

CRANFIELD UNIVERSITY

SVETLIN ISAEV

ADVANCED FLOW TECHNOLOGIES FOR THE CONTROLLED &
CONTINUOUS MANUFACTURE OF NANOSCALE MATERIALS

SCHOOL OF AEROSPACE, TRANSPORT AND MANUFACTURE

SUBMITTED IN PARTIAL FULLFILMENT OF THE
REQUIREMENTS FOR THE DEGREE OF DOCTOR OF
PHILOSOPHY

Academic Year: 2019 - 2020

Supervisor: Prof Harris Makatsoris
2019

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ABSTRACT

Batch processes have been successfully used in the process industry over two centuries. However, changing customer demands and discovery of novel products have led the scientists and engineers to develop new manufacturing methods for the process industry. High-value products such as nanomaterials, smart and functional materials require precise process control for the entire product. Controlling of particle size and shape becomes more difficult in the large scale batch processes. Therefore, over the past few decades, there has been an increasing interest in the flow processing techniques due to their inherent benefits, such as better heat and mass transfer and small control volumes. Continuous Oscillatory Baffled Reactor (COBR) is a novel type of flow reactor. COBR combines oscillatory motion and periodically placed baffled flow channels to generate plug flow conditions, providing better mixing control similar to microreactors. Plug flow conditions can be achieved with the combination of optimum net flow, oscillatory amplitude and frequency using COBRs. With this new reactor and mixing concept, high-value products can be manufactured more efficiently using uniform mixing conditions and better temperature control. This will decrease the reaction time and production cost of novel products, use less energy, and increase time-to-market of novel products. The aim of this research is to develop a scalable and continuous manufacturing platform using continuous oscillatory baffled reactors to produce high-value products in low cost.

The focus of this study includes developing modular oscillatory baffled reactors, characterisation of modular oscillatory baffled reactors using experimental methods, developing scale-up methodology from laboratory scale to industrial production size and demonstration of nanomaterial synthesis using modular oscillatory flow reactor.

Modular reactor concept was patented by Prof Harris Makatsoris Research Group. In this study, a new version of modular OBR was developed including reactor design principles. Improved heating/cooling channels were integrated for better heat and mass transfer. A novel oscillation mechanism was developed for

fully automated process control (net flow, oscillatory amplitude and frequency). Micro and meso scale modular OBRs were used for characterisation experiments and scale-up methodology development. A systematic scale-up methodology was presented based on experimental results and Design of Experiment (DoE) method.

Characterisation experiments were performed for the investigation of wide range operating combinations. Full factorial Design of Experiment (DoE) was used to create 100 systematic experiments for each scale to measure residence time distribution. The mass transfer was measured using tracer and tanks-in-series calculations. The experimental results were analysed to identify the most influencing process parameters and dimensionless number for the plug flow conditions. Based on the experimental analysis, a scale-up methodology was developed to predict future processing parameters for different tube diameters.

Quick discovery and continuous manufacturing of novel functional nanomaterial using modular oscillatory baffled reactor are also presented. The case study involved transferring Spin-crossover (SCO) material production from batch to flow processing and controlling particle size and shape. Wide range of mixing concentrations and flow conditions were explored using response surface methodology. Overall experiment results showed that the modular flow reactor is highly capable of controlling particle size and shape to manufacture on-demand particle properties. Production of nanoparticles ranging from 100 nm to 1500 in various shapes (sphere, crystal, rod, needle and column) was successfully demonstrated for the first time in this study. SCO material production in various scales was illustrated using a derived scale-up methodology in this thesis.

Keywords:

Continuous Manufacturing; Modular Oscillatory Baffled Reactor; Nanotechnology, Process Scale-up, Advanced Nanomaterials, Product and Process Formulation

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TABLE OF CONTENTS

ABSTRACT	I
ACKNOWLEDGEMENTS.....	III
LIST OF FIGURES	VII
LIST OF TABLES	XII
LIST OF ABBREVIATIONS	XIV
1 INTRODUCTION.....	1
1.1 Overview	1
1.2 Background of the Study.....	1
1.3 Research Problem	4
1.4 Research Aim and Objectives.....	5
1.5 Scope and Motivation	6
1.5.1 OFM	6
1.5.2 Continuous Oscillatory Baffled Reactor	9
1.5.3 Plug Flow	10
1.6 Research Method and Analysis	12
1.7 Limitations of the Study.....	13
1.8 Outline of the Thesis	13
2 LITERATURE REVIEW	16
2.1 Introduction	16
2.2 Oscillatory Flow Mixing	21
2.2.1 Dimensionless Groups to Describe and Control of O.F.M.	21
2.3 History of the Oscillatory Flow Mixing	23
2.4 Background of Oscillatory Flow Reactors	28
2.4.1 Modular Oscillatory Baffled Reactor	29
2.5 Design Elements and Considerations for the OBR Development	33
2.5.1 Geometrical Design Parameters	33
2.5.2 Commonly Used Oscillation Mechanism in the Literature	37
2.6 Design of Experiments (DoE) for Statistical Analysis.....	38
2.7 Functional Nanomaterials	39
2.7.1 What is Nanomaterial?	40
2.8 Manufacturing of Nanomaterials	41
2.8.1 Nanomaterial Synthesis in Flow	42
3 REACTOR DEVELOPMENT AND EXPERIMENTAL METHOD	43
3.1 Introduction	43
3.2 Reactor Design Guideline	44
3.3 Development of a Novel OBR.....	45
3.3.1 Meso Scale OBR Design and Development.....	47
3.3.2 Oscillatory Mechanism Design	61
3.4 Experimental Methods	71

3.4.1 Macromixing – Residence Time Distribution	71
3.4.2 Micromixing – Tanks-in-Series Model	74
4 CHARACTERISATION EXPERIMENTS	77
4.1 Tracer Experiments.....	77
4.2 Experimental Design – Design of Experiments (DoE).....	81
4.2.1 Process Factors Selection.....	82
4.2.2 Selection of Full Factorial Experimental Design for the Characterization Experiments	83
4.2.3 Selection of Response Surface Experimental Design Method for SCO Synthesis.....	84
5 REACTOR CHARACTERIZATION EXPERIMENT RESULTS and SCALE- UP METHODOLOGY	85
5.1 Micro Scale (4 mm Diameter) Reactor RTD Results.....	85
5.1.1 Reactor Length versus Plug Flow Performance	86
5.1.2 Correlation between Tanks-in-series Number and Velocity Ratio	87
5.1.3 The Correlation between Str Number and Tanks-in-series.....	91
5.1.4 Independent Process Variable and Their effect on the Outcome	92
5.2 Meso-Scale Reactor (ϕ 8 mm) RTD Results.....	97
5.2.1 Correlation Between Velocity Ratio and Tanks-in-series numbers... 97	
5.2.2 The correlation between Str Number and Plug Flow Quality	102
5.2.3 The Effect of Key Process Parameters for the ϕ 8 mm Reactor	102
5.3 Repeatability of the Characterization Experiments	106
5.4 Scale-up Methodology – Correlation Between Micro and Meso Scale OBR Mechanisms.....	111
5.4.1 Distributions of the Experimental Data	112
5.4.2 Correlation between the Velocity Ratio and Number of Tanks	114
5.4.3 Scale-up Correlation Between Number of Tanks and Reynolds Number	116
5.4.4 Scale-up Correlation Between Number of Tanks and Oscillatory Reynolds Number.....	117
5.4.5 Scale-up Correlation Between Number of Tanks and Strouhal Number	119
5.4.6 Development of Scale-up Rule.....	120
5.5 Chapter Summary.....	122
6 SYNTHESIS OF SPIN CROSSOVER MATERIALS IN FLOW.....	124
6.1 Introduction of Spin Crossover Materials	124
6.2 Preparation of Precursors	125
6.2.1 Iron Precursor.....	125
6.2.2 Triazole Precursor	125
6.3 Characterisation of Spin Crossover Materials	126
6.4 Experimental Procedure	126

6.5 Experiments and Results	128
6.5.1 Screening Experiments – Transferring from Batch to Flow	128
6.5.2 DoE for Continuous SCO Nanomaterial Manufacturing	133
6.5.3 DoE Outcomes – Response Surface Analysis and Results	137
6.5.4 The Effect of the Dimensionless Numbers on the Nanoparticle Size and Shape Control	150
6.5.5 Consistency Experiments	155
6.5.6 Repeatability Experiments	157
6.6 Process Design Method for Industrial Scale Production of SCO Nanoparticles	162
6.6.1 Comparison Between OBR Production Rate and Batch Processing Rate	166
6.7 Chapter Summary	168
7 DISCUSSION	169
7.1 Design Improvements for Modular Continuous OBR Platform	169
7.2 Modular OBR characterization and its performance compared to the traditional OBRs	170
7.3 Scale-up Experiments Outcome	173
7.4 Nanomaterial Synthesis with Modular OBR	174
8 CONCLUSIONS AND SUGGESTIONS FOR FUTURE WORK	176
8.1 Conclusions	176
8.2 Future Implications	180
REFERENCES	182
Appendix A : Micro and Meso Scale Reactor Characterization Experimental Parameters, Response Results and RTD Profiles	191
Appendix B : DoE Experiment Setup Parameters for SCO Synthesis and SEM and DLS Results	209

LIST OF FIGURES

Figure 1.1 OFM	7
Figure 1.2 Flow patterns in a single baffled tank (a) and dividing the volume of (a) into twelve equal sizes of baffled tanks.....	9
Figure 1.3 Conventional and modular OBRs	10
Figure 1.4 Velocity profiles in a tubular system for laminar, turbulent and plug flows (Levenspiel, 1999)	11
Figure 2.1 Batch and continuous flow applications in academic research during the last 20 years	17
Figure 2.2 Recent publication numbers on OBR research and development...	19
Figure 2.3 Representing of Oscillatory Flow Mixing (Stonestreet & Veeken, 1999)	21
Figure 2.4 Geometrical parameters used for OBR reactor design and development	23
Figure 2.5 Butter Churning - Ancient Oscillatory Flow Mixing Method (Interesting, 1944)	23
Figure 2.6 Oscillatory blood mixing membrane (Bellhouse, et al., 1973).....	24
Figure 2.7 Butter Churner - Back and forth Ancient Churning Reactor (Collections, 2016)	28
Figure 2.8 Centillion Micro Scale OBR Disk (Makatsoris, et al., 2011)	30
Figure 2.9 Confluent PVM Precision Syringe Pump	32
Figure 2.10 A timeline of various baffle shapes have been tested in the previous OBR studies	36
Figure 2.11 Cam Double-Piston Oscillatory Mechanism (Dickens, et al., 1989)	37
Figure 2.12 DoE applications in the scientific researches	39
Figure 2.13 Objects in different scales (Image adapted from “A snapshot of nanotechnology”, National Cancer Institute).....	41
Figure 2.14 - Top down and bottom-up approached for nanomaterial production (Su & Chang, 2018).....	42
Figure 3.1 8 mm Modular OBR Design.....	46
Figure 3.2 Reaction, assembly and heating/cooling passages.....	48
Figure 3.3 Meso Scale OBR Disk Design.....	48

Figure 3.4 Special modular OBR disks for inline process monitoring	49
Figure 3.5 Meso-scale OBR with integrated inline measurement probes	50
Figure 3.6 Demonstration of the inline measurement setup with meso-scale OBR and Ocean Optics Spectrometer	51
Figure 3.7 Meso-scale OBR with spiral heating and cooling channels.	52
Figure 3.8 a) Half/half temperature control b) Full temperature control c) Demonstration of heating/cooling fluid flow	53
Figure 3.9 Meso scale OBR disks with spiral heating/cooling channels (Acrylic and PTFE materials).....	53
Figure 3.10 Flexible baffle design for various inner baffle geometry (sharp or round)	56
Figure 3.11 Demonstration of the heating/cooling capability	57
Figure 3.12 ANSYS CFD Heat transfer simulations for the uniform temperature control.....	58
Figure 3.13 ANSYS Simulation of separated temperature control zones by spiral channel design	58
Figure 3.14 Piston engagement points	62
Figure 3.15 Manual amplitude controlled oscillation mechanism.....	63
Figure 3.16 Twin Scotch Yoke oscillation mechanism for meso reactor	64
Figure 3.17 Automated oscillatory frequency and amplitude control mechanism	65
Figure 3.18 a) Fixed amplitude positions b) Lead screw mechanism for amplitude control.....	66
Figure 3.19 Meso scale modular OBR system	68
Figure 3.20 High definition rendering of the meso-scale OBR platform.....	68
Figure 3.21 Meso-scale reactor made from stainless steel	69
Figure 3.22 Wiring diagram of the stepper motor control.....	70
Figure 3.23 Experimental Setup of a RTD Measurement (Fogler, 2011).....	72
Figure 3.24 Concentration-time curves for tracer injection and response (Fogler, 2011)	73
Figure 3.25 Tanks-in-Series Model	75

Figure 3.26 Tanks-in-series model curve for various numbers of CSTRs in series. As the number increases, flow patterns in the reactor behave as plug flow reactor (Fogler, 2011)	76
Figure 4.1 Experimental Setup of the Tracer Measurements	78
Figure 4.2 Experimental Setup of Tracer Measurement	79
Figure 4.3 Reactor Configuration and Tracer Measurement	81
Figure 5.1 Relationship between reactor length and plug flow performance	87
Figure 5.2 Micro Reactor Full DoE Results for the RTD Measurements	88
Figure 5.3 RTD results on velocity ratio for micro reactor ($Re_n = 5.3$; $x=0.5$ - 2.5 mm, $f=1$ - 5 Hz).....	88
Figure 5.4 RTD results on velocity ratio for micro reactor ($Re_n = 10.6$; $x=0.5$ - 2.5 mm, $f=1$ - 5 Hz).....	89
Figure 5.5 RTD results on velocity ratio for micro reactor ($Re_n = 15.9$; $x=0.5$ - 2.5 mm, $f=1$ - 5 Hz).....	90
Figure 5.6 RTD results on velocity ratio for micro reactor ($Re_n = 21.2$; $x=0.5$ - 2.5 mm, $f=1$ - 5 Hz).....	91
Figure 5.7 The effect of Str Number on number of tanks.....	92
Figure 5.8 Effect summary and actual by predicted plot for the full fit model....	93
Figure 5.9 Effect leverage plots a) amplitude, b) frequency, c) amplitude*net flow and d) net flow	94
Figure 5.10 Prediction profiler for the independent process variables	95
Figure 5.11 Prediction function for the Tanks-in-series number based on full factorial of input variables	96
Figure 5.12 Prediction function for the tanks-in-series number according to only independent variables.....	96
Figure 5.13 Full DoE Results for the meso-scale reactor RTD results	98
Figure 5.14 RTD results on velocity ratio for meso reactor ($Re_n = 5.3$; $x=1$ - 3 mm, $f=0.25$ - 1.25 Hz).....	99
Figure 5.15 RTD results on velocity ratio for meso reactor ($Re_n = 10.6$; $x=1$ - 5 mm, $f=0.25$ - 1.25 Hz).....	100
Figure 5.16 RTD results on velocity ratio for meso reactor ($Re_n = 15.9$; $x=1$ - 5 mm, $f=0.25$ - 1.25 Hz).....	101
Figure 5.17 RTD results on velocity ratio for meso reactor ($Re_n = 21.2$; $x=1$ - 5 mm, $f=0.25$ - 1.25 Hz).....	101

Figure 5.18 The effect of Str number on the number of tanks for meso-scale reactor	102
Figure 5.19 Effect summary and actual by predicted plot for the meso-scale experimental results.....	103
Figure 5.20 Effect leverage plots a) amplitude, b) frequency, c) amplitude*frequency and d) net flow	104
Figure 5.21 Prediction profiler for the meso-scale modular OBR	105
Figure 5.22 Prediction function for the target meso-scale reactor tanks-in-series number	105
Figure 5.23 Repeatability results for the micro-scale reactor characterization experiments	108
Figure 5.24 Repeatability results for the meso-scale reactor characterisation experiments	109
Figure 5.25 Distribution reports for micro and meso scale reactor results.....	113
Figure 5.26 Correlation between magnitude of the dispersion effect and tube diameter adapted from (Nagy, et al., 2012)	114
Figure 5.27 Scale-up correlation according to Number of tanks versus velocity ratio.....	115
Figure 5.28 Scale-up correlation according to Number of tanks versus Reynolds number	117
Figure 5.29 Scale-up correlation according to number of tanks and Re_o	118
Figure 5.30 Scale-up correlation according to number of tanks and Str number a) micro-scale b) meso-scale.....	119
Figure 5.31 Scale-up rule for the process parameters	122
Figure 6.1 Low-Spin, High-Spin SCO Structure	125
Figure 6.2 Experimental Setup for the SCO Nanomaterial Synthesis	127
Figure 6.3 Schematic diagram of the continuous SCO nanoparticle synthesis platform.....	127
Figure 6.4 SCO compound synthesis in flow reactor and batch	129
Figure 6.5 Experimental setup for screening of SCO synthesis in modular OBR platform.....	130
Figure 6.6 SEM results for batch, OBR and OBR without oscillation experiments	132

Figure 6.7 Various SCO component particle shapes obtained from DoE results	137
Figure 6.8 The most significant effects for SCO particle size and shape control in the OBR.....	138
Figure 6.9 Interaction plots of the SCO process parameters for APS	142
Figure 6.10 Main effect plots of frequency, amplitude and residence time on the APS	143
Figure 6.11 Main effect plots of triazole and iron concentrations on the APS.	144
Figure 6.12 Contour and surface plots of amplitude x frequency for APS effect	145
Figure 6.13 Contour and surface plots of residence time x frequency for APS effect.....	147
Figure 6.14 Contour and surface plots of residence time x amplitude for APS effect.....	148
Figure 6.15 Contour and surface plots of concentration of iron x concentration of triazole for APS effect	149
Figure 6.16 Effect of the Strouhal number on particle size and shape	151
Figure 6.17 Effect of the Reynolds Number on particle size and shape	152
Figure 6.18 Effect of the Oscillatory Reynolds Number on particle size and shape	153
Figure 6.19 Effect of the Velocity Ratio on particle size and shape control	155
Figure 6.20 Sedimentation occurred during consistency experiments	157
Figure 6.21 APS measurements for original DoE and repeated experiments	158
Figure 6.22 SEM images of original DoE and repeat experiments	160
Figure A.1 RTD profiles for micro scale Reactor at $Re_n = 5.3$	197
Figure A.2 RTD profiles for micro scale Reactor at $Re_n = 10.6$	198
Figure A.3 RTD profiles for micro scale Reactor at $Re_n = 15.9$	199
Figure A.4 RTD profiles for micro scale Reactor at $Re_n = 21.2$	200
Figure A.5 RTD profiles for meso-scale reactor at $Re_n = 5.3$	205
Figure A.6 RTD profiles for meso-scale reactor at $Re_n = 10.6$	206
Figure A.7 RTD profiles for meso-scale reactor at $Re_n = 15.9$	207
Figure A.8 RTD profiles for meso-scale reactor at $Re_n = 21.2$	208

LIST OF TABLES

Table 2.1 Key process control parameters for batch and continuous processing	17
Table 2.2 Oscillatory mixing control parameters.....	22
Table 2.3 Summary of Literature Review	26
Table 2.4 Micro Scale OBR Specs	31
Table 2.5 Dimensions of Nanomaterials.....	40
Table 3.1 Meso-scale OBR Specifications	55
Table 3.2 Performance comparison between original and modified modular OBR designs	60
Table 3.3 Scotch yoke mechanism bill of materials.....	67
Table 3.4 Conversion of the stepper motor control to process frequency.....	71
Table 4.1 Reactor and Tracer Volumes.....	80
Table 4.2 4 mm Reactor Input Factors	82
Table 4.3 8 mm Reactor Input Factors	82
Table 5.1 Input parameters for the investigation of reactor length versus plug flow performance	86
Table 5.2 Accuracy of the Tracer Experiments.....	107
Table 5.3 Repeatability experiments in the plug flow regime.....	110
Table 6.1 Screening experiments and process parameters for investigation of SCO compound synthesis in flow conditions	130
Table 6.2 Screening experiments and dimensionless numbers	131
Table 6.3 Product and Process Variation Levels	133
Table 6.4 Design of Experiments with Response Surface Methodology based on low and high five input variables.....	135
Table 6.5 Dimensionless numbers and DoE Responses.....	136
Table 6.6 DoE Analysis - Model Summary	139
Table 6.7 Analysis of Variance	140
Table 6.8 Particle size measurements for the process consistency control....	156
Table 6.9 APS size and shape comparison for original and repeat experiments of DoE 5, 7, 14, 20 and 30.....	161

Table 6.10 Modular OBR design and process parameter for various production scales	165
Table 6.11 Production Rate Calculation between batch and modular OBR process.....	167
Table 7.1 Comparison of the characterization results with the literature	173
Table 8.1 Linking objectives to conclusions.....	176
Table A.1 Mixing conditions and dimensionless numbers used based on full factorial DoE for Micro-scale reactor chracterization experiments and response results	192
Table A.2 Mixing conditions and dimensionless numbers used based on full factorial DoE for meso-scale reactor characterization experiments and response results	201

LIST OF ABBREVIATIONS

ABS	Acrylonitrile Butadiene Styrene
AI	Artificial Intelligence
APS	Average Particle Size
COBR	Continuous Oscillatory Baffled Reactor
CSTR	Continuous Stirred Tank Reactor
CSTM	Continuous Stirrer Tank Mixing
DF	Degree of Freedom
DLS	Dynamic Light Scattering
D_0	Orifice Diameter
DoE	Design of Experiment
f	Oscillatory Frequency
HS	High Spin
L	Baffle Spacing
I	Baffle Thickness
LS	Low Spin
OBR	Oscillatory Baffled Reactor
OFM	Oscillatory Flow Mixing
OFR	Oscillatory Flow Reactor
PEEK	Polyetheretherketone
PFR	Plug Flow Reactor
PTFE	Polytetrafluoroethylene
Re_n	Reynolds Number
Re_o	Oscillatory Reynolds Number
RPC	Reciprocating-plate Extraction Column
RPM	Revolution Per Minute
RTD	Residence Time Distribution
RTD	Residence Time
SCO	Spin Crossover
SEM	Scanning Electron Microscope
Str	Strouhal Number
TiN	Tanks-in-Series
t_m	Mean Residence Time
X_0	Centre-to-peak Oscillatory Amplitude

1 INTRODUCTION

“Imagination is the highest form of research.”

Albert Einstein

1.1 Overview

Mixing has been important for processing of products since the early days of human history. Mixing uses the principles of the heat and mass transfer to convert heterogeneous physical products to more homogeneous systems. Today, in any industrial production, we can find some form of mixing. For example, blending Active Pharmaceutical Ingredients (API) to ensure homogeneous mixing of all ingredients in the pharmaceutical industry, stirring ingredients in the food and beverage industry, agitating chemical ingredients for the fine chemistry, and mixing vegetable oils and alcohols in the bioprocessing industry. The device used to mix products in the industrial applications is called a chemical reactor. The mixing speed and time have a direct influence on the final product quality and properties. In order to control the product properties and mixing conditions, various reactor designs and mixing methods have been developed by scientists. However, uniform mixing and scale-up issues are still fundamental challenges in the processing industry. These issues are addressed in this study. A novel mixing method named Oscillatory Flow Mixing (OFM) for uniform mixing, and modular oscillatory baffled reactor for process scale-up are proposed in this thesis. This introductory chapter discusses the background of this thesis, including the aim and objectives of the research, research problem and limitations.

1.2 Background of the Study

The process industry has been dominated by batch processes for the last two-three centuries. Long term industry acceptance provides some benefits to make batch processes more popular. It is low risk for the investors and companies from a regulatory perspective. Process regulations and standards are well defined to produce specific batches of products. The implementation of the batch technology and equipment is relatively cheaper compared to new technologies,

which also makes the batch processes more preferable. However, batch processing has some major limitations. They are usually more difficult to scale-up by maintaining similar product properties from the discovery phase to the industrial production stage. This scale-up difficulty is due to heat and mass transfer problems. It is very unpredictable to control heat and mass transfer behaviours in the larger scale batch processes, and there is no scientifically proven scale-up methodology. This also leads to increased time-to-market for successful products. In addition, poor mixing conditions in the batch processes limits the discovery and commercial production of novel products. Today, market and consumer needs have been increased much more than in the past. The evolution of market demands requires novel products with desired properties. This demand can only be delivered by controlling the desired structural properties of new materials in both molecular and microscopic levels. The scale and mixing capabilities of the traditional batch reactors do not allow the control of particle size and geometry in the molecular scales. Wider mixing conditions are essential to produce functional nanomaterials in the industrial scales.

Mixing technology has been evolved in recent years. Various mixing methods and devices have been developed. The continuous process is becoming more popular due to its inherent benefits, such as better heat and mass transfer, scalable process conditions, smaller control volumes, safer and less energy consumption, smaller equipment footprint, decreased time-to-market and rapid discovery of novel products. Mixing and reaction occur inside the micro and meso scale tubular systems in continuous chemistry. Smaller tube diameters provide smaller control volumes, which results in better heat and mass transfer throughout the entire production process. Fluid dynamics in the flow environments are well established by empirical correlations between dimensionless numbers. Similar mixing conditions can be achieved from smaller to larger tube sizes using dimensionless numbers. Geometrical scale-up can quickly be achieved by maintaining dimensionless numbers for any tube diameter. Also, small mixing volumes perform particle mixing and reaction in the molecular levels. Precise flow rate control, from microlitre to litres per minute, of

today's highly sophisticated industrial pumps, fulfil more extensive operating and mixing conditions in the continuous manufacturing systems. Wider operating conditions and small mixing volume encourage scientist to discover novel functional materials and rapid scale-up of discovered materials from laboratory scale to industrial scales. Efficient heat transfer is another important driver of flow chemistry. Surface area to volume ratio is significantly higher in the tubular reactor systems compared to the batch process. Larger surface area to volume ratio provides efficient heat transfer capabilities in the flow processing.

Microreactors are the most popular flow reactors in chemical synthesis. Their tube diameter, under 1 mm, creates Dean Vortices (a form of vortices directed from the centre of the tube towards the outer tube wall) within very low values of Reynolds Number (Re). However, their production capacities are limited to make final products in the industrial channels. Once tube diameters are increased to scale-up microreactors, some challenges occur. In addition to pressure drop, very high net flows are required to maintain similar flow conditions. Higher flow rates result in very long reactor lengths (in most cases tens of kilometres) to maintain the same reaction residence time. Significantly higher flow rate and longer reactor lengths make this approach unpractical for the industrial size production. An external force is required for the larger tube diameters to maintain fluid dynamics and mixing conditions. Oscillatory Baffled Flow Reactor (OBFR) has recently been developed to deliver practical solutions for the industrial-scale production of fine chemicals. In OBFR technology, the mixing is independent of the net flow. The mixing conditions can be controlled using only oscillatory frequency, amplitude and geometry of the baffles.

Manufacturing of nanomaterials plays an important role in not only lowering the cost and enabling sustainable productions but also in the control of operating conditions to produce nanoscale smart materials. Materials are made from atoms, and their properties come from how those atoms are arranged and their size. For example, silicon atoms can be converted to semiconductor chips by changing the position and size of the atoms using correct operating parameters and manufacturing techniques. Batchwise techniques have been successfully

performed to synthesise chemical compounds for decades. Batchwise production is the production of chemical compounds by mixing all ingredients in a vessel and stirring them for some period until finally, we stop the production to take the final product out. However, this method has some limitations in terms of control, automation, uniform mixing and heat and mass transfer, which make the discovery of novel products difficult. On the other hand, miniaturisation in material size and processing industry requires novel nanofabrication techniques to achieve mixing control in nanoscales. OFM technology is a new product synthesis method to achieve uniform size and shape control of synthetic nanomaterials during their processing. In this study, manufacturing of nanoscale materials is presented using OBFR.

1.3 Research Problem

Standard chemical apparatus, such as glass round bottom flasks, stirring magnets, blenders and mixing tanks are still actively used today, since their invention. A standard procedure for a chemical reaction and synthesis to deliver fine products today can easily be recognised compared to a hundred years ago. On the other hand, market demand and consumer needs are more sophisticated than a century ago. Demand for novel products are increased in the recent years. However, traditional process equipments have some limitations to rapidly discover and manufacture novel products. Inconsistency in the mixing quality is a fundamental problem in the batch processes (Torotwa & Ji, 2018). Impeller creates great turbulence in the impeller regions, which is usually at the centre of the vessel. The power of turbulence and mixing uniformity decrease from impeller regions towards the wall regions. In the worst batch reactor design scenario, dead mixing zones can be observed. In the batch process, it is almost impossible to achieve a uniform mixing profile in the entire reactor volume. Inconsistent mixing conditions also lead to reproducibility issues. Each batch setup, even with the same setting and conditions will deliver products with different properties. Poor heat and mass transfer is another important industrial problem with bulk processing techniques (Helal, et al., 2018). High energy and insulation costs are required in batch reactors due to their low surface-to-volume ratio (Souza, et al.,

2018). Heat and mass transfer issue also creates a scale-up problem, which becomes a much larger engineering challenge in larger scales. During the last two decades, discovery in the synthesis and processing of nanomaterials has shown great opportunity to deliver functional novel materials for almost every area and discipline in science and engineering. Nanotechnology has been used in commercial products, such as pharmaceutical coating, electronic devices, magnetic storages, textiles and food and beverage products. However, the production of these materials with a lower manufacturing cost is still a vital industrial challenge (Roco, et al., 2010).

Based on the research background discussed in the previous section, this study will develop an alternative processing method called “OFM” in order to provide better heat and mass transfer, rapid novel product discovery, uniform mixing and scalable production. The next section presents the aim and key objectives of this research.

1.4 Research Aim and Objectives

As presented in the research background and problem, there is an urgent need to develop a novel mixing method which will eliminate the limitations of batch processing. The fundamental aim of the project is to develop an automated continuous oscillatory baffle flow reactor for controllable and scalable nanomaterial synthesis. The key research objectives to be addressed in this study are listed below:

- 1)** To develop a continuous oscillatory baffled reactor, which will provide uniform mixing conditions and better heat and mass transfer including in-situ monitoring and full process automation capabilities.
- 2)** To investigate the impact of process parameters to characterise modular OBR.
- 3)** To develop a systematic scale-up approach and define clear steps to design process parameters from laboratory to industrial scales.
- 4)** To demonstrate production of nanomaterials in the modular OBR by controlling particle size and shape for demand-driven nanomaterial

synthesis. Simulate the production of nanomaterial scenarios from laboratory industrial scale using modular OBR platform.

1.5 Scope and Motivation

Flow chemistry has received great interest in recent years, both from academia and industry because of its inherent advantages for pharmaceutical, food and beverage, agrochemicals, oil & gas, functional nanomaterials and fine chemicals manufacturing. However, due to the lack of proven robust and sustainable flow reactor development, coupled with the vast structures of the batch production capability, flow reactor applications have not yet been widely employed in nanomaterials manufacturing.

The proposed investigation combines three basic principles; OFM, plug flow and modular oscillatory baffled reactor. Each is fundamental and how they are used during this research will be briefly presented in this section.

1.5.1 OFM

OFM has been developed in the last two-three decades for industrial applications of providing efficient and controlled mixing in continuous tubular systems. Mixing occurs in the flow system with the combination of the dynamic effect of oscillation and static effect of periodically placed baffles along the tube. A piston-driven oscillation mechanism is attached to the one side of the tube which moves the entire fluid forward and backwards. Once the fluid crosses the baffles, this creates eddies after and before the sharp edges of the baffles according to the oscillation phase, as shown in Fig.1.1. When the oscillatory motion is in the forward phase, eddies occur after the baffle cavity (red vortex as shown in Fig.1.1); when the oscillatory motion returns to the backward phase, eddies are created before the baffle edges (black vortex as shown in Fig.1.1). Consequently, each baffled zone behaves as a mixing zone. The entire tube acts as a series of small oscillatory mixing zones.

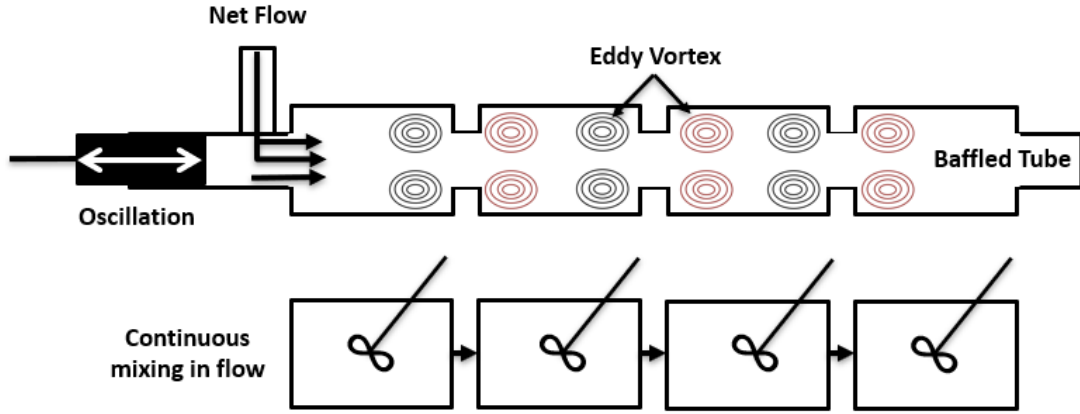


Figure 1.1 OFM

The mixing conditions and residence time distribution (RTD) in OFM are controlled by three dimensionless numbers; net flow Reynolds number (Re_n), oscillatory Reynolds number (Re_o), Strouhal number (Str) (Ni, et al., 2002).

$$Re_n = \frac{\rho du}{\mu} \quad (1)$$

$$Re_o = \frac{x_o 2\pi f d \rho}{\mu} \quad (2)$$

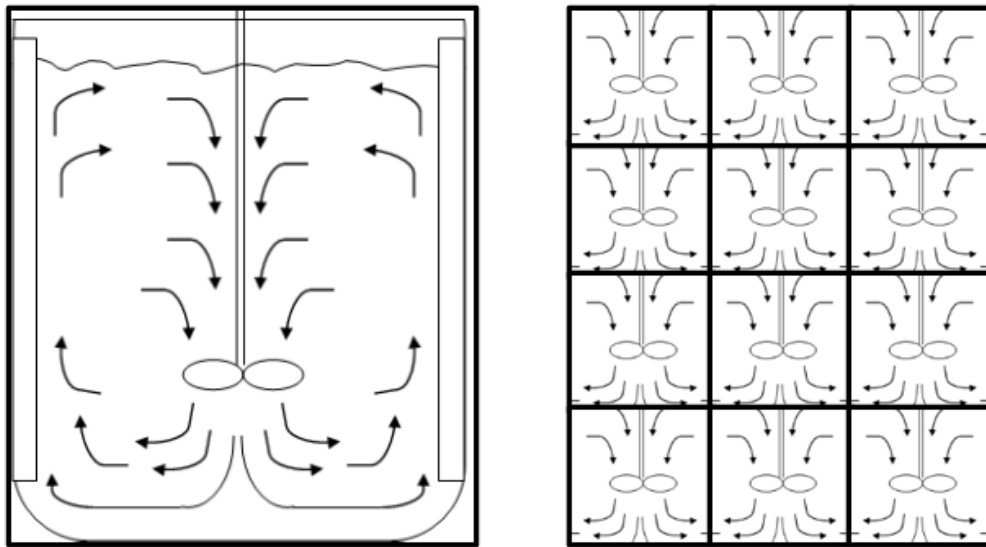
$$Str = \frac{D}{4\pi x_o} \quad (3)$$

Where, d is the tube diameter (m), ρ the fluid density (kg/m^3), μ the fluid viscosity (kg/ms), u the mean superficial flow velocity (m/s), x_o the centre-to-peak oscillation amplitude (m) and f the oscillation frequency (Hz). Net flow Reynolds number describes the state of the flow. Oscillatory Reynolds number characterise the mixing intensity in OBR, a wide range of Re_o can be achieved by changing the amplitude and/or frequency of oscillation. The mixing intensity can be categorised in the three Re_o regimes; if $Re_o < 250$, the mixing is soft, and the flow is 2D-axisymmetric. If $250 < Re_o < 2000$, the flow becomes more turbulent and if $Re_o > 2000$, the flow is fully turbulent in OBR (Stonestreet & Veecken, 1999). The Str number describes the vortex propagation, and it is the tube diameter to oscillation amplitude ratio. The widely used Str number range is between 0.15 and 4 (Ni & Gough, 1997).

OFM provides some significant advantages for the process industry. Some of the key benefits are as follow:

- Better heat and mass transfer
- Minimal control volumes
- Better control of reaction time
- Radial mixing in continuous motion
- Scalable flow patterns maintaining same dimensionless numbers

Fig.1.2 is used to explain the advantages of the OFM compared to traditional Continuous Stirred Tank Mixing (CSTM). The flow patterns are shown in Fig.1.2a; the mixing is more intense around the impeller. In other words, the material mixed well near the impeller, and there is a poor mixing on the materials far from the impeller. This inconsistency gets worse with larger amount of materials (industrial production scales). Imagine the same volume is divided into a (n) number of equal volume zones as illustrated in Fig.1.2b, and consider each volume zone is acting as a mixer. In this case, mixing will be more uniform in the entire volume. OFM behaves precisely like this phenomenon. Some group of elements are mixed in the small mixing regimes continuously and leave the system as a well mixed small group of elements instead of one single bulk element.



a) Flow patterns in baffled tank **b)** Consider dividing the volume of (a) into twelve equal size baffled tanks

Figure 1.2 Flow patterns in a single baffled tank (a) and dividing the volume of (a) into twelve equal sizes of baffled tanks

1.5.2 Continuous Oscillatory Baffled Reactor

Oscillatory Baffled Reactor (OBR) was used in this study in order to create OFM. Modular OBR was invented by Prof Harris Makatsoris and his research group (Makatsoris, et al., 2011). Traditional OBRs are constructed from a fixed length of tubes, on the other hand, modular OBR is made from “slices” rather than “tubes”, and slices can be aligned linearly to behave a continuous tube. The entire reactor comprises of any number of standard modules that, once assembled, combine into continuous OBR system of the desired length. Each module consists of baffled conduits and several baffle free conduits, which are designed for assembly and heating/cooling purposes. This invented design configuration enables the reduction of manufacturing costs and increases its flexibility to rapid construction according to various length and sizes.

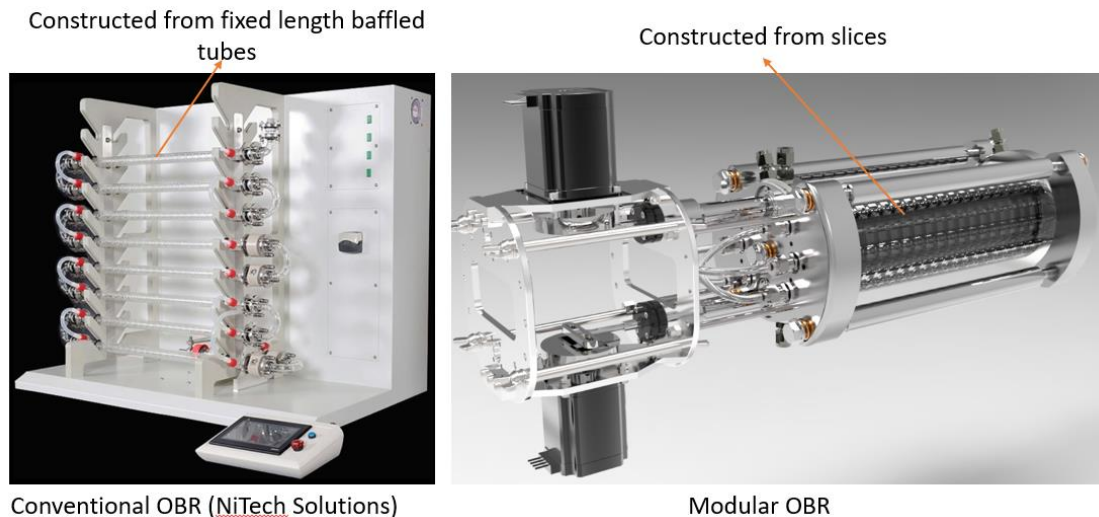


Figure 1.3 Conventional and modular OBRs

Traditional and modular OBR design is presented in Fig.1.3. Following Prof Makatsoris' earlier invention of modular OBR, significant design and development were performed in this study to improve modular OBR performance. A novel oscillation mechanism, spiral heating/cooling channels and integration of inline measurement probes are key development features, and these are explained in more detail in Chapter 3. Major benefits of modular OBR are summarised below:

- Designed as slices for modularity
- Cheaper and quicker manufacturing process
- A novel oscillation mechanism which enables automated oscillatory frequency and amplitude control
- Better heating/cooling performance due larger surface area to volume ratio
- Precise control of net flow and oscillatory power (frequency and amplitude)
- Inline measurement probes (temperature, UV-VIS spectrometers etc.)
- Smaller footprint

1.5.3 Plug Flow

Modular OBR and OFM technology are used to develop plug flow regimes. Velocity profiles can be used to explain flow regimes in a tubular system. Laminar flow has parabolic velocity profiles, incoming velocity is equal at the centre of the

tube, gradually decreasing toward the wall until it comes to zero velocity profiles due to viscosity. As a result, the materials in the centre leave the system first, and the elements near the wall exit the system last. In the turbulent flow, velocity profiles are more chaotic, and their directions and magnitude are difficult to predict along the tube. In the plug flow conditions, all the velocity profiles in the axial direction are uniform and equal to input velocity (u) as shown in Fig.1.4. There is no mixing in the axial direction; all mixing occurs in the radial direction, which also results in equal residence time for all molecules in the reactor system.

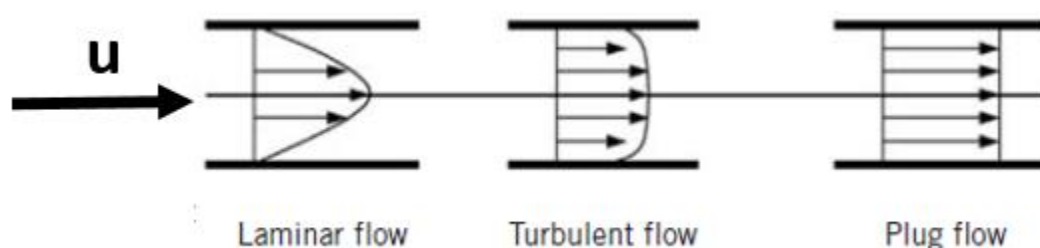


Figure 1.4 Velocity profiles in a tubular system for laminar, turbulent and plug flows (Levenspiel, 1999)

The benefits of the plug flow are listed below:

- Provide uniform mixing for the entire product
- All molecules spend the same residence time in the reactor
- Mixing in the radial direction which creates a better mass transfer
- No back-mixing in the system

OFM, modular OBR and plug flow are the fundamentals of this study to develop a scalable flow process for nanomaterial manufacturing. The scale-up methodology will cover the production size, starting from laboratory to full industrial production. Most processes in the high-value chemicals industry have three processing scales; the lab-scale process has a few kilograms per hour, pilot-scale production capacity is around 50 kg/h, and industrial-scale production requires 300 kg/h (Khinast & Bresciani, 2017).

1.6 Research Method and Analysis

The proposed research investigation is based on modular oscillatory flow reactor development and experimental characterisation of the reactor, to develop a scale-up methodology using characterisation experiments and demonstration of the nanomaterial synthesis using the modular oscillatory flow reactor.

Micro scale modular reactor was developed and patented by Prof Harris Makatsoris and his research group (Makatsoris, et al., 2011). Significant development work was done for the meso scale reactor in this thesis. Meso scale reactor was scaled up using the power of two. Dimensional scale-up ratios identified in the original patent of micro scale reactor were used in the construction of the geometrical dimensions of the meso scale reactor. The arrangement of the baffled channels was optimised for a maximum reactor volume target. A new heating/cooling concept was developed for better heat transfer. A Scotch-yoke oscillation mechanism, including an automated amplitude control feature, was designed for sinusoidal motion and automated process control.

Characterisation of the oscillatory baffled reactors is not something new. Various OBRs have been developed and characterised by previous researchers (Harvey, et al., 2001; Ni, et al., 1998; Phan & Harvey, 2010). However, characterisation of modular OBR is studied first time in this investigation. Technical and manufacturing advantages of the modular reactor over the traditional OBR are presented in Chapter 3. With the characterisation experiments of micro and meso scale modular OBR, its mixing performance and plug flow conditions have been proven. In addition, characterisation experiments are a kind of user guideline to identify optimum operating conditions for the desired process. The data collected from characterisation experiments based on a systematic experimental approach of two scales were used to develop a scale-up methodology. Tracer experiments were conducted for the characterisation of the reactor. Tanks-in-series model was chosen to analyse the experimental data.

As a final investigation, demonstration of the nanoparticle synthesis was presented using meso scale modular OBR. Iron and triazole were mixed to create spin crossover (SCO) nanoparticles. Design of experimental method was used to investigate the impact of the three process variables (oscillation amplitude and frequency and net flow) and concentration of each reagent over final product size and shape. Dynamic light scattering (DLS) was used to measure nanoparticle size, and scanning electron microscope (SEM) was employed for the particle shape analysis.

1.7 Limitations of the Study

As this research is proposed to develop a novel continuous manufacturing platform for controllable and scalable nanomaterial synthesis, the review of the literature suggests some important considerations. Rheological complexity is a major issue. As explained in the research background, flow chemistry uses tubular mechanisms. The most common tube sizes are under 10 mm, and it is much lower (<2 mm) for microreactors, therefore, high viscous materials can easily block the systems. The viscosity of the materials must be checked before the process, and it must be controlled during the processing because viscosity might be different after the reaction, which will cause clogging issues.

Range of the oscillatory motion is another issue which must be considered in the early stages of OFM technology. There are certain limits to each mechanism, such as max rpm and torque ranges for selected motors to drive the oscillation mechanism and limits of the stroke. These limitations will consequently affect the selection of optimum combinations to achieve plug flow conditions.

1.8 Outline of the Thesis

The outline of this thesis follows the guidelines for the doctoral theses provided by Cranfield University. The study starts identifying the research problem, which leads the focus of flow manufacturing and development of the OBR reactor. Rationales of the study are presented by the background research and reviewing the methods and techniques that were used in the past. The performance of the

proposed method was evaluated via experiments. Moreover, in the last section of the thesis, results are discussed, including further suggestions to improve the proposed model. The thesis consists of eight chapters, and each chapter is presented as follows:

Chapter 1: Introduction presents the needs of the research, research questions, brief research background, objectives of the research, research topics and expected contribution for academy and industry.

Chapter 2: Literature review includes comprehensive background for the fundamentals of flow processing, OFM, development of flow reactors, design elements of the oscillatory flow reactor, Design of Experiment (DoE) method and nanomaterial synthesis.

Chapter 3: Reactor development and experimental procedure introduce the sets of reactors and continuous manufacturing platform designed and constructed for the characterisation and scale-up experiments, OBR design principals and brief explanation of experimental method using residence time distribution measurements and tanks-in-series model.

Chapter 4: Characterisation experiments focus on the experimental procedure conducted in this research covering experimental design based on DoE for micro and meso scale reactors, selection of key process and oscillation parameters, measurement method, tracer selection, data collection and data analysis.

Chapter 5: Reactor characterisation and scale-up methodology results discuss the findings of the characterisation experiments of two set up reactors and scale-up methodology from micro to meso scale. The most significant process and oscillatory parameters were identified by analysing the obtained data from characterisation experiments. Dynamic similarity law was employed to develop a scale-up model between two different sizes of diameters. The trend and behaviour of the dimensionless numbers on the plug flow performance were compared between two scales.

Chapter 6: Synthesis of Spin Crossover (SCO) nanomaterials in flow presents the production of nanomaterials in OBR environment. The chapter includes a selection of chemical composite and transferring the recipe from a batch process to flow process, a systematic experimental procedure. Characterisation of the particles and interpretation of the results with analysing obtained experimental data. Simulation of the nanoparticle in various production scales were presented at the end of the chapter.

Chapter 7 and 8 provides the summary of the research by discussing the key findings, potential future works and finally, limitations of the research.

Supplementary information as an appendix and list of the references are provided at the end of this thesis.

2 LITERATURE REVIEW

*“Research is to see what everybody else has seen,
and to think what nobody else has thought.”*

Albert Szent-Gyorgyi

2.1 Introduction

The use and development of the continuous manufacturing systems started a long time ago for the process industry and has rapidly increased due to its proven benefits. Their use will continue to increase exponentially, as shown in Fig.2.1, whereas the traditional “batch-processing” will continue to exist for a limited number of applications. The publication numbers were obtained from Science Direct by searching “Batch processing” and “Continuous Processing”. The principles of a traditional batch processing and continuous flow processing differ in certain ways. In the batch processing, all reagents are loaded into the cylindrical vessels or tanks, then blenders or propellers are used for mixing for a certain period, and when the reaction is completed, the process is stopped, and the final product is collected from the batch reactor. After this, the whole process is repeated for the next volume. The reactor dimensions are in the range of centimetres for batch processing. Flow processing, as a new technology, uses tubular reactors and dimensions are in the range of micro and millimetres. Reagents are continuously pumped into the tubular reactors, where they travel and react within tubes, and the final product can be collected at the end of the flow reactor as a continuous stream. Key process control parameters for the batch and continuous processing are shown in Tab.2.1. The transition from batch to continuous for the control factors can also be seen.

Table 2.1 Key process control parameters for batch and continuous processing

Key Process Control Factors	
Batch Processing	Flow Processing
Concentration	Flow Rates
Mixing (Propeller rpm)	Mixing (flow regimes – Reynolds Number)
Temperature	
Reaction Time	

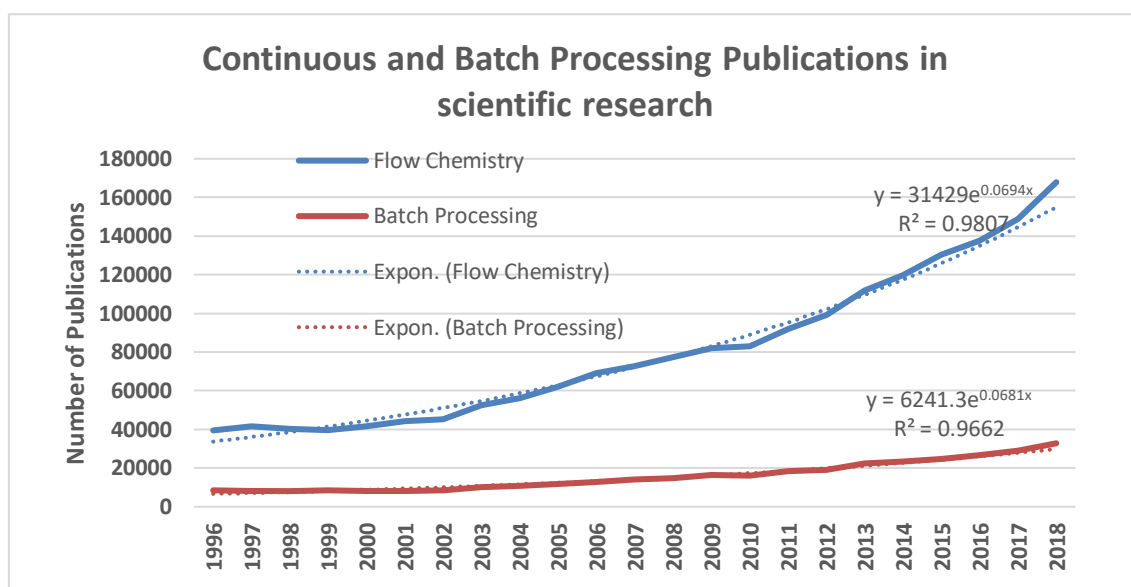


Figure 2.1 Batch and continuous flow applications in academic research during the last 20 years

Continuous flow reactors are something new in modern research laboratories. However, in the petrochemical industry, products have always been manufactured using continuous flow processing in a considerably large scale. Continuous stirred tank reactors (CSTR) are the early examples of the continuous reactors which are used for mixing, reactions, and process intensifications in the chemical process industry. In these types of reactors, the mixing resembles that of batch reactors. Propellers are used to mix particles inside the tanks. More than

one tank can be used in serial connection. There is a continuous inlet and outlet flow from the start of the reaction to the end of the reactor system in CSTR technology.

Tubular reactors were developed as an alternative technology to CSTRs. Raw materials are continuously fed into the reactor from the inlet, and on the other end of the reactor, the final product is continuously collected. The mixing and reaction occur inside the tube due to flow behaviours, such as laminar, turbulence and plug flows or obstacles to create vortices. Main advantages of the tubular reactor over batch and CSTRs are excellent heat transfer due to its large surface-to-volume ratio, and predictable flow patterns in every scale by maintaining similar flow conditions (constant Re_n numbers in various tube diameters). Micro reactors are the most commonly used tubular reactors in the chemical process industry and research labs. Micro reactors can be manufactured from various materials such as silicon, quartz, glass metals and polymers. Their tube diameters range from hundred microns to only a few millimetres, and they are mostly used in small scale synthesis, screening or discovery processes. Micro reactors can provide very rapid mixing and reaction due to short diffusion distances (Nguyen & Wu, 2005). Heat transfer is another important benefit of micro reactors (Watts & Wiles, 2012). Multi-step synthesis can be employed by constructing many arrangements of multiple microreactors (Trojanowicz, 2016). A micro reactor can be fully integrated with feedback control systems and Artificial Intelligence (AI) to develop a “self-learning” chemical synthesis system (McMullen, et al., 2010).

The success and performance of the microreactors have led to the tubular reactor developments in the larger volumes and tube diameters. Once a new product is discovered by using microreactors, mesoscale flow reactors can be used to move the production from small discovery scales to larger pilot or commercial production volumes. Various mesoscale flow reactors have been developed in recent years. Parallel capillary flow reactor was introduced by Strying and Parracho (Strying & Parracho, 2009). The reactor is formed up of a capillary block including 120 capillary tubes with 3 mm diameter and 30 mm lengths, headspace, bottom space inlet manifold and spacer plate. Pressure driven pumping system

was used to produce up to 190 ml/h of organic components. Syrris developed many commercial glass flow mesoscale reactors ranging from grams to kilograms per hour production capacity (Syrris, 2019). Glass and stainless-steel tubes of 1 to 8 mm diameter with covered heating/cooling shell were used and their commercial products were successfully used in many academic/industrial applications (Momo, et al., 2015; Pirotte, et al., 2015; Bagley, et al., 2010). Vapourtec also constructed commercially available meso-scale flow reactors by using a coil, housed inside an insulated glass manifold, which allowed a controlled temperature to be established by circulating heated or cooled air around the reactor (Vapourtec, 2019). Performance of the Vapourtec flow reactors was evaluated in many academic research applications (Capel, et al., 2018; Tadele, et al., 2017). Oscillatory baffled flow reactors are the recent version of the tubular flow reactors because of their unique flow channel design and oscillation integration, and there has been a great interest in recent years, as shown in Fig.2.2. OBRs are the main interest of this study; therefore, they will be comprehensively reviewed and discussed in the following sections.

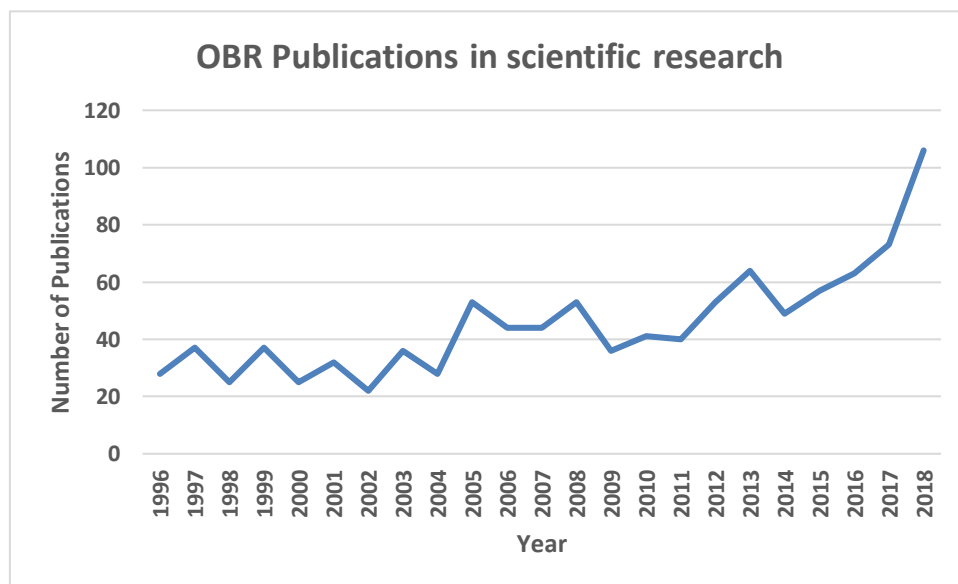


Figure 2.2 Recent publication numbers on OBR research and development

Continuous processing sometimes referred to as flow chemistry, green chemistry, flow processing, green processing, or continuous flow processing, offers better heat and mass transfer and quicker reaction time over batch processing methods to discover new products and process these products to make them more efficient and sustainable. Advantages of the flow chemistry are listed below:

Safe processing – hazardous chemicals can be safely produced using flow reactors. Because of small control volume and tube diameters relative to batch reactors, if something goes wrong, the damage can be minimized in the flow process. How to eliminate the safety concerns using flow chemistry were explained by reviewing active pharmaceutical ingredients applications in flow by B. Gutmann and his colleagues (Gutmann, et al., 2015).

Systematic scale-up – flow patterns are well studied in tubular systems. Dimensionless numbers can be used to predict flow regimes in any size of the tube. Flow chemistry allows developing a systematic scale-up approach with minimal experimental effort (Piccinno, et al., 2016).

Rapid product discovery – the reaction time is relatively quicker in flow processes compare to batch systems. A small number of reactants in the narrow channels can be rapidly synthesised. Multiple flow channels can be used in parallel by tuning process and/or composition parameters to run multiple experiments simultaneously using flow reactors (Richmond, et al., 2012).

Precise product control – crystal shape and size are important properties for any type of product, narrow particle size distribution is always preferable for better quality. Operating conditions play a significant influence on the properties of crystal products. Operating parameters and temperature can be precisely controlled during the entire process in the flow technologies (Yu, et al., 2007).

Improved heat/mass transfer – flow reactors have a high surface area to volume ratios which enables much better heat and mass transfer performances

and small tube diameters offers excellent transport performance consuming less energy (Gutmann, et al., 2015).

2.2 Oscillatory Flow Mixing

Continuous oscillatory flow mixing is a novel mixing technology for the modern process industry. A liquid or multiphase mixture axially oscillates in the cleverly designed tubular systems. The tube consists of periodically placed orifice baffles. At the one end or in the multiple places of the conduit, there is an oscillation mechanism based on piston, diaphragms or bellows to generate an axial backward and forward movement of the whole materials inside the reactor. The combination of oscillation and baffle restrictions induces vortex formation by passing through liquids which creates radial mixing among the whole reactor as shown in Fig.2.3.

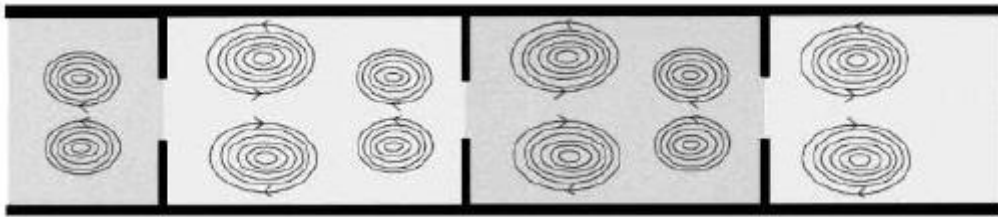


Figure 2.3 Representing of Oscillatory Flow Mixing (Stonestreet & Veeken, 1999)

2.2.1 Dimensionless Groups to Describe and Control of O.F.M.

The mixing conditions and residence time in OBR are controlled by three dimensionless numbers and two geometrical ratios (Ni, et al., 2002):

1. Net flow Reynolds number (Re_n),
2. Oscillatory Reynolds number (Re_o),
3. Strouhal number (Str)
4. Baffle spacing (L/D)
5. Baffle free area ($\alpha = D_o/D$).

Mixing is independent in OFM systems and its governed by the intensity of the oscillations. Oscillatory Reynolds number characterize the mixing intensity in OBR, a wide range of Re_o can be achieved by changing the amplitude and/or

frequency of oscillation. The mixing intensity can be categorized in the three Re_o regimes; if $Re_o < 250$, the mixing is soft, and the flow is 2D-axi-symmetric. If $250 < Re_o < 2000$, the flow becomes more turbulent and if $Re_o > 2000$ the flow is fully turbulent in OBR (Stonestreet & Veeken, 1999). The Str number (St) describes the vortex propagation and it is tube diameter to oscillation amplitude ratio. The widely used Str number range is between 0.15 and 4 (Ni & Gough, 1997).

Full list of parameters is presented in the Tab.2.2. Fig.2.4 shows mixing control parameters in the oscillatory baffled flow channel. The effected parameters can be categorized under three groups. Geometrical parameters are related with the dimensions of flow reactor such as tube diameter, orifice diameter and baffle spacing. Second group is operating parameters which is linked with the pumping and oscillation mechanisms for example net flow or mean flow velocity, oscillatory frequency and amplitude. The last group is fluid parameters that comes from the physical properties of the reactants inside the tube such as fluid density and viscosity. Fluid density and viscosity change the fluid mechanics, therefor they must be taken into considerations.

Table 2.2 Oscillatory mixing control parameters

Variable Parameters for Oscillatory-Baffled Flow					
Geometric Parameters		Operating Parameters		Fluid Parameters	
D	Tube Diameter (m)	u	mean flow velocity (m/s)	ρ	Density (kg/m ³)
D₀	Orifice Diameter (m)	ω	angular frequency of oscillation (radian/s)	μ	Viscosity (m ² /s)
L	Baffle Spacing (m)	X₀	centre-to-peak amplitude of oscillation (m)		

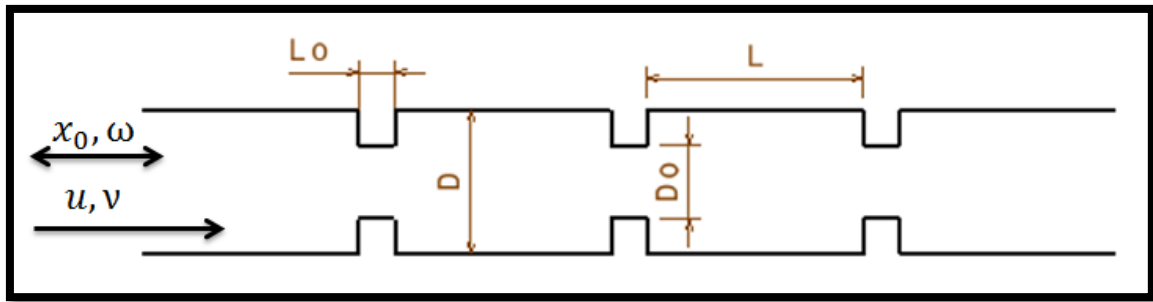


Figure 2.4 Geometrical parameters used for OFR reactor design and development

2.3 History of the Oscillatory Flow Mixing

Oscillatory mixing has been used by humans for hundreds of years. Butter churner is one of the great examples of ancient oscillatory mixing method. Churning is a technique to separate out the yellow fat from the buttermilk to produce butter. Around 15 centuries ago, farmers develop a very simple churning reactor from wood (Interesting, 1944). A stick called dasher or churn dash was moved up and down in a cylindrical container. The stick included a wooden circle with holes around it to create mixing vortexes after each movement as shown in Fig.2.5.



Figure 2.5 Butter Churning - Ancient Oscillatory Flow Mixing Method (Interesting, 1944)

Continuous oscillatory flow mixing and its control are relatively recent research areas. Reciprocating-plate extraction column (RPC) or pulsed packed/plate (PPC) are the earliest industrial example of the oscillatory flow mixing. The primary applications were phase separation and droplet breakage between two immiscible liquids (Karr, 1959). In 1973, Bellhouse et al. (Bellhouse, et al., 1973) combined the oscillation and furrowed membrane for blood mixing and to increase gas transfer for the first time. As shown in Fig.2.6, furrowed channel enables to create vortices are formed in the hollows and those vortices provide continuous blood mixing among the channels.

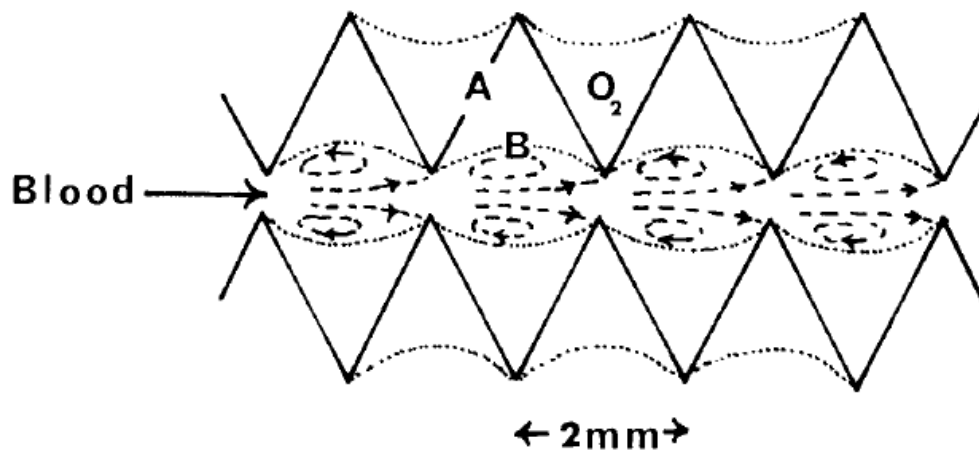


Figure 2.6 Oscillatory blood mixing membrane (Bellhouse, et al., 1973)

Numerical calculation of the flow patterns in furrowed channel were presented by I. Sobey (Sobey, 1980). He used the time-dependent two-dimensional Navier-Stokes equations to show the flow patterns of the arbitrary oscillatory flow. The numerical solutions of part 1 of the low patterns were supported with his experimental observations in part 2 (Stephanoff, et al., 1980). These two papers were the first papers to investigate the effect of Str number and Reynolds number over the flow patterns in the constricted channels. Sobey continued researching the effect of Strouhal number in oscillatory flow and he classified the structure of the flow cycle as small, intermediate or large according to the Str number (Sobey, 1983). He observed a quasi-steady flow with small Str number; however, viscosity was the main driver within the larger Str numbers.

In the late 1980s, baffle geometry with combination of oscillation was introduced by Dickens (Dickens, et al., 1989). The authors experimentally obtained that near plug flow can be achieved in a single tubular system with the appropriate combination of baffle shape and oscillatory Reynolds number. The relation between intensity of the oscillatory power and geometry of baffles (sharp, rectangular or cylindrical) in ducts was reported in (Brunold, et al., 1989).

X. Ni and his research group have conducted extensive range of study to understand mixing phenomena in the oscillatory baffled flow reactor for numerous applications since 1993. Particle image velocimetry (PIV) technique was first used to monitor velocity vector profiles and strain rate distribution for laminar and oscillatory flows in a baffled tube (Ni, et al., 1995). The experimental measurement of the mass transfer of oxygen into yeast culture in a pulsed baffled bioreactor presented by Ni (Ni, et al., 1995) for bioprocessing applications. Formulation of dimensionless groups used in the characterisation of oscillatory baffled flow was studied in (Ni & Gough, 1997). Droplet size and size distribution in suspensions using oscillatory-baffled reactor was investigated and uniform size distribution was experimentally observed by Ni (Ni, et al., 1998). Ni continued his research on the oscillatory flow mixing by publishing a systematic approach to understand the effect of geometrical parameters on mixing time in batch oscillatory baffled columns (Ni, et al., 1998). Scale-up correlation of axial dispersion between close-fit and loose-fit baffles in batch and flow oscillatory mixing was examined by (Ni, et al., 2001). The developments in computational modelling and inexpensive powerful computing hardware enabled scientists to develop numerical models for oscillatory flow mixing simulations (Jian & Ni, 2003).

The early promising studies in 1990s and the inherent mixing advantages, encouraged more scientist and research groups to develop oscillatory flow mixing technology and novel oscillatory baffled flow reactors. Tanks-in-series model was used to investigate the effect of various combination of dimensionless group on the residence time distribution in oscillatory baffled tube reactors by Stonestreet & Veeken (Stonestreet & Veeken, 1999).

It was an important study to provide flexibility in the practical choice of the dimensionless groups. Continuous production of sterols using a pilot-scale oscillatory flow reactor was demonstrated by (Harvey, et al., 2001). This was one of the first promising study to move industrial application from inefficient batch process to more efficient and safe continuous processing. Harvey established a mixing based design methodology for full scale Oscillatory Flow Reactors (OFRs) by maintaining geometric and dynamic similarity using wide range of dimensionless groups (Stonertreet & Harvey, 2002). The reaction time of biodiesel production was shortened using OFRs for transesterification of rapeseed oil with methanol and NaOH by (Harvey, et al., 2003). After 2000, scientists started to develop screening oscillatory flow meso-reactors using small tube dimeters <15 mm for relatively small production volumes but wider range of final product synthesis (modularity). Harvey, et al. demonstrated that the mixing observed in larger dimensions can be achieved with smaller scales of oscillatory flow reactor and smooth constrictions, they published an experimental and numerical study to compere mixing similarity in larger and smaller scales (Reis, et al., 2005). Three different reactor baffle shapes (integral, helical and axial circular) were develop under 5 mm diameter in order to evaluate the mixing performance within in different baffle shapes (Phan & Harvey, 2010). A summary of the prvious oscillatory flox mixing researches can be found in the Tab.2.3.

Table 2.3 Summary of Literature Review

Author(s)	Aim/Summary	Range of Dimensionless Groups		
		Re_n	Re_o	Str
(Bellhouse, et al., 1973)	To develop an oxygenator using pulsating flow and furrowed channels.	300 ml/min	18 ml stroke volume, (80 and 120)/min frequency	Furrows with 0.5 mm depth, 0.4 mm spacing
(Sobey, 1983)	Investigation of the occurrence of separation based on various Strouhal and Reynolds Numbers	7-30 30-75	-	0.00 – 0.1
(Dickens, et al., 1989)	Experimental examination of the oscillatory baffled flow effect on the residence time distribution measurements	110	~0.3	0 – 3000

(Ni, et al., 1995)	To develop an oscillatory baffled bioreactor for yeast culturing	-	0.56	4385 – 10965
(Ni, et al., 1998)	The investigation of the droplet size and size distribution in a batch oscillatory-baffled reactor	-	0.26 – 3.97	313 – 46992
(Fitch, et al., 2001)	Characterisation of flexible baffles in an oscillatory-baffled column for low and uniform shear stress for bioprocessing applications.	-	1000 – 4030	0.49 – 1.98
(Harvey, et al., 2003)	Continuous biodiesel production using oscillatory-baffled flow reactor	175 – 3195	0 – 3.97	0 – 31954
(Reis, et al., 2005)	Characterisation of an oscillatory baffled flow mesoreactor for safe chemical processing with smaller reactor volumes			12 – 335
(Zheng, et al., 2007)	To compare the biodiesel reaction with conventional stirrer tanks and continuous OBRs	1.9	67 – 301	0.13 – 0.4
(Lawton, et al., 2009)	Demonstration of the active pharmaceutical ingredient and continuous crystallization using COBC reactor		2300 – 6150	0.05 – 0.13
(Phan & Harvey, 2010)	Design and development of meso-scale OBR reactors with various baffle shapes for improved plug flow conditions	4.3 – 34	0 – 600	0.1 – 0.8
(Nogueria, et al., 2012)	Investigation of flow dynamics in the oscillatory flow with tri-orifice baffled OBR.	-	1.0	646
(Abbott, 2015)	Demonstration of the bioprocessing using continuous OBR	73 – 259	0.55 – 3.32	127 – 905
(Ahmed, et al., 2017)	Scale-up of continuous oscillatory helical baffled reactor	25 – 250	0.17 – 0.37	67.5 – 14820
(McDonough, et al., 2019)	Characterisation of OBR reaction kinetics for optimised operating conditions.	5 – 40	0 – 0.2	50 – 1000

2.4 Background of Oscillatory Flow Reactors

Oscillatory flow reactors consist of cleverly designed tubular conduits and oscillation mechanisms to oscillate the materials inside the reactor. Tubular reactor consists of periodically spaced baffles with specific ratios to tube diameter and baffle spacing length. At the one end or in the multiple places of the conduit, there is an oscillation mechanism based on piston, diaphragms or bellows to generate an axial backward and forward movement of the whole materials inside the reactor.



**Figure 2.7 Butter Churner - Back and forth Ancient Churning Reactor
(Collections, 2016)**

Earliest butter churns are the first example of the OBR. The working principle of the old butter churns was very simple they convert human power into physical agitation using a stick and milk holding vessel. Very basic design of the earliest vertical butter churn made from wood is shown in the Fig.2.7.

A batch type pulsed baffled reactor was introduced by Ni and Gao (Ni, et al., 1995). The reactor was made from Perspex with 50 mm diameter and 500 mm length. It has 1 L of liquid volume. Baffles were made from PTFE and six baffles were used for the entire reactor length. Three sizes OBR reactor were developed

by K. B. Smith at Cambridge University (Smith, 1999). He used reactors in 24, 54- and 150-mm diameter with volume of 0.45 L, 4.6 L and 79.5 L respectively. For the first time, he introduced multi-orifice baffle design for the 150 mm reactor in order to simplify manufacturing and assembly of the reactor kits. Baffles were inserted into a straight tube, there was 1 mm clearance between baffles and tube wall. Servo-hydraulic mechanism was chosen to oscillate fluid inside the reactor. P.Stonestreet and P.M.J. Van Der Veecken (Stonestreet & Veecken, 1999) developed a stainless steel OBR with 24 mm tube diameter and 1.4 m length. Each tube was connected with U-bends to construct 2.9 m length reactor and 1.3 Litres volume. Each tube was fitted with 38 baffle cavities. A Piston based oscillation mechanism including variable amplitude and frequency control was used to move the fluid. Meso-scale reactors with 7.5 mm tube diameter was presented by A. N. Phan and A. Harvey (Phan & Harvey, 2010). They introduced various baffle shape such as central, helical and integral. Baffled rods were inserted inside 7.5 mm tubes. They used syringe pump to create oscillatory motion. Nitech solutions have been developing commercial OBRs for various industries including various scales from lab to full industrial sizes (NiTech, n.d.).

2.4.1 Modular Oscillatory Baffled Reactor

Microreactors are very important laboratory tools for academic research, and also for chemical and pharmaceutical product development. Small size reactors with excellent heat and mass transfer, provides green chemistry by minimising the waste material and energy, which results in cost-effective and time-efficient ways to discover new materials and with a small footprint.

Modular oscillatory baffled reactor in 4 mm diameter was developed and patented by research group led by Prof Harris Makatsoris at Brunel University London (Makatsoris, et al., 2011) as shown in Fig.2.8. Centillion OBR was used to investigate plug flow conditions in micro scale and then develop a scale-up model for 8 mm diameter.

