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(54) Title: MICRO-GRAVITY GENERATING DEVICE

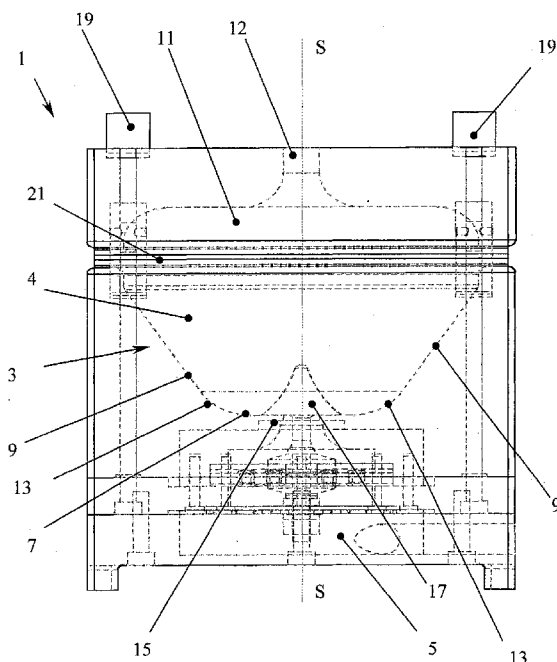


FIG. 1

(57) Abstract: A micro-gravity generating device (1) is described, comprising at least one flow chamber (3) to which at least one supplying circuit (5) is connected, adapted to supply the interior of such flow chamber (3) with at least one fluid (F), such flow chamber (3) delimiting at least internally the volume defined by at least one lower vase (4) composed of at least one base (7) and at least lateral slanted walls (9), and at least one upper cover (11), such base (7) being connected on its perimeter to such lateral slanted walls (9) by interposing at least one junction profile (13).



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MICRO-GRAVITY GENERATING DEVICE

5

The present invention refers to a micro-gravity generating device.

Devices are known in the art that are able to generate a micro-gravity condition for a solvent
10 contained inside a flow chamber: examples of such devices are disclosed in EP2265708, RU2355751, US20110027880, WO2008073348, US2010120136. Such devices belonging to the prior art obtain the micro-gravity conditions by means of rotary
15 components handled by actuators. The presence of such rotary components however has some inconveniences.

In fact, the presence of complex interfaces for coupling rotary components creates problems in
20 keeping sterility, in application where this is necessary, favouring the occurrence of sources of pollution.

Moreover, the presence of rotary components requires the use of moving couplings between pipes
25 and flow chamber in order to perform the fluid re-

circulation, consequently increasing both the difficulties in designing and assembling and the construction costs.

Moreover, known generating devices require a
5 current supply necessary for handling the rotary components.

Document RU-C1-2 355 752 discloses a device according to the preamble of Claim 1.

Therefore, object of the present invention is
10 solving the above prior art problems by providing a device able to generate micro-gravity even if there are no rotary components.

Another object of the present invention is providing a passive micro-gravity generating device
15 able to exploit a fluid-dynamics inside a flow chamber with an optimised geometry to generate micro-gravity at low costs.

The above and other objects and advantages of the invention, as will appear from the following
20 description, are obtained with a micro-gravity generating device as described in claim 1.

Preferred embodiments and non-trivial variations of the present invention are the subject matter of the dependent claims.

25 It is intended that the claims are an integral

part of the present specification.

It will be immediately obvious that numerous variations and modifications (for example related to shape, sizes, arrangements and parts with
5 equivalent functionality) can be made to what is described, without departing from the scope of the invention as appears from the enclosed claims.

