

AIR-LIFT BIOREACTOR

1. FIELD OF THE INVENTION

[0001] The present invention relates to a bioreactor, particularly to an air-lift bioreactor.

5 2. DESCRIPTION OF THE PRIOR ART

[0002] In general, bioreactors are used to cultivate micro-organisms, plant cells and animal cells. Aeration stirred-type bioreactors may be applied to the fermentation of micro-organisms and the culture of plant cells. While an air-lift bioreactor is used to cultivate micro-organisms, it is
10 called the air-lift fermenter. In the air-lift fermenter, the aeration rate thereof is generally 1vvm (air volume/culture volume/min). As the cultivation of animal cells needs a smaller aeration rate, the aeration rate thereof is usually as low as 0.05vvm. In such a low aeration rate, the flowrates of air and liquid are too low to generate a stable circulation
15 system. Thus, the mass transfer rates of oxygen and nutrient are too low to achieve a better cultivation efficiency. Therefore, animal cells are normally cultivated in agitation type bioreactors.

[0003] An air-lift bioreactor may be divided into four sections: the riser, the downcomer, the base and the gas separator. While an air-lift
20 bioreactor is used in suspension cell culture, it may achieve a scale of 20000 liters. While an air-lift bioreactor is used in micro-organism culture, it can even achieve a scale of 1500000 liters. However, it is unsuitable to cultivate more viscous medium in air-lift bioreactors when

considering the higher energy dissipation rate and lower circulation rate thereof. In the animal cell cultivation process, the air flow rate is too low to drive more viscous culture medium and to generate a suitable recirculation environment. The higher the flow rate of the liquid in the downcomer is, the more the gas bubbles carried by the liquid and the more the air holdup form in the downcomer and riser.

[0004] A China patent CN 202297606U discloses a bioreactor suitable for self-suspension culture of animal cells or suspension culture of micro-carriers, wherein agitation, aeration and filtration are integrated to reduce the shear-induced damage of the cultured animal cells which is caused by the impeller and the deep aeration process of the stirred-type bioreactor. A Taiwan patent M531483 discloses a biological reaction system, which can enhance the circulation efficiency of the culture liquid medium, and which has an arc-shaped inner bottom surface, a manifold disposed outside the column, and an aeration device connected with the column, whereby to achieve air-lift circulation and enhance the growth efficiency of the cultured objects.

SUMMARY OF THE INVENTION

[0005] In order to solve the abovementioned problems, the present invention provides an air-lift bioreactor suitable for low-aeration rate recirculation systems, wherein an air sparger and a flow amplifier are used to form the dynamic force for driving gas bubbles and culture medium, whereby to perform the circulation efficiency of air-lift bioreactors.

[0006] In order to solve the abovementioned problems, the present invention provides an air-lift bioreactor including a flow amplifier to accelerate the flow of the culture medium such that the inner draft tube which is used to partition the circulation flows of the culture medium may
5 be omitted, so as to make the air-lift bioreactor use flexibly and scale up easily, wherefore the efficiency of cultivating animal cells is enhanced.

[0007] An air-lift bioreactor is provided herein, which includes a vessel having a first space allowing a culture medium to flow therein; a flow amplifier disposed inside the first space of the vessel and including an
10 annular body, a fluid inlet disposed on the annular body, and a gap, wherein a portion of the culture medium enter the annular body from the fluid inlet and flow to the first space through the gap; and a sparger disposed inside the first space of the vessel and generating a plurality of gas bubbles in the culture medium, wherein the flow direction of the gas
15 bubbles is different from the flow direction of the portion of the culture medium flowing into the first space through the gap.

[0008] In one embodiment, a first end of the vessel is opposite to a second end of the vessel, the flow amplifier is disposed in the vicinity of the first end, and the sparger is disposed in the vicinity of the second end.

[0009] In one embodiment, the air-lift bioreactor further includes an inner draft tube disposed inside the first space of the vessel, wherein the culture medium flow through a second space provided by the inner draft tube, the annular body of the flow amplifier is disposed between the inner draft tube and the vessel, and the sparger is disposed inside the second space of the
20

inner draft tube.

