CLAIMS

1. A droplet generation method, adopting a droplet generation device and a droplet receiver, wherein, a first liquid is placed in the droplet receiver, ~~characterized in that,~~wherein the droplet generation device comprises a fluid passage, an accommodating cavity with a ~~variable~~ volume which is variable and a droplet generation tube having ~~relatively distant~~ a first port and a second port, wherein the first port communicates with the accommodating cavity, and an inner diameter of the second port of the droplet generation tube is not smaller than 0.1 mm; the droplet generation method comprises following steps:

S1, transferring a second liquid into the droplet generation tube, wherein the second liquid is a liquid immiscible with the first liquid;

S2, inserting the droplet generation tube into the first liquid, and keeping the second port of the droplet generation tube being below the liquid surface of the first liquid;

S3, controlling the accommodating cavity to make its volume change periodically, and injecting a driving fluid into the fluid passage to drive the movement of the second liquid.

2. The droplet generation method according to claim 1, ~~characterized in that~~wherein, in step S3, droplets are formed in the droplet generation tube, and then flow out through the second port and enter the droplet receiver.

3. The droplet generation method according to claim 1, ~~characterized in that~~wherein, in step S3, the droplet generation tube and the droplet receiver remain relatively stationary~~.~~; and/or

~~4. The droplet generation method according to claim 1, characterized in that,~~ the periodic change is a compression-recovery reciprocating change, or an expansion-recovery reciprocating change, or a compression-recovery-expansion-recovery reciprocating change~~.~~; and/or

~~5. The droplet generation method according to claim 1, characterized in that,~~ in step S3, the accommodating cavity, the droplet generation tube, and the droplet receiver are arranged in sequence from top to bottom, the first port of the droplet generation tube is communicated with the bottom of the accommodating cavity, and a center line of the accommodating cavity, an axial line of the droplet generation tube, a center line of the first port, and a center line of the second port are coincident and extend in a vertical direction.

~~6~~4. The droplet generation method according to claim 1, ~~characterized in that~~wherein, the

inner diameter of the second port is~~ not smaller than 0.1 mm, preferably~~ greater than 0.2 mm, more preferably 0.2 to 1 mm, still more preferably 0.3 mm to 1 mm, particularly preferably 0.3 mm to 0.6 mm; and/or,

the inner diameter of the first port is larger than the inner diameter of the second port; and/or,

the droplet generation tube comprises a tapered tube portion, and two ends of the tapered tube portion respectively form the first port and the second port, the taper of the tapered tube portion is 0.05 to 0.2; and/or,

the frequency of the periodic change is 10 Hz to 1 KHz, preferably 50 Hz to 600 Hz, further preferably 80 Hz to 600 Hz, more preferably 100 Hz to 600 Hz, more preferably 150 Hz to 600 Hz, still more preferably 150 Hz to 500 Hz, particularly preferably 150 Hz to 300 Hz.

~~7~~5. The droplet generation method according to claim ~~6~~4, ~~characterized in that~~wherein, at least a part of the wall constituting the accommodating cavity is a movable part, which may be driven to move outward or inward when an external force is applied, thereby increasing or decreasing the volume of the accommodating cavity.

~~8~~6. The droplet generation method according to claim ~~7~~5, ~~characterized in that~~wherein, the movable part is composed of a metal or non-metal diaphragm; and/or, one or more of the top or the surrounding side walls of the accommodating cavity are provided with the movable part.

~~9~~7. The droplet generation method according to claim ~~7~~5, ~~characterized in that~~wherein, the movable part is connected with a vibration mechanism through a connecting mechanism, and in step S3, the vibration mechanism drives the movable part to vibrate reciprocally and synchronously to control the volume of the accommodating cavity to change periodically; or,

a vibrating mechanism is set abut against the movable part, and in step S3, the vibrating mechanism transmit its reciprocating vibration to the movable part to make it vibrate, so as to control the volume of the accommodating cavity to change periodically.

