

Title: Assessment of the Mixing Capabilities of the Asynt Vortex System.

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Summary

Access to equipment that permits the rapid screening of a range of reaction conditions in parallel is essential for efficient process development. The Asynt Vortex overhead stirrer system, shown below, allows three reactions to be stirred using a single overhead stirrer and heated to temperatures up to 200°C.



With such equipment it is of critical importance that the reaction conditions can be both precisely controlled and are consistent across all

reaction vessels used to ensure that any measured differences are genuine and not merely artefacts of the variability of the system. In the following report the consistency of the mixing of the Vortex system with three reaction vessels was assessed by measuring the bulk mixing and extraction times in each vessel and comparing this data with a stand alone vessel.

Introduction

Many reactions are controlled using the addition of one reagent to a stirred solution containing the other reactants in what is commonly referred to as a semi-batch reaction. The use of a controlled addition of one reagent can be advantageous for a number of reasons including limiting side reactions and controlling exothermic reactions. Using a semi-batch set-up the selectivity and impurity profiles of fast reactions or reactions involving reactive intermediates are often affected by the mixing efficiency, therefore when conducting reactions in parallel it is important that the mixing characteristics of each vessel are identical.

Two methods were used to assess the consistency of the mixing across the three reaction vessels, the first monitored the time taken for a single phase system to become 95% mixed at three different viscosities and the second measured the 80% extraction time with increasing agitation rate.

Bulk Mixing Time

The Vortex was set-up with three 250 ml multi-neck round-bottom flasks each fitted with identical PTFE stirrer shafts with swing-out impellers, to each of the vessel was added 200 ml of a glycerol / water mix. The agitation rate of each vessel was set to 200 rpm and two drops of phenolphthalein solution was added to each vessel. To each vessel was pipetted 1.0 ml of 1.0 M Sodium Hydroxide solution, resulting in a bright pink colour. 1.05 ml of 1.0 M Hydrochloric acid was then added subsurface, in one aliquot to the first vessel and the timer started, the time for complete de-colourisation was recorded. This was then repeated with the second and third vessels.

The whole procedure was repeated for glycerol/water mixes containing increasing amounts of glycerol. Each time the vessel was emptied and washed out by siphoning the material from the flask so as to not alter the set-up. The results are shown below:

Vessel	Mass Fraction of Glycerol		
	0.6	0.7	0.8
	Time taken for neutralisation /s	Time taken for neutralisation /s	Time taken for neutralisation /s
1	2.6	3.7	5.6
2	2.2	4.2	6.7
3	2.3	3.4	4.8

The experimental error using this arrangement was estimated at +/- 1 s given the degree of subjectivity in determining the exact end-point, taking this

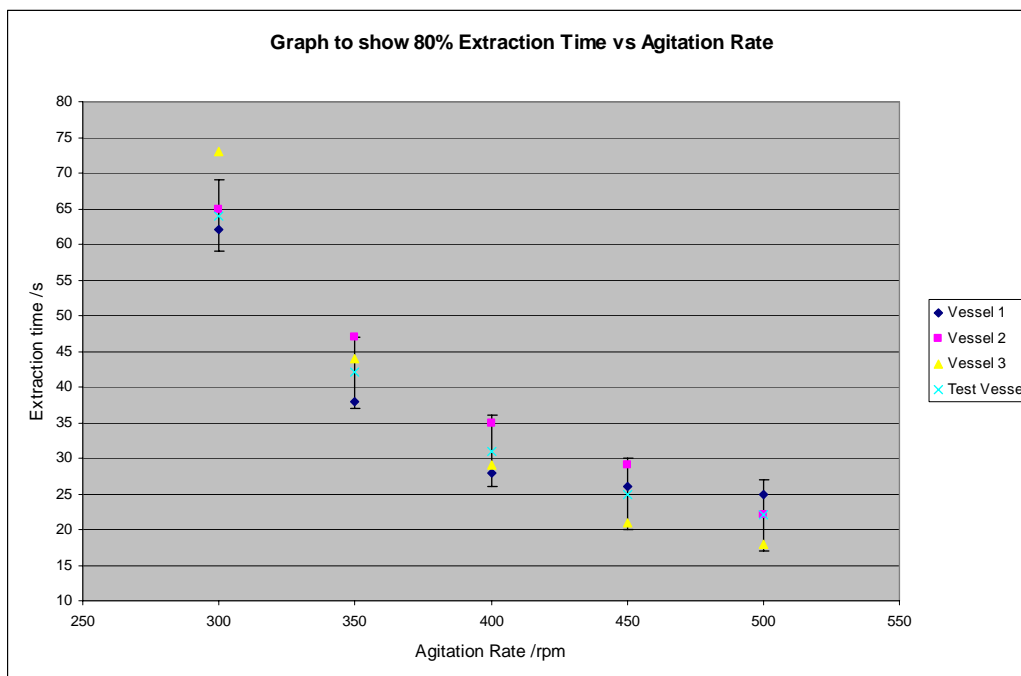
into account no significant differences in the bulk mixing times were observed over the range of conditions tested.

80% Extraction Time

The rate of extraction of one component from an organic phase into an aqueous phase is dependent on the droplet size of the dispersed phase in the continuous phase, which is itself partly dependent on the quality of the mixing. A simple measure of the extraction time can be done by measuring the time taken for a known excess of an organic soluble acid to neutralise an aqueous sodium hydroxide solution. If the Vortex is set up with three identical reaction vessels then the extraction times measured in each case should be comparable.

Two solutions were prepared, Solution A (0.216 M acetic acid in toluene) and Solution B (0.2 M sodium hydroxide solution) and the Vortex was set-up with three 3-neck 250 ml round-bottom flasks with identical PTFE stirrer shafts with swing-out impellers. To each vessel was added 80 ml of Solution B along with a few drops of phenolphthalein indicator, the agitation rate was then set to the desired value and switched off. Solution A (92.6 ml) was then carefully added to each vessel so as to minimise any disruption at the interface. The agitator was then switched on and the time taken for each solution to decolourise was recorded. This procedure was repeated over a range of agitation rates and using both the Vortex and a stand-alone arrangement. Repeat measurements of the extraction times in the stand alone vessel were recorded to determine the amount of natural variation in system which was found to be +/- 5 s. As with the bulk mixing set-up the material from each vessel siphoned off so that the set-up remained unchanged over the course of the measurements. The data is shown below:

Agitation Rate / rpm	80% Extraction Times /s			
	Vessel 1	Vessel 2	Vessel 3	Test Vessel
300	62	65	73	64
350	38	47	44	42
400	28	35	29	31
450	26	29	21	25
500	25	22	18	22



The data shows that over the agitation rates 350-500 rpm all three reaction vessels gave 80% extraction times within the natural variability of the system. At 300 rpm one data point was outside the range but at this lower agitation rate the mixing rate was insufficient to ensure adequate dispersion of the organic phase into the aqueous phase.

Conclusion

From the experiments conducted in can be concluded that no significant difference was measured in the mixing capability of a reaction vessel connected to a Vortex system when compared to a stand-alone single reaction vessel set-up. In addition the mixing characteristics across the three reaction vessels set up on the Vortex system were, within experimental error, the same. Therefore the Vortex system constitutes a useful addition for any laboratory conducting parallel synthesis minimising both the necessary laboratory footprint required and reducing the cost significantly by replacing three overhead stirrers with one. The integration of the Vortex with the DrySyn Multi hotplates allows heating of the three reaction vessels using a single hotplate also reducing the space requirements and costs when compared to a standard set-up without the mess and safety concerns of using a conventional oil bath system.