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EVALUATING THE ROLE OF GEOMETRICAL FEATURES OF A TAYLOR VORTEX BIOREACTOR TO CULTURE ANIMAL CELLS BY USING COMPUTATIONAL FLUID DYNAMICS

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RESUMO - Taylor bioreactor is fast becoming the next bioreactor to culture animal cells due to milder shear and homogenous flow structures through-out the bioreactor in comparison to the traditional stirred tank. However, there is not much information in the literature about how geometrical aspects of the Taylor bioreactor may affect the culture of animal cells which could result in poor efficiency. As a result, six different geometrical conditions of Taylor bioreactor are presented, related to off-bottom clearance and the external cylinders' bottom shape, after conducting a detailed grid and time-step independence study and validating with experimental results. Simulations were conducted at Reynolds number of 12077 and Taylor number of 5331 with a radius ratio of 0.84 and aspect ratio of 19.8. Through-out the bulk zone equivalent of 80 % of the gap-width, the mean velocity was found to be around 50 % of the maximum with similar gradients which is encouraging for cultivating of animal cells in Taylor bioreactor in comparison with spinner flask and stirred tank bioreactors where the gradients are much less uniform. Curved bottom surfaces of the external cylinder and higher off-bottom clearance areas adversely affect the flow structures creating dead-zone areas in the off-bottom clearance area.

INTRODUCTION

The interest in culturing animal cells has increased significantly in the last 20 years due to the need of large-scale production of monoclonal antibodies, hormones, vaccines, recombinant proteins and, more recently, the production of specialized cells for applications in tissue engineering and cell therapy (Agarwal, 2013, Heathman *et al.*, 2015, Mason *et al.*, 2012) . Accordingly, a wide variety of cell lines have been cultivated in the reliable, well known and easy to scale-up stirred tank bioreactor with a design adapted from the fermenters used for microbial cultures (Stanbury *et al.*, 1995).

In order to cultivate the animal cells in stirred tank bioreactor (Stanbury *et al.*, 1995), some fine adjustments in the geometrical design of the fermenters were required to reduce the damage of cells due to shear stress, heat and contamination. In the design one of the most important but controversial item is the bottom geometry of the tank, which as per these authors should be hemispherical or concave to ensure better mixing at lower impeller rotational speed. On the contrary, Charles and Wilson (1994) stated that this requirement is not acceptable since there is no firm evidence to support this belief in addition to the fact that several stirred tank bioreactors with flat bottom have worked well in commercial applications and with the benefit of 50% lower cost of the tank. Reuveny (1990) and Smith (1994) advocate the use of concave bottom, considering the usage of flat bottom to be inappropriate because of formation of stagnant regions in the bottom corners which can cause particle accumulation. In the case of animal cell culture, sedimentation problems can hinder the operation of the bioreactor during the cell adhesion process and during the actual cultivation by forming aggregates because of the large size of the particles (cells, cells clusters and microcarriers) (Ibrahim and Niewnow, 2004).

A study conducted by Chaudacek (1985) showed that the accumulation of high density solids, such as silica, in flat bottom tanks can be eliminated by using axial impellers and implementing modifications in the geometry of the tank. Ibrahim and Nienow (2004) applied this reasoning to low density solids, such as microcarriers, and validated the geometry modification principle using rounded corners in the bottom of the tank and a conical indentation in the region under the impeller. Although, stirred tank is the first bioreactor type for culturing animal cells from laboratory scale to industrial scale, it was not until the study of Ibrahim and Nienow (2004) that there was a better definition of technical criteria demonstrating an advantage of modified bottom with respect to the flat bottom for bioprocesses.