The present invention will be better described by some preferred embodiments thereof, provided as
10 a non-limiting example, with reference to the enclosed drawings, in which:

- Figure 1 shows a side sectional view of a preferred embodiment of the micro-gravity generating device according to the present
15 invention in a first operating position thereof;
- Figure 2 shows a side sectional view of a preferred embodiment of the micro-gravity generating device according to the present invention in a second operating position thereof;
- 20 - Figure 3 shows an axial-symmetrical discrete 2D computational simulation of the micro-gravity generating device according to the present invention;
- Figure 4 shows a colour-metric map of the
25 fluid speed values inside the micro-gravity

generating device according to the present invention;

- Figure 5 shows a colour-metric map of the fluid vortex values inside the micro-gravity generating device according to the present invention; and

- Figure 6 shows a colour-metric map of the fluid deformation speed values inside the micro-gravity generating device according to the present invention.

In general, the device according to the present invention is adapted to generate micro-gravity conditions in systems in which it is necessary preferably to perform perfusion or fluid re-circulation such as, for example, bio-reactors. For such purpose, as will be described below in more detail, the device according to the present invention comprises at least one flow chamber characterised by an internal geometry, designed with the help of information deriving from *in silico* studies, adapted to produce the detachment of the fluid vein from the wall of such chamber within a certain speed range of the inlet fluid and to generate vortexes able to keep particles with different sizes in suspension, ensuring a laminar

speed in every point of the chamber itself, under certain operating conditions, avoiding the use of rotary devices.

With particular reference therefore to Figures 1 and 2, it is possible to note that the micro-gravity generating device 1 according to the present invention comprises at least one flow chamber 3 to which at least one supplying circuit 5, preferably of the hydraulic type, is connected, adapted to supply the interior of such flow chamber 3 with at least one fluid F, such flow chamber 3 being such as to delimit, at least internally, a volume defined by at least one lower vase 4 composed of at least one base 7 and at least lateral slanted walls 9, and at least one upper cover 11, such base 7 being connected on its perimeter to such lateral slanted walls 9 by interposing at least one curvilinear junction profile 13.

According to the invention, the flow chamber 3 is axial-symmetrical with respect to an axis of symmetry S-S. Moreover, the supplying circuit 5 supplies fluid F inside the flow chamber 3 through at least one supplying opening 15 placed through the base 7 in a coaxial position with respect to such axis of symmetry S-S.

Moreover, between such supplying circuit 5 and such internal volume of the flow chamber 3, at least one check valve is interposed, arranged next to such supplying opening 15. The check valve results open (as shown, for example, in Figure 2) only under fluid F re-circulation conditions, being automatically closed (as shown, for example, in Figure 1) as soon as the flow is stopped, thereby preventing the contents of chamber 3 from out-flowing when the device 1 is inactive.

Preferably, such check valve comprises at least one plunger 17 inside the internal volume of the lower vase 4 and adapted to be moved vertically and coaxially with respect to the axis of symmetry S-S in order to open or close the supplying opening 15 (and therefore allow the passage of fluid F inside the flow chamber 3, or not), such plunger 17 being preferably shaped as a right circular frustum of cone.

Preferably, the lateral slanted walls 9, the base 7 and the junction profile 13 are mutually integral and made of the same material.

Obviously, the device 1 according to the present invention can be equipped with a suitable supporting structure 19 that guarantees placement

and necessary stability for the flow chamber 3.

Moreover, the internal volume of the flow chamber 3 can be divided by at least one filtering layer 21 interposed between the lower vase 4 and the cover 11, such filtering layer being adapted to block elements being present inside fluid F from occasionally flow out.

The cover 11 can further be equipped with at least one discharge duct 12 for fluid F.

As stated, the geometry of the internal volume of the flow chamber 3 is devised in order to favour the occurrence of stationary vortexes V in fluid F (solute - solvent solution) supplied by the supplying circuit 5 in order to create a micro-gravity and mixing condition for the solute without the help of rotary components. Advantageously therefore, in order to determine the above geometry, the various components of the flow chamber 3 comply with characteristic dimensional relationships. Therefore, given:

- A the diameter of the base 7;
- B the height of the lower vase 4;
- C the diameter of the supplying opening 15;
- R the radius of curvature of the junction profile 13;

