NEWSLETTER

Solving a Batch Reactor Scale-Up Failure Using VisiMix

No.10- December 2025

Introduction

Scaling up a batch reaction from pilot to production scale often presents challenges that are not immediately evident during development. Even when standard scale-up criteria such as geometric similarity and equivalent mixing time are applied, differences in local hydrodynamics can significantly influence reaction selectivity and product quality. These subtle variations—particularly in reactant distribution and concentration uniformity—are difficult to detect experimentally but can have a substantial impact on competitive or fast reactions.

Mixing simulation provides a structured and reliable approach to evaluate these effects before and after scale-up. By enabling engineers to visualize and quantify mixing behaviour across scales, VisiMix supports faster diagnosis of scale-up deviations and helps identify actionable improvements.

In this newsletter, we highlight a **real case study** where a batch reactor scale-up led to increased by-product formation despite matching mixing times. Using VisiMix Turbulent, the engineering team identified the underlying issue and implemented a straightforward modification to the feeding strategy, resulting in a successful resolution.

The Challenge

A pharmaceutical manufacturer attempted to scale up an organic reaction that involved a desired main reaction and an undesired competing side reaction:

- **Main reaction: A + B → C**
- **Side reaction: B + B → D**

At the development stage, the reaction was carried out in a **2 L reactor,** where the product consistently met purity requirements and the formation of by-product D remained minimal. This provided confidence that the process was well understood under small-scale mixing conditions.

During scale-up to a **1230 L production reactor,** the team applied **mixing time equivalence** as the primary criterion, assuming that similar global mixing performance would ensure comparable reaction selectivity. However, upon executing the process at production scale, several unexpected issues emerged:

- **Higher by-product formation** (reaction B + B → D)
- **Lower purity of main product (C)**
- **Inconsistent reaction behavior** despite matching mixing time

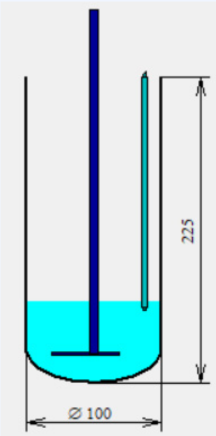
These deviations indicated that, although overall mixing time was matched, the local hydrodynamics and distribution of reactant B were not replicated at the larger scale. Since the reaction scheme clearly shows that by-product formation increases at high local concentrations of B, any non-uniformity in mixing can significantly impact selectivity. This demonstrated that mixing time alone was insufficient for scaling, and a deeper assessment of mixing behaviour and reactant distribution was necessary to identify the root cause.

VisiMix Simulation Approach

The team utilized VisiMix Turbulent and conducted a detailed simulation.

Step-1: Laboratory simulation:

VisiMix Turbulent was first used to simulate the 2 L reactor to understand its hydrodynamics and reaction environment. The simulation evaluated key parameters such as macromixing time, the influence of the baffle, the impeller flow pattern, the local concentration profile of reactant B, and the fast reaction behavior for the main reaction (A + B → C). This established a clear baseline of the conditions that originally produced the desired product quality at pilot scale.



TANK WITH ELLIPTICAL BOTTOM

Inside diameter	100	mm
Total tank height	224.8	mm
Total volume	1.7	l
Level of media	59.26	mm
Volume of media	0.4	l

DE DIETRICH BEAVERTAIL BAFFLE

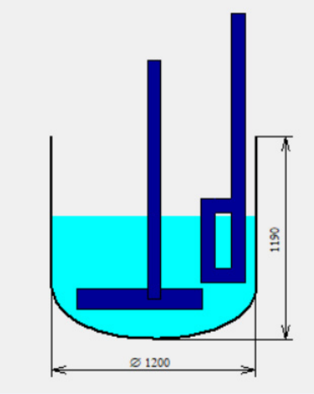
Number	1	
Width	5	mm
Dist. from bottom	55	mm
Dist. from wall	10	mm

GLASS LINED IMPELLER 1

Tip diameter (D)	60	mm
Number of blades	3	
Width of blade	3	mm
Dist. from bottom	20	mm
Rotational speed	250	Rpm
Motor power	0.1	KW

Step-2: Production Simulation:

Similarly, a second VisiMix model was created for the 1230 L production reactor, and the key scale-up parameters were evaluated to understand how the mixing environment differed from the pilot scale.