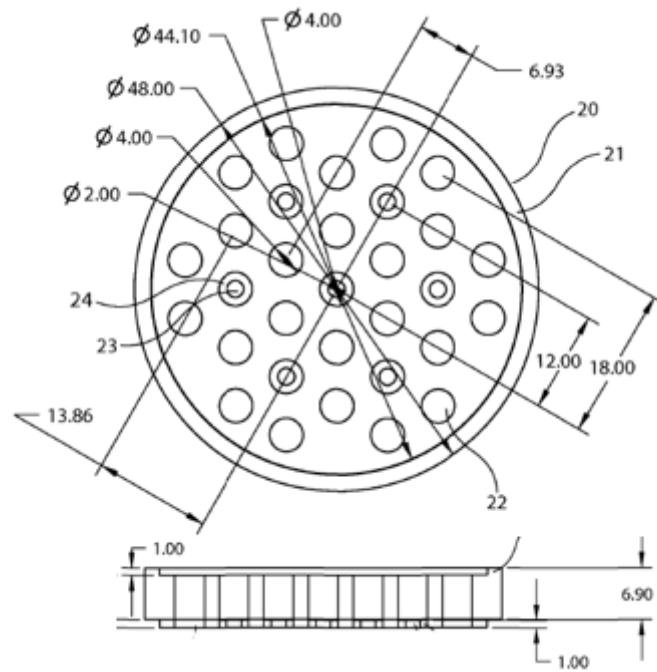


Figure 2.8 Centillion Micro Scale OBR Disk (Makatsoris, et al., 2011)

The modular design configuration provides great flexibility for manufacturing the reactor and rapid configuration of the reactor volume under various reactor volume requirement conditions. The functional sizes of the OBR such as baffle spacing (L), baffle restriction ratio (α), and baffle thickness (l) are same as standard OBR design (Brunold, et al., 1989; Ni, et al., 1998) as shown in Tab.2.4.

Table 2.4 Micro Scale OBR Specs

Baffle Conduit Parameters	
Baffled conduit diameter (D)	4 mm
Baffle constriction diameter (d_o)	2 mm
Baffle spacing (L)	6 mm
Orifice thickness (l)	1 mm
Key Geometrical Ratios for OBR Design	
Baffle spacing (L)	1.5 D
Baffle contraction ratio (α)	0.5
Modular Disk Parameters	
Disk Outside Diameter	$\phi 60$ mm
Disk thickness	8 mm
Number of flow channels	7
Number of service channels	24
Micro Scale OBR Parameters	
Reactor length	168 mm
Reactor volume	18.45 mL

Each reactor disk was machined using Polyetheretherketone (PEEK) and stainless-steel material. 24 middle and 2 end disks were assembled using threaded rods and nuts. Each disk has 7 O-rings placed around flow channels to prevent any leaks. Chromatographic tubing of 1/8" OD (3.175 mm) and 1/6" ID (1.59 mm) was used to transfer liquids from stock solutions to the OBR channels using continuous pumps.

2.4.1.1 Oscillation Control for Modular OBR

The Confluent PVM Precision Syringe pump was used to control oscillation frequency and amplitude. It is a self-contained pump and valve module designed for a variety of liquid handling applications as shown in Fig.2.9.

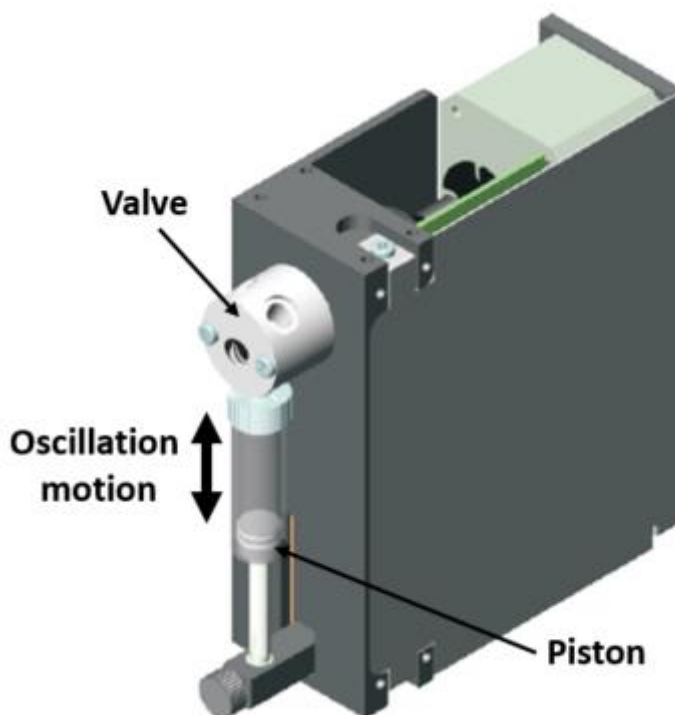


Figure 2.9 Confluent PVM Precision Syringe Pump

It's a stepper motor driven syringe pump which has 30 mm peak-to-peak stroke, that can provide from 0 to 15 mm amplitude range. Pump has 3000 steps resolution, which means 0.01 mm amplitude resolution up to 15 mm. Maximum speed of the pumps is 6000 steps per second, at the smallest amplitude that can reach max frequency of 10 Hz.

The pump can be controlled by an external computer. LabView control software was used to control piston position and speed using RS232 connection. Single or multiple command strings were used to send to the pump and the relevant responses returned. A separate code was written for each set of amplitude and frequency combination.

2.5 Design Elements and Considerations for the OBR Development

Reactor development is a complex process which requires defining the sequence of geometrical and operating parameters in order to develop a robust, sustainable and scalable mixing device. Varying design options may be needed for different reaction and mixing purposes. A typical configuration of OBR consists of two main sections; the tubular section which is also called static part of the reactor, oscillation mechanism is the dynamic part of the reactor which creates a range of amplitude and frequency combinations to achieve various mixing conditions. Geometrical design parameters and oscillation mechanisms are reviewed in this section.

2.5.1 Geometrical Design Parameters

In the development of the Oscillatory Baffle Flow Reactors, there are five important geometrical parameters.

1. Tube Diameter (D)
2. Baffle Thickness (δ)
3. Baffle Spacing (L)
4. Baffle Open Area (α)
5. Baffle Shape

In this section, relevant background literature is presented to identify optimum geometrical parameters.

2.5.1.1 Tube Diameter

Identifying optimum tube diameter of an OBR involves understanding of flow patterns inside the tube, economic analysis, production capacity, physical properties of the manufactured materials, system pressure and temperature, manufacturing technique to develop the reactor and tubing material. Almost in every industry the capital investment of the piping network including pumping equipment is in the range of 25-40% compare to the total facility investment

(Walas, 1990). Also, the required power for pumping depends on tube diameter, flow rate, overall reactor length and tube characteristics (surface roughness etc.).

To provide plug flow conditions, optimum tube diameter has vital importance. Previous OBR designs were observed for better understanding of the optimum tube diameter for the plug flow conditions. There is a clear distinction in terms of tube diameter used in the literature. First OBR development and experiments were mainly performed with large tube diameters (over 20mm diameter).

However, after 2000s, tube diameters became smaller (less than 15mm); meso-scale reactors. There are two main reasons of this trend change in the tube dimension; manufacturing capabilities and market demand for the increased product variety. The manufacturing capability was limited to produce baffles in small tube diameter and it was very expensive, however this was solved with advances in manufacturing such as micro-machining. Before 2000s, the market had been driven with the products, which manufacturers produced for the customer. Companies could survive with only a few products by producing them in very large volumes that was required large production plants. However, this trend was shifted to consumer driven production after 2000s. With this trend, consumer demanded more product variations. Manufacturing requirements were also changed to more agile and modular platforms instead of very large reactor tanks or tubes. OBR technology followed the changing trend by reducing the tube diameter into small scales (under 10 mm) in order to produce less product volumes but more product options such as parallel production with small platforms.

2.5.1.2 Baffle Thickness

Six different baffle thickness were evaluated including 1, 3, 6, 12, 24, and 48 mm in 50 mm OBR to understand optimum baffle thickness (Ni, et al., 1998). The researchers observed that larger baffle thickness increased the vortices “cling time” from a baffle edge prior to process of shedding. Increased cling time resulted in vortex deformation, therefore optimum baffle thickness was identified as 2-3 mm.

2.5.1.3 Baffle Spacing

Distance between two baffles is important to achieve uniform and effective mixing conditions. The shape and length of the vortex formation can be defined by the space between two baffles. Vortices require enough space to fully expand spread among the inter-baffle regions. If the space is too large, that results in insufficient propagation through the entire volume of the inter-baffle zone, producing stagnant regions (Abbott, et al., 2013). If the distance is too short, vortex interacts with the baffles which results limited growth of vortices within each inter-baffle zone (Ni, et al., 1998).

First study on effect of baffle space was published in 1989 (Brunold, et al., 1989). The effects on mixing of three different baffle spacings as 1D, 1.5D and 2D (D is tube diameter) were investigated. 1.5D of baffle spacing was found as optimum for the most range of oscillation combinations. Similar research was conducted by pulsating the fluid by Ni and Gough, they suggested the optimum spacing as 1.8D (Ni & Gough, 1997). Ni et.al. investigated the effects of baffle spacing by employing baffle oscillating instead of pulsating the fluid (Ni, et al., 1998), 2D as baffle spacing was observed for the mechanism of baffle oscillating. A Design of Experiment (DoE) was employed for establishing the relationships between four major geometrical parameters (Ejim, et al., 2017), results showed that the mixing is independent of baffle spacing.

2.5.1.4 Baffle Open Area

Width of the mixing vortices in each baffle zone is controlled by the baffle open area (α). Larger inter-baffle areas create narrow vortices which result poor mixing eddies. Smaller baffle diameters enable larger constrictions for the fluid passing through each baffle. Consequently, constricted fluid creates wider vortex formation resulting better mixing performance. Seven different ratio of the baffle open area in the range of 11% to 51% were investigated using tracer experiment (Ni, et al., 1998). Authors have reported the optimum baffle open area ratios is 20 to 22% by obtaining the shortest mixing time.

2.5.1.5 Baffle Shape

Various baffle geometries including sharp edges, smooth edges, integral, central axial, helical and wire wool were developed, and their performance was experimentally tested by the previous researchers. Each design has advantages for a different application.

One of the first oscillatory flow researchers (Brunold, et al., 1989) observed sharp edges as bent or baffled inserts can generate large scale eddy mixing in the fluid flow. This study was an important guidance for the development of the future baffle geometries. A novel baffle design as “flexible baffles” was proposed by Fitch and Ni (Fitch, et al., 2001). A flexible material was sandwiched between two stainless steel baffle plates, the aim of developing the flexible baffle was to minimise the volume-averaged strain rates. Various baffle shapes used in the past OBR development studies are shown in Fig.2.10. Helical, integral and central baffle shapes were developed by A.N. Phan and A. Harvey for meso-scale OBR development.(Phan & Harvey, 2010).

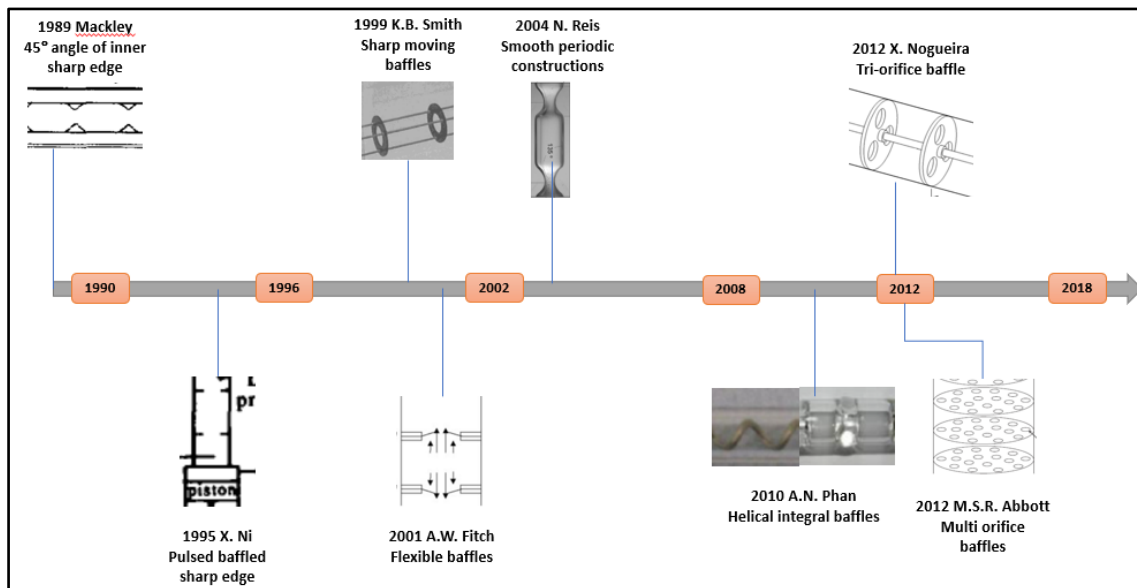


Figure 2.10 A timeline of various baffle shapes have been tested in the previous OBR studies

2.5.2 Commonly Used Oscillation Mechanism in the Literature

A range of different mechanical devices have been designed to create oscillation motion. Sinusoidal wave form was dominated in the previous OBR studies. Max and min oscillation conditions depend on selected oscillation mechanism.

Cam piston oscillatory mechanism was employed by Dickens (Dickens, et al., 1989) as shown in Fig.2.11. Two connected pistons were driven by a cam device. Amplitude and frequency could be tuned within range of 0-5 mm and 0-3.5 Hz respectively.

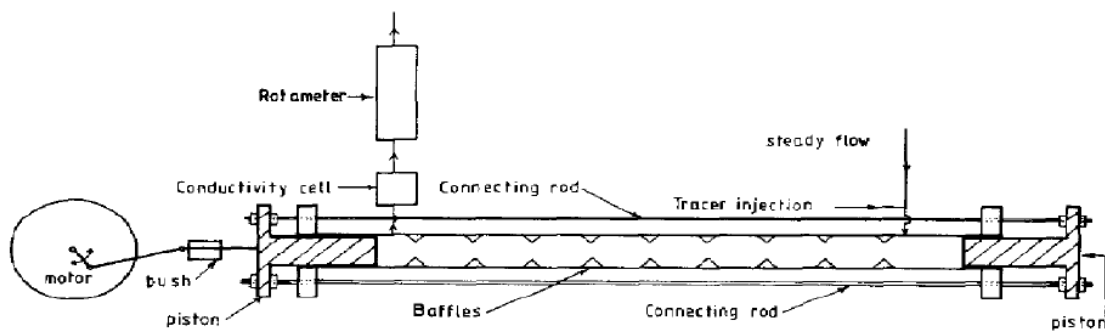


Figure 2.11 Cam Double-Piston Oscillatory Mechanism (Dickens, et al., 1989)

Electromagnetic moving coil with bellow oscillatory performed well to oscillate a 0.45 litre reactor volume (Smith, 1999). The mechanism provides enough power and stroke/frequency range for meso-scale reactors. The limitation of the system was its scalability and the fact that the same mechanism cannot create enough pressure for the large-scale reactors.

Pneumatic piston oscillatory mechanism was used by Mackley and Ni for the 25 mm tube diameter of 6.3 m length OBR (Mackley & Ni, 1993). The oscillatory mechanism consists of pneumatic cylinder, linear transducer and oscillation drive control unit. Stroke of the oscillation is control with various lengths of stoppers placed on the shaft of the pneumatic piston. Square wave pulse was used to control the motion of the piston within the frequency range of 0.5 – 9 Hz. Bellow type oscillation mechanism provides good fluid sealing. The limitations with this mechanism are the cost for large scales, the time required to change amplitude, and poor amplitude control precision.

Servo-hydraulic piston oscillatory mechanism was developed by Smith (Smith, 1999). The hydraulic mechanism provides very high pressures to oscillate large volume of fluids. The mechanism was used for 54 and 150-mm tube diameters of 4.6 and 79.5 litres tube volume respectively. The motion of the piston can be controlled by various wave forms such as sinusoidal, triangular or trapezoidal. The only concern with this mechanism is that it is not suitable for small scales because of its footprint and additional maintained for lubricant etc.

2.6 Design of Experiments (DoE) for Statistical Analysis

Product and process improvement has vital importance in any industry. The methods and tools for identifying the process quality and efficiency are evolving by the recent improvement on the computation and data analysis tools. Statistics is the core element to understand the relationship between input and response variables. It is easy to collect various type of data such as numbers, characters, images etc after each experiment, however data on its own has no meaning. Data must be interpreted to become meaningful to understand process dynamics. Statics takes a core place to interpret the experimental data.

DoE is very powerful statistical tool traditionally used by scientists and industry. The usage of the DoE has increased exponentially in the last two decades as shown in Fig.2.12. The publication numbers per year were obtained from Science Direct by searching “Design of Experiment” in the title search section. The trend is represented by an exponential regression model. Future usage of the DoE can be predicted with exponential regression formula. According to the last two decades publications, it can be clearly expected that the grow of DoE usage will continue. DoE is not something new it has been used for decades, however as shown in Fig.2.12, there is a sharp increased on its usage in the recent years. User-friendly commercial and non-commercial statistical software lead its recent years` popularity. Users can easily create set of experiments using Minitab, Statistica, SPSS, JMP, R, Microsoft Excel etc. Outcome of the statistical analysis can be presented using suitable graphic representation options such as contour, plot, etc.

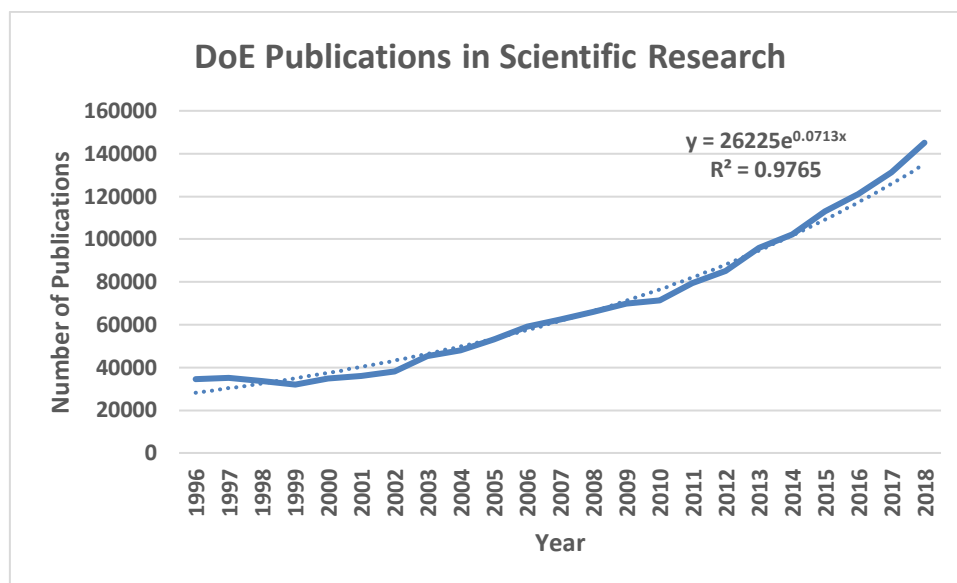


Figure 2.12 DoE applications in the scientific researches

DoE can be used for process monitoring, product/process optimisation and formulation, robust experiment design and developing prediction models. DoE has been successfully performed in various manufacturing and non-manufacturing applications such as increasing protein yield by testing various enzymes in the dairy industry (Emmons & Binns, 1990), improvement of the cheese quality in the food industry (Ellekjar, et al., 1995), process optimization for the microencapsulation processes to protect active ingredients from external damages in the pharmaceutical industry (Paulo & Santos, 2017), minimization of variance for decision making (Anand, et al., 2010), and identifying optimum therapy plan for brain tumour treatment in medicine (Miki, et al., 2018).

2.7 Functional Nanomaterials

Nanoparticles receive great interest from both scientific and synthesis perspectives. Properties of the materials depend on their size. Nanomaterials provide the potential discovery of new applications and properties. Throughout history, enormous work has been done to design and produce nanoscale materials. This work has significantly changed every human-made object in the last two decades in terms of their performance and quality. Nano-scale materials can be successfully used in various engineering domains such as molecular

electronics, coating, textiles, digital information, display devices, foods, drugs, and biotechnology industries. All these materials have wide variable properties and when those are produced in nanoparticle sizes, they can prove another set of new properties.

2.7.1 What is Nanomaterial?

Nanomaterial is an object that has at least one dimension in the 1-100 nm nanoscale size. Nanomaterials are categorised according to their dimensions as shown in Tab.2.5.

Table 2.5 Dimensions of Nanomaterials

Nanomaterial Dimension	Example
All three dimensions < 100 nm	Nanoparticles, quantum dots, nonoshells, nanorings, microcapsules
Two dimensions < 100 nm	Nanotubes, fibres, nanowires
One dimension < 100 nm	Thin films, layers and coatings

Normally the upper limit is taken as 100 nm by the nanoscience community, but this is a fluid limit: most often greater dimensions sometimes up to 200 nm are defined as nanomaterials (Fillipponi & Sutherland, 2013). A valuable question can be raised: “*Why 100 nm and not 250 nm or even not 1 to 1000 nm?*”. The answer is that nanoscience is not just about the science of the small, but it is the science to investigate the effect of small dimensions on creating new physical properties. The definition itself focuses the influence that the dimension has on a certain material rather than at what exact dimension this effect arises. Fig.2.13 shows the nanomaterial scales comparing some of the daily used products.

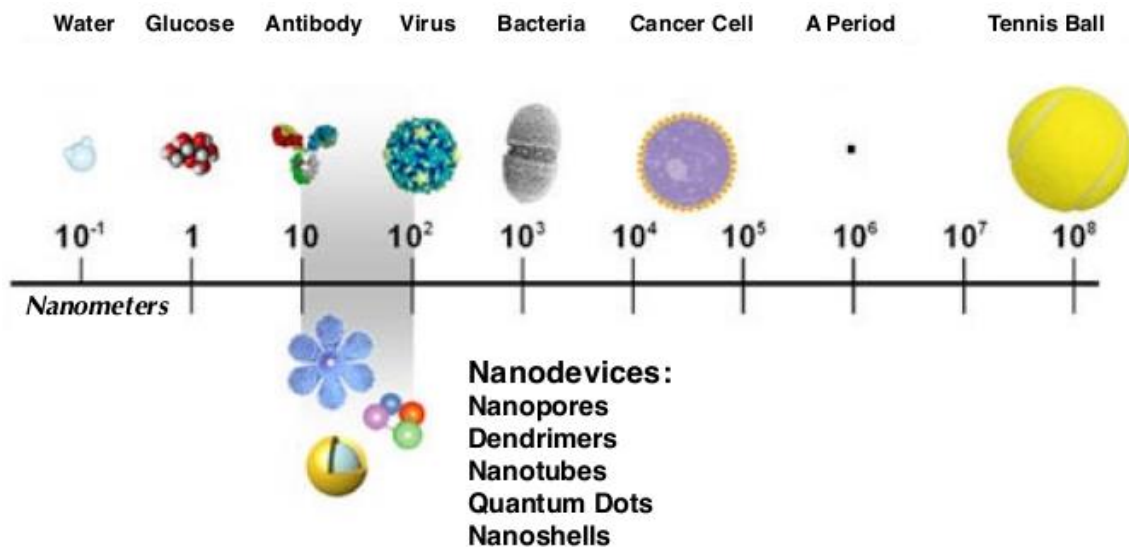


Figure 2.13 Objects in different scales (Image adapted from “A snapshot of nanotechnology”, National Cancer Institute)

2.8 Manufacturing of Nanomaterials

As known, all substances are composed of atoms, which can be assembled in many ways to achieve the desired final product. Manufacturing process, chemistry and geometric arrangement of the atoms can influence properties of the material. If it was possible to build matter, atom by atom, we could make diamond from graphite by rearranging the carbon atoms.

Number of methods have been developed to make nanomaterials in the last few decades. The methods to produce nanomaterials can be categorized into two groups as shown in Fig.2.14. Top-down approach, in which the process begins with a bulk material to grain them to nanoscale size by using mainly mechanical forces. Bottom-up approach, which builds the nanoparticles from finer scales such as atom by atom. The selection of manufacturing methods is directly linked to the final nanomaterial's properties and functionalities, as well as scalability and production costs.

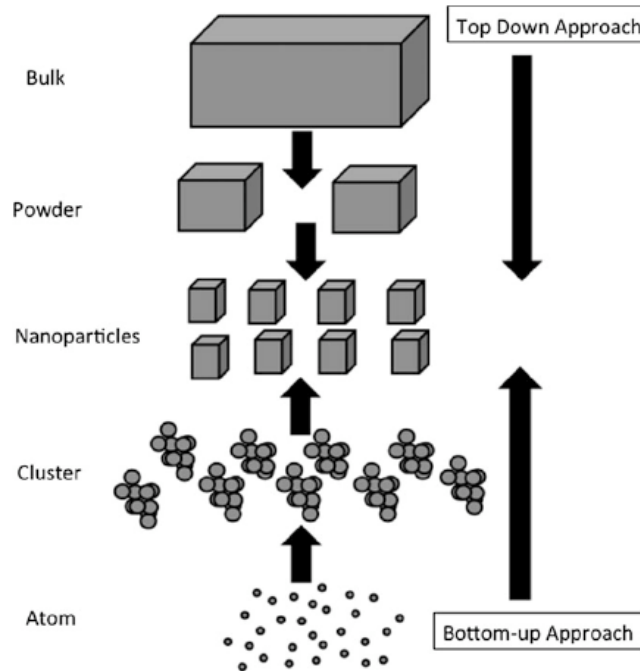


Figure 2.14 - Top down and bottom-up approached for nanomaterial production (Su & Chang, 2018)

2.8.1 Nanomaterial Synthesis in Flow

Nowadays, nanoparticles are widely used across many industries such as painting, coating, electronics, textiles and biotechnology. There have been several financial and manufacturing challenges in developing functional nanoparticle components as stated above. On the other hand, flow processing introduces a new synthesis method to overcome batch type process limitations. Gold nanoparticles are one of the most attractive nonmaterial for chemical and biological applications. One of the first studies to produce gold nanoparticles using glass-silicon microreactor was published by Wagner and Kohler (Wagner & Kohler, 2005). Following the optimum conditions of flow rate, pH and excess of reducing solvent, narrow sized particle distributions of 5-50 nm were achieved. Lin et al. reported a significant reduction in the reaction temperature of silver nanoparticle synthesis by using stainless-steel tubular coil (Lin, et al., 2004).

3 REACTOR DEVELOPMENT AND EXPERIMENTAL METHOD

“If you want to find the secrets of the universe, think in terms of energy, frequency and vibration.”

Nikola Tesla

3.1 Introduction

In this chapter, the development of meso-scale modular OBR and construction of the continuous manufacturing platform is presented. It begins with the reactor design guideline. As a starting design point, modular OBR (Makatsoris, et al., 2011) was studied and its scaling ratios were used to develop a meso scale modular OBR. New heating/cooling channels were introduced to develop better heat transfer for the meso scale OBR and that feature can be scalable for any size. Performance of the spiral heating/cooling channels was measured with CFD simulations and experimental measurement. Various channel arrangement was presented to deliver solutions for challenging process requirements such as rapid heating/cooling, regional heat control and single or dual spiral heating channels. Sharp and smooth baffle edges and their most economic manufacturing methods were explained.

A novel oscillation mechanism was developed. It's novelty comes from the amplitude control feature which is designed based on lead screw mechanism and provides significant time benefit to change the amplitude very quickly. Fully automated amplitude and frequency control is explained in this chapter. Fully automated oscillation and net flow control will open the doors for self-optimising continuous processes to discover limitless combinations with reducing operational cost and time. Furthermore, this chapter discusses the advantages and limitations of the developed meso-scale modular OBR.

3.2 Reactor Design Guideline

Considering all influencing aspects and factors in the design of the reactor will save time and cost to develop efficient processing platforms. Therefore, a list of design considerations is summarised below:

- **Reactor Geometries:** Diameter size, baffle shape, reactor length and footprint must be identified in the beginning of the reactor design based on the target applications and their required production volume.
- **Temperature:** Working temperature is important for the material selection to construct the OBR reactor.
- **Software Selection:** Software is important to control actuators, sensors and pumps in the whole platform. Therefore, a simple software and user-interface is preferable to enable the control and operation by anyone.
- **Data Collection:** Today, we are in the data age, the system needs simultaneous and continuous data transferring for the post-process calculations of the experimental outcomes.
- **Integration of analytical measurements equipment:** access ports are required to collect processing measurements such as temperature, pH, conductivity or spectrometer.
- **Appearance:** Aesthetic requirements can limit the material selection. For example, transparent reactors are generally preferred in the labs, because scientists would like to monitor the process and reactions. In that case, borosilicate glass is the primary material in the lab tools. Again, styling is an important feature that must be considered by the designer. Such as shape, look, and surfaces, they must all be appropriate for human-machine interaction.
- **Life expectancy:** Many functional parts must meet certain life-cycle expectations and regulatory requirements. Life expectancy involves the period in tough chemical conditions and high/low temperature environments.
- **Geometrical dimensioning and tolerance:** Whole system consist of many sub-components, which need tight tolerances for proper fit and

function. The cost, effect of the load, manufacturing method and temperature must be considered for the calculation of the correct tolerance and absolute size.

- **Manufacturing (for the reactor components):** Each material has some specific manufacturing requirements. First, the material of the components needs to be identified and the appropriate manufacturing process needs to be selected for the corresponding material, and finally, the reactor can be designed based on pre-defined material and process. Each process, such as injection moulding, glassblowing, CNC-machining etc. have unique design requirements.
- **Reactor Volume:** The size and volume of the reactor are important to decide the processing method, cost, material selection and assembly process.
- **Cost:** It is particularly important to control your budget to build the whole reactor system.
- **Assembly:** Design must be simple enough to assemble and disassemble when necessary. The reactors may require cleaning after each product or experiment to prevent contamination, therefore, the reactor must be disassembled quickly even by non-experts or technical people.

3.3 Development of a Novel OBR

Scale-up is a common problem for any type of industrial application. Process conditions in the laboratory scales cannot reliably predict in the large-scale productions with using conventional processes of stirred tank reactors or continuous stirred tank reactors. The main advantage of an OBR is the predictable scale-up from laboratory to industrial productions by maintaining dynamic flow conditions. St , Re_n and Re_o are kept constant in order to provide similar fluid dynamics for the flow in various production scales. Two different scales of reactors were designed and constructed to develop a scale-up model.

The current state of the art to design OBR is to use long straight tubes and conduits. All conventional reactors were developed by using tubes and conduits.

However, in this thesis, for the first time, the modular design concept was used to characterise and measure its plug flow performance. Micro scale modular OBR was presented in the second chapter. Dimensional scale-up ratios of modular OBR reactor were used to construct meso-scale OBR (Makatsoris, et al., 2011). The entire reactor comprises of any number of standard sections that, once assembled will combine into continuous OBR system of a desired length. Each section consists of 7 baffled conduits and number of baffle free conduits which are designed for assembly, as well as heating and cooling purposes. The reactor is made up of “slices” rather than “tubes” and slices can be aligned linearly. Therefore, conduits can form a tube as shown in Fig.3.1. This design configuration enables us to reduce the length of the reactor, which is a considerable improvement for the OBR technology especially for the industrial scale OBRs to successfully provide smaller machine footprints compare to batch processes and traditional OBR platforms.

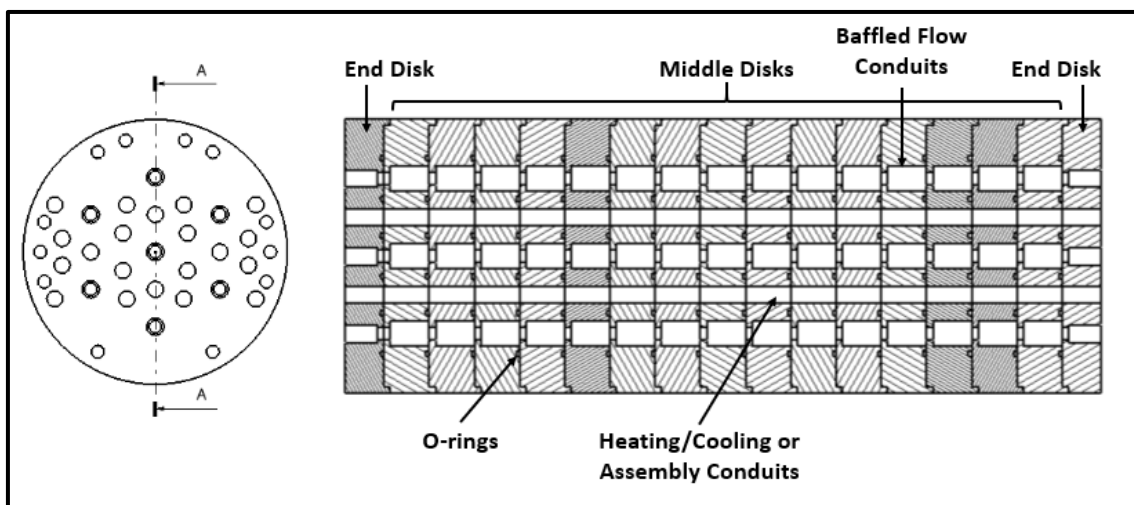


Figure 3.1 8 mm Modular OBR Design

The modular design concept provides great flexibility for manufacturing of the reactor components and assembly. The presented reactor design can be manufactured by using variety of conventional techniques at low cost and by additive manufacturing techniques (3D printing). 5 different were built with two different manufacturing methods, from 4 different materials and in 2 different scales. The micro-scale reactor has been manufactured by using CNC machining

method in stainless steel and Polytetrafluoroethylene (PTFE). The meso-scale reactor, which is scaled by a factor of 2, has been prototyped by using additive manufacturing in Acrylonitrile Butadiene Styrene (ABS) and CNC machining in PTFE, acrylic and stainless steel.

As well as manufacturing advantages, another key benefit of this sectioned design reactor is the flexibility to be disassembled for cleaning and reassembled again. Simply, the “lego-like” ability to be reconfigured into any required length; the ability to integrate monitoring and measurement devices like “plug and play”; the ability to control temperature via cooling or heating fluid flow; and the ability to produce multi-step chemical processes via serial or parallel reactor connections.

3.3.1 Meso Scale OBR Design and Development

Patented modular OBR (Makatsoris, et al., 2011) ratios were used to develop and construct a meso scale OBR. Diameter was increased from 4 mm to 8 mm and all functional OBR ratios were kept same as the patent. The footprint of the disk was increased to 85 mm in diameter and 16 mm in thickness. Disk has 7 baffled reaction channels. In the first meso-scale OBR design, heating/cooling channels were very similar to the original design. But, number of the service passages was increased to 32, to allow more efficient heating and cooling channels, and also to allow more threaded rods to assemble the modular disks as shown in Fig.3.2.

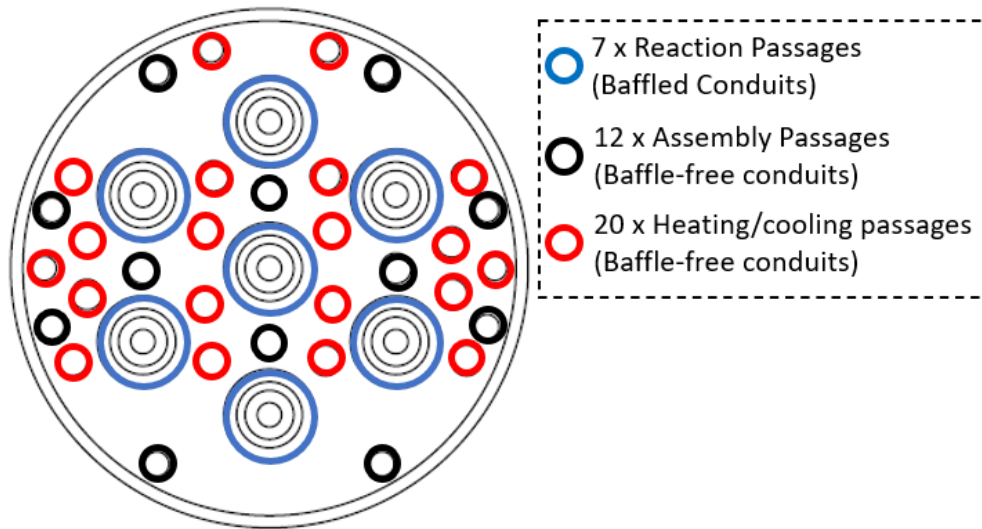


Figure 3.2 Reaction, assembly and heating/cooling passages

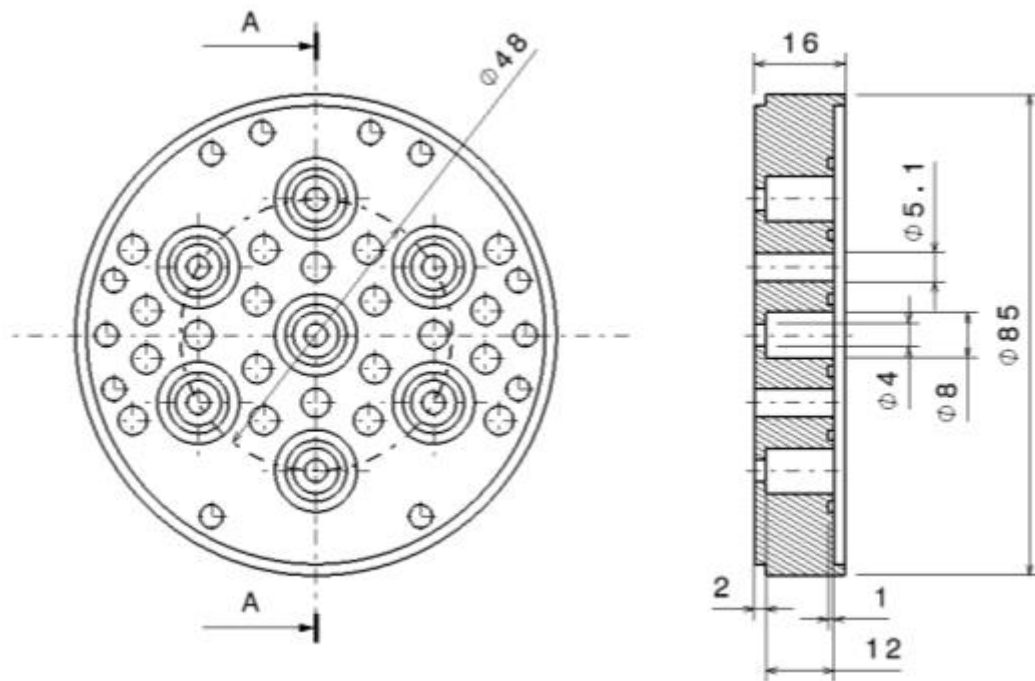


Figure 3.3 Meso Scale OBR Disk Design

Overall dimensions of the meso-scale OBR disk are shown in Fig.3.3. There is one baffled channel in the centre of the disk, another 6 baffled flow channels were placed equally at a 60° angle on the 48 mm diameter axis of the centre. In-line measurements techniques have become very important in the recent years. Process industry prefer to monitor the production and product quality during the

processing, and if something goes wrong, prefer to react immediately to minimise the waste product and time. Therefore, special channels from side face of the modular disk were designed to enable the integration of standard inline analytical tools such as spectrometer, pH, temperature and turbidity measurement probes.

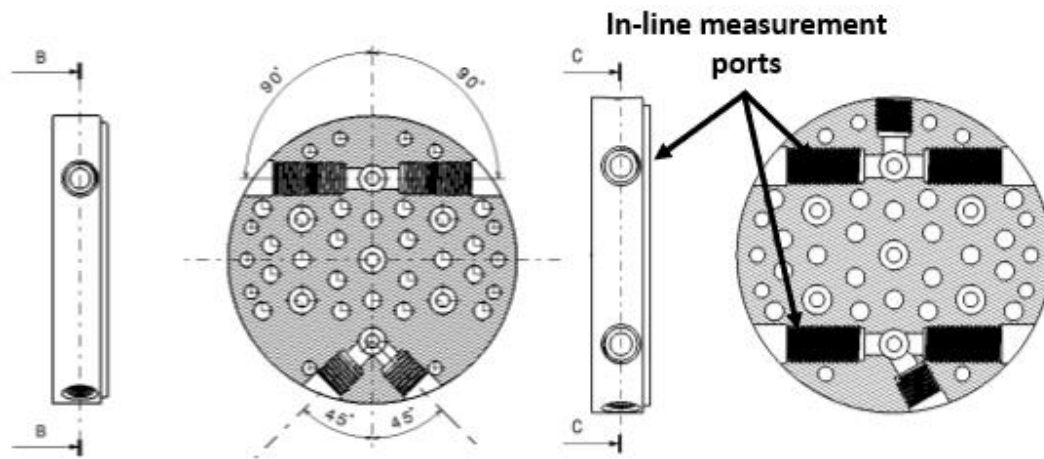


Figure 3.4 Special modular OBR disks for inline process monitoring

The position and number of the monitoring ports depend on required measurement techniques. Various combinations were considered in the meso-scale OBR development stage, and prototype of these combinations were developed to cover a wider range of inline measurement techniques as much as possible, as shown in Fig.3.4 and Fig.3.5. Access ports have standard industrial thread size. Any standard probe can be just plugged and played. Absorbance and colour measurements are most popular techniques in the process industry. Optical fibres can be placed opposite to each other (180°), at 90° or any specific angle for transmission and receiving.

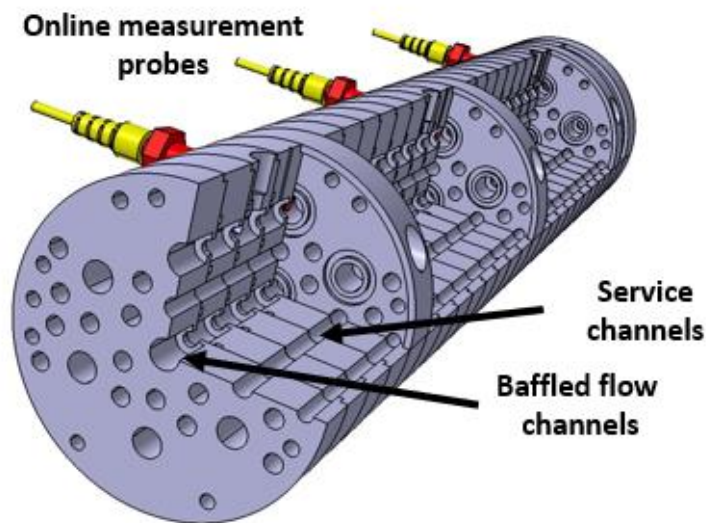


Figure 3.5 Meso-scale OBR with integrated inline measurement probes

The performance of the in-line monitoring has been successfully measured by integrated special modular OBR disks and Ocean optics spectrometer for the absorbance measurements as shown in Fig.3.6. NIR measurements can also be performed by using NIR fibers and spectrometer. Temperature measurement was monitored by using inline thermocouples.

Original design of heating/cooling channels was simple and easy to manufacture by using only straight holes for assembly and service channels. However, some difficulties were observed in the daily operation of the reactor. These difficulties are summarised below and further development was performed to overcome these drawbacks:

- Required large number of O-rings to seal each disk (7 for reaction passages and 20 for heating/cooling passages). Reaction fluid and heating cooling fluid travel through channels and they must be leak-free. This operation significantly increases the cost and time to assemble the reactor.
- Each passage must be connected with U-bend tubes on the both side of the reactor. As that can be seen on the Fig.3.2, conduits are very close to

each other, consequently there is very limited space to tight U-bend assembly nuts.

- Significant amount of effort is required to assembly the reactor.

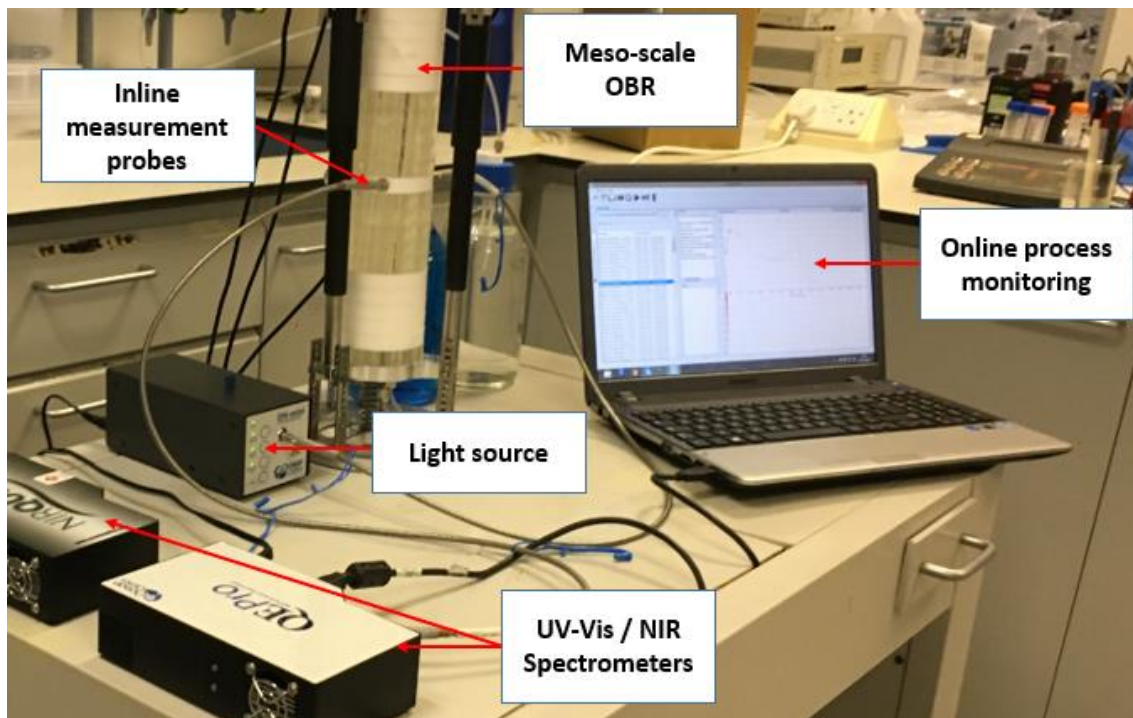


Figure 3.6 Demonstration of the inline measurement setup with meso-scale OBR and Ocean Optics Spectrometer

A major improvement has been made by the second version of the meso scale modular OBR disks as shown in Fig.3.7. The shape of the disk was changed to a “ring” shape by removing the central baffle for better packaging of flow channels and to increase reactor volume. The number of baffled channels was increased from 7 to 8 which consequently increased the volume of the disk of the entire reactor. 8 baffled holes are positioned at 22.5° of angle space inside the 85 mm diameter ring. The ring shape provides lower cost for manufacturing, less weight, easy assembly, and more baffled reaction channels and volume per disk. However, the most important feature of the new design is the spiral heating/cooling channels as shown in Fig.3.7. Spiral channels eliminate the assembly difficulties due to single input/output ports for heating/cooling fluid, it does not need U-bend connections compare to previous version. Addition to easy

assembly benefit, it ensures better heat transfer with increased surface area to volume ratio and uniformly placed around the reaction channels.

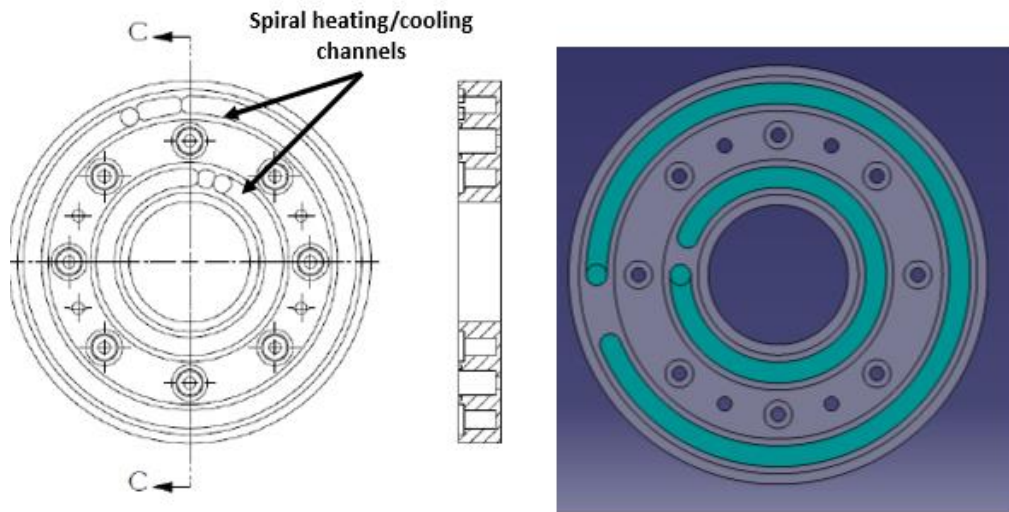


Figure 3.7 Meso-scale OBR with spiral heating and cooling channels.

Two large spiral channels (approximately 340°) are designed to surround baffled channels. One spiral channel is in the inside the baffled channels and the second one is on the outer side of the baffled channels within the same distance from the centre of the baffled conduits. Heating/cooling fluid travels among the spiral channel and passes to next channel as shown in Fig.3.8c. With only one fluid inlet and outlet, the temperature of the entire reactor can be controlled, which does not require any U-bend connections which is significant improvement compare to the original heating/cooling conduit version. The length of the spiral channel can be customised for flexible temperature control. For example, it can be two separate spiral channels as shown in Fig.3.8a, which will allow two sperate temperature zones to be able to control individually. In this case, half of the reactor can be cooled, and another half can be heated.

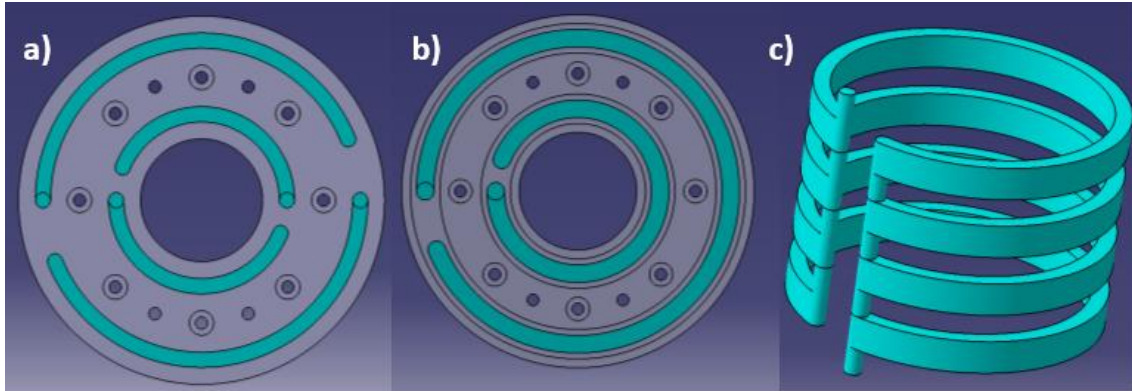


Figure 3.8 a) Half/half temperature control b) Full temperature control c) Demonstration of heating/cooling fluid flow

Some materials have better thermal conductivity such as aluminium, copper, steel etc. In that case, the design can be simplified by removing outer spiral ring to reduce its manufacturing and operation cost. Another advantage is that less quantity of O-rings is required for sealing. In the original straight heating/cooling channels, one O-ring is required for each conduit (that means 20 O-rings per disk to seal all heating/cooling passages in a disk) which means higher cost and longer assembly time. The whole spiral channel can be sealed by two O-rings or a gasket can be designed for the whole disk.



Figure 3.9 Meso scale OBR disks with spiral heating/cooling channels (Acrylic and PTFE materials)

Three different materials (stainless-steel, acrylic and PTFE) were used to construct meso-scale OBR with spiral heating/cooling channels. Acrylic provides see-through feature during reaction and is a great material for light transmission as shown in Fig.3.9. Some bioprocess applications require light, such as algae cultivation, therefore, acrylic is great candidate for bioprocessing applications. Steel has excellent thermal conductivity and good chemical resistance. The stainless-steel reactor can be heated up to 250 °C and cooled up to -50 °C. Stainless steel is also cheap material to build cost effective reactors. Conventional CNC machining was built to manufacture micro and meso scale disks, however, in the industrial scales, CNC machining might not be a cost-effective solution due to longer machining times would be needed. In the pilot and industrial scales, we recommend considering alternative manufacturing methods such as welding standard tubes to develop baffled channels. PTFE is the most versatile plastic in terms of chemical compatibility. It can be used with reactive and corrosive chemicals. PTFE is also food grade material which can be used for food and beverage processing.

The size and important features of the meso-scale OBR are shown in Table.3.1 for two different design versions. With the ring shape design, more volume and number of baffled holes can be achieved.

Table 3.1 Meso-scale OBR Specifications

	Original Design	Modified Design
Baffle Conduit Parameters		
Baffled conduit diameter (D)	8 mm	8 mm
Baffle constriction diameter (d _o)	4 mm	4 mm
Baffle spacing (L)	12 mm	12 mm
Orifice thickness (l)	2 mm	2 mm
Key Geometrical Ratios for OBR Design		
Baffle spacing (L)	1.5 D	1.5 D
Baffle contraction ratio (α)	0.5	0.5
Modular Disk Parameters		
Disk Outside Diameter	φ85 mm	φ110 mm
Disk thickness	14 mm	14 mm
Number of flow channels	7	8
Number of service channels	24	4 plus spiral heating/cooling channels
Micro Scale OBR Parameters		
Reactor length	192 mm	192 mm
Reactor volume	~62 mL	~70 mL

Flexible design is important for any type of manufacturing but for process industry it is vital. Because process industry is more varied and complicated, each chemical application has its own unique process characteristics. Only flexible modular reactor can be used in the wide range of applications. The geometry of the baffle edges has been a big debate since the beginning of the OBR technology. A number of baffle geometries have been investigated by the

previous researches (Phan & Harvey, 2010) and a recent study investigated the smooth or sharp baffled edges in terms of their mixing performance (Ejim, et al., 2017). “Sharp” or “round” baffle does not mean that the specific shape should always be applied to all process applications. The appropriate baffled shape should be selected to achieve max efficiency from each process. Each chemical processing is unique; therefore, the OBR geometry design may need to be tailored based on specific needs. Modular disk feature also allows to construct OBR with mixed baffled edge, for example one disk could be with round edge baffle and another disk could be with sharp edge baffle. Mixed baffled-edge combination could potentially increase innovation of new products with undiscovered new product properties.

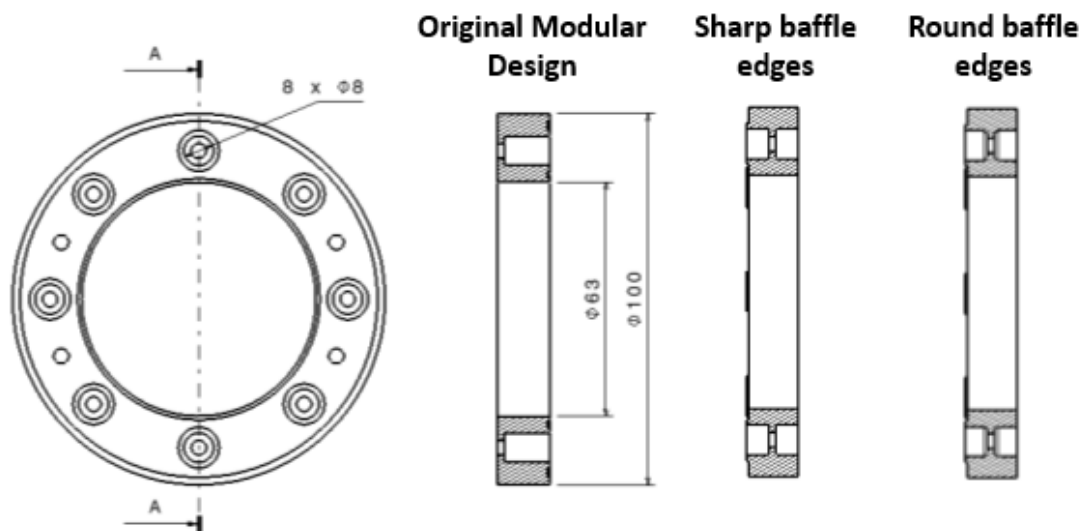


Figure 3.10 Flexible baffle design for various inner baffle geometry (sharp or round)

Each baffled design has their own merit benefits for some specific applications. Sharp edges can create more aggressive eddies which is good for high shear stress required applications. Round shapes can generate smoother eddies, for which perfect mixing regimes for the low shear stress is required in applications such as bioprocessing. Therefore, the original patented design was modified to achieve various baffle geometry shapes. In the original design, the baffle was placed on the one side of the modular disk which limits the creation of a round baffle edge on one side of the disk. The baffle was moved to middle with modified

design as shown in Fig.3.10. Once the baffle is in the middle of the disk, then we can create number of different shapes, like round, sharp, cone etc. for the baffle edges. Round shape baffle edges are also good for the injection moulding processing to construct large number of modular disks.

Heating/cooling performance of the spiral channels were tested by using experimental and computational models. After assembling 18 modular disks half acrylic half PTFE, the heating fluid was heated over 100 °C and circulated inside the inner and outer spiral channels. As shown in Fig.3.11, only one inlet and outlet ports were used to circulate the heating fluid. We observed around 60 °C temperature readings inside the baffled reaction channels.

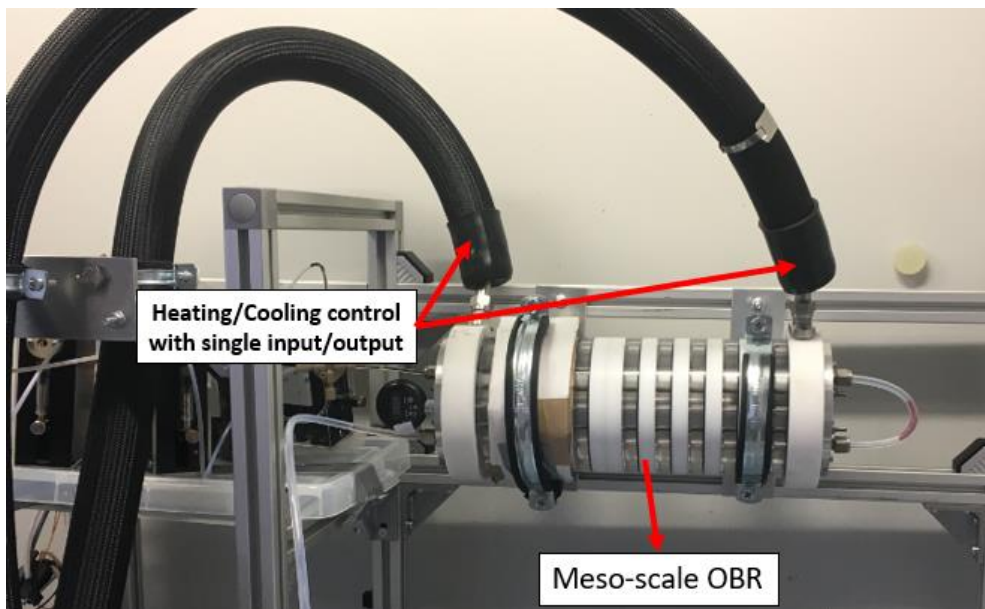


Figure 3.11 Demonstration of the heating/cooling capability

Because of cost and time limitations, we did not prototype all design options as mentioned above for the multiple temperature control zones. However, we proved the concept of the design using ANSYS Fluent Heat Transfer Simulations as shown in Fig.3.12 and Fig.3.13. Once a heating fluid passed around the reactions channels by following the spiral channels from inside and outside, uniform heating and cooling profiles were achieved for all reaction channels as shown in Fig.3.12.

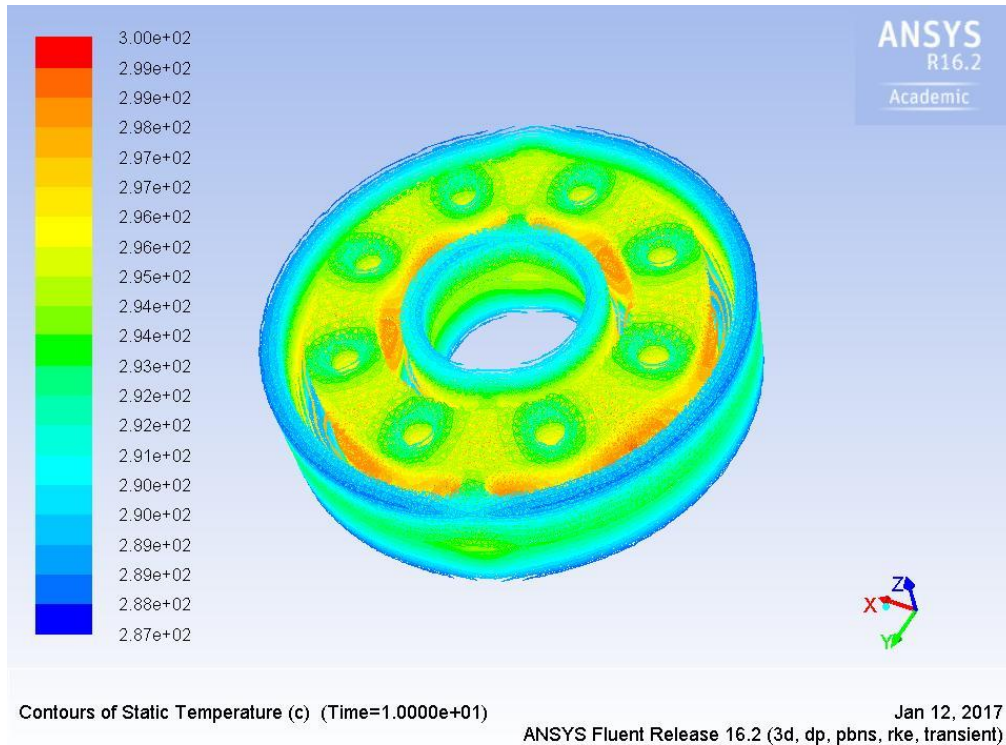


Figure 3.12 ANSYS CFD Heat transfer simulations for the uniform temperature control

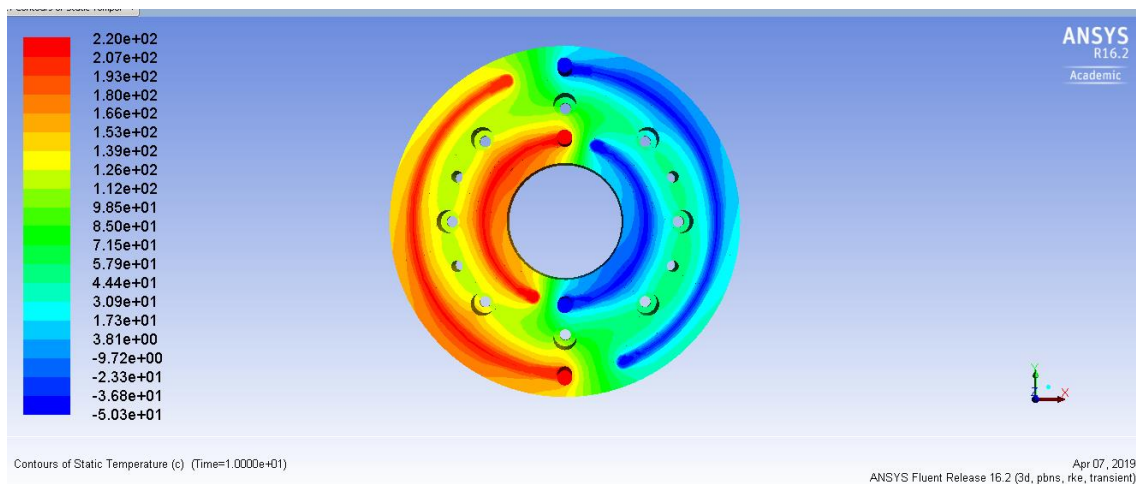


Figure 3.13 ANSYS Simulation of separated temperature control zones by spiral channel design

Simulation of the heating/cooling fluid flow is shown in Fig.3.12 and Fig.3.13. The temperature of the flow channels was successfully simulated for each design option. With the single circular channel, we observed uniform temperature profiles for eight reaction channels. The wall temperature of the flow channel was

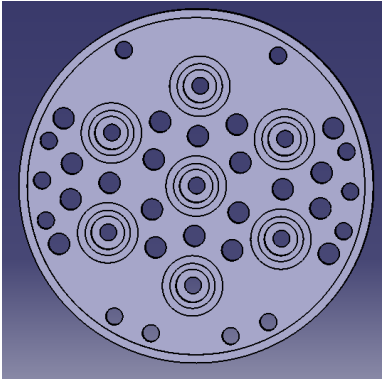
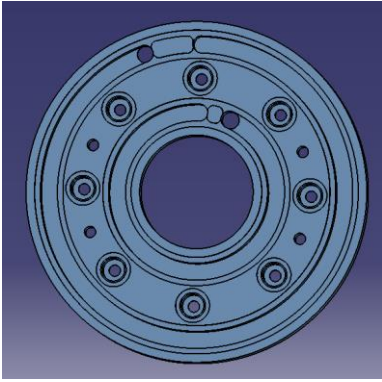
very close to the fluid temperature. The more interesting simulation was with half cooling and half heating. The proposed spiral channels (as two individual arc) can control two separate temperature control zones, which is an excellent feature for some applications. Some chemical reactions require instant cooling and heating, which can be achieved by the proposed heating/cooling system without any additional reactor.

Tab.3.2 provides an overview to show performance differences between two designs of modular OBR. Surface area to volume (S/V) ratio is an important factor to measure heat transfer performance. Larger S/V ratio means, more heating/cooling fluid can contact with the reactor disk, consequently that can quickly maintain the desired temperature of the system and will require less energy to keep it in the desired reaction temperature during the entire process. Original patented design has very low S/V ratio as 0.0033, this number is calculated in the use of 20 service channels (ϕ 5mm) for heating and cooling. It has minimum contact surface due to straight holes. With the spiral channels, S/V ratio significantly increased as 0.164. Two spiral grooves become from 8 mm diameter and 12 mm depth. Large grooves on the both side of reaction channels increase the surfaces between heating/cooling fluid and reactor disk.

The weight was compared based on Stainless Steel 316L, patented design is lighter than modified design as 0.523 kg and 0.76 kg respectively. This is due to footprint of each disk, modified design requires larger foot print to place the spiral channels around the reaction passages. Larger footprint provides to add one additional reaction passage which increases the reaction volume from 4.39 mL to 5.02 mL.

Design changes also make differences in its manufacturing and assembly. Manufacturing of original design is cheaper and quicker as requires drilling only straight holes. However, spiral channels in the modified design require longer machining and more expensive. Machinability of the stainless steel is one of the difficult materials. Therefore, drill diameter and groove depth must be considered for optimise the cost and manufacturing of spiral channels.

Table 3.2 Performance comparison between original and modified modular OBR designs

Specifications	Original Design	Modified Design
		
Surface Area to Volume Ratios (S/V)	0.0033	0.164
Weight (kg)	0.523	0.76
Reaction Volume (mL)	4.39	5.02
Manufacturability	Only drilling straight holes	Requires special process for spiral channels
Assembly	More complicated and takes longer time as have more additional parts	Easier and quicker due to simple design and less parts
Additional Parts	<p>12 assembly rods and 24 nuts (for each of rod)</p> <p>20 O-rings for heating/cooling sealing</p> <p>7 O-rings for sealing of reaction passages</p> <p>10 U-bend connection for heating cooling</p>	<p>4 assembly rods and 8 nuts (for each side of rod)</p> <p>4 O-rings for sealing of spiral heating/cooling channels</p> <p>8 O-rings for sealing of flow passages</p>

As that can be seen on the Tab.3.2, additional part number for assembly was significantly reduced. In the original design, assembly rods and service channel numbers were very high. Each heating cooling channel requires an O-ring for sealing and a U-bend for creating a continuous service channel. Spiral heating/cooling channel has a clever design to create continuous service channel and does not require additional connectors. Heating/cooling fluid can be circulated with only one input and output connectors.

3.3.2 Oscillatory Mechanism Design

Agitation is the fundamental of any type chemical process applications. Efficient agitation relies on an effective oscillation mechanism in OBR technology. Therefore, its design is vital important. One of the biggest innovations of this thesis is to introduce a fully automated oscillatory amplitude and frequency control mechanism for the first time in OBR industry. Best of our knowledge that was not possible before, all previous oscillatory mechanisms are required manual workforce to change its amplitude, but in this section, an automated oscillatory amplitude control mechanism was developed and presented.

Well known Scotch-yoke mechanism was used to drive the piston and generate sinusoidal motion to oscillate entire fluid inside reactor. Two versions of the oscillatory mechanism were developed; the first one was based on manually changeable roller pin and second version was automated changeable roller pin to control oscillatory amplitude.

Initial Version of Oscillatory Mechanism

The initial design was built on simplicity. The mechanism consists of a cam, roller, pin, piston, piston shaft and block and actuator as shown in Fig.3.14 and Fig.3.15. All these parts were mounted on the assembly wall and aligned with the first flow channel of the modular reactor. Two process control parameters were necessary as oscillatory amplitude and frequency. Frequency was controlled with changing the rotation speed of the actuator. In the higher RPMs (revolution per minute), piston is moved higher forward-backward cycles; in the slower RPMs, piston

moves slower. Amplitude control was challenging, piston is attached to rotating cam on a fixed point and the distance between attached point and centre of the cam defines the oscillatory amplitude. This attached point must be changed when different amplitude value is required. The initial idea was to open number of fix threaded holes, which are placed at a fixed distance from the centre of the rotating cam as shown in Fig.3.14. Then, roller pin could be manually replaced to corresponding threaded hole according to the required amplitude. The roller pin was chosen as on the shelf item, it's specifications are M3 screw thread and 5 mm roller diameter. Therefore, M3 threaded holes was required, that means each hole has 3 mm diameter and 1 mm space was given between each hole. This design could provide 20 amplitude options ranging from 1 mm to 20 mm with 1 mm resolution inside 50 mm cam shaft diameter as shown in Fig.3.14. However, this combination and resolution could easily be modified by designing a new cam including various stroke options, if different amplitude range and resolution were required. Replacing the cam part is very simple by only engaging and disengaging a single screw.

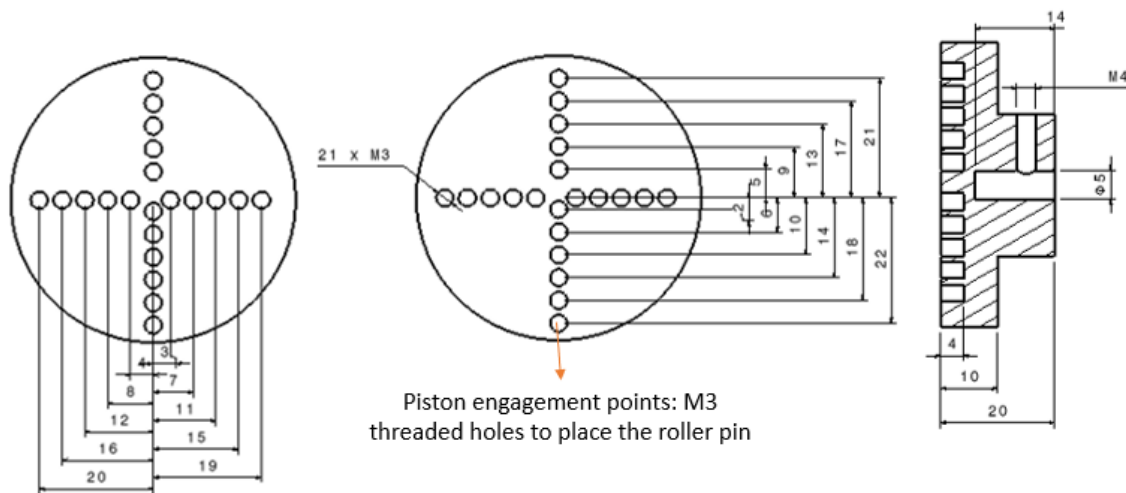


Figure 3.14 Piston engagement points

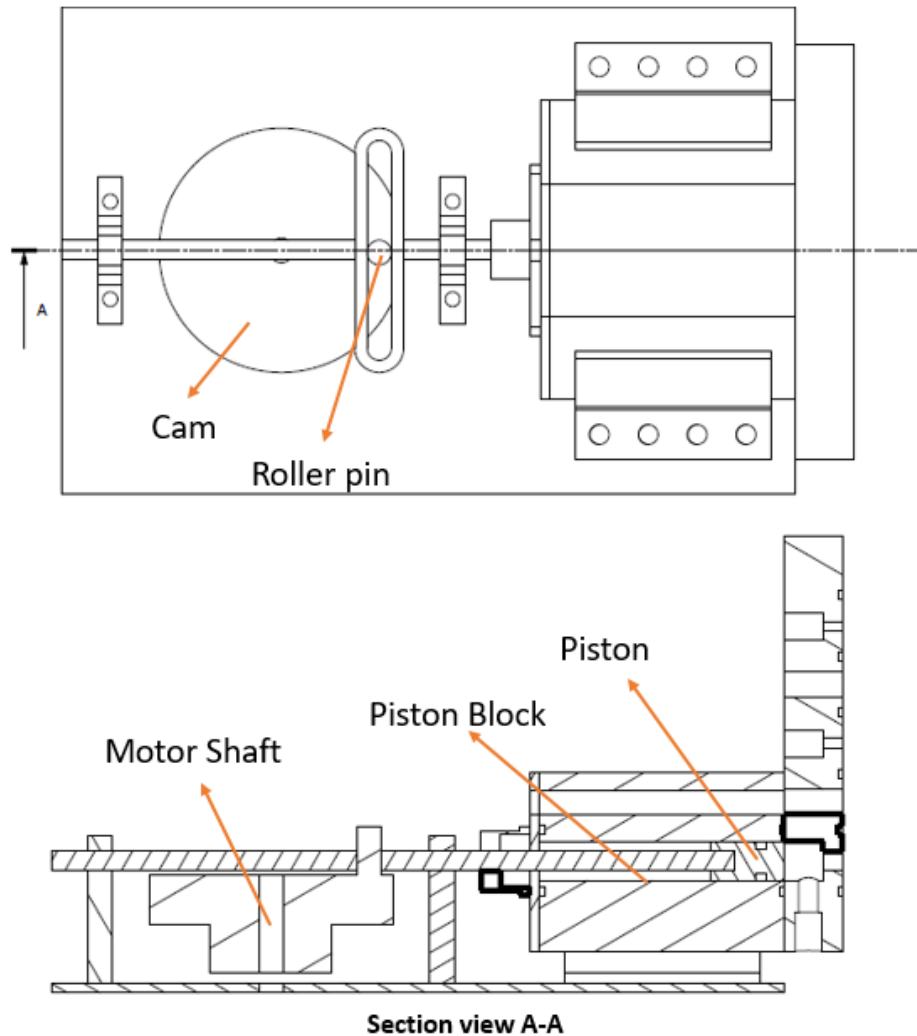


Figure 3.15 Manual amplitude controlled oscillation mechanism

The initial mechanism provides enough oscillatory amplitude and frequency ranges, but there are some drawbacks as summarised below:

- Limited amplitude resolution: it was only possible to change amplitude with the resolution of 1 mm due to fixed roller pin engagement points.
- Time consuming: the roller pin engagement point must be manually changed every time. This operation was taken at least a few minutes; the system must be stopped, the roller must be dismantled and engaged to another fixing point.
- Needs special tool: Roller pin engagement and disengagement always need a screwdriver.