[0010] In one embodiment, the air-lift bioreactor further includes an inner draft tube disposed inside the first space of the vessel, wherein the culture medium flow through a second space provided by the inner draft tube, the
5 annular body of the flow amplifier is disposed inside the inner draft tube, and the sparger is disposed between the inner draft tube and the vessel.

[0011] In one embodiment, the annular body of the flow amplifier is closer to a sidewall of the vessel than the sparger.

[0012] In one embodiment, the sparger is closer to a sidewall of the vessel
10 than the annular body of the flow amplifier.

[0013] In one embodiment, the sparger includes a plurality of annular tubes, a plurality of interconnection channels interconnecting with an air inlet, the plurality of the interconnection channels interconnects the plurality of the annular tubes, and a plurality of bubble via-holes is formed
15 on the annular tubes.

[0014] In one embodiment, the annular tubes are arranged concentrically.

[0015] In one embodiment, the sparger is made of metallic material or plastic material.

[0016] In one embodiment, the flow amplifier is used to accelerate the
20 portion of culture medium flowing therethrough.

BRIEF DESCRIPTION OF THE DRAWINGS

[0017] Fig. 1 is a perspective view schematically showing an assembled air-lift bioreactor according to a first embodiment of the present invention.

[0018] Fig. 2 is an exploded view schematically showing the air-lift
5 bioreactor according to the first embodiment of the present invention.

[0019] Fig. 3 is a perspective top view schematically showing a sparger according to the first embodiment of the present invention.

[0020] Fig. 4 is a perspective side view schematically showing a sparger according to the first embodiment of the present invention.

10 [0021] Fig. 5 is a perspective top view schematically showing a flow amplifier according to the first embodiment of the present invention.

[0022] Fig. 6 is a perspective side view schematically showing a flow amplifier according to the first embodiment of the present invention.

[0023] Fig. 7 is a partial cross-sectional view schematically showing a
15 flow amplifier according to the first embodiment of the present invention.

[0024] Fig. 8 is a perspective view schematically showing an assembled air-lift bioreactor according to a second embodiment of the present invention.

[0025] Fig. 9 is a perspective view schematically showing an assembled
20 air-lift bioreactor according to a third embodiment of the present invention.

[0026] Fig. 10 is a perspective view schematically showing an assembled

air-lift bioreactor according to a fourth embodiment of the present invention.

DESCRIPTION OF THE PREFERRED EMBODIMENT

5 **[0027]** Fig. 1 is a perspective view schematically showing an assembled air-lift bioreactor according to a first embodiment of the present invention. Fig. 2 is an exploded view schematically showing the air-lift bioreactor according to the first embodiment of the present invention. Referring to Fig. 1 and Fig. 2, the air-lift bioreactor 1 of the present invention includes
10 a vessel 10, an inner draft tube 20, a sparger 30, and a flow amplifier 40. The vessel 10 provides a first space 11 to accommodate the inner draft tube 20, the sparger 30 and the flow amplifier 40, and the medium for cultivating cells flows inside the vessel 10. The liquid level 19 of the medium is higher than the flow amplifier 40. In the first embodiment, the
15 inner draft tube 20 provides a second space 21 where the culture medium may pass. The vessel 10 encircles the inner draft tube 20 like a sleeve and a portion of the first space 11 may be kept between the sidewall of the vessel 10 and the sidewall of the inner draft tube 20, and the first space 11 interconnects with the second space 21. An open first end 22 of the inner
20 draft tube 20 is in the vicinity of a first end 12 of the vessel 10. An open second end 24 of the inner draft tube 20 neighbors a second end 14 of the vessel 10. The flow amplifier 40 is disposed on the inner draft tube 20 and in the vicinity of the open first end 22 of the inner draft tube 20. The sparger 30 is disposed between the vessel 10 and the inner draft tube 20

and in the vicinity of the open second end 24 of the inner draft tube 20. The first ends are opposite to the second ends. The vessel 10 may be equipped with one or more interconnection channels (not shown in drawings) to connect with external tubes and external devices (not shown in the drawings). A cover (not shown in the drawings) may be disposed on the first end 12 of the vessel 10 or designed to have any channels connected with external tubes and external devices. Thereby, the culture medium may flow back to the air-lift bioreactor 1 through the external tubes and external devices which are connected with the vessel 10. In order to explain conveniently, the first ends are called the tops of the air-lift bioreactor 1, and the second ends are called the bottoms of the air-lift bioreactor 1, thereafter. In order to describe the characteristics of the present invention clearly, the channels through which the vessel 10 is connected with the exterior are simplified or omitted in the drawings. However, the present invention is not limited by the drawings.

