



(12) **EUROPEAN PATENT APPLICATION**

(43) Date of publication:
20.06.2001 Bulletin 2001/25

(51) Int Cl.7: **B03C 5/02**

(21) Application number: **99125151.3**

(22) Date of filing: **16.12.1999**

(84) Designated Contracting States:
**AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE**
Designated Extension States:
AL LT LV MK RO SI

(72) Inventors:
• **Prior, Adalbert Dr.**
6841 Götzis (AT)
• **Byers, Charles Dr.**
Menlo Park, CA 94025 (US)

(71) Applicant: **PRIOR ENGINEERING AG**
8008 Zürich (CH)

(74) Representative: **Büchel, Kurt F., Dr.**
Büchel, Kaminski & Partner,
Letzanaweg 25
9495 Triesen (LI)

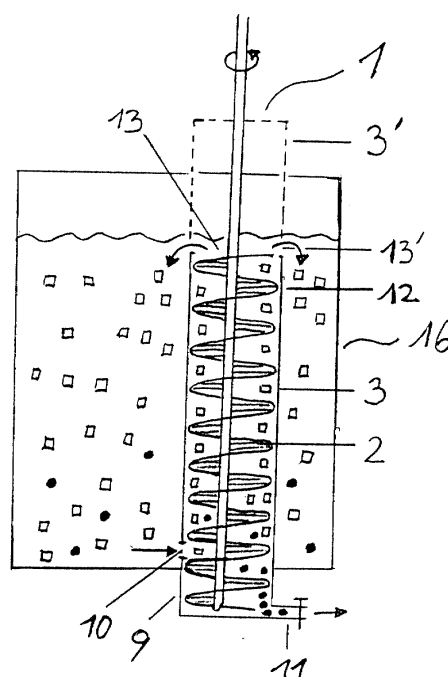
(54) **Device and method for separating particles by dielectrophoresis**

(57) The invention relates to a device (1) for continuous separation of a desired fraction of particulate matter from a liquid suspension containing such particulate matter, the device (1) comprising electrode elements (2, 3) and means for generating an alternating non-uniform dielectric field between said electrode elements, wherein a first electrode (2) has the form of a screw conveyor and is rotatable around its longitudinal axis, and a second electrode (3) is arranged at a distance opposite to

the first electrode and has a form other than the screw conveyor, and preferably has the form of a tubular housing (3) surrounding the screw conveyor electrode (2). The device (1) may be placed inside or outside a container (16) containing a liquid particle suspension.

The invention also relates to applications of said device for preparative purposes in the fields of microbiology, biotechnology and medicine, and particularly for the separation of polarizable biological matter such as plant, animal or human cells.

Fig. 5



Description

[0001] The invention relates to a device and a method for separation of suspended particulate matter from a liquid based on the principle of dielectrophoretic displacement in a non-uniform electric field.

[0002] Dielectrophoresis is a translational migration of a particle caused by polarization effects in a non-uniform electric field. It is well known that non-uniform, preferably alternating, electric fields causing dielectrophoresis can be utilized for characterizing, sorting and separating biological matter such as cells suspended in a fluid. Cells differ in their dielectrophoretic properties according to their biophysical constitution including size, shape or conductivity. Therefore, distinctly different cells like viable and nonviable cells, cancer and normal cells or cells of different kinds may be separated from each other by selectively attracting or repelling one type of cell at a higher extent than the other cells or kinds of cells by specifically adjusting the strength and frequency of the non-uniform electric field as desired.

[0003] US 4,326,934 discloses an arrangement wherein a continuous dielectrophoresis within an isomotive field is employed. A dielectrophoresis conduit is positioned between the electrodes through which the particles are flowed and selectively deflected out of the stream-centered cell suspension flow. The taught apparatus separates different types of cells in an approximately stream-centered mixture comprising two or more cell types.

[0004] US 5,489,506 stipulates a necessity of carrying the cells in deionized solution to achieve sufficient separation. A coaxial stream with cells in a deionized medium surrounded by a sheathing carrier fluid is passed through a separation chamber and the cell stream is spread apart so that the attracted cells are directed toward one end of the chamber while the less attracted cells are distributed at various positions in the outbound stream.

[0005] US 5,888,370 discloses amongst others a separation chamber outside or inside of which one or more electrode elements may be arranged in a geometrical relationship to each other. By specifically energizing these electrodes in a sequential manner particles passing by the electrodes inside the chamber may be attracted by the electrodes thereby slowing down their velocity of migration in the flow direction of the main stream. The velocity profile of the particles travelling through the separation chamber allows to distinguish different particle fractions and thus allows their separation.

[0006] US 5,858,192 suggests the arrangement of a plurality of electrodes in a particular spiral electrode array for the separation chamber disclosed in the aforementioned US 5,888,370.

[0007] WO 98/10869 describes a further concept of particle separation by dielectrophoresis employing travelling wave field migration, wherein negative dielectrophoretic forces are applied, i.e. such as to actively repel

polarizable particles from the electrodes.

