Made available by Hasselt University Library in https://documentserver.uhasselt.be

Batch reactor scale-up of the mixing-sensitive Bechamp reaction based on the heat pulse method Peer-reviewed author version

CAMPS, Lennart; Groth, Urs; Moens; Kuhn, Simon; THOMASSEN, Leen & BRAEKEN, Leen (2022) Batch reactor scale-up of the mixing-sensitive Bechamp reaction based on the heat pulse method. In: CHEMICAL ENGINEERING SCIENCE, 247, (Art N° 116928).

DOI: 10.1016/j.ces.2021.116928 Handle: http://hdl.handle.net/1942/35987

Batch reactor scale-up of the mixing-sensitive Bechamp reaction based on the heat pulse method

Lennart Camps^a*, Luc Moens^b, Urs Groth^c, Leen Braeken^a, Simon Kuhn^d, Leen C.J. Thomassen^a

^aKU Leuven, Department of Chemical Engineering, Centre for Industrial Process Technology, Diepenbeek Campus, Agoralaan Building B box 8, B-3590 Diepenbeek BELGIUM ^bJanssen, Turnhoutseweg 30, 2340 Beerse BELGIUM

^cMettler Toledo GmbH, Heuwinkelstrasse 3, 8606 Nänikon SWITZERLAND

^dKU Leuven, Department of Chemical engineering, Celestijnenlaan 200F, 3001 Leuven BELGIUM

Corresponding Author

*E-mail: Lennart.camps@kuleuven.be; Leen.thomassen@kuleuven.be

HIGHLIGHTS

- 1. Heat-mixing model from 1 to 35 L is developed for mesomixing-sensitive batch processes
- 2. A proof-of-concept scale-up of the mesomixing-sensitive Bechamp reaction validates the model
- 3. The model can be used to perform a scale-down from the pilot to lab scale
- 4. The model can support reactor design and optimisation

ABSTRACT

Knowledge and control of mixing in batch processes can prevent yield losses during scale-up. Therefore, in this study, a new heat-mixing model based ono the measurement of the heat distribution after an applied heat pulse, is proposed. The model was developed to predict mesomixing and support scale-up, scale-down, and design and optimisation of batch reactors. The proposed model considers the influences of rotational speed, stirrer type, solvent, stirrer-to-tank diameter, liquid-height-to-tank diameter, injection time, and pumping number. A strong correlation between the mixing time of the heat pulse method and the mass-transfer coefficient of the mixing-sensitive Bechamp reaction was observed.

KEYWORDS

heat pulse method, scale-up batch reactor, mixing scales, heat and mass mixing, mesomixing, mixing-sensitive solid-liquid reaction.

1. Introduction

Scale-up refers to the transfer of a process to a larger scale and is often a difficult and critical step in industrial production because mass and heat transfer in reactors are influenced by the scale of the process, type of equipment, and process control parameters. Slow mass transfer or mixing causes a slow supply of reagents, thereby limiting the conversion of the reaction with the potential formation of impurities. However, preventing fast side reactions at the industrial scale is difficult (Klaewkla et al., 2011; Paul et al., 2004; Perry et al., 1997; Schwolow et al., 2014). Mixing-related scale-up problems occur when mixing conditions in larger reactors are less effective than those at a smaller scale.

1.1. Mixing scales

A good understanding of the factors that influence mixing and the influence of mixing on a reaction is crucial for the scale-up of batch processes. Three mixing scales are differentiated herein: macromixing, mesomixing, and micromixing. Macromixing is mixing at the largest scale with the circulation time (t_e) as a characteristic value for single-phase macromixing. Mesomixing is the break-up process of large eddies induced by stirrer energy, and it handles the distribution of the feed over the reactor content and the break up of the feed in smaller swirls. As the maximum eddy size is equal to the width of the impeller blades, mixing due to eddies occurs at the meso-scale. The blend time or mixing time signifies the time required to obtain a certain level (%) of homogeneity after an initially inhomogeneous mixture and is characteristic of single-phase mesomixing. Most often, a 95% mixing time (θ_{95}) is used (Bonvillani et al., 2006; Sardeshpande et al., 2016).

The time scale of mesomixing, as shown in Equation 1, is related to energy dissipation (ϵ). Energy dissipation represents the amount of energy that the stirrer added to the mixture in the reactor. Equation 2 shows energy dissipation that depends on the power number (N_p), stirrer diameter (D), rotational speed (N), and volume (V) (Paul et al., 2004).

$$\theta_{95} \sim \varepsilon^{-\frac{1}{3}} \tag{1}$$

$$\varepsilon = \frac{N_p * N^3 * D^5}{V} \tag{2}$$

Micromixing represents mixing at the smallest scale at which the reaction occurs. At this scale, diffusion becomes the most important mixing mechanism for the mass transfer between these lamellar structures. For single-phase micromixing, the micromixing time (t_m) was used as the characteristic value. The micromixing time depends on the kinematic viscosity (v) and energy

dissipation, as shown in Equation 3 (Akiti, 2007; Al-hengari, 2011; Baldyga, 1989; Kukukova et al., 2009; Paul et al., 2004).

$$t_{\rm m} = 17.2 * \left(\frac{\nu}{\varepsilon}\right)^{\frac{1}{2}}$$
(3)

Depending on the dominant mixing scale in the batch process, a different scale-up approach should be used. The scale-up of micromixing- and macromixing-sensitive processes has been thoroughly described by Paul et al. (Monsalve Bravo, 2014; Paul et al., 2004). This study focuses on mesomixing-controlled batch processes.

1.2. Mesomixing scale-up methods

To successfully perform the scale-up of a batch process, mixing it and how it affects the process must be understood (Kukukova et al., 2009; Paul et al., 2004). There are two main approaches to scale-up mesomixing-sensitive processes: scale-up can be based on computational fluid dynamics (CFD) modelling and on mixing time. CFD modelling can describe mixing at different mixing scales depending on the models and equations used. As CFD is based on theoretical models, the simulation of mixing in the reactor requires experimental validation (Kresta et al., 2016; Paul et al., 2004; Sardeshpande & Ranade, 2012).

The scale-up of mesomixing-sensitive processes is often based on the characteristic mixing time. A constant mixing time during scale-up results in the same mesomixing conditions for all reactors (Kukukova et al., 2009; Paul et al., 2004).