- α the slanting angle of the lateral slanted walls 9;
- β the conical angle of the plunger 17;
- D the hollow space between the base of the
5 plunger 17 and the base 7 of the lower vase 4;
- E the height of the plunger 17;
- F the diameter of the base of the plunger 17,

the following dimensional relationships are obtained:

- 10 - A/B is included between 0.4 and 0.7;
- A/C is included between 1 and 1.5;
- B/C is included between 2 and 3;
- R/B is included between 0.2 and 0.5;
- R/A is included between 0.4 and 0.8;
- 15 - α is included between 40° and 60° ;
- β is included between 20° and 40° ;
- E/F is included between 0.5 and 0.9;
- D/C is included between 0.05 and 0.1;
- C/F is included between 0.6 and 1.3.

20 Moreover, advantageously, the inlet speed of fluid F inside the flow chamber 3 through the supplying opening 15 is included between 0.05 m/s and 0.15 m/s.

At steady state, fluid F is pumped inside the
25 flow chamber 3, through the supplying duct 5 and

the related supplying opening 15, where, following the vein detachment induced (and controlled) by the slant of the side walls 9, stationary vortexes V and hydrodynamic forces are formed, that are able to compensate the force of gravity and to avoid the solute sedimentation on the bottom of the chamber 3.

Therefore, in order to study the efficiency of the proposed geometric solution in order to obtain the micro-gravity condition, the Applicant has performed CFD simulations. In particular, aim of the CFD simulations was to establish whether the internal geometry of the flow chamber 3 is able to ensure a homogeneous distribution of the cell-hydrogel aggregates, fluctuating inside the chamber 3 itself, in order to obtain the suspension of the aggregates, avoiding their sedimentation on the chamber bottom, their packing and their collision against the filter.

In the particular case of use of the device for cellular culture on hydrogels, geometry and dimensions both of the chamber and of the valve and fluid inlet parameters have therefore been defined taking into account those information obtained from the performed Computational Fluid-Dynamic (CFD)

Simulations.

In the particular case of use of the device for cellular culture on hydrogels, a device 1 according to the present invention has therefore
5 been made and experimentally tested, with the following characteristic dimensions:

- A = 16 mm;
- B = 29.5 mm;
- C = 12 mm;
- 10 - R = 9.95 mm;
- $\alpha = 50^\circ$;
- $\beta = 30^\circ$;
- D = 1 mm;
- E = 10 mm;
- 15 - F = 13 mm.

Figure 2 shows the discrete axial-symmetrical 2D computational simulation of the device 1 according to the present invention, while Figures 4 to 6 propose colour-metric maps obtained during the
20 simulation tests of the above-described device 1 according to the present invention.

The simulated fluid F is the culture fluid (density = 1006.5 kg/m³, viscosity = $1.003 \cdot 10^{-3}$ kg/(m·s)), for which inlet speeds have been imposed
25 in the above-mentioned range (0.05 m/s - 0.15 m/s)

that guarantees Reynolds numbers lower than 1000 (laminar fluid condition) both in the entry section and in the shrinking section downstream of the entry (section A in Figure 3). Since the device 1
5 has an axial symmetry, for the computational simulation, it has been possible to adopt an axial-symmetrical 2d domain. The geometry has been made discrete with 206275 triangular cells (through the Gambit software supplied by ANSYS Inc., and making
10 the simulation of Figure 3). Simulations have been performed under stationary conditions with single-phase flow, the outlet pressure of the duct 5 has been set to a reference value and the non-sliding condition for the flow has been set to the walls 9
15 (vparete = 0 m/s). The numeric results have been obtained by solving the Navier-Stokes equation for uncompressed fluids by means of the finished-volumes method, used by the Fluent software (supplied by ANSYS Inc.).

20 In order to evaluate the efficiency of the device 1 in guaranteeing the micro-gravity conditions and the possible presence of critical shearing effort values for the cells, motion field (speed and vortex contours) and deformation speed
25 (for a Newton fluid the shearing effort is

proportional to the deformation speed by means of the fluid viscosity multiplying constant) have been analysed.