TANK WITH ELLIPTICAL BOTTOM

Inside diameter	1200	mm
Total tank height	1190	mm
Total volume	1233	l
Level of media	718.9	mm
Volume of media	700	l

TUBULAR BAFFLE-2

Number	1	
Tube diameter (D)	3.6	in
Length (L)	500	mm
Dist. from bottom	330	mm
Dist. from wall	59	mm
Angle to radius (fi)	0	deg

GLASS LINED IMPELLER 1

Tip diameter (D)	900	mm
Number of blades	3	
Width of blade	133	mm
Dist. from bottom	225	mm
Rotational speed	50	Rpm
Motor power	3.3	KW

KEY SIMULATION FINDINGS

- **Macro mixing time:**

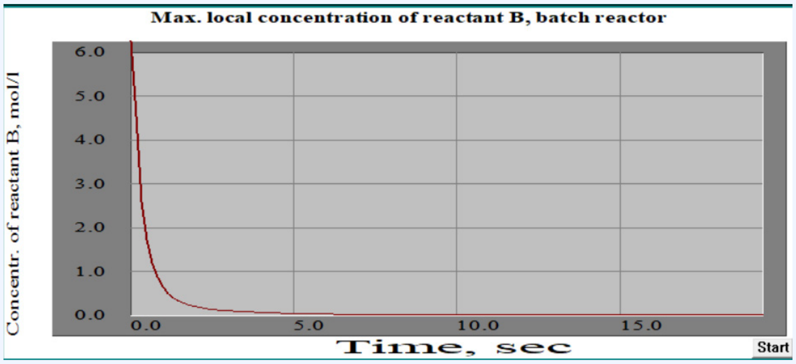
In lab: **13.5 sec**

In production reactor: **11.7 sec**

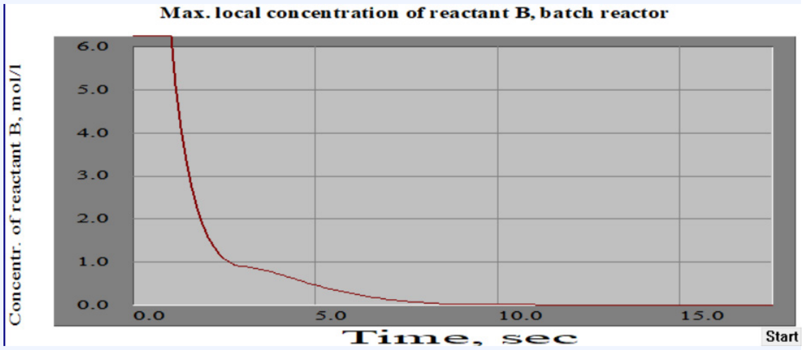
Pilot and production reactors showed similar mixing times, confirming that the mixing time was not the source of the problem.

- **Distribution of reactant B**

VisiMix simulated reactant B concentration in both reactors.



Lab reactor

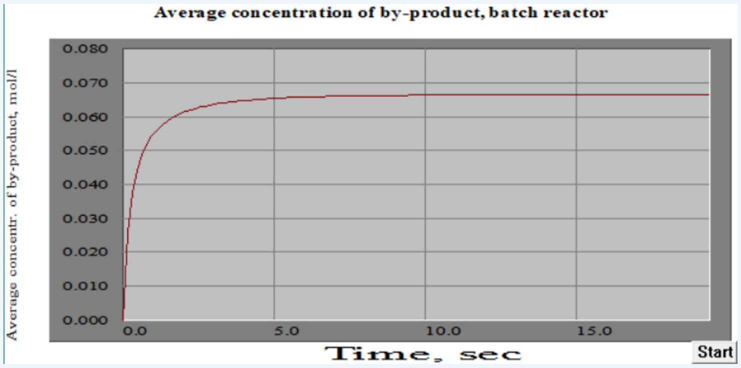


Production reactor

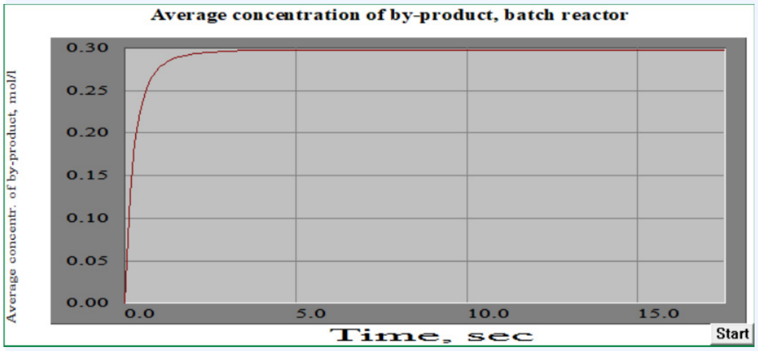
It was observed that:

- The production reactor exhibited 3× longer duration of high local concentration of reactant B.
- This led directly to higher by-product formation due to the side reaction.