Typically, a 95% mixing time was used. The 95% mixing time is based on the homogeneity criterion, which uses the time needed to pass the threshold of 5% from perfect mixing (Bonvillani et al., 2006; Cabaret et al., 2007; Paul et al., 2004; Post, 2010; Rousseaux et al., 2001; Sardeshpande et al., 2016).

Different mixing parameters have been reported to influence the mesomixing time: volume (V), tank height (Z), tank diameter (T), rotational speed (N), stirrer diameter (D), pumping number (N_q), and injection time (t_{inj}). The relation between the mixing time and these mixing parameters has been described in the literature and can be seen in Equations 4–8, with n_1 to n_4 positive decimals (Dickey, 2015; Houcine et al., 2000; James et al., 2017; Paul et al., 2004; Post, 2010).

$$\theta_{95} \sim N^{-1} \tag{4}$$

$$\theta_{95} \sim N_q^{-n_1} \tag{5}$$

$$\theta_{95} \sim \left(\frac{Z}{T}\right)^{n_2} \tag{6}$$

$$\theta_{95} \sim \left(\frac{D}{T}\right)^{-n_3} \tag{7}$$

$$\theta_{95} \sim t_{inj}^{n_4} \tag{8}$$

An increase in rotational speed, pumping number, or stirrer-to-tank diameter improves mixing and consequently results in shorter mixing times, while an increase in tank height or injection time leads to longer mixing times.

Different methods are used to measure the mixing time in batch reactors, and each method has advantages and disadvantages, as described in the review by Ascanio et al. (Ascanio, 2015). Recently, the heat pulse method has been proposed as a new method to characterise the mixing time in batch reactors (Camps et al., 2020).

1.3 Heat pulse method

Camps et al. developed a physical method that uses a heat pulse to measure local mass mixing (Camps et al., 2020). A heat-mixing model distinguishes the contributions of mixing and thermal conduction to 95% mixing time of the heat pulse method. This makes it possible to use the heat pulse method to measure mass mixing in batch reactors (Camps et al., 2020).

Till date, the heat pulse method has only been performed on a 1-L reactor. The objective of this research is to use the heat pulse method on different reactors from the lab scale to pilot scale at varying mixing parameters such as stirrer type, rotational speeds, solvent, baffle, injection time, stirrer diameter, and liquid height. These data were then used to create a scale-up method for mesomixing. Finally, this scale-up method was validated with a mesomixing-sensitive reaction: the Bechamp reaction.

2. Materials and Methods

2.1. Reactor setup

Heat pulse experiments were performed in 1-L, 4-L, 10-L, and 35-L reactors, while the Bechamp reaction was performed in 1-L, 4-L, and 35-L reactors. The reactor setup and the used stirrer types, 45° pitched blade turbine (4PBT), four curved blade turbines (4CBT), and Rushton turbines (6R), are shown in Figure 1. The corresponding dimensions and locations of the temperature sensors (T1-7) are listed in Table 1.





Figure 1. Reactor setup and (A) 4PBT, (B) 4CBT, and (C) 6R

V		1 L	4 L	10 L	35 L
L					
N (RPM)		50-800	100-800	100-500	40–250
T (mm)		99	140	210	400
Z (mm)		105	210	280	300
D (mm)		46	50, 70, 90	93	133, 200
C (mm)		20	35	50	50
Stirrer type		4PBT	4PBT, 6R, 4CBT	4PBT	4PBT, 6R
W (mm)		15	23	30	67
Inj	Z (mm)	37	60	82	120
-	D (mm)	20	20, 30, 40	42	62,95
Baffle	D (mm)	15	14	20	40
	# baffles	0, 1	0, 1, 4	0	0, 4
T1	Z _{T1} (mm)	/	30	45	45
	D_{T1} (mm)	/	55	100	105
T2	Z _{T2} (mm)	37	60	82	120
	$D_{T2} (mm)$	40	55	100	105
T3	Z _{T3} (mm)	57	100	120	170
	D _{T3} (mm)	40	55	100	105
T4	Z _{T4} (mm)	77	150	180	220
	D _{T4} (mm)	40	55	100	105
T5	Z _{T5} (mm)	/	190	230	270
	D _{T5} (mm)	/	55	100	105
T6	Z_{T6} (mm)	/	100	120	170
	$D_{T6} (mm)$	/	55	100	105
Τ7	Z _{T7} (mm)	/	100	120	170
	$D_{T7} (mm)$	/	55	100	105

Table 1. Reactor setup and experimental parameters

2.2. Heat pulse method

All experiments were performed at 20 °C under isoperibolic conditions (a constant temperature difference between the jacket and the reactor). Pt100 1/10 DIN temperature sensors of OMEGA Engineering were used (temperature sensor diameter: 2 mm). For the 1-L scale, three temperature sensors were used, while the 4-L, 10-L, and 35-L scales used seven temperature sensors. Experiments with varying number of temperature sensors indicated that the presence of these temperature sensors did not change the flow pattern in the reactor and consequently did not have an impact on the mixing conditions in the reactor.

Data were collected every 1.6 s using the National Instruments NI9216 and LabView. The time lag of the temperature sensor is corrected, and a loess filter is applied to minimise the noise of the temperature profile in accordance with Camps et al.'s protocol (Camps et al., 2020).

The relative temperature sensor distance is equal to the distance between the temperature sensor and the injection location compared to the tank diameter: $(D_T+D_{inj})/Z$ for T1–T5 and $(D^2_T+D^2_{inj})^{0.5}/Z$ for T6 and T7. Only the temperature sensors located at a relative temperature sensor distance above 0.3 mm are used to calculate the 95% mixing time. The results indicate that for smaller relative temperature sensor distances, an increase in 95% mixing time occurs owing to the slow release of accumulated heat in the sensor. Temperature sensors were placed more than 10 mm from the liquid surface to minimise temperature fluctuations caused by evaporation. Closer to the surface, heat exchange with the environment increases, thereby lowering the signal-to-noise ratio. The signal-to-noise ratio of the temperature probe is the ratio between the measured temperature increase caused by the injected heat and the temperature fluctuations due to the temperature control system. To accurately measure the 95% mixing time, the signal-to-noise ratio is preferably above 10.

