protein, such as a TEP, from a population of cells comprising the cells displaying, preferably secreting said protein, comprising:

a. microfluidic channels,
b. a reaction chamber for mixing magnetic beads in suspension, wherein the reaction chamber has at least one inlet and at least one outlet channel for introducing and removing a fluid into and from, respectively, said reaction chamber,
c. a cell sample container in fluid communication with the reaction chamber through the inlet channel,
d. at least one washing reagent container in fluid communication with the reaction chamber through the inlet channel,
e. a waste container in fluid communication with the reaction chamber through the outlet channel,

wherein, each container of c. to d. is further in communication through one of the microfluidic channels to a venting pore comprising an air filtering element.

In another aspect, there is provided a cartridge for selecting cells based on their level of display of, and secretion of, a protein from a population of cells comprising the cells displaying, and secreting, said protein, according to the method described herein comprising:

a. microfluidic channels,
b. a reaction chamber for mixing magnetic beads in suspension, wherein the reaction chamber has at least one inlet and at least one outlet channel for introducing and removing a fluid into and from said reaction chamber,
c. a cell sample container in fluid communication with the reaction chamber through the inlet channel,
d. at least one washing reagent container in fluid communication with the reaction chamber through the inlet channel,
e. a waste container in fluid communication with the reaction chamber through the outlet channel,

wherein, each container of c- d is further in communication through one of the microfluidic channels to a venting pore comprising an air filtering element, and wherein capture beads in the form of functionalized superparamagnetic beads and carrier beads in the form of ferromagnetic beads are contained in the reaction chamber.

The disclosure is also directed to an integrated system for selecting cells, e.g. recombinant cells, based on their level of display, and preferably secretion (release from a surface of a cell; shedding), of a protein, e.g., a TEP, expressed on the surface of the cells, from a population of cells comprising cells displaying, preferably secreting, said protein, wherein the system comprises a cartridge comprising:

a. microfluidic channels,
b. a reaction chamber for mixing magnetic beads in suspension; wherein the reaction chamber has at least a first inlet and at least a second outlet channel for introducing and removing a fluid into and from said reaction chamber,
c. a cell sample container in fluid communication with the reaction chamber through the inlet channel,
d. at least one washing reagent container in fluid communication with the reaction chamber through the inlet channel,
e. a waste container in fluid communication with the reaction chamber through the outlet channel, wherein each container of c. to d. is further in communication through one of the microfluidic channels to an venting pore comprising an air filtering element;

f. one or more devices that create a controllable magnetic field (magnetic field devices= MFDs), in particular one or more electromagnets, arranged around or at the reaction chamber;

g. data processing equipment (e.g. a computer) configured to adjust a magnetic field created by the MTD(s) within the reaction chamber via frequency and/ or amplitude adjustments, wherein each frequency and/ or amplitude adjustment defines an operation mode within the reaction chamber.

In another aspect, there is provided an integrated system for selecting cells based on their level of display of, and secretion of, a protein from a population of cells comprising the cells displaying, and secreting, said protein, comprising:

a. microfluidic channels,

b. a reaction chamber for mixing magnetic beads in suspension; wherein the reaction chamber has at least a first inlet and at least a second outlet channel for introducing and removing a fluid into and from said reaction chamber,

c. a cell sample container in fluid communication with the reaction chamber through the inlet channel,

d. at least one washing reagent container in fluid communication with the reaction chamber through the inlet channel,

e. a waste container in fluid communication with the reaction chamber through the outlet channel, wherein each container of c-d is further in communication through one of the microfluidic channels to a venting pore comprising an air filtering element; and wherein the reaction chamber comprises a mixture of carrier beads in the form of ferromagnetic beads and capture beads in the form of functionalized superparamagnetic beads; and comprising

f. one or more devices that create a controllable magnetic field (magnetic field devices= MFDs), arranged around or at the reaction chamber;

g. data processing equipment configured to adjust the magnetic field created by the MFDs within the reaction chamber via frequency and/ or amplitude adjustments, wherein each frequency and/ or amplitude adjustment defines an operation mode within the reaction chamber,

wherein the data processing equipment is configured to set a succession of said operation modes comprising a mixing mode, a capture mode, an immobilization mode, a bead separation mode and a recovery mode, wherein

the data processing equipment is adapted to set the MFDs to operate:

- in a circular or alternating mode at 1-1000 Hz, and at 0.1 to 10,000 mA, during the mixing and bead separation mode;
- in circular or alternating mode at a frequency and amplitude lower than in the mixing mode, such as at 0.5 to 40 Hz and at 300 to 600 mA, during the capture mode;
- at 0 Hz and at an amplitude ,such as at 300 to 600 mA, during the immobilization mode; and
- at an, relative to the immobilization mode, increased frequency, such as between 40 Hz-500Hz and at a lowered amplitude, such as at 30-300 mA during the recovery mode.

The data processing equipment may be configured to set a succession of said operation modes comprising a mixing mode, a capture mode, an immobilization mode, a bead separation mode and/or a recovery mode.

The data processing equipment may be adapted to set the MFDs to operate:

- in a circular or alternating mode at 1-1000 Hz, preferably 40 Hz- 500Hz and at 0.1 to 10,000 mA, preferably 200-500 mA during the mixing and bead separation mode, wherein, e.g., the circular mode may switch between clockwise and counterclockwise;
- in circular or alternating mode at a frequency and amplitude lower than in the mixing mode, such as at 0.5 to 40 Hz and at 300 to 600 mA, during the capture mode;
- at 0 Hz and at an amplitude, such as at 300 to 600 mA, during the immobilization mode; and
- at an, relative to the immobilization mode, increased frequency, such as between 40 Hz-500Hz and at a lowered amplitude, such as at 30-300 mA during the recovery mode.

The reaction chamber of the system or cartridge may comprise a mixture of carrier and capture beads.

The cartridge may further include a recovery container for receiving magnetically labelled cells, preferably magnetically labelled recombinant cells from the reaction chamber.

The cartridge or system may further comprise at least one second inlet and at least one second outlet channel in fluid communication with said reaction chamber, wherein the second inlet channel diverges off the at least one first outlet channel and the second outlet channel diverges off the at least one first inlet channel, wherein the recovery container is in fluid communication with the reaction chamber through the second inlet channel and the second outlet channel is connected to a further venting pore comprising an air filtering element.

The air venting pore of the recovery container may be connected to a pump for recovering the magnetically labelled cells within the reaction chamber by pumping air through the venting pore of the recovery container so that the reaction chamber content is flushed into the recovery container through an inlet channel.

The reaction chamber volume may be between 10 µl and 500 µl.

The cartridge may be self-contained and/or disposable.

The disclosure is also directed at a kit comprising, in one container, a cartridge as described herein, wherein the reaction chamber may comprise capture beads and carrier beads (which may alternatively be contained in a further container), and, in a separate container, instructions of how to use the capture beads and carrier beads in the cartridge.

In another aspect, there is provided a kit comprising, in one container, a cartridge comprising:

a. microfluidic channels,

b. a reaction chamber for mixing magnetic beads in suspension, wherein the reaction chamber has at least one inlet and at least one outlet channel for introducing and removing a fluid into and from said reaction chamber,

c. a cell sample container in fluid communication with the reaction chamber through the inlet channel,

d. at least one washing reagent container in fluid communication with the reaction chamber through the inlet channel,

e. a waste container in fluid communication with the reaction chamber through the outlet channel,

wherein, each container of c-d is further in communication through one of the microfluidic channels to a venting pore comprising an air filtering element;

wherein capture beads in the form of functionalized superparamagnetic beads and carrier beads in the form of ferromagnetic beads are contained in the reaction chamber or are provided in a further container, and, in a separate container, instructions of how to use the capture beads and carrier beads in the cartridge.

The capture beads may be superparamagnetic beads and the carrier beads may be ferromagnetic beads, wherein the ratio of superparamagnetic beads to ferromagnetic beads is between 2:1 and 50:1.

The disclosure is also directed at cells identified and preferably selected via the methods, systems and/or cartridges described herein.

The disclosure is also directed at an isolated population of cells comprising, preferably recombinant cells secreting a transgene expression product, at a level of more than 20, 40, 60, 80 pcd, wherein the isolated population of claims does not contain more 40% of a original cell population from which the isolated cell population was isolated.