As a result of such studies, in laboratory scale stirred tank bioreactors to culture animal cells, in general practice, the outer cylinder usually has a curved geometry on the bottom. The three well-known industrial suppliers of the stirred tank laboratory scale bioreactors, New Brunsswick, Infors HT and Applikon biotechnology, have curved (dished outwards) geometry of the outer cylinder. However, the demand of newer and more shear sensitive cell cultures require newer bioreactor types that generate milder hydrodynamic forces in comparison to the stirred tank (Jain and Kumar, 2008). The Taylor bioreactor due to lower and uniform distribution of shear is fast becoming a strong candidate to replace the traditional stirred tank in the cultivation of animal cells by presenting a lower and more uniform shear (Curran and Black, 2004, 2005, Gong *et al.*, 2006, Haut *et al.*, 2003, O´Connor *et al.*, 2002, Santiago *et al.*, 2011, Tanzeglock, 2008, Zhu *et al.*, 2010).

However, in the case of Taylor bioreactor, there is empirical evidence of accumulation of particles at the bottom of the bioreactor which hinders the process of cell adhesion and proliferation. Considering the lack of information for bioreactors using the Taylor vortex principle to culture animal cells with different geometrical conditions, carrying out studies in this direction becomes extremely important and necessary since the geometry modifications can greatly influence the bioprocess efficiency.

Consequently, the shape of the outer cylinder and the height at which the inner cylinder is placed above the outer cylinder, or off-bottom clearance - obc, are considered as parameters which can lead to stagnant zones in a Taylor bioreactor. For example, if the inner cylinder is placed too high, there could be stagnant zones in the bottom of the tank because with only inner rotating cylinder tangential velocity has the biggest impact on the flow structures, thus implying that in the off-bottom clearance area there may not be sufficient amount of mixing due to weak axial flow.

However, as far as the authors are aware, the off-bottom clearance and shapes of the outer cylinders' base have not been investigated for Taylor bioreactor, but are of significant practical importance especially for culturing of anchorage dependent cells on microcarriers. Therefore, the main purpose of this article is to elucidate a favorable geometry for the particle suspension in a Taylor bioreactor at energy dissipation rates that are lower to those considered sub-lethal for the cells by providing an analysis of the flow structures and identifying the locations where the stagnation may occur using a computational fluid dynamics (CFD) validated model.

Best practice numerical methods are employed, and due attention is paid towards grid and time-step independence mesh. The shear-stress transport with curvature correction (SST-CC) turbulence model is employed in this study considering its more accurate prediction of the magnitude and location of the maxima of the turbulence kinetic energy and its dissipation in a stirred vessel (Singh *et al.*, 2011) in comparison to the k-ε, shear-stress transport (SST), Reynolds stress model (RSM) and scale adaptive simulation shear-stress transport (SAS-SST) turbulence models. The numerical model will be validated by comparison with the PIV & numerical study presented by Coufort (2004) and Coufort *et al.*, (2005) on the grounds of similar radius ratio of 0.87 and 0.84 (this study), consideration of only inner cylinder rotation and similar Reynolds number of 10995 and 12000 (this study).

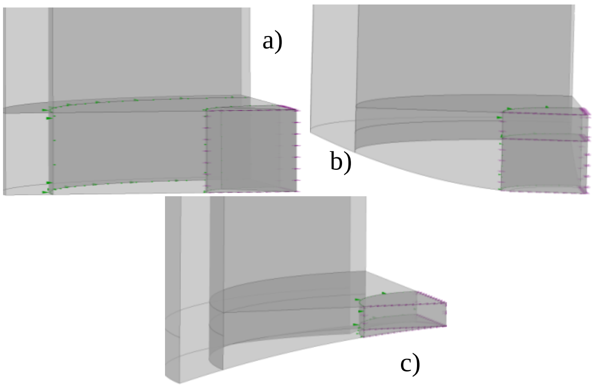
Computational Model

Description of case set-up: The inner, r_i, and outer, r_o, cylinder radius of 54.5 and 65 mm, respectively, and a height, h, of 210 mm was used in this study. This leads to a gap width, $b = r_o - r_i$, radius ratio, $\eta_{rr} = r_i/r_o$, and aspect ratio, Γ, of 10.6, 0.84 and 19.8, respectively. The angular velocity, ω, of 200 rpm or 20.94 rad/s was tested in this study with the Reynolds number, $Re = r_i\omega(r_o - r_i)/\nu$, and Taylor number, $Ta = r_i^{1/2}\omega(r_o - r_i)^{3/2}/\nu$, of 12077 and 5331, respectively. Water at 20 ºC was used as the working fluid.

