improve the ability to assess at an early stage and predict the efficacy of, for example, cancer treatment regimens, including traditional chemotherapy, molecularly targeted agents and immunotherapy, which can be obtained in accordance with the present inventions.

SUMMARY OF THE INVENTIONS

[0015A] According to a first aspect, there is provid ed a flow chamber for separating particles in a sample comprising: an exterior surface area and an interior surface area, the interior surface defining a floor and a ceiling; a first port positioned for fluid communication with an interior surface area of the flow chamber; a second port positioned for fluid communication with the interior surface area of the flow chamber; an electrode element affixed to a floor area of the flow chamber, wherein the electrode comprises: a first electrode zone that is associated with a first inter-electrode pitch that extends from a midpoint of one of a plurality of first conductive traces to a midpoint of an adjacent first conductive trace in the first zone, the first zone configured to generate a first electric field when an electrical signal is applied; and a second electrode zone that is associated with a second inter-electrode pitch that extends from a midpoint of one of a plurality of second conductive traces to a midpoint

of an adjacent second conductive trace in the second zone, the second zone configured to generate a second electric field with at least one of a different magnitude, a different depth of field, and a different spatial profile than the first electric field when the electrical signal is applied; wherein the first inter-electrode pitch has a different width than the second inter-electrode pitch; and wherein a first inter-electrode gap associated with the first zone and a second inter-electrode gap associated with the second zone are of the same width and a first conductive trace width associated with the plurality of first conductive traces and a second conductive trace width associated with the plurality of second conductive traces are of a different width.

[0015B] According to a second aspect, there is provided a method for separating a target particle in a fluidic sample using dielectrophoresis in a flow chamber, the flow chamber being a flow chamber for separating particles in a sample, the flow chamber comprising: an exterior surface area and an interior surface area, the interior surface defining a floor and a ceiling; a first port positioned for fluid communication with an interior surface area of the flow chamber; a second port positioned for fluid communication with the interior surface area of the flow chamber; an electrode element affixed to a floor area of the flow chamber, wherein the electrode comprises: a first electrode zone that is associated with a first inter-electrode pitch that extends from a midpoint of one of a plurality of first conductive traces to a midpoint of an adjacent first conductive trace in the first zone, the first zone configured to generate a first electric field when an electrical signal is applied; and a second electrode zone that is associated with a second inter-electrode pitch that extends from a midpoint of one of a plurality of second conductive traces to a midpoint of an adjacent second conductive trace in the second zone, the second zone configured to generate a second electric field with at least one of a different magnitude, a different depth of field, and a different spatial profile than the first electric field when the electrical signal is applied; wherein the

first inter-electrode pitch has a different width than the second inter-electrode pitch; and wherein a first inter-electrode gap associated with the first zone and a second inter-electrode gap associated with the second zone are of the same width and a first conductive trace width associated with the plurality of first conductive traces and a second conductive trace width associated with the plurality of second conductive traces are of a different width, the method comprising: a) continuously introducing a sample containing the target particle into an infusion port; b) continuously introducing an elution buffer into a flow port; wherein the sample and the elution buffer form a fluidic suspension in a flow chamber; c) exposing the fluidic suspension to an electric field in a defined region of the flow chamber, wherein the electric field is produced by the electrode element; and d) collecting the target molecule.

[0015C] In an example, , an electrode is provided, the electrode comprising:

a first electrode zone that provides a first inter-electrode pitch that extends from a midpoint of one of a plurality of first conductive traces to a midpoint of an adjacent first conductive trace in the first zone, the first zone configured to generate a first electric field when an electrical signal is applied; and

a second electrode zone that provides a second inter-electrode pitch that extends from a midpoint of one of a plurality of second conductive traces to a midpoint of an adjacent second conductive trace in the second zone, the second zone configured to generate a second electric field with at least one of a different magnitude, a different depth of field, and a different spatial profile than the first electric field when the electrical signal is applied.

[0015D] Various examples further provide an electrode comprising first zone configured to generate a first electric field when an electrical signal is applied, and second zone configured to generate a second electric field with at least one of a different magnitude,

a different depth of field, and a different spatial profile than the first electric field when the electrical signal is applied.