All experiments of the heat pulse method were performed with a hot liquid injection because the flow rate and injection time were easily adapted to deliver the required thermal energy pulse for different reactor volumes. The hot liquid injection location, indicated by 'inj', can be seen in Figure 1 and is situated close to the stirrer in order to ensure that the injection location has no influence on mixing. Therefore, mixing was measured at the location of the temperature sensor. Table 2 lists the specifications of the hot liquid injection applied to the different reactors.

V		1 L	4 L	10 L	35 L
V_{flow} (mL/s)		0.3–3	12	30	100
T _{hot liquid} (°C)		80	80	80	80
ΔT_{reator} (°C)		0.1–1	1	1	1
$t_{inj}(s)$		10	1, 10, 30	10	10, 30
Tubing	D _{int} (mm)	2	4	4	8
	Туре	Watson Marlow	PolyFluor	PolyFluor	PolyFluor
	Company				
Pump	Туре	PhD 2000	302S	302S	EcoGold
	Company	Harvard	Watson	Watson	Lauda
		Apparatus	Marlow	Marlow	

Table 2. Hot liquid injection setup

As mixing depends on the dynamic viscosity (μ), density (ρ), heat capacity (c_p), and thermal conductivity (k) of solvents, several solvents are used during the development of the scale-up method. An important heat-mixing characteristic is the Prandtl number that represents the ratio between the momentum diffusivity and thermal diffusivity, as shown in Equation 9.

$$Pr = \frac{v}{\alpha} = \frac{\mu * c_p}{k} \tag{9}$$

Toluene, propionic acid, water, ethylene glycol, 2-octanol, and 2-propanol were used as solvents, and their characteristics are listed in a previous paper by Camps et al. (2020). The solvents cover

a wide range of parameters that influence heat mixing while keeping other parameters constant. In this manner, a model which maps all these influences on heat transfer can be developed. For example, a comparison between propionic acid and water is appealing because both have similar solvent characteristics, except for thermal diffusivity. By comparing the influence of water and propionic acid on heat mixing, the influence of thermal diffusivity was studied.

2.3. Pumping number

The pumping number or flow number indicates the amount of fluid, moved by a stirrer at a certain rotational speed, and is dependent on the reactor size and geometry. The pumping numbers of lab- and pilot-scale batch reactors have an important influence on mixing but are not often described in the literature. Therefore, CFD modelling in the rotating machinery mixer model of Comsol Multiphysics® 4.4 is used to calculate the pumping numbers of the different reactors and stirrers. The k-ɛ turbulence model solves the Reynolds-averaged Navier–Stokes equations (RANS) (Paul et al., 2004). No-slip boundary conditions were applied to solid surfaces. Tetrahedral meshes with a normal size result in pumping numbers are mesh-independent. Relative tolerances below 0.001 for the stationary solver of the RANS equation lead to the modelling solution of the pumping number (Alliet-Gaubert et al., 2006; Brucato et al., 2000; Sommerfeld & Decker, 2004; Torotwa & Changying, 2018).

2.4. Vortex depth

At high rotational speeds, centrifugal forces on the liquid can create vortices in unbaffled reactors. This changes the mixing pattern and thus affects the mixing in batch reactors. The vortex depth is visually determined but can also be calculated using the equations summarised by Markopoulos & Kontogeorgaki (Markopoulos & Kontogeorgaki, 1995). These equations use a

vortex factor ($h_v/h_{v,max}$), which is the ratio of the vortex depth (h_v) to the maximal vortex depth ($h_{v,max}$), where the vortex reaches the stirrer blades (Devi & Kumar, 2017; Dickey, 2015; Markopoulos & Kontogeorgaki, 1995; Myers et al., 2002).

2.5. Bechamp reaction

Agrawal et al., Devlin et al., and Popat et al. described the reaction mechanism of the mixingsensitive Bechamp reaction, where aromatic nitro compounds are reduced by the oxidation of iron particles. The three reaction steps are shown in Equations 10, 11, and 12.

$$\Phi \text{-NO}_2 + \text{Fe}^0 + 2 \text{ H}^+ \rightarrow \Phi \text{-NO} + \text{Fe}^{2+} + \text{H}_2\text{O}$$
(10)

$$\Phi - \mathrm{NO} + \mathrm{Fe}^{0} + 2 \mathrm{H}^{+} \rightarrow \Phi - \mathrm{NHOH} + \mathrm{Fe}^{2+}$$
(11)

$$\Phi\text{-NHOH} + \text{Fe}^0 + 2 \text{ H}^+ \rightarrow \Phi\text{-NH}_2 + \text{Fe}^{2+} + \text{H}_2\text{O}$$
(12)

The Bechamp reaction was performed at three different reactor volumes: 1 L, 4 L, and 35 L, which has 0.8 L, 4 L, and 35 L of demineralised water, respectively. The reagents, except the iron particles, were heated to 60 °C and maintained at this temperature for at least 30 min to fully homogenise nitrobenzene in the reaction mixture. The reaction started when iron particles were added to the reactor. The reagents used are listed in Table 3.

Substance	Company	Purity (%)	Amount		
			1 L	4 L	35 L
Fe ⁰ 5-9 micron	Sigma-Aldrich	/	2.0 g	8.0 g	70 g
Formic acid	Sigma-Aldrich	98	1.3 g	5.4 g	47 g
Nitrobenzene	Sigma-Aldrich	99	1.6 g	6.3 g	55 g

Table 3. Bechamp reaction reagents

A 1-mL sample was taken after 0, 1, 2, 4, 7, 9, 14, 19, and 29 min to measure the concentration during the reaction. This sample was added to 5 mL of toluene (Sigma-Aldrich, 99.8%) and cooled

in an ice bath to stop the reaction. After extraction, the toluene fraction was analysed by splitless GC-FID analysis with an HP-5ms column and N₂ as the carrier gas. After the temperature increased by 5 °C/min between the starting temperatures of 100 °C and 130 °C, the temperature was increased by 25 °C/min until a temperature of 300 °C was reached. A calibration curve was used to determine the concentrations of nitrobenzene and aniline.

