hydrodynamic separation device has a single inlet for taking in the liquid medium and at least two outlets for discharging the liquid medium separated, wherein the cell-rich fraction is discharged from one of the at least two outlets, and the cell-poor fraction is discharged from the other outlet. The cell culture system may be configured to further comprise: an urging device that urges the liquid medium with a flow pressure for supplying the liquid medium to the hydrodynamic separation device; and a pressure control mechanism that controls pressure environment so that the pressure difference between the liquid medium introduced to the hydrodynamic separation device and the liquid medium derived from the hydrodynamic separation device is equal to or less than a predetermined value.

[0020]

Moreover, according to an aspect of the present disclosure, a subject of a cell culture method is to comprise: a cell culture for culturing cells in a liquid medium; a hydrodynamic separation to separate the liquid medium supplied from the cell culture into a cell-rich fraction having a relatively high cell density and a cell-poor fraction having a relatively low cell density, using a vortex flow generated by flow through a curved flow channel having a rectangular cross-section; and a filtration separation in which the cells are removed from the cell-poor fraction separated by the hydrodynamic separation with a filter, and the liquid medium is recovered.

[0021]

Moreover, according to another aspect of the present disclosure, a subject of the cell culture method is to comprise: a cell culture for culturing cells in a liquid medium; a hydrodynamic separation to separate the liquid medium supplied from the cell culture into a cell-rich fraction having a relatively high cell density and a cell-poor fraction having a relatively low cell density, using a vortex flow generated by flow through a curved flow channel

having a rectangular cross-section; a medium return in which the cell-poor faction is supplied to the cell culture to reduce the cell density of the liquid medium in the cell culture; and a filtration separation in which cells are removed from the liquid medium supplied from the cell culture with a filter and the liquid medium is recovered.

Advantageous Effects of Invention

[0022]

According to the present disclosure, a cell culture system and a cell culture method capable of efficiently separating and removing cells from a liquid medium containing cultured cell to recover the liquid medium and efficiently performing cell culture by taking advantage of continuous culture are provided. Then it is possible to obtain efficiently the useful substances produced by cells.

Brief Description of Drawings

[0023]

[FIG. 1] FIG. 1 is a schematic configuration diagram showing the first embodiment of a cell culture system.
[FIG. 2] FIG. 2 is a schematic configuration diagram showing the second embodiment of the cell culture system.
[FIG. 3] FIG. 3 is a schematic configuration diagram showing the third embodiment of the cell culture system.
[FIG. 4] FIG. 4 is a schematic configuration diagram showing the fourth embodiment of the cell culture system.
[FIG. 5] FIG. 5 is a graph showing the relationship between the Dean number and the separation efficiency in cell separation by a hydrodynamic separation device.
[FIG. 6] FIG. 6 is a graph showing the relationship between pumps used in cell separation and cell viability.

Description of Embodiments

[0024]

Description for embodiments of the present disclosure

new liquid medium C0 supplied to the culture step.

[0054]

When the concentration of the useful substance in the liquid medium recovered from the filtration separation step is low, it may be discarded or supplied to the culture tank 2 for reuse in consideration of its glucose concentration and the like. For example, if the supply flow rate of the new liquid medium required for the culture tank is low and the amount of liquid medium in the culture tank cannot be kept constant by continuous processing while maintaining the rated flow rate in the hydrodynamic separation step, the supply to the hydrodynamic separation step may be performed intermittently. As a result, the amount of liquid medium in the culture tank can be maintained while maintaining the rated flow rate in the hydrodynamic separation step and performing suitable separation. When intermittent hydrodynamic separation is performed, increasing the frequency of switching the supply to the hydrodynamic separation step and performing fine intermittent operation are effective in suppressing the concentration fluctuation in the liquid medium of the culture tank.

[0055]

When the liquid medium in the cell culture step reaches a predetermined cell density, an excess amount of cells are discharged as bleeds based on the prediction of an increase in cell density due to proliferation. At the same time, the supply amount of the new liquid medium is adjusted to maintain the liquid amount and cell density of the liquid medium in the culture tank at predetermined amounts.