[0015E] Various example still further provide a chamber for separating particles in a sample comprising:

an exterior surface area and an interior surface area, the interior surface defining a floor and a ceiling;

a first port positioned for fluid communication with an interior surface area of the chamber;

a second port positioned for fluid communication with the interior surface area of the chamber;

an electrode element affixed to a floor area of the chamber, wherein the electrode comprises:

a first electrode zone that is associated with a first inter-electrode pitch that extends from a midpoint of one of a plurality of first conductive traces to a midpoint of an adjacent first conductive trace in the first zone, the first zone configured to generate a first electric field when an electrical signal is applied;

and

a second electrode zone that is associated with a second inter-electrode pitch that extends from a midpoint of one of a plurality of second conductive traces to a midpoint of an adjacent second conductive trace in the second zone, the second zone configured to generate a second electric field with at least one of a different magnitude, a different depth of field, and a different spatial profile than the first electric field when the electrical signal is applied.

[0015F] The first inter-electrode pitch may have a different width than the second inter-electrode pitch.

[0015G] A first inter-electrode gap associated with the first zone and a second inter-electrode gap associated with the second zone may be of the same width and a first conductive trace width associated with the plurality of first conductive traces and a second conductive trace width associated with the plurality of second conductive traces may be of a different width.

[0015H] The first zone may be positioned upstream of the second zone and closer to the second port for generating a first dielectrophoretic force upon a sample. The first electrode zone may have a shorter depth of field than the second electrode zone.

[0015I] The first electrode zone may be fabricated on a flex circuit and laminated to the floor of the flow chamber. Similarly, the second electrode zone may be fabricated on a flex circuit and laminated to the floor of the flow chamber.

[0015J] The electrode may further include a third zone associated with a third inter-electrode gap and a plurality of third conductive traces, the third zone configured to generate a third electric field that is of a different magnitude than the second electric field when the electrical signal is applied.

[0015K] The chamber may be oriented such that the elution buffer flows at least one of vertically, or at a slope, to facilitate reducing a sedimentation force component.

[0015L] At least one of the plurality of first conductive traces and the plurality of second conductive traces may be oriented at an angle with the flow of the fluidic suspension.

[0015M] Various examples yet further provide an electrode coupled to the floor of the flow chamber and to an electrical power source comprising:

a first zone that is associated with a first inter-electrode pitch that extends from a midpoint of one of a plurality of first conductive traces to a midpoint of an adjacent first conductive trace in the first zone, the first zone configured to generate a first electric field when an electrical signal is applied; and

a second zone that is associated with a second inter-electrode pitch that extends from a midpoint of one of a plurality of second conductive traces to a midpoint of an adjacent second conductive trace in the second zone, the second zone configured to generate a second electric field with at least one of a different magnitude, a different depth of field, and a different spatial profile than the first electric field when the electrical signal is applied, wherein the first electric field and the second electric field generate dielectrophoretic forces.

[0015N] The first inter-electrode pitch may have a different width than the second inter-electrode pitch.

[0015O] A first inter-electrode gap associated with a first zone and the second inter-electrode gap associated with the second zone may be of the same width, and a first conductive trace width associated with the plurality of first conductive traces and a second conductive trace width associated with the plurality of second conductive traces may be of a different width.

[0015P] Various examples further provide a method for separating a target particle in a fluidic sample using dielectrophoresis in a flow chamber, the method comprising:

a) continuously introducing a sample containing the target particle into an infusion port;

b) continuously introducing an elution buffer into a flow port; wherein the sample and the elution buffer form a fluidic suspension in a flow chamber;

c) exposing the fluidic suspension to an electric field in a defined region of the flow chamber, wherein the electric field is produced by an electrode coupled to the floor of the chamber, wherein the electrode comprises:

a first zone that is associated with a plurality of first conductive tracks and a first inter-electrode gap that generate a first electric field when an electric signal is applied; and

a second zone that is associated with a plurality of second conductive tracks and a second inter-electrode gap that generate a second electric field of a different magnitude than the first electric field when the electric signal is applied, wherein the first electric field and the second electric field generate dielectrophoretic forces that separates the target particle from the fluidic suspension; and

d) collecting the target molecule.

[0015Q] The elution buffer may have a conductivity of from about 5 mS/m to about 250 mS/m. The elution buffer may particularly have a conductivity of about 30 mS/m. The sample may be contained in a sample buffer having a conductivity of from about 5 mS/m to about 250 mS/m.

[0015R] The electric field comprises an AC voltage of from about 2 Vp-p to about 8 Vp-p, and wherein the frequency of applied voltage comprises from about 10 kHz to about 30 MHz.