[0008] The above discussed prior art systems have in common that their electrodes are arranged and/or operated in sophisticated or even complicated ways to achieve the desired separation effect. None of these systems was described to contain movable parts. The electrodes rest fixed at their determined locations. Moreover, most of these systems are described for and effectively applicable only in a micro scale, e.g. for analytical purposes. Contrary to the prior art, the present invention provides a device and method that is primarily designed and applied for preparative purposes, particularly for the separation of viable from non-viable cells in a lab-scale, semi-industrial or industrial scale tissue cell culture facility. Its simple arrangement and convenient handling is a remarkable improvement over existing systems. Also, whereas in the known prior art systems the electrode elements do not take part in the generation of a liquid suspension flow, the electrode elements according to the present invention may contribute to or may even be the sole source for the generation of the liquid suspension flow.

[0009] An advantage of the instant invention is its flexible operability: When applied to separate different fractions of biological matter, e.g. cells in a cell culture suspension, it may be operated to retain the desired, e.g., viable, biological matter in its regular culture medium while removing non-desired, e.g., non-viable material, from the suspension together with a fraction of the liquid medium, which fraction of liquid medium may thereafter be replenished using fresh medium.

[0010] The present invention relates to a device for continuous separation of a desired fraction of particulate matter from a liquid suspension containing such particulate matter, which device comprises electrode elements and means for generating an alternating non-uniform dielectric field between said electrode elements, and wherein a first electrode has the form of a screw conveyor and is rotatable around its longitudinal axis, and a second electrode is arranged at a distance opposite to the first electrode and has a form other than the screw conveyor.

[0011] The second electrode may be a plane or curved board or a plurality of plane or curved boards, a wall of a pipe-like or tube-like housing or another element that is different in form and shape from the first electrode. In a preferred embodiment the second electrode is provided in the form of a housing that at least partially surrounds the screw conveyor electrode along its longitudinal axis. Partially surrounding means that the housing may be in the form of a curved board that does not entirely circumferentially surround the screw conveyor or that the housing may be fully cylindrical but does not cover the entire length of the screw conveyor.

[0012] The electrodes are preferably mounted such as to be in direct fluid contact with the fluid suspension containing the particulate matter. However, in principle

they can also be mounted in a "dry" manner, e.g., outside a fluid flow channel or else be coated with non conductive material. For instance, the second electrode may itself be the housing surrounding the first electrode or else may be a conductive material arranged along the inner or outer surface of such a housing.

[0013] The pair of electrodes may be placed inside a container containing a fluid suspension of particulate matter or may be placed outside such a container, preferably in a recirculation line ("external loop") of such a container.

[0014] For the purpose of the present invention the first and second electrodes have to be arranged in a manner that polarizable particles exposed to the alternating non-uniform dielectric field may migrate selectively towards or away from the highest field strength at the outermost circumferential edge of the conveyor screw. The distance between the oppositely energized electrodes is adjusted such as to prevent occurrence of a short circuit between the electrodes. It should preferably not exceed 1 mm and in most case ranges from 0.1 to 1 mm.

[0015] It is preferred that the screw conveyor and its corresponding housing may be energized along its entire length or along a section thereof. Also, the screw conveyor may have a hollow shaft for receiving equipment for electrical current supply. It may also be connected with means for thermoregulation and thus may serve, e.g., as a cooling rod, in order to avoid damaging biological material due to field-induced increase in temperature. Where necessary, cooling may also be accomplished using a double-walled housing as the second electrode.

[0016] Where the housing is of a fully cylindrical, pipe-like shape it contains at one end an inlet section having at least one opening for receiving the liquid suspension, and at the opposite end an outlet section having one or more outlet openings.

[0017] Where the screw conveyor and the housing are arranged in a non-horizontal, more or less upright position and the flow of the liquid suspension is directed upwardly, the inlet section may also have at least an outlet opening for continuously or batchwise draining off sedimented particulate matter. The housing may be of uniform width or may comprise at its inlet section an expansion chamber for reducing the flow velocity of the incoming liquid suspension. The expansion chamber may have any suitable form that allows to reduce the flow velocity and to allow for sedimentation of particles that are not attracted or even actively repelled by the dielectric field generated between the screw conveyor and the housing. It thus may have a conical shape with its wider end directed towards the incoming liquid suspension or a cylindrical shape having a larger diameter than the adjacent section of the housing. It is preferred that the screw conveyor electrode is arranged within the housing in a way such as to at least partially extend into the expansion chamber and most preferably to extend

across the entire length of the expansion chamber.

[0018] In case of a cylindrical expansion chamber it is preferred that the expansion chamber is eccentrically connected to the adjacent narrower section of the housing and thus to the screw conveyor and is mounted such as to form a close gap of approximately 0.1 to 1 mm between screw conveyor and closest wall of the expansion chamber while leaving more space between the opposite side of the screw conveyor and the corresponding most distant wall of the expansion chamber.

This arrangement allows to energize just that part of the wall of the expansion chamber that forms the narrow gap with the lower section of the screw conveyor that extends into the expansion chamber. It also allows to only energize that lower section of the screw conveyor and thus to generate a dielectric field exclusively within the narrow gap, while leaving the remaining sections of the screw conveyor and of the housing free from dielectric field generation. As soon as the non-uniform alternating dielectric field has been established and adjusted to the electrophoretic properties of the desired particle fraction of the suspension, the desired particle fraction is preferentially attracted towards the narrow gap and gets concentrated there resulting in a preferential transfer of the attracted particles towards the adjacent narrower and optionally field-free section of the housing, where further transport of the particles enriched in the attracted particle fraction is performed primarily by the rotation of the conveyor screw.