Agrawal et al. and Popat et al. performed kinetic studies on the Bechamp reaction and observed that mass transfer, more specifically the adsorption on the iron surface, is the limiting step in the reduction of nitroaromatic compounds. Each of the three reaction steps can be presented as a firstorder reaction, where the reaction rate of each reaction step is determined by mass transfer, as shown in Equation 13 (Agrawal & Tratnyek, 1996; Popat & Padhiyar, 2013).

$$\frac{dC}{dt} = k_m * a * C \tag{13}$$

The least-squares method was used to fit the model with the reaction profile and to determine the mass-transfer coefficients of the reaction steps. The mass-transfer coefficient (k_m) of the third reaction step (phenylhydroxylamine to aniline) was used as a characteristic value for the reaction because mixing influences were more easily detected in the third reaction. Before the third reaction occurs, the first and second reaction steps have already oxidised part of the limiting amount of iron particles. This decrease in interfacial area slows the reaction and makes mixing influences easier to observe. Equation 14 is used to determine the amount of unoxidised iron surface (a) during the reaction (Agrawal & Tratnyek, 1996; Choe et al., 2004; Kirk et al., 2004; Popat & Padhiyar, 2013).

$$\frac{da}{dt} = -\frac{dC_{nitrosobenzene}}{dt} - \frac{dC_{phenylhydroxylamine}}{dt} - \frac{dC_{aniline}}{dt}$$
(14)

3. Results and Discussion

3.1. Heat pulse method

Injection rate. To accurately measure the mixing time of the heat pulse method at different reactor volumes, the signal-to-noise ratio of the temperature probe above 10 is preferred. Therefore, the pulse power or injection time changes with increasing reactor volume. There are two ways to increase pulse power. First, the temperature of the injected hot liquid can be increased up to the boiling temperature of the solvent. Second, the volumetric flow rate of the injected liquid can be increased. Figure 2 shows the influence of the flow rate on the 95% mixing time at an injection time of 10 s in a 1-L reactor with 800 mL of water at 100 rpm.



Figure 2. Influence of flow rate on the 95% mixing time with the 4PBT in a 1-L reactor

Earlier reported experiments by Camps et al. are all performed at a flow rate of 0.3 mL/s in a 1-L reactor (Camps et al., 2020). At a flow rate below 1.0 mL/s, eddies break up the added fluid to the smallest scale, preventing accumulation of the hot liquid at the mesoscale. Therefore, the heat pulse method measures micromixing. By increasing the flow rate to 1.5 mL/s or higher, a shift from micromixing to the mesomixing regime is experimentally noticeable. The hot liquid accumulates at the mesoscale, indicating that mesomixing influences the heat pulse method at flow rates above 1.5 mL/s. The indication of the mesomixing regime at flow rates above 1.5 mL/s is confirmed by the 95% mixing time, which is related to the reciprocal of the rotational speed (Paul et al., 2004). The signal-to-noise ratio increased as the volumetric flow rate increased. Therefore, the heat pulse method is easier to perform in the mesomixing regime than in the micromixing regime (Kresta et al., 2016; Paul et al., 2004).

Mixing parameters. Different mixing parameters were tested on the four different reactors: solvent characteristics (Prandtl number), vortex formation $(h_v/h_{v,max})$, volume (V), tank height (Z), tank diameter (T), rotational speed (N), stirrer diameter (D), pumping number (N_q) , and injection time (t_{inj}) . Figure 3 shows the influence of the mixing parameters on the 95% mixing time. The experiments shown in Figure 3 were performed with an injection time of 10 s, except for Figure 3F. The figure also shows the model trends, which will be discussed in the heat-mixing model section.



Figure 3. Influence of (A) stirrer-to-tank diameter, (B) stirrer type, (C) baffles, (D) volume, (E) solvent, and injection time (F) on 95% mixing time. Markers with error bars indicate experimental data points (n = 3), whereas the predicted values by the model as shown in Equation (9) are presented by lines.

All measurements and trends in Figure 3 are expressed as a function of rotational speed. When the rotational speed increased, the 95% mixing time decreased. However, at high rotational speeds, the rotational speed only has a limited influence on the 95% mixing time as all curves flatten. Figure 3A shows the influence of the stirrer on the tank diameter. A larger stirrer diameter results in more stirrer energy transferred to the liquid, and eddies with more energy are induced, thereby improving mixing and reducing the 95% mixing time. However, this increase in the stirrer energy also accelerated the formation of a vortex. For example, by increasing the stirrer-to-tank diameter from 1/2 to 2/3 in a 4-L reactor, the vortex reaches the stirrer at a rotational speed of 200 rpm instead of 400 rpm.

The stirrer type changes the pumping number, which has an influence on the 95% mixing time, as shown in Figure 3B. The pumping numbers were simulated by COMSOL CFD modelling. Table 4 shows the simulated pumping numbers of the four downward pitched blade turbines (4PBT), six bladed Rushton turbines (6R), and four curved blade turbines (4CBT) on the 1-L, 4-L, 10-L, and 35-L scales.

V	D/T	4PBT	6R	4CBT
1 L	1/2	0.8		/
4 L	1/3	/	/	2.6
	1/2	0.8	1.3	2.2
	2/3	/	/	1.8
10 L	1/2	0.8	/	/
35 L	1/2	1.5	/	/
	1/3	/	2.5	/

Table 4. Pumping numbers in the 1-L, 4-L, 10-L and 35-L reactors for the 4PBT, 6R and 4CBT

 determined by CFD

4CBT has a higher pumping number than 6R and 4PBT. By increasing the stirrer to the tank diameter, the pumping number decreased. An increase in the pumping number results in a higher flow of liquid in the reactor and therefore better mixing and a reduction in the 95% mixing time (Figure 4B).

Figure 3C shows the influence of baffles in the 35-L reactor. At low rotational speeds, there is no vortex formation, and the fully baffled (4 baffles) and unbaffled reactor setups have similar 95% mixing times. Once a vortex is present in the reactor, which occurs at 100 rpm in the unbaffled reactor, mixing no longer improves.

Figure 3D shows a decrease in 95% mixing time with increasing stirring speed for the 1-, 4-, 10-, and 35-L reactors. The stirrer-to-tank diameter and liquid-height-to-tank diameter determine the mixing performance so that for the reactors with varying (D/T and Z/T), no clear trend for increasing reactor size was detected.

