CLAIMS

1. A method for charging/discharging fluids from a microfluidic device, wherein said method comprises:

a) providing a kit comprising:

a tip;

a microfluidic device comprising a reversed open microwell system, the reversed open microwell system comprising an array of open microwells, at least one microchannel, at least one input port for at least one reagent and/or for one or more biological samples, and at least one output port for the at least one reagent and/or one or more biological samples, said input and output ports being in microfluidic communication with one or more of said at least one microchannels, wherein said at least one microchannel has a cross-section area of micrometric dimensions and is configured to provide a fluid to microwells of said array of open microwells;

a discharge region which comprises: an unloading container in fluid connection with said microfluidic device by means of at least one unloading channel and one outlet door, wherein said unloading channel emerges from said at least one microchannel and is a siphon;

wherein said tip comprises a proximal portion intended to cooperate with a fluid dispensing system and a distal portion, said proximal portion of generally tubular configuration and said distal portion is open tapered wherein the terminal base of said distal portion is made of plastic has an outer diameter of dimension d**3**, and the upper base of said distal portion has an outer diameter of dimension d**4**, wherein a distance between

said upper base and said terminal base of said distal portion is h**2**, the half-opening of a truncated cone formed by said distal portion is (90°-β), and said proximal portion has a height of h**3**; wherein said input port comprises a plastic vertical channel leading into said at least one microchannel, an upward opening of said vertical channel having a diameter of d**2**, where d**3**<d**2**, said vertical channel is a channel tapered downwards having an upper base and a lower base, said lower base having a diameter of dimension d**1**, said vertical channel having a height h**1** and a half-opening of the truncated cone formed by said tapered channel being (90°-α1); said tip and said vertical channel being dimensioned so as to produce an interference coupling therebetween; wherein said microfluidic device is charged with at least a first fluid; and

b) exerting a pressure on said at least a first fluid entering said microfluidic device; or

c) arranging a discharge region wherein said discharge channel has a diameter such as to make said fluid pass from said microfluidic device to said discharge channel by capillarity;

wherein a volume V of said at least a first fluid is smaller than or equal to the volume of said discharge container, and said at least first fluid reaches said discharge container in a unidirectional manner.

2. The method for charging/discharging fluids according to claim 1, wherein said method further comprises:

introducing a second or further fluid through said input port in said microfluidic device, wherein said first, second and/or further fluids are independently equal or different from one another and are selected from the group comprising liquids and gases; and

said second and/or further fluid completely replaces in said microchannel or in said microchannel and in said reversed open microwells, when present in said microfluidic device, the fluid introduced before;

wherein said first, second and/or further fluids do not mix with one another.

3. A method for the large-scale high-content analysis of biological samples, comprising the following steps:

providing a kit comprising:

a tip;

a microfluidic device comprising a reversed open microwell system, the reversed open microwell system comprising an array of open microwells, at least one microchannel, at least one input port for at least one reagent and/or for one or more biological samples, and at least one output port for the at least one reagent and/or one or more biological samples, said input and output ports being in microfluidic communication with one or more of said at least one microchannels, wherein said at least one microchannel has a cross-section area of micrometric dimensions and is configured to provide a fluid to microwells of said array of open microwells;

a discharge region which comprises: an unloading container in fluid connection with said microfluidic device by means of at least one unloading channel and one outlet door

wherein said unloading channel emerges from said at least one microchannel and is a siphon;

wherein said tip comprises a proximal portion intended to cooperate with a fluid dispensing system and a distal portion, said proximal portion of generally tubular configuration and said distal portion is open tapered wherein the terminal base of said distal portion is made of plastic has an outer diameter of dimension d**3**, and the upper base of said distal portion has an outer diameter of dimension d**4**, wherein a distance between said upper base and said terminal base of said distal portion is h**2**, the half-opening of a truncated cone formed by said distal portion is ($90°\beta$), and said proximal portion has a height of h**3**; wherein said input port comprises a plastic vertical channel leading into said at least one microchannel, an upward opening of said vertical channel having a diameter of d**2**, where d**3**<d**2**, said vertical channel is a channel tapered downwards having an upper base and a lower base, said lower base having a diameter of dimension d**1**, said vertical channel having a height h**1** and a half-opening of the truncated cone formed by said tapered channel being ($90°-\alpha 1$); said tip and said vertical channel being dimensioned so as to produce an interference coupling

therebetween;

providing an automated management system of said reversed open microwell system, the automated management system comprising the features of: an incubator at controlled temperature, humidity and CO2 level,

a fluid dispensing system, and phase-contrast and fluorescence image acquisition;

placing said reversed open microwell system in said automated system;

charging reagents through one or more of said input ports, wherein said reagents comprise at least one of: filling buffer, washing solution, one or more drugs, one or more dyes, one or more labeled antibodies, and one or more cell viability markers;

charging said one or more biological samples through one or more of said input ports;

acquiring images from one or more of said microwells, wherein said images are defined images T**0**; and

classifying the cells displayed, wherein said classification is made with morphological and/or functional parameters detected from the images T**0**.

4. The high-content analysis method according to claim **3**, further comprising, after the introduction of said reversed open microwell system in said automated system: filling at least one said microchannel with filling buffer; and acquiring images from one or more of said microwells, either individually or by subgroups, wherein said images are defined baseline images; wherein said classification is made with morphological and/or functional parameters detected by the comparison of images T**0** with said baseline images.

5. The high-content analysis method according to claim **3**, wherein said biological sample comprises about 10-20 cells.

6. The high-content analysis method according to claim **3** wherein, at the end of said method, the surviving cells are harvested and used in subsequent analyses.

7. The high-content analysis high-content analysis method according to claim **3**, wherein said method further comprises: charging a fluid into said tip; positioning said tip above said input port and inserting it into said input port to reach an interference coupling position between said distal region of said tip and said vertical channel in said input port; releasing the fluid contained in said tip in said microfluidic device through said input port or, with the same tip, suctioning fluid already contained in said microfluidic device.

8. The high-content analysis method according to claim **7**, wherein said microfluidic device of said kit further comprises a discharge region which comprises: a discharge container in fluidic connection with said microfluidic device through at least one discharge channel and an output port, and said method further comprises forcing said fluid, pushed by a pressure applied in said input port in said microfluidic device, unidirectionally into said discharge container, where a volume V of said fluid is smaller than or equal to the volume of said discharge container.

9. The high-content analysis method according to claim **3**, further comprising dyeing said cells with at least one of: one or more dyes, one or more labeled antibodies, and one or more cell viability markers.