[0019] Whether or not to energize the housing and the screw conveyor along its entire length mainly depends on the desired degree of sharpness of separation and of the ease of separation of the particle fractions due to electrophoretic similarity or distinction, respectively.

[0020] In another embodiment of the present invention the screw conveyor electrode is placed inside a cylindrical housing and screw and housing are mounted in a non-horizontal position, e.g. either in a vertical position or at an angle between vertical and horizontal. The electrodes may then be connected to an alternate voltage source and energized and adjusted in a way such that the non-uniform dielectric field generated between screw conveyor and housing does not attract but instead repel polarizable particles from the edge of the screw conveyor. This particular way of operation, which is not generally reserved to non-horizontally positioned arrangements of screw conveyor and housing, allows to selectively deflect a desired particle fraction from the screw conveyor and thus to enable gravitational sedimentation of that particle fraction, while preferentially conveying non-affected particles or particle fractions along with the rotating screw in the direction of the flow of the main stream of the suspension.

[0021] The repelled, sedimented particles may be drained off at an outlet opening of the housing that is located at a lower level than the outlet opening or openings, if there are more than one, for the main stream of the suspension. It is preferred that the lower outlet is

located at the bottom of the inlet section of the housing, and if there is an expansion chamber, at the bottom of the expansion chamber. The at least one outlet opening for the main stream, which primarily contains the non-affected particles, is preferably located at the top of the opposite end of the housing.

[0022] For some applications it might also be advantageous to reverse the direction of rotation of the screw conveyor or even to reverse the whole arrangement of first and second electrode, i.e., of screw conveyor and housing, such as to convey particles in the direction of gravitation, i.e. in a downward direction. This may be useful, for instance, if the electrode arrangement is placed in a non-horizontal, preferably vertical, position inside a container filled with the particle suspension, e.g., a bioreactor that contains a tissue cell culture, and is operated to enrich the culture in living cells while removing non-living cells from the bioreactor. If the dielectric field is adjusted such as to attract the living cells towards high field strength at the edge of the conveyor screw, the non-affected cells may pass through the housing at a shorter interval than the attracted cells that are retained by the dielectric field, resulting in an increased cell concentration of attracted cells in the close vicinity of the conveyor screw inside the housing. The non-affected particles, e.g., the non-viable cells in this example, may be drained off at the bottom of the housing, together with a fraction of the cell culture nutrient medium, which may be re-supplemented to the bioreactor by external feeding pipes connected to the bioreactor for supplying various fluids, in particular cleaning, nourishing, pH-adjusting or otherwise supplementing or correcting fluids to the cell culture suspension.

[0023] It may also be useful to run the dielectric field intermittently, i.e., to allow the electrode arrangement to be field-free for a defined interval, in order to enable attracted particles accumulated inside the housing to get washed out and reenter the suspension where they have been collected from. It may also be advantageous in some cases to reverse the direction of rotation of the conveyor screw and/or of the field characteristics of the dielectric field, in order to achieve similar goals.

[0024] It is also a part of the present invention to provide for an arrangement of a plurality of energized pairs of electrodes, i.e. of screw conveyors and housings, either connected in series or in parallel, depending on whether the objective is to improve the throughput or the sharpness of separation. They may also be connected in a cascading arrangement to separate three or more particle fractions from a suspension.

[0025] The distance between the first and second electrodes, between the inner surface of the housing and the outer edge of the conveyor screw, should not exceed 1 mm, and preferably should be between 0.1 and 1 mm. Broader gaps would require higher energy and higher field strength for maintaining a permanent non-uniform dielectric field, which would not only cause an undesired increase of temperature in the field zone

but might also directly damage biological material travelling through the field.

[0026] In a particular embodiment, the screw conveyor may at the circumferential outer edge of the screw thread comprise a narrow, preferably 0.1 to 0.9 mm broad, zone that is made of non-conductive material and does not take part in dielectric field generation nor in dielectric field maintenance. Alternatively, the entire screw conveyor may be of non-conductive material. However, it then contains, at a distance of 0.1 to 0.9 mm from the outer circumferential edge of the screw thread, a continuous layer of conductive material, which layer in effect constitutes the first electrode. This particular arrangement can significantly improve the separation efficiency in upright positioned electrode arrangements. Field strength and frequency of the dielectric field together with the rotational speed of the screw conveyor may be adjusted such as to allow particles attracted by the highest field strength at the end of the conductive material of the screw thread to be more efficiently caught and collected by the flanks of the screw thread and conveyed against gravitational forces, while non-attracted matter will more easily sediment in the gap between screw and housing.

[0027] Where the screw conveyor is not the sole source for generating a flow of the suspension through the dielectric field, additional means such as pumps, impellers, and the like will need to be provided.

[0028] While the present invention is generally suitable for the separation of any polarizable particulate matter in a liquid suspension, it is preferred that its main application is in the fields of microbiology, biotechnology and medicine, for the separation of polarizable biological matter. Such biological matter includes viruses or prions, cell components such as chromosomes or biomolecules such as oligonucleotides, nucleic acids, etc., as well as prokaryotic and eukaryotic cells, and preferably comprises plant, animal or human tissue cells. It may be used to separate different kinds of biological material such as cancerous and non-cancerous cells from each other but it may also be applied to remove viable from non-viable cells.