[0056]

The cell density may be measured by sampling the liquid medium or directly measured with a detector of a cell measuring apparatus. In the cell culture system 1, the liquid medium supplied to the filtration separation step is a cell-poor fraction obtained by hydrodynamic

CLAIMS

[Claim 1] A cell culture system, comprising:

a culture tank that contains a liquid medium containing cells to be cultured;

a hydrodynamic separation device having a curved flow channel having a rectangular cross-section, and separating the liquid medium supplied from the culture tank into a cell-rich fraction having a relatively high cell density and a cell-poor fraction having a relatively low cell density, using a vortex flow generated by flow through the curved flow channel; and

a filtration separator having a filter to remove cells from the cell-poor fraction separated by the hydrodynamic separation device and recover the liquid medium.

[Claim 2] The cell culture system according to claim 1, further comprising:

a first return path connecting the hydrodynamic separation device and the culture tank to supply the cell-rich fraction to the culture tank; and

a second return path connecting the hydrodynamic separation device and the culture tank to supply the cells removed from the cell-poor fraction to the culture tank.

[Claim 3] The cell culture system according to claim 2, further comprising:

a discharge path to discharge a part of the liquid medium containing the cells to the outside as a bleed.

[Claim 4] The cell culture system according to claim 3, wherein the discharge path is provided as a branch from the first return path, to discard a part or the entire of the cell-rich fraction.

[Claim 5] The cell culture system according to claim 2, wherein the filter of the filtration separator is a depth filter, and further comprising:

a discharge path to discard the cell-rich fraction to the outside as a bleed.

[Claim 6] The cell culture system according to claim 5, further comprising:

a medium replenishment path for supplying a new liquid medium to the culture tank; and

an additional filtration separator having a filter for removing the cells from the liquid medium supplied from the culture tank and collecting the liquid medium.

[Claim 7] A cell culture system, comprising:

a culture tank that contains a liquid medium containing cells to be cultured;

a hydrodynamic separation device having a curved flow channel having a rectangular cross-section, and separating the liquid medium supplied from the culture tank into a cell-rich fraction having a relatively high cell density and a cell-poor fraction having a relatively low cell density, using a vortex flow generated by flow through the curved flow channel;

a medium return path that connects the hydrodynamic separation device and the culture tank and supplies the cell-poor fraction to the culture tank to reduce the cell density of the liquid medium in the culture tank; and

a filtration separator having a filter to remove the cells from the liquid medium supplied from the culture tank and recover the liquid medium.

[Claim 8] The cell culture system according to claim 7, further comprising:

a return path that connects the filtration separator and the culture tank and supplies a residual liquid medium

containing the cells removed by the filtration separator, to the culture tank.

[Claim 9] The cell culture system according to any one of claims 1 to 8, wherein the hydrodynamic separation device has a single inlet for taking in the liquid medium and at least two outlets for discharging the liquid medium separated, wherein the cell-rich fraction is discharged from one of the at least two outlets, and the cell-poor fraction is discharged from the other outlet.

[Claim 10] The cell culture system according to any one of claim 1 to 9, further comprising:

an urging device that urges the liquid medium with a flow pressure for supplying the liquid medium to the hydrodynamic separation device; and

a pressure control mechanism that controls pressure environment so that the pressure difference between the liquid medium introduced to the hydrodynamic separation device and the liquid medium derived from the hydrodynamic separation device is equal to or less than a predetermined value.

[Claim 11] A cell culture method, comprising:

a cell culture for culturing cells in a liquid medium;

a hydrodynamic separation to separate the liquid medium supplied from the cell culture into a cell-rich fraction having a relatively high cell density and a cell-poor fraction having a relatively low cell density, using a vortex flow generated by flow through a curved flow channel having a rectangular cross-section; and

a filtration separation in which the cells are removed from the cell-poor fraction separated by the hydrodynamic separation with a filter, and the liquid medium is recovered.

[Claim 12] A cell culture method, comprising:

a cell culture for culturing cells in a liquid medium;

a hydrodynamic separation to separate the liquid medium supplied from the cell culture into a cell-rich fraction having a relatively high cell density and a cell-poor fraction having a relatively low cell density, using a vortex flow generated by flow through a curved flow channel having a rectangular cross-section;

a medium return in which the cell-poor faction is supplied to the cell culture to reduce the cell density of the liquid medium in the cell culture; and

a filtration separation in which cells are removed from the liquid medium supplied from the cell culture with a filter and the liquid medium is recovered.