Three different bottom shapes of the outer cylinder were tested: flat, dished and dished inwards, as shown in Figure 1. The geometries flat bottom and dished bottom are commonly used shapes in laboratory scale bioreactors; while, dished inwards shape was tested based on the idea that with this configuration type accumulation of animal cells in the middle of the bottom of the bioreactor could be reduced. In terms of the off-bottom clearances, four different values were tested, 0, 5, 10 and 15 mm, with only the flat bottom geometry of the outer cylinder. Both the dished outwards and inwards geometries of the outer cylinder had an off-bottom clearance of 15 mm. In total, six different geometries were tested: four for flat-bottom at obc = 0, 5, 10 and 15 mm, and one each for dished and dished inwards at 15 mm obc.

The geometry for each of these six test cases was divided into multiple sections: three for flat bottom geometries and four for the other two cases. The idea behind this multiple geometry was to accommodate sliding-mesh technique and implement sweep mesh on the inner and outer surfaces. Because of the impossibility of implementing the sweep mesh in the complete off-bottom clearance area, another small section was created in the off-bottom clearance area. Moreover, in the two geometries with curved surfaces on the bottom of the outer cylinder, another section was created covering the curved surfaces again in view of the implementation of the sweep mesh in the gap-width area. The top of the bioreactor is considered as symmetry because when working with animal cells the top is a free surface. Furthermore, due to the symmetrical flow conditions and to reduce the computational effort, only 25 % of the geometry was modelled using cyclic symmetry.

Figure 1: Three different shapes (Flat (a), Dished outwards (b) and Dished inwards (c)) of the outer bottom cylinder at 15 mm off-bottom clearance, respectively, for each geometry.



Turbulence Modeling: In this study, an unsteady-Reynolds averaged Navier-Stokes based SST-CC turbulence model is used. The equations used for this model can be found in version 14.0 of ANSYS-CFX software. The SST turbulence model was developed by Menter (1994), and the curvature correction that is used with the SST turbulence model is a recent development of Smirnov and Menter (2009). The curvature correction sensitizes the SST turbulence model to streamline curvature and rotation, thus correcting a key limitation of two-equation turbulence models. This curvature correction clearly improved the predictions of the SST turbulence model in a tank stirred with Rushton turbine, as shown by Singh *et al.*, (2011). In addition, Poncet *et al.*, (2011) stated that in the core region the turbulence is almost isotropic, thereby confirming the usage of two-equation turbulence model which assumes isotropic turbulence.

Although, these simulations were carried out with a geometrical mesh having a radial mesh value of 80 μm or in other words very close to the Kolmogorov scale of turbulence, the DNS or large eddy simulation (LES) models were not tested due to limited computational resources and time. A DNS or LES model would have required simulating a full-scale geometry instead of one-fourth geometry being used in this case, thereby increasing the computational effort by four times. In addition, it is known that DNS and LES models requires collection of large-amount of simulated time-steps to achieve statistical averaging of data (Hartmann *et al.*, 2004). Considering the number of geometries tested, it became impractical to use either DNS or LES because of this limitation of time and computational resources.

Computational mesh and time-step: In a Taylor bioreactor, rotating inner cylinder generates, mainly, tangential-velocity which is spread through the radial direction in the gap-width. As a result the mesh was refined mainly in the radial direction and the final selected mesh had 96 nodes in the radial gap-width area, 432 nodes in the radial off-bottom clearance area and 2.4 million nodes in total. There were 210 and 102 nodes in the axial and tangential directions, respectively. The time-step of 1^{o} rotation was selected after its comparison with 0.5^{o} rotation showed little improvement in accuracy.

