Optimization of Computer Fluid Dynamics Modeling Using Experimentally Obtained Characteristics of Stirred-Tank Fermentors

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Abstract

Scale-up of bioprocess cultures from bench scale to pilot or production scale requires identifying key engineering characteristics to produce predictable and proportional product yields at each scale. The power number is an important scale-up characteristic of stirred-tank bioreactors as it allows the calculation of impeller power at each scale, thus, enabling constant power-based scale-up. As computer fluid dynamics (CFD) simulation is becoming an economically necessary part of the industrial bioreactor and fermentor design, it is important that CFD results closely match experimentally measured characteristics such as the power number. The default parameters of commercially available CFD software, such as ANSYS® Fluent®, are set to give good results in the most general range of fluid flow conditions; however, they may not be optimal for the specific operating conditions used in bioprocess applications. In this study, we show how we tailored the general default parameters of a CFD model to allow CFD results to better match a specific flow condition used in bioprocess, the flow inside of a stirred-tank fermentor. The characteristic we used as our benchmark is the fermentor's experimentally measured power numbers over a practical range of impeller tip speeds suitable for bacterial fermentation. The results are CFD settings which produced power numbers that agree with our experimental result, and a validated CFD model system that will better predict the performance of new fermentors as we scale up our designs.

> It is most economical to develop new biological and pharmaceutical processes at the smallest scales possible; ideally with equipment that can fit on a laboratory bench.
> Only when a bioprocess produces desirable results at the bench and pilot scales it should be scaled up to the manufacturing scale.
> The Eppendorf BioBLU® Single-Use Vessel portfolio meets this bench-scale requirement with working volumes ranging from 65 mL to 40 L.

Fermentors used in this study

> Bench-scale: BioBLU 3f Single-Use Vessel > Pilot-scale: BioFlo® 610 stainless-steel fermentor

Fig. 1: A. BioBLU 3f Single-Use Vessel. **B.** BioFlo 610 fermentation system.

Table 1: Vessel specifications

	BioBLU 3f	BioFlo 610 100 L
Maximum gas flow (SLPM)	5.6	150.0
Maximum gas flow (VVM)	1.5	1.5
Vessel type	Single-Use	Stainless steel
Working volume (L)	1.25 – 3.75	32.0 – 100.0
V_{max} height* (mm/in)	220.7/8.7	904.0/35.6
Vessel inner diameter (ID) (mm/in)	147.1/5.8	381.0/15.0
V_{max} height: vessel ID	1.5	2.4

*: V_{max} height = height from bottom of the vessel to liquid top surface at maximum vessel working volume

Table 2: Impeller specifications

	BioBLU 3f	BioFlo 610 100 L
Impeller style	Rushton-type	
Impeller material	Polycarbonate	316 L
Impeller quantity	3	3
Impeller diameter (D) (mm/in)	55.9/2.2	165.1/6.5
Impeller spacing (mm/in)	46.0/1.8	254.0/10.0
Impeller diameter: vessel ID	0.38	0.43
Blade height (mm/in)	14.0/0.55	28.4/1.12
Max. agitation (rpm)	1,200	500
Max. tip speed (m/s)	3.51	4.32

Power number

The bioreactor characteristic used as the benchmark to compare the CFD model to the experimental result is the power number.

$$\text{Power number } Np = \frac{2\,\pi\,(M\text{-}M_d)}{\rho\,N^2 d^5}$$

M: torque (N · m)
M_d: dry vessel torque (N · m)
ρ: fluid density (kg/m³)
N: agitation speed (rps)
d: impeller outer diameter (m)

Torque measurement

Experimental torque measurement
The moment on the impeller shaft is measured with a custom torque measuring system that is installed between the electric motor and the impeller drive shaft coupling on top of the BioBLU 3f vessel (Fig. 2A) and at the bottom of the BioFlo 610 vessel (Fig. 2B)

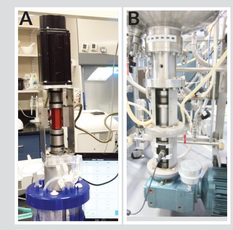

Fig. 2: A. A drive motor and custom torque measuring assembly on top of a BioBLU 3f Single-Use Vessel. **B.** Torque measuring assembly beneath a BioFlo 610 fermentor.