The solvent characteristics were described by the Prandtl number (Figure 3E). 2-Octanol has a higher Prandtl number than water (109 versus 6.99) because 2-octanol has higher viscosity and lower thermal conductivity. A higher Prandtl number deteriorates mixing and therefore increases the mixing time by 95%.

Finally, the injection time was studied (Figure 3F). When the injection time was increased at a constant injection rate, the 95% mixing time also increased. Experiments were performed with injection times of 1, 10, and 30 s, and all experiments were mesomixing-sensitive. However, when the injection time is further increased or the injected volume is decreased, the 95% mixing time can become micromixing-sensitive because longer injection times give the eddies more time to break up the fluid elements. In this study, only experiments in the mesomixing regime were performed.

Heat-mixing model. In total, 316 experiments were performed to study the influence of mixing on the 95% mixing times of the heat pulse method. Our developed heat-mixing model is based on the literature correlations between mixing parameters and the 95% mixing time, as shown in Equations 4–8. In addition, the power number, Prandtl number, and vortex depth were considered. The best fit for the constants and factors of each relevant factor influencing mesomixing was calculated using the least-squares method. This results in a heat-mixing model to determine mixing in the mesomixing regime, as shown in Equation 15.

$$\theta_{95} = \frac{7 * (P_T)^{0.1} * 1.6^{\frac{h_v}{h_v,max}} * \left(\frac{Z}{T}\right)^1}{N * \left(\frac{D}{T}\right)^1 * N_q^{0,7}} + t_{inj}$$
(15)

Figure 4 shows the statistical correlation between the predicted 95% mixing times of the model and the experimental 95% mixing times.



Substance	Value	
R ²	0.948	
Correlation coefficient	0.974	
Maximum error	7.28 s	
Average error	1.28 s	
Mean squared error	2.67 s	

Figure 4. Linear relation between the predicted and experimental values with a 20% error margin (- -) and statistical values of the model

The predicted and laboratory values correspond well, with less than 20% error between the model and experimental values of the 95% mixing time for 99% of the measurements. The heatmixing model with $R^2 = 0.95$, has a significantly higher R^2 value compared to the often-used model based on energy dissipation only (Equation 1), with $R^2 = 0.71$.

This mesomixing model uses the pumping number instead of the power number to describe the contribution of the stirrer to the model. As micromixing relies on the energy that can be used to break up fluid elements to smaller sizes, it depends on the power number, as described by Camps et al. (2020) and others. However, mesomixing occurs at a larger scale and thus depends on the distribution of these fluid elements over the reactor content. Therefore, the amount of liquid that the stirrer can move (the pumping number) is more relevant. This is also confirmed by the higher R^2 value of the mesomixing scale-up model with either the pumping number ($R^2 = 0.95$) or the power number ($R^2 = 0.89$).

For all experimental parameters, as shown in Figure 3, the trends predicted by the model are visualised by full lines. There were no significant differences between the lab and model values when introducing different stirrer types, solvents, injection times, and stirrers-to-tank diameters D/T of 1/2 and 1/3 (Figure 3B, E, F, A). However, for D/T=1/3, the model overestimated the mixing performance at low rotational speeds (Figure 3A). Figure 3C shows a good match between the model and lab values, indicating that the model is able to predict the influence of vortex formation. However, the model overestimated the experimental 95% mixing times at low rotational speeds in a small reactor volume (1 L and 4 L) with baffles. This is because the baffles concentrate mixing near the stirrer; therefore, the overall mixing performance is poorer. The developed model did not consider this influence. This deviation is expected to be insignificant because experiments at the lab scale are mainly performed at relatively high rotational speeds.

Baffles are applied to prevent the formation of a vortex, which mainly occurs in pilot- and industrial-scale reactors (≥ 10 L) and at relatively high rotational speeds.

The mixing times of the different reactor volumes were predicted using the model (Figure 3D). In the model, the stirrer-to-tank diameter and liquid-height-to-tank diameter are used to account for the reactor volume.

3.2. Bechamp reaction

Mass-transfer coefficient.



Figure 5. Concentration profile of nitrobenzene (■) and aniline (●) and the modelled values of nitrobenzene (—) and aniline (- -) in the 4-L reactor at 500 RPM with the 4PBT

Figure 5 shows the concentration profiles of nitrobenzene and aniline in the 4-L reactor at 500 rpm with 4PBT. The concentration of nitrobenzene decreased until all iron was oxidised after 540 s, where the nitrobenzene concentration no longer changed. Nitrobenzene reacts with nitrosobenzene and further reduces to phenylhydroxylamine and aniline. These intermediate reaction steps to aniline cause a small delay in aniline formation. The concentration of aniline

increased until a plateau was reached at 540 s, indicating that the Fe^0 surface atoms were exhausted. Only the concentrations of nitrobenzene and aniline were measured; therefore, the mass balance is not complete, as shown in Figure 5.

Figure 5 shows a good match between the experimental and modelled values of the first-order reaction of Equation 13 with a maximal error of 25%. There are two reasons for the underestimation of aniline concentration by the model. First, it is assumed that after every reaction step, the formed product is desorbed from the iron surface and transferred back to the aqueous solution. For the next reaction, the reagent is adsorbed to the iron surface again, where it reacts further. In reality, not all formed products return to aqueous solutions, and some of the formed product will immediately further react with the Fe²⁺ ion or with a neighbouring Fe⁰ atom (Agrawal & Tratnyek, 1996). Second, the available reaction spots at the iron surface are estimated to decrease linearly with an increase in the reaction products. In reality, oxidised Fe²⁺ ions can further react with Fe³⁺ and Fe₃O₄ (Popat & Padhiyar, 2013). Therefore, the decrease in reaction spots at the iron surface is not linear, which has a small impact on the profile of the interfacial area during the reaction and, therefore, on the concentration profile of aniline.

The mass-transfer coefficient of the reaction was calculated based on Equation 9, using the concentration profile of aniline. The mass-transfer coefficient at 500 RPM with 4PBT in the 4-L reactor was 0.009 s^{-1} .

