

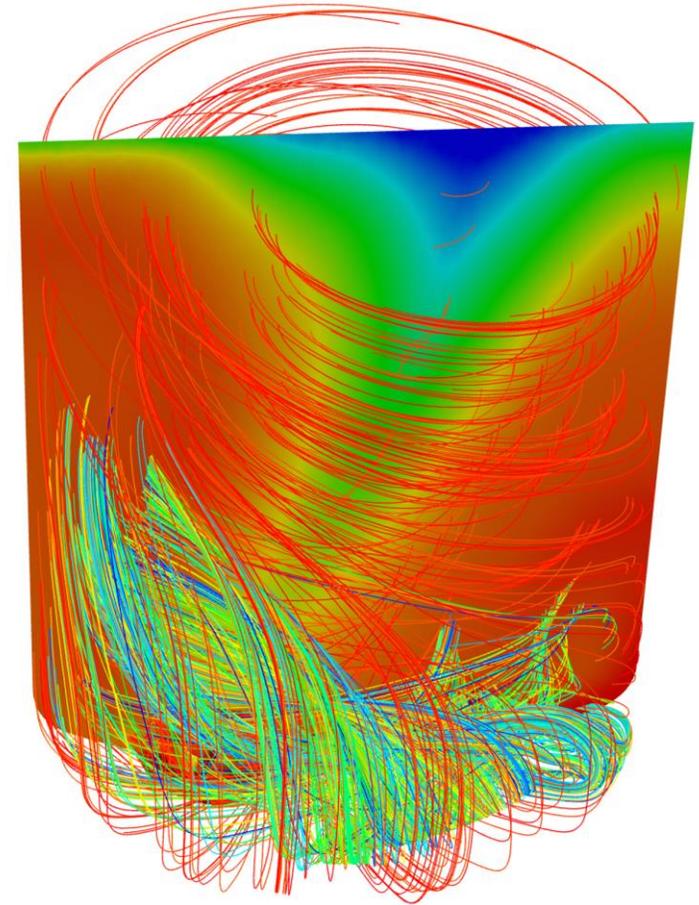


ASEPTCONN AG  
competence in fluid handling

**Mixing Process** Transfer and  
Scale Up for Stirring Tanks by  
Using **CFD Simulations**

Phys. Cosmin Vatra

07.11.2022

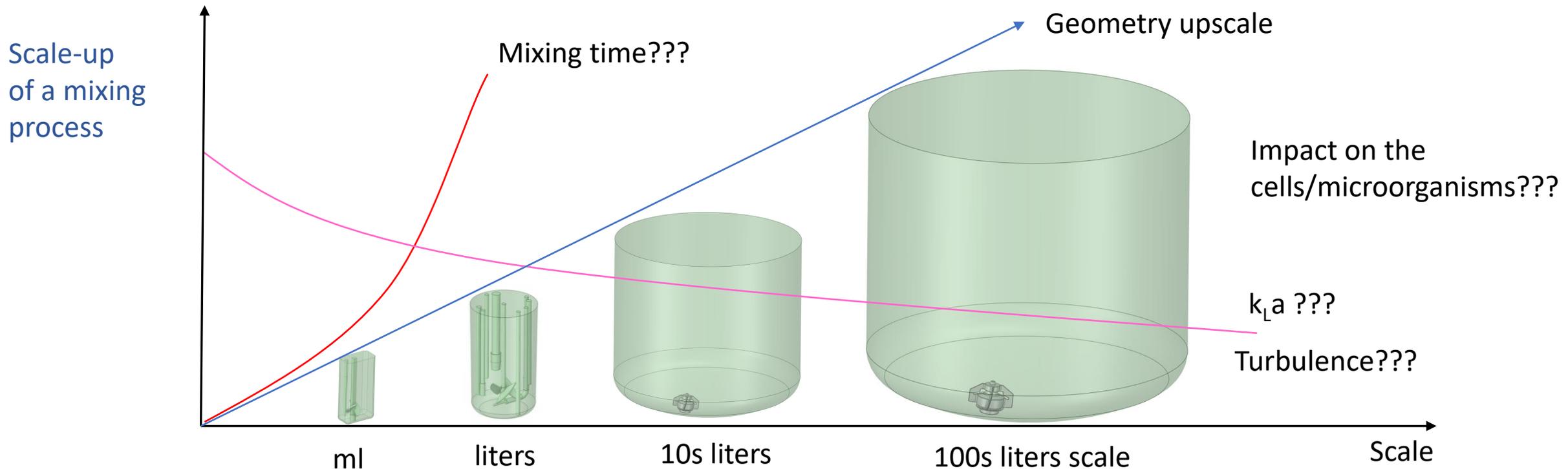


# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations



Mixing processes in stirring tanks or bioreactors are involving nonlinear phenomenon due to which the transfer or scale-up from one specific geometry (tank and one or more mixers) to another is not possible based on simple proportionality criteria. The question is how can we guarantee the mixing efficiency?

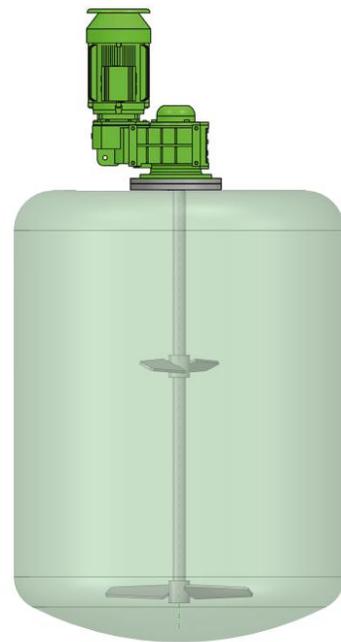


# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations



Even if we are transferring the process to a new system having the same scale, we have the same question: How can we guarantee the mixing efficiency?