As clearly stated on the system drawbacks above, the initial mechanism needs improvement to make it more efficient in the lab and industrial environments.

Automated Oscillatory Amplitude and Frequency Control

Improved version of the oscillation mechanism was developed after the initial version. Scotch-yoke oscillatory mechanism consists of stepper motor (1 or 4), piston (2), piston house (3 or 5), and cam mechanism attached to the stepper motor shaft and roller pin as shown in Fig.3.16. Two identical piston mechanism in synchronized positions (opposite phases) can be used in the full reactor. Alternatively, it can be used as single piston mechanism for the shorter residence time as shown in Fig.3.17.

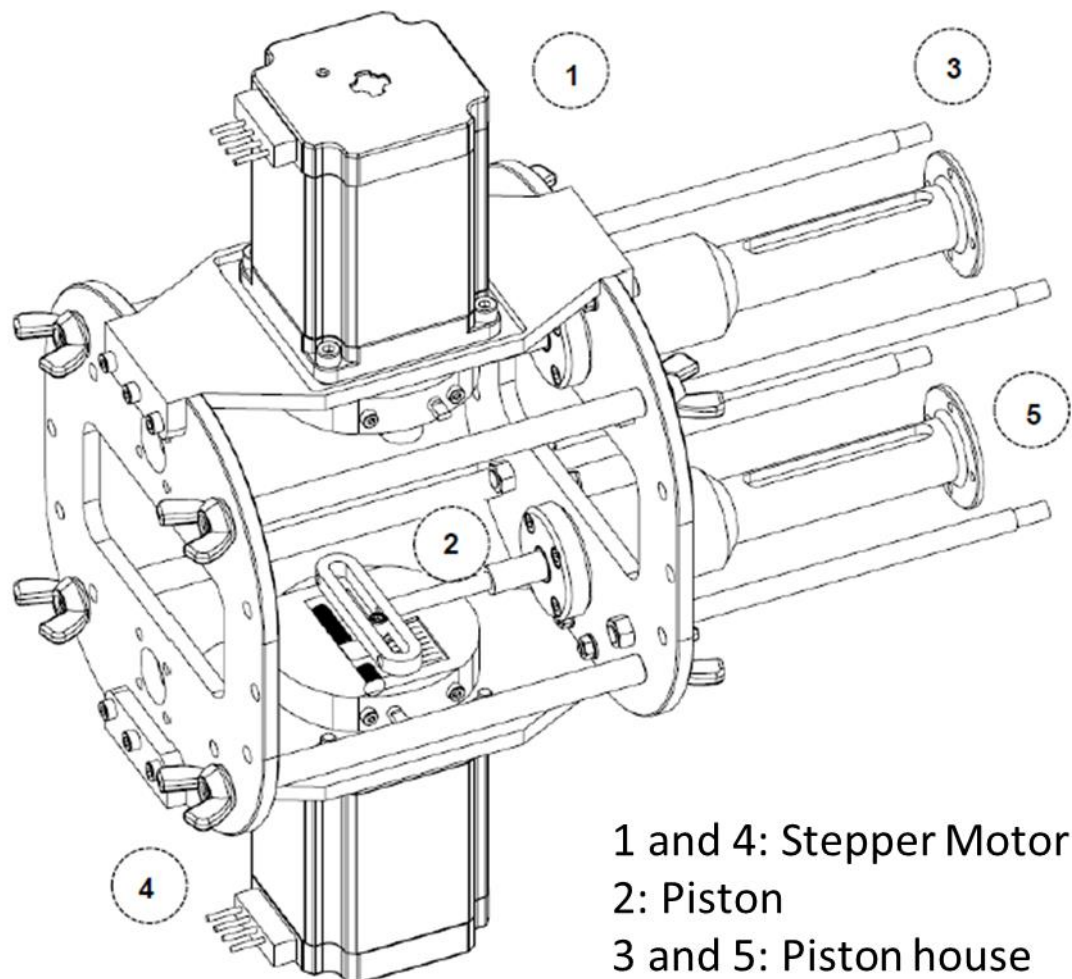


Figure 3.16 Twin Scotch Yoke oscillation mechanism for meso reactor

The entire mechanism was self-designed and built in the Cranfield University lab and workshop. The components were a combination of self-designed parts and on-the-shelf parts as shown in Table.3.3. The design idea was based on simpler, low-cost, flexible and easy maintenance fundamentals. The whole system consists of 7 in house-built components by considering low cost and light material design conditions, 5 on-the-shelf engineering parts and two control units.

There was significant improvement on the amplitude control. Leadscrew mechanism was integrated into the rotating cam as shown in Fig.3.17. The roller pin is placed on a leadscrew nut and the nut has a pointer, which reflects its position from centre of the cam as millimetre on the scale and is moved up and down by rotating a metric lead screw. Lead screw mechanism consists of screw and nut. Screw translated rotary motion into linear motion, consequently nut moves up and down. The pitch or lead defines the amount of travel that nut moves along the screw for every complete revolution. This design reduced the time to change amplitude compared to the first version. If the mechanism is designed with 2mm screw pitch, stroke changes 2 mm in every complete rotation. Lead screw mechanism can be operated manually or with a small servo motor to change its location which will provide automated amplitude control.

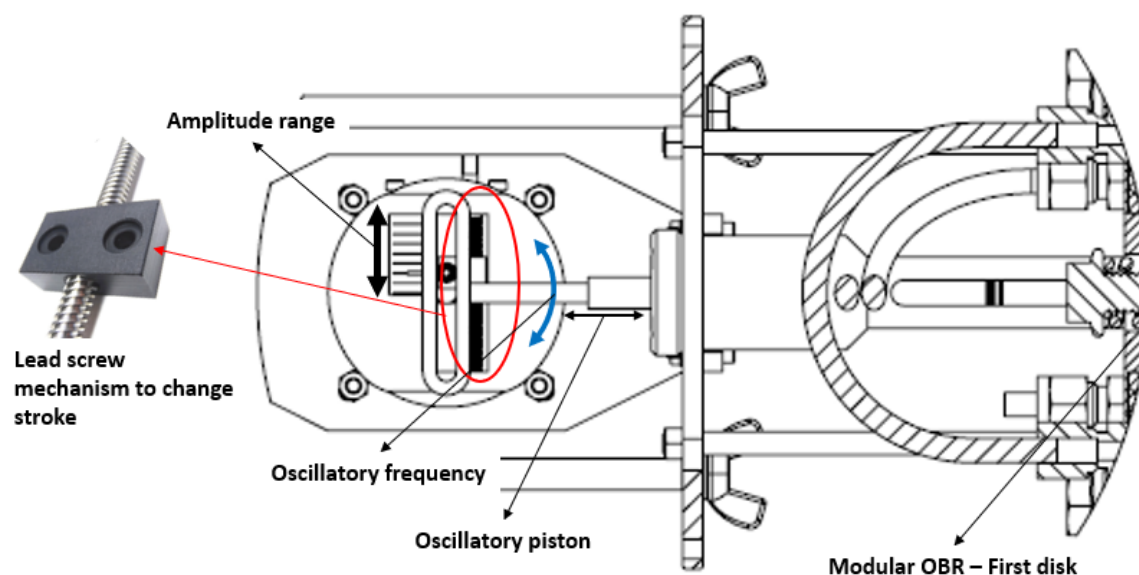


Figure 3.17 Automated oscillatory frequency and amplitude control mechanism

Amplitude can be precisely controlled between 0 to 20 mm range with two decimal points which was not possible in the earlier version as compared in the Fig.3.18. Frequency is controlled by a stepper motor within the range of 0-6 Hz with very precise resolution. Range of the frequency comes from motor specs. Nema-17 was selected because of its low cost and easy control. The motor is mounted to the motor block by 4 screws, 5 mm motor shaft was coupled to the roller cam. Same as amplitude range, frequency range can be increased or decreased by changing actuator.

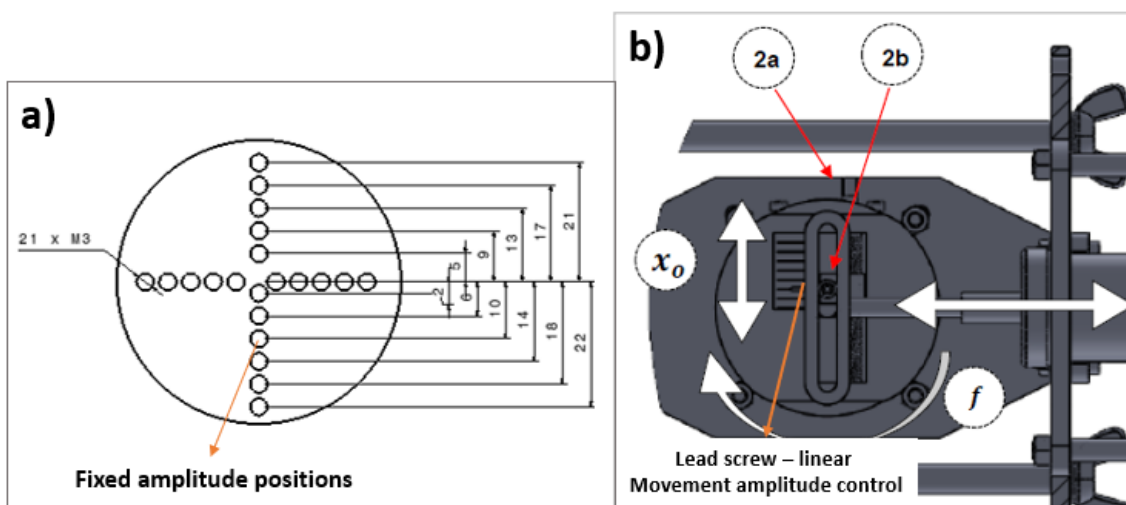


Figure 3.18 a) Fixed amplitude positions b) Lead screw mechanism for amplitude control

The cost of the whole system is shown in Tab.3.3. With a low cost (estimated of £280), a precise and reliable oscillation system was developed. The same oscillation mechanism was used for all $\phi 8$ mm reactor characterization experiments and spin-crossover material synthesis without any mechanical or leaking problem. The cost was not the only design feature of the current oscillation mechanism, another crucial factor is that it allows a scalable design. The identical oscillation mechanism can be built for any size reactor. Each on-the-shelf component can be ordered for any standard industrial processing size. Two larger sizes of $\phi 22$ mm and $\phi 38$ mm have already built in the same research group for larger pilot scales. However, this scotch-yoke oscillation mechanism was used first time in this thesis with $\phi 8$ mm reactor.

Table 3.3 Scotch yoke mechanism bill of materials

Scotch Yoke Mechanism Design and Development Cost					
Part		Supplier	Quantity	Unit Price (£)	Total Price (£)
On the Shelf Parts	Nema 17 stepper motor	RS Components	1	22.13	22.13
	Linear Bearing	Bearingboys	3	24.06	72.18
	Borosilicate glass piston tube	Aimer	1	3.00	3.00
	Arduni uno controller	RS Compenents	1	19.00	19.00
	Stepper motor driver	Amazon	1	8.00	8.00
	5mm Cam Roller	RS Components	2	4.70	9.40
In-house built components	Piston Block	Workshop	1		
	Motor Block	Workshop	1		
	Connector	Workshop	1		
	Roller block	Worksop	2		
	Roller shaft	Workshop	2		
	Total Estimated Cost of in house-built components				
	Total Mechanism Cost				280.71

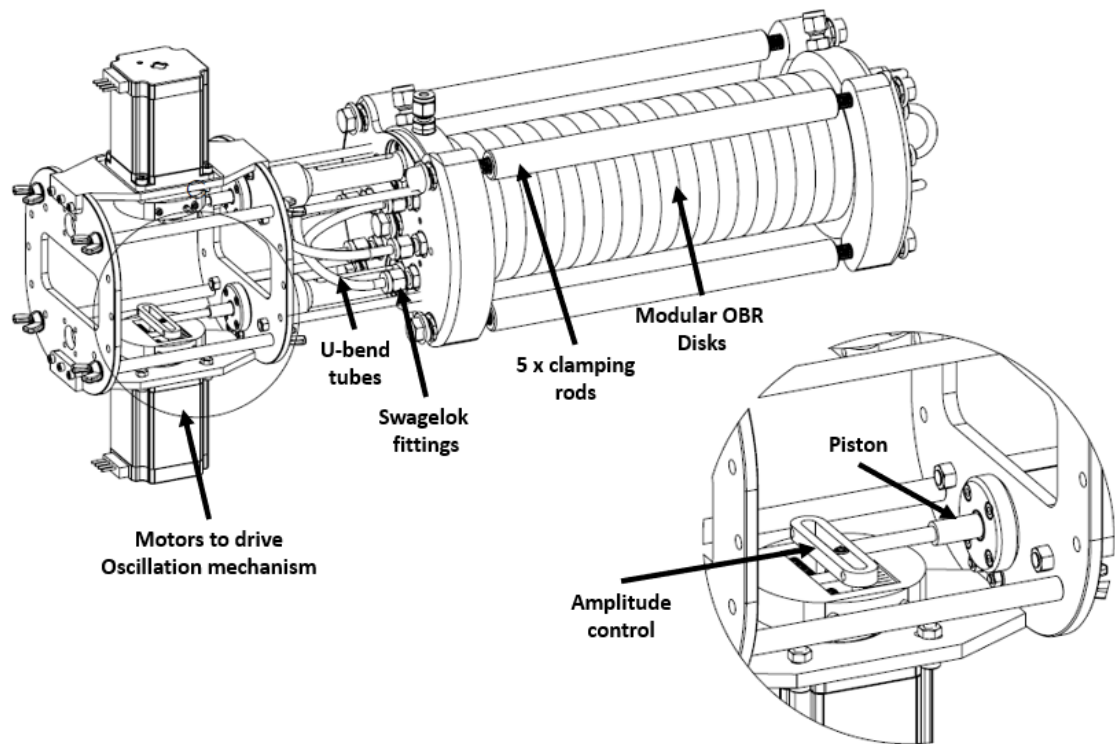


Figure 3.19 Meso scale modular OBR system

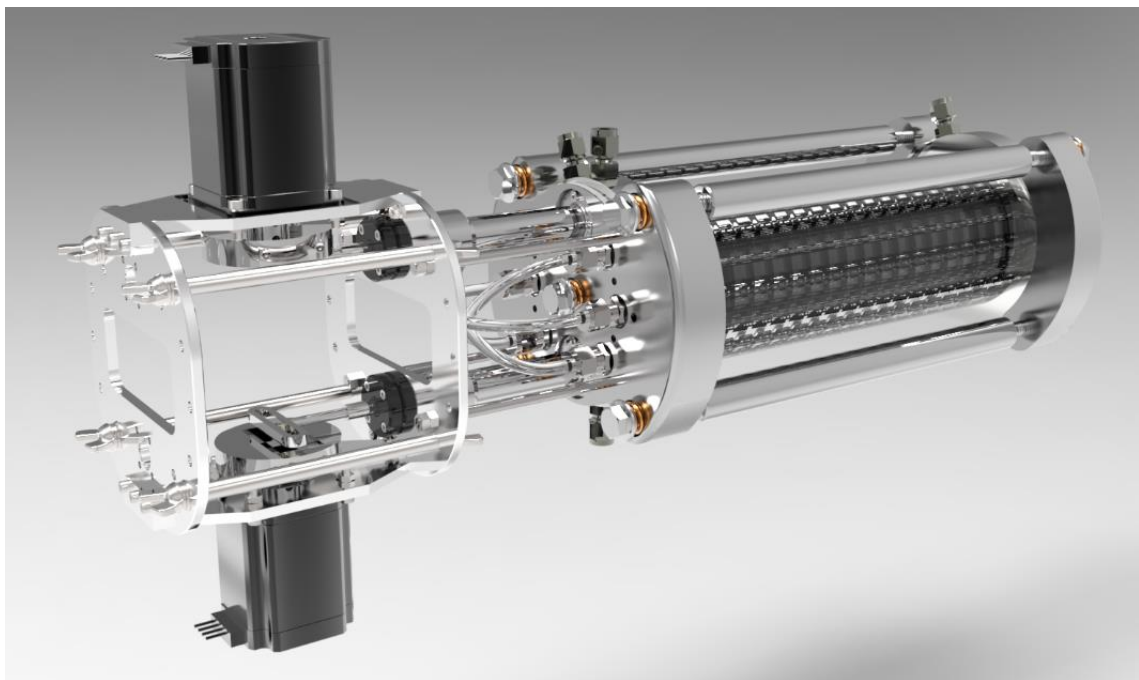


Figure 3.20 High definition rendering of the meso-scale OBR platform

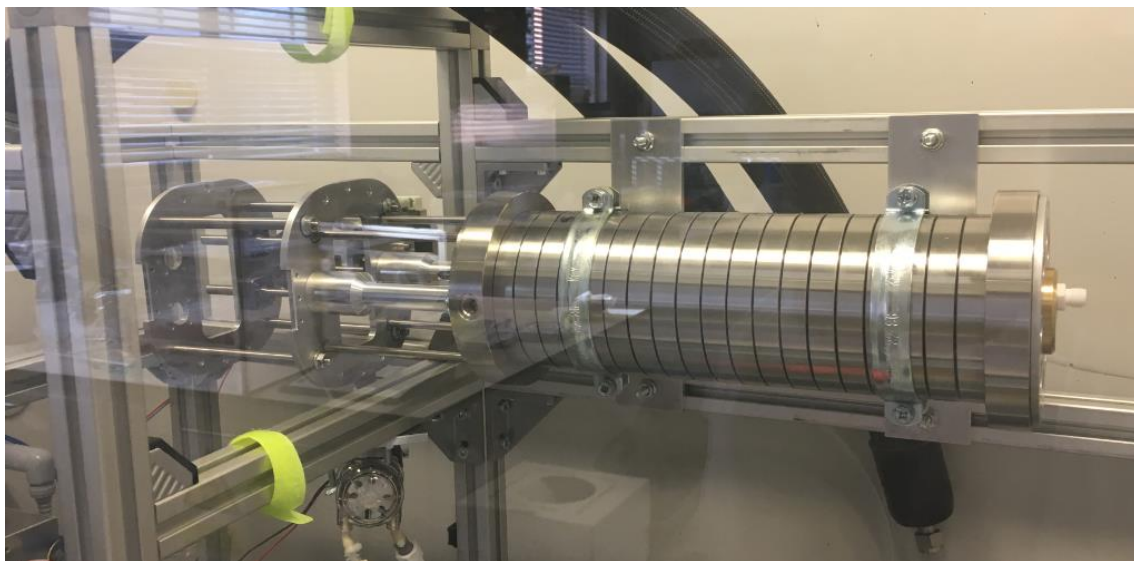


Figure 3.21 Meso-scale reactor made from stainless steel

3D assembly model of the meso scale reactor is shown in Fig.3.19 and Fig.3.20. Fig.3.21 shows actual setup of the modified meso scale reactor.

3.3.2.1 Meso Scale OBR Net Flow Control

Net flow was controlled by using two types of pumps. Syringe pumps were used in the micro-scale reactor net flow control. Eldex reciprocating piston pumps were alternative pumping kits to maintain net flow. Eldex pumps can provide precise flow rate control between 0-10 ml/min at high pressures.

3.3.2.2 Meso Scale OBR Oscillation Control (Software Design)

Arduino Uno control board and A4988 stepper motor driver were used to control four-wire bipolar Nema-17 stepper motor. The wiring diagram is shown in Fig.3.22.

Arduino Uno is a microcontroller board consists of 14 digital input/output pins (6 can be used as PWM outputs), 6 analogue inputs, a USB connection, a power jack and reset button. It can be powered from a computer with a USB cable or an AC to DC adapter. Each stepper motor requires 2 digital pin connections to control direction and speed. An Arduino Uno microcontroller can control up to 8 stepper motors. Arduino software is used for control coding.

A4988 is a very powerful bipolar stepper motor driver. It has two power inputs; one for its internal microcontroller and the other one for the motor, which can be up to 35 Volts per 2A of maximum current per phase or continuous current phase of 1A phase. Required min operating voltage is 8 volts. A4988 datasheet is used for the correct pin connection.

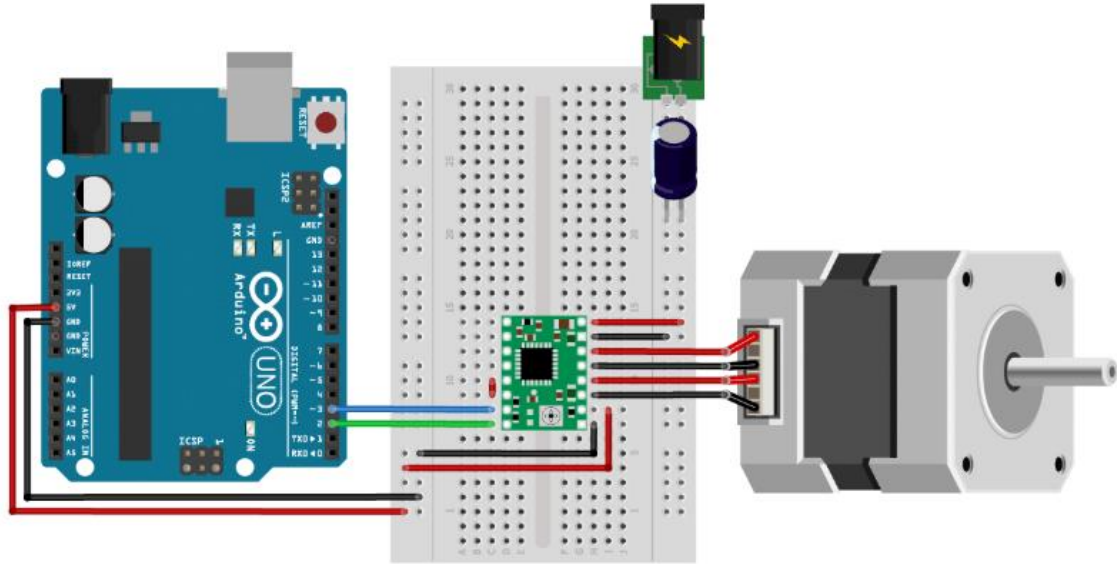


Figure 3.22 Wiring diagram of the stepper motor control

NEMA 17 is commonly used in the robotics, 3d printers and smaller CNC mills. It is a very reliable and low-cost motor. Larger NEMA motor can be found for the large-scale applications. The motor has 200 steps with a 1.8° angle.

In the assembly, the Arduino Uno microcontroller is connected to the A4988 motor driver which is connected to the stepper motor and 12 V power supply. A setup function was defined to control the motor speed as rpm (revolution per minute) as. RPM can be converted to the frequency by using the Eq.4.

$$1 \text{ rpm} = \frac{1}{60} \text{ Hz} \quad (4)$$

In the $\phi 8$ mm reactor, 1 – 5 Hz with the resolution of 1 was used for the characterization experiments. The corresponding rpm number for each frequency is shown Tab.3.4.

Table 3.4 Conversion of the stepper motor control to process frequency

Stepper motor speed code (rpm)	Corresponding oscillatory frequency (Hz)
60	1
120	2
180	3
240	4
300	5

3.4 Experimental Methods

There are several different types of batch and continuous chemical reactors. In the first part of this chapter, the design guideline to develop a continuous flow reactor were clearly defined. The mixing performance is vital for any type of reactor. Two important aspects of the mixing; characterization and conversion are necessary in order to investigate the mixing quality inside the reactor. Several different models for reactor characterisation are presented in the literature; two primary methods reported in this thesis to evaluate the performance of the proposed reactor. These are characterisation using the residence time distribution function (Ch 3.4.1), and conversion by employing the tanks-in-series model (Ch 3.4.2).

Tracer experiments are used to determine micromixing and macromixing information in a reactor system. **Macromixing** defines a distribution of residence times without specifying the exchange of matter between the reactant elements. However, **micromixing** specify the mixing of the molecules inside the reactor. Special terms and major functions to characterise and model a non-ideal reactor are discussed in the following sections.

3.4.1 Macromixing – Residence Time Distribution

The time atoms and molecules have spent in the reactor is named as the residence time of the particles in the reactor. The distributions of residence times

of particles inside the reactor from 0 to t is termed as residence time distribution (RTD). All particles in the reactor stay exactly at the same residence time in the ideal batch and flow reactors (Levenspiel, 1999). However, in the real world it is practically very difficult to design an ideal chemical reactor. Therefore, residence time distribution knowledge is used to characterize the behaviour of nonideal chemical reactors. The theory of using RTD in the analysis of macromixing inside the reactor was first proposed by MacMulling and Weber (MacMullin & Weber, 1935) and later, this theory was functionally defined by Prof P. V. Danckwerts (Danckwerts, 1953).

3.4.1.1 Measurement of the RTD

RTD is measured experimentally by using a nonreactive and easily detectable species called the tracer. Physical properties of the tracer should be identical to the feeding solution in order to increase solubility. A known amount of tracer is injected into the carried fluid in the inlet of the reactor as quickly as possible. Then the outlet concentration of the tracer is measured as a function of time 0 and t as shown in Fig.3.23. Then this data is converted to a residence time distribution, which tells how long each fraction of the tracer stays in the reactor. Pulse and step input are the two most commonly used tracer injection methods.

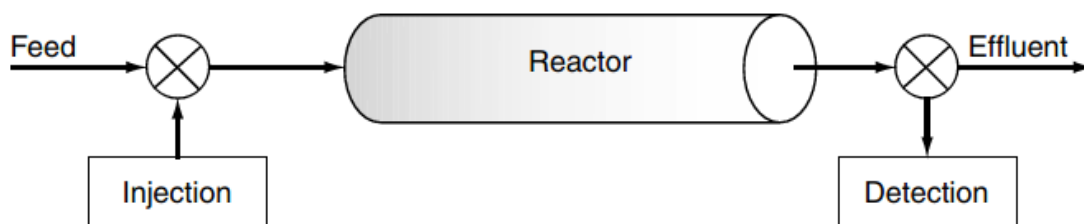


Figure 3.23 Experimental Setup of a RTD Measurement (Fogler, 2011)

3.4.1.2 Pulse Input Experiments

A known amount of tracer is injected into entrance of the reactor as quickly as possible. Then the outlet concentration of the effluent is measured as a function of time. The concentration – time curves for tracer injection in the inlet and tracer response at the exit are shown in Fig.3.24.

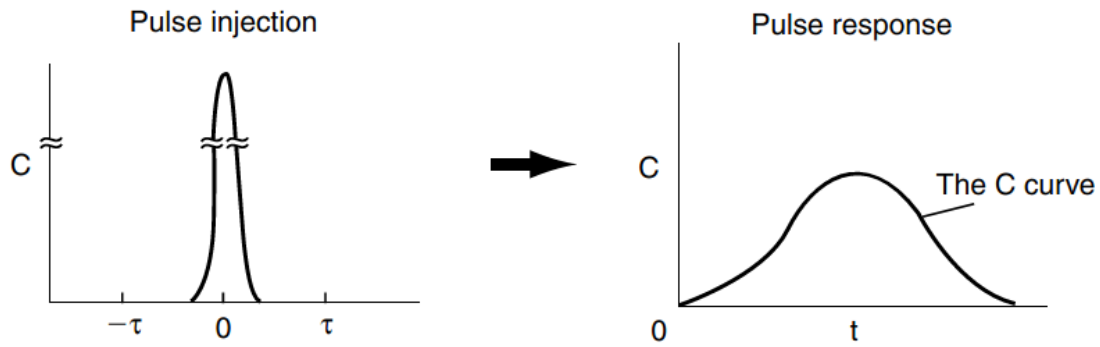


Figure 3.24 Concentration-time curves for tracer injection and response (Fogler, 2011)

The Residence Time Distribution (RTD) function $E(t)$ can be calculated from the tracer concentration $C(t)$ by using the Eq.5.

$$E(t) = \frac{C(t)}{\int_0^{\infty} C(t) dt} \quad (5)$$

$E(t)$ function can tell us how long different molecules stayed in the reactor, therefore, sometimes $E(t)$ function is called exit-age distribution function. It is appealing that most previous studies used this model for reactor analysis.

At the first moment of the RTD function, $E(t)$ is equal to the mean residence time t_m . In the constant volumetric flow without dispersion, no matter which RTD a reactor has, nominal space time (τ) is equal to the mean residence time t_m (Fogler, 2006). Mean residence time represents the average time the molecules spend in the reactor. Mean residence time can be calculated by using Eq.6.

$$t_m = \frac{\int_0^{\infty} tE(t) dt}{\int_0^{\infty} E(t) dt} = \int_0^{\infty} tE(t) dt \quad (6)$$

RTDs are compared by their moments instead of their entire distributions. There are two moments most commonly used to characterize the RTD. These are mean

residence time (t_m), and variance (σ^2). Variance is the second moment of the standard deviation and defined as Eq.7.

$$\sigma^2 = \int_0^{\infty} (t - t_m)^2 E(t) dt \quad (7)$$

Variance represents the “spread” of the distribution; the greater the value of the variance, the spread. We will use mean residence time and variance in order to calculate the equivalent number of the tanks-in-series for each experiment in the next chapter.

Generally, normalized RTD is used instead of the $E(t)$ function. Θ is called as dimensionless time and defined as Eq.8.

$$\theta = \frac{t}{\tau} \quad (8)$$

And dimensionless RTD function $E(\Theta)$ is defined as Eq.9.

$$E(\theta) = \tau E(t) \quad (9)$$

Flow performance of various tube sizes of the reactors can be compared using normalized RTD function.

3.4.2 Micromixing – Tanks-in-Series Model

There are numbers of formulated models to describe nonideal flow reactors such as segregation model, maximum mixedness model, tanks-in-series model, and dispersion model (Fogler, 2011). Dispersion and tanks-in-series are the most commonly used models to study plug flow conditions. They are almost identical so any of these models can be used. In the analysis of tracer experiments, tanks-in-series model will be used due its simplicity. The tanks-in-series model adapted from the literature to understand mixing performance in the reactor. The tanks-in-series (TiN) model is the most robust and successful method to characterise fluid

mixing in a reactor. This model provides a direct physical representation of the oscillatory flow mixing performance in the non-ideal reactors.

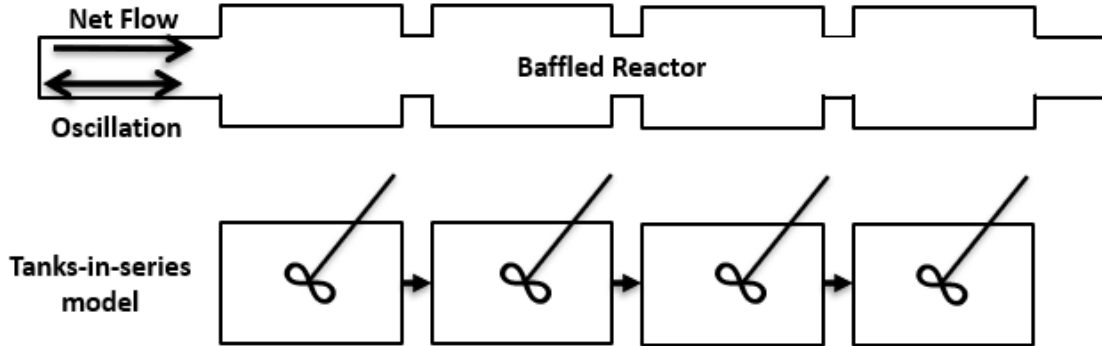


Figure 3.25 Tanks-in-Series Model

The tanks-in-series model considers that the reactor behaves as a series of N equal-sized stirrer tanks as shown in Fig.3.25. The number of the tanks (N) can be calculated by using variance and mean residence time as defined in Eq.10 and Eq.11.

$$\sigma(\theta)^2 = \frac{\sigma(t)^2}{\tau^2} = \int_0^{\infty} (\theta - 1)^2 E(\theta) d\theta = \frac{1}{N} \quad (10)$$

$$N = \frac{1}{\sigma(\theta)^2} \quad (11)$$

Normalized RTD curve can be matched with the model curve to determine number of the tanks (N). Model curve is shown in Fig.3.26. If the number is small, the reactor characteristics act as a single or a smaller CSTR. If the number of tanks is high, the reactor characteristics is called as Plug Flow Reactor (PFR). With the curve matching, the sum of square differences between the tracer measurements and the calculated values from Equation – 9 can be minimized.

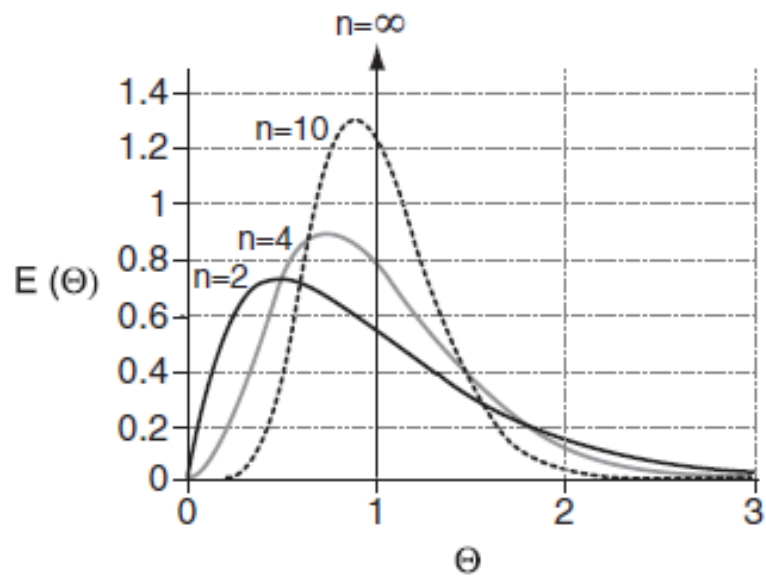


Figure 3.26 Tanks-in-series model curve for various numbers of CSTRs in series. As the number increases, flow patterns in the reactor behave as plug flow reactor (Fogler, 2011)

4 CHARACTERISATION EXPERIMENTS

“It does not matter how beautiful your theory is, it does not matter how smart you are. If it does not agree with experiments, it’s wrong.”

Richard P. Feynman

4.1 Tracer Experiments

Tracer is used to determine RTDs in any type of reactor. There are different types of tracers such as dye, salt solution, smoke or radioactive particles. Selection of the tracer is vital in order to collect reliable measurements. Physical properties of the tracer should be similar to that of the reacting mixture and be completely soluble in the carrier material. It also should not interfere with the reactor material (for example, it should not be absorbed by the walls of the reactor) (Fogler, 2006). Radioactive particles have advantages such as detection, easy monitoring without sampling directly from walls, and better sensitivity, however, they are not appropriate because of high cost, health and safety issues, and the need of large quantities of material for each experiment (H. Muhr & David, 1999). Several problems have also been identified for the salt-based tracers in the past (Mackley & Ni, 1993). Their disadvantages include inaccurate measurements due to density differences, large volume of injection, and poor mass-weighted averaging across the tube-cross section.

After a detailed study on the selection of tracer type and its measurement technique, an optical method was selected. Optical measurement technique has been successfully used in the determination of the RTD profiles for plug flow reactors. There are great advantages of applying coloured tracer, such as not disturbing the flow inside the reactor. It is also very cheap to use, very easy and robust to detect, and it can be easily captured with flow cell at the end of each flow channel.

The concentration of the food grade blue tracer dye was measured at the effluent. Some amount of the light passes through the sample without interacting with it, the rest of the light is absorbed by the sample in an absorption measurement. Deuterium & Halogen light source (Ocean Optics DH-mini) were used to produce strong light across the UV-Vis range. Two 450 μm extreme solarisation-resistant optical fibres were used to transmit and receive the light through the flow cell. A low cell of a UV-Vis spectrometer (Ocean Optics QE Pro Series) at fixed wavelength range (198nm – 998nm) was integrated at the end of the reactor. The exit concentration of tracer was collected at time intervals of 1s by using OcenView software. As the blue tracer passes through the flow cell between the receiver and detector fibres, the average concentration of the tracer can be calculated corresponding to the measured optical density. Experimental setup of the tracer measurement is shown in the Fig.4.1.

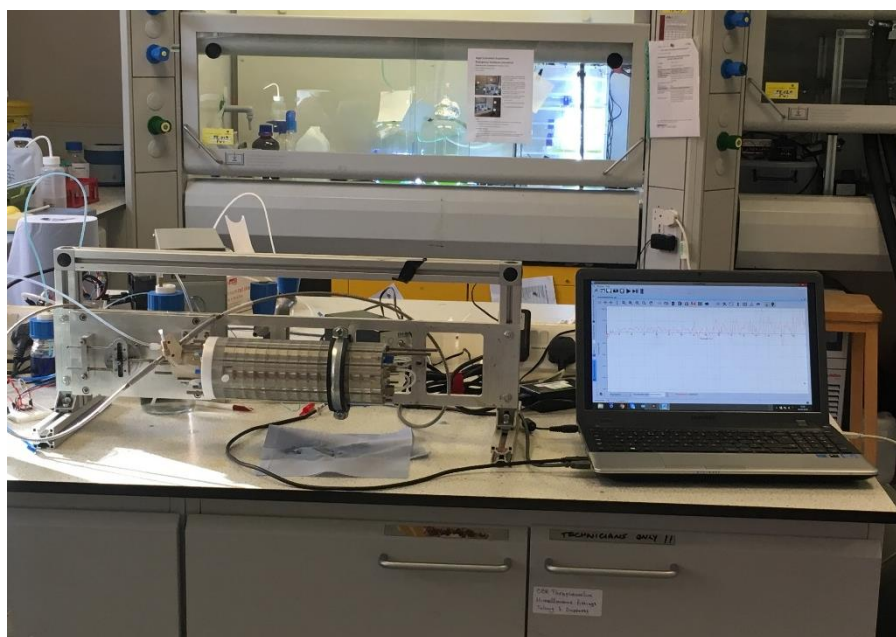


Figure 4.1 Experimental Setup of the Tracer Measurements

The aim of the tracer experiments was to develop a plug flow model as function of reactor length and various operating conditions (residence time and oscillation combinations). Pulse input and step tracer experiments are the two primary experimental methods to characterize non-ideal reactors. Pulse input technique

was used to evaluate the performance of the plug flow. 8 mm meso-scale reactor with 7 channels (each flow channel has 15 baffled disks) was used for the tracer experiments. Second disk was designed specifically for tracer injection, a 3 mm hole was designed with 90° angle through flow channel which enables to inject the tracer directly into the entrance of the reactor as shown in Fig.4.2. A pulse of tracer was injected into the reactor quickly, and then the effluent concentration was measured as a function of time at the exit of the reactor. Once the exit concentration of blue tracer was obtained, the residence time distribution and dimensionless residence time distributions were determined using concentration-time profiles. Finally, the tanks-in-series model was used to describe the performance of the oscillatory baffled flow reactor.

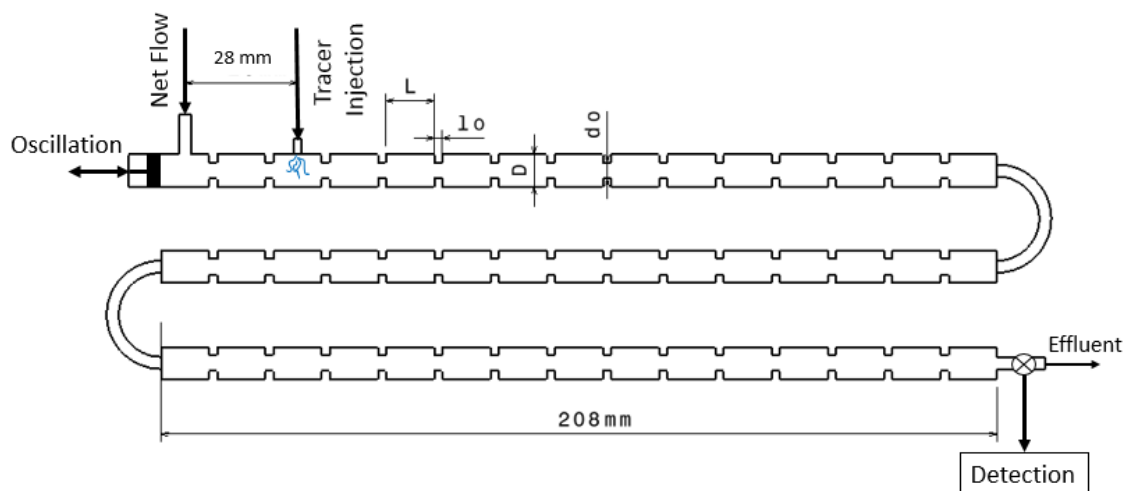


Figure 4.2 Experimental Setup of Tracer Measurement

In the 8 mm reactor channel, the tracer was injected directly through the side injection port. The Confluent PVM syringe pump was used for tracer injection. The Confluent PVM syringe pump can provide great control of the tracer volume, very short pulsing time (just under 0.5s), and automation for tracer injection. Volume of the tracer used for injection depends of the volume of the reactor. The volume of the tracer used for each flow channel is shown in Tab.4.1.

Tracer selection has crucial importance to obtain robust results. Food grade blue dye was selected because of its high optical density at low concentrations, which,

even in very dilute solutions, can easily be detected by using a spectrometer. More dilute solutions mean lower concentration difference between the tracer and carried fluid.

Table 4.1 Reactor and Tracer Volumes

Number of Flow Channel(s)	Volume of Flow channel(s) (ml)	Volume of U-Bend(s) (ml)	Total Reactor Volume (ml)	Tracer Volume (ml)
1	9.42	0.095	9.51	0.1
2	18.84	0.286	19.126	0.1
3	28.27	0.477	28.75	0.1
4	37.69	0.668	38.36	0.12
5	47.12	0.859	47.98	0.12
6	56.54	1.05	57.59	0.12
7	65.97	1.241	67.21	0.14

The position of the spectrometer was changed by placing it after each channel in order to investigate the effect of the reactor length over plug flow performance as shown in Fig.4.3.

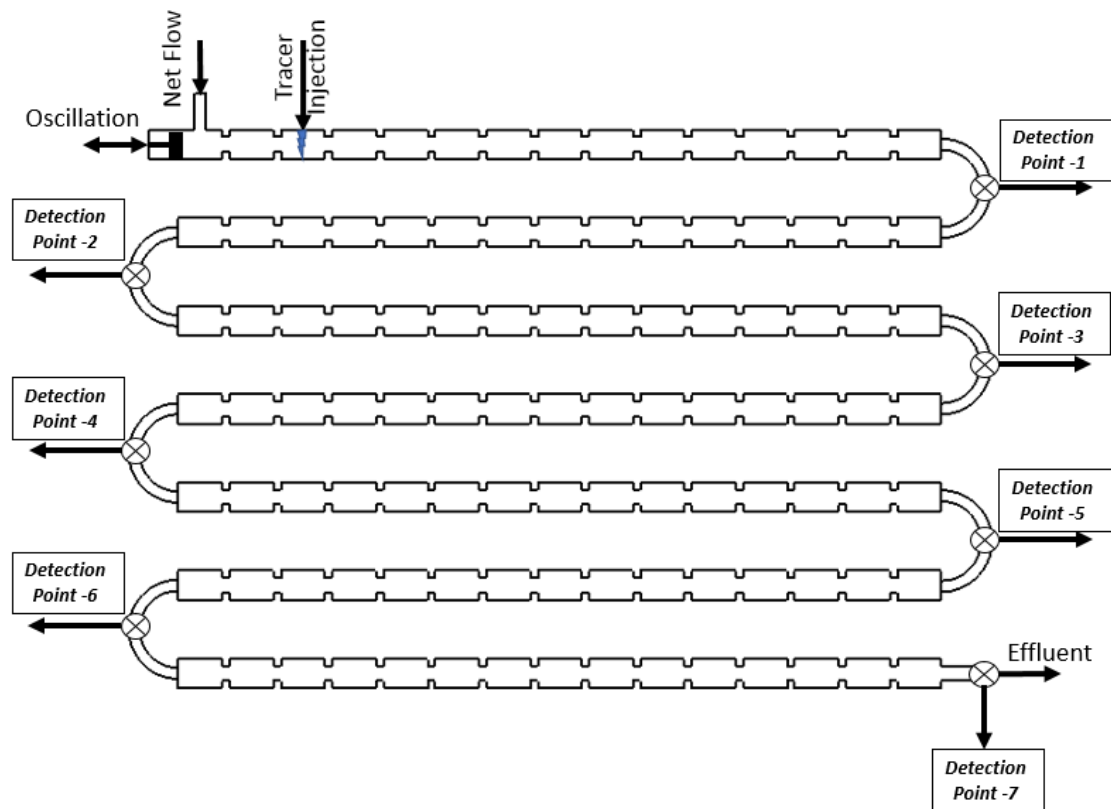


Figure 4.3 Reactor Configuration and Tracer Measurement

4.2 Experimental Design – Design of Experiments (DoE)

An experimental design was developed to identify optimum operating combinations to achieve plug flow conditions. Plug flow can be considered as a function of net flow, oscillation amplitude, and frequency. Design of experiments (DoE) method can be used for systematic investigation of the operating variables that affect the plug flow conditions. There are number of statistical techniques available in the DoE. Full factorial design was chosen to measure all combinations for a comprehensive investigation of the operating parameters. The aim is to get most information from the minimum set of experiments to develop a reliable characterization study.

Three factorial design (amplitude, frequency and net flow) was determined including with 5 levels for amplitude and frequency, and 4 levels for the net flow as shown in Tab.4.2 for the micro scale reactor and Tab.4.3 for the meso scale reactor. There were two key considerations to identify factor levels; first, velocity

ratio (Re_o/Re_n), and second, the limits of the oscillation mechanism and net flow. For example, we can reach asset of maximum amplitude and frequency for each system. Two sets of designs considered for development, one for small and one for large reactor. Each design requires 100 experiments, same Re_o and Re_n were kept for each experiment by maintaining frequency and amplitude from small reactor to large size reactor.

4.2.1 Process Factors Selection

Selection of a set of input factors is needed to determine their effect on an outcome variable. Two set of factors for small and large reactors respectively are shown below.

Table 4.2 4 mm Reactor Input Factors

Factors	Levels				
Amplitude (mm)	0.5	1	1.5	2	2.5
Frequency (Hz)	1	2	3	2	5
Net Flow (ml/min)	1	2	3	4	

Same oscillatory and net flow Reynolds numbers were kept for 8 mm internal diameter reactor. In order to achieve similar flow conditions, the dynamic scaling rule was performed. For example, oscillation of 1 mm amplitude, 1 Hz frequency in 4 mm diameter, was increased two times in amplitude (2 mm) and decreased 4 times in frequency (0.25 Hz), in order to achieve same Str and Net flow Reynolds numbers. The net flow required was increased two times due to doubled diameter to achieve the same Re_n in 8 mm diameter. Similar scaling law were used for all experiments.

Table 4.3 8 mm Reactor Input Factors

Factors	Levels				
Amplitude (mm)	1	2	3	4	5
Frequency (Hz)	0.25	0.50	0.75	1	1.25
Net Flow (ml/min)	2	4	6	8	

4.2.2 Selection of Full Factorial Experimental Design for the Characterization Experiments

Chemical and industrial products enter into our daily lives after series of complex experimental processes. The aim of the DoE is to collect precise data and complete information about a process with a minimum number of experiments and the lowest possible cost and shortest time. DoE provides number of experimental design methods to achieve this aim such as, screening design, full factorial design, fractional factorial design, and response surface methodology and mixture design (Durakovic, 2017). Each method has its own advantages and disadvantages. Before starting the experimental design, the selection of the experimental method is crucial in order to achieve research objectives in terms of time, cost and accuracy. The following research can be helpful to identify the experimental method (Lazic, 2004):

- What is the research objective?
- What are the factors that influence the responses?
- How many factors and levels affect the response?
- What is the data collection type?
- What is the data analysis required after data collection?

Considering these research questions, we decided to use the full factorial experimental design method in the characterization experiments. This method requires large number of experiments to investigate the combinations of all factors, but it was necessary to capture the big picture. Requirements of the characterization experiments are summarized as follows:

- Research objective was to investigate the plug flow conditions in the modular OBR using a wide range of factor combinations. Plug flow space as a function of the input variables was the key outcome of the experiments.
- It was a large experimental set as 100 per scale and 200 experiments in total for both tube diameters. It was time consuming but worth to complete it.

- Experiments does not cost anything. Deionized water was used as carrier fluid with very low amount of food grade blue tracer. One bottle of tracer cost is only a few pounds and it was enough for all experiments.
- The data was collected using spectrometer and again the life of a spectrometer can go up to 20000 hours.
- The data analysis was done by using tanks-in-series calculation method. A MATLAB code was developed to process the data after each experiment. With the power of computational software, the spectrometer readings were calculated simultaneously to generate response data.
- JMP software was used for the final analysis of the DoE results.

4.2.3 Selection of Response Surface Experimental Design Method for SCO Synthesis

SCO material production is expensive and requires lots of time-consuming analysis to characterise final products. Therefore, method selection is very crucial to collect the maximum amount of information with minimum experiment numbers and cost. Below factors were considered to select experimental design method for the SCO material;

- Cost of chemical ingredients
- Required knowledge of physical and chemical properties of each chemical components and materials.
- Lab requirements for conducting experiments (time, health & safety, working hours etc)
- Lab equipment to run experiments and collect samples.
- Analysis of final products using SEM and DLS for particle size and shape investigation.
- Analysis of the results to identify the most influencing parts.

5 REACTOR CHARACTERIZATION EXPERIMENT RESULTS and SCALE-UP METHODOLOGY

*“An experiment is a question which science poses to
Nature, and a measurement is the recording of
Nature`s answer.”*

Max Planck

This chapter presents the experimental data and analysis of flow conditions in OBR for wide range of oscillation and net flow conditions of two different scales. Following the experimental method described in the previous chapters and performed DoE technique, RTD measurements based on TIS model were conducted for each scale of reactor (4 mm and 8 mm reactor diameters). The fundamental goal of these experiments was to compare the experimental outcome for two different scales and develop a scale-up model in order to successfully move material productions from laboratory scales to industrial production scales.

First, experimental results of each diameter are presented and then the results are compared for two different sizes to find relationships between two scales. Chapter closes with a systematic scale-up methodology and clear instruction explaining how to use it various scale-up scenarios.

5.1 Micro Scale (4 mm Diameter) Reactor RTD Results

This section describes the data and analysis of micro reactor characterisation experiment results for a wide range oscillatory and net flow conditions. The main objective of these experiments was to understand the plug flow conditions and performance as a function of three independent variables (amplitude, frequency and net flow) for the micro-scale reactor. The second objective of this section is to compare micro-scale results to meso-scale results in order to develop a scale-up model as a function of the tube diameter.

5.1.1 Reactor Length versus Plug Flow Performance

The first investigation was to understand the relationship between reactor length and plug flow conditions. As mentioned in the previous chapter, the entire reactor system consists of 7 independent reaction channels. These channels are connected with U-shape tubes to tune the reactor length according to the various reaction requirements. Input parameters were decided based on literature review as a starting point. Velocity ratio was investigated by Phan and Harvey previously (Phan & Harvey, 2010), best plug flow conditions were observed at velocity ratio between 5-15. Three frequencies, 1.5, 1.75 and 2 Hz were used and the amplitude was kept the same as 2mm for all experiments. Net flow was 10 ml/min as shown in Table.5.1.

Table 5.1 Input parameters for the investigation of reactor length versus plug flow performance

Net Flow and Oscillation Parameters						
Flow Rate (ml/min)	x (mm)	f (Hz)	Str	Ren	Reo	Velocity Ratio
10	2	1.5	0.318	26.45	150.37	5.68
10	2	1.75	0.318	26.45	175.43	6.63
10	2	2	0.318	26.45	200.5	7.58

Tracer experiments were conducted at each channel from 1 to 7 and Tanks-in-series numbers were calculated. Fig.5.1 shows the trend between reactor length and plug flow performance. Increased reactor length results in better plug flow performance. This outcome was expected. In simple terms, molecules spend more time in the reactor under same mixing conditions and consequently better mixing performance was observed.

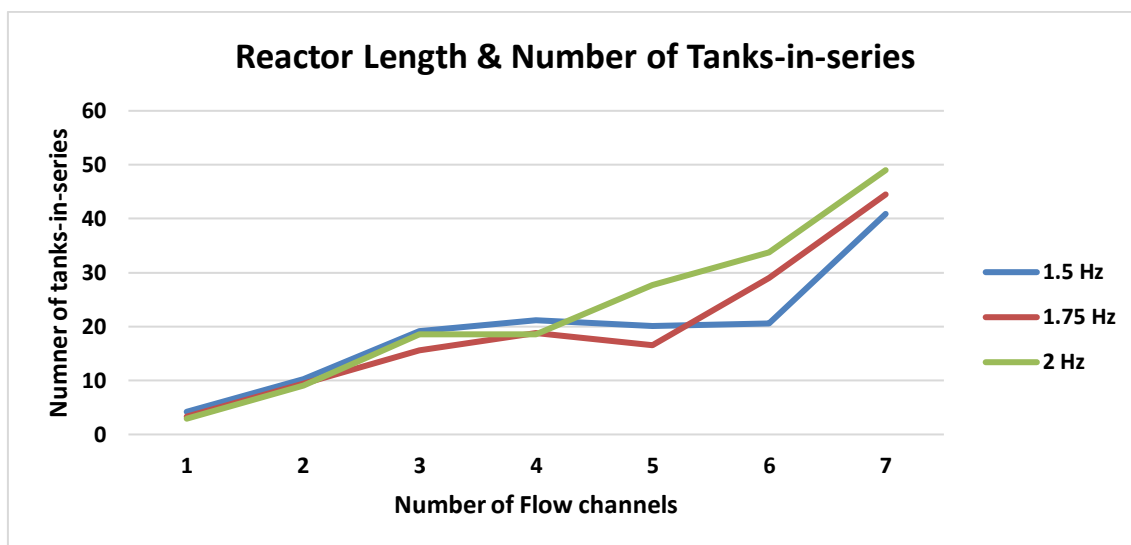


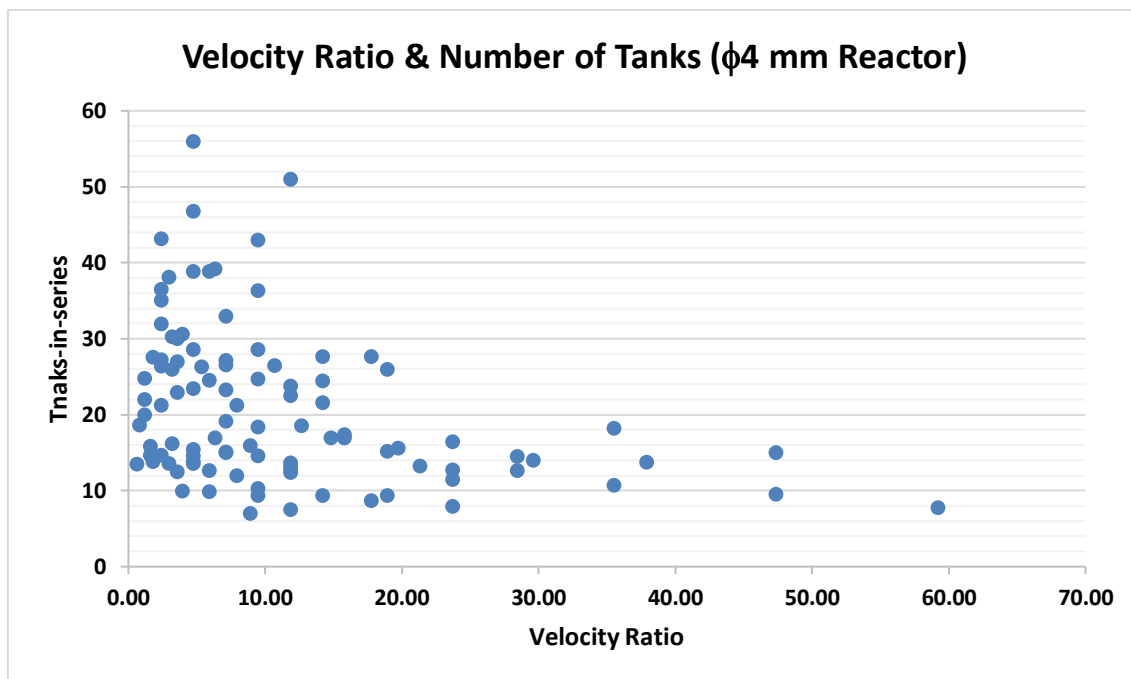
Figure 5.1 Relationship between reactor length and plug flow performance

5.1.2 Correlation between Tanks-in-series Number and Velocity Ratio

There is a significant difference in the flow conditions according to the response of the various operational combinations. This clearly shows the importance of the operational factor selection and how they affect the quality of mixing performance.

4 different flow rates as 1, 2, 3 and 4 ml/min was used for the RTD measurements. Each flow rate has 25 measurements as a combination of 5 different amplitudes and frequencies. First, the effect of the velocity ratio against four different net flows was investigated. Velocity ratio (ψ) is the ratio of the oscillatory Reynolds number to net Reynolds number. Entire experimental list including combinations of mixing conditions, dimensionless number and response results in Appendix.A (Table.A.1 and Figures A.1 to A.4 for micro-scale reactor and Table.A.2. and Figures A.5 to A.8 for meso-scale reactor).

First of all, similar trend as conventional OBRs was observed for velocity ratios versus number of tanks (Phan & Harvey, 2010), (Harvey, et al., 2001) as shown in Fig.5.2. The number of TiS increased at velocity ratios between 5 and 20. In the cases where velocity ratio was over 20 and below 5, lower TiS numbers were observed.



The best plug flow conditions were observed with lower net flow. It is because the wider range of velocity ratio can be used with the same amplitude and frequency combinations for smaller net flows as shown in Fig.5.3. Top three maximum number of TIS were achieved at 1 mm amplitude and at three different frequencies.

The mixing performance was decreased when we increased the flow rate as shown in Fig.5.4. The velocity ratio around 10 was identified as the best performance for the $Re_n = 10.6$ in 4 mm diameter. Smaller amplitudes (0.5 and 1 mm) also resulted in a better performance similar to the 1 ml/min net flow results.

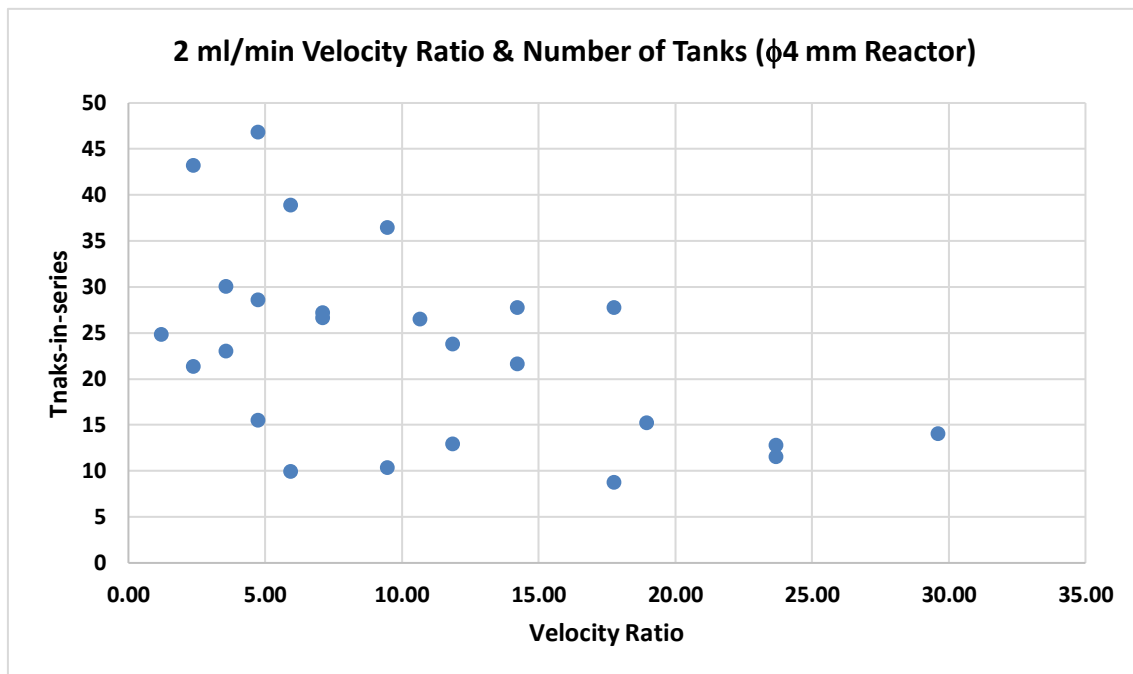


Figure 5.4 RTD results on velocity ratio for micro reactor ($Re_n = 10.6$; $x=0.5-2.5$ mm, $f=1-5$ Hz)

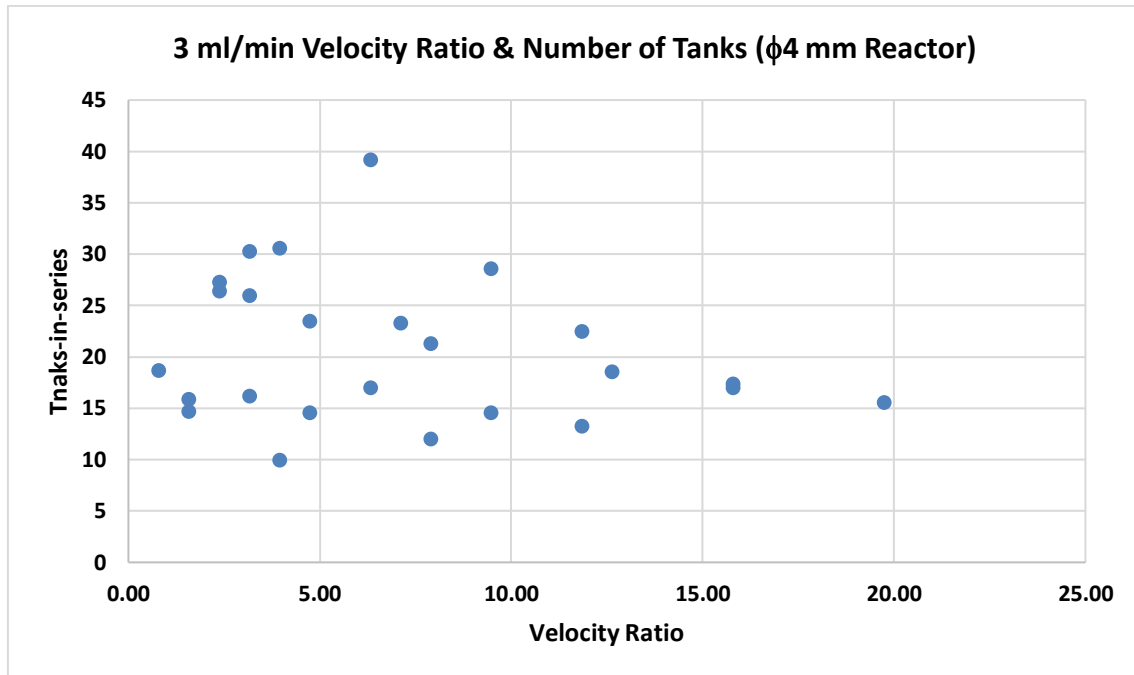


Figure 5.5 RTD results on velocity ratio for micro reactor (Ren = 15.9; x=0.5-2.5 mm, f=1-5 Hz)

The mixing performance decreased with increasing net flow Reynolds numbers as shown in Fig.5.5 and Fig.5.6. However, the performance of the reactor used in this study was better than the similar diameter reactors used in the literature. For example, Phan and Harvey (Phan & Harvey, 2010) observed a maximum number of 26 TIS with their mesoscale reactors. We observed up to a number of 56 TIS in this study. The main reason for the difference is the number of the baffles. 156 baffle cavities were used in the Phan and Harvey's research, whereas we used 185 baffled zone. Also, the pumps were different, and a more accurate continuous operational flow pump was used in this study, which made a significant difference in order to achieve continuous flow in the system compared to syringe pumps. First attempt was to use syringe pumps by synchronising two syringe pumps, but it did not work. Pumps were out of sync after some time, which disturbed the flow in the reactor.

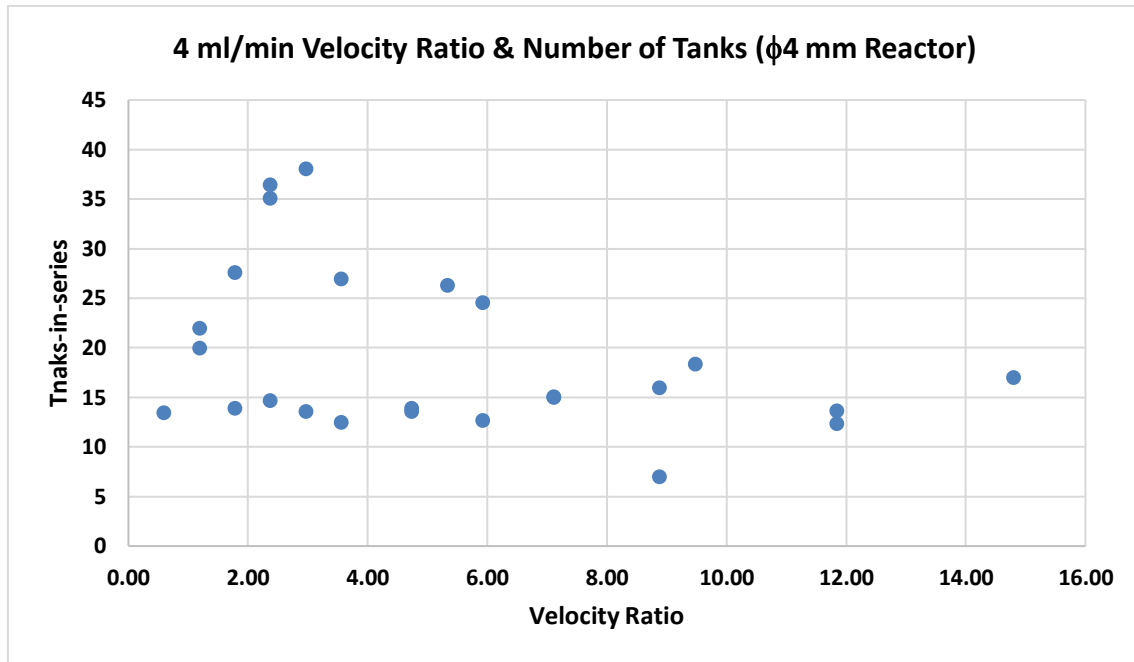


Figure 5.6 RTD results on velocity ratio for micro reactor ($Re_n = 21.2$; $x=0.5-2.5$ mm, $f=1-5$ Hz)

5.1.3 The Correlation between Str Number and Tanks-in-series

Another dimensionless number called Strouhal Number was investigated against the number of tanks. Str number represents the ratio between tube diameter and oscillation amplitude and is an important dimensionless number for scale-up. By maintaining similar Str number for different tube diameters, oscillation amplitude can be calculated for each scale.

Str numbers varied between 0.127 and 0.637. As shown in Fig.5.7, there is no clear trend on Str Number against number of tanks.

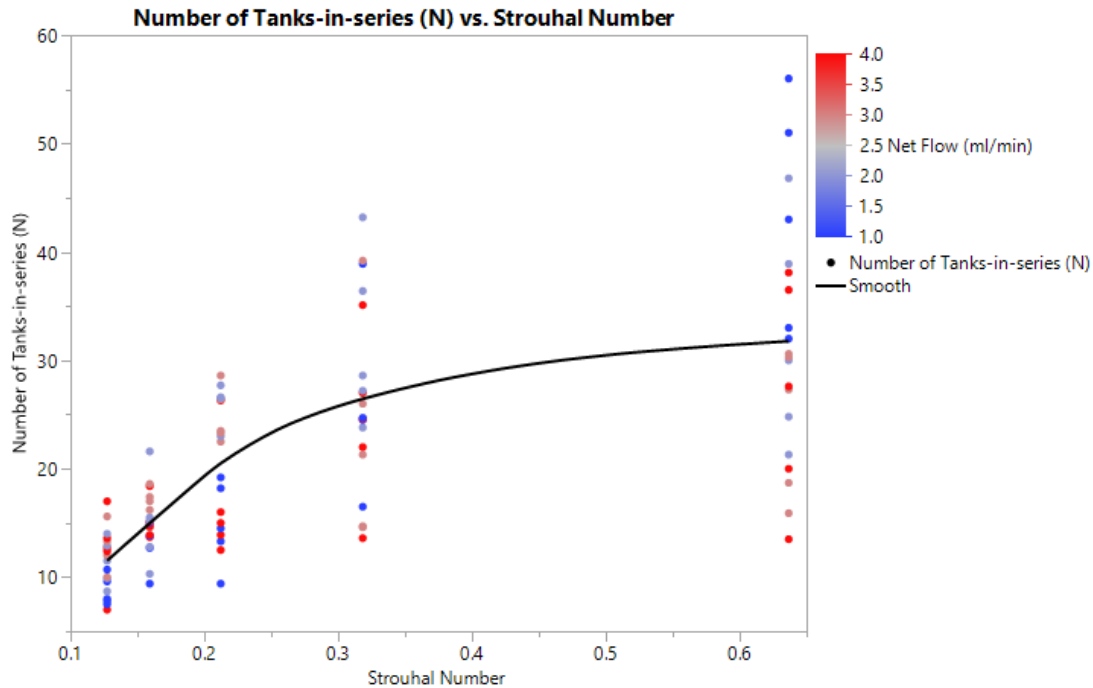


Figure 5.7 The effect of Str Number on number of tanks.

5.1.4 Independent Process Variable and Their effect on the Outcome

All graphs and statistical computations in this chapter were performed by using JMP statistical Software. The key outcomes of implemented statistical analysis are, to understand which independent variables significant effect on the plug flow performance have, what is the robustness of the model used in terms of standard deviation and p-values, and finally, what is the model to predict further experiments. Calculated tanks-in-series numbers for each experiment were used as a response variable of the model. Amplitude, frequency and net flow are independent process variables.

Actual predicted plot was prepared by using the Standard Least Squares personality within the Fit Model. The model includes regression and analysis of variance, covariance and designed experiments. Fig.5.8 presents the information about the model. The plot consists of confidence line (red) and horizontal line (blue). These lines provide a visual indication of whether the model is significant at the %5 level. If the confidence region between the confidence curves contains

the horizontal line, then the effect is not significant. If the confidence curves cross the horizontal line, then the effect is significant.

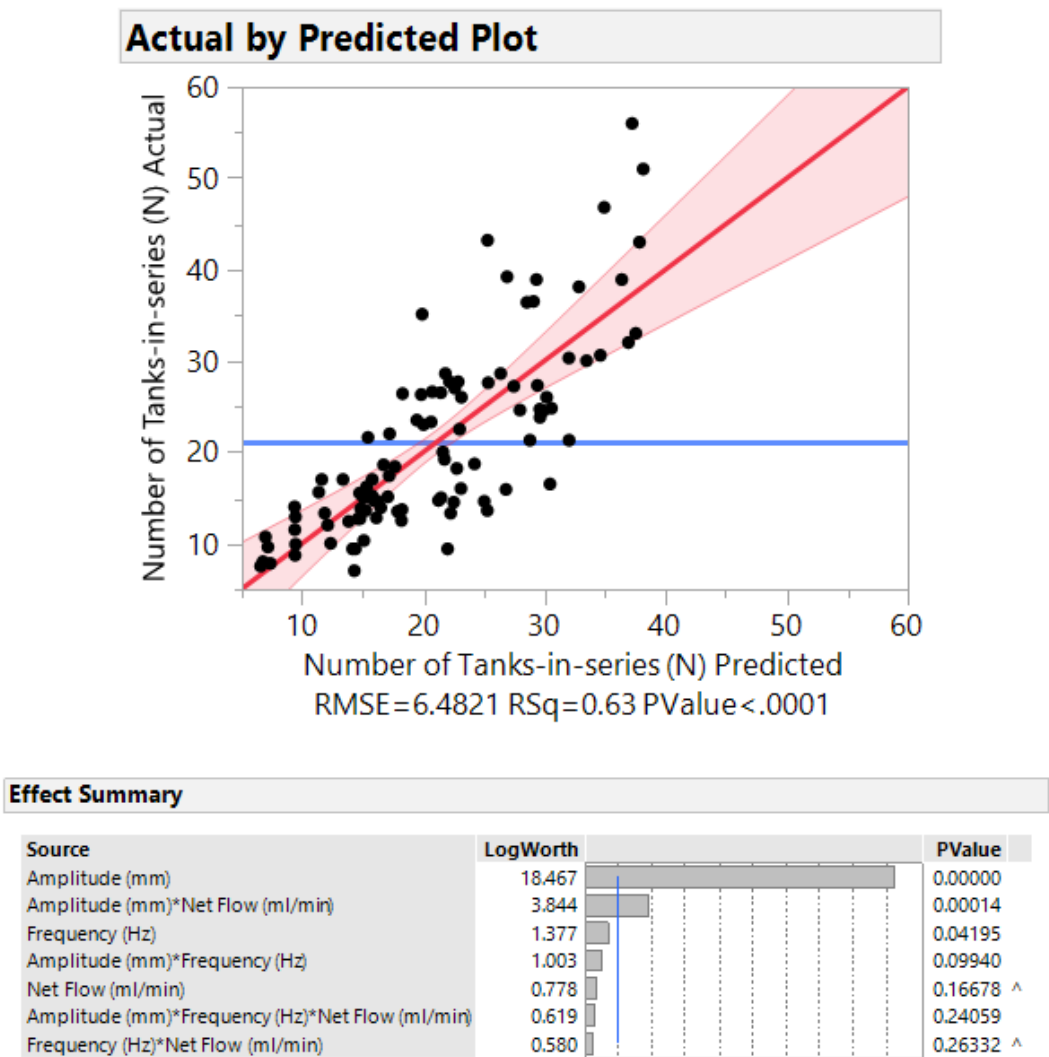


Figure 5.8 Effect summary and actual by predicted plot for the full fit model

The plot shows no evidence of lack of the fit which means the overall model is significant as $p < 0.0001$ and $RSq = 0.63$. All independent variables and their full factorial combinations are significant at the 0.05 level. However, their effects are not at the same level. Amplitude is the biggest influencer as shown in the effect summary, with a LogWorth of 18.46, which is much higher than other factors. Amplitude with net flow is the second biggest influencer as shown in the effect summary.