For an inlet fluid speed equal to 0.10 m/s
5 (Reynolds_{ingresso} = 400, Re_A = 620) the colour-metric maps shown in Figures 4 and 5 are obtained, in which Figure 4 shows the colour-metric map of the speed values and Figure 5 shows the colour-metric map of the vortex values.

10 Observing Figures 4 and 5, it is then possible to note that a vortex is formed, following the fluid vein detachment from the wall 9, that allows keeping in suspension particles with different sizes, avoiding the use of rotary devices.

15 The fluid vein detachment brings about the formation of a great vortex structure that is able to compensate, with the hydrodynamic forces that are generated in the bio-reactor, the force of gravity acting on the hydrogels, avoiding their
20 sedimentation. Such vein detachment, that brings about the vortex formation, is guaranteed through the appropriate sizing of the chamber 3, in particular by the slanting of the side wall and the curvature of the junction profile with the base of
25 the lower vase: at steady state, the profile

curvature and the chamber wall slanting allow the inlet fluid, having a fluid-dynamic structure shaped as a jet, to rise along the side wall till the fluid vein detachment from the wall with the following formation of the above vortex due to an inertia effect.

Moreover, in order to evaluate the possible presence of critical shearing effort values for the cultivated cells (critical value due to cellular damage = 2 Pa), the deformation speed distribution has been analysed, as shown in Figure 6. By multiplying the maximum value of the deformation speed, present in the area where there are cells, due to the fluid viscosity it is possible to obtain the maximum value of the shearing effort (0.6 Pa), that is much lower than the critical value.

From the obtained results, the adopted geometric solution and the speed value imposed as inlet to the fluid thereby allow the device 1 according to the present invention to obtain a micro-gravity condition, with non-critical shearing effort values for the cells being present inside the chamber.

The device 1 according to the present invention further allows obtaining the following

advantages:

- the absence of rotary components removes the need of moving couplings between pipes and chamber in order to perform the fluid re-circulation, lowering both design and assembling difficulties and building costs;
- the absence of complex interfaces for coupling rotary components reduces the problems of keeping the sterility, in applications where this is necessary, favouring a design without pollution sources;
- the device 1 is devised in such a way as to ensure a laminar fluid-dynamic state in any point of the chamber 3, ensuring thereby a tolerable level of shearing efforts from living cells, in the application where this is required;
- the device 1 has easily scalable dimensions, possibly allowing to strongly reduce the overall sizes also due to the absence of rotary actuators, this allowing to use the device without problems, for example, like bio-reactor for tissue engineering, making it able to be easily inserted inside commercial incubators like those commonly used for cellular growths;
- the device 1, operating in series with the

other devices, does not require other energy sources to obtain the micro-gravity condition for the solute.

CLAIMS

1. Micro-gravity generating device (1) comprising
at least one flow chamber (3) to which at least one
supplying circuit (5) is connected, adapted to
5 supply an interior of said flow chamber (3) with at
least one fluid (F), and at least one upper cover
(11), characterised in that:

said flow chamber (3) delimits at least
internally a volume defined by at least one lower
10 vase (4) composed of at least one base (7) and at
least lateral slanted walls (9),

said base (7) is connected on its perimeter to
said lateral slanted walls (9) by interposing at
least one curvilinear junction profile (13),

15 said flow chamber (3) is axial-symmetrical
with respect to an axis of symmetry (S-S),

said supplying circuit (5) is adapted to
supply said fluid (F) inside said flow chamber (3)
through at least one supplying opening (15) placed
20 through said base (7) in a coaxial position with
respect to said axis of symmetry (S-S).

2. Micro-gravity generating device (1) according to
claim 1, characterised in that between said
supplying circuit (5) and said internal volume of
25 said flow chamber (3), at least one check valve is

interposed, arranged next to said supplying opening (15).

3. Micro-gravity generating device (1) according to claim 2, characterised in that said check valve
5 comprises at least one plunger (17) inside said internal volume of said lower vase (4) and adapted to be moved vertically and coaxially to said axis of symmetry (S-S) in order to open or close said supplying opening (15), said plunger (17) being
10 preferably shaped as a right circular frustum of cone.