Average by-product concentration profiles



Lab reactor



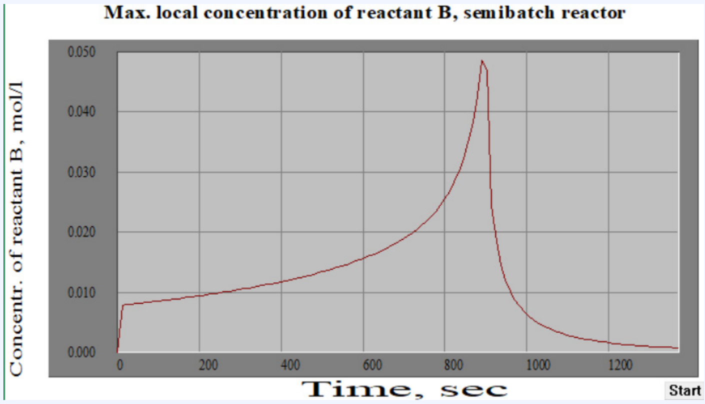
Production reactor

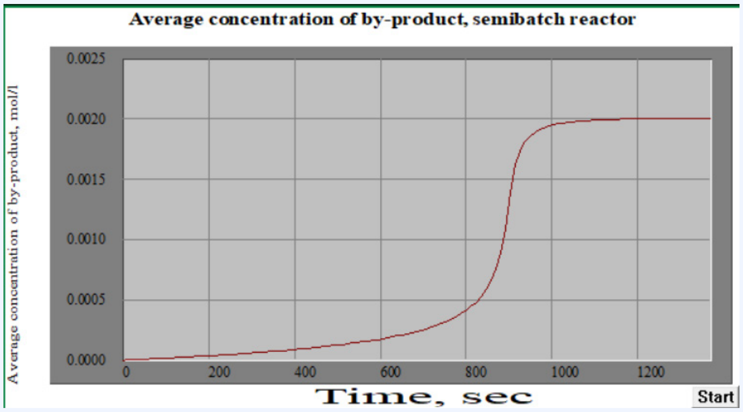
The results of calculation of the by-product concentration presented in the graphs are obvious enough and can explain the unsuccessful scaling-up.

Semi Batch Feeding Strategy

A semi-batch feeding strategy was simulated by adding reactant B gradually over 15 minutes instead of instant dumping. VisiMix was used to model multiple feeding durations to evaluate their impact on mixing uniformity and the suppression of local concentration peaks. The simulations clearly demonstrated that controlled, gradual addition significantly reduced the maximum local concentration of reactant B and minimized the likelihood of the competing side reaction.

This approach provided a practical and effective method to improve product quality during scale-up without altering the reactor design.





- The modeling results show a significant reduction in the maximum local concentration of reactant B under the semi-batch feeding strategy.
- The average concentration of the by-product is also lower compared to the batch (instant addition) case.

This strategy was implemented at the plant.

Key Observations

- Although mixing time was matched between the pilot and production reactors, the larger reactor showed prolonged high local concentration of reactant B after feeding.
- Instant addition of reactant B in the 1230 L reactor resulted in non-uniform distribution, significantly different from the pilot-scale behavior.

- These concentration spikes directly favored the undesired side reaction (B + B → D), causing higher by-product formation.
- Semi-batch simulations demonstrated that gradual feeding over 15 minutes significantly reduced concentration gradients and enhanced overall mixing uniformity in the production reactor.

Conclusion

- Matching macromixing time alone was insufficient to ensure successful scale-up for a reaction involving fast competitive pathways.
- VisiMix identified the **root cause** of scale-up deviation as high local concentration zones during instantaneous feeding at production scale.
- A controlled semi-batch feeding strategy effectively **minimized concentration spikes,** reducing the rate of undesired side reaction.
- This approach led to **improved product purity,** lower by-product formation, and better reproducibility at production scale.
- The solution required **no equipment modifications,** demonstrating a practical and efficient optimization pathway.
- This case highlights VisiMix as a **critical tool for predicting mixing behavior, preventing scale-up failures, and enabling right-first-time process transfer.**