[0029] The present invention further comprises to recirculate back at least a portion of a separated fluid fraction to the inlet opening of the housing containing the screw conveyor, to repeat the separation procedure resulting in a higher degree of separation.

[0030] In order to further illustrate the present invention Figures 1 to 4 are set forth, wherein

- Fig. 1 is a schematic illustration of a screw conveyor or electrode inside a tubular housing;
- Fig. 2a is a schematic illustration of a layered section of the screw thread;
- Fig. 2b is a schematic illustration of a layered section of the screw thread inside a tubular housing;
- Fig. 3 is a schematic view of a screw conveyor

electrode and surrounding housing placed inside a container containing a liquid particle suspension;

Fig. 4 is a schematic view of a screw conveyor electrode and surrounding housing placed in an external recirculation line of a bioreactor; and

Fig. 5 is a schematic view of a screw conveyor electrode inside its surrounding housing specifically arranged inside and outside of a container containing a liquid particle suspension;

[0031] Figure 1 schematically illustrates a preferred arrangement of a pair of electrodes 1 according to the present invention, wherein the screw conveyor electrode 2 is placed inside a tubular housing 3 and which upon rotation of the screw and generation of a non-uniform alternating dielectric field 4 between the outermost edge of the screw thread and the inner surface of the surrounding housing efficiently separates polarizable particle fractions by attracting one fraction 5 (symbolized by open squares) towards the screw while leaving other fractions 6 (symbolized by full circles) unaffected. While the attracted particle fraction 5 is captured by the screw thread and subsequently conveyed in the direction of the screw rotation symbolized by arrows on top of the drawing, the non-attracted particle fraction may prevailingly sediment by gravitation in the gap between screw 2 and housing 3, as indicated by arrows at the bottom of the drawing.

[0032] Fig. 2a is a detail view of a section of the conveyor screw 2 in a particular embodiment, wherein a narrow zone 7 at the outermost circumferential edge of the screw thread is made of non-conductive material and does not take part in the generation and maintenance of the dielectric field, while the adjacent area of the thread consists of a conductive material A and is part of the field generating system and, in effect, constitutes the first electrode.

[0033] In Fig. 2b it is schematically illustrated that in a particular embodiment of the present invention the screw 2 inside the housing 3 is made of non-conductive material while it is layered with a conductive material B leaving a narrow zone 7 at the outermost edge of the screw thread non-conductive. This arrangement improves the efficiency of capture of attracted particles by the flanks of the screw conveyor and hence improves their smooth advancement against gravitational forces.

[0034] Fig. 3 illustrates a closed containment 8 containing a particle suspension comprising two (at least electrophoretically) different particle fractions, symbolized by open squares and full circles. Inside the containment 8 a pair of electrodes in the form of a screw conveyor and a tube-like housing is placed in a vertical position. The housing 3 comprises an inlet section 9 at the bottom end of the housing and an outlet section 12 at the opposite end of the housing 3. The inlet section 9

may be designed as an expansion chamber 14, into which the conveyor screw 2 extends in an eccentric manner. The inlet section 9 comprises at least one inlet opening 10 for receiving the incoming flow of the liquid particle suspension, and at least one outlet opening 11 for draining off a sedimented fraction of the particulate matter of the suspension. It is particularly preferred that the screw conveyor 2 extends to a level below the inlet opening 10 in order to better allow for the polarizable particles to get entrapped by the dielectric field and caught and advanced by the screw thread. Such an arrangement allows to prevailingly elevate the particle fraction attracted by the dielectric field while it facilitates sedimentation of non-attracted particle fractions in the expansion chamber.

[0035] The sections of the screw and the housing adjacent to the expansion chamber 14 may or may not be energized for dielectric field generation, depending on the pre-separation efficiency within the expansion chamber.

[0036] The pitch of the screw may be constant across the entire length of the screw (as indicated in Fig. 5) or may be different with two or more sections of the screw, e.g., smaller at the one end of the screw that extends into the inlet section 9 or expansion chamber 14 of the housing 3, and bigger at the adjacent section of the screw outside the inlet section 9 or expansion chamber 14 of the housing 3. The resulting flat convolution and the increased number of turns of the screw there will be particularly advantageous in arrangements using an expansion chamber as well as in arrangements wherein only the inlet section 9 or a part thereof and the corresponding section of the screw are energized for generating the dielectric field.

[0037] Fig. 4 gives an impression of another embodiment of the present invention, wherein a screw conveyor electrode 2 and a housing 3 are arranged in or as a part of an external loop of a bioreactor system 15. Although in Fig. 4 the electrode arrangement is shown in a vertical position, it is to be understood and shall be embraced by the present invention that the electrode arrangement may also be in a horizontal position or at any angle between horizontal and vertical. If in a horizontal position, the inlet section 9 may not contain an expansion chamber 14 nor an outlet opening 11 but instead may comprise an outlet opening 11' at the outlet section 12, at a lower level than outlet opening 13, e.g. opposite the outlet opening 13, for discharging sedimented material.

