several researchers. Alternative techniques to detect attached cells by substrate impedance sensing require cell coverage on the electrode surface to reach near unity for detectable measurements. Studies using non-optical methods to detect few cells on large surface areas in a relatively large volume—including even the microliter volumes of microscale devices have not yet been reported, despite the need for non-optical detection methods in microfluidic applications.

Detection and enumeration of cells are essential for medical diagnostics, especially AIDS, cancer diagnosis, and pathogen detection. While most existing methods to detect cells are optical (i.e., microscopy), electrical detection is significantly simpler, cheaper, and more amenable to point of care devices. To date, electrical detection and enumeration of intact cells based on impedance spectroscopy (i.e., detection of changes in electrical impedance caused by the presence of cells) have proven to be extremely practical and inexpensive, but limited to large cell populations or homogenous cell types (e.g., Coulter counting of red blood cells).

SUMMARY ~~OF THE INVENTION~~

In one ~~aspect~~example, ~~the invention features~~disclosed herein is a method of counting cells (e.g., mammalian, fungal, protist, or bacterial cells) in a sample by introducing the sample into a channel, lysing the cells in the channel, and measuring at least one property of at least one cellular component resulting from the lysing. In this ~~aspect~~example, the cellular component is indicative of the number of cells lysed in the channel.

In another ~~aspect~~example, ~~the invention features~~disclosed herein is a method of counting cells (e.g., a mammalian, fungal, protest, or bacterial cell) in a sample including the steps of introducing the sample into a channel (e.g., a microfluidic channel), introducing a

non-conductive solution into the channel (e.g., a sugar solution), applying an electric field to the channel, measuring the impedance of the channel, replacing the non-conductive solution with a lysing non-conductive solution (e.g., a detergent solution) and allowing at least one cell to lyse, applying an electric field to the channel, and measuring the impedance of the channel. In this ~~aspect~~example a decrease in the impedance after lysis is indicative of the number of the cells in the sample. In this ~~aspect~~example, the impedance is measured, for example, using a top down electrode, IDT electrode, or a two rail electrode. Desirably, the impedance of the non-conductive solution prior to lysis is greater than 1,000 ohms, greater than 10,000 ohms, greater than 100,000 ohms, greater than 1,000,000 ohms or greater.

In another ~~aspect~~example, ~~the invention features~~disclosed herein is a method of diagnosing a condition in a subject by introducing a sample (e.g., a human blood sample) containing a population of cells (e.g., CD4 helper cells) into a channel, lysing the population of cells in the channel, and measuring at least one property of at least one cellular component resulting from the lysing. In this ~~aspect~~example, the cellular component is indicative of the number of cells lysed in the channel and the number of cells is diagnostic for the condition.

In one aspect, the present invention refers to a kit for counting cells in a sample, said kit comprising: a microfluidic device, wherein said microfluidic device comprises a microfluidic channel and an electrode to measure an impedance within said microfluidic channel, and wherein said microfluidic channel comprises a surface on which binding moieties can adhere; an isotonic, low conductivity solution for establishing a baseline impedance in the microfluidic channel; and a lysing hypotonic, low conductivity solution for replacing the isotonic, low conductivity solution in the microfluidic channel and for lysing cells within the microfluidic channel.

In another aspect, the present invention refers to a microfluidic device for counting cells, wherein the microfluidic device comprises: a microfluidic channel; one or more electrodes adjacent to the microfluidic channel for measuring an impedance within said microfluidic channel, wherein said one or more electrodes are selected from the group consisting of a top down electrode, an IDT electrode, and a two rail electrode; and anti-CD4 antibodies for immobilizing mammalian cells, wherein the anti-CD4 antibodies are bound to a wall of the microfluidic channel.

In another ~~aspect~~example, ~~the invention features~~disclosed herein is a kit for counting cells including a device, a non-conductive solution (e.g., a sugar solution), and a lysing non-conductive solution (e.g., a detergent solution). In this ~~aspect~~example, the device includes a microfluidic channel and an electrode (.e.g., top down electrode, IDT electrode, and a two rail electrode) to measure the impedance of the microfluidic channel. In any of the forging ~~aspects~~examples, the detergent can be triton-X or tween-20.

In any of the forgoing ~~aspects~~examples, the cellular component can be an ion (e.g., potassium, calcium, and sodium) or an enzyme (e.g., lactate dehydrogenase).

In any of the forgoing ~~aspects~~examples, the property resulting from the lysing can be impedance. In this ~~aspect~~example, the impedance can be measured using a top down electrode, IDT electrode, and a two rail electrode.

In any of the forgoing ~~aspects~~examples, impedance can be, for example, measured using a single frequency (e.g., 760 Hz) or using an ion sensitive electrode (e.g., a potassium, sodium or calcium ion-specific electrode).

Alternatively, the property resulting from lysing can be mass. In this ~~aspect~~example, the mass can be measured using a micro- or nano-mechanical resonator.

In any of the forgoing ~~aspects~~examples, the measuring can include optical detection, surface plasmon resonance, or a lateral flow diffusion assay.

In one preferred ~~embodiment~~example, the property is measured using fluorescent probes and the ion is potassium. In another preferred ~~embodiment~~example, the cellular component is a nucleus, and the property resulting from the lysing is impedance. In yet another preferred ~~embodiment~~example, the microfluidic channel has a volume of 10 μl.

In any of the above methods, the population of cells and the condition can be selected from Table 1.

Table 1

Cell Population	**Condition**
Neutrophil	Effects of Immunosuppressive drug treatment
Monocyte	Differential blood count
Lymphocyte	AIDS
Lymphocyte	Effects of Immunosuppressive drug treatment
Lymphocyte B	Immune response to infection
Circulating tumor cells	Cancer
Dendritic cells	Immune responses
Red blood cells	Malaria
Tuberculosis sensitive CD8 T cell	Latent tuberculosis
Platelets	Effects of anti-thrombotic drug

carrying out the invention that are obvious to those skilled in the art are intended to be within the scope of the invention.

Other embodiments are in the claims.

~~What is claimed is:~~