[0028] Fig. 3 is a perspective top view schematically showing a sparger according to the first embodiment of the present invention. Fig. 4 is a perspective side view schematically showing a sparger according to the first embodiment of the present invention. Referring to Figs. 1-4, by increasing the area of the air flow and reducing the size of the gas bubbles, the sparger 30 may enhance air/oxygen transfer and contribute the driving force to recirculation of the air-lift bioreactor 1. The sparger 30 may include a plurality of hollow tubes 32 arranged concentrically. One or more interconnection channels 34 may be disposed between the tubes 32 to

interconnect the tubes 32 and stabilize the structure of the sparger 30. An air inlet 36 is disposed in one of the tubes 32 and used to connect with an external air pumping device (not shown in the drawings) and fill air from the air pumping device into the interconnected tubes 32. The filled air enters each tube 32 through the interconnection channels 34. In one embodiment, the wall of each tube 32 has a plurality of bubble via-holes 38. The air inside the tube 32 is dissipated through the bubble via-holes 38 into the culture medium between the vessel 10 and the inner draft tube 20 to generate upward flows. The tubes 32 may be made of metallic material, plastic material or appropriate material. The present invention does not limit the number of the concentric annular tubes 32. The more the number of the concentric annular tubes 32 is, the larger the area available for the bubble via-holes 38 is. The bubble via-holes 38 may be distributed on the tubes in a regular mode or an irregular mode. For example, in the regular mode, the bubble via-holes 38 may be distributed along the circumference of the tube 32 equidistantly; in the irregular mode, the bubble via-holes 38 may be distributed in different positions of the tube 32, and the densities of the bubble via-holes 38 are different in different tubes 32. Besides, the sizes of the bubble via-holes 38 may be identical or different. The smaller bubble via-holes 38 may generate smaller gas bubbles.

[0029] Fig. 5 is a perspective top view schematically showing a flow amplifier according to the first embodiment of the present invention. Fig. 6 is a perspective side view schematically showing a flow amplifier according to the first embodiment of the present invention. Fig. 7 is a

sectional view schematically showing a flow amplifier according to the first embodiment of the present invention. Referring to Fig. 1, Fig. 2, and Figs. 5-7, the flow amplifier 40 includes a hollow annular body 42 and a fluid inlet 46 interconnecting with a space 45 encircled by the annular body 42. The height h of the space 45 may be adjusted according to requirement. The inner sidewall 44 of the annular body 42 has a gap 47 interconnecting with the space 45 encircled by the annular body 42. Furthermore, the inner sidewall 44 of the annular body 42 may be tilt and protruding towards the second space 21 of the inner draft tube 20 to form a path longer than the outer sidewall of the annular body 42 when medium passes through the space 45, so as to form negative pressure area that may drive the medium on the top of the flow amplifier 40 to flow downward. As shown in Fig.7, such a configuration of the annual body 42 may form thicker area neighboring the gap 47 than the one neighboring the closed end of the annual body 42 for the space 45. Next, the fluid inlet 46 allows the culture medium which flows back from the external tube(not shown in figures) to enter the flow amplifier 40. Through the arrangement of the space 45 encircled by the annular body 45 and the gap 47, the flow amplifier 40 pressurizes the culture medium therethrough with pushing force to form a negative pressure area. The negative pressure area accelerates intermediate flow 15 in the vicinity of the first end 12 and outside the inner draft tube 20 to flow into the space 21 of the inner draft tube 20. Besides, the pushing force from the flow amplifier 40 accelerates the culture medium inside the space 21 of the inner draft tube

20 to generate a higher-speed downward flow 17 to reach the bottoms of the inner draft tube 20 and the vessel 10 (the second end 14), which favors the recirculation of the culture medium. The design of the flow amplifier enables the present invention to achieve the effect of accelerating
5 higher-viscosity culture medium.