4. Micro-gravity generating device (1) according to claim 2, characterised in that said internal volume of said flow chamber (3) is divided by at least one
15 filtering layer (21) interposed between said lower vase (4) and said cover (11).

5. Micro-gravity generating device (1) according to any one of the previous claims, characterised in that, let A be the diameter of said base (7), B the
20 height of said lower vase (4), C the diameter of said supplying opening (15), R the radius of curvature of said junction profile (13), α the slanting angle of said lateral slanted walls (9), β the conical angle of said plunger (17), D the
25 hollow space between a base of said plunger (17)

and said base (7) of said lower vase (4), E the height of said plunger (17), F the diameter of said base of said plunger (17), A/B is included between 0.4 and 0.7, A/C is included between 1 and 1.5, B/C is included between 2 and 3, R/B is included between 0.2 and 0.5, R/A is included between 0.4 and 0.8, α is included between 40° and 60° , β is included between 20° and 40° , E/F is included between 0.5 and 0.9, D/C is included between 0.05 and 0.1, C/F is included between 0.6 and 1.3.

6. Micro-gravity generating device (1) according to any one of the previous claims, characterised in that said fluid (F) is adapted to enter inside said flow chamber (3) through said supplying opening (15) with an inlet speed included between 0.05 m/s and 0.15 m/s.