CFD methods

For the CFD modeling, ANSYS Fluent software is used with Fluent's RANS solver (Reynolds Averaged Navier-Stokes). RANS solves the continuity (2) and conservation of momentum (3) equations for fluid through the control volumes delineated by the meshed geometry.

$$\frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \vec{\upsilon}) = 0 \qquad (2)$$

$$\frac{\partial (\rho\ \bar{\upsilon})}{\partial t} + \nabla \cdot (\rho \cdot \bar{\upsilon} \cdot \bar{\upsilon}) = -\nabla p + \nabla\ \bar{\bar{\tau}} + \rho \cdot \bar{g} + \bar{F} \qquad (3)$$

K-ε turbulence models solve the two transport equations for kinetic energy (κ) and eddy energy dissipation (ε). In the Realizable κ-ε model, the kinetic energy transport equation is:

$$\frac{\partial (\rho\kappa)}{\partial t} + \nabla \cdot (\rho \cdot \kappa \cdot \bar{\upsilon}) = \nabla \left[\left(\mu + \frac{\mu_\tau}{\sigma_\kappa} \right) \nabla \kappa \right] + G_\kappa + G_b - \rho \cdot \varepsilon - Y_M + S_\kappa \qquad (4)$$

and the eddy energy dissipation transport equation is:

$$\frac{\partial (\rho\varepsilon)}{\partial t} + \nabla \cdot (\rho \cdot \varepsilon \cdot \bar{\upsilon}) = \nabla \left[\left(\mu + \frac{\mu_\tau}{\sigma_\varepsilon} \right) \nabla \varepsilon \right] + C_{1\varepsilon} (G_\kappa + C_{3\varepsilon}\, G_b) - C_{2\varepsilon} \rho \frac{\varepsilon^2}{\kappa} + S_\kappa \qquad (5)$$

ρ: density,
$\bar{\upsilon}$: velocity vector;
p: pressure
$\bar{\bar{\tau}}$: viscous shear stress tensor
$\bar{g}$: gravity
$\bar{F}$: external force
$\sigma_\kappa, \sigma_\varepsilon$: Prandtl numbers
G_κ: kinetic energy generation
G_b: buoyancy generation
Y_M: fluctuating effects
S_κ: external energy source term

$\mu_\tau = \rho C_\mu \frac{\kappa^2}{\varepsilon}$: turbulent viscosity

$C_\mu, C_{1\varepsilon}, C_{2\varepsilon}, C_{3\varepsilon}$: constants derived from experiments conducted on a wide range of flows

Optimization of the CFD for bioreactor modeling involved adjusting the values of these constants from their default values.

Justification
The constants in the turbulence models are usually based on empirical measurements of general flows like pipe flow or open flow. We are changing the constants specifically for stirred bioreactors. The flow range may be in the laminar-to-turbulent transition where most default constants are set for fully turbulent flow.

Assumptions
There are over 100 assumptions that are made in the computer simulation. Making these assumptions is not a trivial matter, as some assumptions might radically change the results. A few of the more important assumptions are:
> Multiple reference frames (MRFs) to model stationary impellers in zones of rotating flow
> Treatment of the water surface as a flat surface rather than a concave air-water interface
> Geometry simplifications such as eliminating or smoothing smaller geometry details
> Mesh density (5 million elements) is assumed to give mesh-independent results.
> Turbulence models are assumed to give good approximation of turbulence.

Results

The CFD software is able to plot the velocity vectors of the water around the inside of the fermentor.

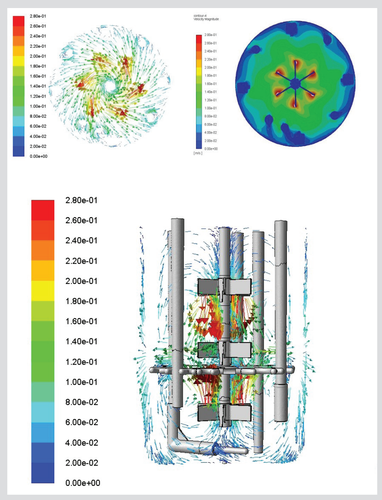

Fig. 3: Velocity vectors and velocity magnitudes in slices through the BioBLU 3f. The vessel contains 3 L of water with an impeller tip speed of 2.8 m/s

The bench-scale BioBLU 3f Np lab values are obtained from a torque meter mounted on top of the BioBLU 3f vessel with the noted impeller configuration. The CFD simulations use the 3-impeller geometry with the noted settings of the turbulence coefficients.