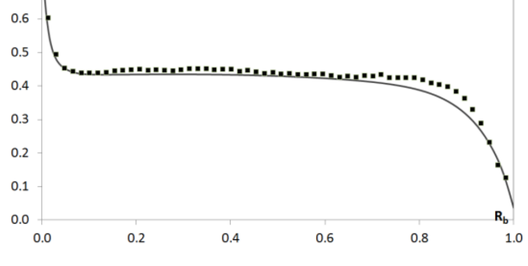
Computational aspects: The high resolution and second order backward Euler schemes were used to model the advection terms and transient terms, respectively, for all the equations The MRF technique was employed to study the transient nature of the flow field. The Convergence criterion of 10^{-5}, which was achieved within a maximum of 5 iterations per time-step, for RMS scaled residuals was employed for the continuity, momentum and turbulence quantities. Double precision arithmetic was applied for all of the simulations. Once a pseudo steady state was achieved, the transient data was collected for only one more revolution since the acquired data would have been a repeat for each further revolution. It took around 7 revolutions to reach the pseudo steady state for each tested grid. All of these simulations were performed on a desktop with eight-core 3.2 GHz AMD Fx-8120 processor and 32 GB of memory RAM. The simulations were run using hpi based parallel processing with 4 cores.

Validation of the Computational Model

As mentioned earlier, the numerical results are validated by comparison with the PIV velocity results of the Coufort (2004) on the grounds of similar radius ratio of 0.87 and 0.84 (this study) and the consideration of only inner cylinder rotation. It is important to note that the velocity flow profile data presented in their study was for 70 rpm and Re= 10995 in comparison to the 200 rpm and Re=12000 in this study in order to compare similar flow conditions.

Because of having similar geometrical and flow configurations, qualitative and quantitative comparisons should be considered valid. Figure 2 shows that both qualitatively and quantitatively the comparison of the tangential velocity flow structure is well depicted by the SST-CC turbulence model in this study. The SST-CC turbulence model not only predicts well the velocity flow structure and its magnitude in the boundary layer but also away from the walls in the centre of the gap-width.

Figure 2: Comparison of numerical tangential velocity results with the PIV results of Coufort (2004).

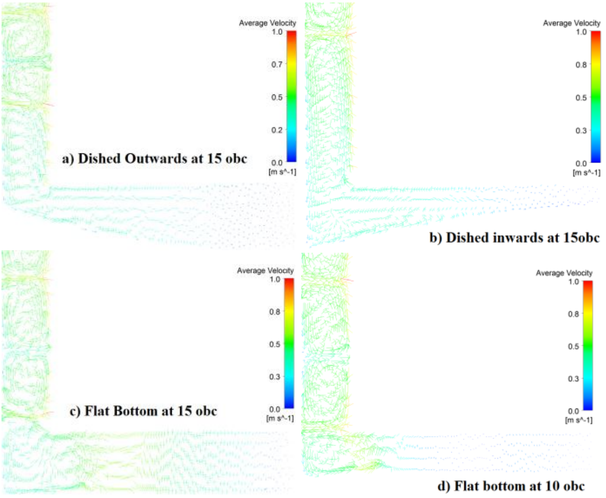


Further validation is done by estimating torque numerically and empirically using the correlation of Wendt (1933) to compare the Power number obtained through these two methods. The Power number, $N_P = P\,b/(\rho V\omega^3 r_i^3)$, used by Coufort (2004) and Douaire *et al.*, (2010) was employed for its caluculation, where P represents power, b represents gap-width, ρ represents density, V represents volume of the bioreactor, ω represents the rotational speed and r_i represents inner cylinder radius. The Power number was found to be of value 1.4×10^{-3}. For a Reynolds number of approximately 11000, similar to this study, Coufort (2004) also observed a Power number of 1.4×10^{-3}.