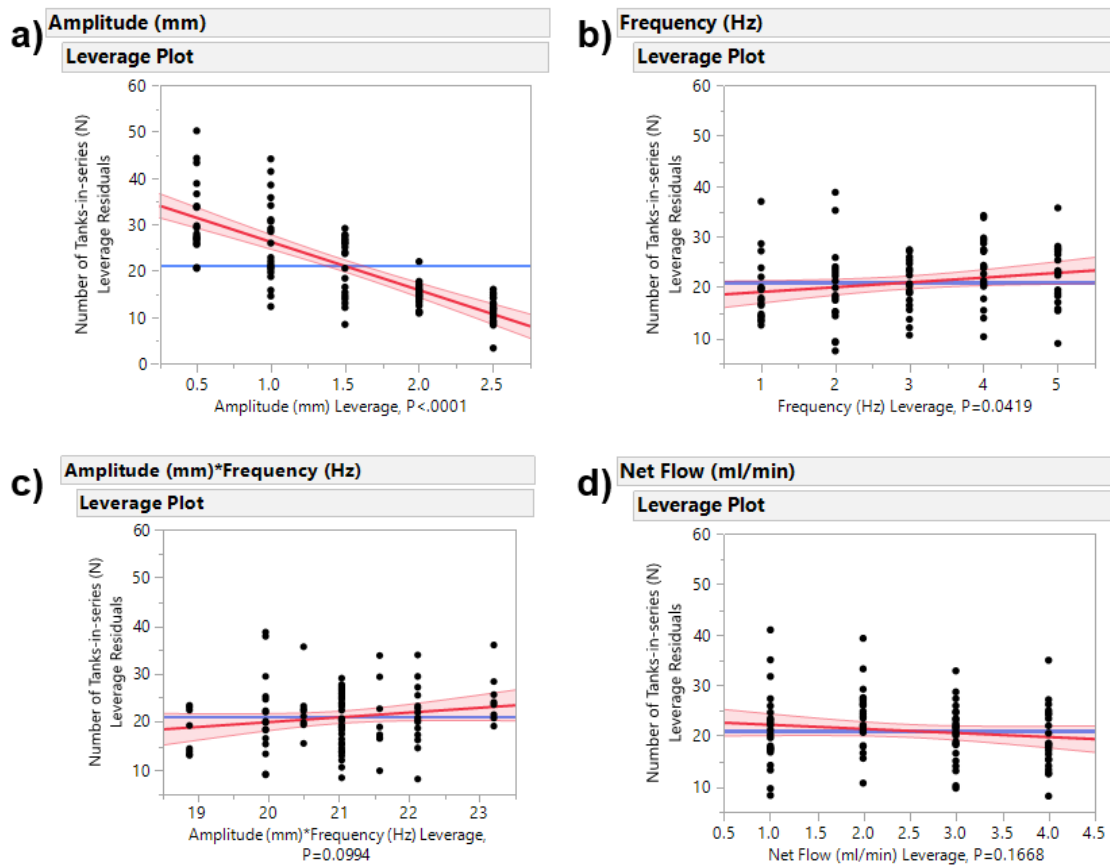


Figure 5.9 Effect leverage plots a) amplitude, b) frequency, c) amplitude*net flow and d) net flow

The effect of leverage plots on an independent variable is useful to see which points might be exerting influence on the whole model. The effect of leverage plots of the top four influencers are shown in the Fig.5.9. Leverage plots consists of a confidence line (red) and horizontal line (blue) like the actual by predicted plot.

As shown in the amplitude leverage plot, confidence curves cross the horizontal line which indicates the oscillation amplitude has the most significant role in the system. From the graph it can be seen that there is a linear trend between amplitude and tanks-in-series number. Lower amplitude creates higher number of tanks-in-series.

Confidence curves are asymptotic to horizontal line in the frequency leverage plot which means that the effect is borderline.

Net flow is not a significant effect as shown in the net flow leverage plot. The horizontal line is inside the confidence curves which means there is no significant effect.

The third outcome of the fit model analysis is “Prediction Profiler”. The prediction model can be used to identify optimal settings of the input factors for a desired response target. A prediction model was constructed to set the tanks-in-series number target within limits of 10 and 32 as shown in the Fig.5.10.

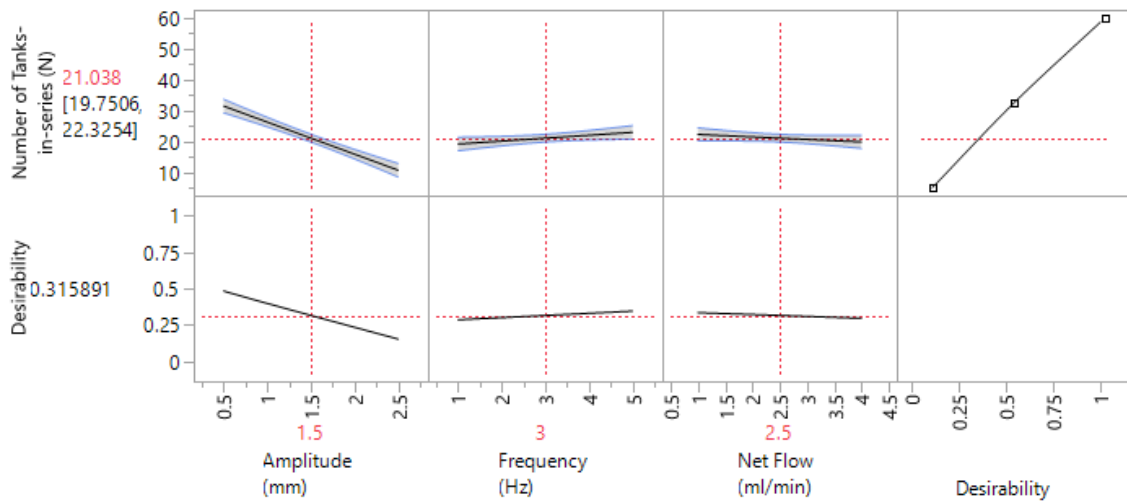


Figure 5.10 Prediction profiler for the independent process variables

The first three plots on the top row of the prediction profiler describes how tanks-in-series number changes when one of the factors change and the remaining two factors are kept the same. For example, when amplitude is 1.5 mm and frequency is 3 Hz, the line in the net flow can be moved towards left and right to show how tanks-in-series changes by dragging the red dashed vertical lines in the columns for net flow. The numbers under the tanks-in-series title on the left defines the predicted number of tanks-in-series (red) and a confidence intervals (black) for mean tanks-in-series for the selected input settings. Top right plot of the prediction profiler shows the desirability function for the tanks-in-series number. The bottom row plots describe the desirability trace for each input factor at the setting of the factor.

The prediction function is an alternative way to predict the response. The equation shown in Fig.5.11 can be used to calculate the number of the tanks-in-series based on independent inputs and their full factorial effects.

Prediction Expression
35.8335
+ -10.408 • Amplitude (mm)
+ 0.9455 • Frequency (Hz)
+ (Amplitude (mm) - 1.5) • ((Frequency (Hz) - 3) • -1.079)
+ -0.808 • Net Flow (ml/min)
+ (Amplitude (mm) - 1.5) • ((Net Flow (ml/min) - 2.5) • 3.2536)
+ (Frequency (Hz) - 3) • ((Net Flow (ml/min) - 2.5) • 0.4614)
+ (Amplitude (mm) - 1.5) • ((Frequency (Hz) - 3) • ((Net Flow (ml/min) - 2.5) • -0.6848))

Figure 5.11 Prediction function for the Tanks-in-series number based on full factorial of input variables

The function can be simplified for only three independent variables without considering their full factorial effect as shown in Fig.5.12. However, its accuracy will be lower than the equation shown in Fig.5.11.

Prediction Expression
35.8335 + -10.408 • Amplitude (mm) + 0.9455 • Frequency (Hz) + -0.808 • Net Flow (ml/min)

Figure 5.12 Prediction function for the tanks-in-series number according to only independent variables

5.2 Meso-Scale Reactor ($\phi 8$ mm) RTD Results

This section presents the data and analysis of meso-scale reactor characterisation experiment results for a wide range of oscillatory and net flow conditions. The scale-up methodology was used to identify amplitude, frequency and net flow numbers by maintaining same Str , Re and Ro numbers as micro-scale reactor system. Basically, DoE of the micro-scale reactor was scaled up for the meso-scale reactor. The main objective of these experiments was to understand the plug flow conditions and performance as a function of three independent variables (amplitude, frequency and net flow) for the meso-scale reactor. And then the results were compared to micro-scale reactor results to develop a scale-up methodology from 4 mm diameter to 8 mm diameter.

However, the oscillation mechanism used in the $\phi 8$ mm reactor was different than the micro-scale reactor. Scotch-yoke oscillation mechanism was developed. This mechanism provides much better sinusoidal motion and wider range of amplitude and frequency combination for the meso-scale reactor. Also, reactor length was different than that of the micro scale reactor. Only three reaction channels were used to keep same reaction volume in two different scales which means residence times are same for two sets of systems. Therefore, we don't expect the exact same tanks-in-series numbers, but similar trends.

5.2.1 Correlation Between Velocity Ratio and Tanks-in-series numbers

Fig.5.13 shows the number of tanks versus velocity ratio for the full set of factorial DoE measurements. It was observed that the trend of the tanks-in-series numbers on the velocity ratios was similar to the micro-scale reactor results and previous studies on OBR (Phan & Harvey, 2010). Maximum tanks-in-series numbers were observed at velocity ratios around 10. In the lowest velocity ratio, the lowest number of tanks were measured; similarly, in the highest velocity ratio, the lowest number of tanks were observed (except 1 measurement which might be due to measurement error). A detailed investigation for each net flow group is presented in the next section.

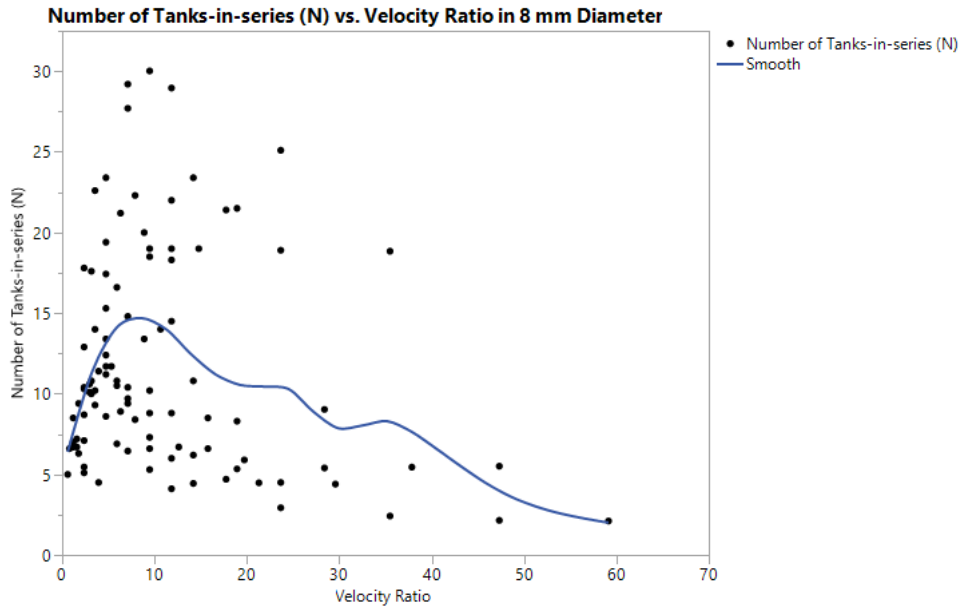


Figure 5.13 Full DoE Results for the meso-scale reactor RTD results

Only 15 experiments were completed for the low flow rate of 2 ml/min. High amplitudes (4 and 5 mm) resulted in very poor tracer measurements in the low flow rates. The dispersion was very large at high amplitudes with a very low net flow rate. After a very long time, the spectrometer still detected blue tracers from the effluent fluid, which is a result of the back-mixing and very bad plug flow conditions. Therefore, 4- and 5-mm amplitude with 2 ml/min net flow results was decided to be taken off from the data. Maximum number of tanks were observed at velocity ratios around 10. However, there is no significant trend due to limited data.

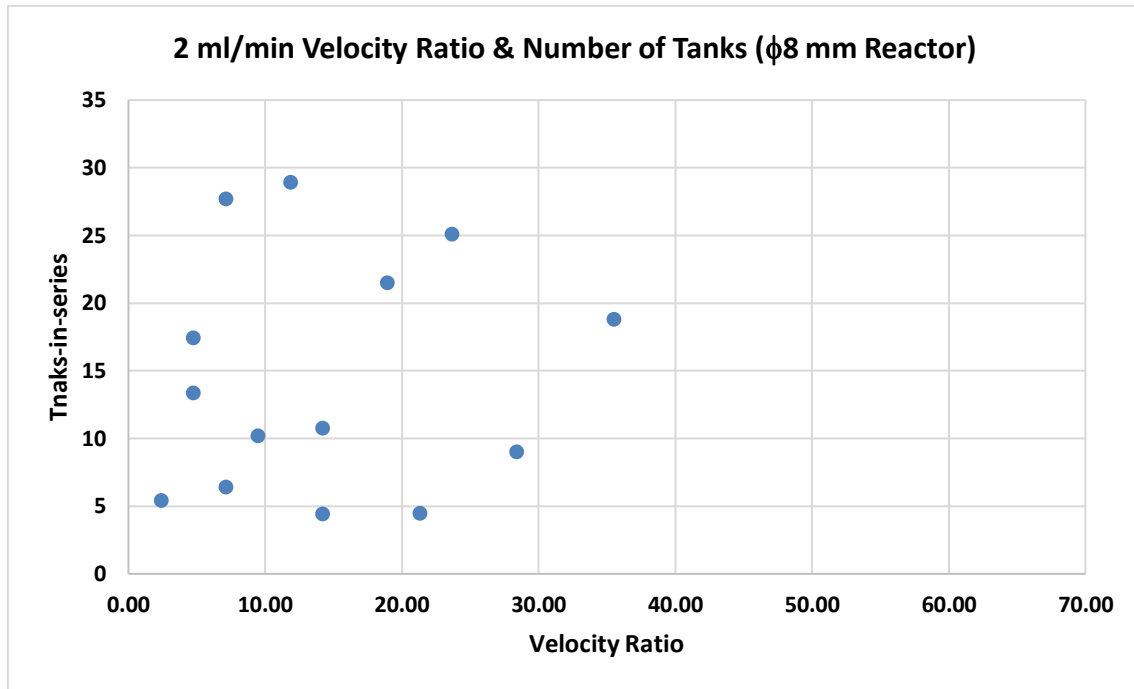


Figure 5.14 RTD results on velocity ratio for meso reactor ($Re_n = 5.3$; $x=1-3$ mm, $f=0.25-1.25$ Hz)

For the second net flow group, there is similar trend between velocity ratio and number of tanks as shown in Fig.5.15. The number of tanks increases until some point of velocity ratio (until $\psi = 15$). After the velocity ratio 15, the number of tanks starts falling. The velocity range is between 0 and 30 in this net flow group.

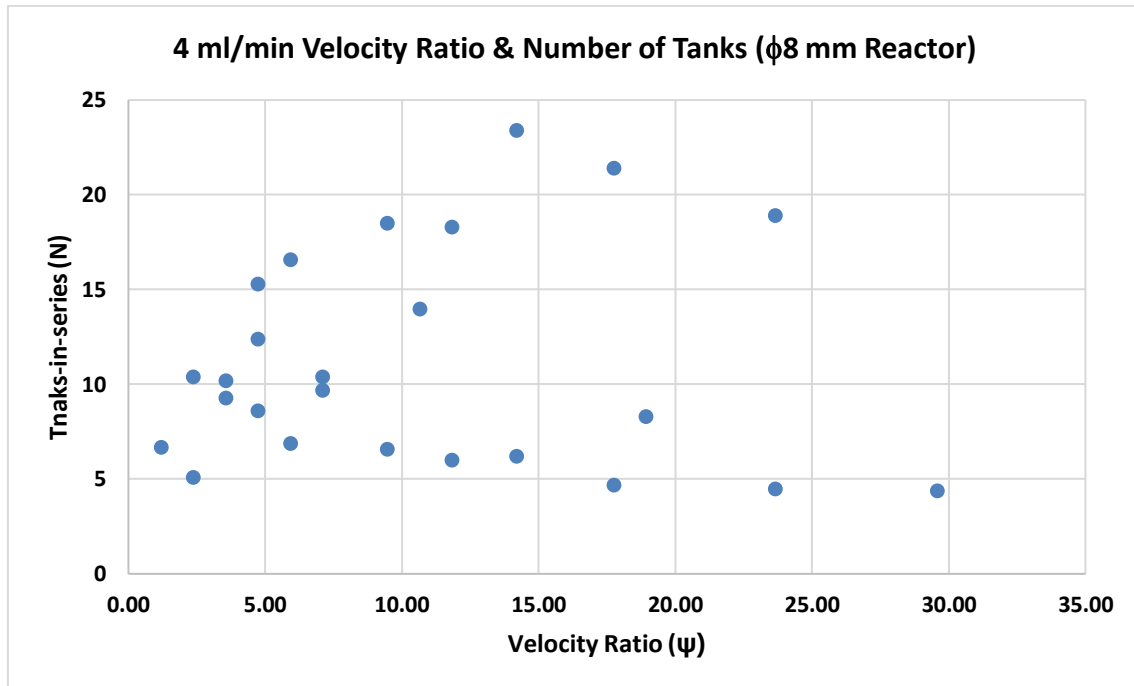


Figure 5.15 RTD results on velocity ratio for meso reactor ($Re_n = 10.6$; $x=1-5$ mm, $f=0.25-1.25$ Hz)

The third net flow (6 ml/min) group has the velocity ratio between 0 to 20, which means there are more data points in the narrow velocity range. Because of that, there is clearer trend between velocity ratio and number of tanks compared to the previous two graphs. Better plug flow conditions were observed at the velocity ratios around 8 as shown in Fig.5.16.

The final group of net flow (8 ml/min) has a velocity ratio between 0 to 15. Similar to the previous net flows, maximum plug flow conditions were observed at velocity ratios around 8 as shown in Fig.5-17.

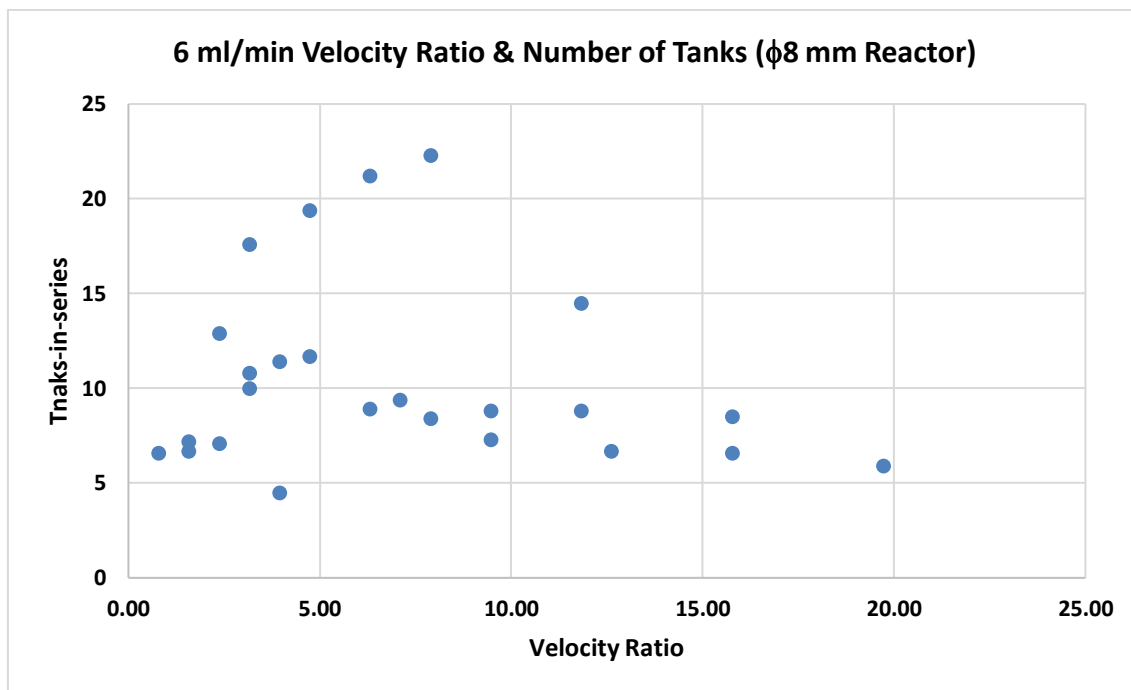


Figure 5.16 RTD results on velocity ratio for meso reactor ($Re_n = 15.9$; $x=1-5$ mm, $f=0.25-1.25$ Hz)

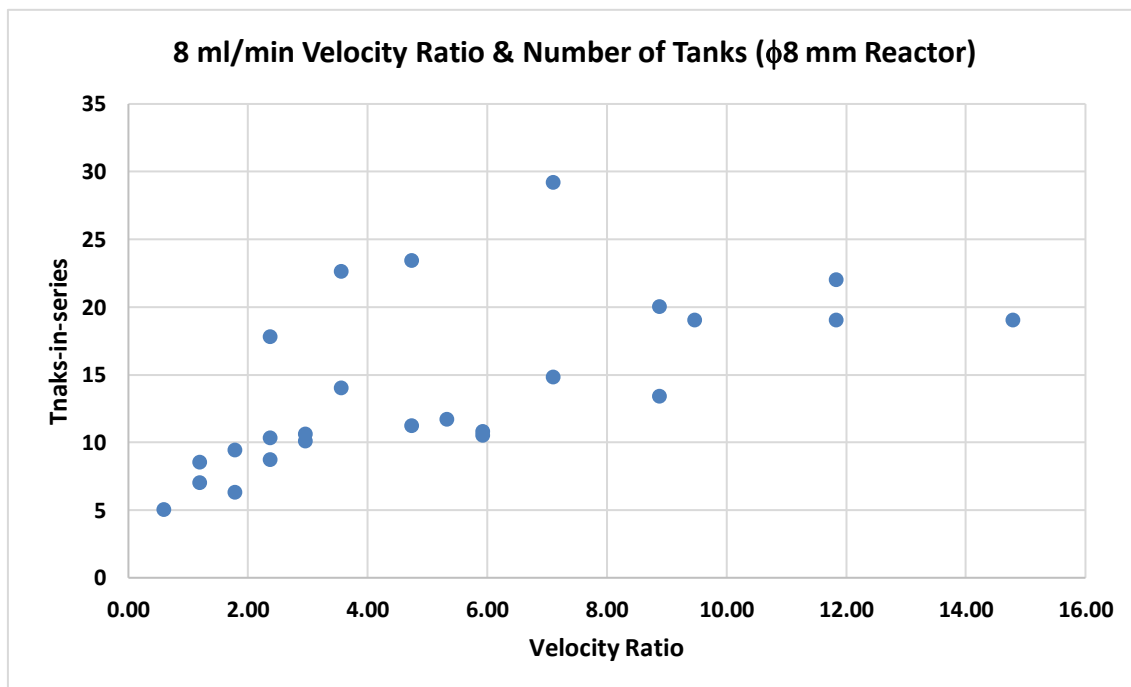


Figure 5.17 RTD results on velocity ratio for meso reactor ($Re_n = 21.2$; $x=1-5$ mm, $f=0.25-1.25$ Hz)

5.2.2 The correlation between Str Number and Plug Flow Quality

Str numbers were plotted against the tanks-in-series number for the entire DoE results as shown in Fig.5.18. Due to simple OBR scale-up rule, same Str numbers were used for micro and meso scale reactors. Regardless of the tube diameter, there is no clear trend between Str number and velocity ratio. Similar plug conditions were observed in various Str numbers.

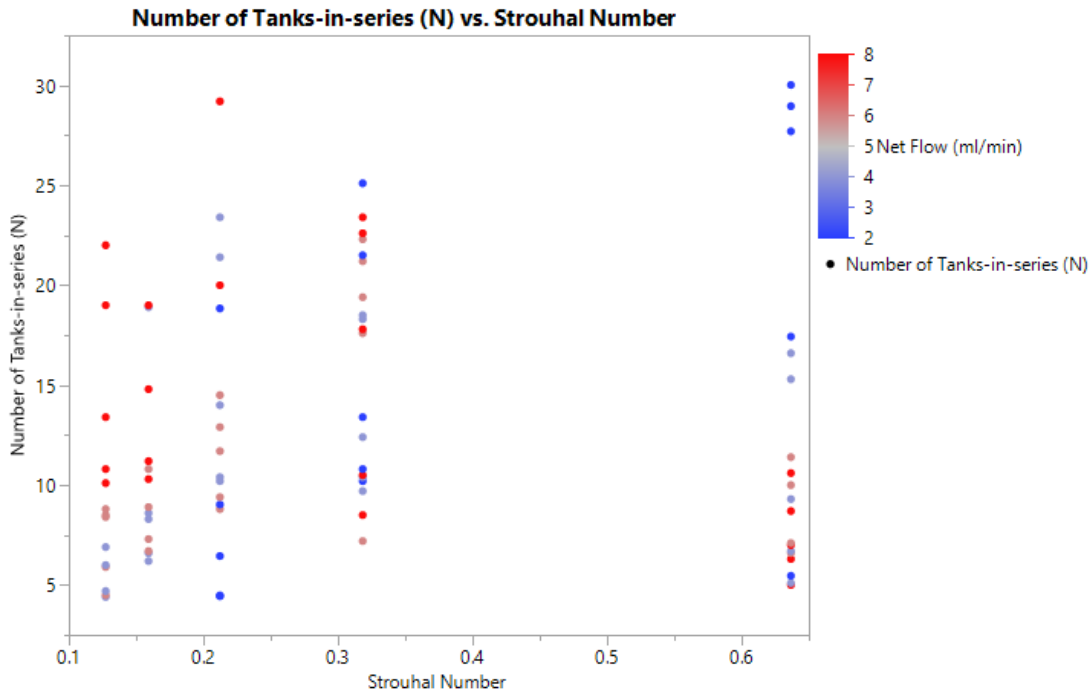


Figure 5.18 The effect of Str number on the number of tanks for meso-scale reactor

5.2.3 The Effect of Key Process Parameters for the $\phi 8$ mm Reactor

A detailed statistical analysis was performed using Jmp software. Tanks-in-series number was calculated for each tracer experiment and 90 data points were used for the fit model. The aim of to study significant factor analysis was three-fold. First aim was to characterize the plug flow behaviour of the meso-scale modular flow reactor by using the similar experimental conditions of micro-scale reactor characterisation. Second, was, to investigate the effect of the independent input variables in the meso scale reactor, and third was to develop a scale-up methodology between meso and micro scale reactors.

Actual predicted plot was calculated using the Standard Least Square method within the Fit Model regression analysis. Fig.5.19 summarizes the fit model analysis results and effect of each variable. As observed on the plot, the overall model is significant as $p < .0001$ and $RSq = 0.50$. All independent variables and their full factorial effects (except frequency*net flow < 0.5) are significant at the 0.5 level. However, the order and magnitude of the variable effects are not the same as the micro-scale reactor. Amplitude with net flow and frequency are the biggest influencers as shown in the effect summary table. Amplitude was observed as the third best influencer input variable.

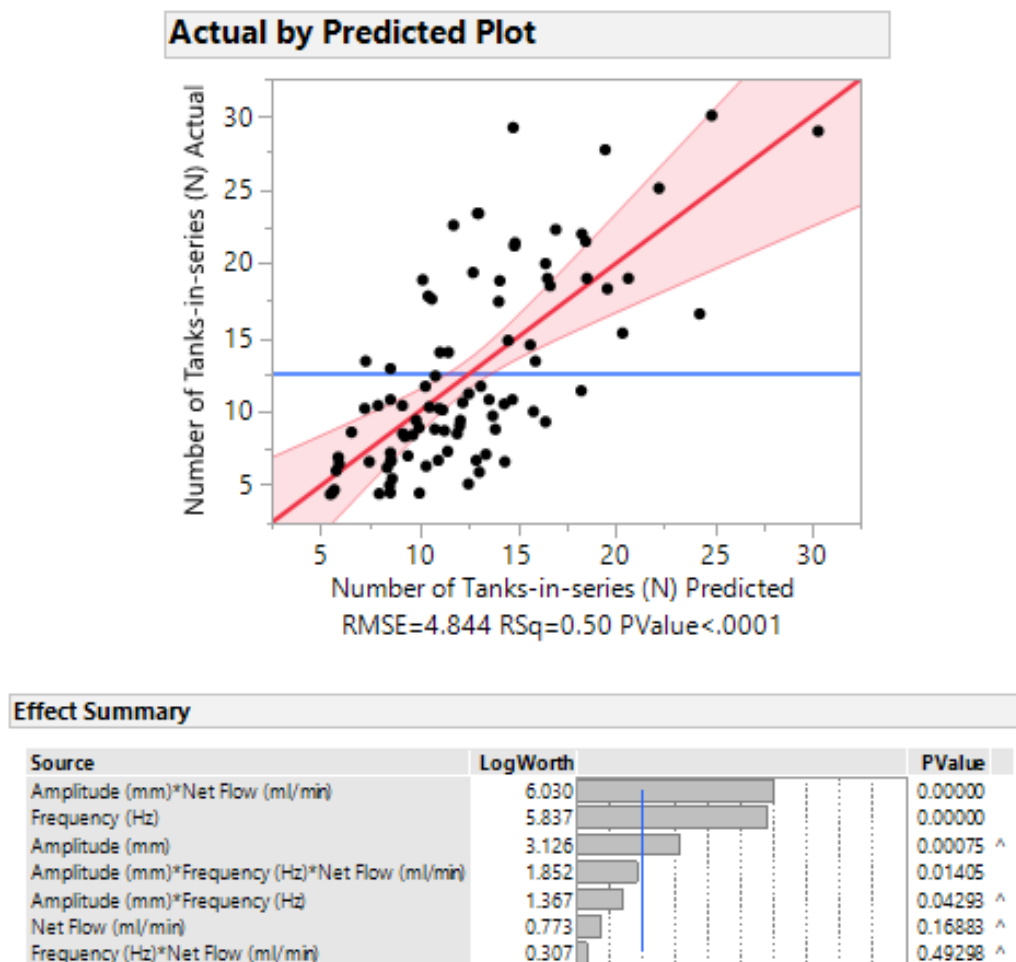


Figure 5.19 Effect summary and actual by predicted plot for the meso-scale experimental results

However, the difference between top three influencers in terms of their magnitude levels are small when compared to micro-scale reactor results. Amplitude was the dominant influencer in the micro-scale OBR system but we did not observe a similar outcome in the meso scale mechanism.

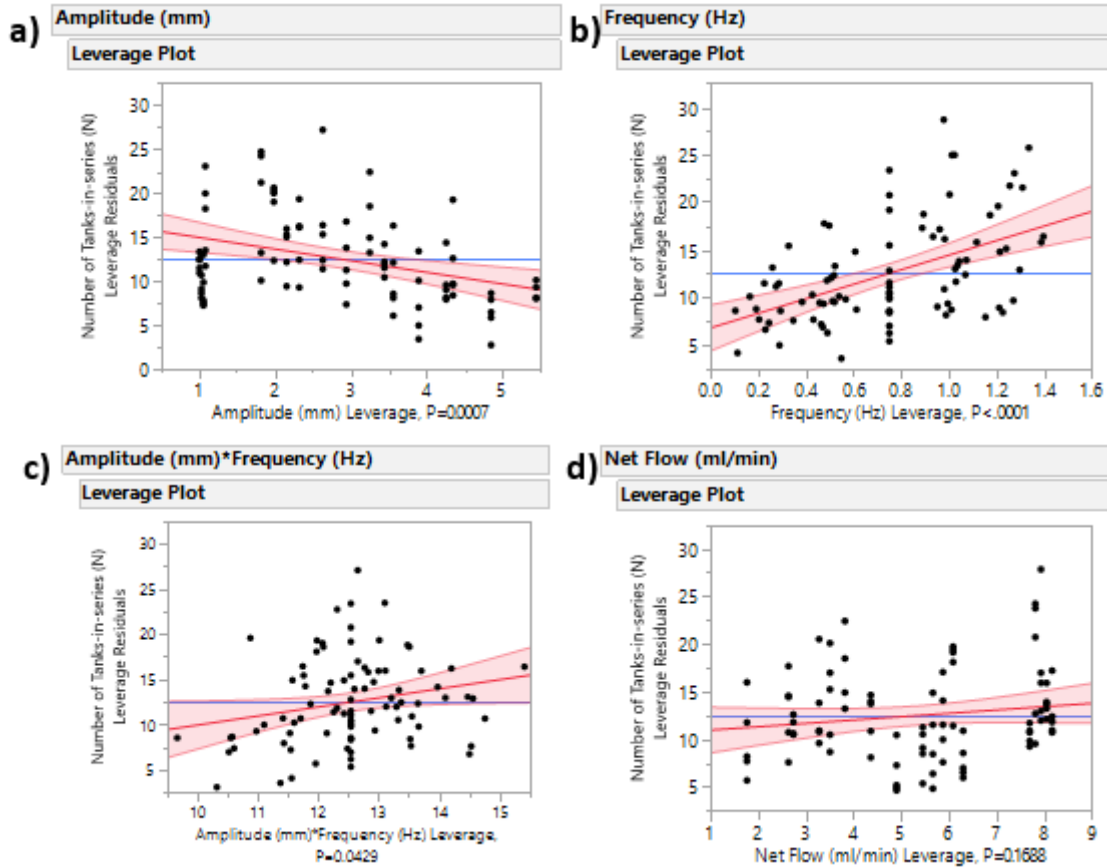


Figure 5.20 Effect leverage plots a) amplitude, b) frequency, c) amplitude*frequency and d) net flow

Effect leverage plots for the variables that had the biggest influence are shown in Fig.5.20. These plots are useful to visualise the points that might be important for the whole model. The interaction between horizontal (blue) and confidence curves (red) explains its importance. As seen on the first three plots (a, b and c), horizontal line crosses the confidence curves, which indicates those variables take significant role in creating the response. The tanks-in-series number response is dependent on both frequency and amplitude. The overall trend between amplitude and N is negatively correlated, indicating that higher

amplitude values tend to result lower tanks-in-series numbers. There is positive relation between frequency and N, indicating that higher frequency values tend to result in higher number of tanks. The effect of net flow is not significant as observed on the plot Fig.5.20d; the horizontal line is within the confidence curves.

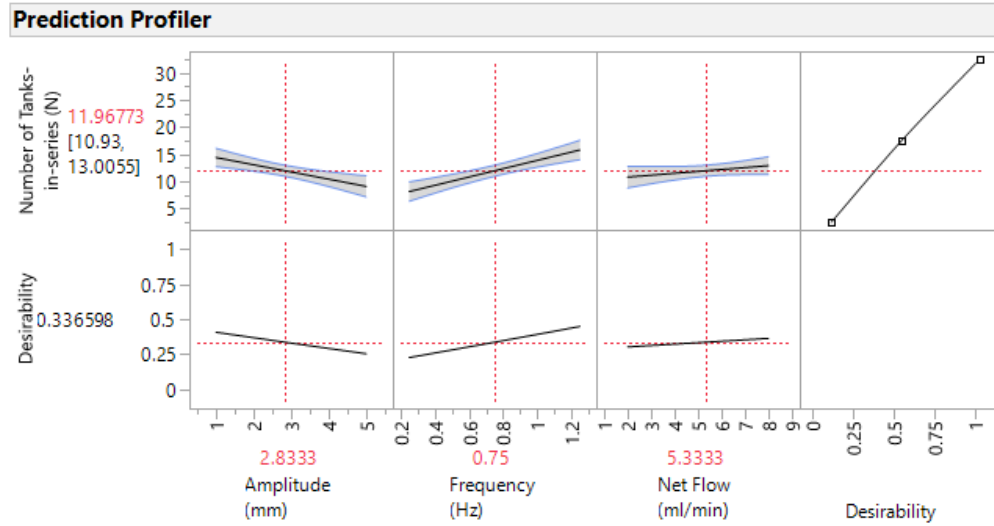


Figure 5.21 Prediction profiler for the meso-scale modular OBR

Prediction model was developed based on prediction profiler for the meso-scale OBR system as shown in Fig.5.21. The model can be used to identify optimum settings of the input variables for the desired number of tanks value or alternatively, prediction equation can be used as shown in Fig.5.22.

Prediction Expression

$$\begin{aligned}
 & 8.1457870607 \\
 & + -1.329121643 \cdot \text{Amplitude (mm)} \\
 & + 7.622368525 \cdot \text{Frequency (Hz)} \\
 & + \left(\text{Amplitude (mm)} - 2.833333333 \right) \cdot \left(\left(\text{Frequency (Hz)} - 0.75 \right) \cdot -2.365089209 \right) \\
 & + 0.3508088468 \cdot \text{Net Flow (ml/min)} \\
 & + \left(\text{Amplitude (mm)} - 2.833333333 \right) \\
 & \cdot \left(\left(\text{Net Flow (ml/min)} - 5.333333333 \right) \cdot 1.0203412322 \right) \\
 & + \left(\text{Amplitude (mm)} - 2.833333333 \right) \\
 & \cdot \left(\left(\text{Frequency (Hz)} - 0.75 \right) \cdot \left(\left(\text{Net Flow (ml/min)} - 5.333333333 \right) \cdot 1.446136655 \right) \right)
 \end{aligned}$$

Figure 5.22 Prediction function for the target meso-scale reactor tanks-in-series number

5.3 Repeatability of the Characterization Experiments

Reproducibility is one of the main benefits of the flow processing. In order to investigate and prove the consistency of the low conditions in the modular OBR reactor, 34 randomly selected experiments (20 from micro scale and 14 from meso scale) from each flow rate set were chosen to repeat. The result of the consistency experiments is shown in Table.5.2.

Repeatability difference has been calculated in terms of percent error of TiS numbers between two sets of results. As that can be seen from the table below, 11 experiment out of 20 have remarkably good repeatability in the micro-scale reactor. These 11 experiments have resulted fractional difference in the range of $\pm 10\%$ compare to the first and repeated experiments. 4 repeated experiments have percentage changes of -10 to -20. Rest of the experiments has shown the worse percent error ranging from -20% to -40%.

Similar fractional difference analysis was conducted for the meso-scale reactor experiments in order to understand the percent error of the experiments. Eight experiments out of fourteen have shown remarkably good repeatability, changes between first and repeated experiments was only in the range of $\pm 6\%$ as shown in the Table.5.2. Two experiments have shown in the range of minus ten to minus twenty percentage difference. And the remaining meso-scale repeated experiments has demonstrated a significant difference. Further investigation was conducted between repeatability results and dimensionless number to understand if there is any correlation between process repeatability and dimensionless numbers.

Table 5.2 Accuracy of the Tracer Experiments

DoE Number	Str Number	Re_n Number	Re_o Number	Velocity Ratio	Number of TiS	Repeat Experiment	% Change
Micro Scale Reactor (4 mm Tube Channel)							
2	0.127	5.29	125.3	23.7	8	7.5	6%
8	0.637	5.29	37.6	7.1	33	39	-18%
10	0.127	10.59	250.6	23.7	11.5	12	-4%
22	0.318	10.59	50.1	4.7	28.6	37.2	-30%
23	0.318	15.88	50.1	3.2	26	36	-38%
32	0.637	10.59	12.5	1.2	24.8	22.8	8%
33	0.637	5.29	25.1	4.7	56	52	7%
39	0.127	15.88	313.3	19.7	15.6	15.2	3%
41	0.212	5.29	75.2	14.2	9.4	12.2	-30%
45	0.127	10.59	313.3	29.6	14	15.5	-11%
55	0.637	21.17	12.5	0.6	13.5	13.6	-1%
59	0.637	15.88	12.5	0.8	18.7	17.2	8%
64	0.212	15.88	112.8	7.1	23.3	26.7	-15%
67	0.127	5.29	313.3	59.2	7.8	8.4	-8%
78	0.212	10.59	112.8	10.7	26.5	27.4	-3%
84	0.127	21.17	313.3	14.8	17	18.6	-9%
86	0.159	15.88	200.5	12.6	18.6	19.6	-5%
94	0.212	21.17	112.8	5.3	26.3	31.5	-20%
95	0.318	21.17	50.1	2.4	35.1	43.4	-24%
98	0.159	21.17	200.5	9.5	18.4	23.2	-26%
Meso Scale Reactor (8 mm Tube Channel)							
9	0.212	21.19	150.4	7.1	29.2	13.6	53%
16	0.318	5.30	25.1	4.7	13.4	13.94	-4%
17	0.318	21.19	125.3	5.9	10.5	22.4	-113%
29	0.318	5.30	100.2	18.9	21.5	21.46	0%
51	0.212	10.59	150.4	14.2	23.4	22.3	5%
56	0.212	21.19	37.6	1.8	9.4	11.4	-21%
61	0.159	15.89	200.5	12.6	6.7	7.11	-6%
62	0.637	10.59	50.1	4.7	15.3	14.7	4%
68	0.637	15.89	50.1	3.2	10	10.5	-5%
76	0.637	21.19	50.1	2.4	8.7	8.7	0%
86	0.318	15.89	100.2	6.3	21.2	23.6	-11%
90	0.637	5.30	50.1	9.5	30.02	28.22	6%
95	0.212	15.89	150.4	9.5	8.8	16.2	-84%
96	0.318	10.59	100.2	9.5	18.5	11.5	38%

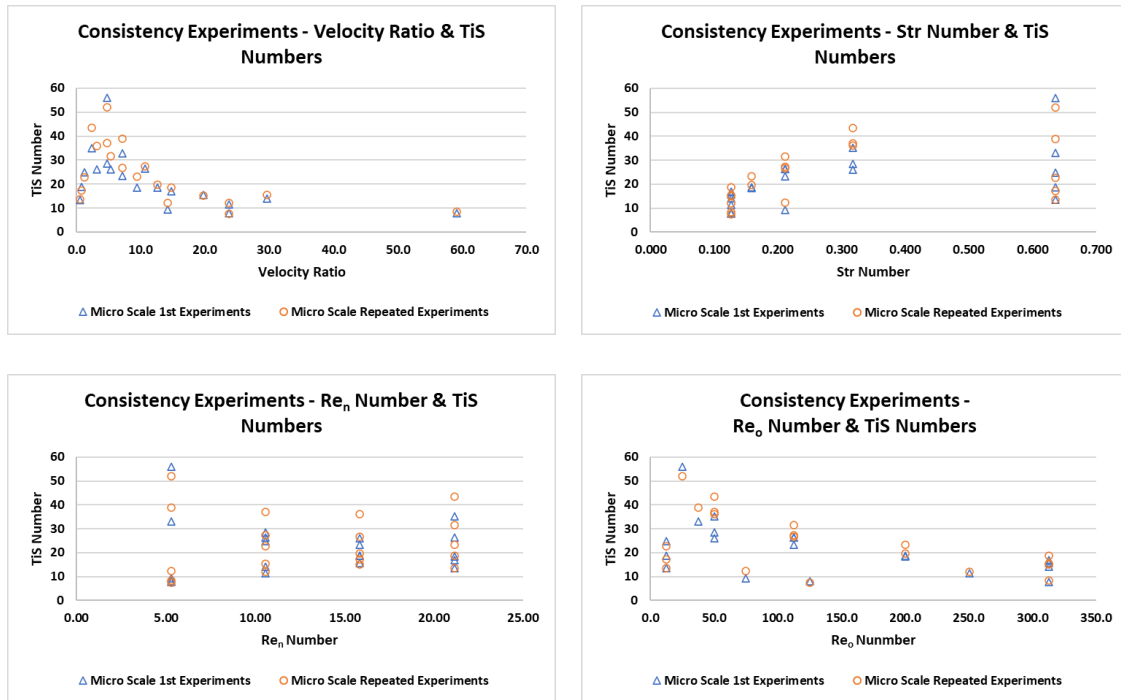


Figure 5.23 Repeatability results for the micro-scale reactor characterization experiments

Fig.5.23 presents the correlation between dimensionless numbers and repeatability of the micro-scale characterization experiments. The first graph presents the relationship between velocity ratio and repeatability results. The velocity ratio over 10 resulted almost identical TiS numbers, however these TiS numbers are under 20. According to the literature, TiS number over 10 can be accepted as a plug flow condition. But, compare to the higher TiS numbers (>40) achieved in this study, TiS numbers under 20 do not have very good plug flow conditions. We observed larger percent errors TiS numbers over 25 in the velocity range of 5 to 10. The relationship between Str number and repeatability experiments is more interesting. With the largest amplitude (Str=0.127), repeatability results were consistent with small difference of percent error. With the two smallest amplitude (Str = 0.637 and 0.318), larger percent error was observed. There is no clear trend between Re_n , Re_o numbers and repeatability as shown in the Fig.5.23.

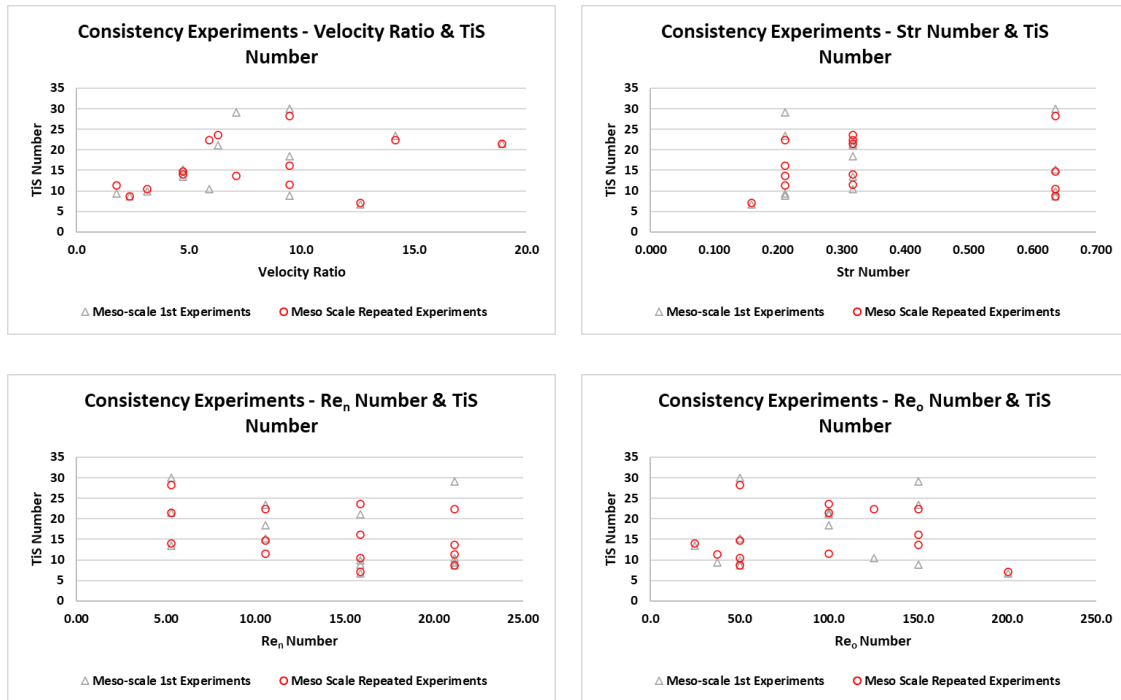


Figure 5.24 Repeatability results for the meso-scale reactor characterisation experiments

The similar investigation was repeated for the meso-scale reactor. The relationship between dimensionless numbers and repeatability for the meso-scale reactor characterization experiments is shown in Fig.5.24. The velocity ratios between 0 to 5 and 10 to 20 have shown good process repeatability with small percent error. Larger fractional difference was observed in the velocity ratio between 5 to 10. Better repeatability was observed with smaller Str numbers, increased Str numbers resulted larger percent error. We did not observe any trend between Re_n , Re_o and repeatability results which was same observation for the micro-scale reactor as well.

The conclusion for the process repeatability analysis is that overall success is 55% (19 successful experiments out of 34). As mentioned above, repeated experiments were randomly selected for screening the full set of experimental points. The dataset is divided into two group plug flow and non-plug flow conditions. A clear distinguished was observed between plug flow regime and non-plug flow conditions for the process repeatability. The consistency rate is higher in the plug flow regimes as shown in Tab.5.3.

Assumptions for the plug flow regimes were distinguished from the literature and characterisation experiments outcome and listed as below:

- In the literature that defined if the TiS number is above 10 then the system behaves as plug flow reactor. TiS number results from characterization experiments were screened and the results over 10 were taken in the Tab.5.3.
- Velocity ratio was the second filtering parameter to identify from plug flow conditions. As presented in Chap.5.1.2 and Chap.5.2.1, velocity is important dimensionless number to achieve plug flow and that had been found the optimum velocity ratio is between 4 and 25 for the modular OBR. Therefore, the velocity ratios between 4 and 25 were taken from the repeatability experiments as shown in Tab.5.2

Table 5.3 Repeatability experiments in the plug flow regime

DoE Number	Str Number	Re _n Number	Re _o Number	Velocity Ratio	Number of TiS	Repeat Experiment	% Change
Micro Scale Reactor (4 mm Tube Channel)							
8	0.637	5.29	37.6	7.1	33	39	-18%
10	0.127	10.59	250.6	23.7	11.5	12	-4%
22	0.318	10.59	50.1	4.7	28.6	37.2	-30%
33	0.637	5.29	25.1	4.7	56	52	7%
39	0.127	15.88	313.3	19.7	15.6	15.2	3%
64	0.212	15.88	112.8	7.1	23.3	26.7	-15%
78	0.212	10.59	112.8	10.7	26.5	27.4	-3%
84	0.127	21.17	313.3	14.8	17	18.6	-9%
86	0.159	15.88	200.5	12.6	18.6	19.6	-5%
94	0.212	21.17	112.8	5.3	26.3	31.5	-20%
98	0.159	21.17	200.5	9.5	18.4	23.2	-26%
Meso Scale Reactor (8 mm Tube Channel)							
9	0.212	21.19	150.4	7.1	29.2	13,6	53%
16	0.318	5.3	25.1	4.7	13.4	13.94	-4%
17	0.318	21.19	125.3	5.9	10.5	22.4	-113%
29	0.318	5.30	100.2	18.9	21.5	21.46	0%
51	0.212	10.59	150.4	14.2	23.4	22.3	5%
62	0.637	10.59	50.1	4.7	15.3	14.7	4%
86	0.318	15.89	100.2	6.3	21.2	23.6	-11%
90	0.637	5.3	50.1	9.5	30.02	28.22	6%
96	0.318	10.59	100.2	9.5	18.5	11.5	38%

It is difficult to obtain identical TiS numbers for each repeated experiment due to number of factors such as control of tracer volume, accuracy of spectrometer, light source and detector, pump speed accuracy etc. Therefore, a range of $\pm 20\%$ was accepted as a successful repeatability rate. In the plug flow regime, 14 (shown in Tab.5.3 with green colour) experiments out of 20 were observed as repeatable experiments which means 70% of repeatability rate. More experimental dataset is recommended as future study by employing a clear method to identify experiments to repeat for example identical dimensionless numbers should be selected for micro and meso scale reactors to increase the confidence rate.

5.4 Scale-up Methodology – Correlation Between Micro and Meso Scale OBR Mechanisms

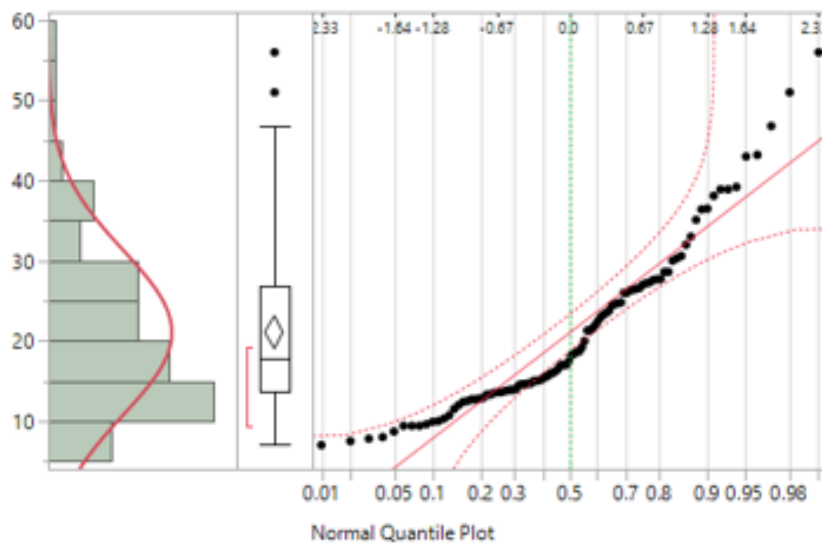
In order to develop scale-up methodology, the number of tanks-in-series was selected. Same dimensionless numbers were used for experiments of 4- and 8-mm diameters. The correlation between two diameter sizes based on dimensionless numbers will be presented in this section. This section presents the key outcomes of this thesis in terms of scale-up principles for modular OBR systems.

First, the missing data points of the meso scale experiments were integrated into the meso-scale dataset using meso-scale reactor prediction model. 10 amplitude and frequency combinations in the 2 ml/min net flow were set as input variables to predict target number of tanks. The model was validated by testing some of the experiments and the predicted value was compared with actual test results. It was observed that the prediction model was successful at predicting missing data points. Each scale has 100 measurement points collected from full factorial DoE for scale-up correlation analysis. The main objective of these experiments was to compare the experimental number of tanks performance under large range of oscillatory and net flow conditions as a function of tube diameter.

5.4.1 Distributions of the Experimental Data

Distribution analysis are shown in Fig.5.25 to assess the normality of the response results. Y-axis of the histograms show the density of the tanks-in-series numbers, which were experimentally measured. Red bracket defines the shortest half of the data which means the densest region. As seen from the results, most micro-scale responses are between 10 to 30 number of tanks as it is 5 to 15 number of tanks for meso-scale responses. Micro-scale dataset has two outliers as shown with two dots on the quantile box, these are disconnected data points from rest of the dataset. Normal quantile plots identify a dataset distributed as a normal or exponential. The data points follow the same trend and behaviour among the normal distribution line for both reactor diameters. The data points are not on the line. They follow their own nonlinear coherent path, but the path is similar for both scales. Normal distributions based on the mean and standard deviation are fitted on the histograms as shown with red curves. Normal distribution lines are also similar for two sizes of the reactor.

a) Distributions of number of tanks (N) in 4 mm diameter



b) Distributions of number of tanks (N) in 8 mm diameter

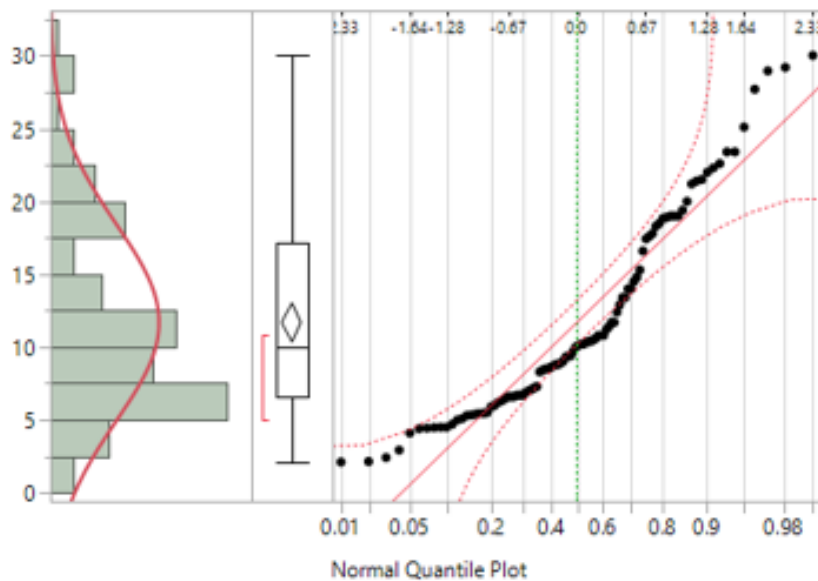


Figure 5.25 Distribution reports for micro and meso scale reactor results

As seen from the results, there is a similar trend. However, the magnitude of the number of tanks are different for the two sizes of tube diameter. This result was expected as mentioned at the beginning of this chapter. When the tube diameter is changed, the residence time is also changed to achieve same mixing

conditions due to changing fluid kinetics and mass transfer, even when similar eddies were used in the system. Reactor dimensions and mixing performance in the small-scale flow systems were investigated by a group of researchers (Nagy, et al., 2012). They developed a correlation model between reactor diameter and residence time using Damkohler number.

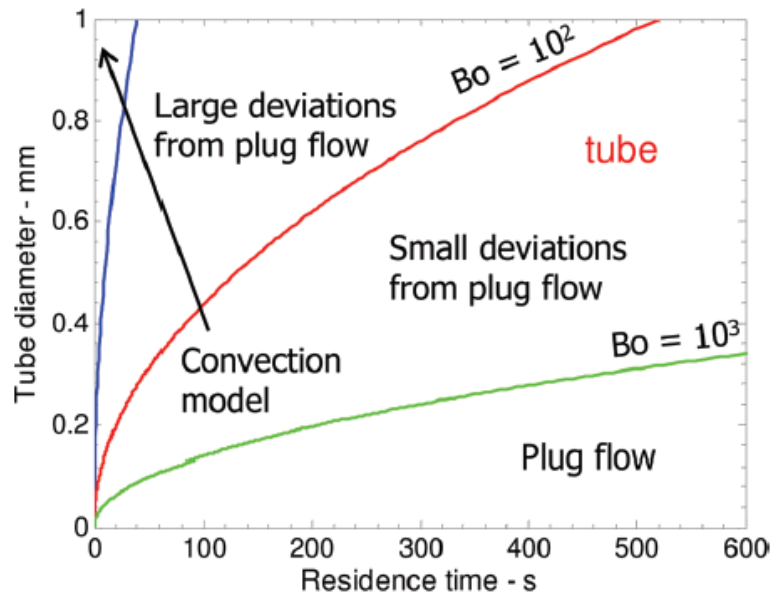


Figure 5.26 Correlation between magnitude of the dispersion effect and tube diameter
adapted from (Nagy, et al., 2012)

The relationship between tube diameter and residence time in the plug flow regime was developed by Nagy et al. as shown in Fig.5.26. Increasing the tube diameter causes increased dispersion effects. If the aim is to achieve same number of tanks for two different size of tube diameter, then residence time must be taken into consideration. This principal was observed in the section 5.3.1, where various mixing performances was measured from different locations of the micro-scale reactor under the same oscillation and flow conditions. Better mixing performance can be achieved by increasing the length of the meso-scale reactor.

5.4.2 Correlation between the Velocity Ratio and Number of Tanks

Fig.5.27 presents measured number of tanks as a function of velocity ratio for micro and meso scale reactors, at a velocity range between 0 and 60. There is a

close match between the regression curves and overall trend for the measured full DoE data points. Three similar distinct regimes can be identified from the results for both scales. First, there is an optimum region in velocity ratio, which gives the highest value for the number of tanks, this optimum velocity region is around 10. Second, the number of tanks increases approximately linearly with the increasing velocity ratio between 0 and 10. Third, the number of tanks decreases with the increasing velocity ratio after 15. Similar results were observed by Phan and Harvey (Phan & Harvey, 2010).

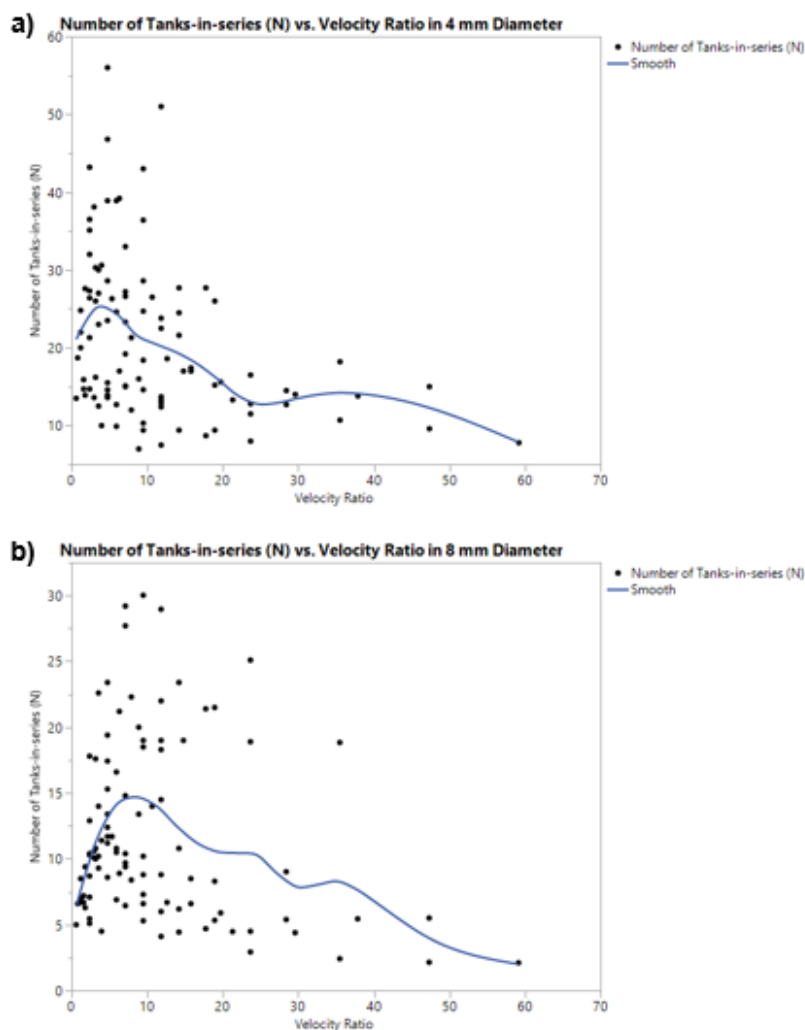


Figure 5.27 Scale-up correlation according to Number of tanks versus velocity ratio

5.4.3 Scale-up Correlation Between Number of Tanks and Reynolds Number

Measured number of tanks as function of Re_n for both scales of reactor systems is shown in Fig.5.28. Four different net flows Re numbers between 5 to 22 with various oscillation conditions were investigated to understand the effect of the net flow on the response. As seen on Fig.5.28, there is no obvious trend between net flow and number of tanks for the both sizes of tube diameters. In the smallest $Re_n = 5.3$, the maximum number of tanks were observed. Then it seems, the number of tanks decreases with increasing net flow. Although, mixing conditions is independent to the net flow in the OBRs, the residence time distribution is an important parameter for the TiS number. With increased flow rate, RTD becomes shorter which means molecules spends shorter time in the same length of the reactor. Consequently, shorter mixing time results lower number of tanks results as shown in Fig.5.28.

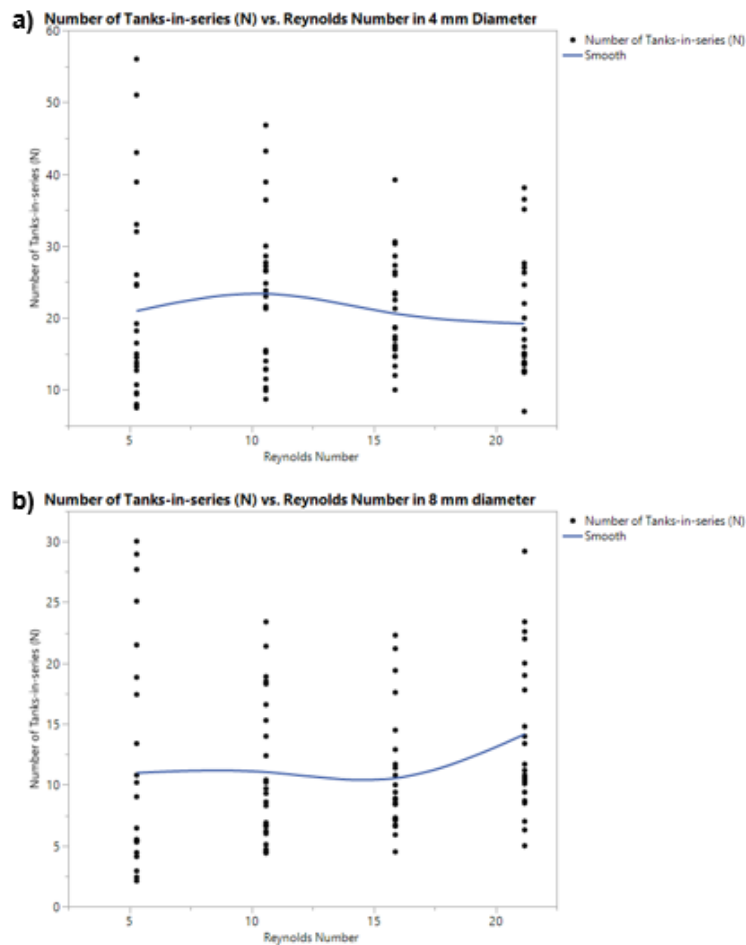


Figure 5.28 Scale-up correlation according to Number of tanks versus Reynolds number

5.4.4 Scale-up Correlation Between Number of Tanks and Oscillatory Reynolds Number

Fig.5.29 presents the measured number of tanks as a function of Re_o for micro (a) and meso (b) scale reactors. There is a noticeable matching trend for both sets of tube diameters (except a few outliers in the meso scale reactor). The optimum number of tanks were observed around $Re_o = 50$ for both sizes. There is a clear trend for the micro reactor after $Re_o = 75$, where increasing oscillatory Reynolds number results poor plug flow conditions. For the meso-scale reactor, there is a trend towards decreasing number of tanks after $Re_o = 75$, but there are a few measured points out of this trend.

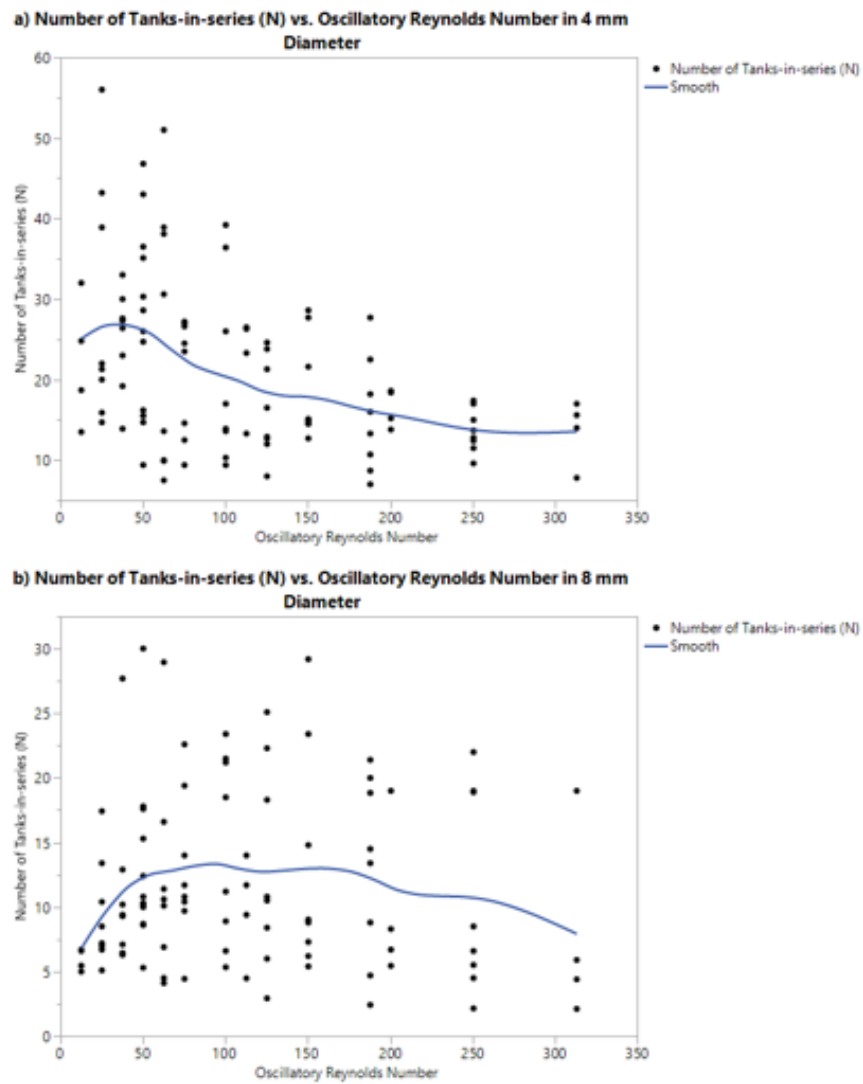


Figure 5.29 Scale-up correlation according to number of tanks and Re_o

5.4.5 Scale-up Correlation Between Number of Tanks and Strouhal Number

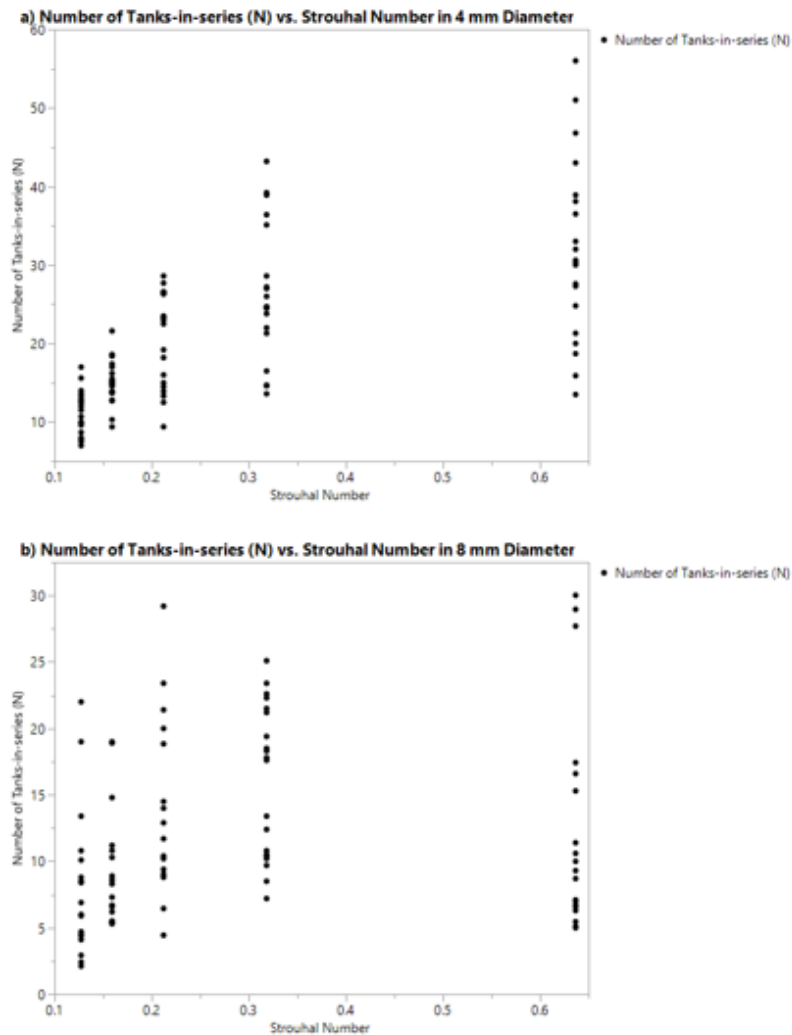


Figure 5.30 Scale-up correlation according to number of tanks and Str number a) micro-scale b) meso-scale

Fig.5.30 shows the measured number of tanks as a function of Str number for micro and meso scale reactors. Five sets of Str numbers were investigated. As seen from the figure above, there is some variation between two the sizes of tube diameters. Three Str numbers (0.159, 0.318 and 0.637) have similar responds for two different scales of the reactor, however, different responses on the different tube diameters were observed for two Str numbers (0.127 and 0.212). Similar results were observed by using Smith for scale-up investigation of 24, 54-

and 150-mm reactors (Smith, 1999). This dissimilarity is due to individual effect of oscillation amplitude and frequency on the plug flow conditions.

5.4.6 Development of Scale-up Rule

RTD studies were performed for the both scales (4 and 8 mm) over a wide range of oscillation and net flow conditions. The RTD results were observed very similar at both scales. Dynamic similarity for the flow patterns was kept same at both scale reactors in this study. There are 5 parameters must be identified based on dynamic similarity law once a system moves to larger or smaller scale. These parameters are as below.

1. Tube diameter (D)
2. Net Flow
3. Oscillatory amplitude (x_0)
4. Oscillatory frequency (f)
5. Residence time (RT)

Calculation of each parameter for a required is explained below.

5.4.6.1 Scale-up Rule for the Tube Diameter

Identifying the tube diameter size is the starting point in the modular OBR scale-up methodology. Production capacity for a specific process is the key driver to identify the tube size in the larger production. The proposed manufacturing platform is suitable to produce high value chemical, pharmaceutical, electronics and smart materials. Most processes in the high value chemicals industry have three processing scales; lab scale process has a few kilograms per hour, pilot scale production capacity is around 50 kg/h and industrial scale production requires 300 kg/h (Khinast & Bresciani, 2017). Max tube diameter is recommended not to exceed 40-50 mm in the worst case, otherwise system will face with mixing and dispersion issues. Larger tube diameter will significantly increase the dispersion effects which means plug flow conditions will start behaving like laminar flow.

Tube diameter is also linked with dimensionless numbers. In order to keep dynamic similarity constant, in the larger scales low oscillation frequency will be required. Achievable oscillation conditions must be considered when increasing the tube diameter for larger scales. Because, it is difficult to achieve very low or high oscillation frequency and amplitude.

5.4.6.2 Scale-up Rule for the Net Flow

Equation (1) is used to identify new net flow in the larger scales. Net flow Reynolds must be kept constant to maintain similar flow conditions for any tube size. There is increasing linear correlation between tube diameter and net flow. If the tube diameter is increased by the scale of two, the net flowrate must be doubled as the tube diameter increases. Increase in the net low rate and tube diameter imply decrease in the flow velocity. Very slow flow velocities could cause sedimentation problems, therefore flow velocity must be considered in the early stage of the scale-up model.

5.4.6.3 Scale-up Rule for the Oscillation Amplitude

Equation (2) is employed to calculate new oscillation amplitude in the larger scales. Str number is kept constant for any size of tube diameter to maintain dynamic similarity. Increasing tube diameter requires increase in the oscillation amplitude with the same scaling ratio. If the tube diameter is increased by the factor of two, amplitude must be doubled.

5.4.6.4 Scale-up Rule for the Oscillation Frequency

Equation (3) is used to identify new oscillation frequency in the larger scales. Oscillatory Reynolds number must be kept constant for any size in order to maintain dynamic similarity. A x factor increase in the tube diameter and oscillation amplitude requires x^2 factor decrease for the oscillation frequency. For example, if the tube diameter is doubled, amplitude must be doubled and that will result four-fold decrease in the system frequency. As that can be seen from the Equation (3), oscillation frequency decreases by the squared of increased tube diameter. If the scaling ratio is selected as very high for the processing scaling,

new oscillation frequency will require very low values that will be difficult to achieve.

5.4.6.5 Scale-up Rule for the Residence Time

Residence time must be increased from lab scale to industry scale. Once tube diameter is increased, the mixing volume of each baffle will be increased as well. Increased RT allows enough time for the process reaction. Otherwise, the rate of mass transfer could be faster than the rate of reaction. As examined in the Chapter 5.1.1, increased reactor length results higher TiS numbers. Additional results from chapter 5.3.1 concludes that the RT must be increased as same scaling factor of tube diameter.