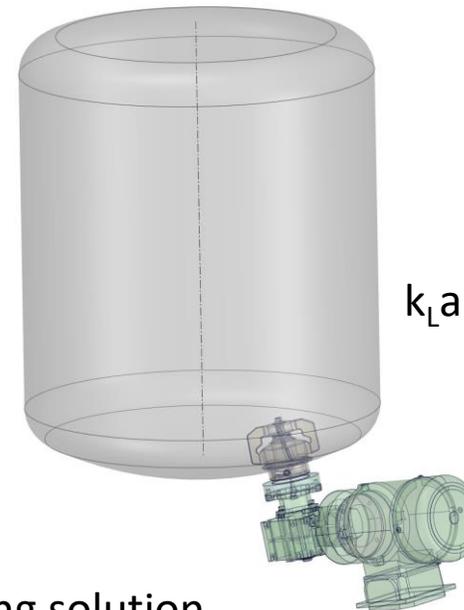
Transfer  
of a mixing process

Mixing time???

Turbulence???

Impact on the  
cells/microorganisms???

$k_L a$  ???



Same scale, but different geometry or mixing solution.

NovAseptic®  
Magnetic coupled mixer

# Mixing Process Transfer and Scale Up for Stirring Tanks

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by Using CFD Simulations



At **Aseptconn**, we can answer to all these questions related to the mixing process transfer and scale-up, with our expertise based on the **CFD simulations!**

# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations



As an example, we are happy to briefly present to you our nice results of the project done for **MSD Animal Health**, a subsidiary of **Merck & Co., Inc.**, **Rahway, NJ, USA**, published in **ChemieXtra** magazine.



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The article was written by me (Msc. Dipl. Phys. Eng. Cosmin Vatra) and Richard Smits, Assoc. Prin. Scientist at MSD Animal Health.

By scanning the QR code, you can read the full article!

CHEMIEXTRA

PUBLIREPORTAGE

## CHEMIEXTRA

Mixing Process Transfer and Scale-Up for Stirring Tanks by Using CFD Simulations

### Two Practical MSD Animal Health Case Studies

Mixing processes in stirring tanks are involving nonlinear phenomenon due to which the transfer or scale-up from one specific geometry (tank and one or more mixers) to another is not possible based on simple proportionality criteria. Comparison between the mixing with two different tank and mixer geometries should consider very complex criteria, and the data obtained with Computational Fluid Dynamics (CFD) simulations are the perfect tool.

MSc. Dipl. Phys. Eng. Cosmin Vatra<sup>1</sup>,  
BSc. Richard Smits<sup>2</sup>

We are presenting hereby the analysis of the transfer of two mixing processes from tanks with paddle type mixers with slow movement, to ones with NovAseptic mixers having pitched impellers.

The first criteria when you transfer or scale-up a mixing process from one geometrical configuration to another, is to check the turbulence regime and try to maintain the same average energy dissipation rate per mass unit. This is a good approach to assure the same dissolving capacity for powders and gases. The second criterion is to check and compare the fluid streams, and internal flows. In case the tanks contain whole cells or microorganism, the third criterion is to check the impact of the new geometry on the cells or microorganisms. If the tanks have fermenter or bioreactor functionalities, the criteria become even more complex and should take into account the volumetric oxygen mass transfer coefficient (k<sub>L</sub>a) and the gas holdup, for which will be important the average value and the distribution through the whole liquid.

Hereby, we are presenting some examples from a project done for MSD Animal Health, a subsidiary of Merck&Co., Inc., Rahway, NJ, USA. The stirring tanks were used in a production phase to mix some liquid ingredients and cells also being present. The tanks do not have spargers for supplying the cells with air or oxygen. Therefore, the k<sub>L</sub>a and gas holdup were not investigated, while the impact on the

CASE no. 1: Comparison of an existing 500 liters tank with a paddle type mixer with a new 500 liters tank geometry equipped with a GMS NovAseptic<sup>®</sup> mixer

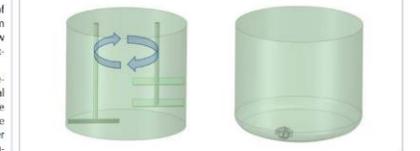


Fig. 1.a: Existing 500 liters tank with paddle mixer. Fig. 1.b: New 500 liters tank with GMS NovAseptic<sup>®</sup> mixer.

CASE no. 2: Comparison of an existing 100 liters tank with a paddle type mixer with a new 100 liters tank geometry equipped with a GM1 NovAseptic<sup>®</sup> mixer



Fig. 12.a: Existing 100 liters tank with paddle mixer. Fig. 12.b: New 100 liters tank with GM1 NovAseptic<sup>®</sup> mixer.

cells was considered, as it has some importance in the process.