Results and Discussion

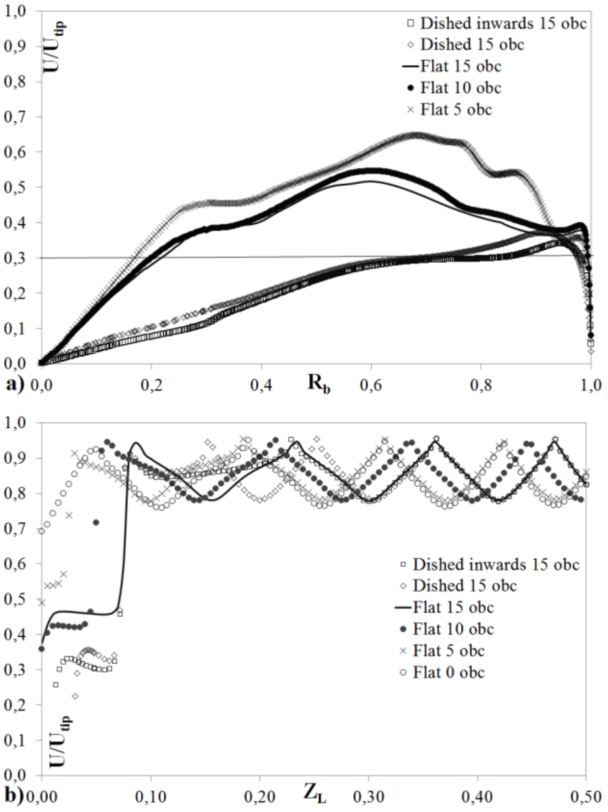
Outer cylinder´s bottom shape: Figure 3 presents vector profiles of the mean velocity for the different shapes of the outer cylinders' base, and Figure 4 shows the mean velocity profiles axially at $R_b = 0.009$ and radially at 1mm below the inner cylinder, to demonstrate the impact of the variation in the shape of the bottom of the outer cylinder and off-bottom clearance area, obc. It can be seen that the dished and dished inward surfaces impact significantly the secondary vortex structure of the bioreactor towards the bottom.

Figure 3: Mean velocity vectors for different shapes and off-bottom clearances.



The Taylor-vortex pair which is nearer to the bottom of the bioreactor for Flat surfaces is pushed up for the dished surfaces. The location of first pair of Taylor-Vortex for these three different bottom surfaces is around 0.08, 0.15 and 0.23 Z_L for flat, dished outward and dished inward surfaces types, respectively. For both dished surfaces before the formation of the Taylor vortex pair, a single vortex is formed and which is much longer for the dished inwards surface in comparison to the dished outwards, as can be seen in Figures 3a, 3b. The axial profiles of velocity (Figure 4b) further confirms the formation of this single vortex and that the profiles for these three different shapes join up around Z_L= 0.3 from bottom, in other words, the flow structure attains similar magnitude in the rest of the axial length.

Figure 4: Dimensionless mean velocity at 1mm below inner cylinder (a) and radial location of 0.1 mm away from the inner wall (b) for different geometry types.



It can be seen that the dished surfaces also impacts significantly the magnitude of the velocity towards the bottom of the bioreactor. The velocity is below 20 % of the tip velocity for $R_b < 0.4$ for dished surfaces in comparison to $R_b < 0.13$ for the flat surface, as shown in the radial velocity flow profile located at 1 mm below the inner cylinder (Figure 4a). Furthermore, for dished surfaces the velocity magnitude remains below 30% in 70% of the area below the inner cylinder and never attains a velocity magnitude value above 40%. Thereby, indicating that the dead-zone, where mixing will not be efficient, is larger for dished surfaces, a pattern which can also be noticed in Figure 4.