[0038] From the bottom of bioreactor 15 the particle suspension is drained off, optionally using a controllable valve and/or pump (not shown in the drawings) and enters the housing 3 at the inlet opening 10. Due to the large diameter of the expansion chamber 14 the flow velocity there is lower than in the input and output lines. The rotating screw, which builds up an alternating non-uniform dielectric field between the screw tips and the closest opposite wall of the housing, attracts primarily

the desired particle fraction (open squares) into the preferably 0.1 to 1 mm narrow gap between the screw tips and the housing (in Fig. 4 located at the bottom left-hand side), and conveys them towards the adjacent narrower section of the housing 3, while non-attracted particles prevailingly sediment already in the expansion chamber 14. The rotational speed of the screw conveyor is preferably adjusted such as to mechanically advance the particles, that got captured by the dielectric field, towards the outlet section 12, while simultaneously keeping the liquid flow slow enough to allow for sedimentation of non-attracted particles, even in the gap between screw tips and housing.

[0039] The present invention also provides for the possibility to reverse the field characteristics of the dielectric field in a way such as to actively repel one particle fraction (e.g. cancerous cells) and thus to add to the gravitational sedimentation of these cells, while allowing others (e.g. non-cancerous cells) to be elevated by the screw.

[0040] The housing 3 at its outlet section 12 may further be connected with external feeding pipes (not illustrated in Fig. 4), e.g., for washing off biological material that possibly adheres to the screw thread, or else for supplementing the bioreactor system 15 with fresh nutrients, pH-adjusting liquids or other needful fluids, and/or just to compensate for the amount of liquid that has been removed along with the non-desired particle fractions via outlet opening 11.

[0041] In Fig. 5 the pair of electrodes is arranged in a vertical position and in a way such that a bottom part of the housing 3 and of the screw conveyor 2 are located outside a container 16 containing the liquid particle suspension, while an adjacent part of the housing 3 and of the screw conveyor 2 are located inside the container 16. This particular arrangement allows to place the inlet opening 10 close to the bottom of container 16 and still provides for a proper capture of the incoming particles by the flanks of the screw and by the dielectric field applied there. In a variation of that embodiment, symbolized by the dashed lines, the upper part 3' of the housing 3 may exit the top of the container. As the housing 3 is not twisted but instead rests fixed in place, this arrangement allows for very simple stabilization and fixation of the housing 3 by corresponding openings in the top and bottom plates of the container, and also allows for safe and non-complicated sealing against those plates, for instance using common gaskets or flanges.

[0042] The outlet section 12 of the housing 3 may end above or below the level of the liquid suspension inside the container 16. It may have just a single outlet opening 13 that extends virtually across the entire diameter of the housing, or it may have one or more smaller outlet openings 13 located on top or at the sidewall of the housing 3 at the outlet section 12. In the variation embodiment, the outlet openings 13' are located at the sidewall of housing 3, at a level above or below the liquid level of the suspension.

[0043] It is generally preferred that in the various embodiments of the present invention the pairs of electrodes, e.g., screw conveyor and housing, are made of a material and/or are constructionally adapted to allow - optionally in situ - sterilization of the electrode device, preferably along with the containment with which it is connected, by hot steam or chemical disinfectants.

[0044] The potential of the present invention may additionally be illustrated by the following example.

Example 1:

[0045] In a C 174 myeloma cell suspension with a cell density of 1×10^6 cells/ml viable and nonviable cells can be separated (along with part of the medium) using a screw conveyor and a surrounding tubular housing as the first and second electrodes according to the present invention, wherein a gap of 300 microns between the outer wall electrode along the inner surface of the housing and the screw conveyor tip electrode is established. An alternating current potential of 30 Volts peak-to-peak (with a maximum field strength of 10^5 V/m) is applied over a frequency range of 5-15 MHz. At the optimal frequency - in this example - of 10 MHz, 98% separation efficiency is achieved in the viable cells, while about 85% of the nonviable cells are removed with the partially spent medium. The conductivities of the media in this example is in the 12,000 to 14,000 $\mu\text{S/cm}$ range.

[0046] It is further understood that the present invention is not limited to the embodiments explicitly disclosed herein but also includes variations therefrom that will be recognized by a person of ordinary skill in the art without inventive contribution or undue experimentation.

Claims

1. A device for continuous separation of a desired fraction of particulate matter from a liquid suspension containing such particulate matter, the device (1) comprising electrode elements (2, 3) and means for generating an alternating non-uniform dielectric field between said electrode elements, wherein

- a first electrode (2) has the form of a screw conveyor and is rotatable around its longitudinal axis, and
- a second electrode (3) is arranged at a distance opposite to the first electrode and has a form other than the screw conveyor.

2. A device according to claim 1, wherein the second electrode (3) is provided in the form of one or more plane or curved boards or walls.

3. A device according to claim 1, wherein the second electrode (3) is provided in the form of a hous-

ing (3) partially or totally surrounding the screw conveyor along its longitudinal axis.

4. A device according to claim 3, wherein the housing (3) is of cylindrical shape, preferably having the form of a hollow tube or pipe, and has at least one inlet opening (10) at one end and at least one outlet opening (13) at its other end, and wherein at least a part of the screw conveyor (2) is arranged inside said housing (3).

5. A device according to any one of claims 1 to 4, wherein a distinct zone (7), preferably having a width of 0.1-1 mm, at the outermost circumferential edge of the screw conveyor (2) is made of non-conductive material which does not take part in dielectric field generation or maintenance.

6. A device according to claim 3 or 4, wherein the distance between the outermost edge of the screw conveyor (2) and the opposite surface of the housing (3) is adjusted such as to avoid occurrence of a short circuit between the screw conveyor and the housing, and preferably ranges from 100 μm to 1000 μm .