Observations:
> The empirical lab Np values are negatively sloped (decrease with speed).
> The CFD results using the laminar model are negatively sloped but still flatter than the lab results.
> The CFD results (blue) using the default turbulence constants ($C_\mu = 0.09$ $C_{2\varepsilon} = 1.7$) are relatively flat.
> Raising the C_μ to 0.22 increases the average Np to near lab results, but the curve has a positive slope that differs from the negative lab slope.
> Lowering dissipation to $C_{2\varepsilon} = 0.3$ gives a negative slope.
> Setting C_μ to 1.20 and $C_{2\varepsilon} = 0.3$ gives a negative slope with an average Np near lab result.

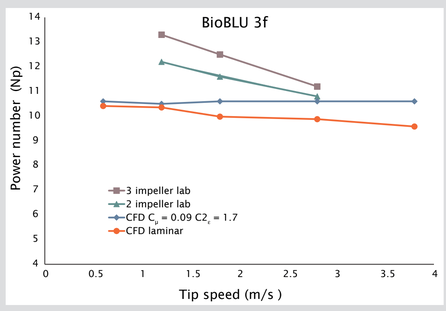

Fig. 4: Power number vs. tip speed experimental and default CFD curves for a 3 L fermentor.

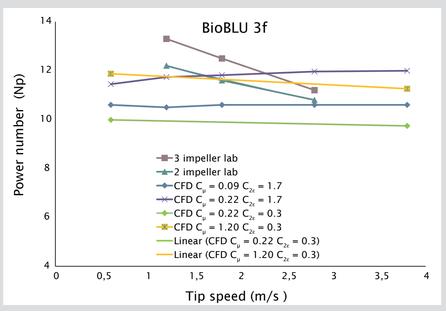

Fig. 5: Power number vs. tip speed experimental and CFD curves for a 3 L fermentor. The added CFD curves are from cases where the turbulence constants are changed from the default values (blue).

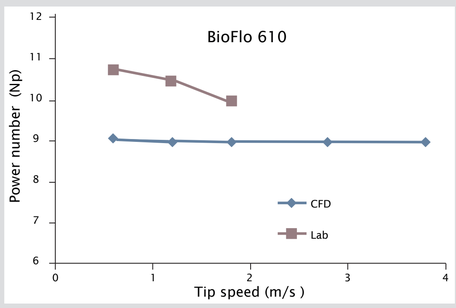

Fig. 6: Power number vs. tip speed experimental and CFD curves for a 100 L BioFlo 610 fermentor.

The 100 L pilot scale BioFlo 610 fermentor lab-obtained power numbers are presented along with CFD results using defaults settings.
> The lab results are negatively sloped vs. the flat CFD default results.
> The next steps are to go through the same optimizing process as the bench scale BioBLU 3f fermentor, and tune the CFD constants to better match the lab results for the pilot scale BioFlo 610 fermentor.

Conclusion

> The use of the Realizable κ-epsilon model is acceptable in CFD modeling of stirred bioreactors.
> Using the default turbulence constants may deliver power number results that are 10 to 15 percent below the power numbers derived from experiments on bench scale-sized bioreactors, and the CFD power number curves are fairly flat compared to the experimentally obtained slopes.
> When the eddy viscosity coefficient, C_μ, is increased to above 0.20, the CFD-derived power number average value increases by 15 percent to match the average values of the experimentally derived power numbers, however, the CFD slope remains flat. The CFD slope can be tuned to give a negative slope like the experimental slope by reducing the $C_{2\varepsilon}$ turbulence constant to one fifth of its default value. The C_μ is increased further to counter the depressed Np values caused by the reduced $C_{2\varepsilon}$.
> The optimized CFD model can be used to scale-up bench-scale processes (1 L to 100 L) to commercial-scale processes (vessels greater than 1000 L).
> This study demonstrates how CFD models can be optimized to specifically predict the performance of bioreactors. The ability of CFD models to predict a commercial-scale process from bench-scale results can save hundreds of hours of design time and prevent costly mistakes in the construction of large commercial-scale bioreactors that may have limited production runs where the cost of design and development really counts.

References

[1] Bin Li and Ma Sha. Scale-Up of Escherichia coli Fermentation from Small Scale to Pilot Scale Using Eppendorf Fermentation Systems. Eppendorf Application Note 306. 2016
[2] ANSYS, Inc. ANSYS Fluent Theory Guide. Release 17.0. January 2016. Canonsburg, PA.

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