Mixing influences. Mixing is the rate-limiting step in the Bechamp reaction. Therefore, the mass-transfer coefficient of the Bechamp reaction was used to characterise the mixing. Figure 6 shows the influences of the rotational speed, stirrer type, stirrer diameter, and baffles on the mass-transfer coefficient. There is typically a 10% experimental error in the results: experiments with the four curved blade turbine (4CBT) at 400 RPM in the 4-L reactor are repeated three times,

resulting in a k_m of 0.018 \pm 0.002 s⁻¹. Other determinations of k_m -values, each based on a concentration profile comprising nine measurements, were performed once.



Figure 6. Influence of (A) rotational speed, (B) stirrer type, (C) stirrer-to-tank diameter, and (D) baffles on the mass-transfer coefficient of the Bechamp reaction

From 250 to 400 rpm, the mass-transfer coefficient increases until the vortex reaches the upper end of the stirrer blades at 500 rpm (Figure 6A). The reduction in the mass-transfer coefficient is caused by the solid-body rotation of the liquid (Assirelli et al., 2008). Moreover, air entrainment, which is caused by the vortex, can oxidise the iron particles resulting in less iron atoms to react in the Bechamp reaction. Indeed, at 500 rpm, the reaction under nitrogen atmosphere has a higher mass-transfer coefficient (0.010 s⁻¹) than that under an air atmosphere (0.008 s⁻¹), indicating that air entrainment oxidises the iron particles.

Figure 6B shows the influence of the stirrer type on the mass-transfer coefficient at 400 rpm in the 4-L reactor. The radial stirrers—6R and 4CBT—have a higher mass-transfer coefficient compared to the axial stirrer—4PBT.

The stirrer-to-tank diameter of 2/3 causes a decrease in the mass-transfer coefficient compared to 1/3 and 1/2, as shown in Figure 6C. The large stirrer diameter resulted in a vortex that reached the upper end of the stirrer blades at 400 rpm. This resulted in a lower mass-transfer coefficient compared to the other stirrer diameters. Furthermore, higher air entrainment causes oxidation of iron particles.

Figure 6D shows the influence of baffles at 400 and 800 rpm in the 4-L reactor. At 400 rpm, the reaction under baffled conditions had a lower mass-transfer coefficient than that under unbaffled conditions. Under these conditions, only a minor vortex was present.

At 800 rpm, the baffles increased the mass-transfer coefficient. The baffles prevented the formation of a vortex that reached the upper end of the stirrer blades and improved mixing in the reactor.

Scale-up of the Bechamp reaction Figure 7 shows the relation between the heat pulse method and the Bechamp reaction because both the heat pulse method and the Bechamp reaction are influenced in the same manner by mixing parameters such as the rotational speed, stirrer-to-tank diameter, stirrer type, and baffles. The results of the heat pulse experiments were expressed as the 95% mixing time minus the injection time. In this manner, only the influence of mixing is considered as the value, and the variation in injection time does not have an impact.

Figure 7. Relation between the 95% mixing time and mass-transfer coefficient at 1 L(\blacksquare), 4 L(\bullet), and 35 L(\blacktriangle)

A linear correlation between 95% mixing time and mass-transfer coefficient was observed, indicating that the reaction was mesomixing-dependent. Better mesomixing indicates a lower 95% mixing time as well as an increase in the mass-transfer coefficient. A 95% mixing time minus the injection time of zero (x = 0) signifies infinitely fast mixing. Therefore, the extrapolated intercept value of 0.022 represents the reaction rate constant, as only the reaction kinetics influence the reaction.

The two groups of results deviate from the trend and are not shown in Figure 7. The results in the baffled reactors at a low rotational speed in the 1- and 4-L reactors and the results in the unbaffled reactors, where the vortex reaches the upper end of the stirrer blades. At low rotational speeds, the baffles cause a decrease in mixing because the baffles concentrate mixing energy around the stirrer to prevent distribution over the entire reactor content. As indicated earlier, baffles are used to prevent the formation of a vortex and are therefore mainly applied at a high rotational speed.

In addition, the linear trend between 95% mixing times and the reaction does not hold when a vortex reaches the upper end of the stirrer blades. The vortex causes air (O_2) entrainment and consequently oxidation of iron, whereby less Fe⁰ is available for the Bechamp reaction. The air entrainment does not affect the heat pulse method; therefore, the experiments wherein a vortex is formed are not relevant to compare the mixing time of the heat pulse method and the mass-transfer coefficient of the Bechamp reaction.

4. Conclusion

We herein describe the development of a heat-mixing model from the lab to the pilot scale in the mesomixing regime. The model includes the influence of the rotational speed, stirrer type, stirrer-to-tank diameter ratio, liquid height-to-tank diameter, pumping number, solvent (Prandtl number), and injection time. An R² of 0.95 confirmed that the model was able to accurately predict mixing in different reactors from 1 L to 35 L.

The heat pulse model was used to scale-up the Bechamp reaction. The mass-transfer coefficient of this solid–liquid reaction was mesomixing-dependent. Therefore, a linear dependency between the mass-transfer coefficient of the reaction and the 95% mixing time of the heat pulse method was observed. However, the scale-up method is unable to predict the mass-transfer coefficient at low rotational speeds in a baffled lab-scale reactor and when a large vortex is present.

Applicability and ranges of heat-mixing model. The developed heat pulse model, which measures mesomixing, has three applications.

The model can be used as a scale-up method for mesomixing-sensitive batch processes.
 Once a mesomixing-sensitive reaction suffices to a reaction criterion (conversion,

selectivity, mass-transfer coefficient, among others), a heat pulse experiment can be performed to measure the 95% mixing time. The scale-up model translates the 95% mixing times at the lab scale to the rotational speed of the pilot-scale reactor. This results in mixing scale-up, where the same mesomixing occurs at the lab and pilot scales. Other parameters besides the rotational speed can also be changed, such as the stirrer-to-tank diameter or stirrer type.

- 2. The model can be used as a scaled-down method for mixing. The 95% mixing time was measured using the heat pulse method, applying the best mixing conditions at the pilot scale. By performing the reaction at the lab scale under mixing conditions with the same 95% mixing time, the scalability of the reaction can be measured. If the reaction criterion (yield, purity, among others) is not achieved, improvements to the mixing conditions in the pilot-scale reactor are needed by changing parameters such as stirrer type, stirrer-to-tank diameter, reactor geometry, and dosing strategy.
- 3. The model can be used for reactor design and optimisation of mixing. The influence of rotational speed, stirrer type, stirrer-to-tank diameter, liquid-height-to-tank diameter, pumping number, solvent (Prandtl number), and injection time on mesomixing were included in the model. Therefore, the method can be used to design the dimensions of a reactor or stirrer or to determine the best mixing conditions in a reactor for a dedicated solvent or reaction mixture.