Such poor magnitude values of the velocity clearly confirm the empirical observations of accumulation of particles in the bottom of bioreactor for the dished outwards bottom structure. This aspect will demand the usage of higher rotational velocities to pick up particles settled at the bottom of bioreactor for these shapes. Usage of high rotational speeds could be detrimental to growth of animal cell cultures which are highly sensitive to the hydrodynamics of the fluid. The dished outwards shape which was found to be beneficial in the case of stirred tank bioreactor is clearly a disruptive factor in the case of Taylor bioreactor. Whereas, the idea that dished inward surface could have aided in reducing the dead zone are in the bottom of the bioreactor is proved wrong, as the velocity magnitude for this surface is smaller as compared to the dished outward. In contrast to the stirred tank, the flat bottom offers a significant advantage over the dished surfaces, especially at lower off-bottom clearance areas.

Off-bottom clearance: In contrast to the dished bottom surfaces, where the impact of the geometry is adversely effective up-to a certain height in the gap-width area, the off-bottom clearance flow structures does not interfere in the flow structures of the gap-width area. As soon as the off-bottom clearance height is finished, similar flow structures with similar magnitudes develop in the gap-width area instantly, as represented by the Figures 3(c), 3(d) and 4(b). However, the off-bottom clearance area has a very big disadvantage of completely zero velocity magnitude values in the centre of the obc region for all geometry types presented here. Higher the off-bottom clearance height will be, larger the volume will be with such poor velocity magnitude values which lead towards the dead-zone area located in the middle of the off-bottom clearance area (Figures 3c 3d and 4a).

The flow structure in the gap-width is generated due to the inner rotating cylinder, and is mainly tangential in nature. The axial flow is of secondary nature only, and is not strong enough to sustain flow in the off-bottom clearance area. Unless there is a change in the geometry to help generate flow in the off-bottom clearance area, it will be important to keep it to a minimum height possible. Considering the high sensitivity of the animal cell lines and that the animal cell cultures are generally operated in batch operation mode, one possible change in the geometry could be the influx of axial flow through recirculation to generate some movement in the off-bottom clearance area. However, the idea of recirculation of the fluid requires significant amount of experimental and numerical study, and it is out of scope of this study.

Energy dissipation rate and Kolmogorov scale: In order to use the Taylor bioreactor, the most important constraint will be to keep the energy dissipation rate (EDR) within the sub-lethal responses of a cell-line in order to achieve the desired results. Godoy-Silva *et al.*, 2009) discovered that when cells are cultured in suspension around 60 $W\ kg^{-1} = m^2 s^{-3}$ maximum EDR, the CHO cell line gave the sub lethal physiological responses that are critical to a bioprocess. CHO cell line is one of the most robust cell lines that exist in present time, but there are many cell lines, especially the ones requiring microcarriers, which are much more sensitive and their sub-lethal response should be found at a much lower value (Mollet *et al.*, 2004).

Ibrahim and Nienow (2004) suggested a volume average EDR value of 0.001 Wkg^{-1} to be considered as a base line for culturing cells on microcarriers in stirred vessels. However, Kaiser *et al.*, (2012) and Hewitt *et al.*, (2001) have successfully cultured mesenchymal stem cells at volume averaged EDR values of 0.0021 and 0.0034 $W\ kg^{-1}$ in spinner flasks, a kind of stirred vessel. Santiago *et al.*, (2011) have successfully cultured CHO-K1 cells on microcarriers in a Taylor bioreactor at 50 rpm for a Reynolds no 3660 and volume average EDR of 0.0037 Wkg^{-1}. Mollet *et al.*, (2004) advocated the employment of local EDR instead of volume averaged EDR due to large difference between these two values in some vessels such as spinner flasks, where the difference between the maximum and volume average EDR is more than 100 times (Hewitt *et al.,* 2011, Kaiser *et al.,* 2012). This could mean that the extremely high local values in the impeller regions of a stirred vessel should also be considered as an important factor as the cell damage could be due to these high local values in the impeller region instead of the small volume averaged EDR values. Moreover, when culturing cells on microcarriers the size of microcarriers also play a relevant role (Hewitt *et al.,* 2011, Croughan *et al.*, 1986).