Read the complete article here:



[www.aseptconn.ch](http://www.aseptconn.ch)

<sup>1</sup>Aseptconn A.G. – Dietikon, Switzerland  
<sup>2</sup>MSD Animal Health – Baarnse, The Netherlands



# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations



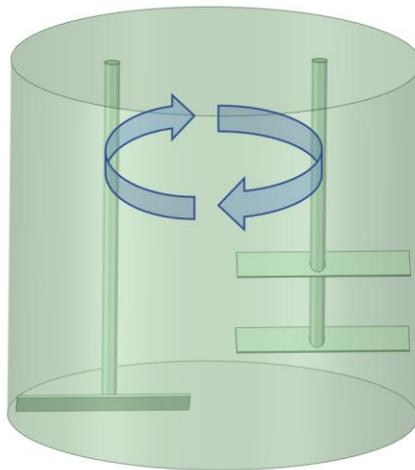
- The first criteria when you transfer or scale-up a mixing process from one geometrical configuration to another, is to check the turbulence regime and try to maintain the same average energy dissipation rate per mass unit. This is a good approach to assure the same dissolving capacity for powders and gases.
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# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations

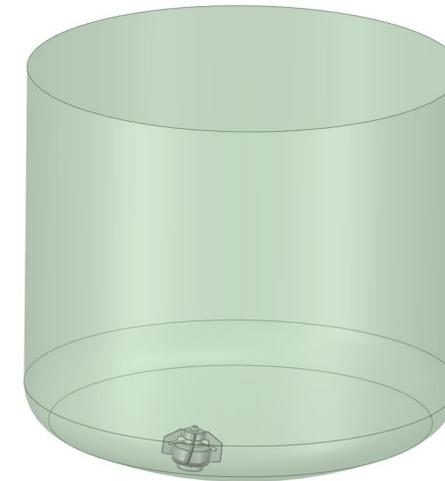


***CASE no. 1: Comparison of an existing 500 liters tank with a paddle type mixer with a new 500 liters tank geometry equipped with a GM5 NovAseptic® mixer***



Existing 500 liters tank with paddle mixer

Transfer  
of the mixing process



New 500 liters tank with GM5  
NovAseptic® magnetic coupled mixer

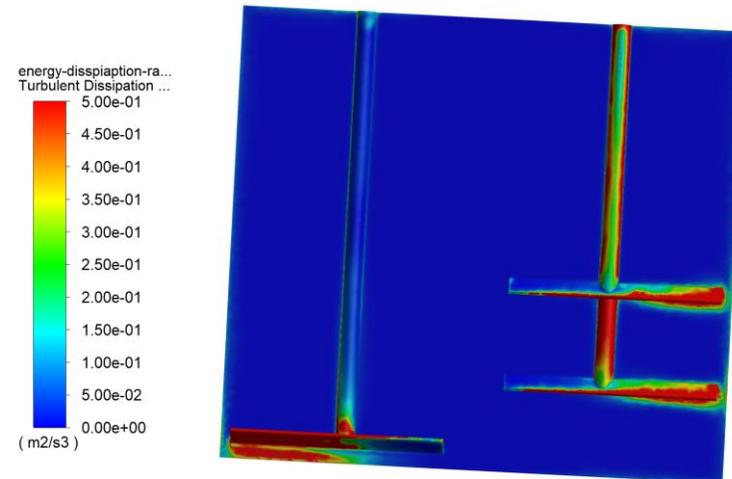
Liquid properties:  
 $\rho=1050 \text{ kg/m}^3$   
 $\mu=1.9 \text{ Pa}\cdot\text{s}$

# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations



The paddle mixer in the existing tank was running at 34 rpm. The CFD simulations done for this tank gave an average energy dissipation per mass unit of  $\varepsilon = 0.02 \text{ m}^2/\text{s}^3$ .