7. A device according to any one of claims 1 to 6, wherein the first and second electrodes (2, 3) are mounted inside a container (8) containing the liquid suspension.

8. A device according to claim 4, wherein the first and second electrodes (2, 3) are arranged to be a part of a pipeline in an external recirculation loop of a container (15) containing the liquid suspension.

9. A device according to claim 7 or 8, wherein said container (8, 15) is a bioreactor.

10. A device according to any one of claims 3 to 9, wherein the housing (3) surrounding the first electrode (2) is arranged in a horizontal or vertical position or at an angle in between horizontal and vertical.

11. A device according to claim 1, wherein a longitudinal section of the screw conveyor (2) is part of the dielectric field generating means and constitutes the first electrode, while another section of the screw conveyor (2) has no electrode function and does not form part of the dielectric field generating means.

12. A device according to claim 10, wherein the housing (3) is arranged in a non-horizontal position and has at its lower end an inlet section (9) for receiving the liquid suspension, and at its upper end an outlet section (12) having one or more outlet

openings (13) for continuously or batchwise draining off or recirculating at least one fraction of the particulate matter contained in the liquid suspension.

13. A device according to claim 12, wherein said inlet section (9) comprises an expansion chamber (14), and wherein the screw conveyor (2) extends into the expansion chamber (14), preferably in an eccentric manner.

14. A device according to claim 12 or 13, wherein the screw conveyor (2) extends to a level below the inlet opening 10, and wherein the pitch of the screw part that extends into the inlet section (9) is preferably smaller than the pitch of the adjacent screw part outside the inlet section (9).

15. A device according to claim 12, wherein said inlet section (9) additionally comprises at least one outlet opening (11), for continuously or batchwise draining off sedimented particulate matter.

16. A device according to claim 10, wherein the housing (3) is arranged in a horizontal position and comprises an inlet section (9) at one end and an outlet section (12) at its other end and wherein the outlet section (12) comprises at least two outlet openings (13, 11') located at different vertical levels, for separating sedimented from non-sedimented particles.

17. A device according to claim 1, wherein the screw conveyor (2) has a hollow shaft and is optionally equipped with means for electrical supply and/or thermoregulation.

18. A method for electrophoretically separating a desired fraction of particles from a liquid suspension containing a mixture of particles having different electrophoretic properties, which method comprises

generating a flow of said liquid suspension and passing said suspension through a space between a rotating screw conveyor (2) that is operated as a first electrode and the surface of a second electrode (3) located opposite the first electrode; generating an alternating non-uniform dielectric field (4) between the screw conveyor (2) and the second electrode (3); adjusting strength and frequency of the dielectric field (4) to selectively attract or repel at least one desired particle fraction contained in the liquid suspension; and collecting, recirculating or discharging said at least one particle fraction after passage of the liquid suspension through the dielectric

field.

19. Method according to claim 18, wherein the second electrode (3) has the form of a tube-like or pipe-like housing, the screw conveyor (2) being located inside said housing, wherein the liquid suspension is introduced to the dielectric field via an inlet section (9) at one end of the housing and leaves the dielectric field via one or more outlet openings (13, 11') located at an outlet section (12) at the opposite end of the housing.

20. Method according to claim 19, wherein the first and second electrodes are arranged in a horizontal position and the dielectric field and the suspension flow are adjusted such as to allow non-attracted or actively repelled particle fractions to sediment underneath the screw conveyor (2) from where they are removed through a first outlet opening (11'), while advancing the attracted or non-repelled particle fraction(s) towards a second outlet opening (13) of said housing located at a level above said first outlet opening (11').

21. Method according to claim 19, wherein the first and second electrodes are arranged in a non-horizontal position, and wherein the flow of the liquid suspension, the rotational speed of the screw conveyor and the dielectric field are adjusted such as to advance the liquid together with particles attracted or not repelled by the dielectric field in an upward direction against gravitational forces, while allowing non-attracted or actively repelled particle fractions to sediment in the space between screw tips and inner surface of the housing, and batchwise or continuously removing the sedimented particles through another outlet opening (11) located at the lower end of the housing (3).

22. Method according to claim 19, wherein the particles of the liquid suspension are eukaryotic cells, preferably plant, animal or human cells, and wherein the cells attracted or actively repelled by the dielectric field are recirculated into the suspension for enriching the suspension in the fraction of these cells, while the corresponding non-attracted or not actively repelled cell fractions are removed from the suspension.

23. Method according to claim 22, wherein the suspension contains viable and non-viable cells and wherein the dielectric field is adjusted such as to attract the viable cells towards the screw conveyor (2) while allowing the non-viable cells to sediment by gravitation.

24. Method according to claim 22, wherein the liquid suspension is a cell culture and the screw conveyor

(2) together with the housing (3) is placed and operated inside a bioreactor (8) containing said cell culture or is placed and operated in an external recirculation loop of a bioreactor (15).

25. Method according to claim 21, wherein the housing (3) at its inlet section contains an expansion chamber (14), and wherein at least a first section of the screw conveyor (2), in as much as it is located inside said expansion chamber (14) is operated as the first electrode, and an opposite wall of the expansion chamber (14) is operated as the second electrode for generating an alternating non-uniform dielectric field, while the remaining section of the screw conveyor (2) and of the housing (3) are optionally kept free from participation in dielectric field generation.