12. A cartridge for selecting cells based on their level of display of, and secretion of, a protein from a population of cells comprising the cells displaying, and secreting, said protein, according to the method of any one of the preceding claims comprising:

a. microfluidic channels,

b. a reaction chamber for mixing magnetic beads in suspension, wherein the reaction chamber has at least one inlet and at least one outlet channel for introducing and removing a fluid into and from said reaction chamber,

c. a cell sample container in fluid communication with the reaction chamber through the inlet channel,

d. at least one washing reagent container in fluid communication with the reaction chamber through the inlet channel,

e. a waste container in fluid communication with the reaction chamber through the outlet channel,

wherein, each container of c- d is further in communication through one of the microfluidic channels to a venting pore comprising an air filtering element, and wherein capture beads in the form of functionalized superparamagnetic beads and carrier beads in the form of ferromagnetic beads are contained in the reaction chamber.

13. An integrated system for selecting cells based on their level of display of, and secretion of, a protein from a population of cells comprising the cells displaying, and secreting, said protein, comprising:

a. microfluidic channels,

b. a reaction chamber for mixing magnetic beads in suspension; wherein the reaction chamber has at least a first inlet and at least a second outlet channel for introducing and removing a fluid into and from said reaction chamber,

c. a cell sample container in fluid communication with the reaction chamber through the inlet channel,

d. at least one washing reagent container in fluid communication with the reaction chamber through the inlet channel,

e. a waste container in fluid communication with the reaction chamber through the outlet channel, wherein each container of c-d is further in communication through

one of the microfluidic channels to a venting pore comprising an air filtering element; and wherein the reaction chamber comprises a mixture of carrier beads in the form of ferromagnetic beads and capture beads in the form of functionalized superparamagnetic beads; and comprising

f. one or more devices that create a controllable magnetic field (magnetic field devices= MFDs), arranged around or at the reaction chamber;

g. data processing equipment configured to adjust the magnetic field created by the MFDs within the reaction chamber via frequency and/ or amplitude adjustments, wherein each frequency and/ or amplitude adjustment defines an operation mode within the reaction chamber,

wherein the data processing equipment is configured to set a succession of said operation modes comprising a mixing mode, a capture mode, an immobilization mode, a bead separation mode and a recovery mode, wherein

the data processing equipment is adapted to set the MFDs to operate:

- in a circular or alternating mode at 1-1000 Hz, and at 0.1 to 10,000 mA, during the mixing and bead separation mode;
- in circular or alternating mode at a frequency and amplitude lower than in the mixing mode, such as at 0.5 to 40 Hz and at 300 to 600 mA, during the capture mode;
- at 0 Hz and at an amplitude ,such as at 300 to 600 mA, during the immobilization mode; and
- at an, relative to the immobilization mode, increased frequency, such as between 40 Hz- 500Hz and at a lowered amplitude, such as at 30-300 mA during the recovery mode.

14. The system of claim 13, wherein the one or more devices that create a controllable magnetic field is one or more electromagnets.

15. The system of claim 13, wherein the circular or alternating mode is set at 40 Hz-500Hz and at 200mA-500 mA during the mixing and bead separation mode.

16. A kit comprising, in one container, a cartridge comprising:

    a. microfluidic channels,

    b. a reaction chamber for mixing magnetic beads in suspension, wherein the reaction chamber has at least one inlet and at least one outlet channel for introducing and removing a fluid into and from said reaction chamber,

    c. a cell sample container in fluid communication with the reaction chamber through the inlet channel,

    d. at least one washing reagent container in fluid communication with the reaction chamber through the inlet channel,

    e. a waste container in fluid communication with the reaction chamber through the outlet channel,

    wherein, each container of c-d is further in communication through one of the microfluidic channels to a venting pore comprising an air filtering element;

    wherein capture beads in the form of functionalized superparamagnetic beads and carrier beads in the form of ferromagnetic beads are contained in the reaction chamber or are provided in a further container, and, in a separate container, instructions of how to use the capture beads and carrier beads in the cartridge.

17. The kit of claim 16, wherein the ratio of superparamagnetic beads to ferromagnetic beads is between 2:1 and 50:1.