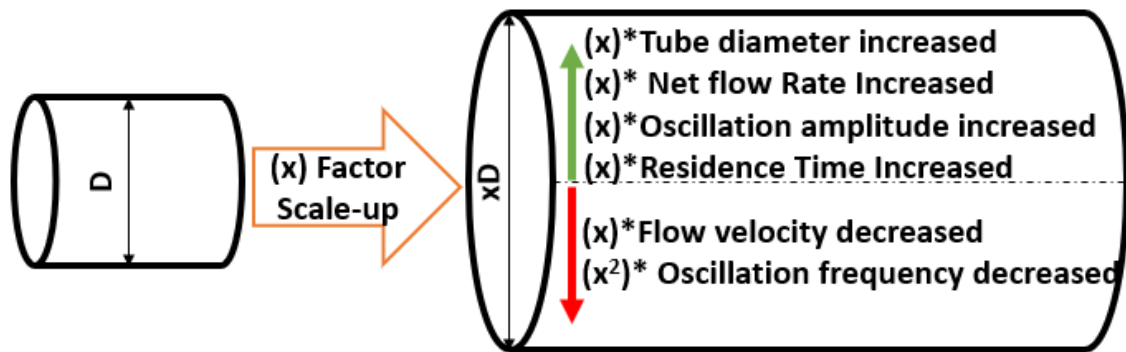


Figure 5.31 Scale-up rule for the process parameters

Fig.5.31 shows the summary of the scale-up rule for the key process parameters.

5.5 Chapter Summary

A full factorial DoE with 100 experiments were conducted for 4 mm and 8 mm tube diameters in order to investigation of plug flow conditions as function of amplitude, frequency and net flow in the modular oscillatory flow reactor. Tanks - in-series model was used to characterise micro and meso scale reactors. The obtained experimental results indicate that both reactors perform plug flow conditions under various oscillatory and net flow conditions.

An increasing linear correlation was observed between reactor length and plug flow performance. Increased reactor length resulted higher TiS numbers.

Amplitude and amplitude x net flow were the most significant influencing factors over plug flow conditions for the micro-scale reactor. Significant effect analysis was slightly different for the meso-scale reactor. The interaction between amplitude and net flow was observed the most significant factor over TiS numbers. Frequency was the second most significant influencer and amplitude became the third most important factor. This difference between micro and meso scale reactors indicates that oscillation amplitude and frequency play independent behaviour in different size tube diameters.

Dimensionless numbers (Reynolds number, oscillatory Reynolds number, Str number and velocity ratio) were used to develop a scale-up methodology. Experimental data and correlation between two scale show that the plug flow conditions in the modular oscillatory baffled reactor is not a function of tube diameter. Similar mixing and plug flow conditions can be achieved using scale-up methodology presented in this chapter.

6 SYNTHESIS OF SPIN CROSSOVER MATERIALS IN FLOW

“There is plenty of room at the bottom.”

Richard Feynman

6.1 Introduction of Spin Crossover Materials

Spin-Crossover (SCO) materials are a special type of nanomaterials. SCO complexes are characterised by a change in electronic configuration of a transition-metal centre as a response to external stimuli such as heat, light, pressure, or changes in magnetic field (Krober, et al., 1994). The combination of the environment and their important physical and chemical properties, enables the use of them as smart sensors for a variety of applications, including data storage, biosensor, temperature and pressure detectors (Letard, et al., 2004). Some animals in the nature such as cuttlefish and chameleons change their appearance depending on their surrounding conditions in order to camouflage (Yoshida & Lahann, 2008). Inspired from the nature, SCO compounds can be developed and synthesized in different nanoscale sizes to produce smart nanomaterials.

A particular SCO component, Fe(II) ion, has a unique physical property. It can switch its electron configurations from low-spin (LS) to high-spin (HS) according to external conditions. Their colour is pink at room temperature, which indicates the HS orientation. When the particles are switched to HS orientation, the colour changes from pink to white at temperatures over 40C⁰ as shown in Fig.6.1. These unique features allow the use of SCO particles for various smart applications like sensors, display or switching devices.

SCO experiments were conducted with the collaboration of Metastable Materials Group at University of Bath. Chemical composition of batch process was introduced by Metastable Materials Group and then it was transferred to OFM process in this study. All experiments were conducted in the Cranfield University

using modular OBR. Particle size and shape measurements were performed at Chemistry department at University of Bath.

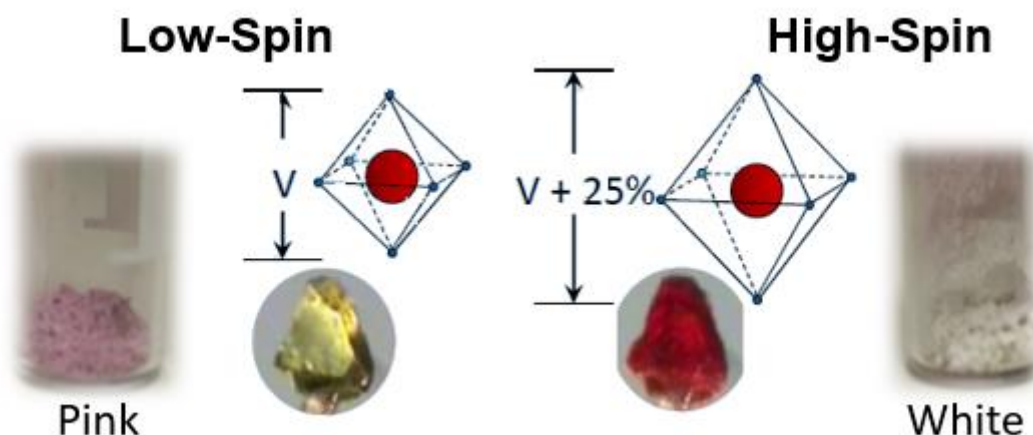


Figure 6.1 Low-Spin, High-Spin SCO Structure

6.2 Preparation of Precursors

Two chemical reagents; Iron II Tetrafluoroborate (BF_4) and 1,2,4 Triazole were purchased from Sigma Aldrich in powder state. Each solution was prepared in various concentrations.

6.2.1 Iron Precursor

BF_4 powder was weighed using high accuracy electronic lab scale balance. The weighed powder was dissolved in 100 mL deionized water. The solution was mixed using magnetic stirrer at 400 rpm around 10 min. When the BF_4 powder was completely dissolved, the mixing was stopped. The solution was taken and connected to the syringe pump to send it into the reactor.

6.2.2 Triazole Precursor

The same solution preparation procedure was used for the triazole precursor. First, the powder form of the triazole was measured using precise lab scale electronic balance. Powder was dissolved in deionized water and mixed by using a magnetic stirrer at 400 rpm for 10 min. Completely dissolved solution was taken

and connected to syringe pump. Mixing concentration was controlled with pump flow rate.

6.3 Characterisation of Spin Crossover Materials

The size and the shape of the nanoparticles were studied by scanning electron microscope (SEM – Supra). Average Particle Size (APS) of the SCO particle were measured using dynamic Light Scattering (DLS) technique with Malvern Zetasizer Nano-S. We obtained a range of nanoparticle shapes and sizes according to different processing conditions and mixing concentrations.

6.4 Experimental Procedure

In traditional chemistry, bath-wise mixing is a traditionally used method to synthesize nanoparticles. Due to inherent issues of batch-type mixing, significant improvement in nanomanufacturing is still required in order to deliver nanomaterials to the mainstream marketplace. Scale-up, cost, sustainability, energy efficiency, process control, repeatability, continuous manufacturing and predictive modelling are problems in nanofabrication. All those issues need to be solved in order to produce low cost nanoparticles in every scale (Roco, et al., 2010). Therefore, we developed a novel continuous oscillatory baffled reactor (COBR) to answer the problems in nanoparticle manufacturing as shown in Fig.6.2. All experiments were performed with laboratory scaled built automated continuous nanoparticle synthesis platform. The continuous synthesis platform consists of solvent feeding section; including TriContinent C-Series precision OEM syringe pumps and solution vessels, scotch-yoke oscillation mechanism to provide oscillatory flow mixing, oscillatory baffled flow reactor, filtration mechanism with 40 nm filter paper and vacuum pump, and LabVIEW based process control software.

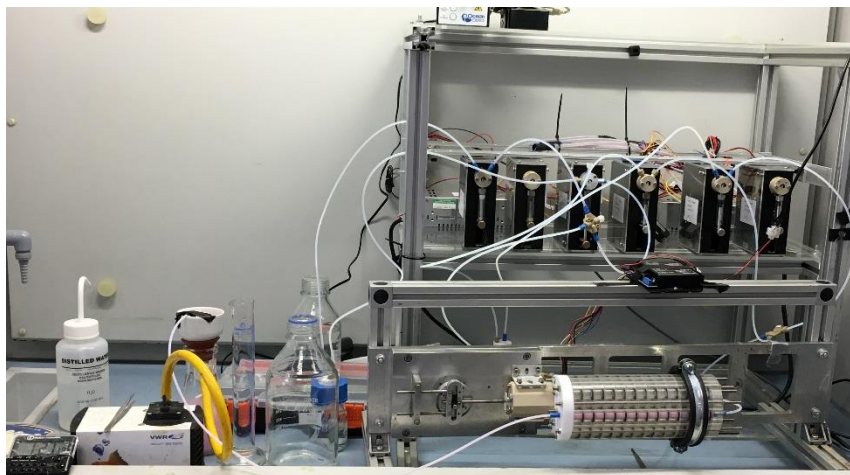


Figure 6.2 Experimental Setup for the SCO Nanomaterial Synthesis

The reactor was filled with deionized water before the reaction to use it as carrier fluid and the system was completely air-free. After each experiment, the reactor was purged with HCl solution to prevent contamination.

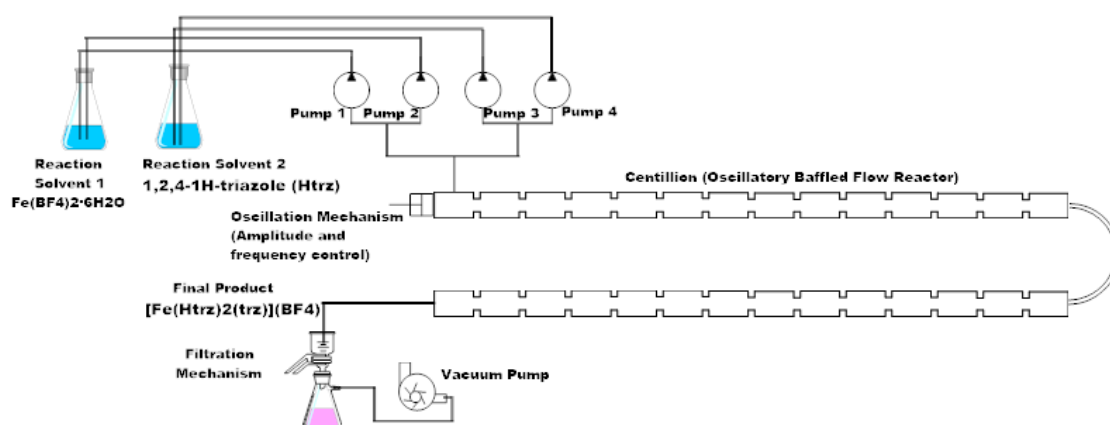


Figure 6.3 Schematic diagram of the continuous SCO nanoparticle synthesis platform

Continuous SCO crystallization experiments were performed in an 8 mm internal diameter modular oscillatory flow reactor. The reactor is formed up of number of cylindrical slices; each slice with seven reaction channels, assembly holes and heating/cooling hole. Each flow channel consists of 8 mm baffle diameter, 12 mm in length, and 4 mm baffle orifice diameter, 2 mm thick. The setup consisted of 13 middle discs, one front and one end disc. This setup provides 182 mm flow

pattern for each channel. Channels are connected by using u-shape chromatographic tubes to increase the flow pattern if necessary. Throughout all experiments, two 364 mm length and four 728 mm length flow channels were employed. Net flow rate in the system was controlled by using Tri-continental Syringe Pumps. Two syringe pumps, which work alternately, were used for each solution in order to provide continuous fluid flow. One pumps the solution, while the other one fills the syringe with the solution. Oscillation was controlled by piston-driven scotch yoke mechanism, which provides smooth sinusoidal oscillatory motion. The process fluid was oscillated at various oscillatory flow mixing conditions by adjusting the amplitude (2 – 6 mm), frequency (1.25 – 6 Hz) and flow rate (0.6 – 7.8 mL/min). The frequency was controlled by changing the speed of the piston movement, and the amplitude (centre-to-peak) by changing the stroke of the piston. Nanoparticles were collected through a tube connected to an outlet piece and separated immediately using Air Cadet vacuum pump with 0.45 μm filter paper. Nanoparticles were collected for each residence time (RT) and filter papers were changed after each residence time in order to calculate the yield.

6.5 Experiments and Results

3 sets of experiments were conducted. First, some trial experiments were performed to understand the potential of SCO production in the OBR environment as it was done for the first time in this study. After initial experiments proved that the synthesis of the SCO manufacturing is possible with OBR, then a systematic experimental design was conducted for the investigation of the product, and process parameters on average particle size and shape control. The final set of experiments was to measure the consistency of the system. One experiment (DoE_14) was repeated simultaneously for 4 hours non-stop processing.

6.5.1 Screening Experiments – Transferring from Batch to Flow

In current chemistry, the batch type mixing is the traditional method to synthesize SCO compounds. In the initial experiments, trial flow results were compared with batch type results. The aim was to collect initial data to understand its behaviour

in the flow environment and develop a systematic DoE setup for further investigation. The batch-wise synthetic route followed the reported previous study (Krober, et al., 1994). Two solutions of triazole and iron (II) tetrafluoroborate hexahydrate of 8.32 g and 8.67 g respectively in 100 ml DI water were mixed at 350 rpm using magnetic stirrer. As shown in Fig.6.4, the complex started to change colour to cloudy pink in 14 min mixing. After successful completion of batch synthesis, SCO synthesis was performed for the first time in the OBR.

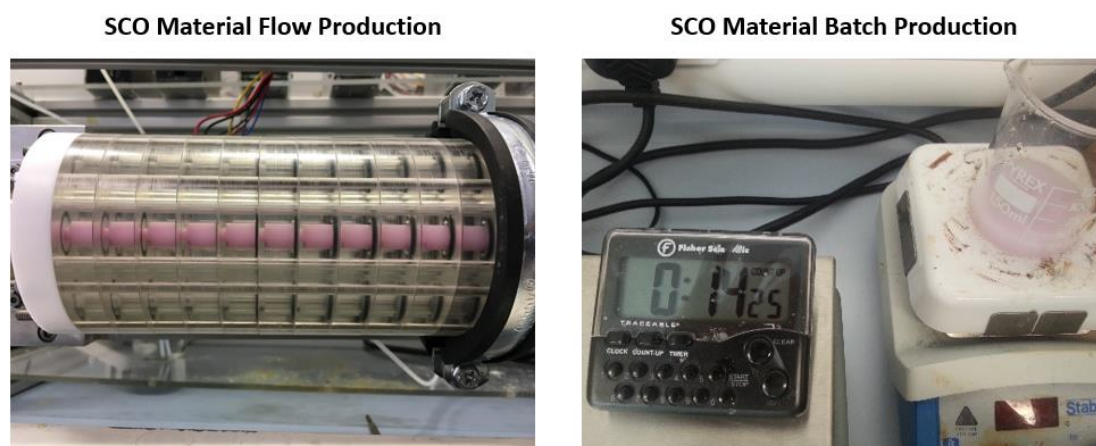


Figure 6.4 SCO compound synthesis in flow reactor and batch

Experimental setup of the modular OBR flow platform is shown in Fig.6.5. The continuous platform consists of modular OBR reactor and 5 syringe pumps. Two synchronised pumps were used for each solution. One of the synchronised pumps refilled the solution, while the other one pumped the solution into the reactor, so that there was continuous pumping at all times. Perspex material was used to build the reactor. With see-through design, the colour change can easily be observed to detect the reaction time. The fifth pump was used to generate oscillation. The piston of the fifth syringe pump can behave as an oscillatory piston instead of a pump. Speed and stroke of the syringe pump piston can be controlled with LabVIEW software in order to achieve required oscillation conditions. The same software was used to control flow rate of solutions. Mixing concentration was %50 for each solution, therefore same pump speeds were used for both solutions to achieve equal mixing volumes.

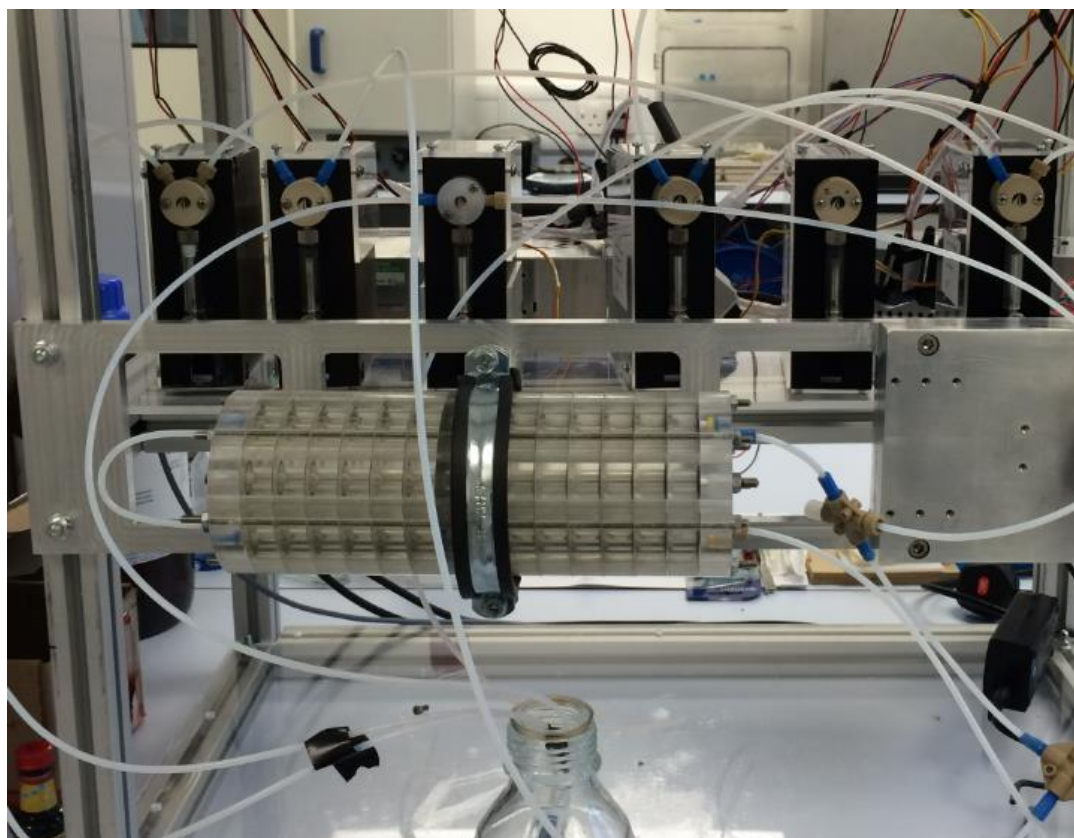


Figure 6.5 Experimental setup for screening of SCO synthesis in modular OBR platform

Parameters of screening experiments are shown in Table.6.1. There are three process parameters; oscillation frequency, amplitude and net flow, and two product variables as concentration of $\text{Fe}(\text{BF}_4)_2 \cdot 6\text{H}_2\text{O}$ (CI), and concentration of triazole (CT).

Table 6.1 Screening experiments and process parameters for investigation of SCO compound synthesis in flow conditions

Screening Experiments	Freq (Hz)	Amp (mm)	Flow Rate (mL/min)	CI (g/100 mL)	CT (g/100 mL)	Number of baffled-flow channels	Observed Reaction Time (min)
S1	2.01	3	2.3	5.25	8.39	2	39
S2	1.58	3.5	1.5	8.3	8.67	2	45
S3	1	2.5	9	5.25	8.67	2	20
S4	2	4	4.5	8.3	8.67	2	30
S5	2	4	4.5	8.3	8.67	4	25
S6	1	2.5	2.5	8.3	8.67	2	36

Full reactor has 7 flow channels, which is the equivalent of a 61.5 mL reactor volume. In the initial experiments only two and four channels were tested. The main reason to shorten reactor volume was to use fewer chemical solutions to save cost. In other words, large amount of chemical solutions would be needed if the full reactor volume was used. As mentioned in Chapter 3, one of the great advantages of the modular reactor design is that the length and volume can be easily configured according to the required application specs. The reactor volume was 17.6 mL and 35.2 mL for 2 and 4 channels use respectively.

Dimensionless numbers used in the initial experiments are shown in Tab.6.2. Various velocity ratios ranging between 5 and 70 were used to investigate the effect of dimensionless numbers for reaction time and particle size.

Table 6.2 Screening experiments and dimensionless numbers

Screening Experiments	Freq (Hz)	Amp (mm)	Flow Rate (mL/min)	Str Number	Re _n Number	Re _o Number	Velocity Ratio	APS (nm)
S1	2.01	3	2.3	0.212	6.08	302.25	49.68	543
S2	1.58	3.5	1.5	0.181	3.96	277	69.86	824
S3	1	2.5	9	0.254	23.8	125.31	5.26	945
S4	2	4	4.5	0.159	11.9	400	33.7	422
S5	2	4	4.5	0.159	11.9	400	33.7	335
S6	1	2.5	2.5	0.254	6.61	125.31	18.94	498

From OBR processing, crystal sizes from 400 nm to 1 μ m with spherical and rod crystal shapes were obtained. The particle sizes were smaller than batch type crystallisation with similar shape. More detailed information for the batch processing results can be found in P. B. Flandrin's PhD research (Flandrin, 2019). The Dynamic Light Scattering (DLS) for particle size measurement of the screening experiments are shown in Tab.6.2. The particle sizes range between 300 nm and 1000 nm. Smallest particle size was observed at velocity ratios of 18 and 33 with high chemical concentrations. As seen in Tab.6.1 and Tab.2.2, processing parameters are important to achieve different reaction times and particle sizes. Same process parameters and chemical concentrations were used for S4 and S5 experiments, where the only difference is the number of flow

channels. 2 flow channels were used in S4 and 4 flow channels were used in S5, which means the products stayed in the reactor two times longer in the S5 experiments, which reduces the colour change (from colourless to cloudy) time from 30 min to 25 min.

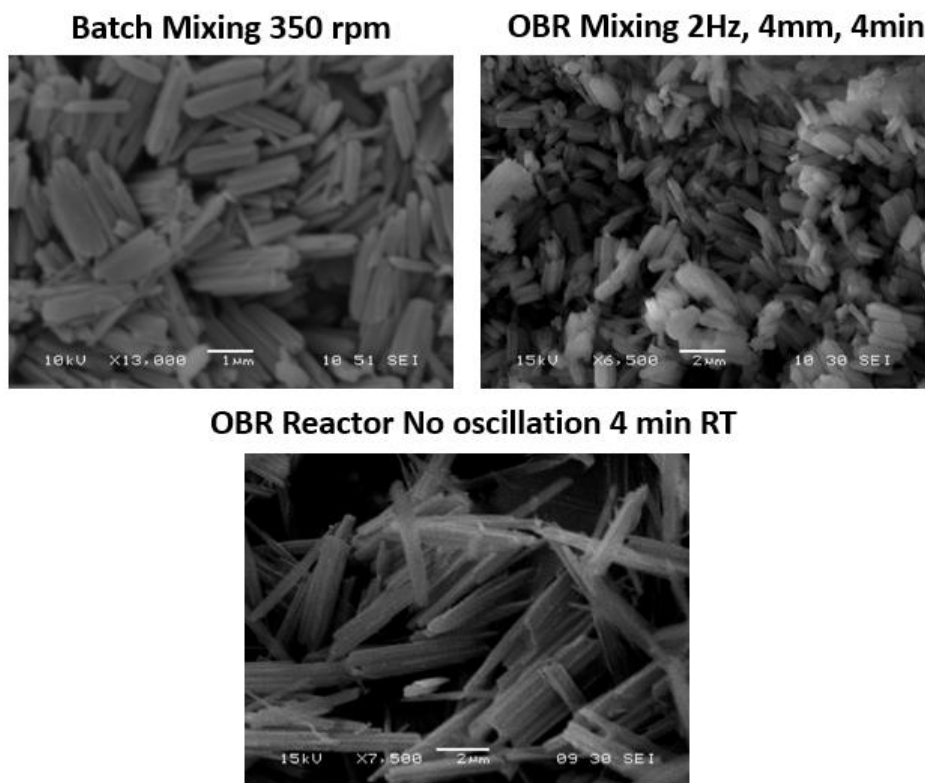


Figure 6.6 SEM results for batch, OBR and OBR without oscillation experiments

Three different processing methods as batch, OBR and OBR without oscillation were used for comparison. Scanning electron microscopy (SEM) was used to analyse the particle shape and size in each experiment as shown in Fig.6.6. As shown in the Fig.6.6, OBR particles are more uniform and smaller when compared to batch type SCO material synthesis. Without oscillation in the modular OBR reactor, rod shaped particles and clusters were observed.

It was difficult to come to a detailed conclusion based on limited screening experiments for the SCO production investigation using modular OBR reactor. However, these experiments clearly demonstrate that, the SCO synthesis is possible with a modular flow reactor. In the next section, a comprehensive Design

of Experiment (DoE) investigation will be presented for detailed understanding of the effect of the oscillatory flow parameters for the particle size and shapes.

6.5.2 DoE for Continuous SCO Nanomaterial Manufacturing

Nanoparticles are very complicated structures including size, shape, composition, magnetic and electrical properties. This complexity cannot be efficiently solved only with empirical studies. Consequently, alternative methods such as multi-scale modelling, artificial intelligence and algorithm optimization are required. Fundamental understanding of chemical materials and accurate predictive models are critically important to manufacture desired particle size and properties of nanomaterials. Towards this target, improvement in only the nanofabrication techniques is not enough. In addition, reliable and repeatable experimental design capabilities are critically important to move from the era of “best-guess” nonmanufacturing to predictive modelling of engineered nanomaterials. Design of Experiments (DOE) was performed in order to minimise the number of experiments, to simultaneously identify all factors that influences the outcome of the reaction, and to develop an accurate predictive model after a set of experiments. Particle size on SCO nanomaterial has been investigated as a function of five process factors. The names of factors, with their variation levels are shown in Tab 6.3. The factors and their levels were selected by studying the previous research on SCO synthesis and considering the range of process limitations.

Table 6.3 Product and Process Variation Levels

Factor	Name	Levels	
		Low	High
X ₁	Frequency	1	4
X ₂	Amplitude	2	4
X ₃	Residence Time	8	20
X ₄	Iron-TFB Concentration	3.374	8.32
X ₅	1,2,4 Triazole Concentration	3.374	8.32

Response surface method was used to investigate the effect of process and chemical variables over the SCO nanoparticle size and shape. Minitab statistical

analysis software was used to develop DoE. Minitab provides central composite and Box-Behnken designs. Central composite designs can fit full quadratic model and it is the most commonly used response for surface designed experiments (Abbott, 2015; Paulo & Santos, 2017). Central composite model was used to develop experimental matrix. The design matrix obtained by using the central composite method with experimental particle size and shape results are shown in Tab.6.4.

For the five variables with low and high levels, there are 32 experiment points as shown in Tab.6.4. Factor levels define the proportions of the “cube” around the whole experiment design. Design points could be inside the cube, on the cube or outside the cube. In central composite design, low and high factor levels are usually not the minimum and maximum values in the design matrix. They are low and high settings for the “cube” portion of the design. The axial points are generally outside the cube. As seen on the design matrix, some values for each factor are different than high or low factor levels.

Table 6.4 Design of Experiments with Response Surface Methodology based on low and high five input variables

Exp No	Frequency (Hz)	Amplitude (mm)	Residence Time (min)	Iron-TFB Concentration (g/100 mL)	1,2,4 Triazole Concentration (g/100 mL)	Average Particle Size (nm)
1	2.25	3	14	5.85	5.85	161.8
2	2.25	5	14	5.85	5.85	496.7
3	2.25	2	14	5.85	5.85	182.7
4	2.25	3	26	5.85	5.85	429
5	2.25	3	14	5.85	5.85	179
6	5.75	3	14	5.85	5.85	166
7	1.25	3	14	5.85	5.85	95.8
8	2.25	3	14	5.85	5.85	165.5
9	2.25	3	14	5.85	5.85	108.2
10	2.25	3	14	5.85	5.85	140.2
11	2.25	3	14	5.85	5.85	121.5
12	2.25	3	2	5.85	5.85	823.9
13	2.25	3	14	5.85	0.90	153.9
14	2.25	3	14	5.85	10.79	236.5
15	2.25	3	14	0.90	5.85	106.2
16	2.25	3	14	10.79	5.85	1211.4
17	4	2	20	8.32	3.37	743.3
18	4	4	8	8.32	3.37	859.5
19	0.5	4	20	8.32	3.37	1120.1
20	0.5	2	8	8.32	3.37	189.8
21	0.5	4	8	8.32	8.32	264.6
22	0.5	2	20	8.32	8.32	1611
23	4	4	20	8.32	8.32	561.8
24	4	2	8	8.32	8.32	574.5
25	4	2	20	3.37	8.32	414.2
26	4	4	8	3.37	8.32	1029.4
27	0.5	4	20	3.37	8.32	787.7
28	0.5	2	8	3.37	8.32	1273.4
29	0.5	2	20	3.37	3.37	575.1
30	0.5	4	8	3.37	3.37	441.8
31	4	4	20	3.37	3.37	858.6
32	4	2	8	3.37	3.37	183.7

Dimensionless numbers used in the design matrix are shown in Tab.6.5. Wide range of dimensionless numbers ($Re_n = 1.6 - 22.17$, $Re_o = 50 - 863$, $St = 0.127 - 0.32$ and $\psi = 8.5 - 362$) were investigated to minimise the cost of experiments by using min experimental number and lowest possible amount of chemicals. Due

to longer RT required for some experiments, we had to use large velocity ratio values. All experiments were performed at room temperature.

Table 6.5 Dimensionless numbers and DoE Responses

Exp No	Strouhal Number	Reynolds Number	Oscillatory Reynolds Number	Velocity Ratio	Average Particle Size (nm)	Particle Shape
1	0.212	3.17	337.7	106.5	161.8	Spherical-shaped
2	0.127	3.17	562.83	177.5	496.7	Column-shaped
3	0.318	3.17	225.13	71.0	182.7	Spherical-shaped
4	0.212	1.69	337.7	199.8	429	Column-shaped
5	0.212	3.17	333.7	105.3	179	Column-shaped
6	0.212	3.17	863	272.2	166	Column-shaped
7	0.212	3.17	187.61	59.2	95.8	Column-shaped
8	0.212	3.17	187.61	59.2	165.5	Spherical-shaped
9	0.212	3.17	187.61	59.2	108.2	Spherical-shaped
10	0.212	3.17	187.61	59.2	140.2	Column-shaped
11	0.212	3.17	187.61	59.2	121.5	Rod-shaped
12	0.212	22.17	187.61	8.5	823.9	Rod-shaped
13	0.212	3.17	187.61	59.2	153.9	Crystal-shaped
14	0.212	3.17	187.61	59.2	236.5	Spherical-shaped
15	0.212	3.17	187.61	59.2	106.2	Needle-shaped
16	0.212	3.17	187.61	59.2	1211.4	Rod-shaped
17	0.318	2.21	400	181.0	743.3	Rod-shaped
18	0.159	5.54	800	144.4	859.5	Rod-shaped
19	0.159	2.21	100	45.2	1120.1	Needle-shaped
20	0.318	5.54	50.03	9.0	189.8	Needle-shaped
21	0.159	5.54	100	18.1	264.6	Column-shaped
22	0.318	2.21	50.03	22.6	1611	Column-shaped
23	0.159	2.21	800	362.0	561.8	Column-shaped
24	0.318	5.54	400	72.2	574.5	Column-shaped
25	0.318	5.54	400	72.2	414.2	Spherical-shape
26	0.159	5.54	800	144.4	1029.4	Rod-shaped
27	0.159	2.21	100	45.2	787.7	Column-shaped
28	0.318	5.54	50.03	9.0	1273.4	Column-shaped
29	0.318	2.21	50	22.6	575.1	Rod-shaped
30	0.159	5.54	100	18.1	441.8	Needle-shaped
31	0.159	2.21	800	362.0	858.6	Rod-shaped
32	0.318	5.54	400	72.2	183.7	Needle-shaped

From the overview of all the experiments, various particle morphologies were observed as shown in Fig.6.7. Four different experiments as DoE_4 column-shaped particles, DoE_12 rod-shaped particles, DoE_14 spherical-shaped

particles and DoE_20 needle-shaped particles are shown in Fig.6.7. The most common morphologies were spherical and column shaped, also known as short-rod, similar to the literature (Moulet, et al., 2016). Needle-shaped, rod-shaped and crystal-shaped SCO particles were also observed with OBR synthesis method. Particle sizes, width and length, can be measured with SEM images. In the DoE experiments, the obtained particle width lies in the range of 50-300 nm and the length is between 100 nm to more than 1.5 μm . SEM images and DLS results for all the DoE experiments can be found in Appendix.B.

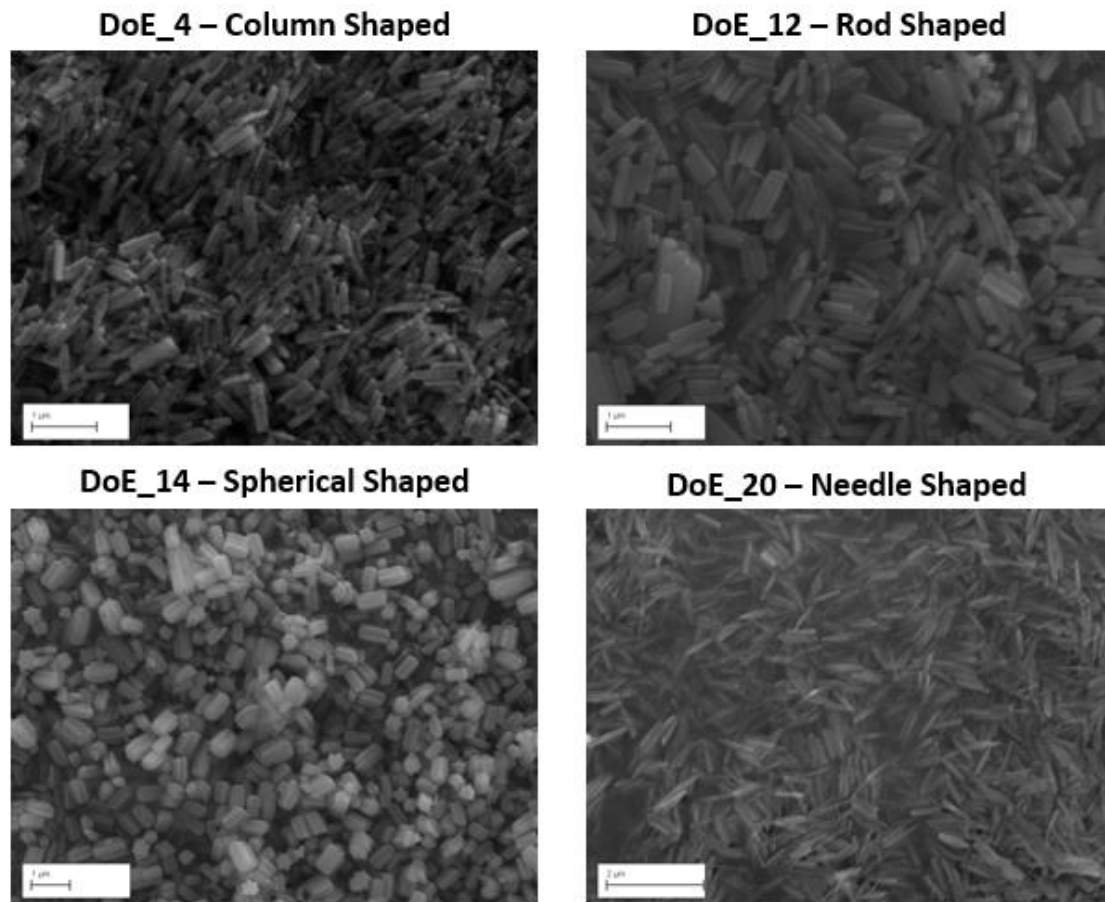


Figure 6.7 Various SCO component particle shapes obtained from DoE results

6.5.3 DoE Outcomes – Response Surface Analysis and Results

The effect of five different input variables on SCO component particle size and morphonology were investigated by performing 32 systematic experiments. Responses of average particle size was measured using DLS and particle shapes

were identified by using SEM images. Average particle size and particle shapes for all experiments are shown in Table.6.5. The results show the importance of the systematic investigation. The wide range of particle sizes and shapes can be obtained depends on combination of input variables.

Pareto chart shows the absolute values of the standardized effects from the most significant effect to the least significant effect and it is very useful to visually identify the most significant effects and compare that to the relative magnitude of the various effects. The reference line (red-dashed line) indicates the significance level, the bars which cross the reference line mean significant effect.

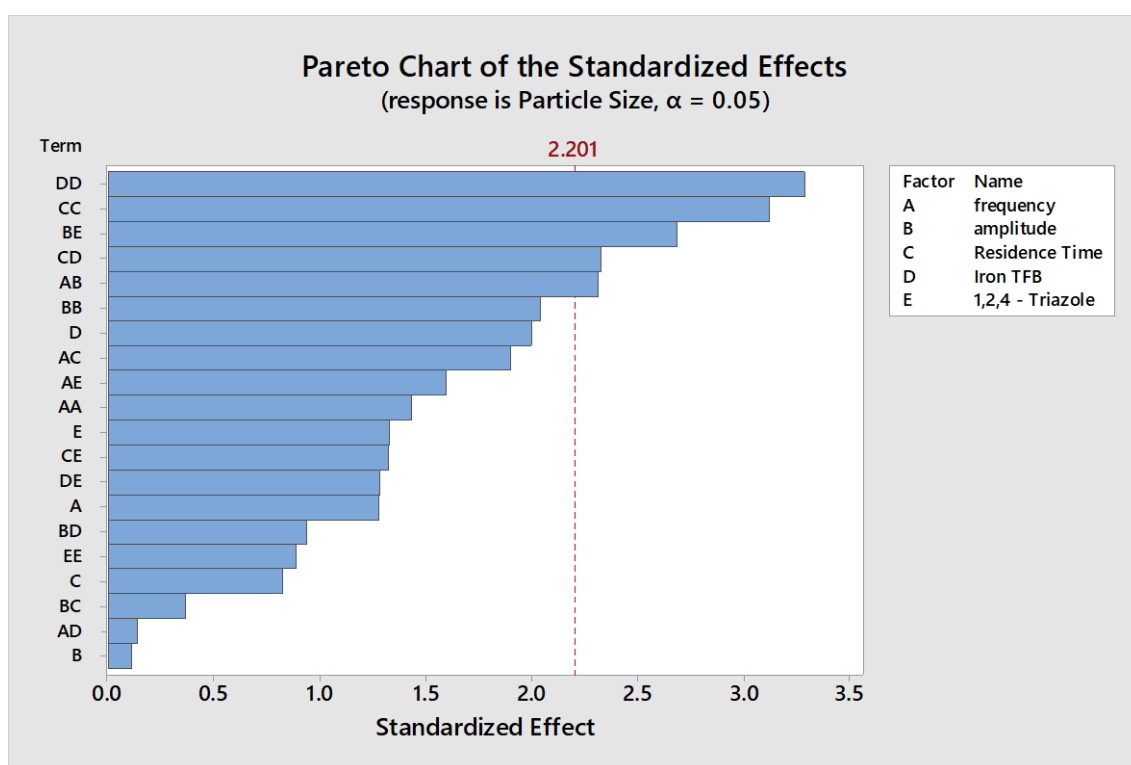


Figure 6.8 The most significant effects for SCO particle size and shape control in the OBR

As shown in Fig.6.8, there are five significant factors for the particle size control. The most significant one is the second order of the Iron TFB concentration; the second most important one is the second order of the residence time and the third most important factor is the interaction between amplitude and triazole concentration. The interaction of the residence time and iron concentration (CD)

and interaction between frequency and amplitude (AB) have almost similar effect just above the significance level.

Table 6.6 summarises how well the model fits in response data. The model has 85.6 % accuracy ($R^2 = 85.64\%$). If R^2 is closer to 100, the accuracy of the fitted model is much better.

Table 6.6 DoE Analysis - Model Summary

S	R-sq	R-sq(adj)	R-sq(pred)
262.131	85.64%	59.53%	0.00%

Analysis of variance table is shown in Table.6.7. This table can be used to read the statistical significance of each factor in the first order, second order and two-way interaction levels. The significance level 0.05 for the p-value was used to determine the factor significance.

DF is total degree of freedom, which defines the amount of information in the data. Adj SS is the adjusted sum of squares that calculates the variation of the different factors of the model. Adj MS is the adjusted mean squares, which measures how much the variation of a term affects the response. F-value presents whether any term in the model is associated with the response by testing the ratio of two variances. The regression model used in the Minitab uses the F-value and Adj SS to calculate the p-values and R^2 statistic. There are some important findings in the analysis of variance table. The p-value for the lack of fit is 0.000, which is less than significance level 0.05. It shows that the model does not correctly specify the relationship between input variables and average particle size which might be due to limited experimental data points.

There are three levels of regression analysis obtained in the data analysis, there are linear, squared and two-way interactions. In the linear regression, concentration of Iron is the most significant input factor as p-value is 0.071, which is the nearest number to the significance level of 0.05. P-values of the frequency, amplitude, residence time and concentration of triazole are higher than significance level of 0.05, which means they don't have significant affect for the

APS. However, frequency (p-value = 0.227) and concentration of triazole (p-value=0.210) are the second most important factors after the concentration of the triazole even they have higher p-values than the significance level.

Table 6.7 Analysis of Variance

Source	DF	Adj SS	Adj MS	F-Value	P-Value
Model	20	4507936	225397	3.28	0.024
Linear	5	557566	111513	1.62	0.234
frequency	1	112726	112726	1.64	0.227
amplitude	1	918	918	0.01	0.910
Residence Time	1	47286	47286	0.69	0.424
Iron TFB	1	275440	275440	4.01	0.071
1,2,4 - Triazole	1	121823	121823	1.77	0.210
Square	5	1967466	393493	5.73	0.008
frequency*frequency	1	141203	141203	2.05	0.180
amplitude*amplitude	1	287676	287676	4.19	0.065
Residence Time*Residence Time	1	669304	669304	9.74	0.010
Iron TFB*Iron TFB	1	743114	743114	10.81	0.007
1,2,4 - Triazole*1,2,4 - Triazole	1	54050	54050	0.79	0.394
2-Way Interaction	10	1966109	196611	2.86	0.050
frequency*amplitude	1	368661	368661	5.37	0.041
frequency*Residence Time	1	248378	248378	3.61	0.084
frequency*Iron TFB	1	1327	1327	0.02	0.892
frequency*1,2,4 - Triazole	1	175373	175373	2.55	0.138
amplitude*Residence Time	1	9472	9472	0.14	0.717
amplitude*Iron TFB	1	60479	60479	0.88	0.368
amplitude*1,2,4 - Triazole	1	496215	496215	7.22	0.021
Residence Time*Iron TFB	1	372253	372253	5.42	0.040
Residence Time*1,2,4 - Triazole	1	120669	120669	1.76	0.212
Iron TFB*1,2,4 - Triazole	1	113283	113283	1.65	0.226
Error	11	755836	68712		
Lack-of-Fit	6	752055	125342	165.73	0.000
Pure Error	5	3782	756		
Total	31	5263772			

In the second order regression level, square of the Iron concentration is the most significant influencing factor as p-value is 0.007. Square of the Residence Time is the second most influencing factor with p-value of 0.010. Second order of all other factors are higher than significance level and they don't have a significant effect to change average particle size of the SCO components.

Two-way interaction analysis shows that (amplitude)x(concentration of triazole) is the most significant factor as p-value is 0.021, followed by (residence time(x(concentration of iron) as p-value = 0.040 and)(frequency)x(amplitude) as p-value=0.041 which are less than significance level. All remaining two-way interaction significance level are higher than significance level of 0.05.

The relationship between process parameters (frequency, amplitude and residence time) and average particle size is shown in Fig.6.9. There are three interaction graphs as frequency x amplitude, frequency x residence time and amplitude x residence time. The effect of three different amplitudes at each frequency can be analysed in the top white box in fig.6.9. The interaction between amplitude and frequency is important as they define the oscillatory Reynolds number and mixing in the system. As that can be seen on the results, 2 mm amplitude (blue solid line in the frequency*amplitude graph) with lowest frequency creates the largest particles due to soft mixing regime. Increasing frequency in the 2 mm amplitude resulted smaller APS due to increased mixing intensity. 3- and 4-mm amplitudes have similar effect in the lowest frequency, and they resulted smaller APSs than 2 mm amplitude. APSs decreased with increased frequency up to 3 Hz, after 3Hz APS started increasing with increased frequency at 3 mm amplitude. 4 mm (green line) resulted larger APSs with increased frequency.

The interaction between frequency and residence time is shown in the bottom-left graph in Fig.6.9. the interactions between frequency*RT and amplitude*RT changes the velocity ratio in the system which was identified an important dimensionless number for the plug flow control. Shortest residence time as 8 min (blue solid line) resulted smaller particles in the low frequency, APS increased

with increased frequency in the 8 min RT. The effect of the 14 min RT is less than 8- and 20-min RTs. Smallest APSs were observed with 14 min RT and 3 Hz frequency. Particle sizes were under 300 nm with all combinations of 14 min RT and frequencies used in the experiments. Longer RT and lower frequencies (0 – 2 Hz) resulted larger APSs. 20 min RT and frequencies over 3 Hz gave smaller APSs.

The final interaction analysis was between amplitude*RT as shown bottom right graph in Fig.6.9. A similar trend was observed for all combinations. Lowest amplitude as 2 mm resulted medium size particles (200 – 400 nm) with all RTs, but smallest APSs were with 14 min RT. The smallest particles were observed with 3 mm amplitude in all RTs. After 3 mm increased amplitude resulted larger particles in the all RT regimes.

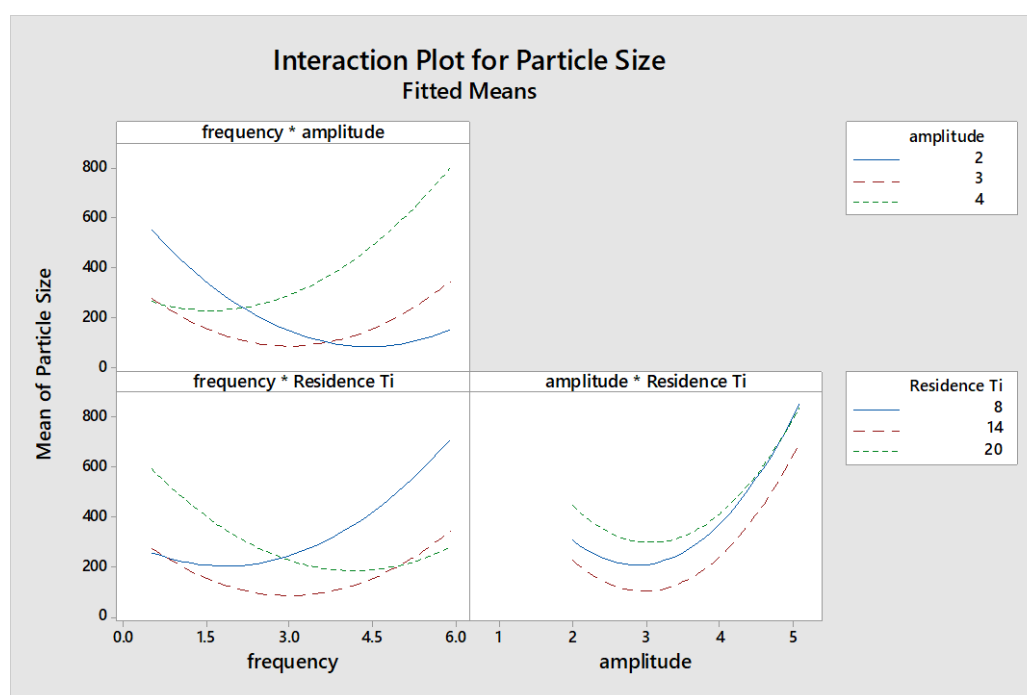


Figure 6.9 Interaction plots of the SCO process parameters for APS

Main effect plots of the process parameters are shown in Fig.6.10. Main effect plots can be used to understand the effect of each factor based on its all levels but without any interaction with other factors.

5 levels of the frequency between 0.5 Hz and 5.75 Hz were investigated in this study. Frequency was the most significant factor as p-value 0.227 lies within three process parameters. The lowest frequency 0.5 Hz resulted in the largest average particle sizes (over 500 nm). From 0.5 Hz to 2.5 Hz, the trend is negative; increased frequency resulted smaller particles. From 2.5 Hz to 5.5 Hz, the trend is positive; increased frequency resulted larger particle sizes.

The optimum amplitude was observed as 3 mm to produce the smallest particle sizes. Increased amplitude from 2 mm to 3 mm resulted decreased in particle sizes (from 700 nm to 100 nm). The trend changed after 3 mm amplitude, increasing amplitude resulted larger particles as shown in Fig.6.10.

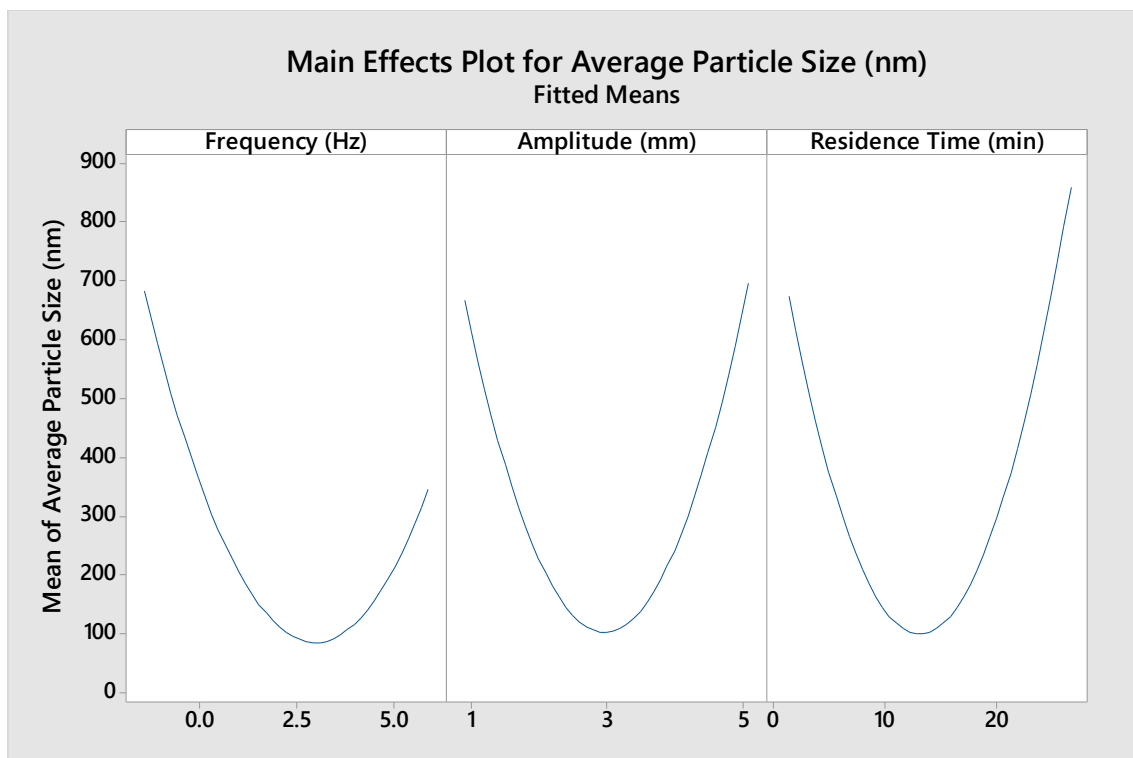


Figure 6.10 Main effect plots of frequency, amplitude and residence time on the APS

Residence time has similar affect as amplitude. Medium size RT as 14 min provided the smallest particles. Increased RT time from 2 min to 14 min resulted decrease in the APS. After 14 min, increased RT gave larger particles as shown in Fig.6.10.

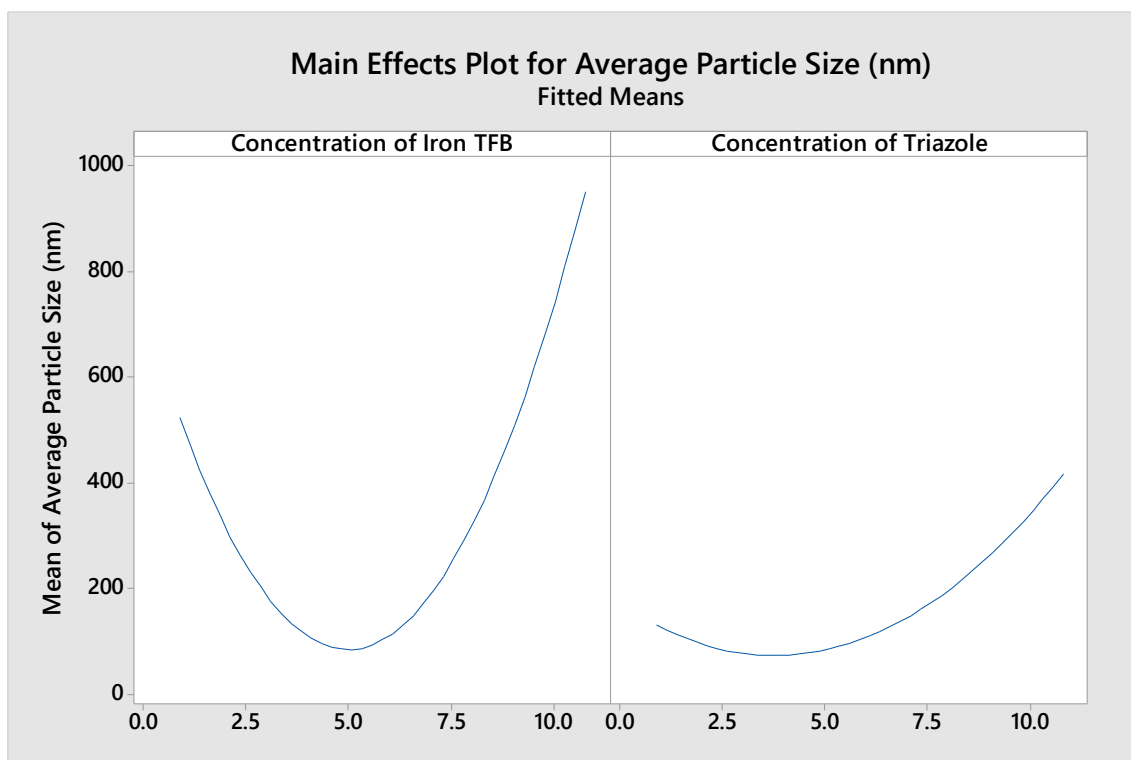


Figure 6.11 Main effect plots of triazole and iron concentrations on the APS

Fig.6.11 shows the main effect plots of the reagent concentrations. 5 % concentration of iron resulted the smallest particles. The particle sizes were increased over 1 μm at highest iron concentrations of over 10 %. Middle range particle sizes, 400 – 600 nm, were observed at lowest concentration of iron solutions.

Triazole concentration had less effect compare to iron concentration. Smallest particles, from 100 nm to 200 nm, were observed concentrations between 0 and 5 %. Largest particle sizes over 500 nm were observed at the concentration over 8 %.

A clear trend was not observed between surfactant concentrations and APS. There were some studies in the literature that reported a correlation between the reagent concentration and SCO particle size (Zhao, et al., 2015). However, they kept the process parameters constant and changed the concentrations, that is the main reason they found a correlation. Here, 5 factor variables were used at a

time with 32 experiments and it is quite difficult to find an independent effect of individual concentrations.

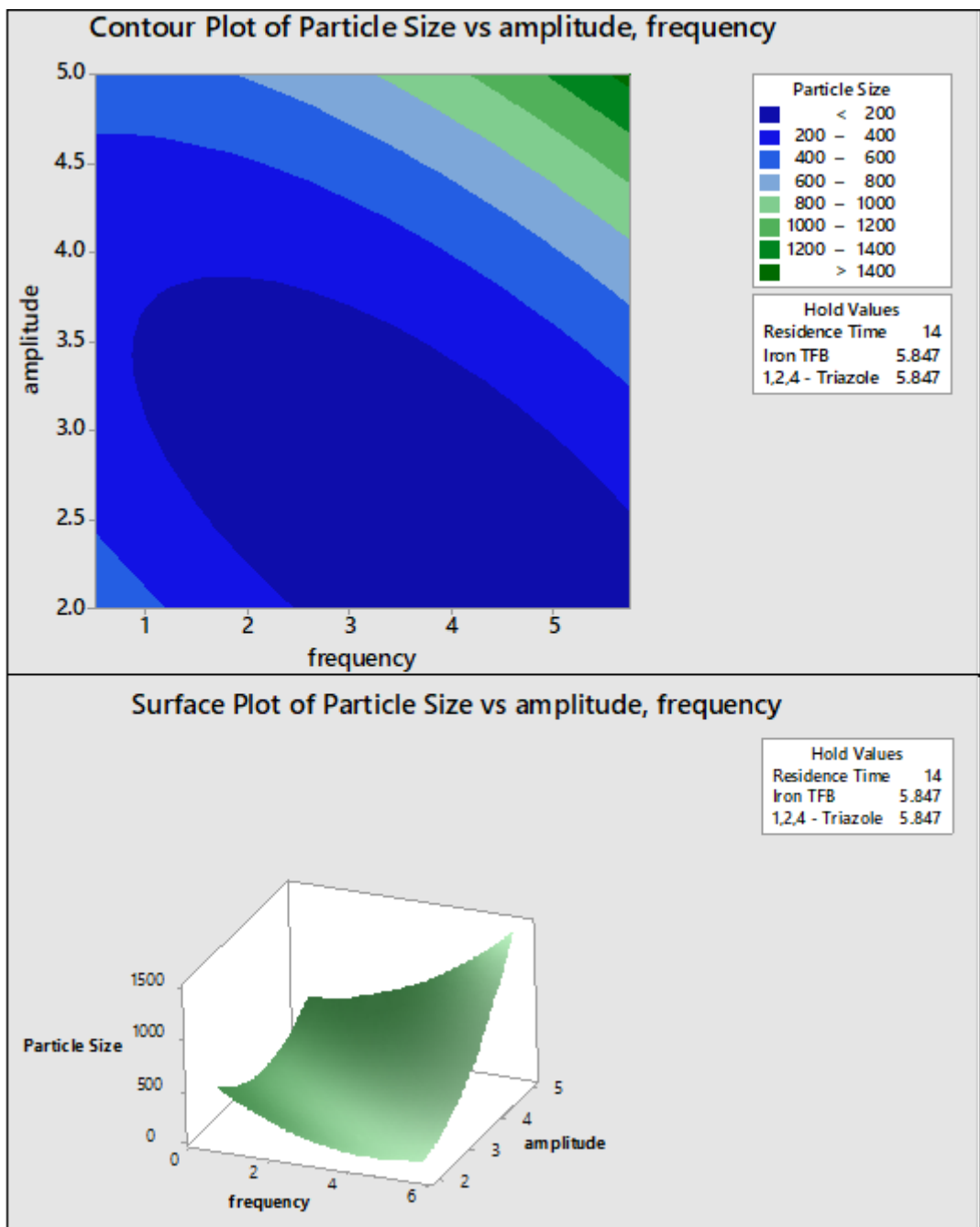


Figure 6.12 Contour and surface plots of amplitude x frequency for APS effect

Potential relationship between response and two input factors are shown in the contour and surface plots from Fig.6.12 to Fig.6.15.

The surface of the APS versus the frequency and amplitude is shown in Fig.6.12. As seen from the contour trend, higher amplitude and frequency resulted in bigger particle sizes (over 800 nm) due to very high oscillatory Reynolds numbers which created turbulent mixing regimes rather than plug flow conditions. Similar results were observed at the lowest amplitude and frequency values, where the APS was observed slightly large as around 600 nm due to soft mixing conditions. In order to produce smaller nanoparticles (less than 200 nm), the optimum frequency and amplitude have to be chosen from the dark blue area (amplitude 2-3.5 mm and frequency between 2.5 and 5 Hz),

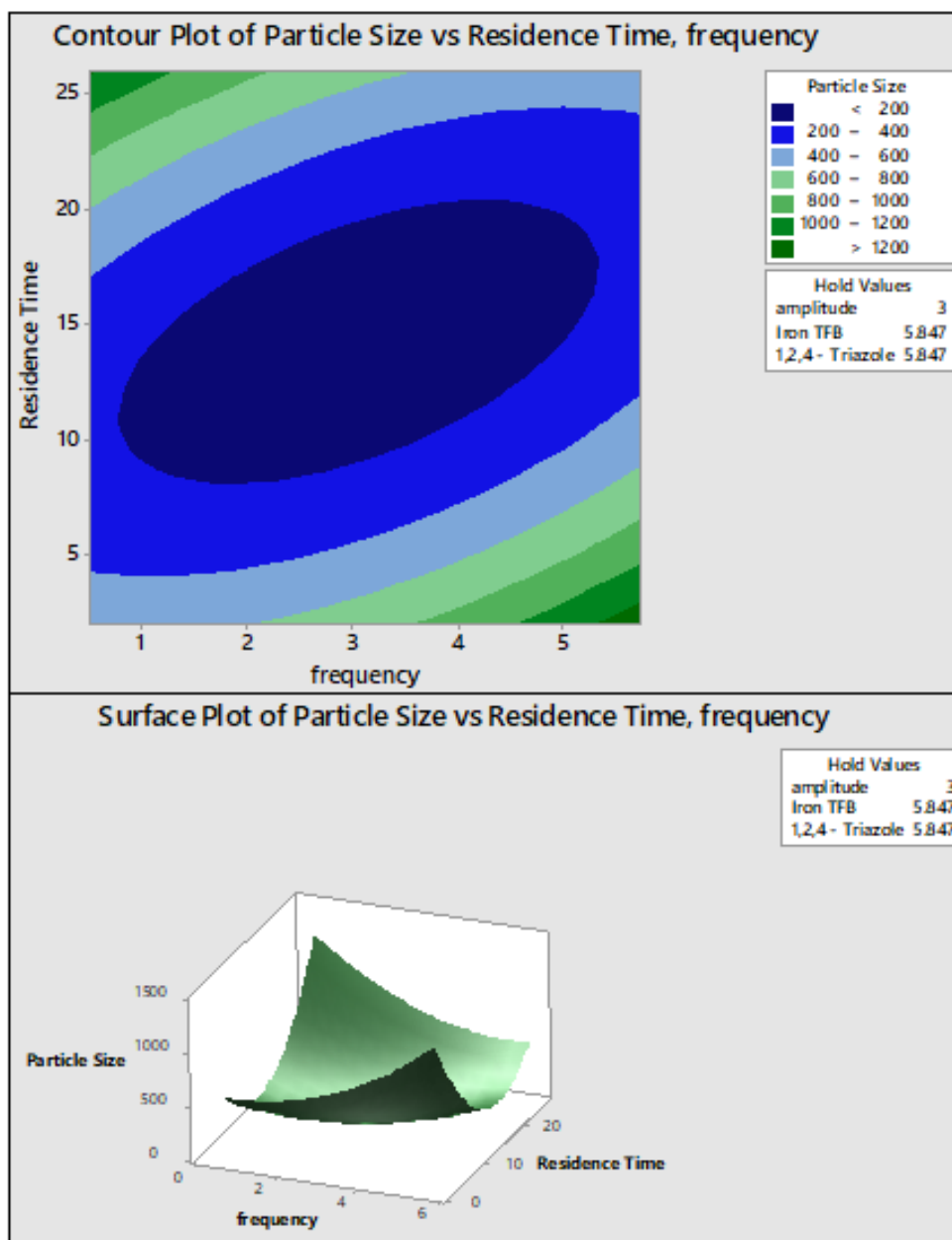


Figure 6.13 Contour and surface plots of residence time x frequency for APS effect

The relationship between the APS versus residence time and frequency is presented in the Fig.6.13. A response surface with simple maximum pattern was observed, as the colour gets darker, the response decreases. The smallest particles (under 200 nm) was observed with the residence time around 14 min and frequencies range of 1 to 5 Hz.

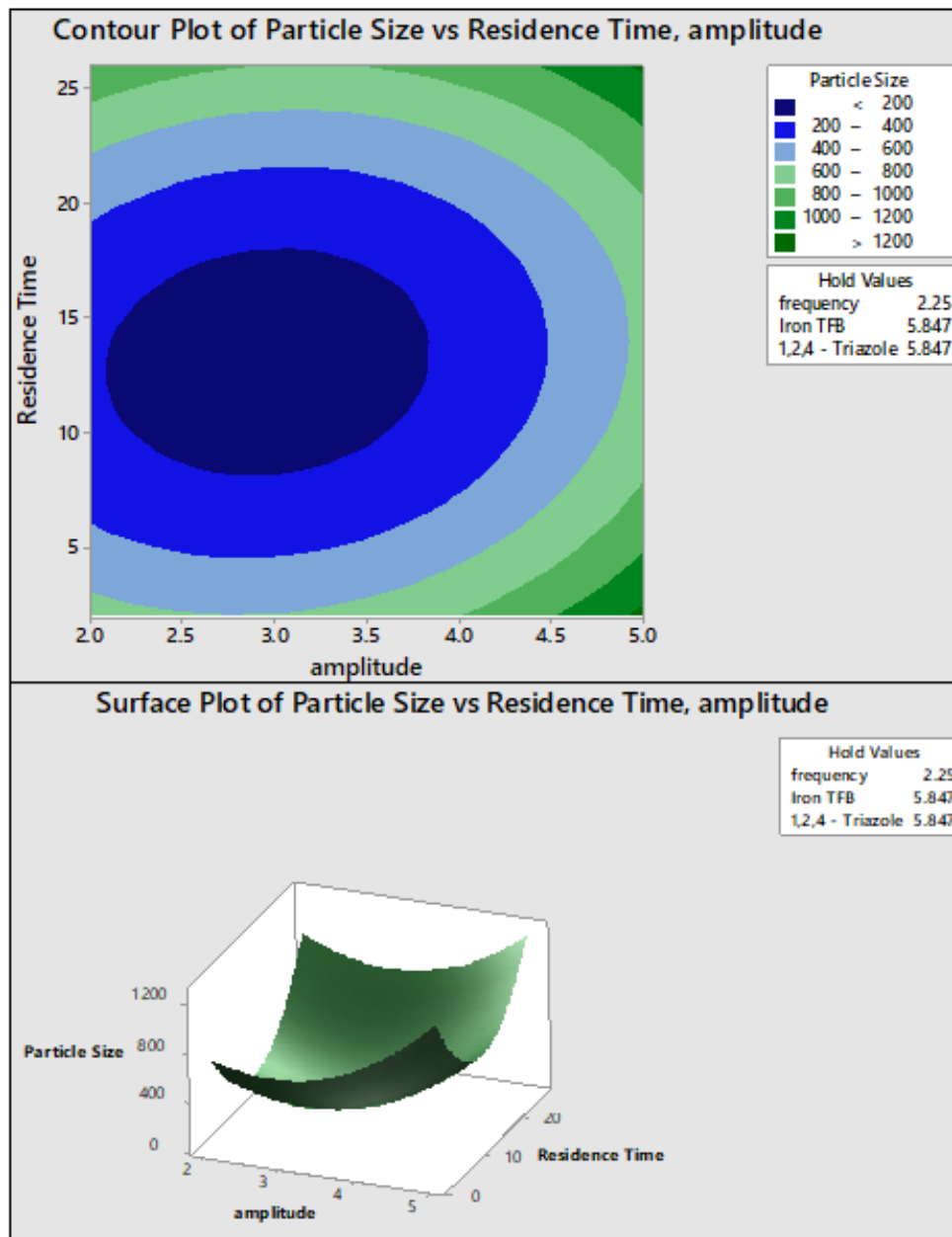


Figure 6.14 Contour and surface plots of residence time x amplitude for APS effect

Fig.6.14 presents the relationship between the amplitude and residence time combinations, and response of APS of SCO components. The darker blue region (middle circle) indicates the smallest particle size, under 200 nm. Using higher amplitudes (over 3.5 mm) large particle sizes were observed (over 800 nm), regardless of residence time as shown in the upper and lower right of the graph.

There is a clear trend for amplitude, where it is the dominant influencer compared to residence time for changing APS. The smallest SCO particles can be observed in the amplitude range of 2.5-3.5 mm and residence times of 8-18 min.

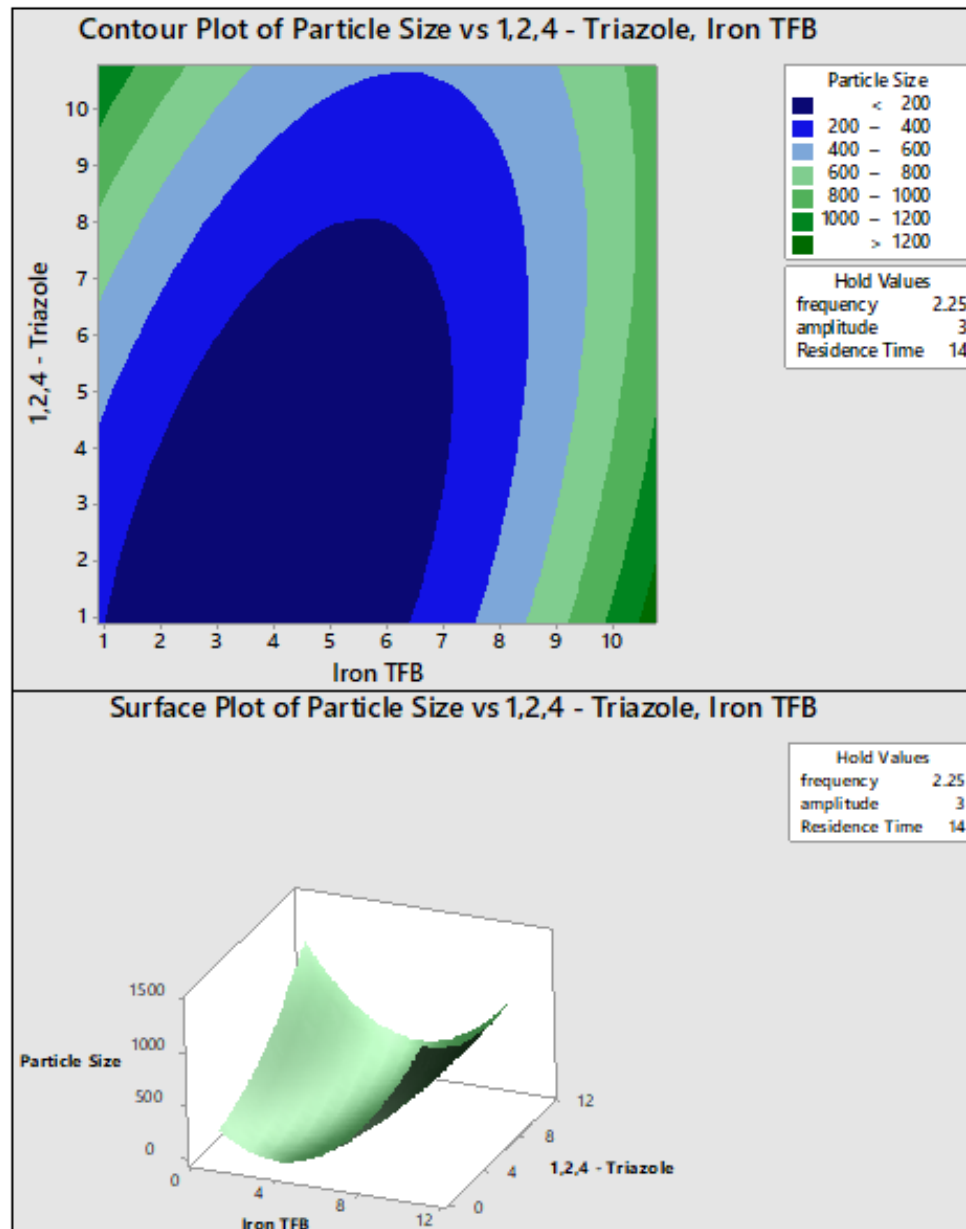


Figure 6.15 Contour and surface plots of concentration of iron x concentration of triazole for APS effect

The response surface of the APS versus reactant concentrations is shown in Fig.6.15. Dark blue region indicates the smallest APS, which can be

manufactured by using a concentration of triazole under % 7 and a concentration of iron between % 1 – % 7. The concentration of triazole has a more significant effect as seen on the 3D surface plot. On the top left corner and right side of the contour plot (dark green regions), the largest particle sizes observed as over 1 μm .

6.5.4 The Effect of the Dimensionless Numbers on the Nanoparticle Size and Shape Control

In this section, the effect of the dimensionless numbers on particle size and shape are reported. As stated in chapter 5, dimensionless numbers are key parameters to change mixing conditions in the OBR technology. Therefore, the outcomes of this section are very important to understand OBR behaviours to produce and control SCO components in the modular OBR reactor.