~~10~~8. The droplet generation method according to claim ~~9~~7, ~~characterized in that~~wherein, a direction of the reciprocating vibration is an up-down direction~~.~~; and/or

~~11. The droplet generation method according to claim 9 or 10, characterized in that,~~ the vibration amplitude is 5 μm to 1000 μm, preferably 5 μm to 600 μm, more preferably 5 μm to 300 μm, further preferably 5 μm to 100 μm, more further preferably 5 μm to 60 μm~~.~~; and/or

~~12. The droplet generation method according to claim 9, characterized in that,~~ when the taper of the tapered tube portion is 0.05 to 0.1, setting the vibration frequency to be 100 Hz to 600 Hz, and the vibration amplitude to be 10 μm to 300 μm; when the taper of the tapered tube portion is 0.1 to 0.2, setting the vibration frequency to be 100 to 300 Hz, and the vibration amplitude to be 10 μm to 600 μm~~.~~; and/or

~~13. The droplet generation method according to claim 1, characterized in that,~~ in step S3, the fluid is a liquid, and the injection speed is 2 to 200 μL/min, preferably 10 to 50 μL/min~~.~~; and/or

~~14. The droplet generation method according to claim 1, characterized in that,~~ the accommodating cavity is an annular cavity with an inner diameter of 4 to 6 mm; and/or, an inner peripheral side wall of the accommodating cavity extends in a vertical direction~~.~~; and/or

~~15. The droplet generation method according to claim 1, characterized in that,~~ the step S1 is performed before the step S2, or the step S1 is performed after the step S2~~.~~; and/or

~~16. The droplet generation method according to claim 1, characterized in that,~~ in step S1, the second liquid is sucked into the ~~the~~ droplet generation tube through the second port of the droplet generation tube, which is followed or not followed by sucking some of the first liquid~~.~~; and/or

~~17. The droplet generation method according to claim 1 or 16, characterized in that,~~ before step S3, the liquid in the droplet generation tube has a section of driving fluid and a section of second liquid in sequence from top to bottom; or, the liquid in the droplet generation tube has a section of driving fluid, a section of second liquid and a section of first liquid in sequence from top to bottom.

~~18~~9. The droplet generation method according to claim 1, ~~characterized in that~~wherein, the droplet generation method comprises a step of cleaning and/or eliminating bubbles of the accommodating cavity and the droplet generation tube after the droplet generation is completed or before the next droplet generation starts~~.~~;

~~19. The droplet generation method according to claim 18, characterized in that~~preferably, two plunger pumps are adopted with different volumes to control the driving fluid, combining with a three-way valve for switching control, wherein the plunger pump with a larger volume is used in the step of cleaning and/or step of eliminating bubbles, and the plunger pump with a smaller volume is used in the step of droplet formation.

~~20~~10. The droplet generation method according to claim 1, ~~characterized in that~~wherein, the first liquid is a continuous phase, and the second liquid is a dispersed phase; and/or, the first liquid is an oil phase, and the second liquid is an aqueous phase~~.~~; and/or

~~21. The droplet generation method according to claim 1 or 20, characterized in that,~~ the first liquid is added with a surfactant; the second liquid is an aqueous phase containing biological or chemical substances to be detected~~.~~; and/or

~~22. The droplet generation method according to claim 1, characterized in that,~~ the droplets are digital PCR droplets or single-cell droplets; and/or, a diameter of the droplets is 50 μm to 250 μm, preferably 200 μm or less, more preferably 150 μm or less, further preferably 120 μm or less, still more preferably 110 μm or less.

~~23~~11. A droplet generation method, the droplet generation method forming droplets by mixing a first liquid and a second liquid immiscible with the first liquid, ~~characterized in that~~wherein, the droplet generation method comprises the following steps:

providing a first cavity stored with the first liquid;

feeding the second liquid into the first liquid through a second cavity having a port for liquid flow in and out, wherein an inner diameter of the port for liquid flow in and out of the second cavity is 0.1 to 1 mm, a third liquid immiscible with the second liquid is used to drive the second liquid to flow, and is applied with vibration, the first liquid is kept ~~relatively~~ stationary with respect to the first cavity and the second cavity, and the first cavity is kept ~~relatively~~ stationary with respect to the second cavity during the feeding of the second liquid,

the second liquid being wrapped by the first liquid to obtain droplets, wherein the first liquid and the third liquid are continuous phases, and the second liquid is a dispersed phase.