26. Method according to any one of claims 18 to 25, wherein the screw conveyor (2) and the second electrode (3) are placed in an upside-down position and the screw conveyor (2) is rotated in the direction of gravitation.

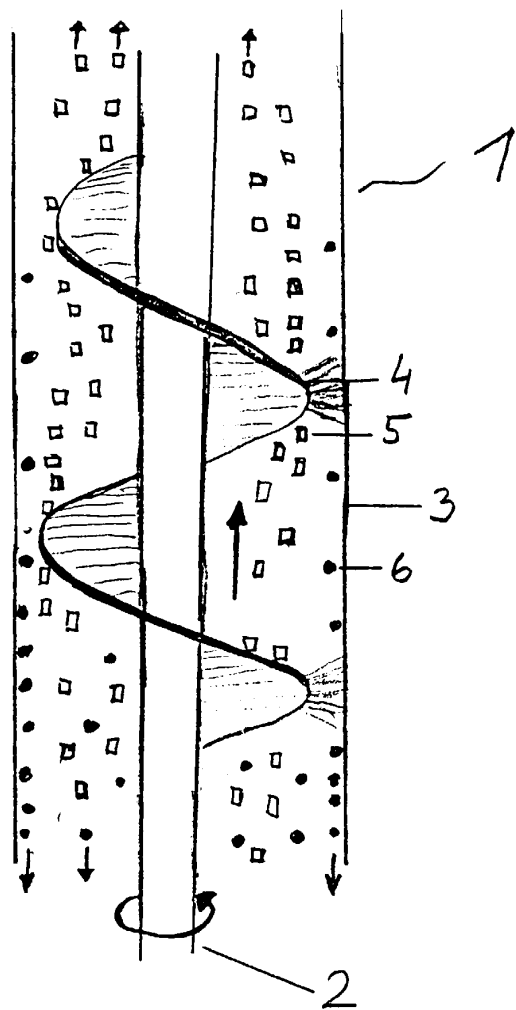


Fig. 1

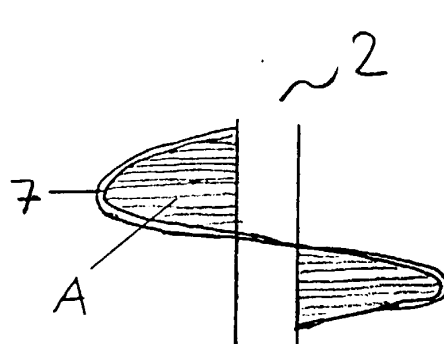


Fig. 2a

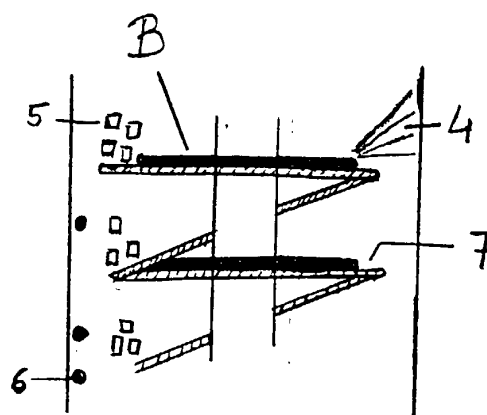


Fig. 2b

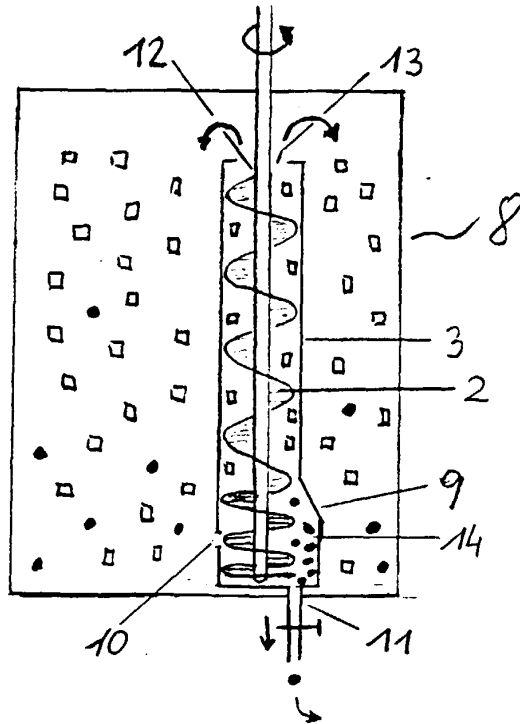


Fig. 3

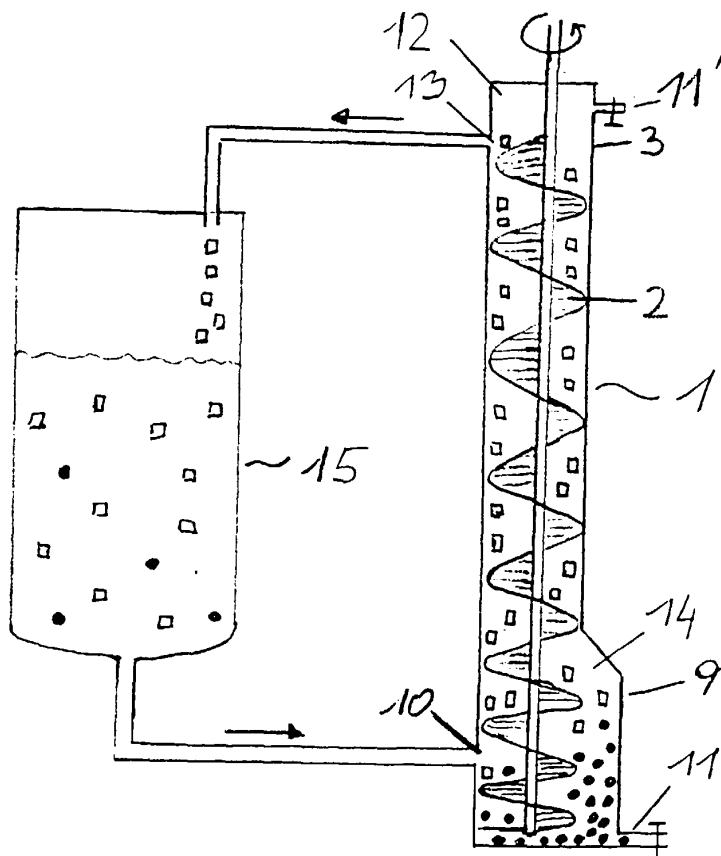
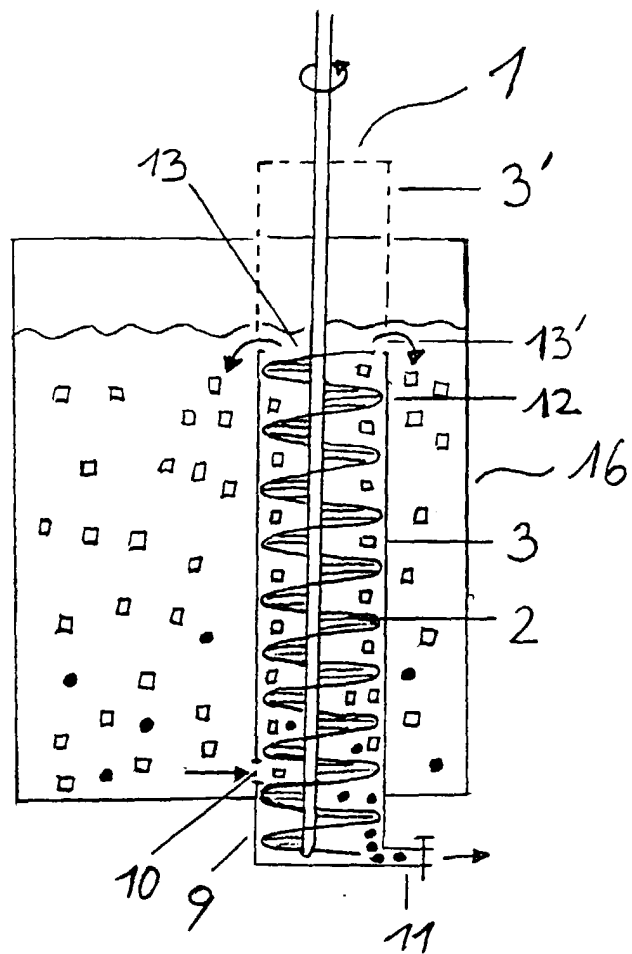


Fig. 4

Fig. 5





European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 99 12 5151

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Y	WO 92 04429 A (GRUNDMANN JUERGEN ; LAU JUERGEN (DE)) 19 March 1992 (1992-03-19) * page 5, paragraph 3 * * page 9, paragraph 3 *	18,22	B03C5/02
A	* page 10, paragraph 4 - paragraph 5; claims 1,4,5; figures 1,7 *	1-4,7, 9-12,19, 21,24,26	
Y	EP 0 645 169 A (AJDARI ARMAND ; LEWINER JACQUES (FR); PROST JACQUES (FR); VIOVY JEA) 29 March 1995 (1995-03-29) * page 5, line 22 - line 33; claims 1-5,8,10,13,16; figures 1-3 * * column 1, line 1 - line 7 *	18,22	
D,A	WO 97 27933 A (HUANG YING ; UNIV TEXAS (US); WANG XIAO BO (US); BECKER FREDERICK F) 7 August 1997 (1997-08-07)		
The present search report has been drawn up for all claims			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			B03C
Place of search	Date of completion of the search	Examiner	
THE HAGUE	26 April 2000	Decanniere, L	
CATEGORY OF CITED DOCUMENTS		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	
X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document			

EPO FORM 1503 03/82 (P04C01)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 99 12 5151

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

26-04-2000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9204429 A	19-03-1992	DE 4028805 A	12-03-1992
		CA 2091452 A	12-03-1992
EP 0645169 A	29-03-1995	FR 2710279 A	31-03-1995
		DE 69404405 D	04-09-1997
		DE 69404405 T	05-02-1998
		US 5593565 A	14-01-1997
WO 9727933 A	07-08-1997	US 5993630 A	30-11-1999
		US 5888370 A	30-03-1999
		AU 1856097 A	22-08-1997
		CA 2245514 A	07-08-1997
		EP 0885055 A	23-12-1998
		US 5993632 A	30-11-1999

EPO FORM P0469

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82