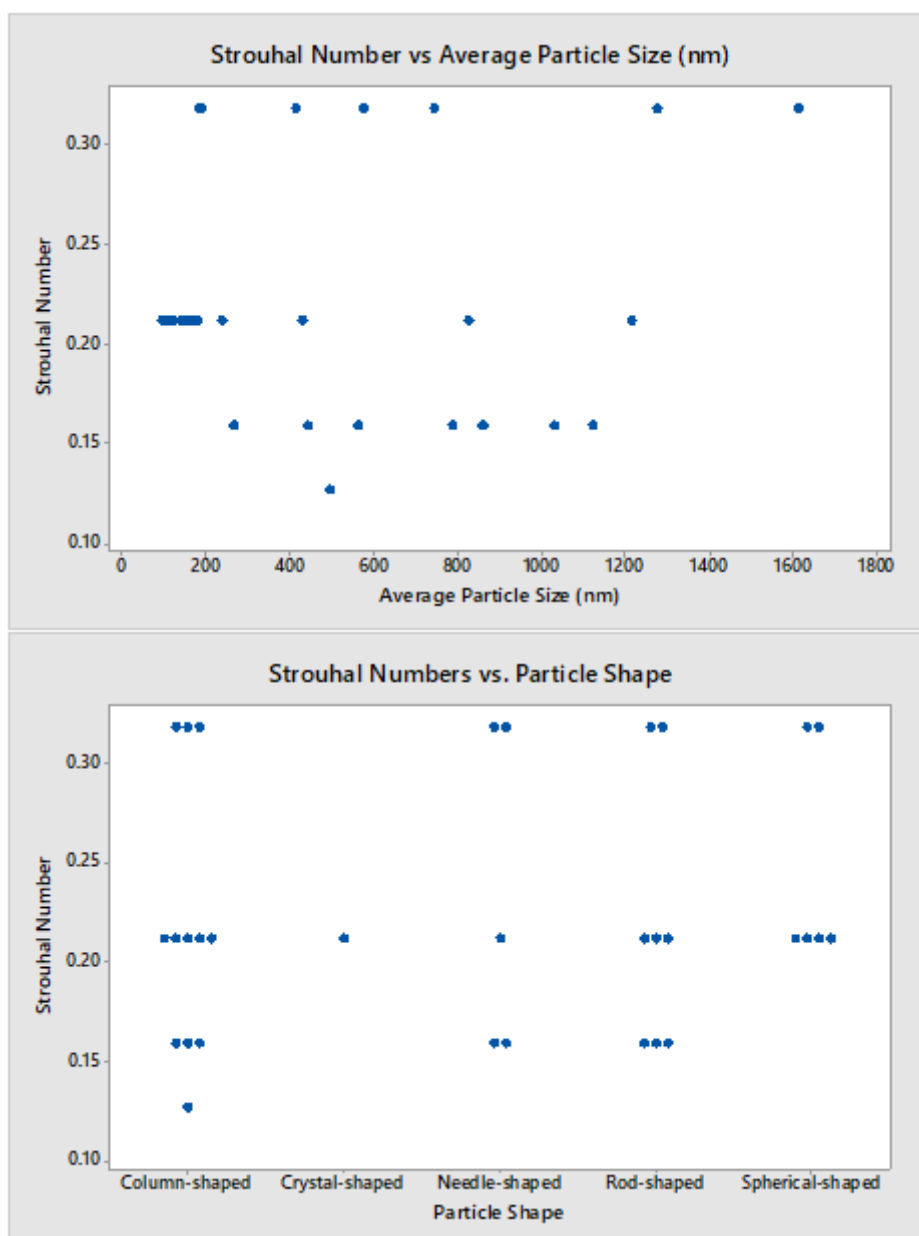


Figure 6.16 Effect of the Strouhal number on particle size and shape

The Str number was varied between 0.12 – 0.32 by using four different values as shown in Fig.6.16. For the median Str number (0.212), most of the experiments resulted Aps under 200 nm. Except for three experiments, where APS was observed between 200 nm and 1200 nm with the Str number 0.212, therefore it is difficult to conclude a correlation between Str = 0.212 and APS. There was only one experiment done by using the smallest Str number, 0.127, therefore, it is difficult to find a trend. For the Str numbers 0.16 and 0.32 there is no correlation

with the APS. With these Str numbers, particle size is widely dispersed between 200 nm and 1400 nm. Similar outcome was observed for the morphology control, where similar crystal shapes were observed in the various Str numbers. This indicates only Str number does not have a significant effect on the control of particle size and shapes. For example, column and crystal shapes were observed at every Str number.

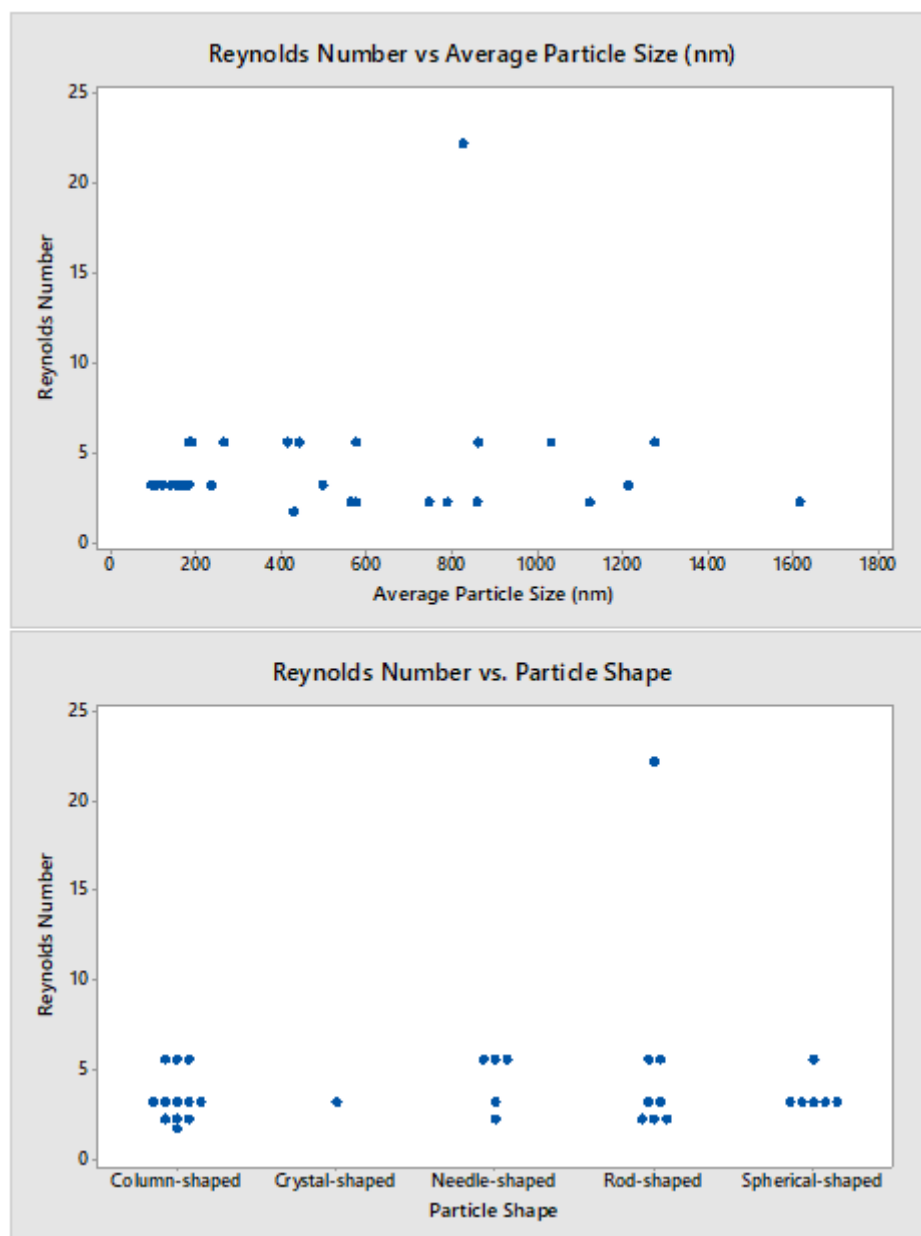


Figure 6.17 Effect of the Reynolds Number on particle size and shape

The effect of the Reynolds number on particle size and shape is shown in Fig.6.17. Reynolds number was varied between 1.69 and 22.17. It is clear from the results that there is no obvious trend between Reynolds number and particle size and shape. In other words, net flow does not influence the mixing in the OBR technology, so mixing is independent from the net flow and the only dominant factor is oscillation. This outcome supports our findings in chapter 5 and the literature studies (Ni & Gough, 1997; Harvey, et al., 2001).

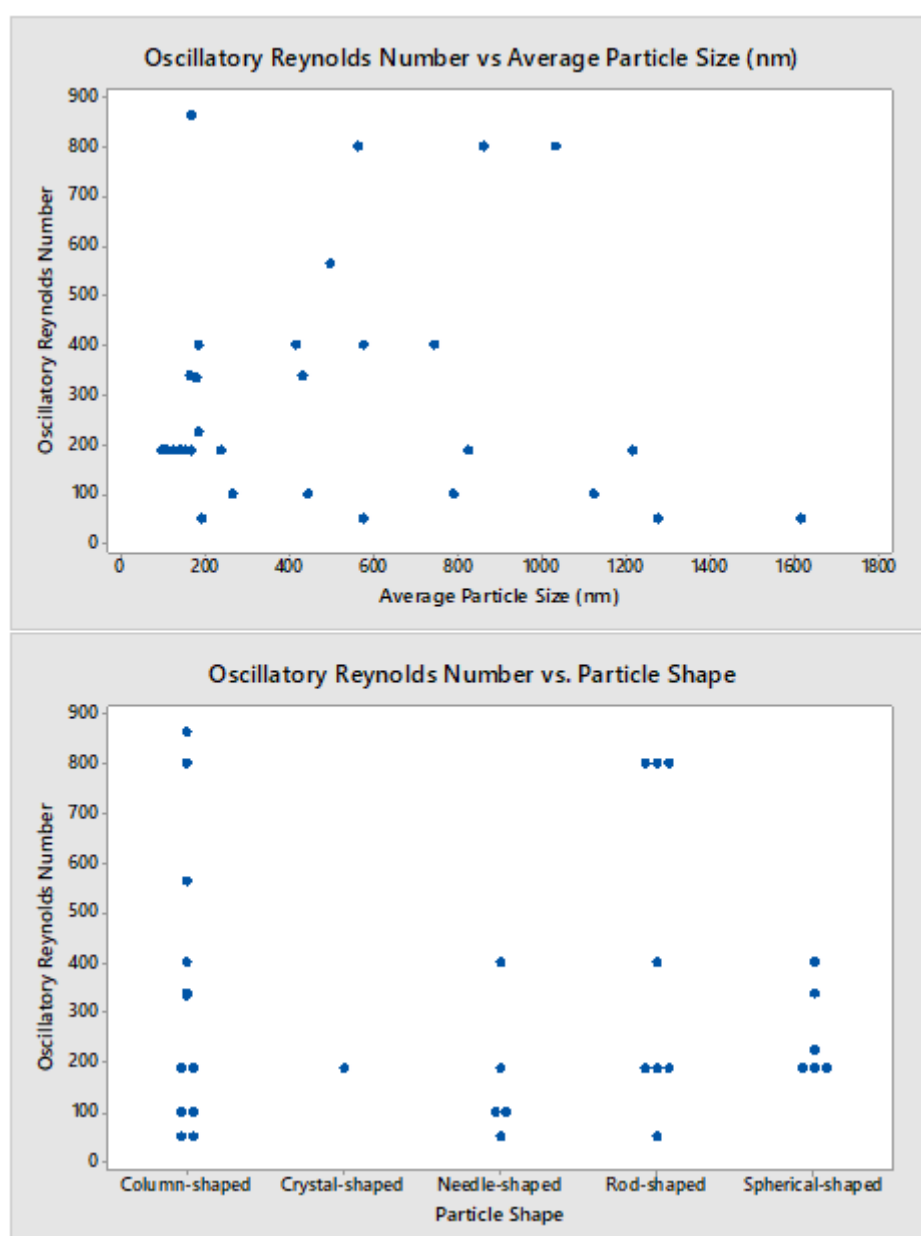


Figure 6.18 Effect of the Oscillatory Reynolds Number on particle size and shape

The effect of the oscillatory Reynolds number on particle size and shape is presented in the Fig.6.18. Wide range of the Re_o numbers were used in the DoE experiments, varying from 50 to 863. For low Re_o numbers (less than 100), there is no correlation with the particle size and shape and oscillatory Reynolds number (soft mixing range). In the region of Re_o numbers between 100 and 300, smaller particle sizes (under 250 nm) were observed. After Re_o 300, as the oscillatory Reynolds number increases, the APS tends to increase from 200 nm to 1 μm . It is difficult to find a correlation between particle shape and oscillatory Reynolds number as seen in the graph above. The only interesting result was for the needle-shaped particles, which were only observed for $Re_o < 200$ (except one outlier).

Fig.6.19 shows the APS and particle shape versus velocity ratio for five different cases of net flow over a wide range of oscillatory Reynolds number. Overall, smaller particles were observed at $0 < \psi < 120$. At a velocity ratio above 120, the APS tends to increase from 200 nm to 800 nm. Largest APS (over 1 μm) was observed at velocity ratios between 0 and 50, however, this is mainly the effect of the high concentrations of the reactants rather than the velocity ratio effect. For the particle shape, a good correlation was observed for the needle and spherical shapes. Needle-shaped SCO particles were observed in the velocity ratio range 0 – 80. Spherical particle shapes were observed in the velocity ratio range from 50 to 80.

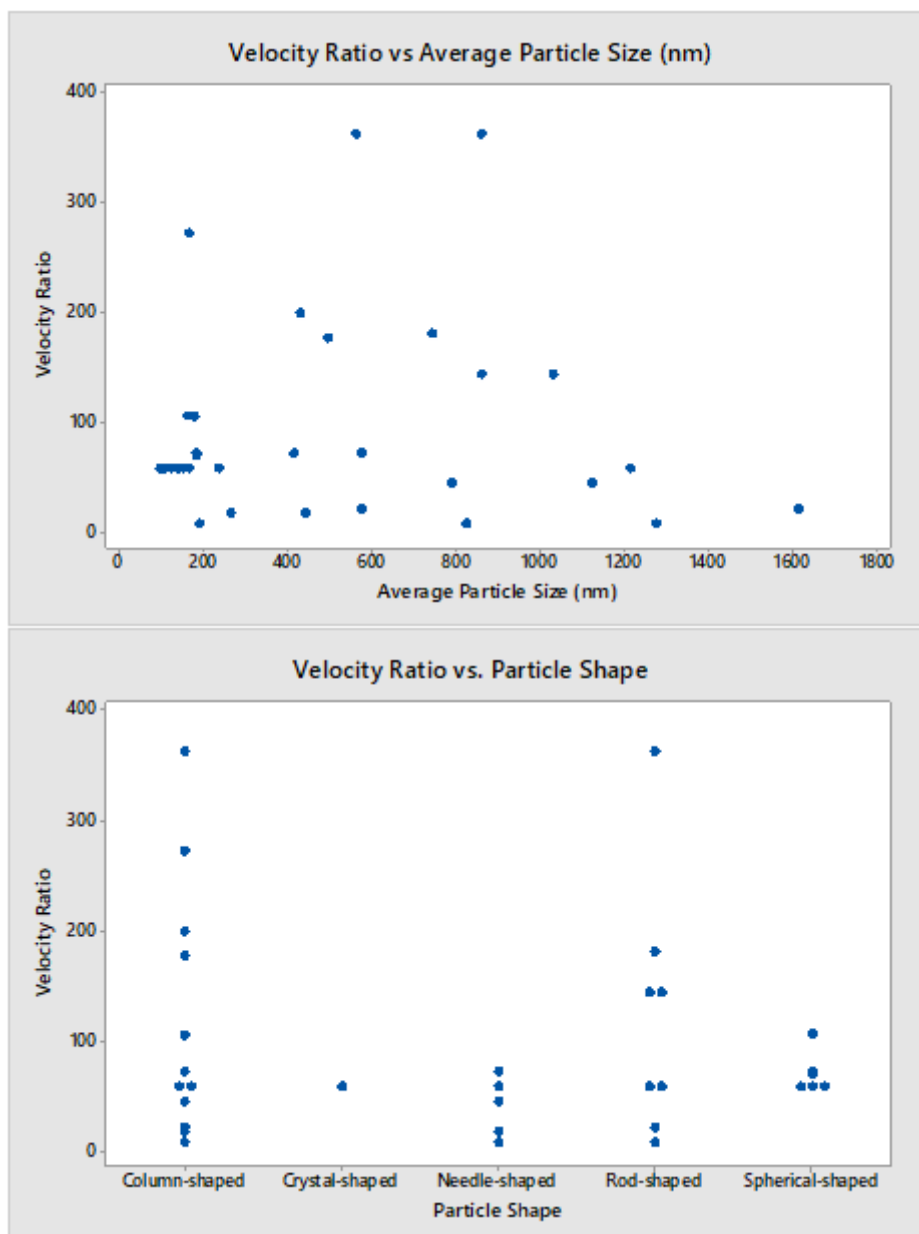


Figure 6.19 Effect of the Velocity Ratio on particle size and shape control

6.5.5 Consistency Experiments

The consistency was measured by running a non-stop four-hour experiment for the DoE_14 (2.25 Hz, 3 mm, 14 min RT, 5.84% CI and 10.79% CT). Every fourteen minutes, samples were collected for the particle size measurement using DLS. APS results for each residence time are shown in Tab.6.8. As seen on the table, APS varied between 500 nm and 1500 nm in the first twelve

samples. A consistency was observed in the last four samples of APS around 400 nm.

Table 6.8 Particle size measurements for the process consistency control

Sample time (every 14 min)	Average Particle Size (nm)
1st RT	549.7
2nd RT	605.8
3rd RT	609.8
4th RT	831.5
5th RT	662.1
6th RT	1581.7
7th RT	869.8
8th RT	624.2
9th RT	661.2
10th RT	791
11th RT	546.8
12th RT	928.5
13th RT	466.8
14th RT	388.9
15th RT	410.4
16th RT	412.4

Sedimentation has occurred during long run consistency experiments as shown in Fig.6.20. The first reactor channel was cloudy, and second reactor channel was pink at 20 min, which indicates the plug flow conditions and SCO reaction occurred in the second channel. These conditions continued until 120 min. After two hours, small sedimentations occurred at the bottom of the sharp-baffled edges inside the second channel. They got bigger after 200 min. Despite increasing sedimentation, the APS remained steady around 400 nm for the samples collected after sedimentation. This suggests that the sedimentation do not disturb the flow conditions in the channel and the reaction is still continuous. The reason for the sedimentation might be dead mixing zones in the baffled conduits. Eddy vortexes does not create uniform mixing in the entire channel. There are some small tiny spaces on the corners that are not affected by the mixing vortexes, which creates sedimentation in the long-term experiments. Another potential reason is the low net flow. The net flow is not enough to push

SCO particles after crystallization. The particles are getting bigger consequently and the density changes, so due to the effect of gravity under low net flow, we can observe sedimentation.

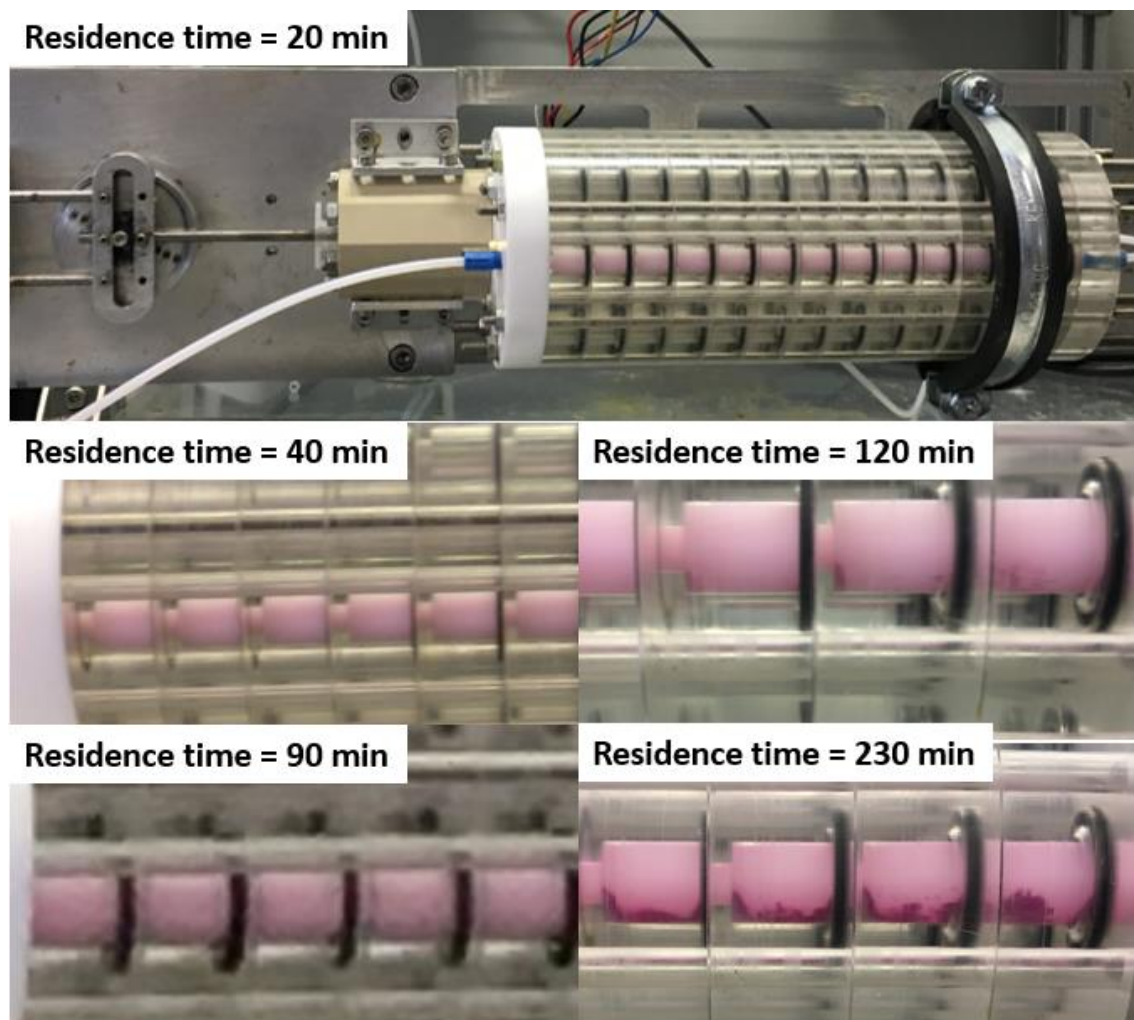


Figure 6.20 Sedimentation occurred during consistency experiments

6.5.6 Repeatability Experiments

Process accuracy of SCO production was measured by repeating experiments of DoE (5, 7, 14, 20 and 30). Same oscillatory/net flow conditions and chemical concentrations as original DoE experiments were used for the repeat experiments. The experiments were conducted at different dates and time intervals in order to check their reproducibility. APS of each experiments was compared to the original DoE results by using DLS particle size measurement as

shown in Fig.6.20. SEM imaging were used to compare their morphology, which are shown in Fig.6.21.

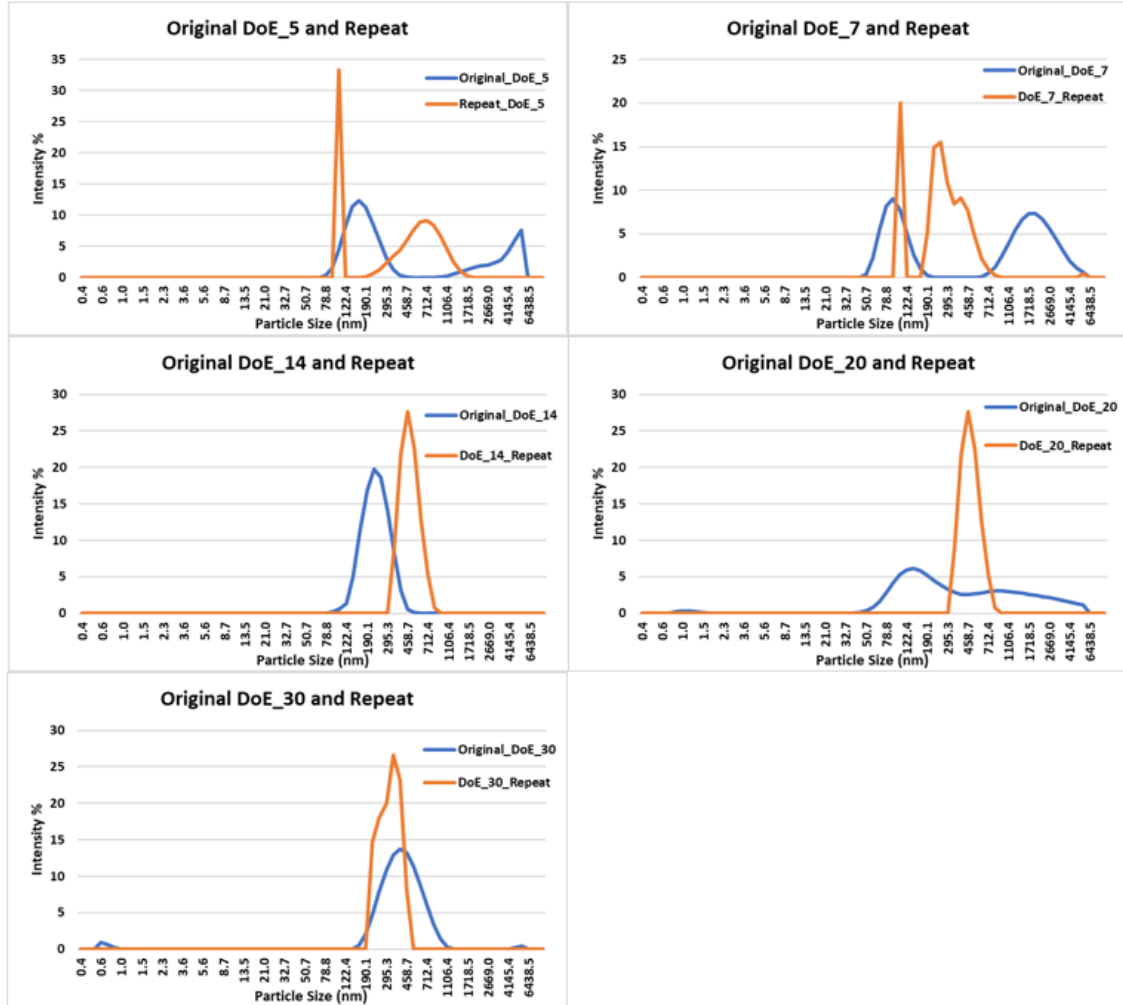
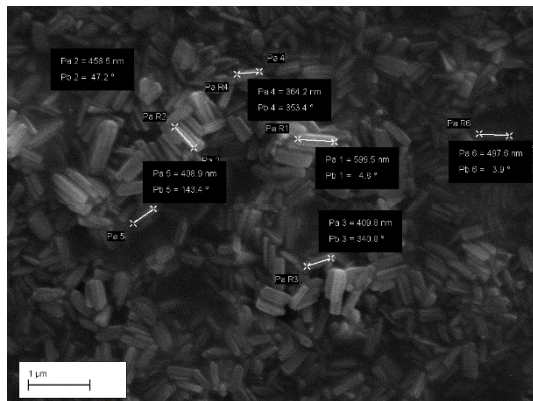


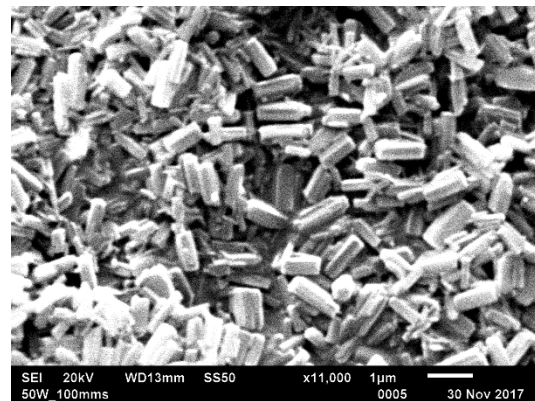
Figure 6.21 APS measurements for original DoE and repeated experiments

In the original DoE experiments, the smallest particles were measured for the DoE_7, 95 nm, with the column-shaped morphology. In the repeat experiment of DoE_7, APS was increased from 91 nm to 255 nm and morphology changed from column-shaped to rod-shaped particles. This experiment was employed with one of the extreme oscillatory conditions ($x = 4$ mm, $f = 4$ Hz, $Re_o = 800$, $\psi = 362$). Due to a very high velocity ratio, the different APS and shapes were observed. As stated in Chapter 5 and literature, higher velocity ratio influences the plug flow in a negative way.

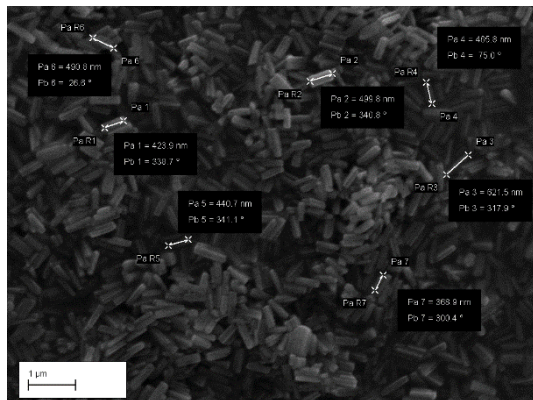
DoE_5_Original



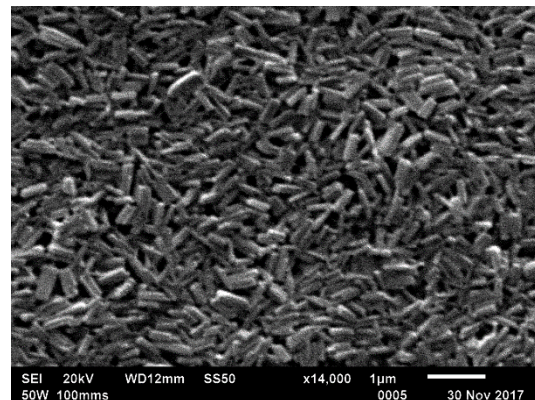
DoE_5_Repeat



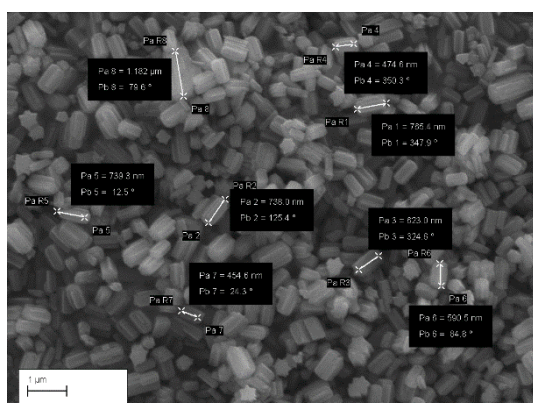
DoE_7_Original



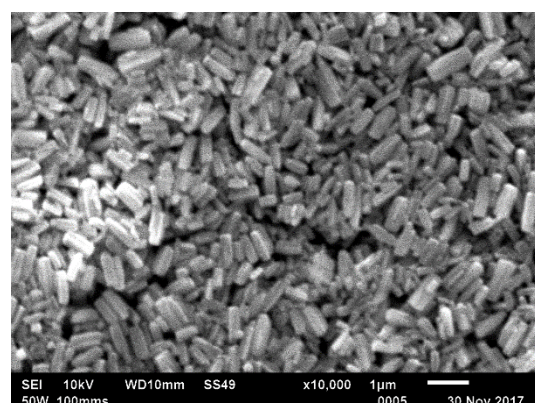
DoE_7_Repeat



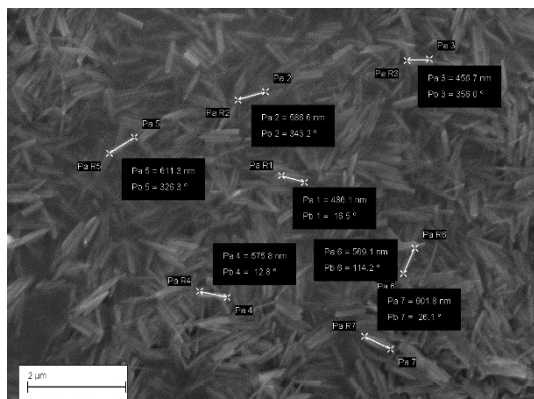
DoE_14_Original



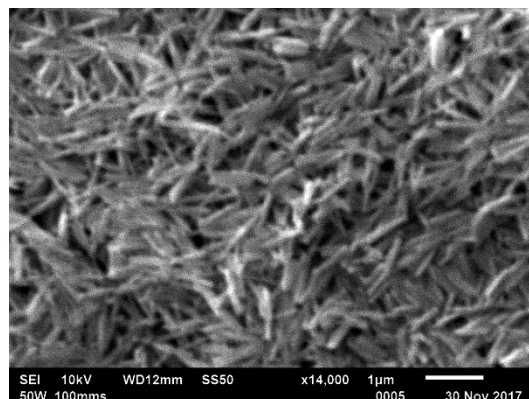
DoE_14_Repeat



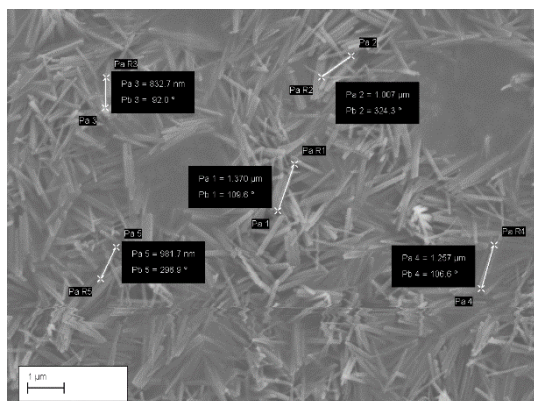
DoE_20_Original



DoE_20_Repeat



DoE_30_Original



DoE_30_Repeat

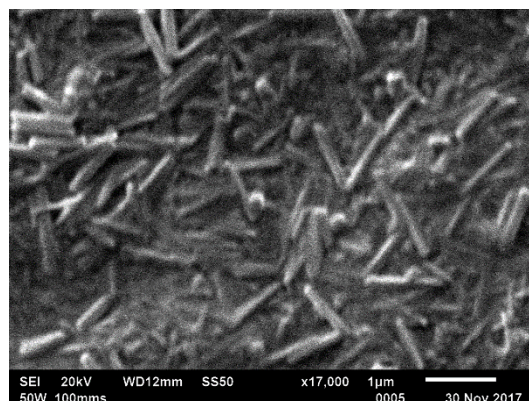


Figure 6.22 SEM images of original DoE and repeat experiments

Both particle size and shape were slightly different between original DoE_14 and repeat experiments. APS of original DoE_14 was 236.5 nm, however, in the repeat experiment, APS was increased to 458 nm. Particle shape changed from spherical-shaped to rod-shaped particles. A difference was observed for the DoE_14 in the repeatability experiments, but if the consistency experiment of DoE_14 is considered, it can be seen that APS was varied between 400 nm to 1500 nm. Some measurement error could have happened in original DoE_14, because in the consistency experiments of 16 samples, 236 nm particles were not observed, which indicates a measurement error in original experiment.

Table 6.9 APS size and shape comparison for original and repeat experiments of DoE 5, 7, 14, 20 and 30

	Original		Repeat	
Experiment	APS (nm)	Particle Shape	APS (nm)	Particle Shape
DoE_5	179	Column-shaped	105	Column-shaped
DoE_7	95.8	Column-shaped	255	Rod-shaped
DoE_14	236.5	Spherical-shaped	458	Rod-shaped
DoE_20	189.8	Needle-shaped	220	Needle-shaped
DoE_30	441.8	Needle-shaped	341	Thicker needle-shaped

DoE_20 resulted the best producibility outcome out of 5 experiments. DLS measurements for APS were very close for each experiment, which also indicates the importance of controlling dimensionless numbers in order to achieve a consistent plug flow condition. As seen on the Table.6.5, the velocity ratio used in the DoE_20 is 9 which is in the good plug flow regime.

As that can be seen from Tab.6.9 and DLS graphs, we have not observed a good reproducibility for the repeated experiments. It needs further investigation and experimental study to achieve a process repeatability. There are some reasons which poorly affected the repeatability experiments. These factors and suggestions to improve process accuracy are listed below:

- Adjust the velocity ratios to achieve better plug flow conditions. As mentioned in the beginning of this chapter, the velocity ratios used in the SCO synthesis was very high, but this was necessary to maintain residence time and cost of chemicals. In other word, more material would be needed if smaller velocity ratios were used and that would be limited the number of total experiments. The suggestion for further studies is to

take the best chemical composition out of this study and use velocity ratios in plug flow regime and conduct repeatability experiments.

- Selection of reliable pumping mechanism. Syringe pumps were used in this study to carry SCO composites from stock vessels to reactor. Two syringe pumps were synchronised for each chemical compound to provide continuous flow. However, we observed that the synchronisation did not perfectly worked in some time frames which cause disturbance providing smooth continuous flow through entire production. High precision continuous flow pumps are recommended to use in further studies.

6.6 Process Design Method for Industrial Scale Production of SCO Nanoparticles

In this section, the process design methodology is presented to illustrate SCO synthesis in three different scales as laboratory, pilot and industrial processing. Production rate was required as starting point for the calculations of key process parameters. The production rate of was studied from literature as 2.5 kg/h for laboratory scale, 50 kg/h for pilot scale and 300 kg/h for industrial scale (Khinast & Bresciani, 2017). These production rates will be illustrated for various tube diameters. There are three ways of increasing production rate; 1) scale-up: increasing the tube diameter, 2) scale-out: to use multiple units in parallel, 3) to increase net flow which requires increase in the reactor length.

First dimensionless numbers must be identified. Re_n , Re_o , Str and velocity ratio were chosen from the characterization experimental results. As that can be seen from Fig.5.13, the optimum velocity ratio for the 8 mm diameter was observed as 8 for the best plug flow performance. This velocity ratio was chosen for calculation. Str number was chosen from Fig.5.18 as optimum Str number was observed 0.2. The production rate of six Reynolds number from 50 to 300 with increment of 50 was for tube diameter of 8-48 mm. Residence time is also required for process design calculations. SCO experiment results were employed to identify required mean residence time. DoE_14 was performed as best experiment in terms of final product quality and consistency. The residence time

of DoE_14 was taken for the process design calculations. DoE_14 residence time is 14 min (0.23 hr). Based on chosen dimensionless numbers and mean residence time (τ), the superficial velocity (u), baffled flow channel length (Σ), reactor volume (V) and production rate (Q) were calculated using Equations from 12 to 15. The bulk physical data of the triazole and iron precursors were measured at room temperature as $\rho = 980 \text{ kg/m}^3$, and $\mu = 0.001 \text{ Pa}\cdot\text{s}$.

$$u = \frac{Re_n * \mu}{D * \rho} \quad (12)$$

$$\Sigma = u * \tau \quad (13)$$

$$V = \Sigma \frac{\pi D^2}{4} \quad (14)$$

$$Q = \frac{V}{\tau} \quad (15)$$

Overall reactor length, tube diameter and production rate are the key parameters. These parameters must be realistic in terms of system feasibility, plug flow conditions and fluid dynamics inside the tube. Ideal dimensionless number conditions for plug flow were identified in the Tab.6.10. Based on dimensionless numbers identified and SCO processing mean residence time of 0.23 hour at 8 mm tube diameter, various production rates were presented in the Tab.6.10. Required reactor parameters as volume and length were calculated for initial design. With the $Re_n = 50$, 1.15 l/hr production rate can be achievable for 5.3 m flow channel length and 8 mm tube diameter. Flow velocity can be increased to increase production rate, with 8 mm tube diameter and $Re_n = 300$, the production rate become 6.92 l/hr, however, the required flow channel length increases from

5.3 m 31.7 m. Flow rate can technically be increased for higher volumes (for example $Re_n = 600$ etc.) which will also increase the production rate. However, at that can be seen from the calculation, increased flow rate leads some design issues such as very long reactor length and very high Re_o to keep the velocity ratio same. Because of this reason, $Re_n = 300$ was kept as upper threshold for the system design. 31.7 m tubular length is achievable, as presented in the Chapter 3, proposed design has 8 flow channels in parallel. 31.7 m flow channel length can be divided into 8 channels, then the reactor length will be approximately 4 m long.

Table 6.10 Modular OBR design and process parameter for various production scales

Mixing Conditions	Diameter (mm)	Scaling Factor	Mean Residence Time (hour)	Superficial velocity (m/s)	Flow Channel Length (m)	Reactor Volume (litre)	Production Rate (Litres/hr)
$\Psi = 8$ $Re_n = 50$ $Re_o = 400$ $Str = 0.2$	8	1	0.23	0.0064	5.3	0.27	1.15
	16	2	0.46	0.0032	5.3	1.06	2.31
	24	3	0.69	0.0021	5.3	2.39	3.46
	32	4	0.92	0.0016	5.3	4.25	4.62
	40	5	1.15	0.0013	5.3	6.64	5.77
	48	6	1.38	0.0011	5.3	9.56	6.92
$\Psi = 8$ $Re_n = 100$ $Re_o = 800$ $Str = 0.2$	8	1	0.23	0.0128	10.6	0.53	2.31
	16	2	0.46	0.0064	10.6	2.12	4.62
	24	3	0.69	0.0043	10.6	4.78	6.92
	32	4	0.92	0.0032	10.6	8.49	9.23
	40	5	1.15	0.0026	10.6	13.27	11.54
	48	6	1.38	0.0021	10.6	19.11	13.85
$\Psi = 8$ $Re_n = 150$ $Re_o = 1200$ $Str = 0.2$	8	1	0.23	0.0191	15.8	0.80	3.46
	16	2	0.46	0.0096	15.8	3.19	6.92
	24	3	0.69	0.0064	15.8	7.17	10.39
	32	4	0.92	0.0048	15.8	12.74	13.85
	40	5	1.15	0.0038	15.8	19.91	17.31
	48	6	1.38	0.0032	15.8	28.67	20.77
$\Psi = 8$ $Re_n = 200$ $Re_o = 1600$ $Str = 0.2$	8	1	0.23	0.0255	21.1	1.06	4.62
	16	2	0.46	0.0128	21.1	4.25	9.23
	24	3	0.69	0.0085	21.1	9.56	13.85
	32	4	0.92	0.0064	21.1	16.99	18.46
	40	5	1.15	0.0051	21.1	26.54	23.08
	48	6	1.38	0.0043	21.1	38.22	27.70
$\Psi = 8$ $Re_n = 250$ $Re_o = 2000$ $Str = 0.2$	8	1	0.23	0.0319	26.4	1.33	5.77
	16	2	0.46	0.0159	26.4	5.31	11.54
	24	3	0.69	0.0106	26.4	11.94	17.31
	32	4	0.92	0.0080	26.4	21.23	23.08
	40	5	1.15	0.0064	26.4	33.18	28.85
	48	6	1.38	0.0053	26.4	47.78	34.62
$\Psi = 8$ $Re_n = 300$ $Re_o = 2400$ $Str = 0.2$	8	1	0.23	0.0383	31.7	1.33	6.92
	16	2	0.46	0.0191	31.7	6.37	13.85
	24	3	0.69	0.0128	31.7	14.33	20.77
	32	4	0.92	0.0096	31.7	25.48	27.70
	40	5	1.15	0.0077	31.7	39.81	34.62
	48	6	1.38	0.0064	31.7	57.33	41.55

Second design scenario is to increase the tube diameter by pre-defined scaling factor. In the case of scaling factor 6, the tube diameter became 48 mm. Same

mixing conditions were used to calculate required reactor length and volume for 48 mm tube diameter. As that can be seen from Tab.6.10, production rate became 6.92 l/hr with the reactor dimensions of 48 mm tube diameter and 5.3 m required flow channel length. With the highest superficial fluid velocity ($Re_n = 300$) in 48 mm diameter and 31.7 m reactor length, the production rate increased up to 41.55 L/hr.

As shown in Tab.6.10, calculated reactor dimensions and production rate is not still enough to produce full industrial scale of 300 L/hr with using single reactor as max production capacity of single unit is 42 L/hr. Operation of multiple units in parallel is required in order to achieve full industrial scale production. 8 units of 48 mm diameter and 31.7 m flow channel length will provide 332 L/hr production of SCO materials. Final design configuration of the reactor can be optimized to provide the best footprint solution. Such as the flow channel length can be divided to a practical configuration considering available platform storage, assembly and manufacturability. The design ratios provided in the Chapter 2.5.1 are employed for baffle, thickness, baffle spacing, baffle open area and baffle shape.

Using multiple units also provides great flexibility and decentralized manufacturing opportunity. As small footprint can be configured for 40 L/hr reactor capacity, it can be setup in the storage of a lorry or van for shipping to specific location or plant. All sensors and actuators can be remotely controlled with today's technology. The whole platform can be controlled from one centre, it does not require many highly skills operator.

6.6.1 Comparison Between OBR Production Rate and Batch Processing Rate

Literature was reviewed to compare production rate of SCO synthesis for batch and flow processes. In the last 3 decades, various academic studies were published for the development of SCO components (Luo, et al., 2016; Krober, et al., 1994; Scepianiak, et al., 2011). However, limited information was provided for the production rate in the previous studies. They mostly investigated SCO components based on various temperature conditions, chemical compositions,

mechanical and magnetic properties. Only one research study was found who provides information about mixing time. L. Moulet and his colleagues published a paper to understand SCO particles shapes in various mixing time and temperatures (Moulet, et al., 2016). The mixing time used in this study was compared with mixing time to synthesis SCO particles in modular OBR reactor. The authors investigated four mixing times (5 min, 1h, 2h and 12h) at 6 various temperature ranging from room temperature (21 °C) to 130 °C in the batch process. In this study, the residence times used to manufacture SCO components in flow were from 2 min to 26 min. Table.6.11 presents mixing time between batch process from literature and residence time from this study including their responses as particle size and shape.

Table 6.11 Production Rate Calculation between batch and modular OBR process

Mixing time for SCO synthesis in batch (Moulet, et al., 2016)				Residence time for SCO synthesis in this study			
Exp No	Mixing Time	Particle Shape	Particle Size	Exp No	Residence Time	Particle size	Particle Shape
1	5 min	75 nm	Rod	DoE_12	2 min	823 nm	Rod
2	1 hour	110 nm	Rod	DoE_32	8 min	183 nm	Needle
3	2 hours	85 nm	Rod	DoE_7	14 min	96 nm	Rod
4	12 hours	80 nm	Rod	DoE_4	26 min	429 nm	Column

As that can be seen from Table.6.11, only 5 min mixing time was worth to compare with residence time conducted in this study. Moulet et al achieved 75 nm sizes with 5 min batch mixing, on the other side, 14 min residence time produced 96 nm particles in this study. In first instance, batch process seems three times quicker than flow. However, additional time is required for batch process to measure precursor volumes, unload and load the reactor after every process cycle. With best scenario additional time calculation for 5 min mixing time will require ~5 min to measure and prepare feeding precursors, ~5 min to load the batch reactor and ~5 min to stop the mixing and unload the final product. These calculations are based on lab experience, the process was demonstrated in the lab and time was recorded for each step. So basically 5 min mixing does not mean real production rate in the batch process, the real production rate is around 15-20 min. Flow processing does not require any additional time or

processing steps. Once the system is setup, that can continuously produce final products until the system is stopped. There is also still opportunity to reduce 14 min residence time by investigating more process conditions.

6.7 Chapter Summary

In this chapter, OBR technology has been described to synthesise SCO components for the first time. Initial screening experiments showed that SCO reaction can be successfully transferred from batch processing to flow processing using modular oscillatory baffled reactor to produce various particle shapes and sizes. After initial experiments, a systemic methodology was developed for SCO material production using modular meso-scale OBR reactor.

Controlled space was investigated by developing a systematic DoE setup to understand the effect of five input variables (net flow, oscillatory amplitude and frequency, triazole concentration and iron concentration). It was discovered through the examination of factor effect, that the concentration of the triazole and interaction between amplitude and frequency are the most important factors to influence the response of the reaction. The desired particle size and morphology can be produced by tuning the processing parameters and chemical concentrations. Five different particle shapes as spherical, rod, column, needle and crystals were observed within the range of 100 nm and 1500 nm. Consistency experiments showed that similar particles and shapes can be manufactured with 4 hours nonstop continuous production. Repeatability experiments resulted some further work is required to manufacture similar product in various timeframes. Velocity ratios and pump selection must be reviewed to achieve repeatable experiments.

Process and reactor design methodology was presented at the end of the chapter for various production sizes starting from laboratory to full industrial scales. There are three ways to increase production capacity. First option is to scale up the tube diameter. Second option is to increase fluid net flow, but this will require longer reactor length and volume to maintain same residence time. Third option is to use multiple reactor units in parallel.

7 DISCUSSION

“Difficult roads often lead to beautiful destinations”

In this thesis, a novel modular oscillatory baffled reactor was characterized in two different tube diameters and scale-up methodology was developed. Same reactor was used to produce SCO nanoparticles and control of its shape and size for the first time using a systematic DoE approach. In this chapter, the outcomes and major achievements will be discussed.

7.1 Design Improvements for Modular Continuous OBR Platform

Original modular OBR concept was patented by Prof Harris and his colleagues (Makatsoris, et al., 2011). The patented reactor was used for the micro-scale characterization experiments. Design changes were introduced for the meso-scale reactor to improve its performance and modularity. As stated in chapter 2.5, baffle shape is essential to generate various shear stresses, and there is still a big debate for optimum baffle shape for a large group of applications. Each application may need different baffle shape; sharp or smooth. In the patented design, there was a limitation to manufacture symmetrical baffle shapes on each side of the baffled edges. The orifice was placed on one side of the disk in the patented design, which always results in a sharp baffle on one side of the reactor. Orifice position was moved from edge to the middle of the baffled conduit, and with this orientation, smooth baffles could be shaped from both sides of the disk. Symmetrical baffle shapes were achieved along the entire reactor. Additional to the symmetrical baffled design, mixed baffled shapes can be combined such as one disk with sharp edges and one disk with smooth edges.

Second design improvement was introduced for the heating/cooling channels. In the patented original design, heating/cooling channels were designed as 26 straight holes connected with U-bend tubes at both ends of the reactor. The patented original heating/cooling design requires a high number of parts to

construct a circulatory system for heating/cooling fluid to travel the entire reactor, such as 26 O-rings for each disk and 26 U-bend tubes and fittings for each end of the reactor. With the modified design, O-ring numbers were decreased to only four per disk, and there is no need of U-bend connection for heating/cooling channels. The heating/cooling fluid can circulate the entire reactor with only one input and one output, without any u-bend connections. Instead of straight channels, one or two spiral heating/cooling channels were designed around reaction channels. Spiral channels do not only provide cost advantage, but they also provide great flexibility for the uniform temperature control. Spiral length can be divided into many sections that can provide individual heating or cooling zones within the same reactor, such as half of the reactor can be cooled when the other one is heated.

The third design improvement was developing a novel oscillation mechanism. In the original patented reactor, the syringe pump was used to create oscillatory motion. This method was not suitable for a large-scale reactor, so a new and unique scotch-yoke oscillation mechanism was developed. It can be scaled for any size reactor. Scotch-yoke mechanism provides smooth sinusoidal motion which is vitally essential for the OBR systems. The unique part of the oscillation mechanism is that a lead-screw mechanism is integrated on the rotating cam. With this mechanism, the amplitude can easily be changed to any stroke size in a short time, compared to all other previous mechanisms. With the integration of micro-scale motor, the mechanism can be fully automated. In other words, net flow, oscillatory amplitude, and frequency can be fully automated without human interaction, which results in a self-optimized continuous OBR platform. As far as we are aware, this is the first fully automated continuous OBR concept in the literature.

7.2 Modular OBR characterization and its performance compared to the traditional OBRs

A full factorial experimental design was conducted to investigate the effects of three processing factors (net flow, oscillatory frequency and amplitude) on the

plug flow conditions. RTD measurements were experimentally collected in the micro and meso scale reactors. Tanks-in-series model was used to characterize micro- and meso-scale modular oscillatory baffled reactors. This was the first study to characterize a modular OBR. Modular OBR design performed better than conventional OBR designs. Better performance comes from the combination of better oscillation mechanism and pump selection. One observation in the experiments was that syringe pumps were not able to provide constant continuous flow in the reactor system. Therefore, high precision syringe pumps were selected for the experiments. The modular design has better dimensional control during the manufacturing of the reactor compare to traditional OBRs. Each disk is separately manufactured that means dimensions of each baffled channel can be precisely controlled. One single straight glass or metal tube is formed to construct baffled channels in the conventional OBRs. That means it is more difficult to control dimensions and alignment for the entire tube. This has not been confirmed by measuring dimensions of conventional OBRs as we have not got any conventional OBR in the laboratory. Dimensional control has to be investigated to measure its effect on the reactor performance for further studies.

The best plug flow condition was observed as 58 tanks-in-series number in the 4 mm tube diameter, and 30 in the 8 mm tube diameter. Amplitude and iteration of (amplitude) x (net flow) were shown to have a significant influence on the plug flow conditions for the micro-scale reactor. For the meso-scale reactor, the most influencing factors showed difference compare to microscale reactor, as the interaction of (amplitude) x (net flow) and frequency became the most significant factor for the plug flow conditions in the meso-scale system. This difference indicates the independent effect of amplitude and frequency in different flow diameters.

As presented in sections 5.1.2 and 5.2.1, the net flow is not the function of mixing in the OBR processing. With the increasing net flow Reynolds number, the flow behaviour becomes naturally more chaotic due to transaction from the laminar regime to turbulent flow regime for both scales. Therefore, better plug flow conditions were observed with a lower Reynolds number ($Re_n = 5.3$) in both

scales. Twenty-five combinations of amplitude and frequency were used for each net flow in this study. At lower Reynolds numbers, better plug conditions were observed with more combinations of oscillation and amplitude. Whereas at higher Reynolds numbers, better plug flow conditions were still observed but with limited combinations of amplitude and frequency, which explains mixing is not a function of net flow, but it becomes more chaotic flow regime at higher Reynolds numbers.

Modular OBR was characterized using tanks-in-series model like the previous studies. One hundred experiments were conducted for each size within the velocity ratio of 0–60, which shows the significant effort to investigate a broader range of net flow and oscillation conditions compared to previous studies. The direct comparison of the results between this study and studies from the literature is quite tricky because of variations in the reactor length, tube diameter and baffle size and shape. Table 7.1 compares the measured tanks-in-series number in this study and the similar flow conditions and reactor dimensions used in the literature. As seen from the table below, the plug flow performance was observed better than the literature in this study with similar flow conditions and reactor dimensions. Advantages of the modular reactor mechanism were discussed in sections 3.2 and 3.3. Better mixing conditions can be achieved with lower manufacturing and assembly cost by using modular reactor. Additional to the modular design, there is a contribution of the pump selection and oscillation mechanism in order to achieve better performance.

Table 7.1 Comparison of the characterization results with the literature

Research	Reactor Dimension		Net Flow Reynolds Number	Oscillatory Reynolds Number	Tanks- in-series number
	Length (mm)	Diameter (mm)			
(Phan & Harvey, 2010)	390	7.5	4.3	64.5	26
Meso-scale in this research	336	8	5.3	62.6	29

The experimental results collected from tracer experiments were consistent with the previous studies in terms of the trend between velocity ratio vs number on tanks correlation, reactor length and plug flow performance.

7.3 Scale-up Experiments Outcome

The tube diameter was increased from 4 mm to 8 mm in order to develop a scale-up methodology. Dynamic scaling law was used to calculate the required process parameters. For example, taking reference of 1 ml/min net flow, 1 Hz oscillation frequency and 1 mm centre-to-peak oscillatory amplitude for 4 mm micro-scale reactor, in order to keep same dimensionless numbers for 8 mm reactor; amplitude increased from 1 mm to 2 mm, the frequency decreased to 0.25 Hz, and net flow increased from 1 ml/min to 2 ml/min. The residence time was kept the same for both scales.

As presented in section 5.3, a similar trend was observed in two different size reactors. Better plug flow conditions were obtained with velocity ratios between 5 and 15 in the micro and meso-scale reactors. At velocity ratios over 15, the flow becomes more asymmetric, resulting in a lower number of tanks. Also, if the velocity ratios are less than 5, poor mixing conditions were observed. Increased oscillatory numbers create chaotic flow regimes. Optimum oscillatory numbers were observed as $50 < Re_o < 150$ for both sizes. Reynolds and Strouhal numbers were independent of the plug flow conditions; there was not any clear trend.

Five design parameters (tube diameter, net flow, oscillatory amplitude and frequency and residence time) were identified for the scale-up rule. There was a correlation between these parameters and scaling factor. Once the tube diameter was increased by the factor of “x”, net flow, oscillation amplitude, and residence time also needed to be increased by the factor of “x”. On the other hand, when the flow velocity was decreased by the factor of “x”, oscillation frequency decreased by the factor of “x²” in order to maintain dynamic similarity.

Different magnitudes of the tanks-in-series number were observed between micro and meso-scale experiments by using the same dimensionless number. This is due to the diameter effect. Changes in the tube diameters result in change in the residence time. Residence time must also be considered to achieve similar magnitudes in various scales.

7.4 Nanomaterial Synthesis with Modular OBR

Synthesis of iron-based spin-crossover nanoparticles was successfully transferred from batch synthesis to the flow processing by using meso-scale flow reactor for the first time in this research. Five particle shapes (column, spherical, needle, rod and crystal) were obtained at a particle range of 100–1500 nm. Response surface methodology was performed to investigate mixing factors and chemical composition. Interaction of amplitude and frequency was the most significant processing factor over average particle size, and concentration of the triazole was the key chemical to influence particle size. A prediction model was developed to predict particle size between 100–1000 nm based on DoE results; however, the prediction model was not successful. More data points were required to develop a robust prediction model. Further studies are required to produce repeatable results each time, where five random selected experiments were repeated in different time frames, similar particle size and morphology were observed in only DoE_20, and it was repeated as shown in section 6.5.6. Sedimentation issue was observed in the four hours non-stop consistency experiments. Two reasons were concluded for the sedimentation and repeatability issues. The first issue is the non-continuous flow due to

synchronisation problem of the dual syringe-pump arrangement. In the long term running (over 2 hours), pumps started losing their synchronisation, which caused the non-continuous net flow. The second reason is prolonged net flow after the density of particles changes due to crystallisation. Some crystals become bigger, which results in precipitation at the bottom of the tube due to gravity.

Synthesis of the nanoparticles was one of the great achievements in this research. Production of uniform nanoparticles was proven using plug flow conditions in the modular OBR. These results represent a significant first step to encourage other researches to investigate the synthesis of more nanoparticles in the meso-scale flow processes.

After the successful production of SCO particles using meso-scale modular OBR, process design methodology was presented to achieve larger production capacities. Dimensionless numbers and residence time of the specific reaction are starting point to identify reactor volume and length and superficial fluid velocity inside the tube. Reactor length and net flow must be realistic for achieving process feasibility and required mixing conditions. For example, if very high Re_n was selected as a starting point in the laboratory experiments that will also require very high Re_o due to velocity ratio between Reynolds and oscillatory Reynolds numbers. It is difficult to achieve very high Re_o number with any type of oscillation mechanism, and even if it were achieved, it would not be practical in terms of cost and fluid dynamics. Low superficial velocity is also not recommended for the system. That may cause sedimentation of particles.

8 CONCLUSIONS AND SUGGESTIONS FOR FUTURE WORK

“If we knew what it was we were doing, it would not be called research, would it?”

Albert Einstein

8.1 Conclusions

In the first chapter of the thesis, a set of objectives were presented. The aim of the research was to develop a scalable, low-cost, modular continuous manufacturing platform for quick discovery and rapid production of advanced nanomaterials. Tab.8.1 shows the summary of the conclusions with referencing to each objective.

Table 8.1 Linking objectives to conclusions

	Objective	Conclusion
1	To develop a fully automated continuous oscillatory baffled reactor.	Design principles were identified for cost-effective reactor development. Based on design principles, a new version of modular OBR was developed, including better heating/cooling channels and fully automated oscillation mechanism.
2	To investigate the impact of process variables and characterize the reactor performance	Characterisation experiments were conducted based on full-factorial DoE for both scales. Tracer experiments were modelled with tanks-in-series method. The most influencing process parameters were identified using analysis of

		variance to identify the impact of each input variable.
3	To develop a systematic scale-up method from laboratory scale to industrial scales.	A scale-up methodology was developed based on dimensionless numbers, tube diameter, residence time and production volume. Multiple options were suggested for production scale-up as increasing tube diameter, increasing net flow or using parallel platforms.
4	To demonstrate the production of nanomaterials in flow and define a guideline to scale-up industrial production levels.	SCO synthesis was transferred from the batch process to flow. Screening experiments were conducted as a starting point to develop a full DoE. Five variables were used based on the response surface method. SCO nanomaterials were successfully manufactured in the flow environment in various particle size and shape. The most influencing parameters were analysed to control particle shape and size. Consistency and repeatability experiments were conducted.

A cost-effective and modular OBR was developed based on the design principles presented in this thesis. The individual and combined impact of net flow, oscillatory amplitude and frequency on plug flow performance, scale-up methodology from micro-scale to meso-scale, and advanced nanomaterial

synthesis in the continuous OBR were investigated. Tanks-in-series model was used to characterize modular micro- and meso-scale OBRs.

A novel modular design was developed to build an oscillatory baffled reactor and oscillation mechanism, including various design versions to address various application requirements. The presented design provides excellent flexibility in terms of manufacturing, cleaning, adjustable reactor length, various baffle shapes such as sharp and rounded, multiple material options, and easy assembly/disassembly. Uniform and efficient temperature control can be achieved with spherical heating/cooling channels among the entire reactor. Scotch-yoke oscillation mechanism provides perfect sinusoidal motion and its scalable to any production size. Fully automated process control was achieved by designing a lead-screw integrated Scotch-yoke oscillation mechanism. Net flow, oscillatory amplitude and frequency can be changed by using control codes without manual human interactions. The fully automated concept could lead the self-optimized processes in the labs and factories.

Significant effects of oscillation parameters were investigated for micro and meso-scale reactors in order to achieve better plug flow conditions. Amplitude was the most significant input variable for the micro scale reactor; however, the interaction between amplitude and net flow showed the most significant effect in the large-scale reactor. This confirmed the individual effect of oscillation parameters and net flow on the plug flow conditions. There was a strong correlation between velocity ratios and plug flow conditions, which indicated that the velocity ratio was the key parameter to achieve plug flow. The optimum velocity was observed between 5 to 20 for both scales. Tanks-in-series number decreased at the velocity ratios below 5 and higher than 20. Net flow did not have a significant effect on the mixing conditions, which confirmed that Re_n is a crucial dimensionless number to control the residence time and production volume. In addition, Re_o is vital to generate optimum mixing conditions. There was no clear trend between Str number and plug flow performance.

Scale-up of modular OBR was studied for 4 and 8-mm diameter reactors by conducting tracer experiments in the wide range of oscillation and net flow conditions. Dimensionless RTD measurements produced very similar flow and mixing behaviours at both scales. In conclusion, dynamic similarity law of dimensionless process numbers (Str , Re_n , Re_o and ψ) can be used to achieve similar mixing and plug conditions in any size of the reactor from lab scale to industrial production scales. Additional to dimensionless numbers, net flow, oscillatory amplitude, and frequency, reactor length must be investigated due to diameter effect. In order to achieve same tanks-in-series number for both scales, reactor length must be longer in larger diameters. A limited investigation was conducted in this study to understand the correlation between reactor length and tube diameter, according to the limited experimental result, there is a linear correlation between reactor diameter and reactor length. However, this phenomenon requires more extensive experiments for a full investigation and to develop a robust correlation between tube diameter and reactor length. In conclusion, the following steps must be followed for the modular OBR scale-up approach:

- Identify the target production volume for the larger system at the beginning.
- Identify the process parameter and dimensions for both systems, such as max and min limits of tube diameter and reactor length, net flow (residence time), oscillatory amplitude, and frequency. Identifying these parameters in the early stage will reduce the unexpected mechanical issues due to process limitations in the later stages. For example, a set of experiments can be conducted at the laboratory scale; once the system is scaled up by 10, the net flow or frequency is impossible to achieve by increasing or decreasing the corresponding parameter 10 folds. Therefore, full process parameters must be ready for all available or potentially available systems before starting the scale-up process design.
- Set a DoE to start laboratory experiments. A micro or laboratory scale modular OBR is selected, velocity ratio must be between 5 to 20.

- Identify the scaling factor for a larger system and follow the calculations presented in Chapter 6.6 to find new process parameters in the larger system.

Production of the SCO nanoparticles in flow was achieved using OBR for the first time in this research. Various forms of nanoparticles, such as column, spherical, needle, and rod, were obtained in a broad spectrum of particle sizes from 100 nm to 1500 nm. Desired particle shape or size can be manufactured by tuning the chemical composition or process conditions. DoE method was used to understand the effect of chemical composition and oscillation conditions over SCO particle size and shape. Second-order of the Iron TFB concentration was observed as the most significant variable. Interaction of the amplitude and frequency was the second most significant parameter. Pump selection is vitally crucial for repeatable experiments. The system must be steady and same at all times to achieve identical flow patterns. We observed that syringe pumps had synchronisation issue in the long term usage, which caused unrepeatable experiments. Consistency required further investigation as sedimentation was observed in the system after 3 hours of continuous DoE_14 experiments.

This study proved that OBR technology enables for quick discovery of novel nanomaterials with tailored properties in the lab scales and immediately scaling the identical lab processes to large scale industrial processes by using dynamic similarity law of corresponding process dimensionless numbers. This process will reduce the cost of nanomaterial production and energy consumption.

8.2 Future Implications

A comprehensive experimental study was presented for better understanding the impact of oscillation and net flow parameters on plug flow, mixing conditions and scale-up methodology in the modular oscillatory baffled reactor. A similar trend of RTD measurements was observed for both scales. However, few difficulties remain to be addressed. A variation was observed in the magnitude of the tanks-in-series number between two scales. This is due to the different tube diameter sizes. In order to achieve the same tanks-in-series number in different tube sizes,

reactor length must be taken into consideration additional to dimensionless numbers. Diameter effect must be considered in the future experiments, various reactor lengths versus tube diameters must be experimentally evaluated to improve the performance of the scale-up model. Initial correlation was found in the Chapter 5 with the limited experimental number. However, this correlation needs improvement with a comprehensive experimental study.

In the SCO experiments, 5 variables were used for 32 experiments. This was necessary as this study was investigated SCO synthesis in the flow first time. A further investigation could be suggested only based on process variables. The effect of each precursor was understood in this study. The optimum concentrations obtained from response surface methodology can be used for further experiments. Investigation of broad mixing conditions could improve the controlling of SCO particle size and shape. Velocity ratio must be taken into centre of new set of experiments. With the optimum velocity ratio range found in the Chapter 5, the performance of the consistency and repeatability experiments could be also improved. Sedimentation was observed in the 4 hours continuous experiment, it is suggested that potential for increasing net flow will solve the sedimentation issue.

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Appendix A : Micro and Meso Scale Reactor Characterization Experimental Parameters, Response Results and RTD Profiles

100 experiments were conducted to investigate plug flow performance using micro-scale reactor. Table.A.1 presents mixing conditions and dimensionless numbers used for the characterization experiments. As a response, TiS numbers were calculated using spectrometer data collected at the exit of the micro-scale reactor. RTD graphs are shown for all corresponding DoE experiments for the micro-scale reactor in Figures A.1 to A.4. Each graph represents a set of Re_n number of 25 experiments for better visual explanation.

Similar approach was employed for meso-scale reactor to present experimental data. Table.A.2 shows mixing conditions and dimensionless numbers used for meso-scale reactor characterization experiments based on full factorial DoE approach. As a response, TiS numbers were calculated. TiS number were calculated using tracer data for 90 of 100 experimental points. TiS numbers for 10 experiments were calculated using prediction model, these experiments are indicated with (P) character in Table.A.2. RTD profiles are shown in Figures A.5 to A.8.