The heat pulse model for the scale-up of mesomixing-sensitive batch processes can only be used within the validated ranges of the injection position and time, solvent parameters, reactor dimensions, and impeller and baffle dimensions:

- The injection was located close to the stirrer, within a distance of 2 cm, and the injection time was varied from 1 s to 30 s. The injection was adjusted to obtain a signal-to-noise ratio of the temperature probe above 10 to enable accurate measurements.
- Prandtl numbers between 1 and 16 times the Prandtl number of water were tested. Around 96% of all commonly used solvents are characterised by Prandtl numbers within this range (Kauffman & Jurs, 2001; Marcus, 2003);
- 3. Experiments were performed in flat and dished bottom reactors with volumes between 1 and 35 L. The liquid-height-to-tank diameter ratio was varied from 0.4 to 1.3. For reactor volumes of 100 mL, the heat pulse method is unable to measure mixing because the temperature sensors are either at a relative temperature sensor distance below 0.3 or very close to the surface, resulting in a signal-to-noise ratio that is too low to perform experiments. However, it is expected that the model will also be applicable to reactors with volumes larger than 35 L. To validate the heat pulse method for scale-up to the production scale, additional tests need to be performed at a large pilot scale (V = 200-600 L) and at the industrial scale (V = 1000-5000 L).
- 4. The heat pulse model is applicable to 4PBT, 4CBT, or 6R single impellers between 30 and 1200 rpm. The stirrer-to-tank diameter ranged from 1/3 to 2/3.
- 5. Experiments were performed in an unbaffled or flat-blade baffled reactor setup with one baffle or four baffles. However, the model overestimates mixing in the 1-L and 4-L reactors at low rotational speeds because the baffles concentrate mixing near the stirrer, resulting in a poorer overall mixing performance.

In future experiments, broader experimental ranges can be validated (larger reactor volumes, other stirrer types, among others), thereby increasing the applicability of the model.

ACKNOWLEDGMENT

The financial support of the KU Leuven Impulsfonds IMP/16/023 is gratefully acknowledged by the authors. Janssen, part of Johnson & Johnson, and Mettler Toledo made this work possible.

NOMENCLATURE

Symbol	Definition	Unit
С	concentration	mole L ⁻¹
c _p	specific heat capacity	J kg ⁻¹ K ⁻¹
D	diameter of the stirrer	m
$h_{\rm v}$	vortex height	m
h _{v,max}	maximal vortex height	m
k	thermal conductivity	$W m^{-1} K^{-1}$
km	mass-transfer coefficient	s ⁻¹
Ν	rotational speed	s ⁻¹
Np	power number	dimensionless
Nq	pumping number	dimensionless
Р	power	W
Pr	Prandtl number	dimensionless
t	time	S
t _{inj}	injection time	S
tm	micromixing time	S
Т	tank diameter	m
V	reactor volume	m ³

28

V_{flow}	volumetric flow	mL s ⁻¹
Ζ	liquid height	m
Greek Lett Symbol	ters Definition	Unit
θ_{95}	95% mixing time	S
μ	dynamic viscosity	Pa s
ρ	density	kg m ⁻³
ν	kinematic viscosity	m ² s ⁻¹

REFERENCES

- Agrawal, A., & Tratnyek, P. G. (1996). Reduction of nitro aromatic compounds by zero-valent iron metal. *Environmental Science and Technology*, 30(1), 153–160. https://doi.org/10.1021/es950211h
- Akiti, O. (2000). Turbulent Mixing And Chemical Reaction In Baffled Stirred Tank Reactors: A
 Comparison Between Experiments And A Novel Micromixing-Based Computational Fluid
 Dynamics Model. New Jersey Institute of Technology. Dissertations.
 https://digitalcommons.njit.edu/dissertations/420
- Al-hengari, S. (2011). Process Intensification : A Study of Micromixing and Residence Time Distribution Characteristics in the Spinning Disc Reactor. Newcastle University. Dissertations. https://theses.ncl.ac.uk/jspui/handle/10443/1771
- Alliet-Gaubert, M., Sardeing, R., Xuereb, C., Hobbes, P., Letellier, B., & Swaels, P. (2006). CFD analysis of industrial multi-staged stirred vessels. *Chemical Engineering and Processing: Process Intensification*, 45(5), 415–427. https://doi.org/10.1016/j.cep.2005.11.003
- Ascanio, G. (2015). Mixing time in stirred vessels: A review of experimental techniques. Chinese

 Journal
 of
 Chemical
 Engineering,
 23(7),
 1065–1076.

 https://doi.org/10.1016/j.cjche.2014.10.022

- Assirelli, M., Bujalski, W., Eaglesham, A., & Nienow, A. W. (2008). Macro- and micromixing studies in an unbaffled vessel agitated by a Rushton turbine. *Chemical Engineering Science*, 63(1), 35–46. https://doi.org/10.1016/j.ces.2007.07.074
- Baldyga, J. ;Bourne J. R. (1989). Simplification of Micromixing Calculations. I. Derivation and Application of new model. *The Chemical Engineering Journal*, 42(2), 83–92. https://doi.org/10.1016/0300-9467(89)85002-6.
- Bonvillani, P., Ferrari, M. P., Ducrós, E. M., & Orejas, J. A. (2006). Theoretical and experimental study of the effects of scale-up on mixing time for a stirred-tank bioreactor. *Brazilian Journal* of Chemical Engineering, 23(1), 1–7. https://doi.org/10.1590/S0104-66322006000100001
- Brucato, A., Ciofalo, M., Grisafi, F., & Tocco, R. (2000). On the simulation of stirred tank reactors via computational fluid dynamics. *Chemical Engineering Science*, 55(2), 291–302. https://doi.org/10.1016/S0009-2509(99)00324-3
- Cabaret, F., Bonnot, S., Fradette, L., & Tanguy, P. A. (2007). Mixing Time Analysis Using Colorimetric Methods and Image Processing. *Industrial & Engineering Chemistry Research*, 46(14), 5032–5042. https://doi.org/10.1021/ie0613265
- Camps, L., Moens, L., Groth, U., Kuhn, S., Braeken, L., & Thomassen, L. C. J. (2020).
 Characterization method for mass mixing in batch reactors based on temperature profiles
 Lennart. *Chemical Engineering Research & Design*, 136248.
 https://doi.org/10.1016/j.cherd.2020.02.004
- Choe, S., Liljestrand, H. M., & Khim, J. (2004). Nitrate reduction by zero-valent iron under different pH regimes. 19, 335–342. https://doi.org/10.1016/j.apgeochem.2003.08.001