[0030] Fig. 8 is a perspective view schematically showing an assembled air-lift bioreactor according to a second embodiment of the present invention. Referring to Fig. 1, Fig. 2 and Fig. 8, in comparison with the first embodiment shown in Fig. 1, the sparger 30 of the air-lift bioreactor 3
10 of the second embodiment is disposed inside the inner draft tube 20 and in the vicinity of the open second end 24 of the inner draft tube 20; the flow amplifier 40 is disposed between the vessel 10 and the inner draft tube 20 and in the vicinity of the open first end 22 of the inner draft tube 20 and the first end 12 of the vessel 10; and the other components of the second
15 embodiment are similar to those of the first embodiment and will not repeat herein. Thus, in the air-lift bioreactor 3, the upward flow 13 is inside the inner draft tube 10; the intermediate flow 15 flows from the inside of the inner draft tube 20 to the outside of the inner draft tube 20; and the downward flow 17 is between the vessel 10 and the inner draft tube
20 20.

[0031] According to the above description, the air-lift bioreactor of the present invention is provided with the sparger and the flow amplifier to establish a superior, stable and free of blind spots circulation system. The culture medium is circulated in a stable and uniform flowrate in all the

regions of the inner draft tube and the vessel. The sparger may increase the area of air flow and decrease the size of gas bubbles to enhance the air/oxygen transfer in the air-lift bioreactor and contribute recirculation driving force to the air-lift bioreactor. The flow amplifier makes use of the difference of fluid flows to form negative pressure area to increase the flow rate of the fluid.

[0032] Fig. 9 is a perspective view schematically showing an assembled air-lift bioreactor according to a third embodiment of the present invention. Refer to Fig. 1, Fig. 2, Fig. 5, Fig. 7, Fig. 8, and Fig. 9. In comparison with the first embodiment and the second embodiment, the air-lift bioreactor 2 of the third embodiment is free of the inner draft tube, and the height h of the annular body of the flow amplifier 50 is larger in the third embodiment. The relative sizes of the sparger 30 and the flow amplifier 50 may be specially designed to distinguish the regions where the upward flow 13 and the downward flow 17 are distributed inside the vessel 10. Viewed from the top, that the projection area of the sparger 30 is larger than that of the flow amplifier 50 may make the upward flow 13 closer to the sidewall of the vessel 10 than the downward flow 17. In other words, the upward flow 13 of the culture medium surrounds the downward flow 17 in the first space 11 of the vessel 10; the intermediate flow 15 in the vicinity of the top (the first end 12) runs from the sidewall of the vessel to the center of the vessel; and the intermediate flow 15 in the vicinity of the bottom (the second end 14) flows from the center of the vessel to the sidewall of the vessel, whereby the culture medium circulates in the first

space 11 of the vessel 10 without blind spots. On the other hand, increasing the height h of the annular body of the flow amplifier 50 not only enables the space 45 of the flow amplifier 50 to accelerate the downward flow 17 but also forms a boundary between the downward flow 17 and the upward flow 13 to avoid the mixture of the flows. Therefore, the flow amplifier 50 can replace the inner draft tube of the ordinary air-lift bioreactors and simplify the structure of air-lift bioreactors. Further, omitting the inner draft tube can make the air-lift bioreactor use flexibly and scale up easily. Therefore, the simplified structure of the air-lift bioreactor is more suitable for animal cell culture and other suspension cell cultures.