Table A.1 Mixing conditions and dimensionless numbers used based on full factorial DoE for Micro-scale reactor chracterization experiments and response results

DoE Number	Amplitude (mm)	Frequency (Hz)	Net Flow (ml/min)	Str Number	Re _n N	Re _o Number	Velocity Ratio	Number of TiS	Repeated Experiment s
1	0.5	4	2	0.637	10.586	50.125	4.74	46.8	
2	2.5	2	1	0.127	5.293	125.312	23.68	8	7.5
3	1.5	4	3	0.212	15.879	150.375	9.47	28.6	
4	1	3	3	0.318	15.879	75.187	4.74	14.6	
5	1.5	5	4	0.212	21.172	187.968	8.88	16	
6	2.5	2	4	0.127	21.172	125.312	5.92	12.7	
7	1	3	2	0.318	10.586	75.187	7.10	27.2	
8	0.5	3	1	0.637	5.293	37.594	7.10	33	39
9	1.5	4	4	0.212	21.172	150.375	7.10	15	
10	2.5	4	2	0.127	10.586	250.624	23.68	11.5	12
11	2	4	1	0.159	5.293	200.500	37.88	13.8	
12	2.5	4	1	0.127	5.293	250.624	47.35	9.6	
13	1	5	3	0.318	15.879	125.312	7.89	21.3	
14	2.5	3	1	0.127	5.293	187.968	35.51	10.7	
15	0.5	2	4	0.637	21.172	25.062	1.18	20	
16	2	1	4	0.159	21.172	50.125	2.37	14.7	
17	0.5	4	3	0.637	15.879	50.125	3.16	30.3	

18	1	4	4	0.318	21.172	100.250	4.74	13.6	
19	1.5	1	4	0.212	21.172	37.594	1.78	13.9	
20	1	5	2	0.318	10.586	125.312	11.84	23.8	
21	2	3	3	0.159	15.879	150.375	9.47	14.6	
22	1	2	2	0.318	10.586	50.125	4.74	28.6	37.2
23	1	2	3	0.318	15.879	50.125	3.16	26	36
24	2.5	1	3	0.127	15.879	62.656	3.95	10	
25	2.5	2	2	0.127	10.586	125.312	11.84	12.9	
26	2.5	2	3	0.127	15.879	125.312	7.89	12	
27	2.5	3	3	0.127	15.879	187.968	11.84	13.3	
28	2	2	4	0.159	21.172	100.250	4.74	13.9	
29	1	4	2	0.318	10.586	100.250	9.47	36.4	
30	1.5	1	2	0.212	10.586	37.594	3.55	23	
31	1.5	1	1	0.212	5.293	37.594	7.10	19.2	
32	0.5	1	2	0.637	10.586	12.531	1.18	24.8	22.8
33	0.5	2	1	0.637	5.293	25.062	4.74	56	81
34	1.5	5	3	0.212	15.879	187.968	11.84	22.5	
35	2.5	3	4	0.127	21.172	187.968	8.88	7	
36	1.5	2	3	0.212	15.879	75.187	4.74	23.5	
37	1.5	2	4	0.212	21.172	75.187	3.55	12.5	
38	1	3	4	0.318	21.172	75.187	3.55	27	

39	2.5	5	3	0.127	15.879	313.280	19.73	15.6	15.2
40	2	4	2	0.159	10.586	200.500	18.94	15.2	
41	1.5	2	1	0.212	5.293	75.187	14.21	9.4	12.2
42	2.5	3	2	0.127	10.586	187.968	17.76	8.7	
43	1.5	5	1	0.212	5.293	187.968	35.51	18.2	
44	2.5	4	4	0.127	21.172	250.624	11.84	12.4	
45	2.5	5	2	0.127	10.586	313.280	29.59	14	15.5
46	0.5	2	2	0.637	10.586	25.062	2.37	21.3	
47	2	5	2	0.159	10.586	250.624	23.68	12.8	
48	2	5	1	0.159	5.293	250.624	47.35	15	
49	0.5	5	1	0.637	5.293	62.656	11.84	51	
50	2	2	2	0.159	10.586	100.250	9.47	10.3	
51	2	2	1	0.159	5.293	100.250	18.94	9.4	
52	0.5	5	4	0.637	21.172	62.656	2.96	38.1	
53	2	5	4	0.159	21.172	250.624	11.84	13.7	
54	0.5	2	3	0.637	15.879	25.062	1.58	15.9	
55	0.5	1	4	0.637	21.172	12.531	0.59	13.5	13.6
56	1	3	1	0.318	5.293	75.187	14.21	24.5	
57	1.5	4	1	0.212	5.293	150.375	28.41	14.5	
58	1	5	4	0.318	21.172	125.312	5.92	24.6	
59	0.5	1	3	0.637	15.879	12.531	0.79	18.7	17.2

60	1.5	4	2	0.212	10.586	150.375	14.21	27.7	
61	1	1	2	0.318	10.586	25.062	2.37	43.2	
62	1	1	1	0.318	5.293	25.062	4.74	38.9	
63	1	2	1	0.318	5.293	50.125	9.47	24.7	
64	1.5	3	3	0.212	15.879	112.781	7.10	23.3	26.7
65	1	5	1	0.318	5.293	125.312	23.68	16.5	
66	1.5	3	1	0.212	5.293	112.781	21.31	13.3	
67	2.5	5	1	0.127	5.293	313.280	59.19	7.8	8.4
68	2	3	1	0.159	5.293	150.375	28.41	12.7	
69	0.5	5	3	0.637	15.879	62.656	3.95	30.6	
70	1	4	1	0.318	5.293	100.250	18.94	26	
71	2	5	3	0.159	15.879	250.624	15.78	17.4	
72	1.5	1	3	0.212	15.879	37.594	2.37	26.4	
73	2	1	3	0.159	15.879	50.125	3.16	16.2	
74	0.5	3	4	0.637	21.172	37.594	1.78	27.6	
75	2	1	1	0.159	5.293	50.125	9.47	9.4	
76	0.5	3	3	0.637	15.879	37.594	2.37	27.3	
77	1.5	5	2	0.212	10.586	187.968	17.76	27.7	
78	1.5	3	2	0.212	10.586	112.781	10.65	26.5	27.4
79	2	3	2	0.159	10.586	150.375	14.21	21.6	
80	2	3	4	0.159	21.172	150.375	7.10	15.1	

81	1	1	3	0.318	15.879	25.062	1.58	14.7	
82	0.5	1	1	0.637	5.293	12.531	2.37	32	
83	1.5	2	2	0.212	10.586	75.187	7.10	26.6	
84	2.5	5	4	0.127	21.172	313.280	14.80	17	18.6
85	2.5	1	4	0.127	21.172	62.656	2.96	13.6	
86	2	4	3	0.159	15.879	200.500	12.63	18.6	19.6
87	2	1	2	0.159	10.586	50.125	4.74	15.5	
88	1	4	3	0.318	15.879	100.250	6.31	39.2	
89	2.5	1	2	0.127	10.586	62.656	5.92	9.9	
90	1	1	4	0.318	21.172	25.062	1.18	22	
91	0.5	5	2	0.637	10.586	62.656	5.92	38.9	
92	2.5	4	3	0.127	15.879	250.624	15.78	17	
93	2	2	3	0.159	15.879	100.250	6.31	17	
94	1.5	3	4	0.212	21.172	112.781	5.33	26.3	31.5
95	1	2	4	0.318	21.172	50.125	2.37	35.1	43.4
96	0.5	4	1	0.637	5.293	50.125	9.47	43	
97	0.5	3	2	0.637	10.586	37.594	3.55	30	
98	2	4	4	0.159	21.172	200.500	9.47	18.4	23.2
99	0.5	4	4	0.637	21.172	50.125	2.37	36.5	
100	2.5	1	1	0.127	5.293	62.656	11.84	7.5	

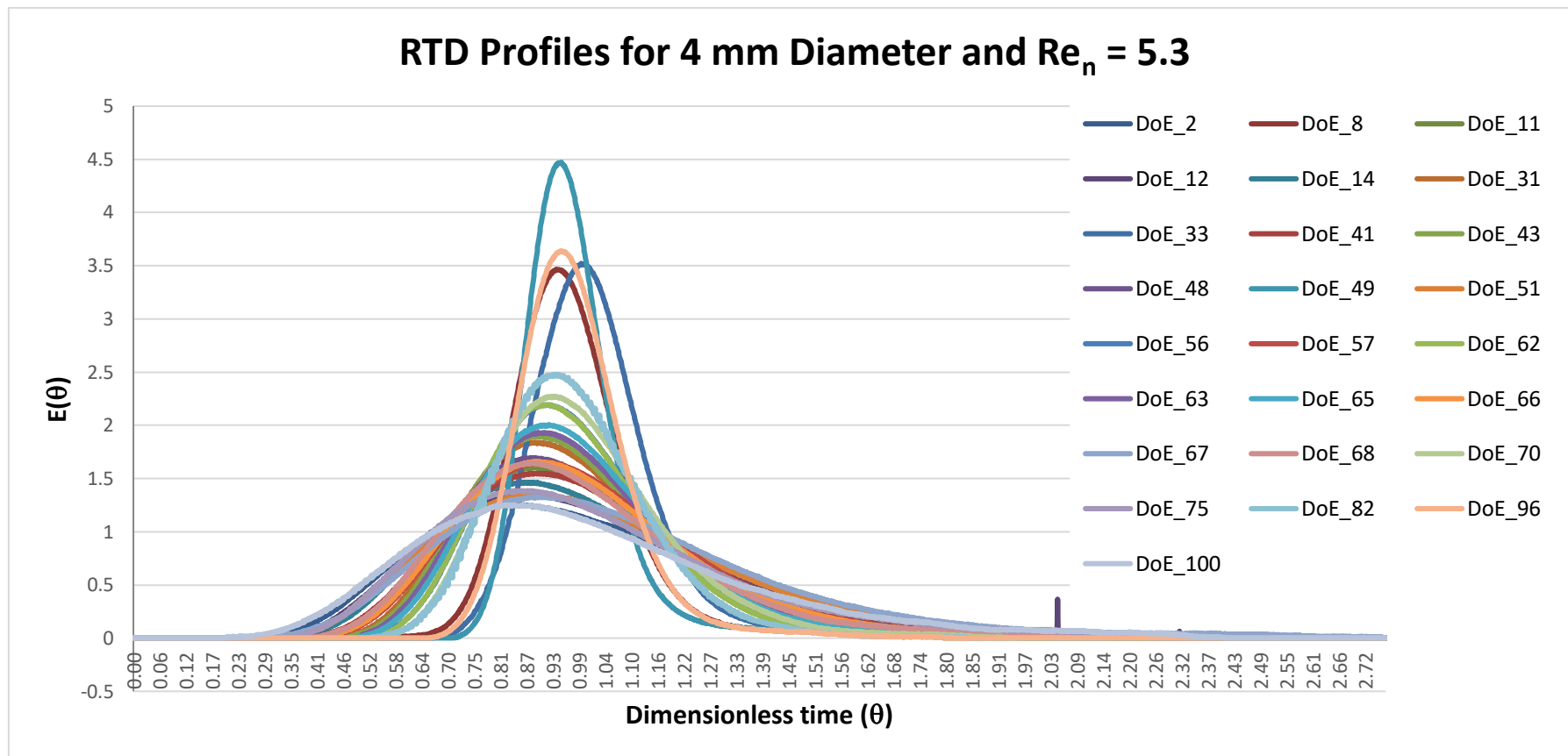


Figure A.1 RTD profiles for micro scale Reactor at $Re_n = 5.3$

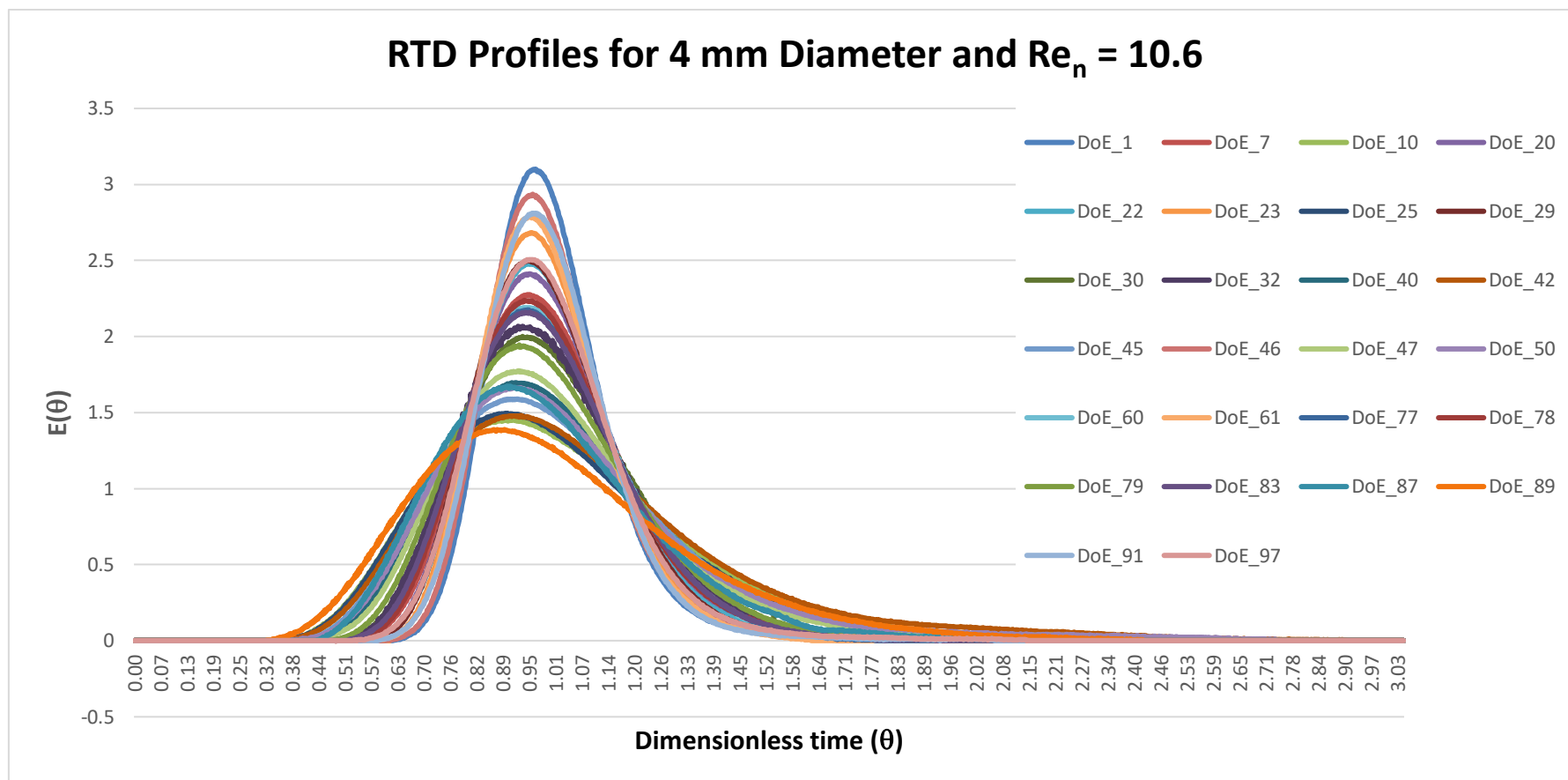


Figure A.2 RTD profiles for micro scale Reactor at $Re_n = 10.6$

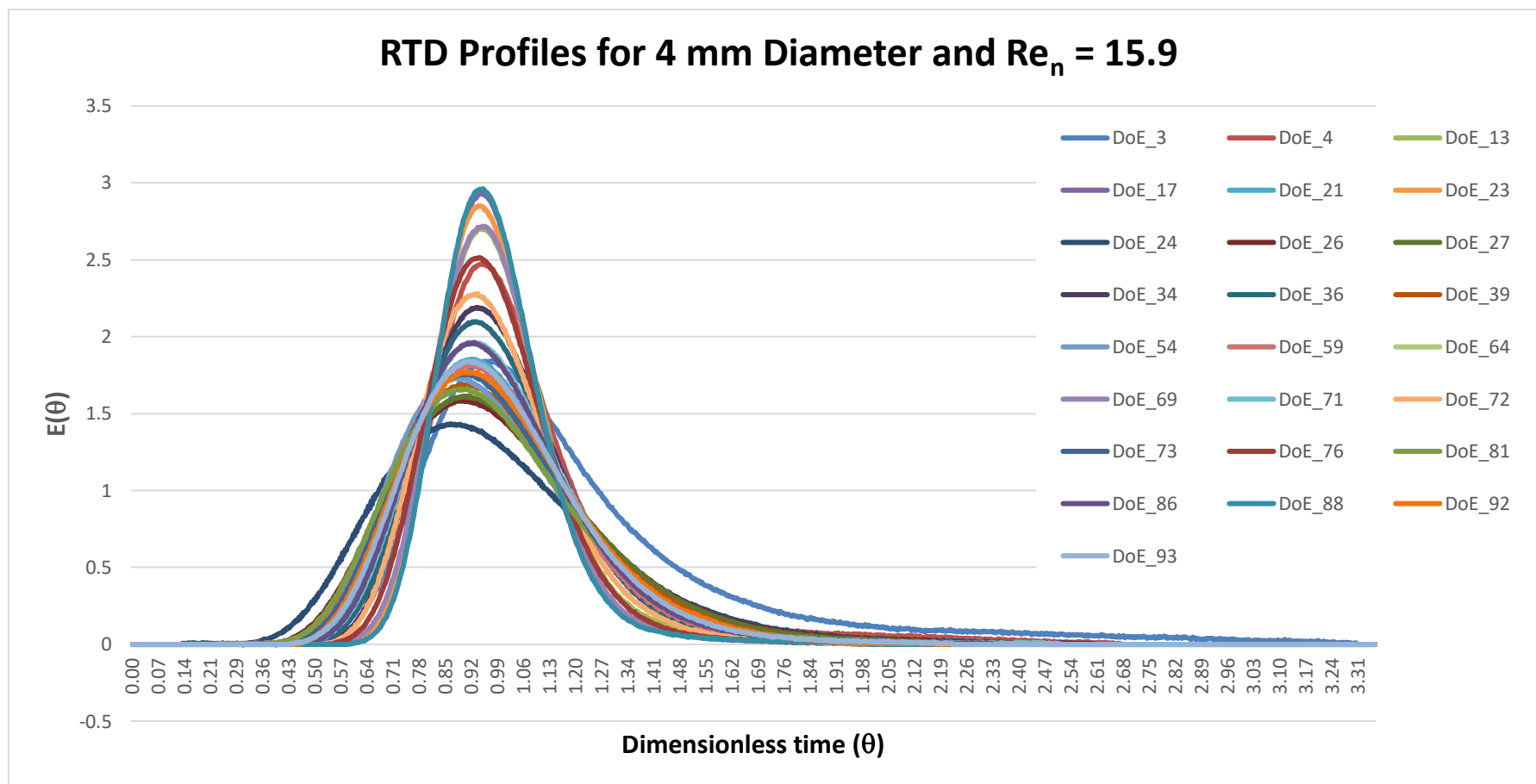


Figure A.3 RTD profiles for micro scale Reactor at $Re_n = 15.9$

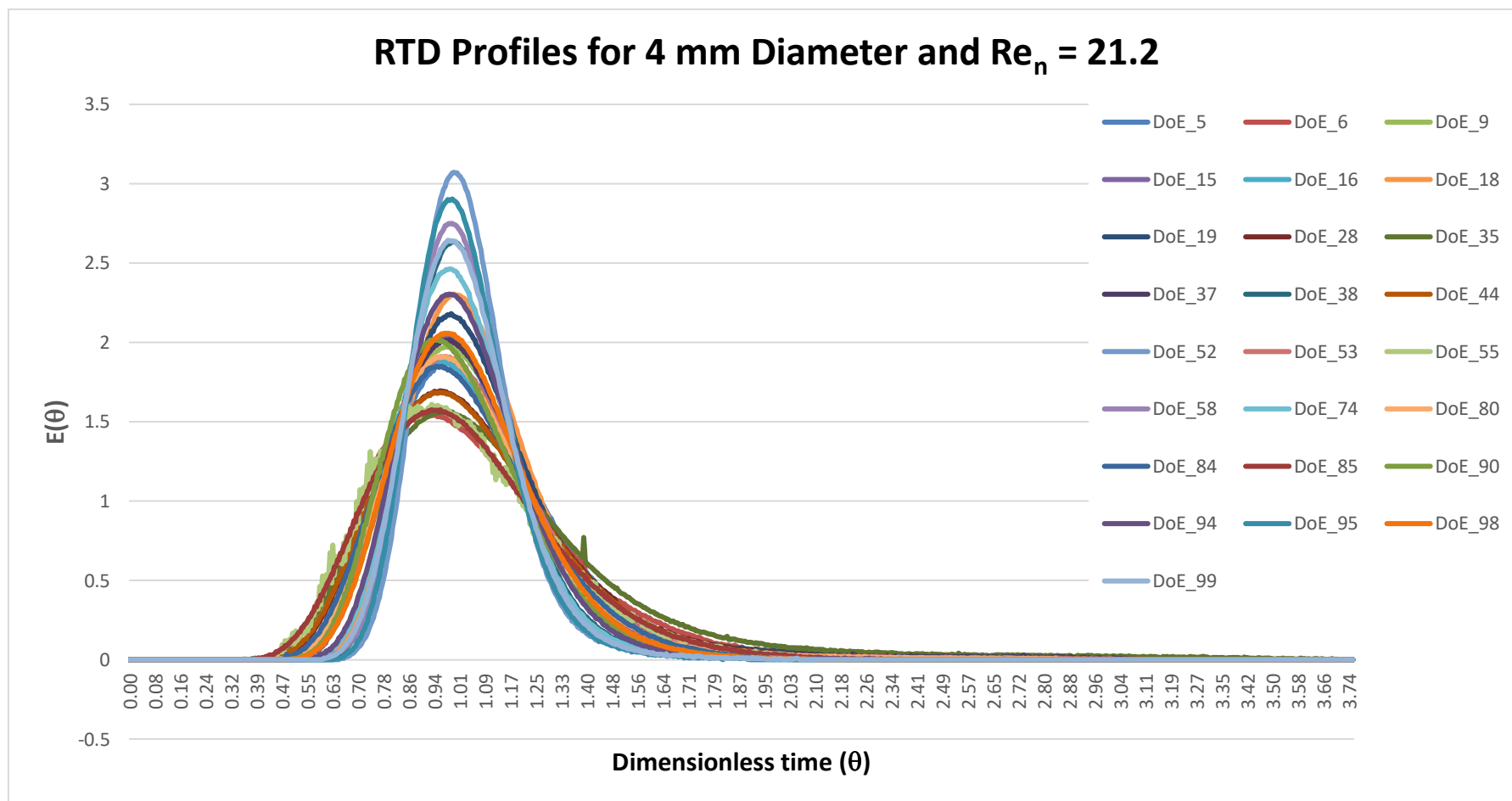


Figure A.4 RTD profiles for micro scale Reactor at $Re_n = 21.2$

Table A.2 Mixing conditions and dimensionless numbers used based on full factorial DoE for meso-scale reactor characterization experiments and response results

DoE Number	Amplitude (mm)	Frequency (Hz)	Net Flow (ml/min)	Str Number	Re_n Numbers	Re_o Numbers	Velocity Ratio	Number of TiS	Repeated Experiments
1	5	0.5	4	0.127	10.594	125.312	11.83	6	
2	2	0.75	8	0.318	21.189	75.187	3.55	22.6	
3	3	0.25	2	0.212	5.297	37.594	7.10	6.45	
4	1	0.25	6	0.637	15.892	12.531	0.79	6.6	
5	1	0.75	8	0.637	21.189	37.594	1.77	6.3	
6	4	0.25	8	0.159	21.189	50.125	2.37	10.3	
7	1	0.75	2	0.637	5.297	37.594	7.10	27.7	
8	4	0.75	4	0.159	10.594	150.375	14.19	6.2	
9	3	1	8	0.212	21.189	150.375	7.10	29.2	13,6
10	3	1.25	2	0.212	5.297	187.968	35.48	18.84	
11	1	0.5	2	0.637	5.297	25.062	4.73	17.43	
12	3	0.75	4	0.212	10.594	112.781	10.65	14	
13	4	0.25	2	0.159	5.297	50.125	9.46	5.3 (P)	
14	3	0.5	8	0.212	21.189	75.187	3.55	14	
15	1	0.25	8	0.637	21.189	12.531	0.59	5	
16	2	0.25	2	0.318	5.297	25.062	4.73	13.4	13.94
17	2	1.25	8	0.318	21.189	125.312	5.91	10.5	22.4
18	4	0.5	2	0.159	5.297	100.250	18.92	5.34 (P)	
19	5	0.75	6	0.127	15.892	187.968	11.83	8.8	
20	4	1	2	0.159	5.297	200.500	37.85	5.45 (P)	
21	1	0.75	6	0.637	15.892	37.594	2.37	7.1	
22	3	0.25	4	0.212	10.594	37.594	3.55	10.2	
23	4	1	8	0.159	21.189	200.500	9.46	19	

24	5	0.5	8	0.127	21.189	125.312	5.91	10.8	
25	4	0.25	6	0.159	15.892	50.125	3.15	10.8	
26	5	1.25	6	0.127	15.892	313.280	19.71	5.9	
27	1	0.5	8	0.637	21.189	25.062	1.18	7	
28	1	1.25	2	0.637	5.297	62.656	11.83	28.96	
29	2	1	2	0.318	5.297	100.250	18.92	21.5	21.46
30	3	0.5	6	0.212	15.892	75.187	4.73	11.7	
31	2	0.25	8	0.318	21.189	25.062	1.18	8.5	
32	2	0.75	2	0.318	5.297	75.187	14.19	10.8	
33	3	0.5	2	0.212	5.297	75.187	14.19	4.44	
34	5	1.25	2	0.127	5.297	313.280	59.14	2.11 (P)	
35	4	0.75	8	0.159	21.189	150.375	7.10	14.8	
36	3	0.75	6	0.212	15.892	112.781	7.10	9.4	
37	3	0.75	2	0.212	5.297	112.781	21.29	4.48	
38	5	0.75	2	0.127	5.297	187.968	35.48	2.42 (P)	
39	1	0.5	4	0.637	10.594	25.062	2.37	5.1	
40	4	1.25	4	0.159	10.594	250.624	23.66	18.9	
41	3	0.5	4	0.212	10.594	75.187	7.10	10.4	
42	3	1.25	8	0.212	21.189	187.968	8.87	20	
43	5	1	4	0.127	10.594	250.624	23.66	4.5	
44	1	1.25	6	0.637	15.892	62.656	3.94	11.4	
45	4	1.25	2	0.159	5.297	250.624	47.31	5.51 (P)	
46	2	1.25	6	0.318	15.892	125.312	7.89	22.3	
47	1	0.25	2	0.637	5.297	12.531	2.37	5.46	
48	2	0.5	8	0.318	21.189	50.125	2.37	17.8	
49	4	0.5	6	0.159	15.892	100.250	6.31	8.9	
50	5	1	6	0.127	15.892	250.624	15.77	8.5	
51	3	1	4	0.212	10.594	150.375	14.19	23.4	22.3

52	5	0.75	8	0.127	21.189	187.968	8.87	13.4	
53	2	0.5	2	0.318	5.297	50.125	9.46	10.2	
54	5	0.25	2	0.127	5.297	62.656	11.83	4.11 (P)	
55	1	1.25	4	0.637	10.594	62.656	5.91	16.6	
56	3	0.25	8	0.212	21.189	37.594	1.77	9.4	11.4
57	4	0.75	6	0.159	15.892	150.375	9.46	7.3	
58	1	0.25	4	0.637	10.594	12.531	1.18	6.7	
59	2	0.5	4	0.318	10.594	50.125	4.73	12.4	
60	3	1	2	0.212	5.297	150.375	28.39	9.03	
61	4	1	6	0.159	15.892	200.500	12.62	6.7	7.11
62	1	1	4	0.637	10.594	50.125	4.73	15.3	14.7
63	4	0.5	8	0.159	21.189	100.250	4.73	11.2	
64	5	0.25	4	0.127	10.594	62.656	5.91	6.9	
65	5	0.75	4	0.127	10.594	187.968	17.74	4.7	
66	1	1.25	8	0.637	21.189	62.656	2.96	10.6	
67	4	1.25	8	0.159	21.189	250.624	11.83	19	
68	1	1	6	0.637	15.892	50.125	3.15	10	10.5
69	2	1	8	0.318	21.189	100.250	4.73	23.4	
70	2	0.75	4	0.318	10.594	75.187	7.10	9.7	
71	5	0.25	8	0.127	21.189	62.656	2.96	10.1	
72	5	1.25	4	0.127	10.594	313.280	29.57	4.4	
73	3	0.25	6	0.212	15.892	37.594	2.37	12.9	
74	2	0.25	6	0.318	15.892	25.062	1.58	7.2	
75	1	0.75	4	0.637	10.594	37.594	3.55	9.3	
76	1	1	8	0.637	21.189	50.125	2.37	8.7	8.7
77	3	1.25	6	0.212	15.892	187.968	11.83	14.5	
78	5	0.25	6	0.127	15.892	62.656	3.94	4.5	
79	2	1.25	4	0.318	10.594	125.312	11.83	18.3	

80	2	1.25	2	0.318	5.297	125.312	23.66	25.1	
81	3	0.75	8	0.212	21.189	112.781	5.32	11.7	
82	4	1.25	6	0.159	15.892	250.624	15.77	6.6	
83	5	0.5	2	0.127	5.297	125.312	23.66	2.93 (P)	
84	4	0.75	2	0.159	5.297	150.375	28.39	5.4 (P)	
85	5	1	2	0.127	5.297	250.624	47.31	2.15 (P)	
86	2	1	6	0.318	15.892	100.250	6.31	21.2	23.6
87	5	0.5	6	0.127	15.892	125.312	7.89	8.4	
88	5	1.25	8	0.127	21.189	313.280	14.79	19	
89	4	0.5	4	0.159	10.594	100.250	9.46	6.6	
90	1	1	2	0.637	5.297	50.125	9.46	30.02	28.22
91	4	0.25	4	0.159	10.594	50.125	4.73	8.6	
92	2	0.75	6	0.318	15.892	75.187	4.73	19.4	
93	2	0.25	4	0.318	10.594	25.062	2.37	10.4	
94	4	1	4	0.159	10.594	200.500	18.92	8.3	
95	3	1	6	0.212	15.892	150.375	9.46	8.8	16.2
96	2	1	4	0.318	10.594	100.250	9.46	18.5	11.5
97	2	0.5	6	0.318	15.892	50.125	3.15	17.6	
98	3	1.25	4	0.212	10.594	187.968	17.74	21.4	
99	1	0.5	6	0.637	15.892	25.062	1.58	6.7	
100	5	1	8	0.127	21.189	250.624	11.83	22	

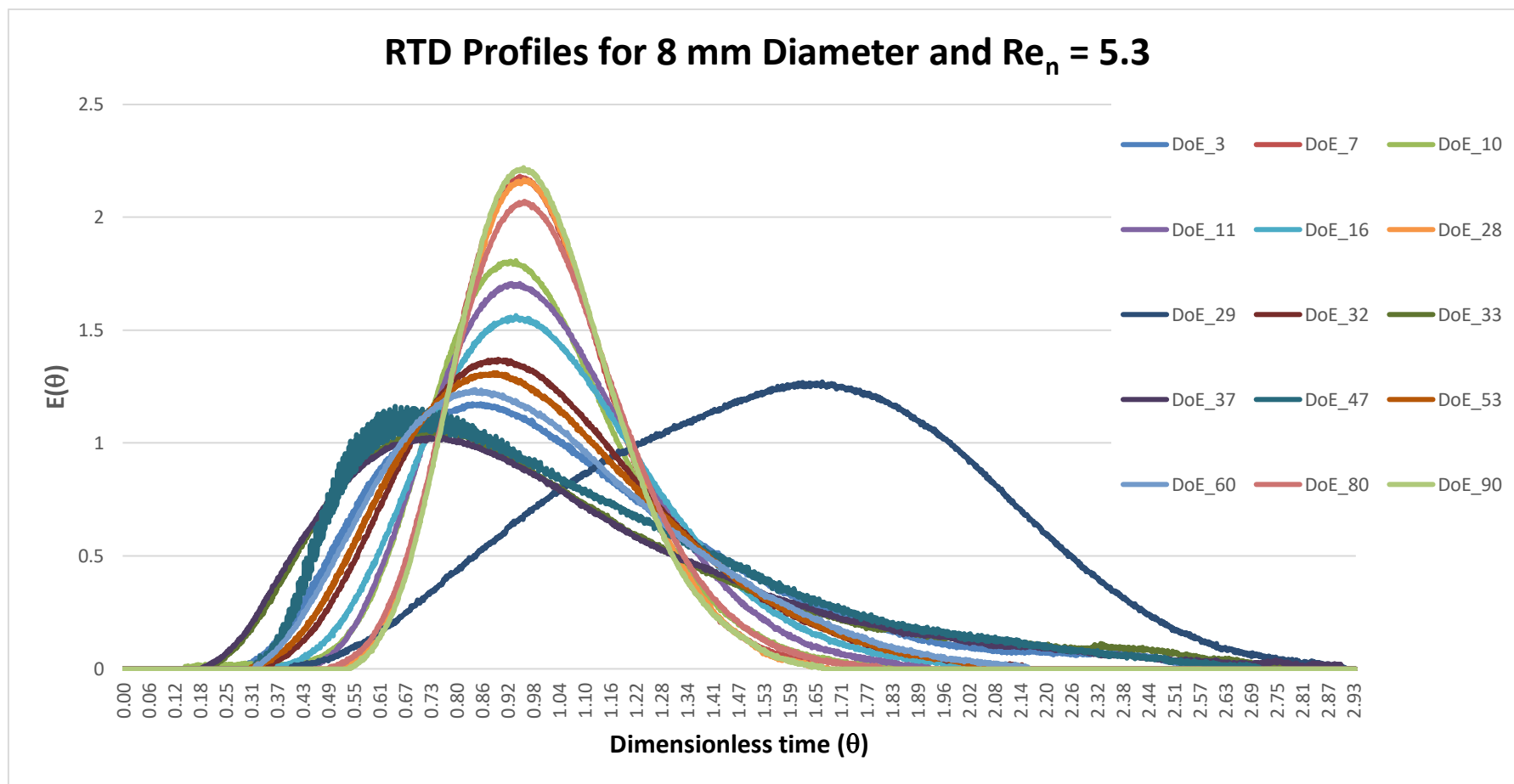


Figure A.5 RTD profiles for meso-scale reactor at $Re_n = 5.3$

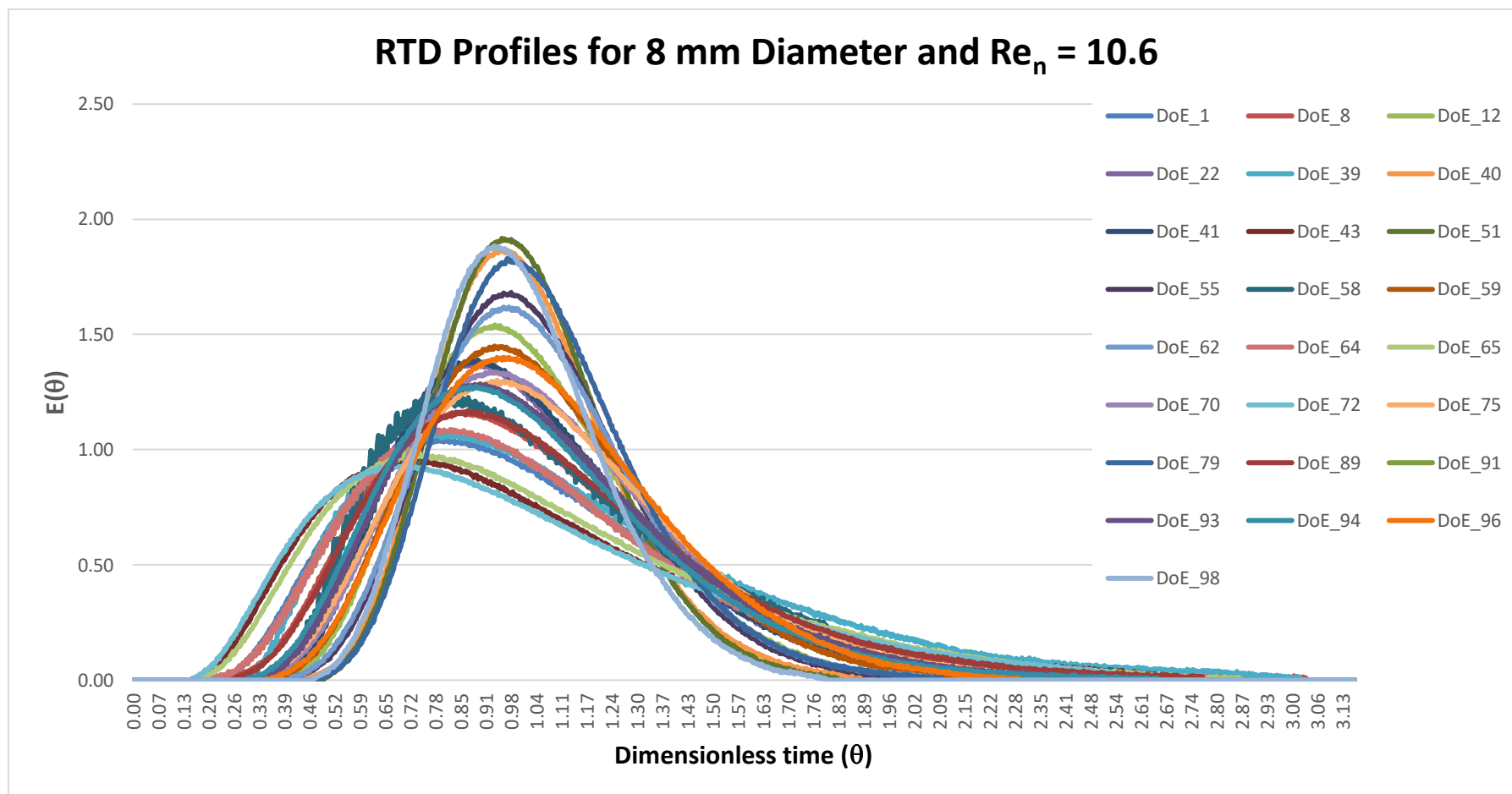


Figure A.6 RTD profiles for meso-scale reactor at $Re_n = 10.6$

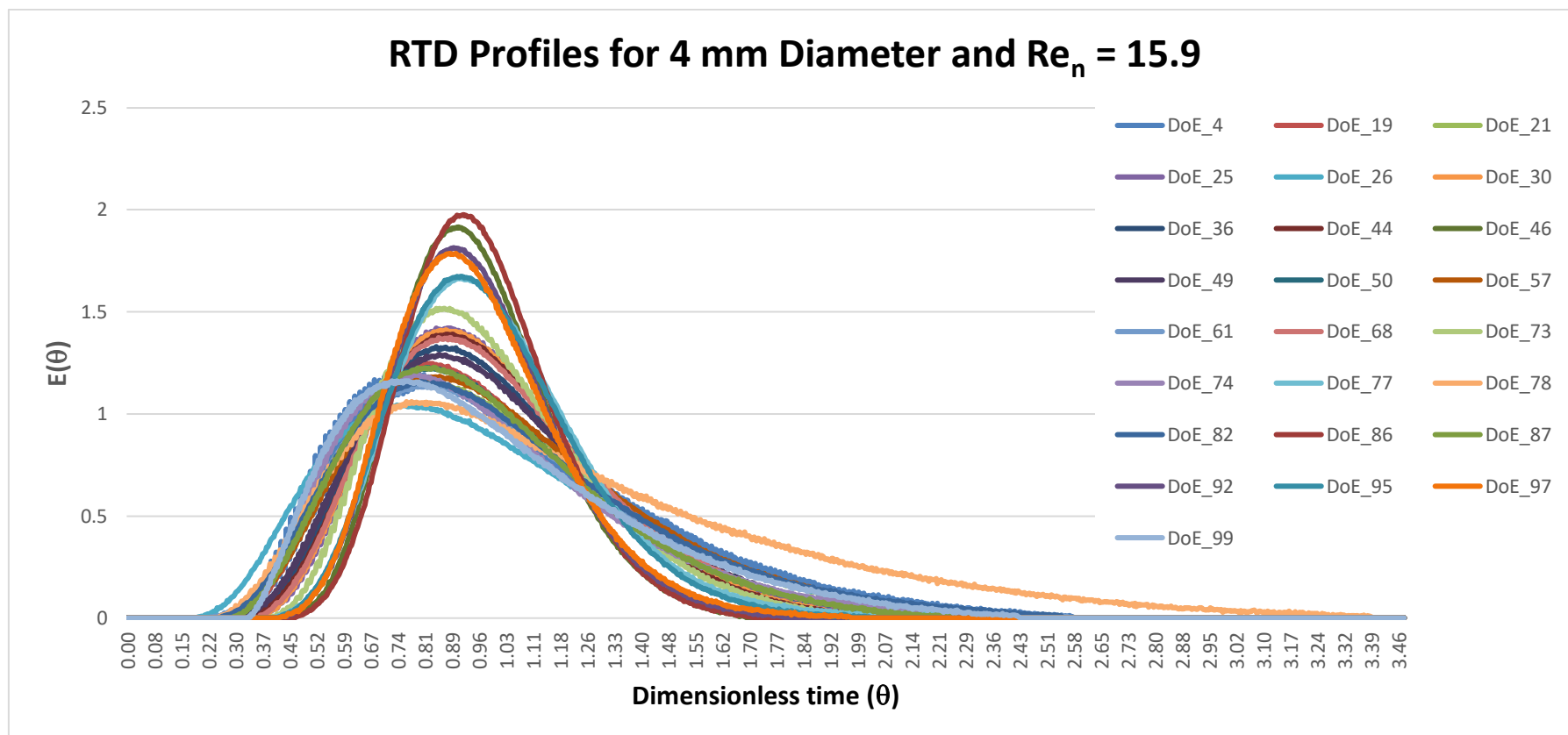


Figure A.7 RTD profiles for meso-scale reactor at $Re_n = 15.9$

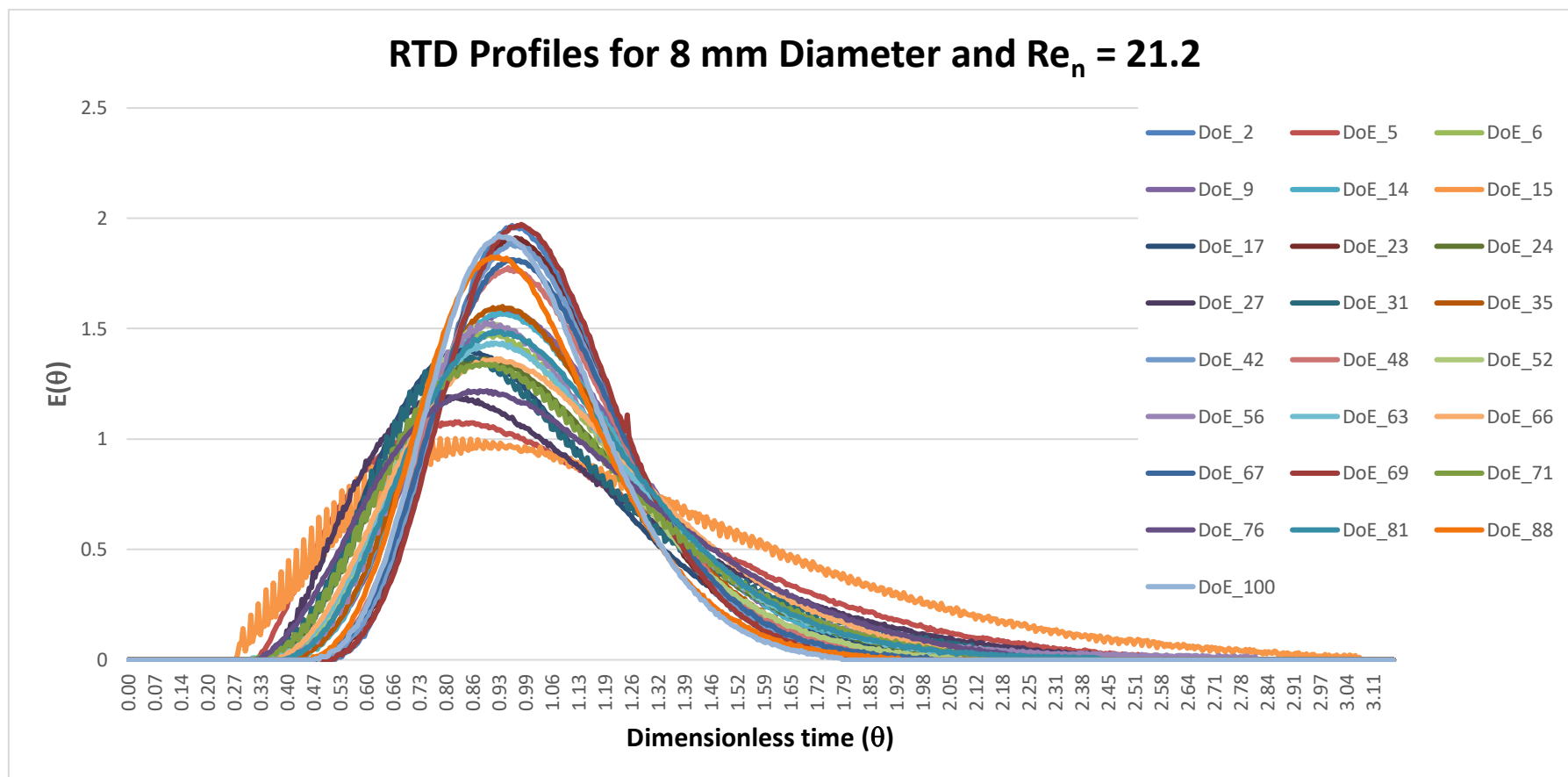


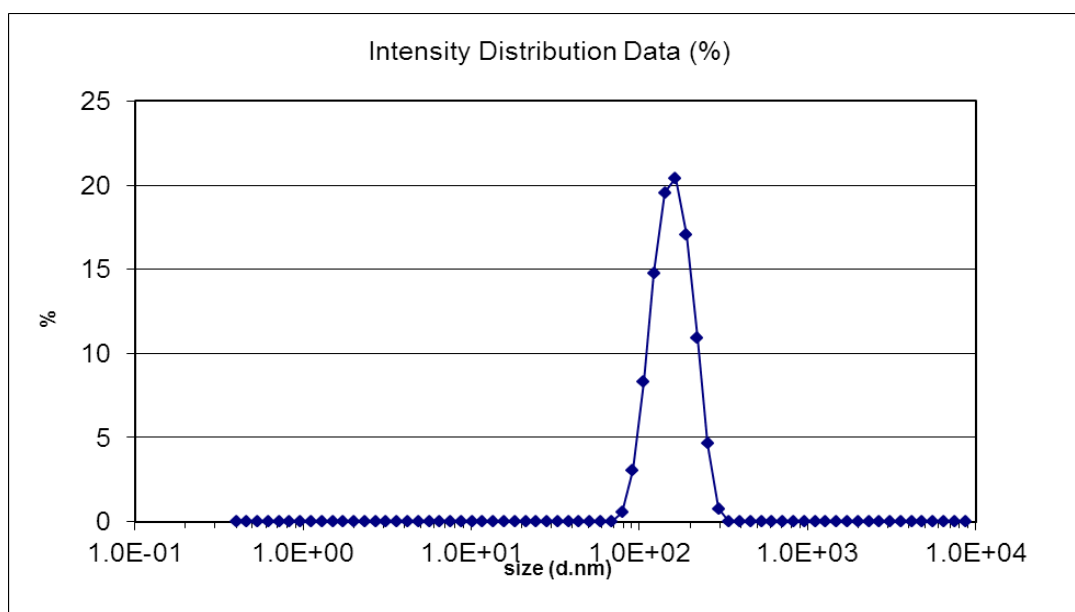
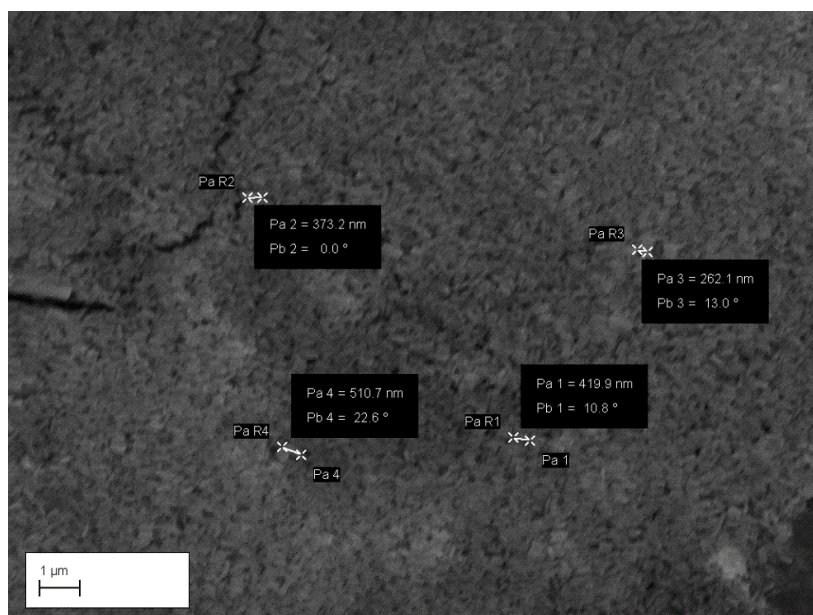
Figure A.8 RTD profiles for meso-scale reactor at $Re_n = 21.2$

Appendix B : DoE Experiment Setup Parameters for SCO Synthesis and SEM and DLS Results

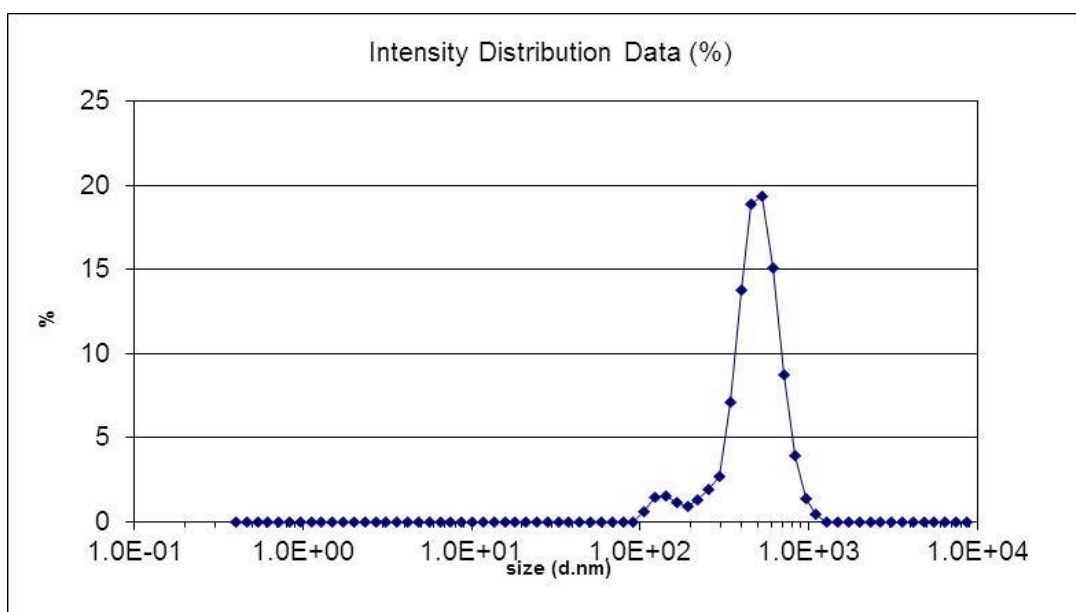
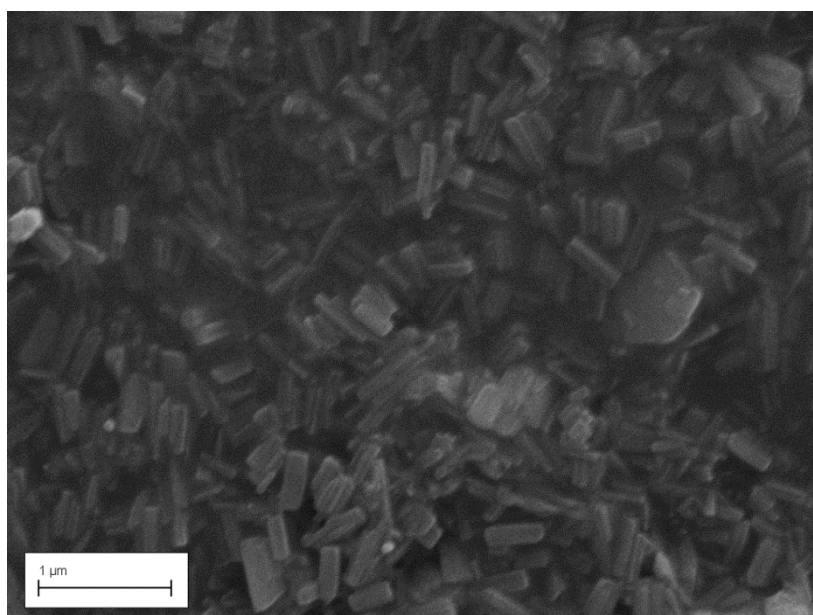
SCO experimental data are presented in pages 192 to 223. Each page represents one experimental point. 32 experiments were created based on response surface method to investigate SCO processing in continuous OBR platform.

Chemical compositions, mixing conditions, dimensionless numbers and response measurements as particle shape and size are given in the table for each corresponding DoE number. The table was followed by a DLS graph to show average particle size measurement of each experiment. And finally, SEM images were included to present particle shapes obtained from each experiment.

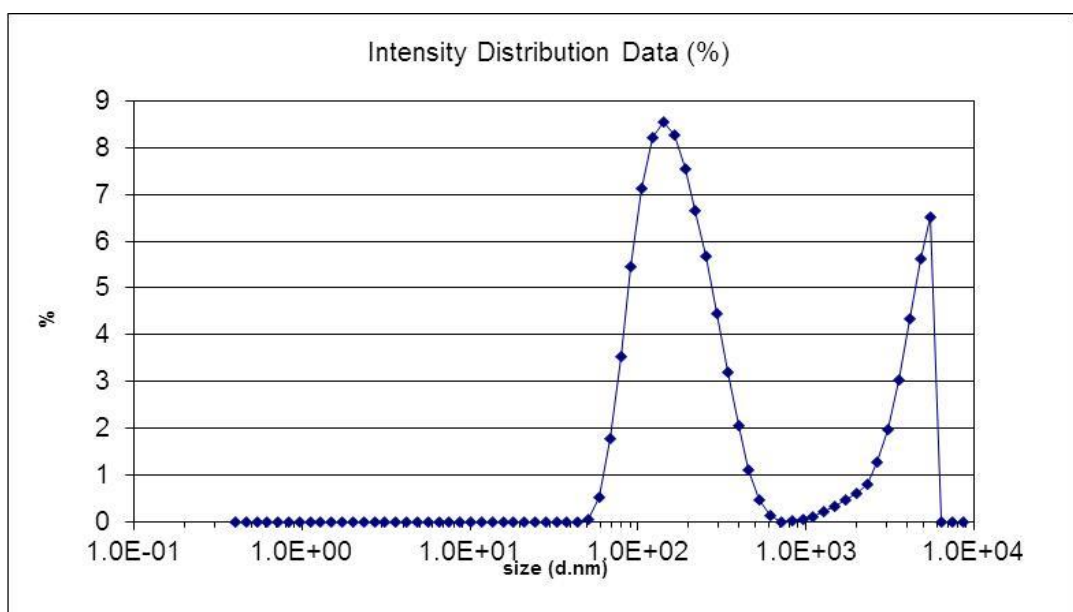
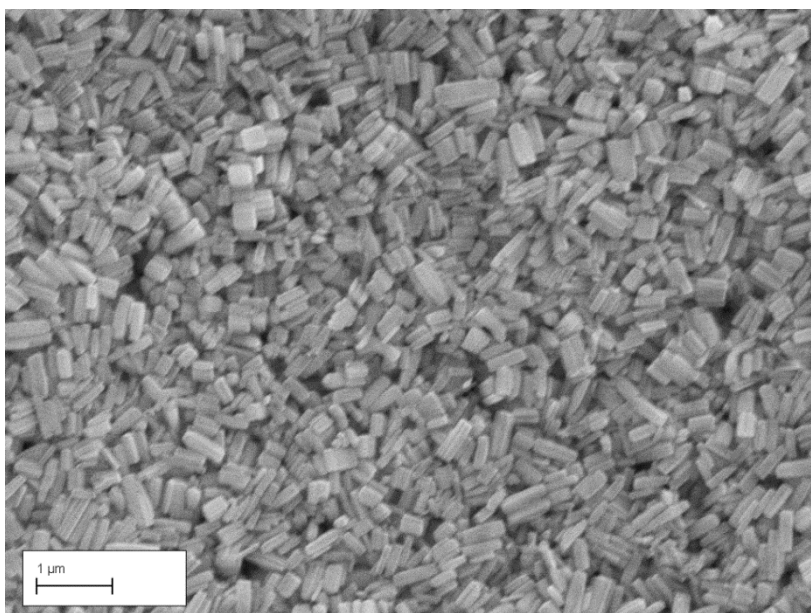
Experiment Number		1		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		337.7	106.5
Results				
APS (nm)			Particle Shape	
161.8			Spherical-shaped	



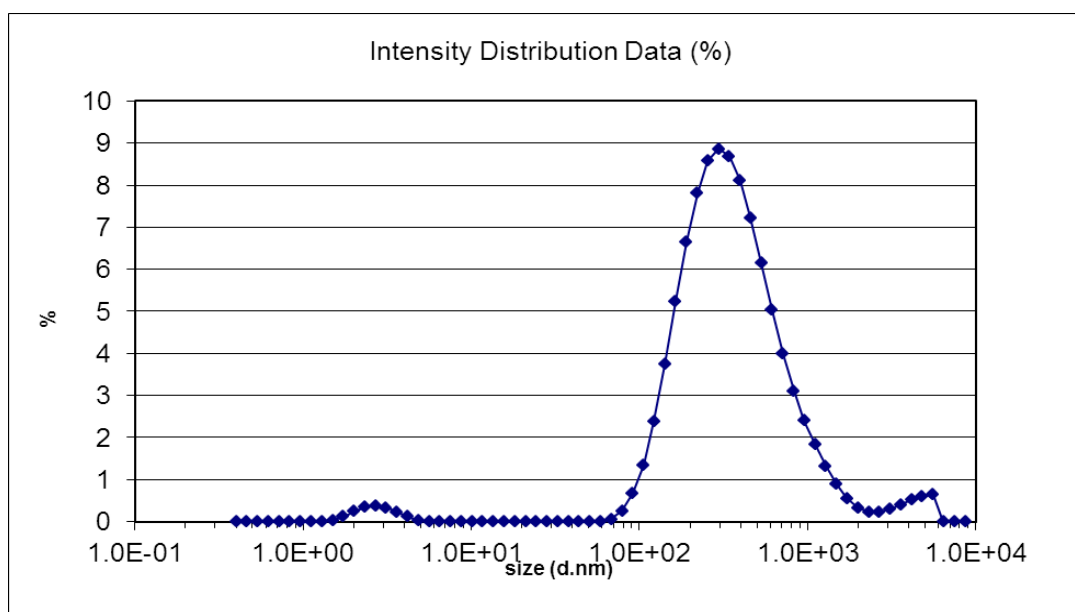
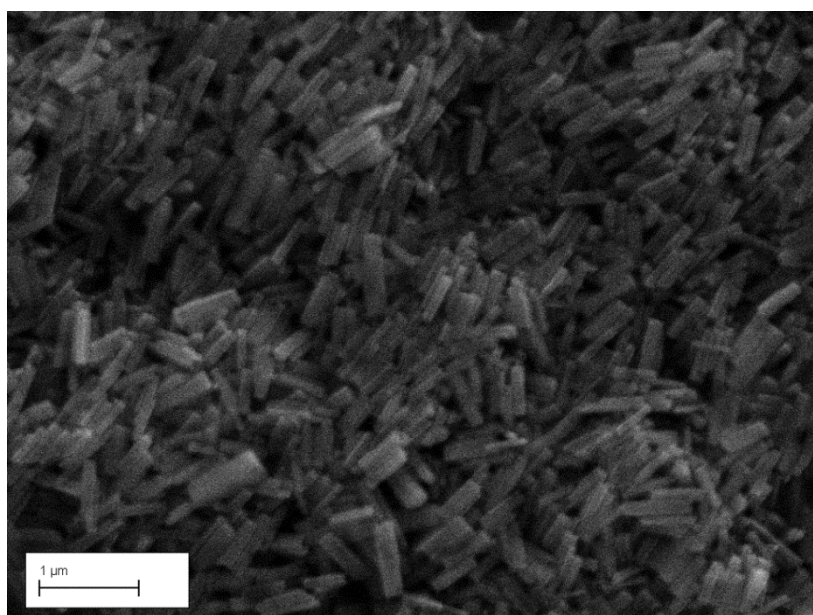
Experiment Number		2		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
02.25	5	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.127	3.17		562.83	177.5
Results				
APS (nm)			Particle Shape	
496.7			Column-shaped	



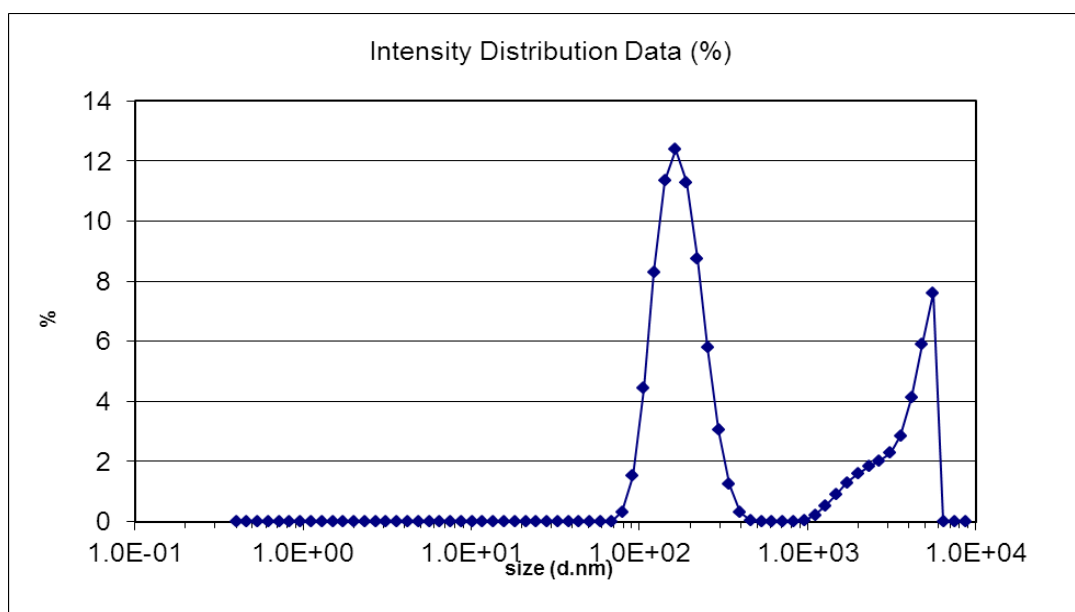
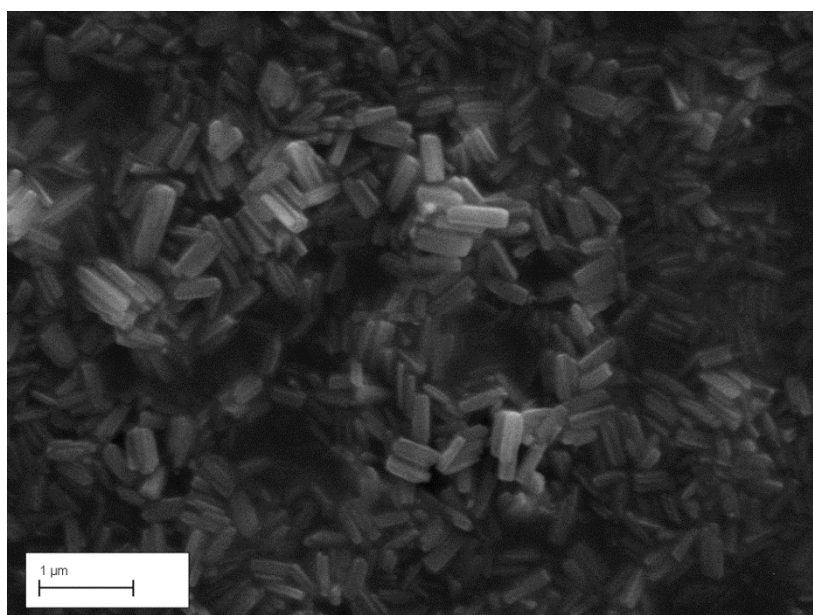
Experiment Number		3		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	2	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.318	3.17		225.13	71
Results				
APS (nm)			Particle Shape	
182.7			Spherical-shaped	



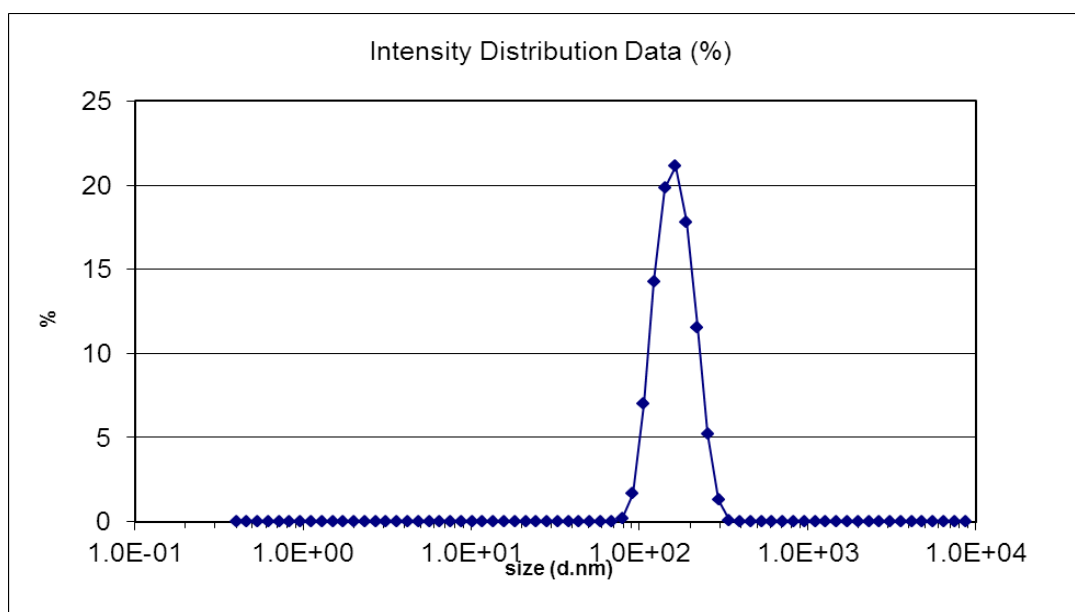
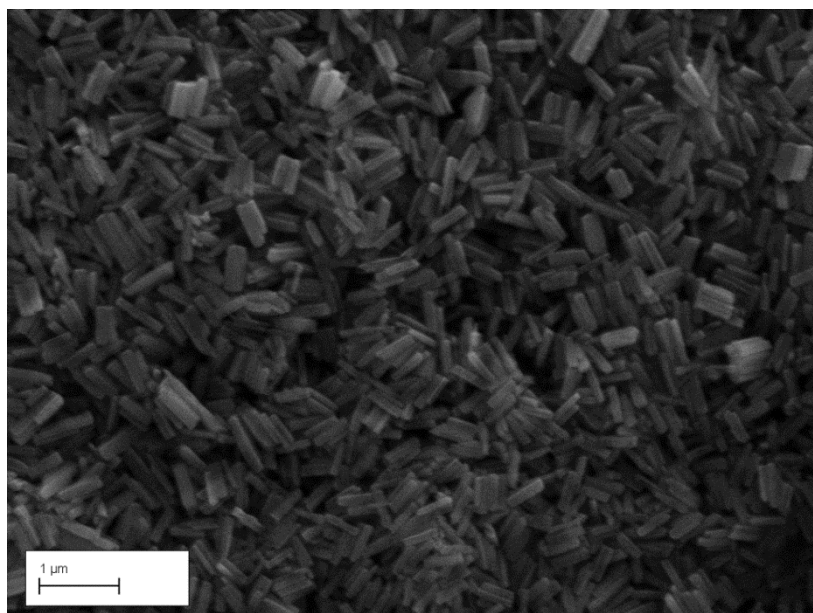
Experiment Number		4		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	26	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	1.69		337.7	199.8
Results				
APS (nm)			Particle Shape	
429			Column-shaped	



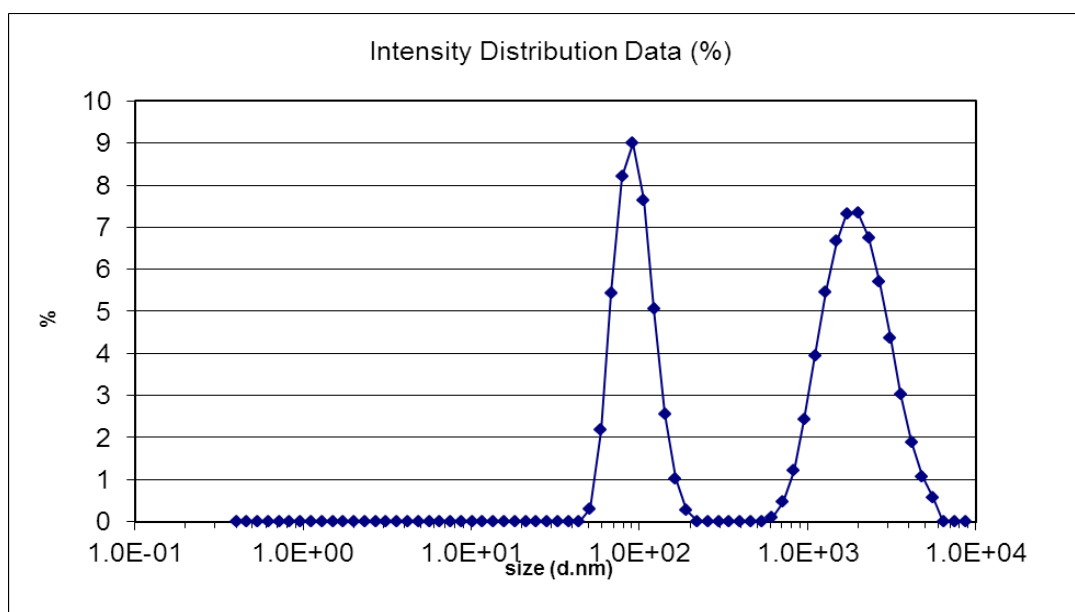
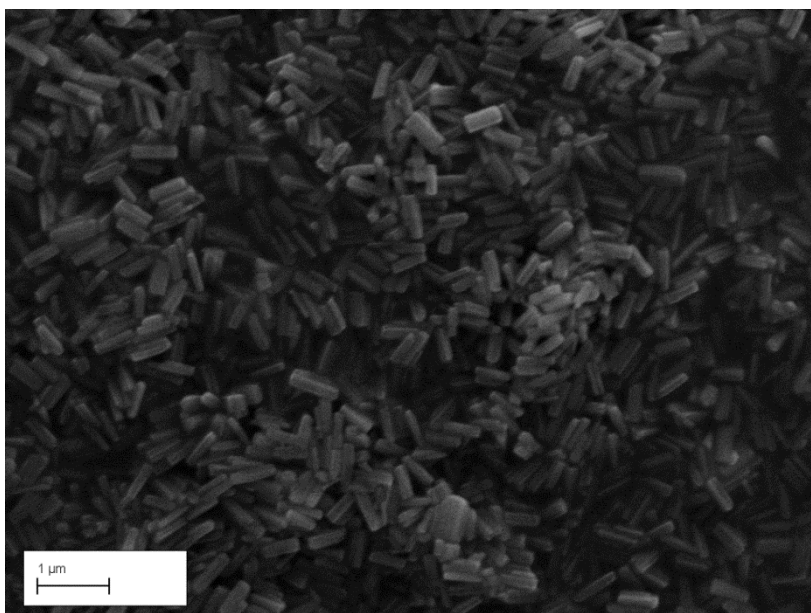
Experiment Number		5		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		337.7	105.2
Results				
APS (nm)			Particle Shape	
179			Column-shaped	



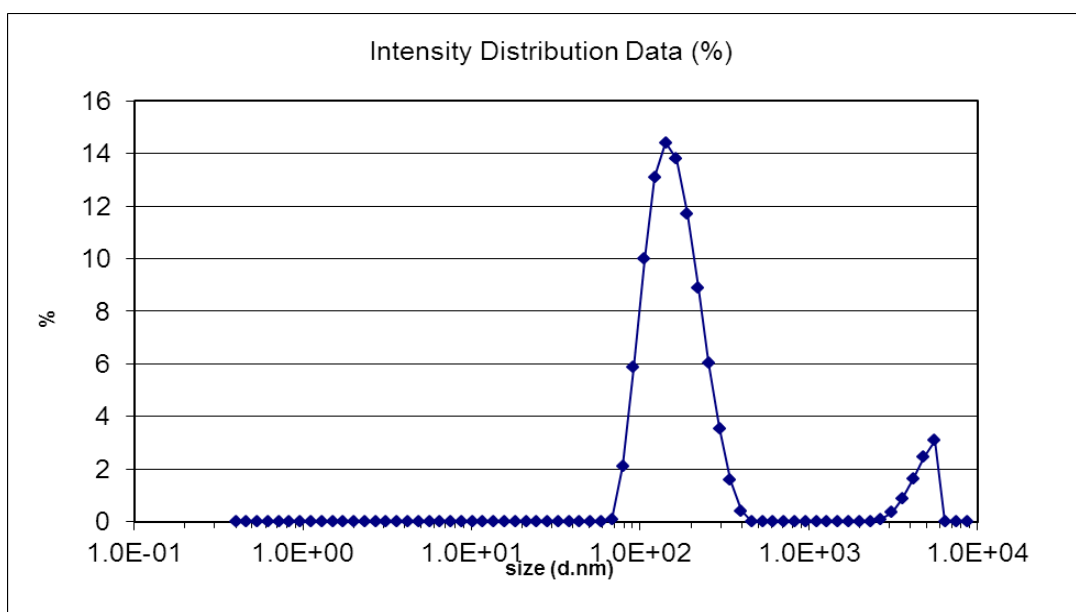
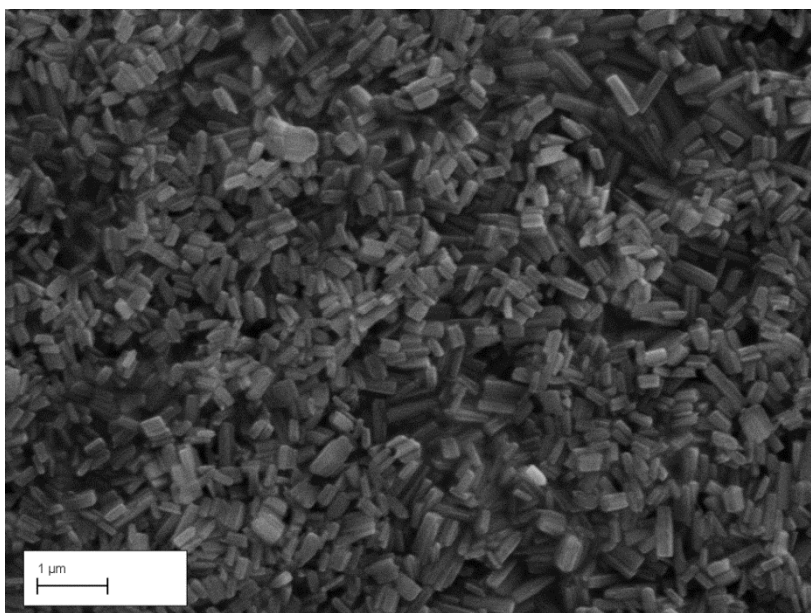
Experiment Number		6		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
5.75	3	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		863	272.2
Results				
APS (nm)			Particle She	
166			Column-shaped	



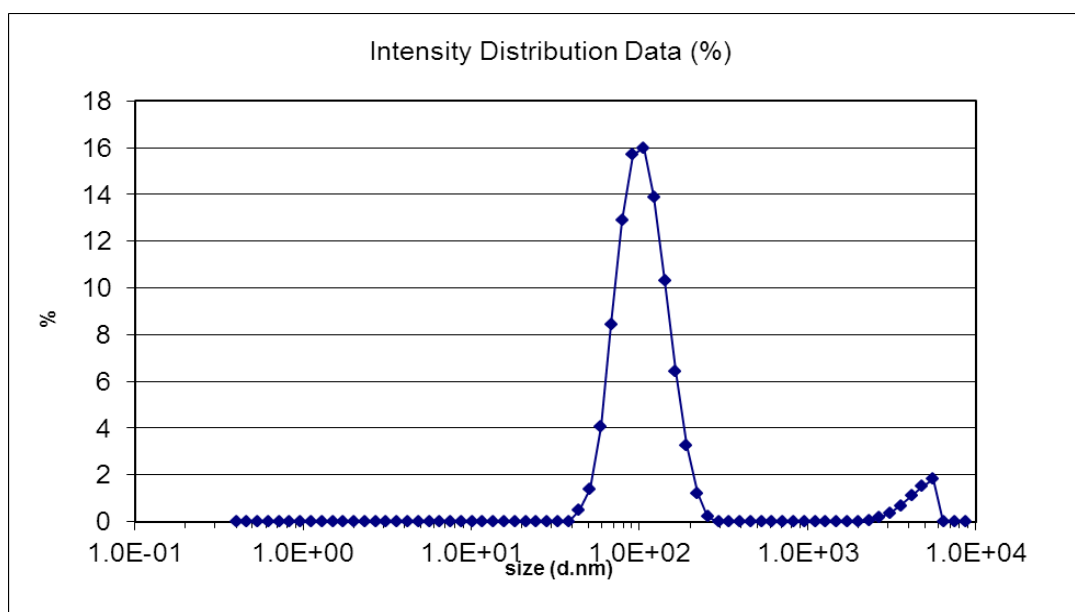
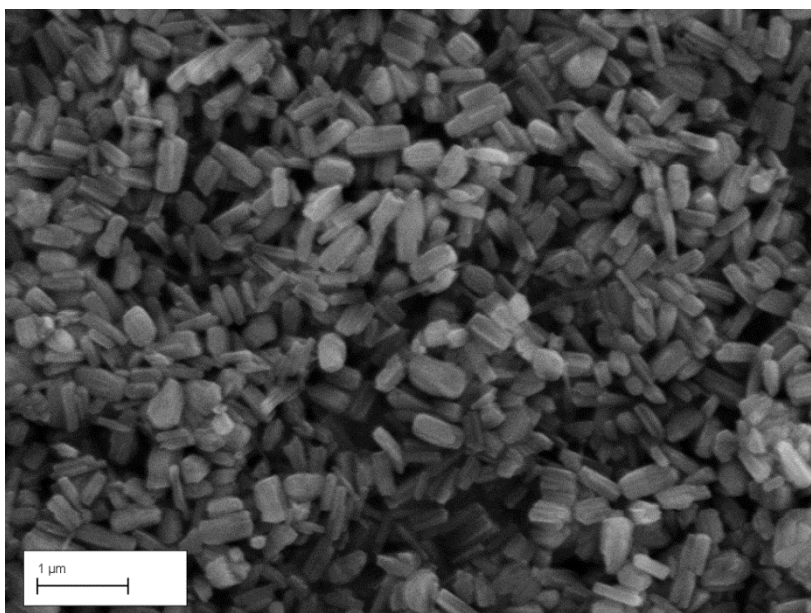
Experiment Number		7		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
1.25	3	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		187.6	59.2
Results				
APS (nm)			Particle Shape	
95.8			Column-shaped	



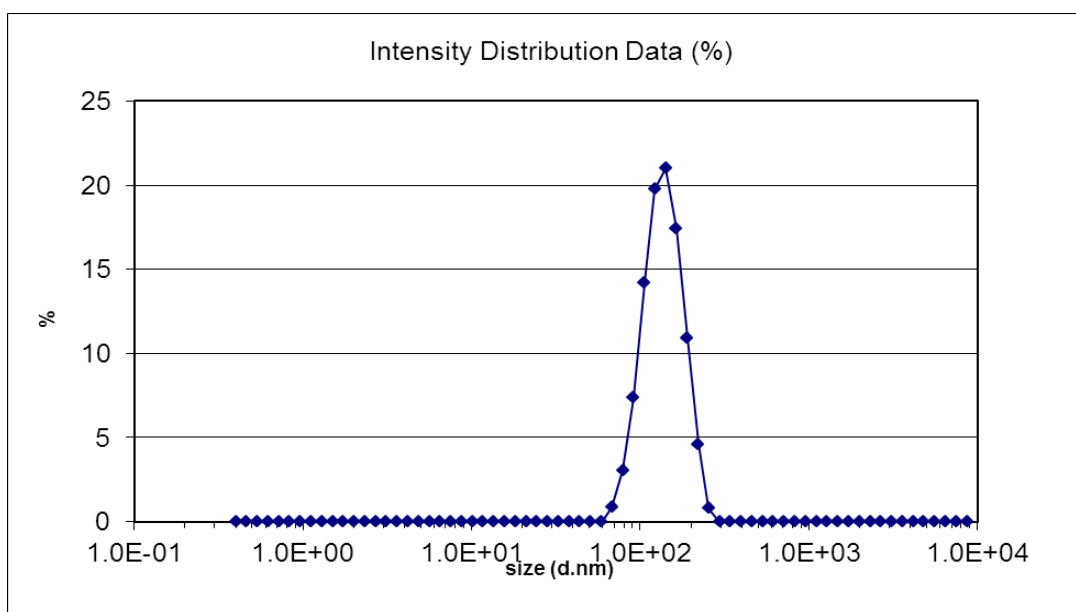
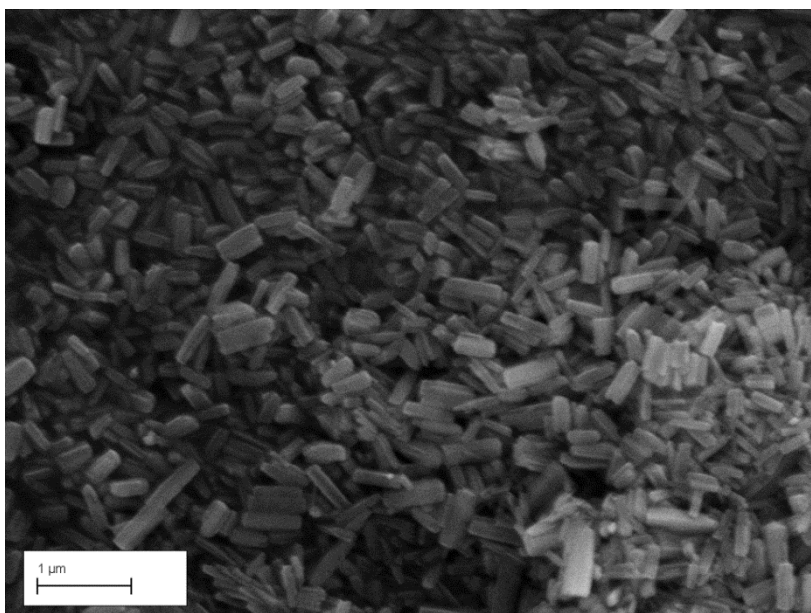
Experiment Number		8		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		187.6	59.2
Results				
APS (nm)			Particle Shape	
165.5			Spherical-shaped	