The analytical and numerical estimations of the Taylor bioreactor at 200 rpm are presented in Table 1 using the Wendt (1933)´s empirical correlation to estimate torque, $\tau = G\rho\upsilon^2 h$, where $G=0.23\left(\left(\eta_{rr}^{3/2}\right)/\left(1-\eta_{rr}\right)\right)^{7/4} Re^{1.7}$ alongside the numerical estimations of the torque for the SST-CC turbulence model.

Table 1: Analytical and numerical estimations of the Taylor bioreactor at 200 rpm.

Parameters	Value (Dimensions)	
	Analytic	Numeric
Moment, τ, N m	0.0077	0.0077
Wall shear stress at inner wall, $\tau_{\omega i} = \tau/(2\pi r_i^2 h)$, N m^{-2}	1.96	1.96
Friction velocity at inner wall, $u_{\tau i}=\sqrt{\tau_{\omega i}/\rho}$, m s^{-1}	0.044	0.044
Max EDR at inner wall, $\varepsilon_{innerwall} = u_{\tau i}^4/\nu$, W kg^{-1}	3.86	3.88
Global power, $P = \tau\omega$, W	0.16	0.16
Avg. EDR, $\langle\varepsilon\rangle = P/(\rho\pi(r_o^2 - r_i^2)L)$, W kg^{-1}	0.192	0.193
Avg. Kolmogorov micro-scale, $\langle\eta\rangle = (\upsilon^3/\langle\varepsilon\rangle)^{1/4}$, μ m	47.7	47.7

The numerical estimations of torque and its derivatives are in complete sync with the analytical estimations. As per global estimates of the EDR, the maximum value of 3.9 W kg^{-1} was obtained located at the inner wall for the rotational speed of 200 rpm. Based on the analytical estimations at 150, 100 and 50 rpm, the maximum and mean EDR value would be of 1.5 and 0.09, 0.45 and 0.033, and 0.06 and 0.006 W kg^{-1}, respectively as shown in Table 2.

In order to compare the data with a different geometry type Re/Re$_T$ ratio will be used as the criteria based on the study of Lathrop *et al.*, (1992). Here Re$_T$ is the Reynolds number related to fully turbulent Reynolds number, and its value for stirred vessels is known to be 2×10^4 and in the case of Taylor reactor Lathrop *et al.*, (1992) have shown that Re$_T$ =1.3×10^4. First of all, the impeller rotational speed is not used because it becomes irrelevant for different scales and geometry types. Reynolds number is relevant for the different scales of the same geometry, but when the geometry is changed the significance of Reynolds number also changes as Re$_T$ values are different for different geometry types: the Re$_T$ values for stirred vessels, Taylor-Vortex bioreactor, pipe flow and flat plate are 2×10^4, 1.3×10^4, 2.3×10^4 and 3.2×10^5, respectively (Lathrop *et al.*, 1992). Therefore, for a better comparison between different geometry types, the Re/Re$_T$ ratio presents the option of comparing similar turbulence flow conditions.

For similar Re/Re$_T$ ratio of ≈ 0.14 in comparison with the spinner vessel of Kaiser *et al.*, (2012), the max and mean EDRs are around 50 and 2 times lower. In comparison with the spinner vessel study of Hewitt *et al.*, (2011), at a higher Re/Re$_T$ value of 0.14 the mean EDR is practically half the value. In a Taylor bioreactor, it is important to note that the maximum value is only achieved in the viscous sub-layer very near to the wall where the cells may never reach due to the nature of the viscous layer of providing resistance to any kind of transfer. Away from the wall, the EDR decreases extremely rapidly and its magnitude is much smaller than the maximum value (Coufort *et al.*, 2004, Tokgoz *et al.*, 2012, Van Hout and Katz, 2011).

Table 2: Summary of energy dissipation rate (EDR) for different geometries.