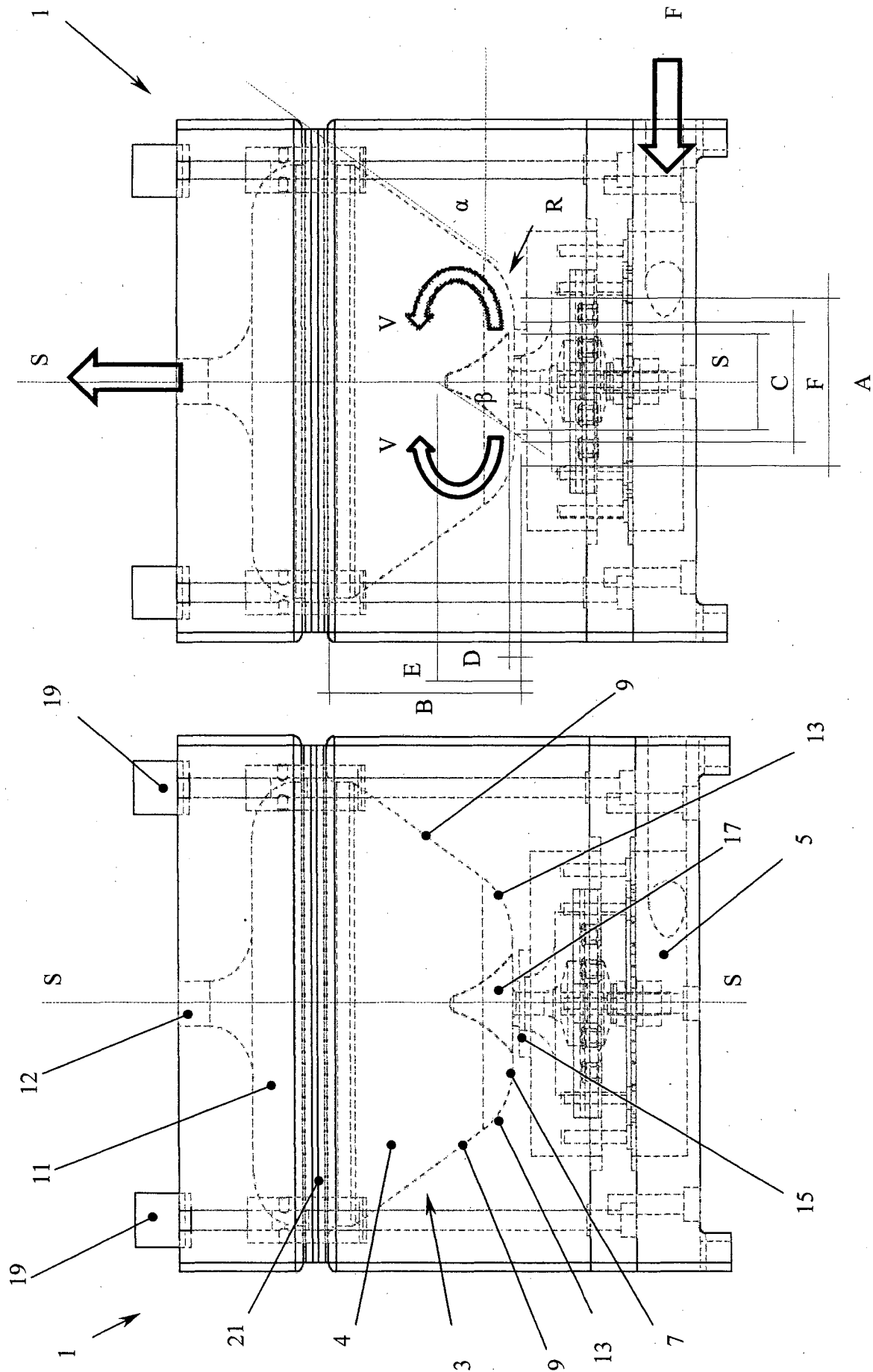


FIG. 1

FIG. 2

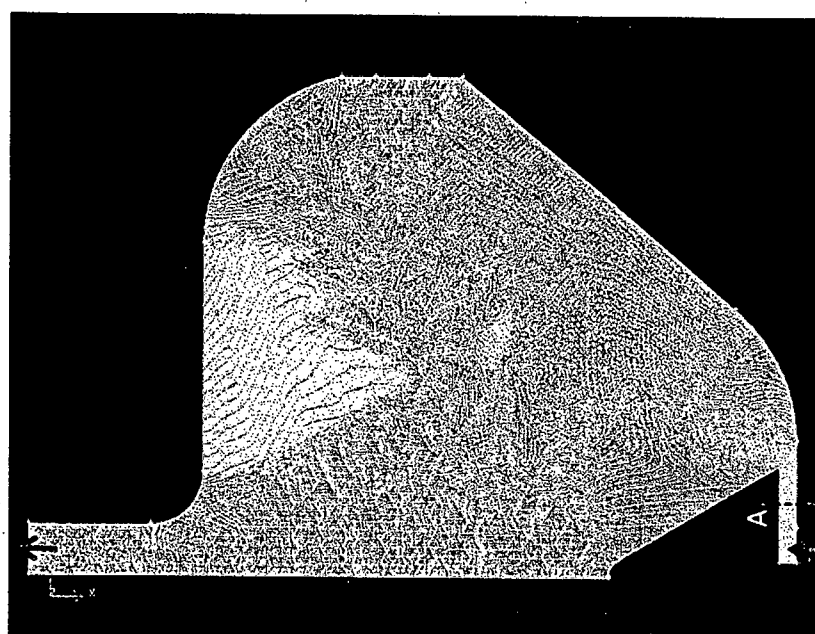


FIG. 3

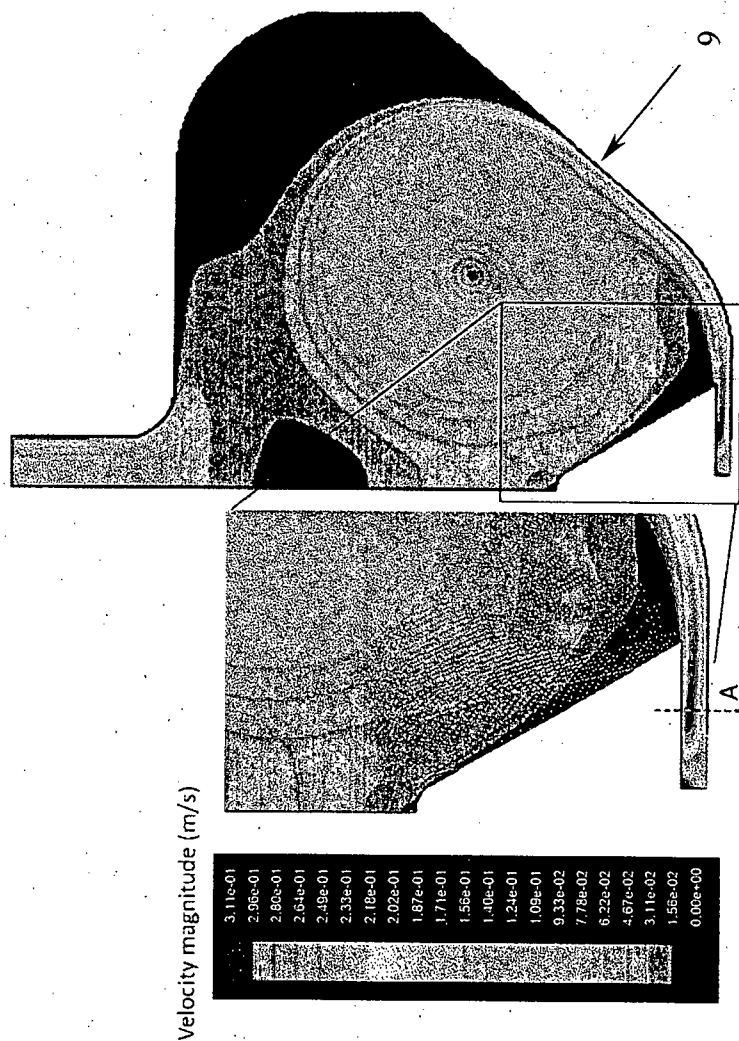


FIG. 4

FIG. 5

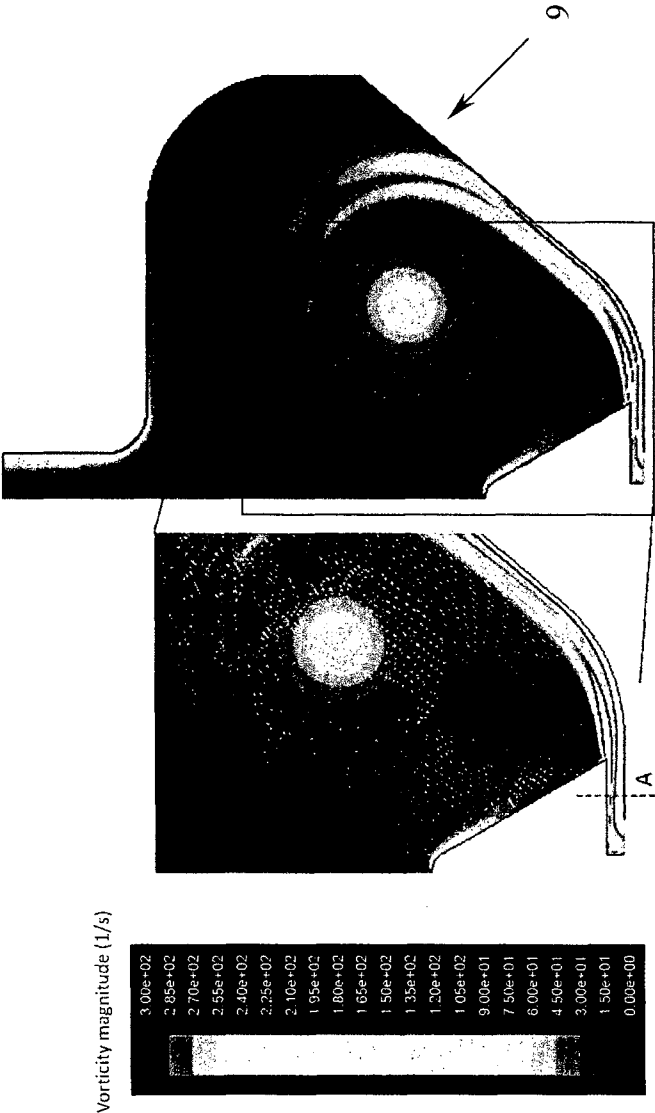
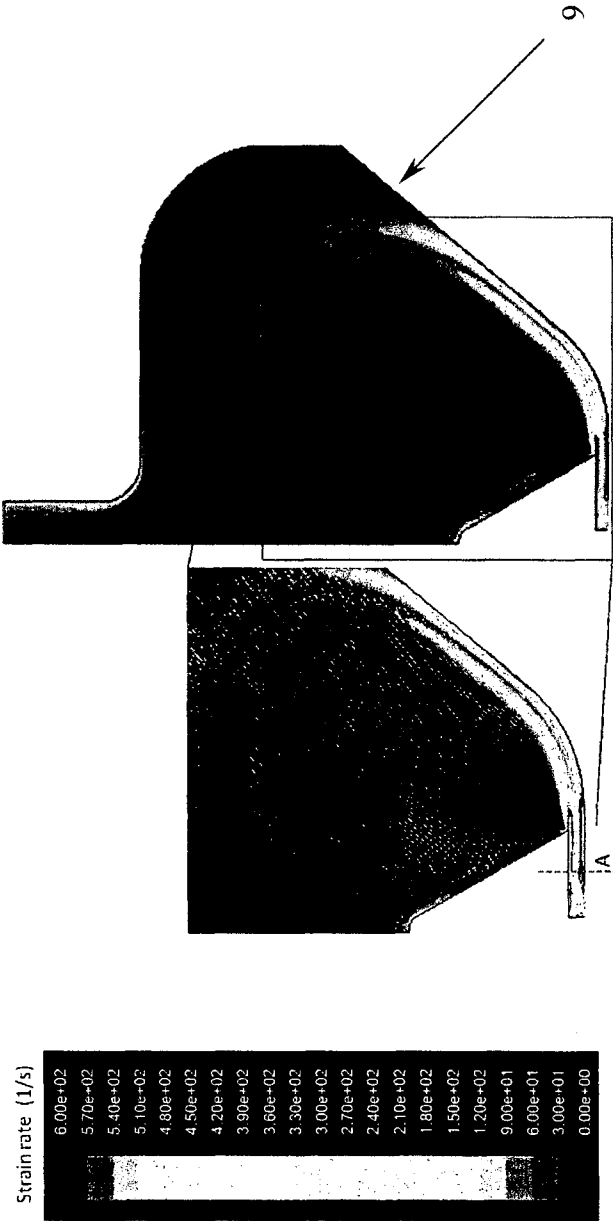


FIG. 6



INTERNATIONAL SEARCH REPORT

International application No

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A. CLASSIFICATION OF SUBJECT MATTER

INV. C12M1/00

ADD.

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

C12M C12N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	RU 2 355 752 C1 (FEDERAL NOE G UCHREZHDENIE NAU [RU]) 20 May 2009 (2009-05-20) cited in the application abstract; figures 1-6 -----	1-6
Y	LIN ET AL.: "The influence of inclination of a solid surface on contact angles due to the effect of line tension", COLLOIDS AND SURFACTANTS A:PHYSICOCHEMICAL AND ENGINEERING ASPECTS, vol. 87, 1994, pages 93-100, XP002666099, page 93 - page 94 -----	1-6
A	US 5 248 613 A (ROUBICEK RUDOLF V [US]) 28 September 1993 (1993-09-28) column 6, line 34 - line 45; figures 1,3-6 ----- -/--	1-6



Further documents are listed in the continuation of Box C.



See patent family annex.

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Date of the actual completion of the international search

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INTERNATIONAL SEARCH REPORT

International application No

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C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 2007/039726 A1 (UNIV LIVERPOOL [GB]; BLACK RICHARD A [GB]; CURRAN STEPHEN JOHN [GB]; B) 12 April 2007 (2007-04-12) claims 1-68; figures 1-4 -----	1-6

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/IT2012/000090

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