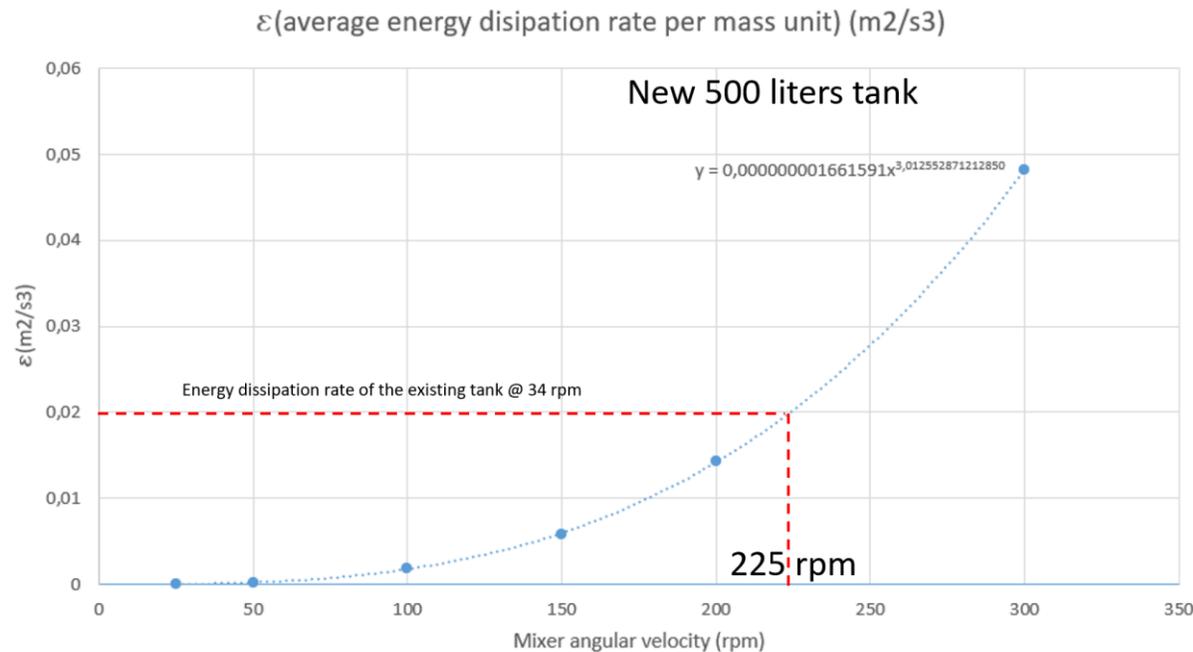


# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations



For the new tank with the NovAseptic® mixer, we have run simulations for different mixer rotational velocities between 25 rpm to 300 rpm, and we had obtained the graphic of  $\epsilon$  as a function of the mixer velocity:



The new tank should run the mixer at 225 rpm, to develop the same energy dissipation rate per mass unit, as the existing tank.



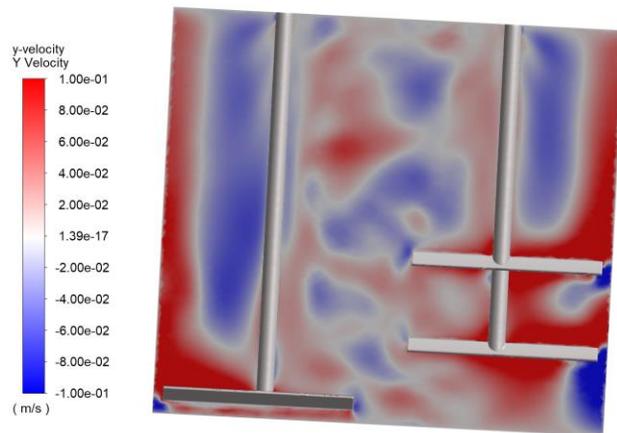
Energy dissipation rate per mass unit for the new 500 liters tank at 225 rpm

# Mixing Process Transfer and Scale Up for Stirring Tanks

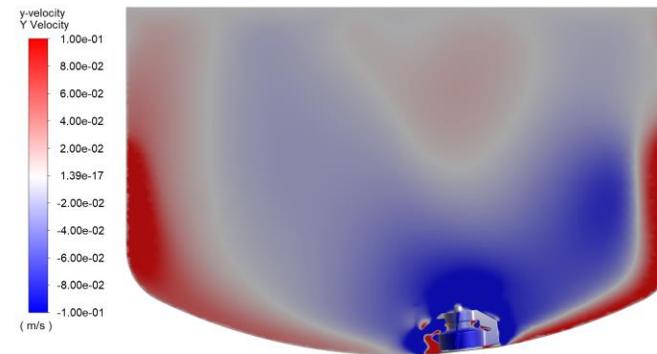
by Using CFD Simulations

Comparison between the vertical flow circulation in both tanks. Velocity on the vertical axis (Y in our case) gives a good picture of the up and down liquid circulation. Representing the vertical velocity colored (from blue to red) symmetrical scale, we will have:

- blue regions: meaning that the fluid is going down (vertical velocity  $< 0$  m/s)
- red regions: meaning that the fluid is going up (vertical velocity  $> 0$  m/s)
- grayed-white: meaning fluid with very low or even zero vertical velocity, which are between the red and blue regions.



**Existing tank (34 rpm): chaotic  
up and down flow regions**



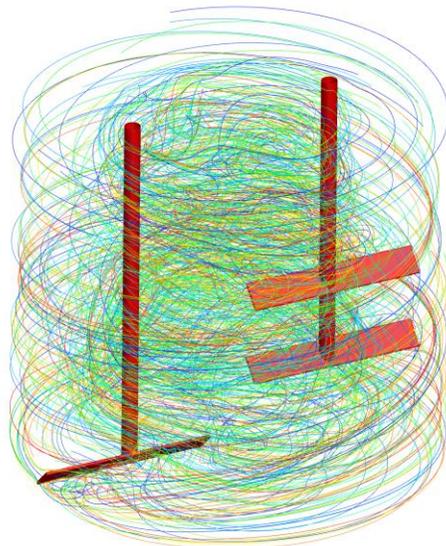
**New tank (225 rpm): good  
up or down flow regions**

# Mixing Process Transfer and Scale Up for Stirring Tanks

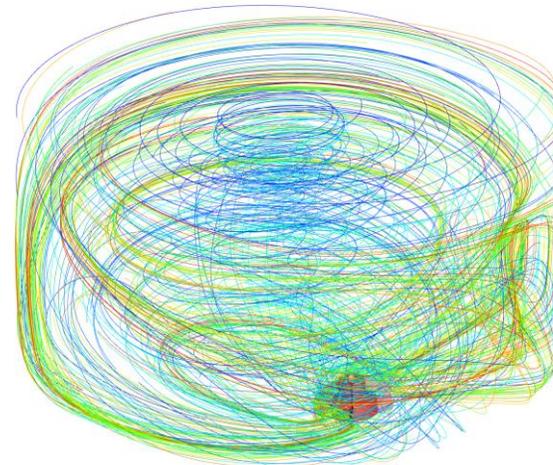
by Using CFD Simulations



The existing tank has chaotic distributed regions with up and down liquid circulation. This means that the fluid is not circulating well between the upper and the lower part of the tank. Contrastingly, the new tank with NovAseptic® mixer, has clear and large areas with up and down liquid circulation into a vortex shape, suggesting that it has better liquid circulations between the upper and the lower part of the tank.