Group	Geometry	Rotational Speed	Reynolds No		EDR Max/Mean
		Rpm	(-)	Re/Re_T	$W\ kg^{-1}$, $m^2\ s^{-3}$
Analytical Estimation	Taylor Bioreactor	200	12077	0.93	3.88/0.193
		150	9058	0.70	1.51/0.09
		100	6039	0.46	0.45/0.033
		50	3019	0.23	0.06/0.006
		30	1812	0.14	0.01/0.002
Kaiser *et al.*, (2012)	Spinner Flask	105	3014	0.15	0.58/0.004
		50	1435	0.07	0.062/0.0006
Hewitt *et al.*, (2011)		50	1690	0.08	(-)/0.0034

It can be further confirmed by the fact that the average EDR, $\langle \varepsilon \rangle$, was found to be 0.193 based on numerical simulations (Table 3). The animal cells are bound to spend the maximum amount of time within a Taylor-vortex in the bulk zone, between R_b = 0.1 to 0.9, where the gradients are much smaller and have similar magnitude (Gong *et al.*, 2006, Hewitt *et al.*, 2011, Kaiser *et al.*, 2012), i.e., similar hydrodynamic conditions in the major part of the reactor. This is a significant advantage for a Taylor bioreactor to be used for culturing animal cells in comparison to the spinner vessel where the probability of cells reaching the high gradient region near the impellers is high and the fluid flow conditions are less uniform with large difference between local and volume averages EDR values. These aspects clearly demonstrate the possibility of using the Taylor bioreactor not only for the suspended cell cultures but also in the case of the microcarrier systems.

Conclusions

The aim of this study was to understand the impact of the changes in the geometrical configuration, namely, off-bottom clearance area and different bottom shapes of the outer cylinder, of a Taylor bioreactor on its flow structure and its practicality as a bioreactor. The bulk zone comprising of the 80 % of the gap-width, where the cell cultures will spend most of the time, has a near constant velocity magnitude of around 50 % of the maximum and VEDR values which are around 10 times smaller in comparison to the boundary layer area, an aspect of great significance which demonstrates the possibility of culturing cells successfully.

The geometrical features of curved surface of outer bottom and off-bottom clearance area which are of practical importance in stirred vessels, impact adversely the flow structures in the Taylor bioreactor due to poor axial velocity component. In comparison with the spinner vessel for similar Re/Re_T ratio, the maximum and mean EDRs were always found to be of lower magnitude values, and due to much less difference between the maximum and the mean values, the Taylor bioreactor presents more uniform structures in comparison to the spinner vessel. These attributes clearly confirm that the Taylor bioreactor is adequate for culturing of animal cells not only in suspension but also for the microcarrier culture systems. This study has provided the authors the guiding light in constructing such a bioreactor which is at present in testing phase with animal cells using the microcarriers.

Acknowledgements

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NOMENCLATURE

b	Gap-width, mm
c	Off-bottom clearance area, mm
h	Height, mm
N_P	Power number, (-)
P	Power, τω, W
Re	Reynolds number, (-)
r	Radial axis, mm
r_i	Inner cylinder radius, mm
r_o	Outer cylinder radius, mm
R_b	Dimensionlized radial axis, r/ b
Ta	Taylor number, (-)
U_{tip}	Tip velocity, r_i ω, m/s
$u_{\tau i}$	Friction velocity at inner wall, $\sqrt{\tau_{\omega i}/\rho}$, m/s
V	Volume, m^3
z	Axial axis, mm
Z_L	Dimensionlized axial axis, z/h
ω	Angular velocity, rad/s
ν	Kinematic viscosity, m^2/s
ε	Avg EDR, $P/(\rho\pi(r_o^2 - r_i^2)L)$, W/kg
$\varepsilon_{innerwall}$	Max EDR at inner wall, $u_{\tau i}^4/\nu$, W/kg
τ	Torque, Nm
$\tau_{\omega i}$	Wall shear stress at inner wall, $\tau/(2\pi r_i^2 h)$, N/m^2
η	Kolmogorov scale, $(\upsilon^3/\langle\varepsilon\rangle)^{1/4}$, µm
η_{rr}	Radius ratio, r_i/r_o
ρ	Density, kg/m^3

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