- Devi, T., & Kumar, B. (2017). Vortex depth analysis in an unbaffled stirred tank reactor with concave blade impeller. *Chemistry and Chemical Technology*. 11(3), 301–307. https://doi.org/10.23939/chcht11.03.301
- Dickey, D. S. (2015). Tackling difficult mixing problems. *Chemical Engineering Progress*, 111(8), 35–42.
- Houcine, J., Plasari, E., & David, R. (2000). Effects of the stirred tank's design on power consumption and mixing time in liquid phase. *Chemical Engineering and Technology*, 23(7), 605–613. https://doi.org/10.1002/1521-4125(200007)23:7<605::AID-CEAT605>3.0.CO;2-0
- James, J., Cooke, M., Kowalski, A., & Rodgers, T. L. (2017). Scale-up of batch rotor-stator mixers. Part 2—Mixing and emulsification. *Chemical Engineering Research and Design*, 124(2), 321–329. https://doi.org/10.1016/j.cherd.2017.06.032
- Kauffman, G. W., & Jurs, P. C. (2001). Prediction of surface tension, viscosity, and thermal conductivity for common organic solvents using quantitative structure-property relationships. *Journal of Chemical Information and Computer Sciences*, *41*(2), 408–418. https://doi.org/10.1021/ci000139t
- Kirk, R. E., Othmer, D. F., Grayson, M., & Eckroth, D. (2004). Kirk-Othmer Encyclopedia of Chemical Technology (p. 540). Wiley.
- Klaewkla, R., Arend, M., & Hoelderich, W. F. (2011). A Review of Mass Transfer Controlling the Reaction Rate in Heterogeneous Catalytic Systems. *Mass Transfer - Advanced Aspects*, 3, 667–684. https://doi.org/10.5772/22962
- Kresta, S. M., Etchels, A. W., Dickey, D. S., & Atiemo-Obeng, V. A. (2016). Advances in Industrial Mixing: A Companion to the Handbook of Industrial Mixing.

https://doi.org/10.1017/CBO9781107415324.004

Kukukova, A., Aubin, J., & Kresta, S. M. (2009). A new definition of mixing and segregation: Three dimensions of a key process variable. *Chemical Engineering Research and Design*, 87(4), 633–647. https://doi.org/10.1016/j.cherd.2009.01.001

Marcus, Y. (2003). The properties of solvents. John Wiley & Sons.

- Markopoulos, J., & Kontogeorgaki, E. (1995). Vortex Depth in Unbaffled Single and Multiple Impeller Agitated Vessels. *Chemical Engineering & Technology*, 18, 68–74. https://doi.org/10.1002/ceat.270180113
- Monsalve Bravo, G. M. (2014). An approximation to the scale-up of batch processes using phenomenological-based models. Universidad Nacional de Colombia. Dissertation. http://www.bdigital.unal.edu.co/12567/
- Myers, K. J., Reeder, M. F., & Fasano, J. B. (2002). Optimize mixing by using the proper baffles. *Chemical Engineering Progress*, 98, 42-47.
- Paul, E. L., Atiemo-Obeng, V. A., & Kresta, S. M. (2004). Handbook of Industrial Mixing. Science and Practice. John Wiley & Sons. https://doi.org/10.1002/0471451452
- Perry, R., Green, D., & Maloney, J. (1997). Perry's chemical engineers' handbook. In *Journal of Chemical Education* (7th Issue). The McGraw-Hill companies. https://doi.org/10.10360071422943
- Popat, V., & Padhiyar, N. (2013). Kinetic Study of Bechamp Process for P-Nitrotoluene Reduction to P-Toluidine. *International Journal of Chemical Engineering and Applications*, 4(6), 401– 405. https://doi.org/10.7763/IJCEA.2013.V4.334
- Post, T. (2010). Understand the real world of mixing. *Chemical Engineering Progress*, 106(3), 25–32. https://doi.org/10.1038/nrmicro1165

- Rousseaux, J.-M., Muhr, H., & Plasari, E. (2001). Mixing and micromixing times in the forced vortex region of unbaffled mixing devices. *The Canadian Journal of Chemical Engineering*, 79(5), 697–707. https://doi.org/10.1002/cjce.5450790501
- Sardeshpande, M. V., Kumar, G., Aditya, T., & Ranade, V. V. (2016). Mixing studies in unbaffled stirred tank reactor using electrical resistance tomography. *Flow Measurement and Instrumentation*, 47(October), 110–121. https://doi.org/10.1016/j.flowmeasinst.2016.01.003
- Sardeshpande, M. V., & Ranade, V. V. (2012). Computational fluid dynamics modelling of solid suspension in stirred tanks. *Current Science*, *102*(11), 1539.
- Schwolow, S., Heikenwälder, B., Abahmane, L., Kockmann, N., & Röder, T. (2014). Kinetic and scale-up investigations of a michael addition in microreactors. *Organic Process Research and Development*, 18(11), 1535–1544. https://doi.org/10.1021/op5002758
- Sommerfeld, M., & Decker, S. (2004). State of the art and future trends in CFD simulation of stirred vessel hydrodynamics. *Chemical Engineering and Technology*, 27(3), 215–224. https://doi.org/10.1002/ceat.200402007
- Torotwa, I., & Changying, J. (2018). A Study of the Mixing Performance of Different Impeller Designs in Stirred Vessels Using Computational Fluid Dynamics. *Designs*, 2(1), 10. https://doi.org/10.3390/designs2010010