~~24.~~ 12. The droplet generation method according to claim 23, ~~characterized in that, the inner diameter of the port for liquid in and out of the second cavity is 0.1 to 1 mm; preferably,~~ wherein, the inner diameter of the port for liquid flow in and out of the second cavity is 0.3 to 0.6 mm; and/or,

a feed speed of the second liquid is 2 to 200 μL/min; preferably, a feed speed of the second liquid is 10 to 50 μL/min; and/or,

a frequency of the vibration is 10 Hz to 1 KHz; and/or,

an amplitude of the vibration is 5 to 1000 μm; preferably, a frequency of the vibration is 150 Hz to 600 Hz; an amplitude of the vibration is 5 to 100 μm~~.~~; and/or

~~25. The droplet generation method according to claim 23, characterized in that,~~ the first liquid and the third liquid are oil phases, and the first liquid is added with a surfactant; the second liquid is an aqueous phase containing biological or chemical substances to be detected~~.~~; and/or

~~26. The droplet generation method according to claim 23, characterized in that,~~ the center line of the port for liquid in and out and the liquid surface of the first liquid are perpendicular~~.~~; and/or

~~27. The droplet generation method according to claim 23, characterized in that,~~ when feeding the second liquid into the first liquid, inserting the port for liquid in and out of the second cavity below the liquid surface of the first liquid; and, firstly filling the second cavity with the third liquid , then sucking the second liquid through the port for liquid in and out of the second cavity to the second cavity which has already been stored with the third liquid, and finally driving the third liquid, so as to drive the second liquid to output from the port for liquid in and out of the second cavity.

~~28~~13. A droplet generation system, comprising a droplet generation device~~, and a droplet receiver used for accommodating a first liquid and droplets, characterized in that~~, wherein the droplet generation device comprises an accommodating cavity with a ~~variable~~ volume which is variable, a control mechanism for controlling periodical change of volume of the accommodating cavity, and a droplet generation tube having a first port and a second port ~~that are relatively distant from each other~~, the first port of the droplet generation tube communicates with the accommodating cavity, the inner diameter of the second port of the droplet generation tube is greater than 0.1 mm, and the droplet generation device further comprises a fluid driving mechanism for introducing a driving fluid into the accommodating cavity.

~~29~~14. The droplet generation system according to claim ~~28~~13, ~~characterized in that~~wherein, the inner diameter of the second port of the droplet generation tube is greater than 0.2 mm and lower than 1 mm; and/or, the inner diameter of the first port is greater than that of the second port; and/or, a volume of the droplet generation tube is 10 to 200 μL; and/or, the droplet generation tube comprises a tapered tube portion having ~~a relatively distant~~ the first port and ~~a~~ the second

port, the inner diameter of the first port is larger than the inner diameter of the second port, and the taper of the tapered tube portion is 0.05 to 0.2~~.~~; and/or

~~30. The droplet generation system according to claim 29, characterized in that,~~ the inner diameter of the second port of the droplet generation tube is 0.3 to 0.6 mm; and/or, the taper of the tapered tube portion is 0.05 to 0.15; and/or, volume of the tapered tube portion is 10 to 200μL; and/or, the inner wall surface of the tapered tube portion is a smooth surface~~.~~; and/or

~~31. The droplet generation system according to claim 28, characterized in that,~~ the periodic change is a compression-recovery reciprocating change, or an expansion-recovery reciprocating change, or a compression-recovery-expansion-recovery reciprocating change.

~~32~~15. The droplet generation system according to claim ~~28~~13, ~~characterized in that~~wherein, the fluid driving mechanism comprises a pump and a fluid passage, the droplet generation device comprises a base, which provides a cylindrical hole, the fluid passage, and a connecting portion for connecting the droplet generation tube, and there are one or more cylindrical holes, one or more fluid passages, and one or more connecting portions for one base, each of the cylindrical hole is cylindrical with both up opening and down opening, and is covered with a diaphragm, which form the accommodating cavity together with the cylindrical hole.

~~33~~16. The droplet generation system according to claim ~~32~~15, ~~characterized in that~~wherein, the accommodating cavity, the droplet generation tube, and the droplet receiver are arranged in sequence from top to bottom, the first port of the droplet generation tube communicates with the down opening of the accommodating cavity, a center line of the accommodating cavity, an axial line of the droplet generation tube, a center line of the first port, and a center line of the second port coincide and extend in a vertical direction~~.~~; and/or

~~34. The droplet generation system according to claim 32, characterized in that,~~ each diaphragm comprises a main body and a movable part, the main body is fixedly connected with the base, the movable part is located over the cylindrical hole, and is connected to the control mechanism through the connecting member~~.~~; and/or

~~35. The droplet generation system according to any one of claims 32 to 34, characterized in that,~~ the diaphragm is a metal or non-metal diaphragm; and/or, a thickness of the diaphragm is 0.005 to 2 mm; and/or, a sealing member is provided between the diaphragm and the base to seal

the accommodating cavity.

