

Claims

1. A bioreactor or fermenter (100) for the culturing of cells or microorganisms in suspension in a liquid medium in industrial scale comprising
5 a vessel (102) containing the culture in a liquid medium having a determined filling height;
a stirrer (120) provided in the vessel to stir the liquid medium;
a first sparger (150) arranged in the bottom portion (105) of the vessel (102) provided
10 to supply gas bubbles (10, 10.1, 10.2, 10.3) continuously to the liquid medium, the gas being selected from air and/or oxygen gas; and
a second sparger (160) arranged in the vessel (102) and provided above the first sparger (150) to supply additional air bubbles and/or additional oxygen gas bubbles (20, 20.1, 20.2, 20.3) continuously to the liquid medium,
15 whereby
the second sparger (160) is located at a position in the bioreactor or fermenter (100) above the first sparger (150) in a distance η whereby η is selected to be in the range from at least about 0.4 m above the first sparger (150) to at most about 0.5 m below the filling height of the bioreactor or fermenter (100) or
20 about 0.4 m above the first sparger to about 2/3 of the filling height of the bioreactor or fermenter (100) or
about 0.4 m above the first sparger to about 1/2 of the filling height of the bioreactor or fermenter (100) or
about 0.4 m to about 3.0 m above the first sparger or about 0.4 m to about 2.5 m
25 above the first sparger or about 0.4 m to about 2.0 m above the first sparger or about 0.4 m to about 1.5 m above the first sparger or
about 0.4 to about 1.0 m above the first sparger or about 0.45 to about 0.90 m above the first sparger or about 0.5 to about 0.80 m above the first sparger or about 0.55 to about 0.70 m above the first sparger or at about 0.6 m above the first sparger.
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2. The bioreactor or fermenter (100) according to claim 1, characterized in that
the bioreactor or fermenter (100) comprises a filling height in the range from about 8 to about 20 m or about 9 to about 15 m or about 9,5 to about 12 m or about 10 m.

3. The bioreactor or fermenter (100) according to claim 1 or 2,
characterized in that
the second sparger (160) is a side-sparger.

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4. The bioreactor or fermenter (100) according to any of the preceding claims 1
to 3,
characterized in that
a third sparger (170) and optional (a) further sparger(s) are provided in the bioreactor
10 or fermenter (100) above the first sparger (150) and the second sparger (160), the
distance between two consecutive spargers (150, 160) (160, 170), one arranged
above the other, is selected to be η .

5. The bioreactor or fermenter (100) according to any of the preceding claims 1
15 to 4,
characterized in that
the stirrer (120) has a stirrer radius r_s which is located around a central axis A
through the bioreactor or fermenter (100),
whereby the first sparger (150) is arranged at a distance from the central axis A of
20 the bioreactor or fermenter (100) such that the gas bubbles (10, 10.1, 10.2, 10.3)
provided enter the liquid medium at a distance which is equal to or less than the
stirrer radius r_s ;
and/or
whereby the second sparger (160) and optional further spargers are arranged at a
25 distance from the central axis A such that the bubbles (20, 20.1, 20.2, 20.3) provided
enter the liquid phase at a distance which is larger than the stirrer radius r_s .

6. The bioreactor or fermenter (100) according to any of the preceding claims 1
to 5,
30 characterized in that
(an) additional stirrer(s) (R2, R3, R4) is(are) provided in addition to the stirrer (120,
R1), the additional stirrer(s) (R2, R3, R4) being located above and/or below the
second sparger (160).

7. The bioreactor or fermenter (100) according to any of the preceding claims 1 to 6,
characterized in that
the first sparger (150), the second sparger (160) and optional further spargers (170)
5 are static spargers selected from tube type spargers such as open-tube spargers,
sintering plates, perforated slabs, ring spargers, spider type spargers, disc type
spargers, sheet type spargers, cup type spargers, and bushing type spargers.
8. The bioreactor or fermenter (100) according to any of the preceding claims 1
10 to 7,
characterized in that
the first sparger (150) is a central sparger or a side sparger and the second sparger
(160) and the optional third sparger (170) and further spargers are side-spargers.
- 15 9. A process to control and adjust the content of dissolved CO₂ and the content
of dissolved O₂ in a liquid medium in a bioreactor or fermenter (100) for the culturing
of cells or microorganisms in suspension in industrial scale comprising a vessel (102)
containing the culture in a liquid medium;
stirring the liquid medium;
20 continuously supplying gas bubbles (10, 10.1, 10.2, 10.3) from a first sparger (150)
arranged in the bottom portion (105) of the vessel (102) to the liquid medium, the gas
being selected from air and/or oxygen gas;
continuously supplying gas bubbles (20, 20.1, 20.2, 20.3) from a second sparger
(160) arranged in the vessel (102) to the liquid medium, the gas being selected from
25 air and/or oxygen gas, whereby the second sparger (160) being arranged above the
first sparger (150) and the second sparger (160) is a side-sparger;
selecting and adjusting a modified gas flow rate $q_{\text{mod}}(\text{O}_2)$ and selecting and adjusting
a modified gas flow rate $q_{\text{mod}}(\text{CO}_2)$ which are both suitable for the culturing process,
based on the gas flow rate q_{sub} of the submerge or first sparger (150) and the gas
30 flow rate q_{side} of the side or second sparger (160), whereby the following equations
apply:

$$q_{\text{mod}}(\text{O}_2) = q_{\text{sub}} + C_{\text{O}_2} \times q_{\text{side}} \quad [1a]$$

and

$$q_{\text{mod}}(\text{CO}_2) = q_{\text{sub}} + C_{\text{CO}_2} \times q_{\text{side}} \quad [1b]$$

wherein

q_{sub} represents the gas flow rate of the submerge or first sparger (150);

5 q_{side} represents the gas flow rate of the side or second sparger (160);

C_{O_2} represents an influence factor C of the volumetric oxygen mass transfer, whereby $C_{\text{O}_2} = 0.15$; and

C_{CO_2} represents an influence factor C of the volumetric carbon dioxide mass transfer, whereby $C_{\text{CO}_2} = 0.6$.

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10. The process according to claim 9, characterized in that q_{sub} is adjusted to be greater than q_{side} .

15 11. The process according to any of the preceding claims 9 or 10, characterized in that

the position of second sparger (160) in the bioreactor or fermenter (100) is selected to be above the first sparger (150) in a distance η whereby η is selected to be in the range from at least about 0.4 m above the first sparger (150) to at most about 0.5 m

20 below the filling height of the bioreactor or fermenter (100) or

about 0.4 m above the first sparger to about 2/3 of the filling height of the bioreactor or fermenter (100) or

about 0.4 m above the first sparger to about 1/2 of the filling height of the bioreactor or fermenter (100) or

25 about 0.4 m to about 3.0 m above the first sparger or about 0.4 m to about 2.5 m above the first sparger or about 0.4 m to about 2.0 m above the first sparger or about 0.4 m to about 1.5 m above the first sparger or

about 0.4 to about 1.0 m above the first sparger or about 0.45 to about 0.90 m above the first sparger or about 0.5 to about 0.80 m above the first sparger or about 0.55 to

30 about 0.70 m above the first sparger or at about 0.6 m above the first sparger.

12. The process according to any of the preceding claims 9 to 11, characterized in that

a third sparger (170) and optional (a) further sparger(s) are provided in the bioreactor or fermenter (100) above the first sparger (150) and second sparger (160), the distance between two consecutive spargers (150, 160) (160, 170), one arranged above the other, is selected to be η .

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13. The process according to any of the preceding claims 9 to 12, characterized in that

the stirrer (120) has a stirrer radius r_s which is located around a central axis A through the bioreactor or fermenter (100),

10 whereby the first sparger (150) is arranged at a distance from the central axis A of the bioreactor or fermenter (100) such that the gas bubbles (10, 10.1, 10.2, 10.3) provided enter the liquid medium at a distance which is equal to or less than the stirrer radius r_s ;

and/or

15 whereby the second sparger (160) is arranged at a distance from the central axis A such that the bubbles (20, 20.1, 20.1, 20.3) provided enter the liquid phase at a distance which is larger than the stirrer radius r_s .

14. The process according to any of the preceding claims 9 to 13,

20 characterized in that

(an) additional stirrer(s) (R2, R3, R4) is(are) provided in addition to the first stirrer (120, R1), the additional stirrer(s) (R2, R3, R4) being located above and/or below the second sparger (160).

25 15. The process according to any of the preceding claims 9 to 14,

characterized in that

the first sparger (150) is a central sparger or a side sparger and the second sparger (160) and the optional third sparger (170) and optional further spargers are side-spargers.

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16. The process according to any of the preceding claims 9 to 15,

characterized in that

the first sparger (150), the second sparger (160) and the optional further spargers are static spargers selected from spargers with a pipe-geometry, for example tube type

spargers such as open-tube spargers, sintering plates, perforated slabs, ring spargers, spider type spargers, disc type spargers, sheet type spargers, cup type spargers, and bushing type spargers.

- 5 17. A process for the culturing of cells or microorganisms in a bioreactor or fermenter (100) according to any of the preceding claims 1 to 8, wherein a second sparger (160) and optional a third sparger (170) and optional (a) further sparger(s) are provided in the bioreactor or fermenter (100) to promote the growth, viability, productivity and/or any other metabolic condition of the cells or microorganisms to be
10 cultivated.

18. A second sparger (160), optional a third sparger (170) and optional (a) further sparger(s) are provided in a bioreactor or fermenter (100) for the culturing of cells or microorganisms according to any of the preceding claims 1 to 8, wherein the
15 spargers (160, 170) are provided in the bioreactor or fermenter (100) to promote the growth, viability, productivity and/or any other metabolic condition of the cells or microorganisms to be cultivated.