[0016] The present inventions are generally directed to instruments (or apparatuses), component devices or parts that can be employed in the instruments, and methods employing

the instruments and/or their component parts, for processing samples of interest (e.g., separating target particles of interest from non-target particles). In one embodiment, an apparatus of the invention generally includes an integrated fluidic device using dielectrophoresis in a continuous, semi-continuous, staged, or intermittent system, that includes a microfluidic chamber capable of enriching and isolating target particles, such as viable and/or fixed circulating tumor cells (CTCs) or disseminated tumor cells (DTCs), from a suspension of target and non-target particles (e.g., a suspension of cells). The apparatus enables the quantitative and/or qualitative analyzing of a subpopulation of the target particle-containing suspension (i.e., the target particles of the suspension), by using, for example

CLAIMS

What is claimed is:

1. A flow chamber for separating particles in a sample comprising:

an exterior surface area and an interior surface area, the interior surface defining a floor and a ceiling;

a first port positioned for fluid communication with an interior surface area of the flow chamber;

a second port positioned for fluid communication with the interior surface area of the flow chamber;

an electrode element affixed to a floor area of the flow chamber, wherein the electrode comprises:

a first electrode zone that is associated with a first inter-electrode pitch that extends from a midpoint of one of a plurality of first conductive traces to a midpoint of an adjacent first conductive trace in the first zone, the first zone configured to generate a first electric field when an electrical signal is applied;

and

a second electrode zone that is associated with a second inter-electrode pitch that extends from a midpoint of one of a plurality of second conductive traces to a midpoint of an adjacent second conductive trace in the second zone, the second zone configured to generate a second electric field with at least one of a different magnitude, a different depth of field, and a different spatial profile than the first electric field when the electrical signal is applied;

wherein the first inter-electrode pitch has a different width than the second inter-electrode pitch; and

wherein a first inter-electrode gap associated with the first zone and a second inter-electrode gap associated with the second zone are of the same width and a first conductive trace width associated with the plurality of first conductive traces and a second conductive trace width associated with the plurality of second conductive traces are of a different width.

2. A method for separating a target particle in a fluidic sample using dielectrophoresis in a flow chamber, the flow chamber being a flow chamber for separating particles in a sample, the flow chamber comprising: an exterior surface area and an interior surface area, the interior surface defining a floor and a ceiling; a first port positioned for fluid communication with an interior surface area of the flow chamber; a second port positioned for fluid communication with the interior surface area of the flow chamber; an electrode element affixed to a floor area of the flow chamber, wherein the electrode comprises:

a first electrode zone that is associated with a first inter-electrode pitch that extends from a midpoint of one of a plurality of first conductive traces to a midpoint of an adjacent first conductive trace in the first zone, the first zone configured to generate a first electric field when an electrical signal is applied; and a second electrode zone that is associated with a second inter-electrode pitch that extends from a midpoint of one of a plurality of second conductive traces to a midpoint of an adjacent second conductive trace in the second zone, the second zone configured to generate a second electric field with at least one of a different magnitude, a different depth of field, and a different spatial profile than the first electric field when the electrical signal is applied; wherein the first inter-electrode pitch has a different width than the second inter-electrode pitch; and wherein a first inter-electrode gap associated with the first zone and a second inter-electrode gap associated with the second zone are of the

same width and a first conductive trace width associated with the plurality of first conductive traces and a second conductive trace width associated with the plurality of second conductive traces are of a different width, the method comprising:

a) continuously introducing a sample containing the target particle into an infusion port;

b) continuously introducing an elution buffer into a flow port; wherein the sample and the elution buffer form a fluidic suspension in a flow chamber;

c) exposing the fluidic suspension to an electric field in a defined region of the flow chamber, wherein the electric field is produced by the electrode element; and

d) collecting the target molecule.

3. The method of claim 2 wherein the elution buffer has a conductivity of from about 5 mS/m to about 250 mS/m.

4. The method of claim 3, wherein the elution buffer has a conductivity of about 30 mS/m.

5. The method of claim 4, wherein the sample is contained in a sample buffer having a conductivity of from about 5 mS/m to about 250 mS/m.

6. The method of any one of claims 2 to 5, wherein the electric field comprises an AC voltage of from about 2 Vp-p to about 8 Vp-p, and wherein the frequency of applied voltage comprises from about 10 kHz to about 30 MHz.