~~36~~17. The droplet generation system according to any one of claims 32 to 34, ~~characterized in that~~wherein, the control mechanism is a vibration mechanism~~,~~.

~~37. The droplet generation system according to claim 36, characterized in that,~~ the vibration mechanism comprises one or more of a galvanometer motor, piezoelectric ceramic, and a voice coil motor; and/or, direction of vibration provided by the vibration mechanism is an up-down direction.

~~38~~18. The droplet generation system according to claim ~~37~~17, ~~characterized in that~~wherein, the droplet generation tube is detachably connected to the connecting portion; and/or, a number of the cylindrical holes, the fluid passages, and the connecting portions for one base is 2 to 20, respectively.

~~39~~19. The droplet generation system according to claim ~~38~~18, ~~characterized in that~~wherein, there are a plurality of cylindrical holes, a plurality of fluid passages, and a plurality of connecting portions, two opposite side portions of the base are respectively higher than a middle part between the two opposite side portions, the plurality of cylindrical holes are independently distributed in the middle part of the base and are arranged in two rows, each fluid passage comprises a vertical passage formed on two opposite side portions of the base and a horizontal passage correspondingly communicating the vertical passage with the cylindrical hole.

~~40~~20. The droplet generation system according to claim ~~39~~19, ~~characterized in that~~wherein, a drainage portion is formed between a port of the horizontal passage and an inner peripheral side wall of the accommodating cavity, so that the liquid from the horizontal passage enters the accommodating cavity in a direction tangent to the circumferential direction of the accommodating cavity~~.~~;

~~41. The droplet generation system according to claim 32, characterized in that~~preferably, one end portion of the fluid passage communicates with the accommodating cavity, and when the fluid is driven from the fluid passage into the accommodating cavity, the fluid forms a vortex in the accommodating cavity and the droplet generation tube that rotates along the circumferential directions of the accommodating cavity and the droplet generation tube~~.~~; or

~~42. The droplet generation system according to claim 32, characterized in that,~~ one end

portion of the fluid passage communicates with the accommodating cavity, the direction in which the fluid is discharged from the fluid passage is deviated from an axial line of the accommodating cavity.

~~43. A droplet generation system, characterized in that, it comprises:~~

~~a container having a first cavity for placing the first liquid, the container having a mouth communicating with the first cavity;~~

~~a sample-adding tube having a second cavity, which is provided with a port for liquid in and out, a liquid injection port and a vibration access port which are respectively communicated with the second cavity, the inner diameter of the port for liquid in and out is 0.1 to 1 mm, the port for liquid in and out is used for sucking the second liquid and the third liquid and outputting the second liquid, the liquid injection port is used for connecting to a drive source, and the vibration access port is used to connect to a vibration source;~~

~~a drive source connected to the liquid injection port;~~

~~and a vibration source applying vibration to the vibration access port.~~

~~44. The droplet generation system according to claim 43, characterized in that, an inner diameter of the port for liquid in and out of the second cavity is 0.3 to 0.6 mm; and/or, the droplet generation system is a digital PCR droplet generation system or a single-cell droplet generation system.~~

~~45. The droplet generation system according to claim 43, characterized in that, the sample-adding tube has a first tube cavity, a second tube cavity and a third tube cavity, which together form the second cavity, the first tube cavity extends along a first direction, one end of which forms the liquid injection port, and another end of which is communicated with the second tube cavity; the second tube cavity is provided with the vibration access port; the third tube cavity extends along a second direction, one end of which is communicated with the second tube cavity, and another end of which forms the port for liquid in and out, wherein the first direction and the second direction are perpendicular;~~

~~the second cavity is narrowed near the port for liquid in and out; a diaphragm is encapsulated at the vibration access port, and the vibration source applies vibration to the diaphragm;~~

~~center lines of the port for liquid in and out and the vibration access port coincide.~~

~~46. The droplet generation device according to any one of claims 28 to 42.~~

~~47. Application of a droplet generation method according to any one of claims 1 to 27, a droplet generation system according to any one of claims 28 to 45 or a droplet generation device according to claim 46 in clinical diagnosis, gene expression analysis or microorganism detection.~~