**Existing tank (34 rpm): chaotic streamlines in the center of the tank**

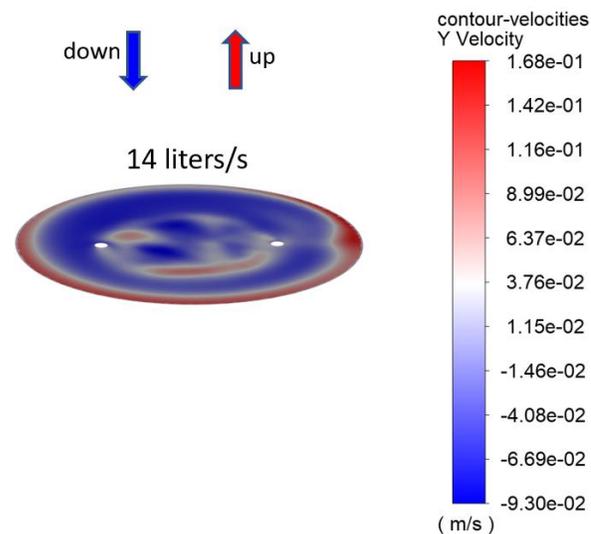


**New tank (225 rpm): good streamlines, having vortex shape**

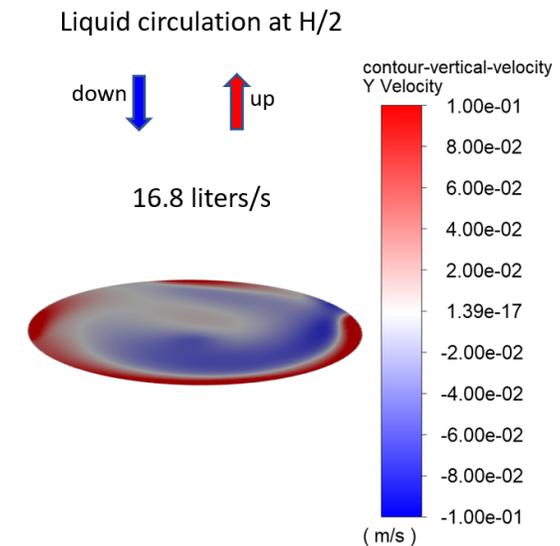
# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations

The up and down flow at halfway up the tank is good in both tanks, but we need to take into consideration that for the existing tank this flow is the result of a chaotic local flow, not a clear stream from top to bottom or bottom to top.



**Existing tank (34 rpm): up and down liquid flow at halfway up the tank**



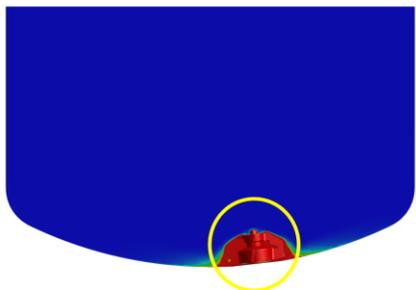
**New tank (200 rpm): up and down liquid flow at halfway up the tank**

# Mixing Process Transfer and Scale Up for Stirring Tanks

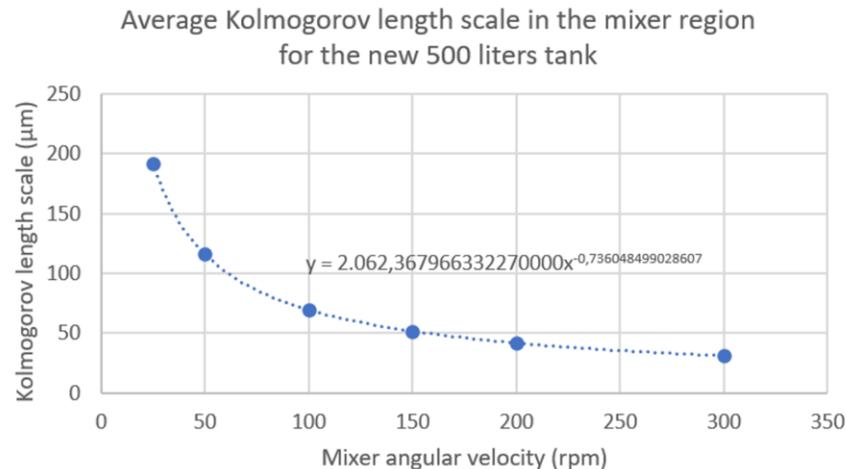
by Using CFD Simulations



Because the new tank with the NovAseptic® mixer should run at a much higher rotational velocity, we should check the impact on the cells. One of the best approaches is to calculate from the CFD data the average of the Kolmogorov length scale in the mixer region. Kolmogorov length scale is establishing the smallest vortices, called eddies, that appear due to the fluid turbulence. If the eddies are equal to or smaller than the cells, then consistent death will appear of the cells. If the eddies are bigger, then the impact will not be significant. We have plotted the CFD data and obtained the average Kolmogorov length scale as a function of the mixer angular velocity:



Mixer fluid region



In our case, the cells have dimensions in the range of 0.2 to 0.5 µm and thus being smaller than the average dimensions of the eddies generated at 225 rpm. Therefore, it is expected that the NovAseptic® mixer at this speed does not have a potential destructive impact on the cells. The same graphic could be used to evaluate the impact on any other cell types.