[0033] Fig. 10 is a perspective view schematically showing an assembled air-lift bioreactor according to a fourth embodiment of the present invention. Refer to Fig. 1, Fig. 2, Fig. 5, Fig. 7, Fig. 8, Fig. 9, and Fig. 10. In comparison with the third embodiment, the air-lift bioreactor 4 of the fourth embodiment is also free of the inner draft tube. Viewed from the top, the projection area of the sparger 30 is smaller than that of the flow amplifier 50. The upward flow 13 is closer to the center of the vessel 10. In other words, the downward flow 17 of the culture medium surrounds the upward flow 13 in the first space 11 of the vessel 10; the intermediate flow 15 near the top runs from the center of the vessel to the sidewall of the vessel; and the intermediate flow 15 near the bottom runs from the sidewall of the vessel to the center of the vessel, whereby the culture medium circulates in the first space 11 of the vessel 10 without

blind spots. It is noted that the air-lift bioreactor 4 may include the flow amplifier of the first and second embodiments whose annular bodies have different height h . In the embodiments without inner draft tube, the position of the flow amplifier disposed in the vessel may be adjusted
5 according to the liquid level of the culture medium as long as the liquid level of the culture medium is higher than the flow amplifier. It is understood that the air-lift bioreactor of the present invention is not limited to use the abovementioned sparger but may match with the conventional bubble distribution component/device. In the embodiments
10 without inner draft tube, the amount of culture medium may be not limited by the height of an ordinary inner draft tube, whereby the flexibility of designing culture environments is increased.

[0034] The embodiments described are only to demonstrate the technical thoughts and characteristics of the present invention to enable the persons
15 skilled in the art to understand, make, and use the present invention. However, these embodiments are not intended to limit the scope of the present invention. Any equivalent modification or variation according to the spirit of the present invention is to be also included by the scope of the present invention.

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CLAIMS

What is claimed is:

1. An air-lift bioreactor comprising:

a vessel having a first space allowing a culture medium to flow
5 therein;

a flow amplifier disposed inside the first space of the vessel and
including an annular body, a fluid inlet disposed on the annular body
and a gap, wherein a portion of the culture medium enters the annular
body through the fluid inlet and flows through the gap to the first
10 space; and

a sparger disposed inside the first space of the vessel and
generating a plurality of gas bubbles in the culture medium, wherein a
flow direction of the gas bubbles is different from a flowing direction
of the portion of the culture medium that flows through the gap into the
15 first space.

2. The air-lift bioreactor according to claim 1, wherein a first end of the
vessel is opposite to a second end of the vessel, the flow amplifier is
disposed in the vicinity of the first end, and the sparger is disposed in
the vicinity of the second end.

3. The air-lift bioreactor according to claim 2, further comprising an
20 inner draft tube disposed inside the first space of the vessel, wherein
the culture medium flows through a second space provided by the inner
draft tube, the annular body of the flow amplifier is disposed between
the inner draft tube and the vessel, and the sparger is disposed inside

the second space of the inner draft tube.

4. The air-lift bioreactor according to claim 2, further comprising an inner draft tube disposed inside the first space of the vessel, wherein the culture medium flow through a second space provided by the inner
5 draft tube, the annular body of the flow amplifier is disposed inside the inner draft tube, and the sparger is disposed between the inner draft tube and the vessel.

5. The air-lift bioreactor according to claim 2, wherein the annular body of the flow amplifier is closer to a sidewall of the vessel than the
10 sparger.

6. The air-lift bioreactor according to claim 2, wherein the sparger is closer to a sidewall of the vessel than the annular body of the flow amplifier.

7. The air-lift bioreactor according to claim 1, claim 2, claim 3, claim 4,
15 claim 5 or claim 6, wherein the sparger includes a plurality of annular tubes, a plurality of interconnection channels, and an air inlet interconnecting with the interconnection channels and the annular bodies; the plurality of interconnection channels interconnects the annular tubes; and a plurality bubble via-holes is formed on the
20 plurality of annular tubes.

8. The air-lift bioreactor according to claim 7, wherein the plurality of annular bodies is disposed concentrically.

9. The air-lift bioreactor according to claim 7, wherein the sparger is made of a metallic material or a plastic material.

10. The air-lift bioreactor according to claim 1, claim 2, claim 3, claim 4, claim 5 or claim 6, wherein the flow amplifier is used to accelerate the culture medium flowing through the flow amplifier.