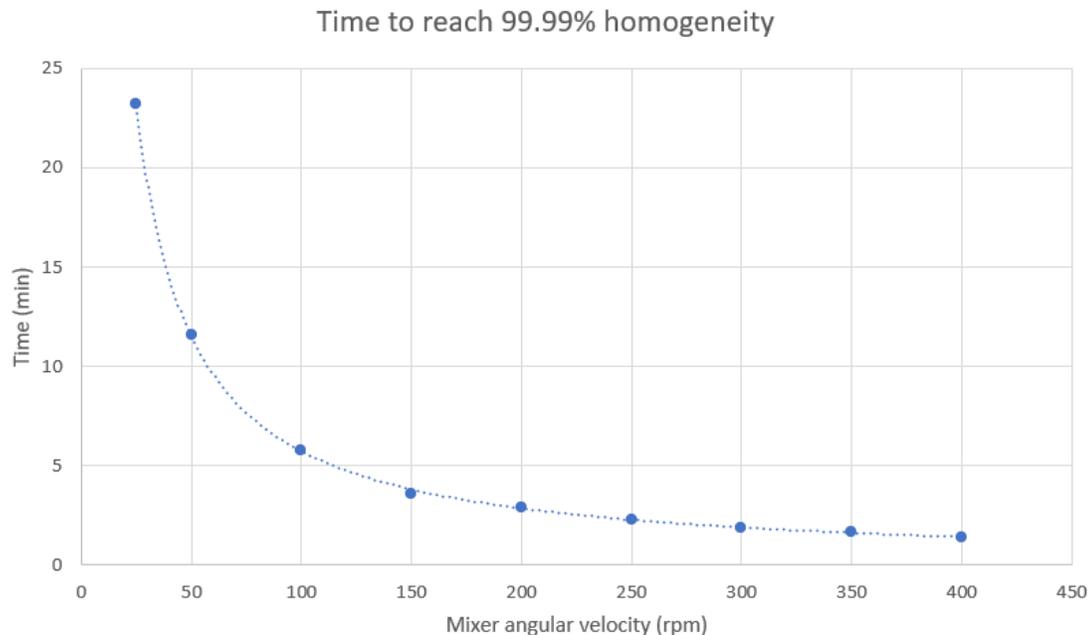
**Average Kolmogorov length scale in the mixer region for the new 500 liters tank**

# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations



The next step was to estimate the mixing time of a passive tracer for the new tank. From the CFD data, we have obtained the bellow graphic:



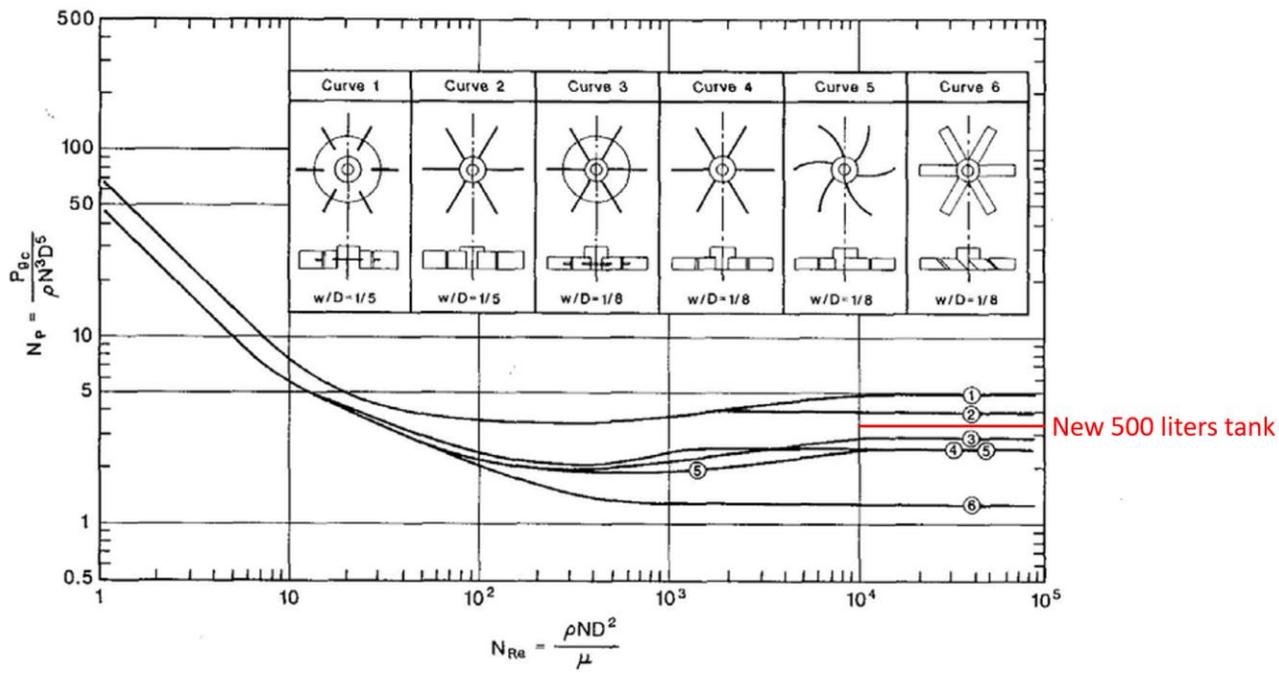
The mixing time to reach 99.99% homogeneity, at 225 rpm, is around 2-3 minutes, which is a very good time for this application.

**Mixing time of a passive tracer for the new 500 liters tank**

# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations

Next point was to calculate the power numbers ( $N_p$ ) of the two tanks as shown in below able and compare them with the common values available from the research literature. The existing tank has a low power number, which means that it has a low capacity to drag the liquid and create radial circulation. The new tank with NovAseptic<sup>®</sup> mixer has a higher power number and can be compared with power numbers of classical Rushton turbines and pitched blade impellers.



Power numbers of existing and new mixer:

Tank	Power number
Existing 500 liters tank with paddle type mixer	0.12
New 500 liters tank with NovAseptic <sup>®</sup> mixer	3.44

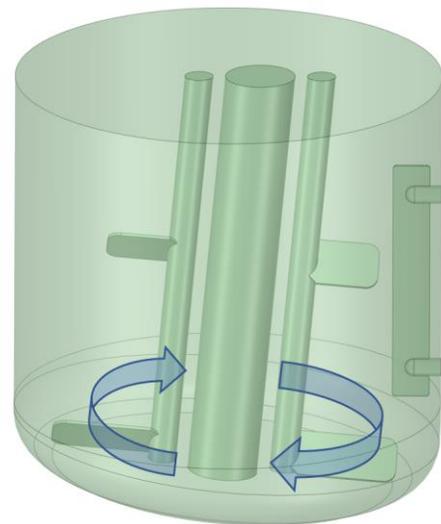
# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations



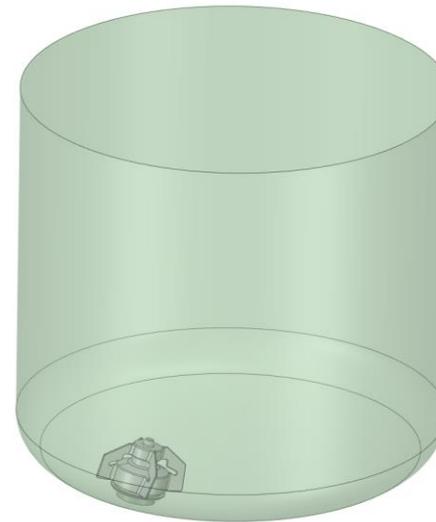
***CASE no. 2: Comparison of an existing 100 liters tank with a paddle type mixer with a new 100 liters tank geometry equipped with a GM1 NovAseptic® mixer***

As the presentation time is limited, we invite you to explore the details of the 2<sup>nd</sup> case directly on the ChemieXtra article, by scanning the below QR code:



**Existing 100 liters tank with paddle mixer**

Transfer  
of the mixing process



**New 100 liters tank with GM1 NovAseptic® mixer**



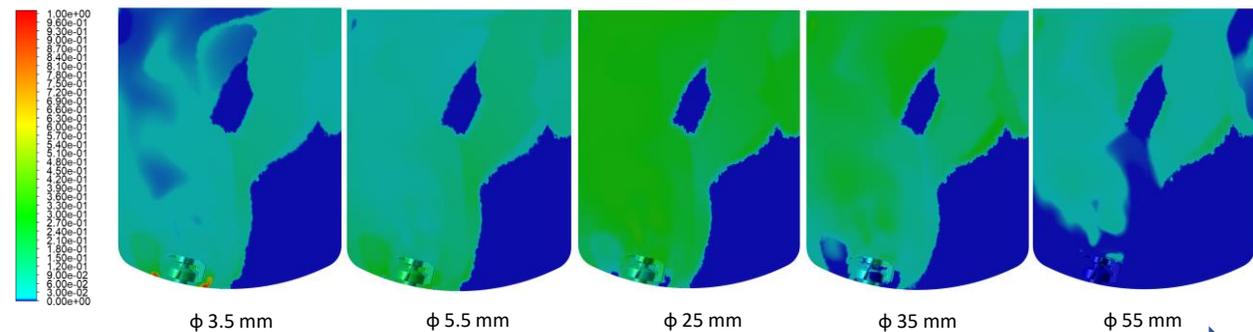
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# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations

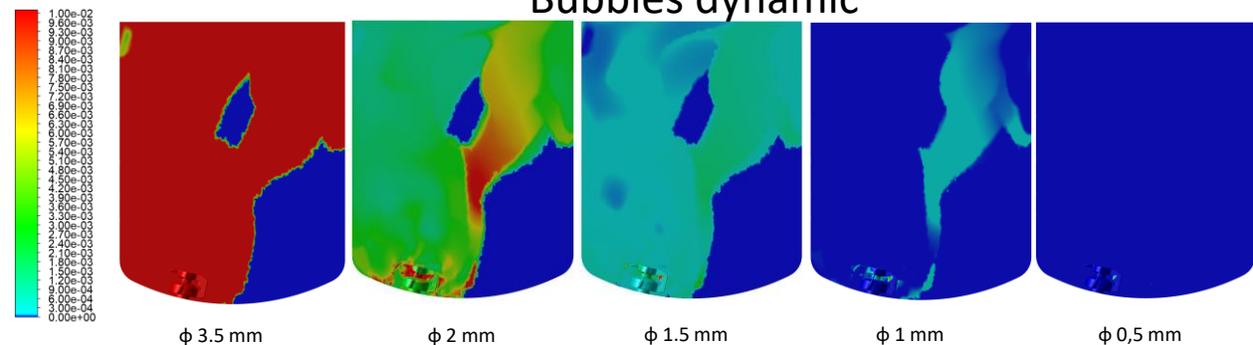


For bioreactors and fermenters, we can do supplementary investigations based on the CFD simulations



Bubbles coalescence

Bubbles dynamic



Bubbles breakage

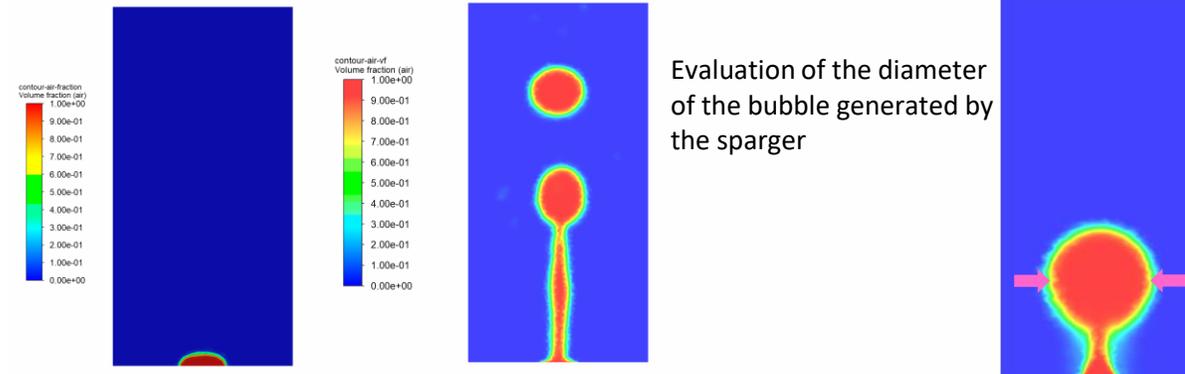
Gas holdup:

Air volume:

Total Volume	(m3)
fluid_mixer	0.00042154673
fluid_tank	0.11649977
Net	0.11692132

Total volume:

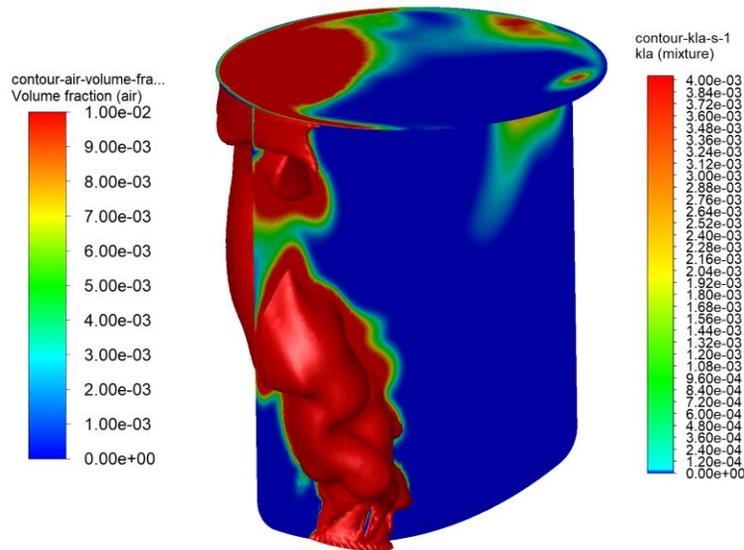
Total Volume	(m3)
fluid_mixer	0.00042154673
fluid_tank	0.11649977
Net	0.11692132



Evaluation of the diameter of the bubble generated by the sparger

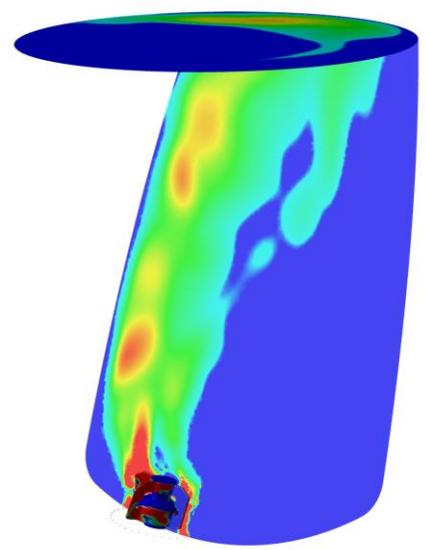
# Mixing Process Transfer and Scale Up for Stirring Tanks

by Using CFD Simulations



mixture	
Volume-Weighted Average	
$k_L$	
fluid_mixer	0.0013236362
fluid_tank	0.00045923409
Net	0.00046235059

mixture	
Volume-Weighted Average	
$a$	
fluid_mixer	176.11447
fluid_tank	3.3332121
Net	3.9561556



mixture	
Volume-Weighted Average	
$k_L a$	
fluid_mixer	0.25577625
fluid_tank	0.0029025925
Net	0.0038143001

- $k_L$  (oxygen mass transfer coeff.)
- $a$  (interfacial area concentration)
- $k_L a$  (volumetric oxygen mass transfer coeff.)

# Mixing Process Transfer and Scale Up for Stirring Tanks

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by Using CFD Simulations



Thank you for your attention!

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