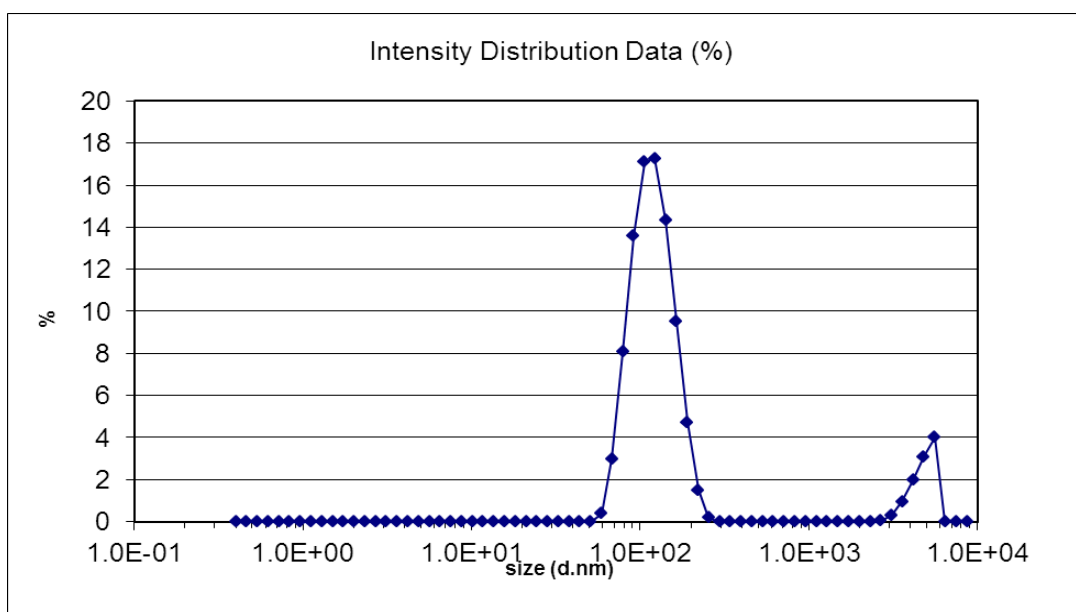
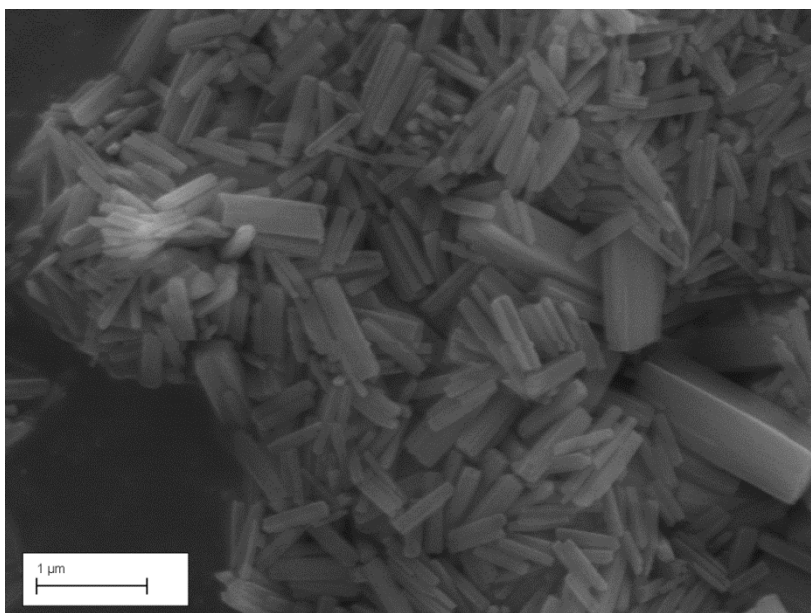
Experiment Number		9		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		187.6	59.2
Results				
APS (nm)			Particle Shape	
108.2			Spherical-shaped	



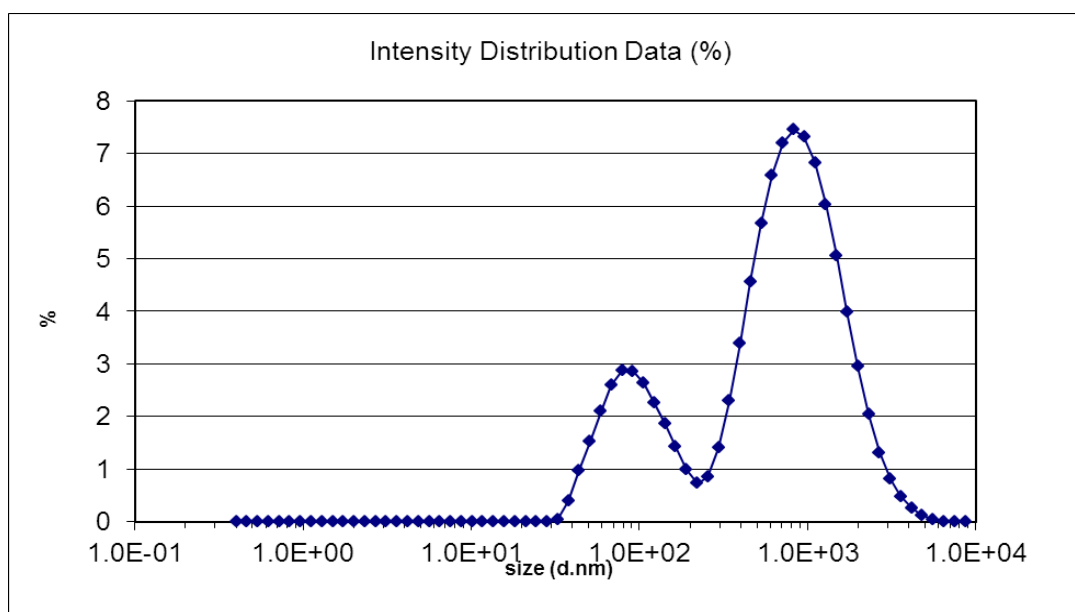
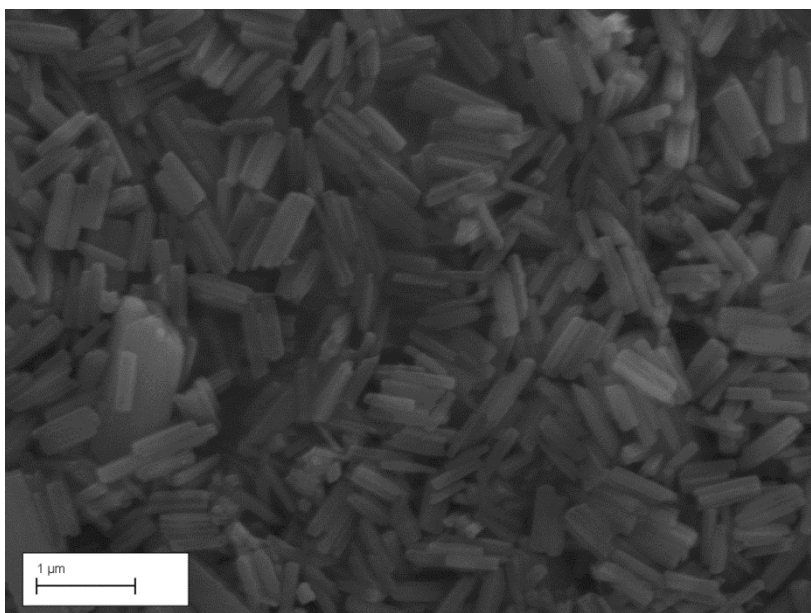
Experiment Number		10		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		187.6	59.2
Results				
APS (nm)			Particle Shape	
140.2			Column-shaped	



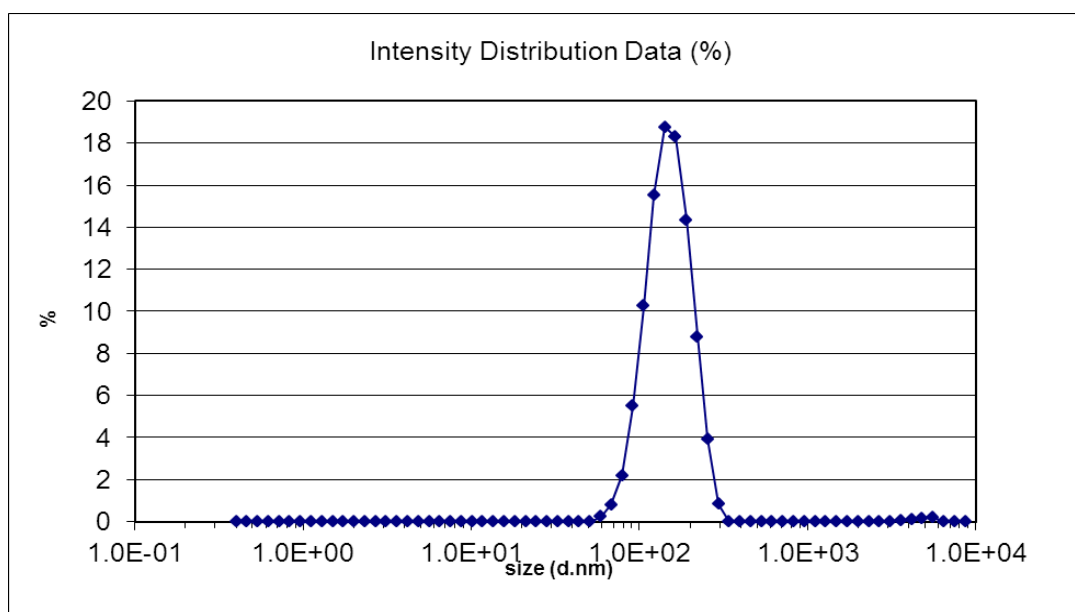
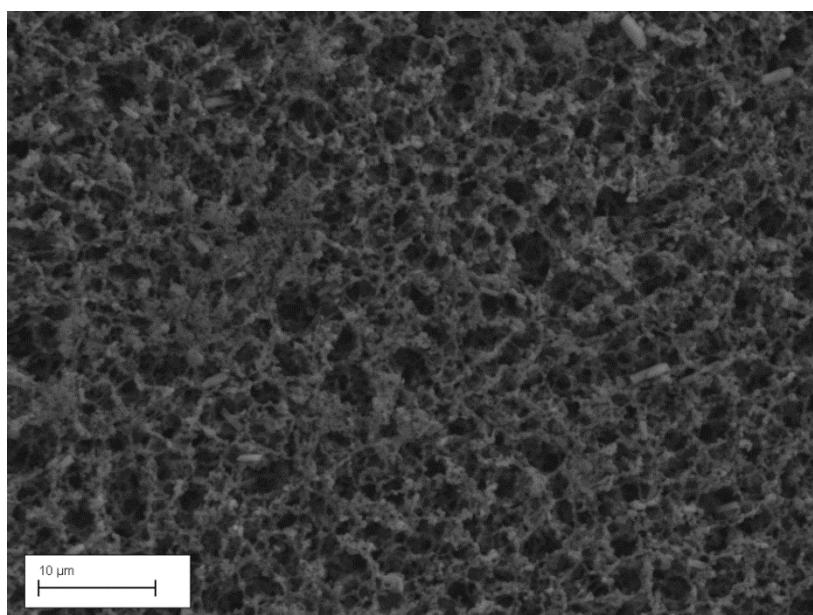
Experiment Number		11		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		187.6	59.2
Results				
APS (nm)			Particle Shape	
121.5			Rod-shaped	



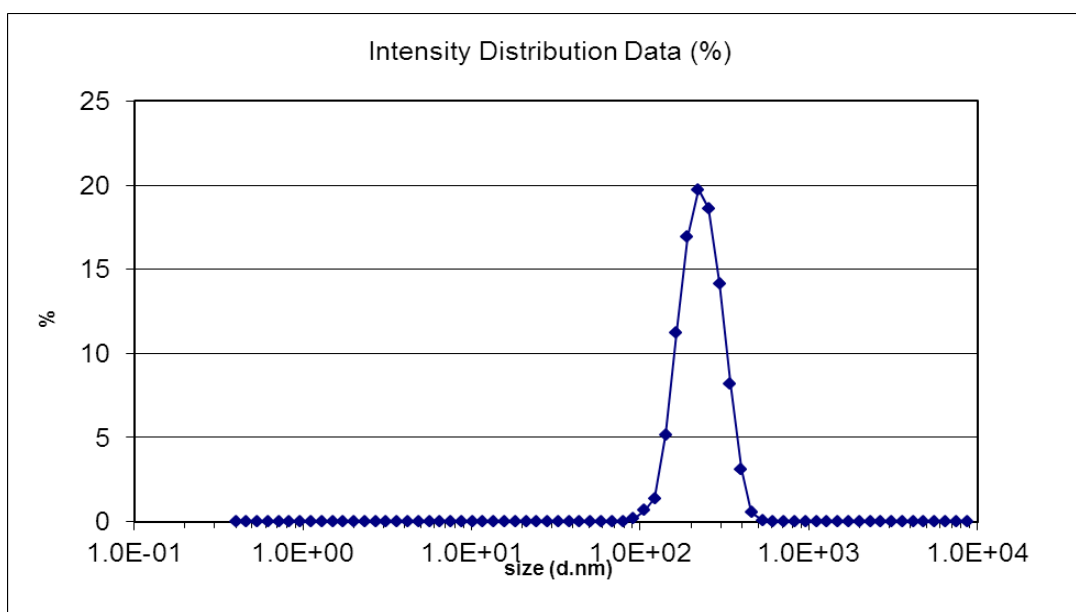
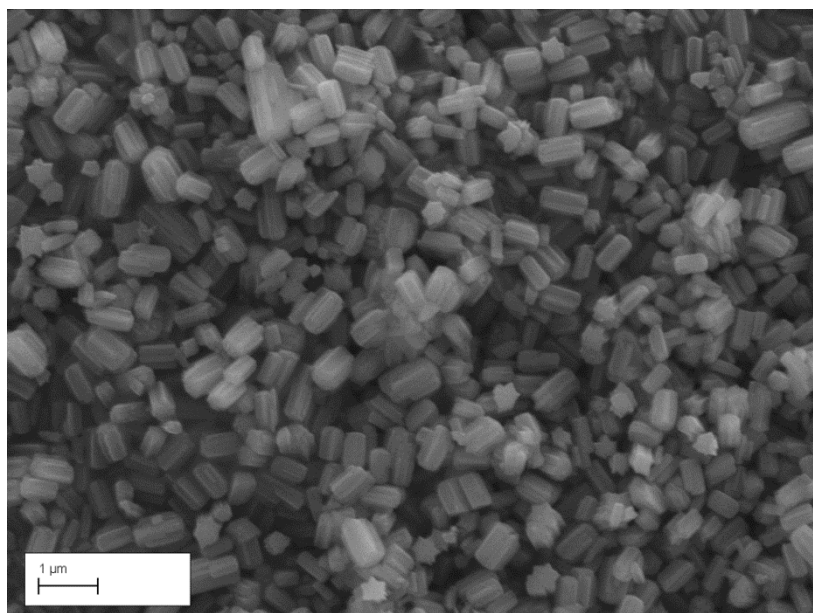
Experiment Number		12		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	5	5.847	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	22.17		187.6	8.46
Results				
APS (nm)			Particle Shape	
823.9			Rod-shaped	



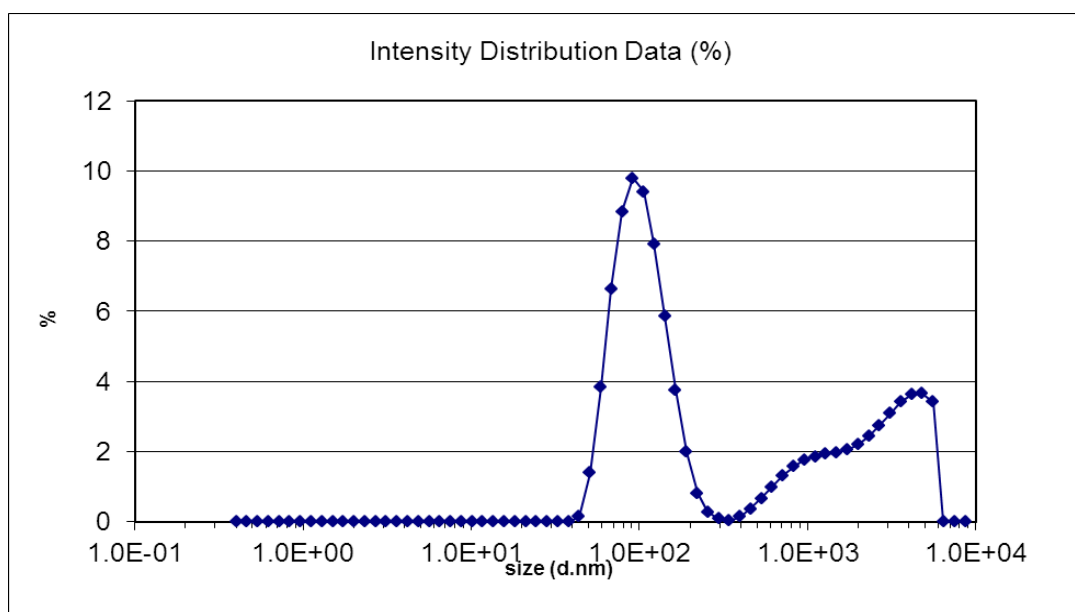
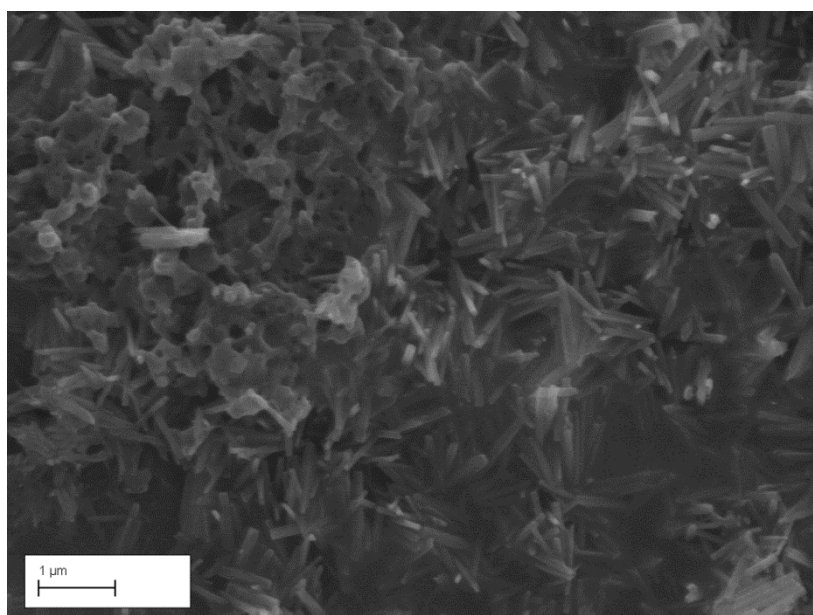
Experiment Number		13		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	5.847	0.901
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		187.6	59.2
Results				
APS (nm)			Particle Shape	
153.9			Crystal-shaped	



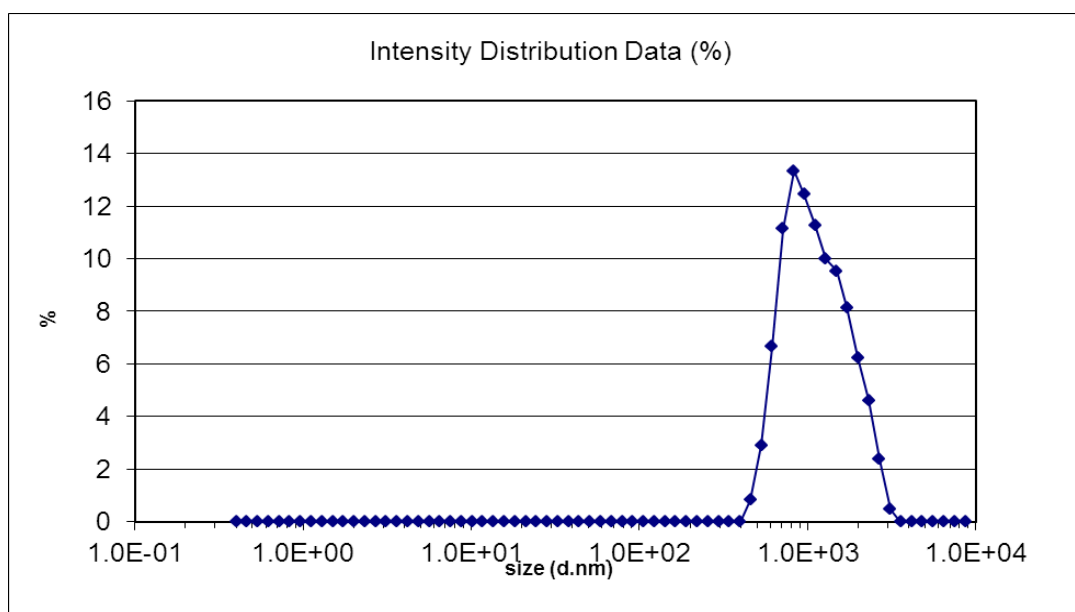
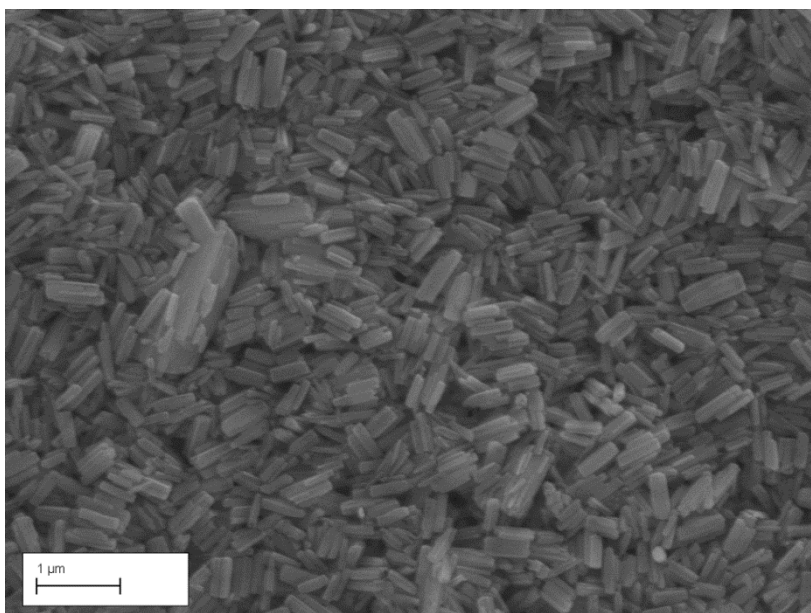
Experiment Number		14		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	5.847	10.793
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		187.6	59.2
Results				
APS (nm)			Particle Shape	
236.5			Spherical-shaped	



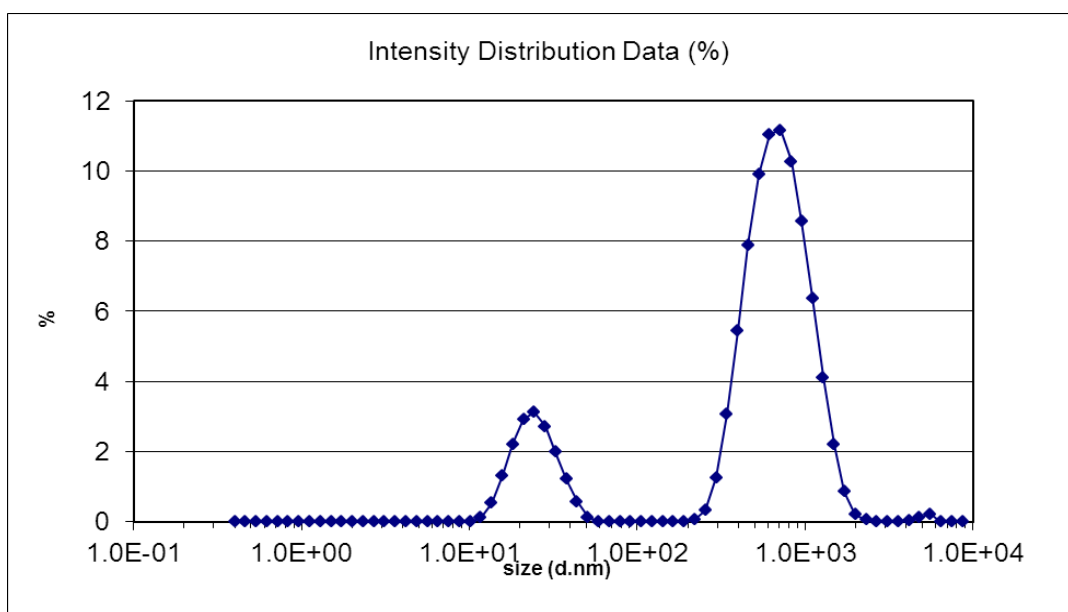
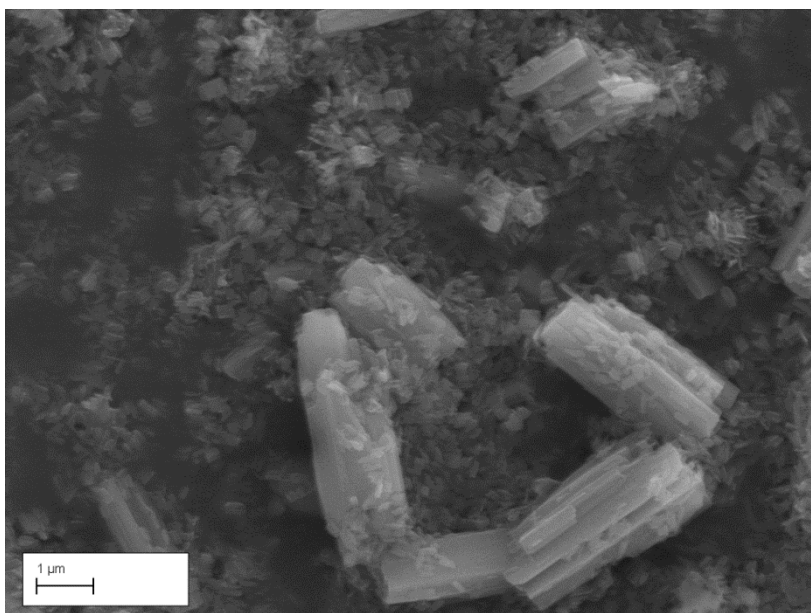
Experiment Number		15		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	0.901	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		187.6	59.2
Results				
APS (nm)			Particle Shape	
106.2			Needle-shaped	



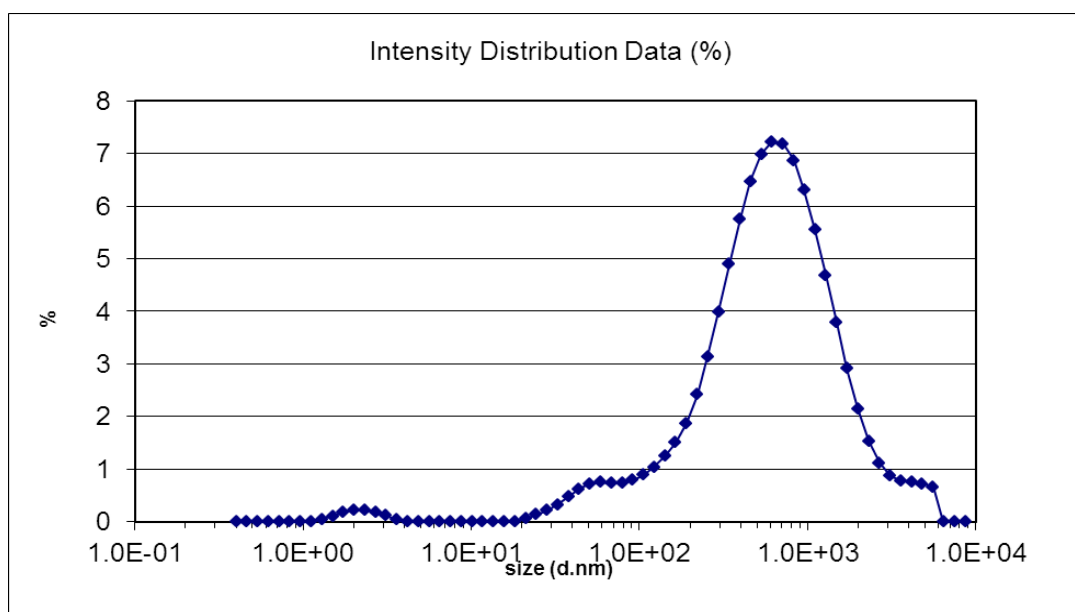
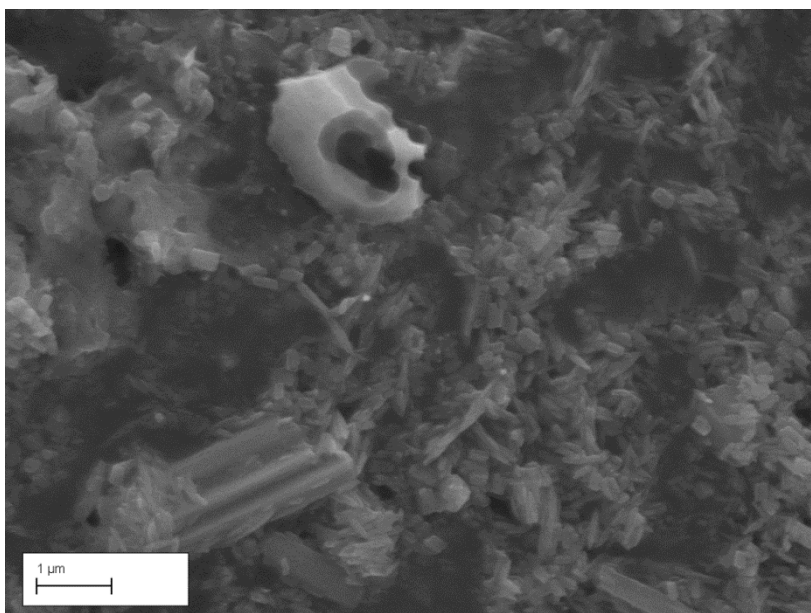
Experiment Number		16		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
2.25	3	14	10.793	5.847
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.212	3.17		187.6	59.2
Results				
APS (nm)			Particle Shape	
1211			Rod-shaped	



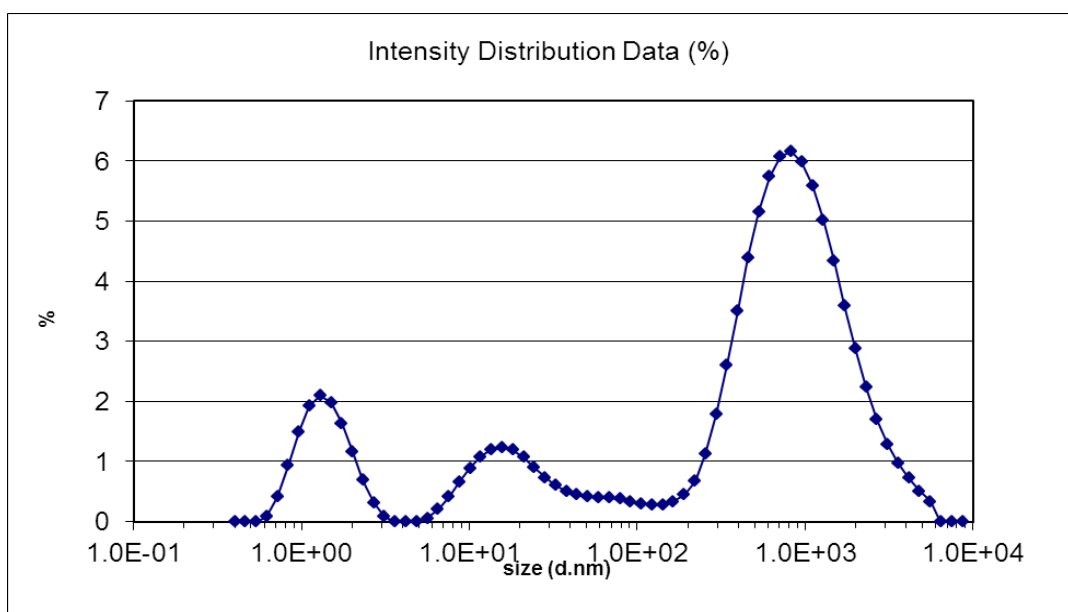
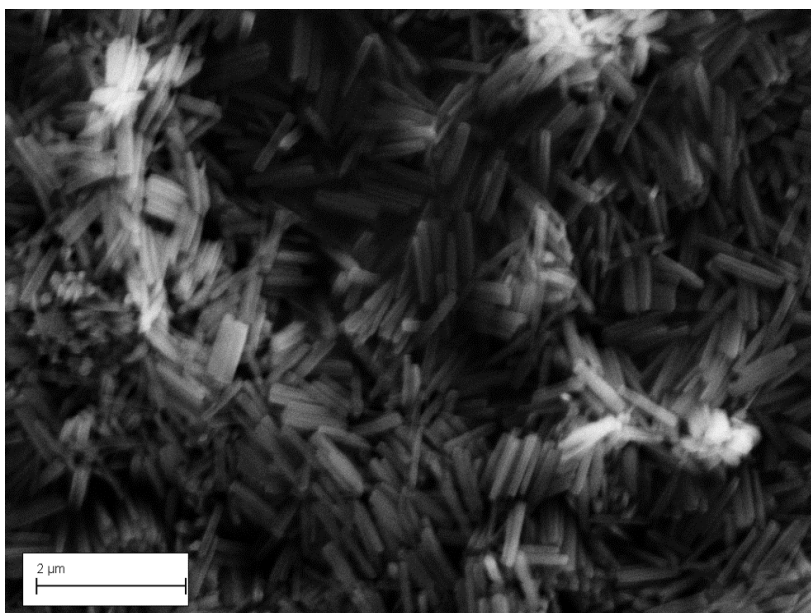
Experiment Number		17		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
4	2	20	8.32	3.374
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.318	2.21		400	181
Results				
APS (nm)			Particle Shape	
743.3			Rod-shaped	



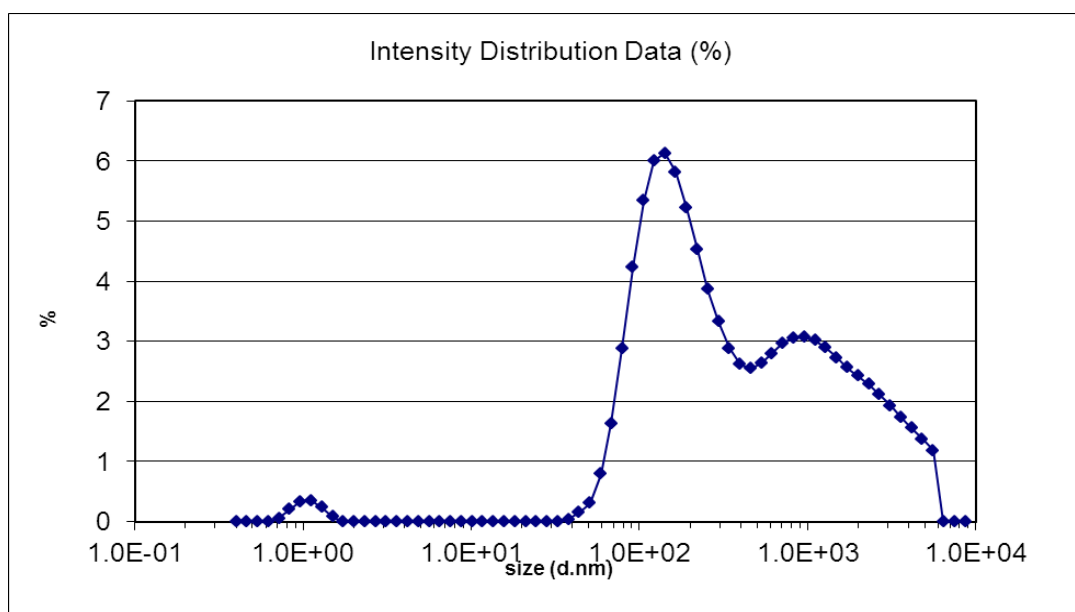
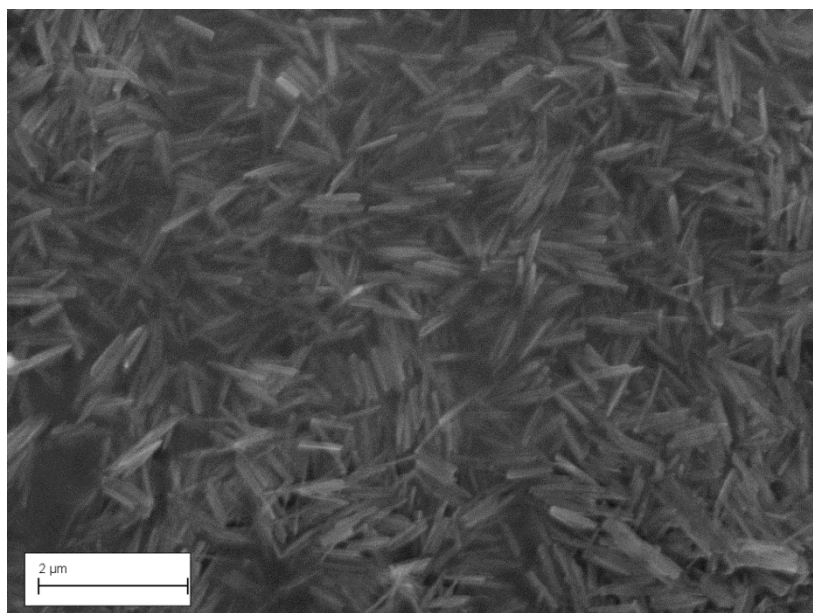
Experiment Number		18		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
4	4	8	8.32	3.374
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.159	5.54		800	144.4
Results				
APS (nm)			Particle Shape	
859.5			Rod-shaped	



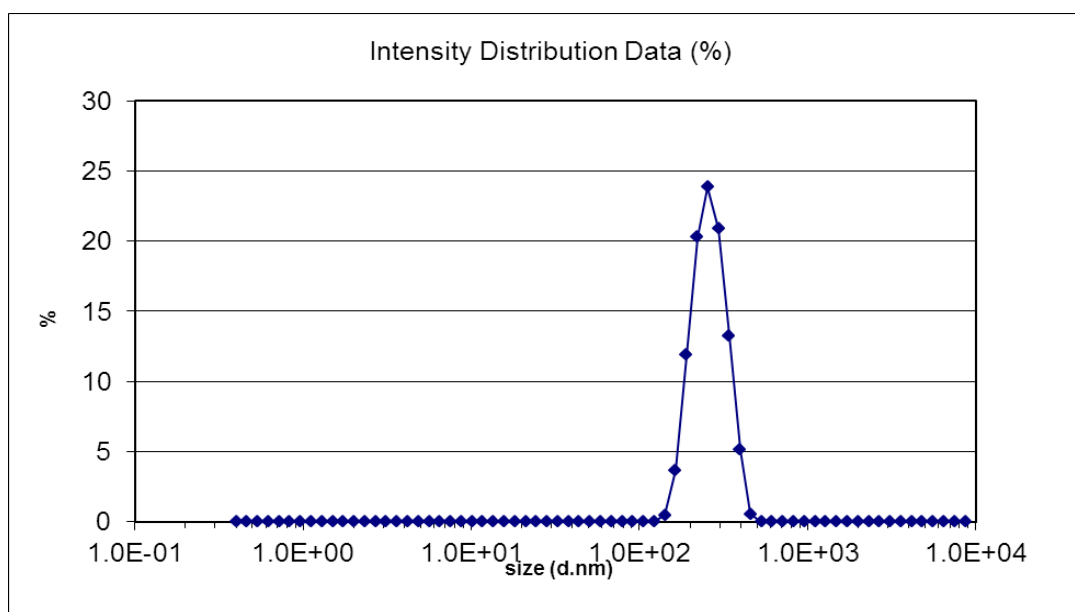
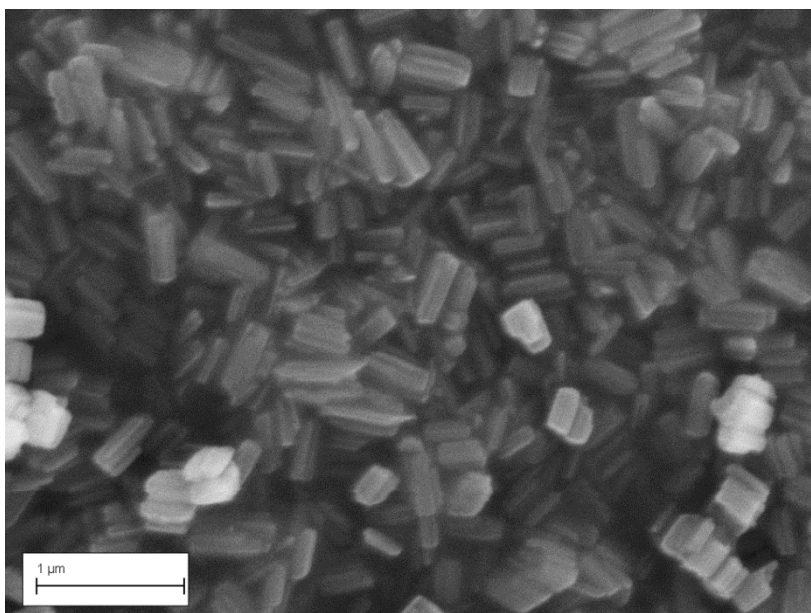
Experiment Number		19		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
0.5	4	20	8.32	3.374
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.159	2.21		100	45.2
Results				
APS (nm)			Particle Shape	
1120			Needle-shaped	



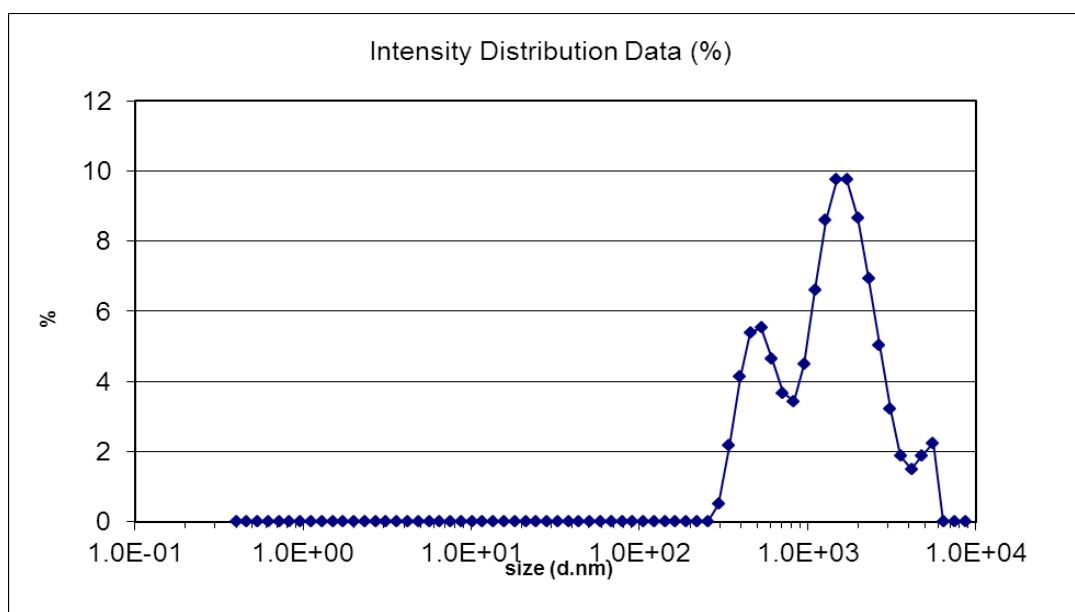
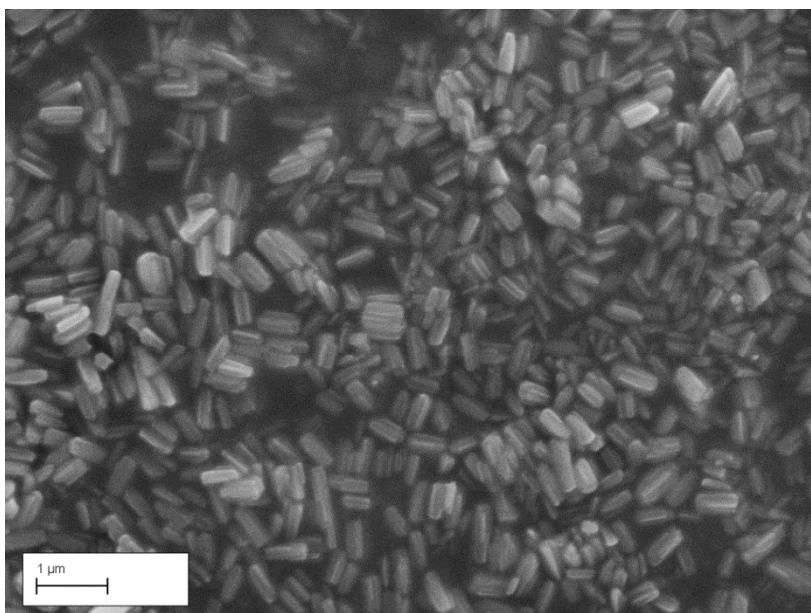
Experiment Number		20		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
0.5	2	8	8.32	3.374
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.318	5.54		50	9
Results				
APS (nm)			Particle Shape	
189.8			Needle-shaped	



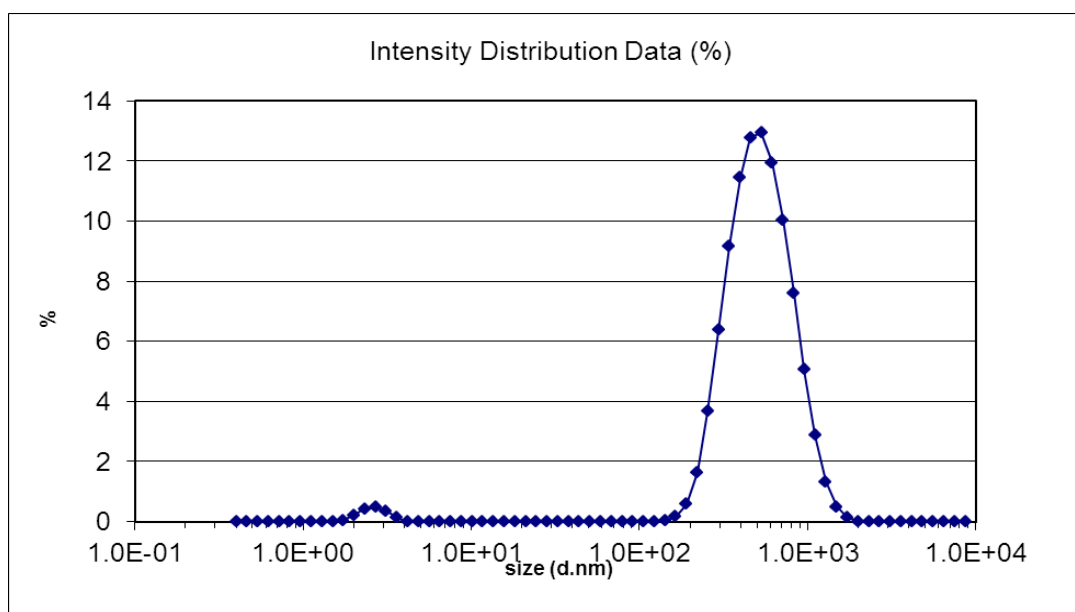
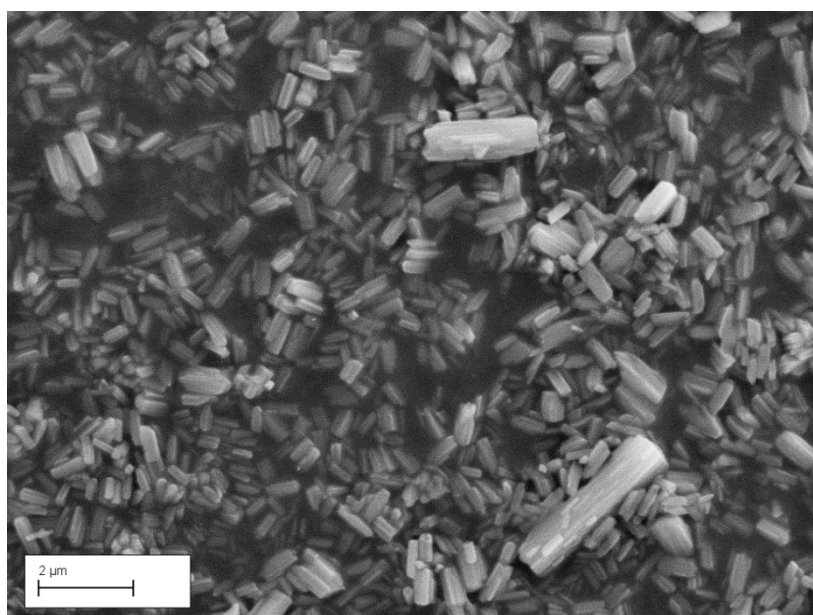
Experiment Number		21		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
0.5	4	8	8.32	8.32
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.159	5.54		100	18
Results				
APS (nm)			Particle Shape	
264.6			Column-shaped	



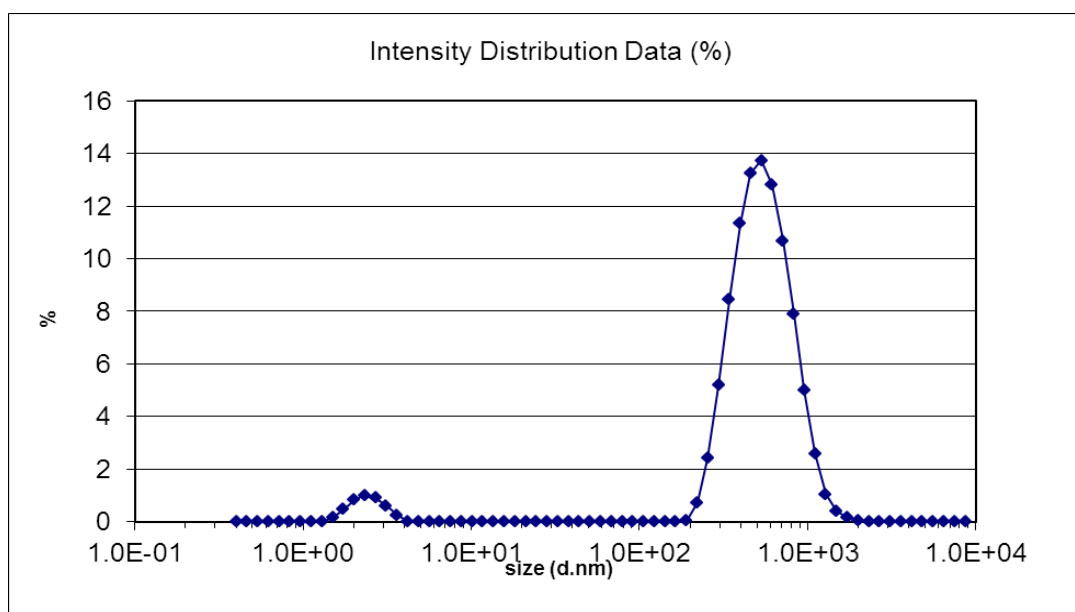
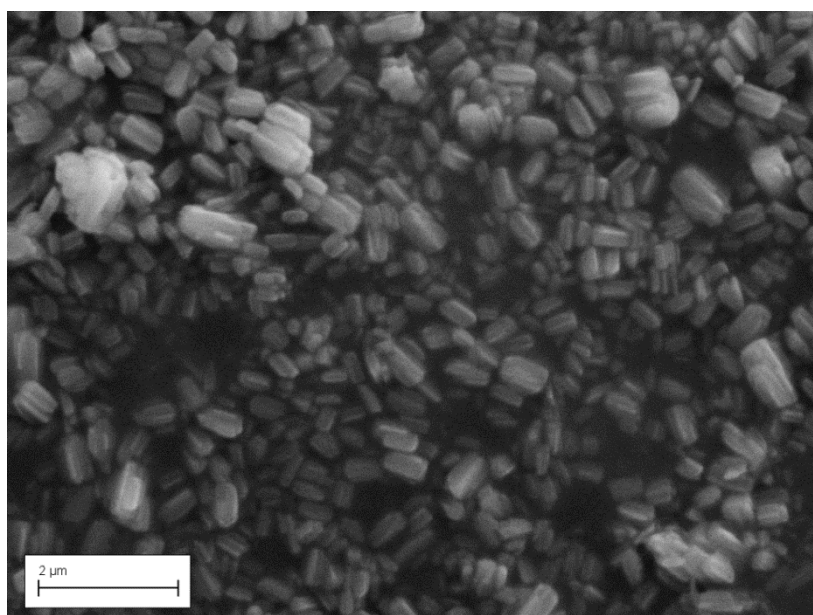
Experiment Number		22		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
0.5	2	20	8.32	8.32
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.318	2.21		50	22.64
Results				
APS (nm)			Particle Shape	
1611			Column-shaped	



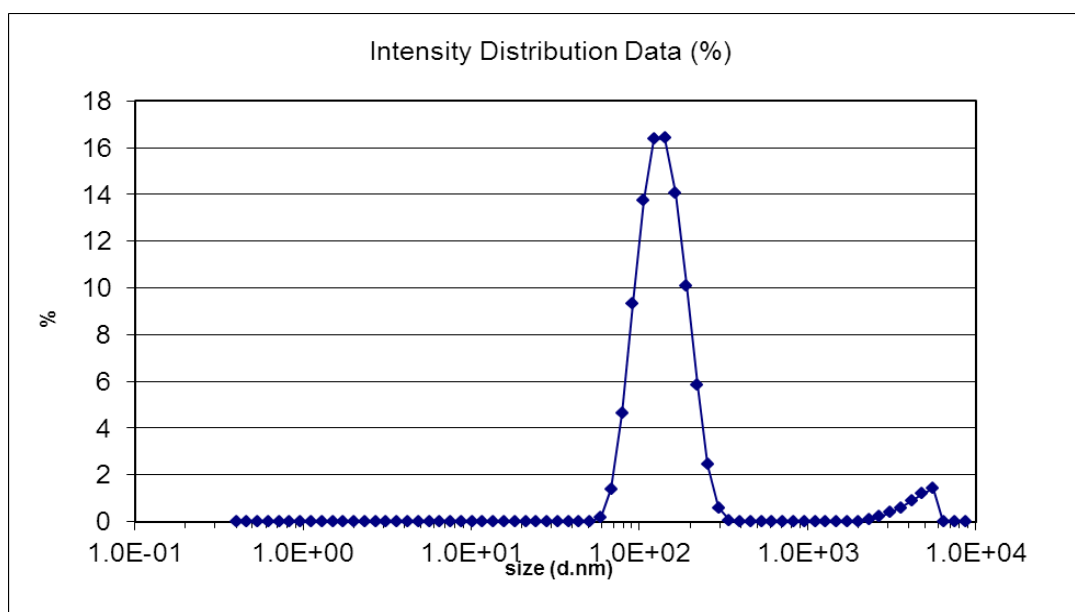
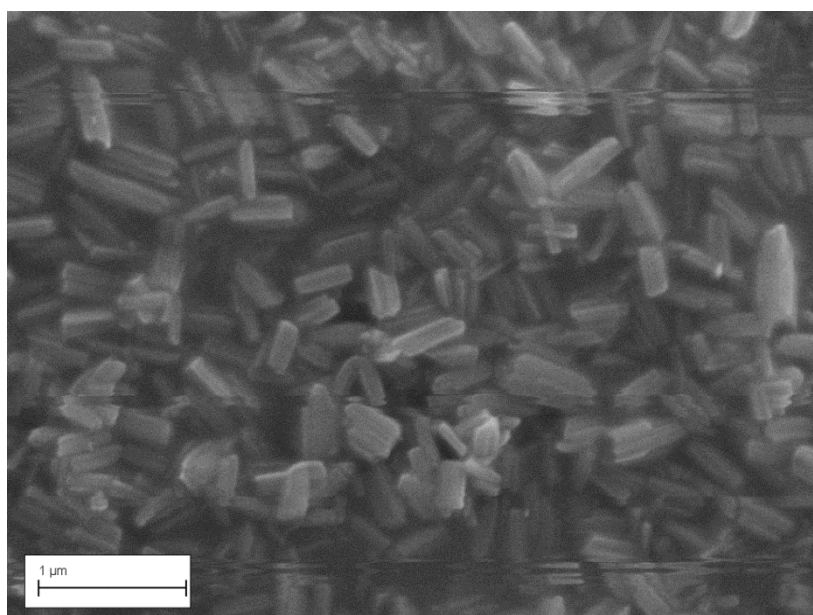
Experiment Number		23		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
4	4	20	8.32	8.32
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.159	2.21		800	362
Results				
APS (nm)			Particle Shape	
561.8			Column-shaped	



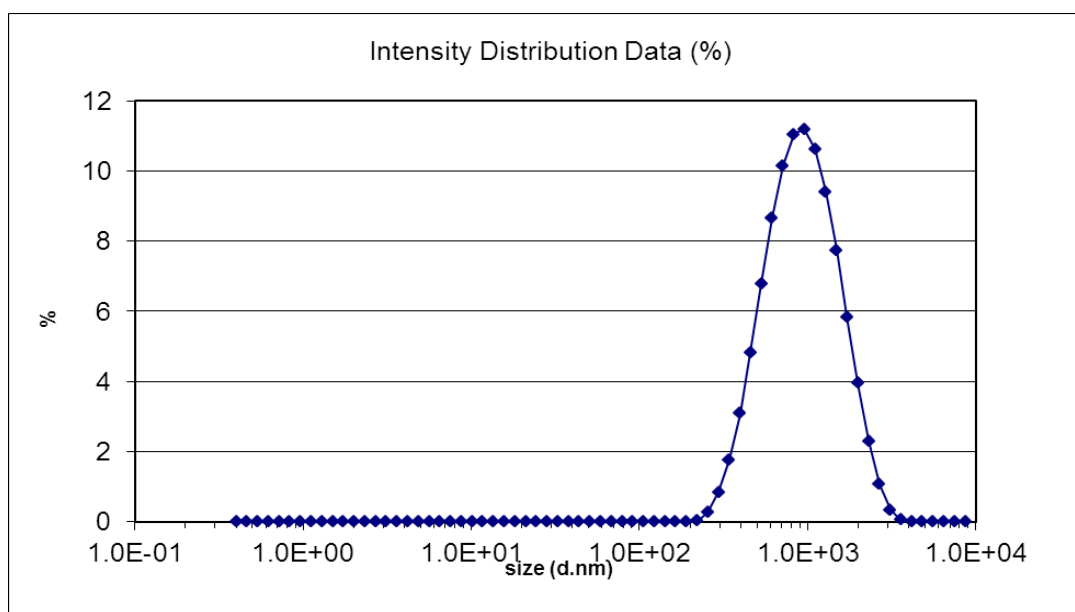
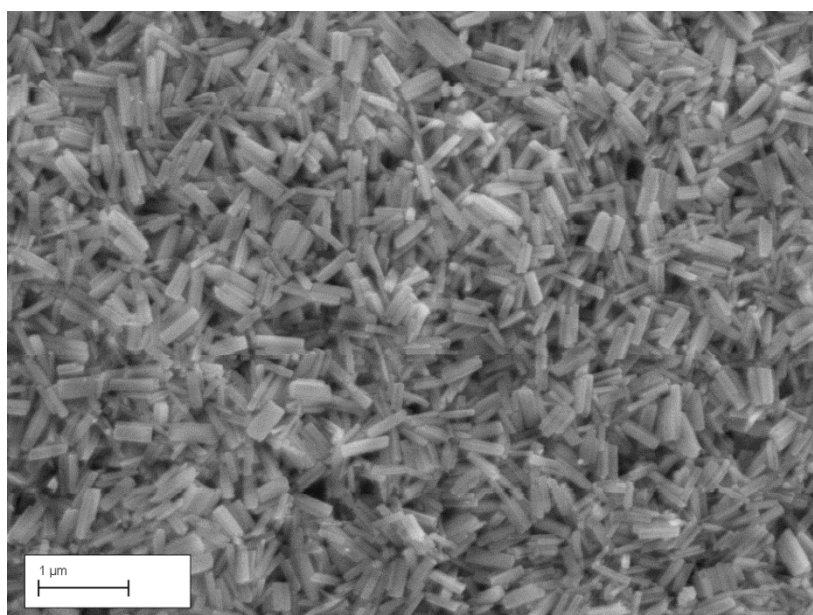
Experiment Number		24		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
4	2	8	8.32	8.32
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.318	5.54		400	72.2
Results				
APS (nm)			Particle Shape	
574.5			Column-shaped	



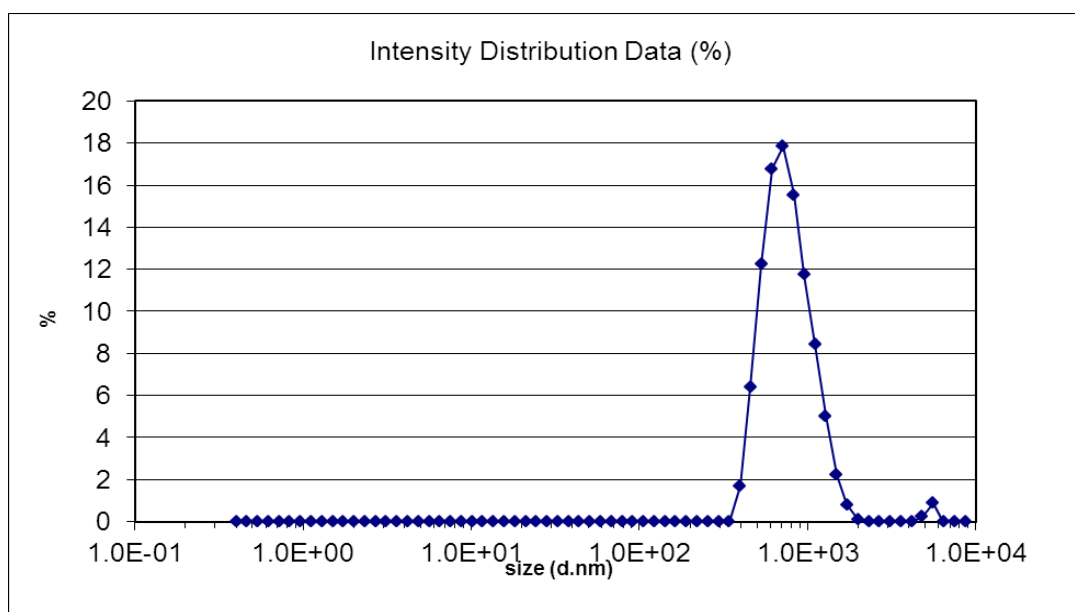
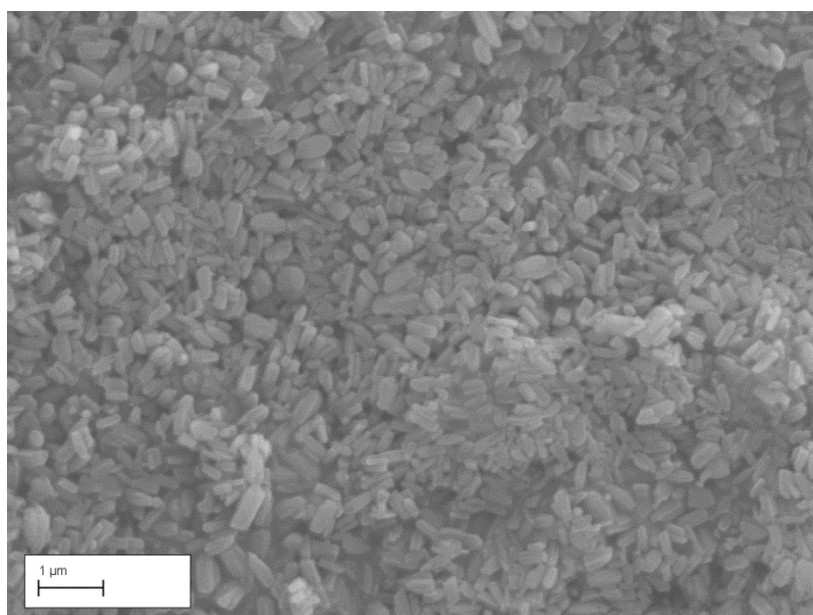
Experiment Number		25		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
4	2	20	3.374	8.32
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.318	5.54		400	72.2
Results				
APS (nm)			Particle Shape	
414.2			Rod-shaped	



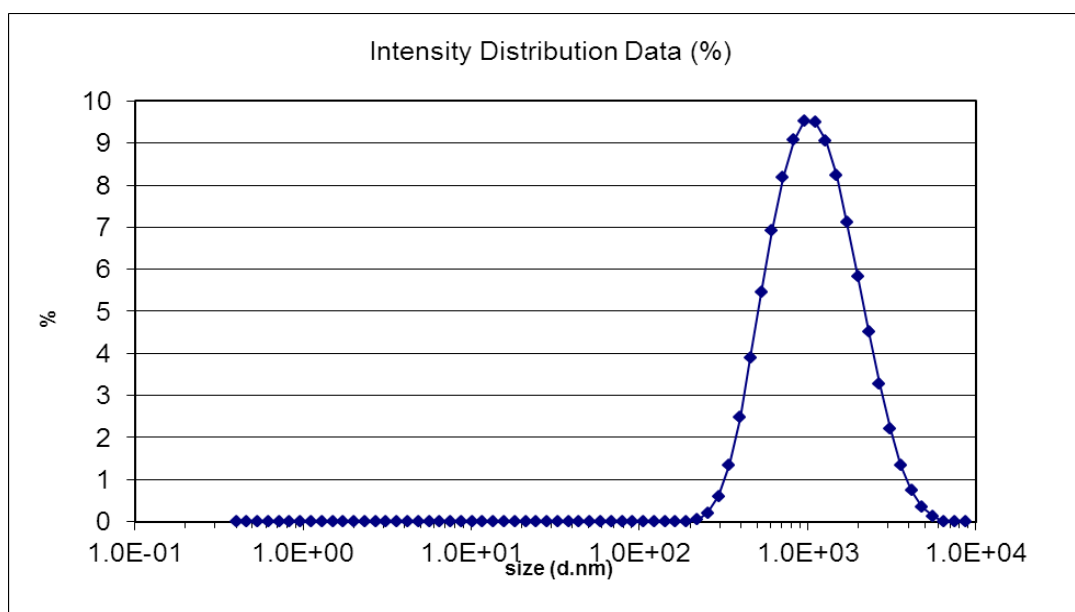
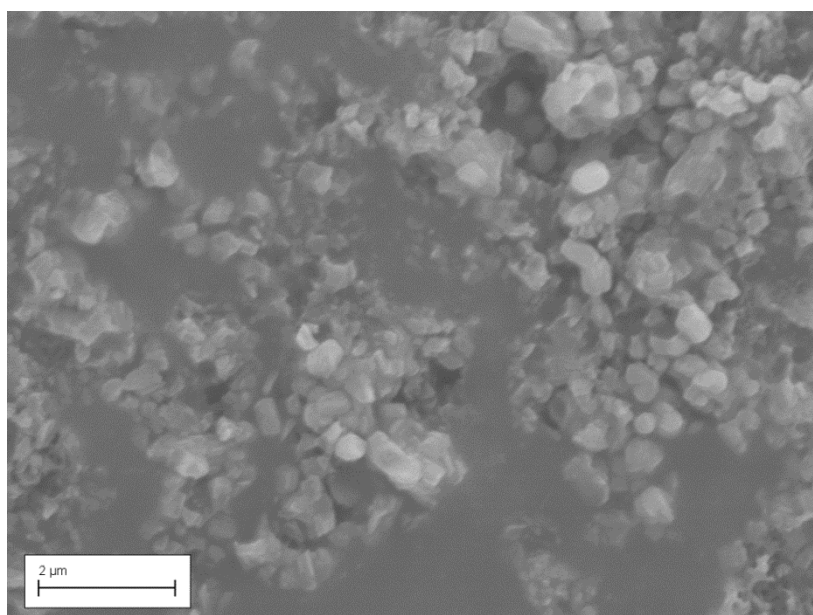
Experiment Number		26		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
4	4	8	3.374	8.32
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.159	5.54		800	144.4
Results				
APS (nm)			Particle Shape	
1029.4			Rod-shaped	



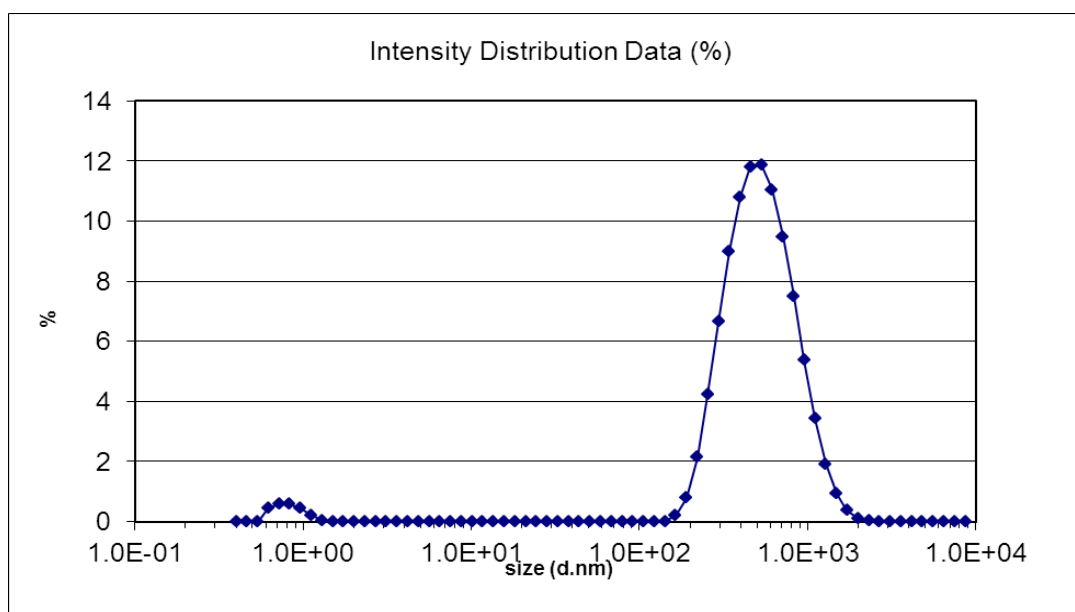
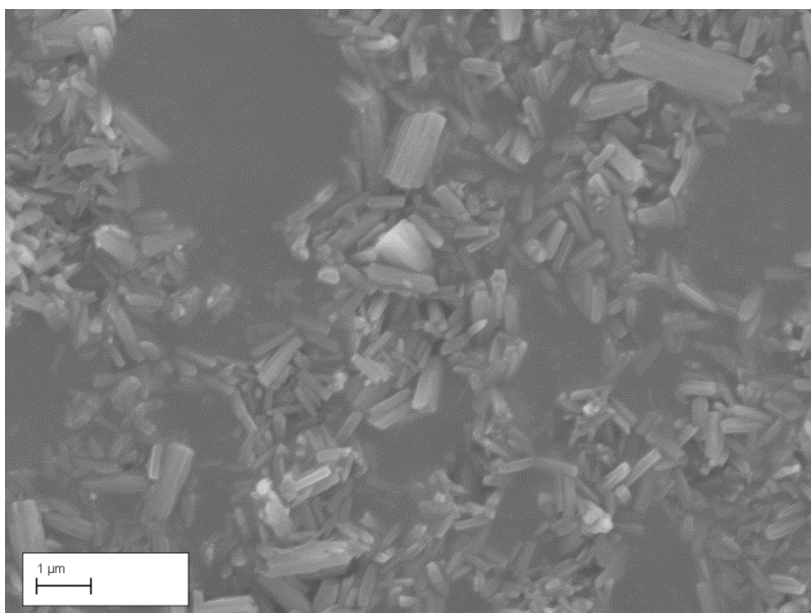
Experiment Number		27		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
0.5	4	20	3.374	8.32
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.159	2.21		100	45.2
Results				
APS (nm)			Particle Shape	
787.7			Column-shaped	



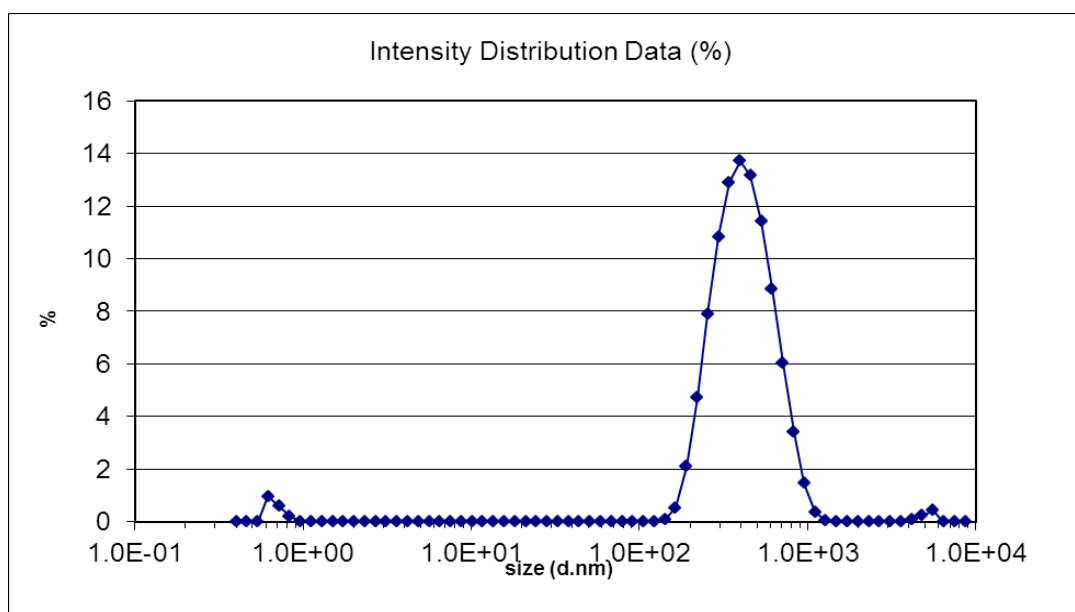
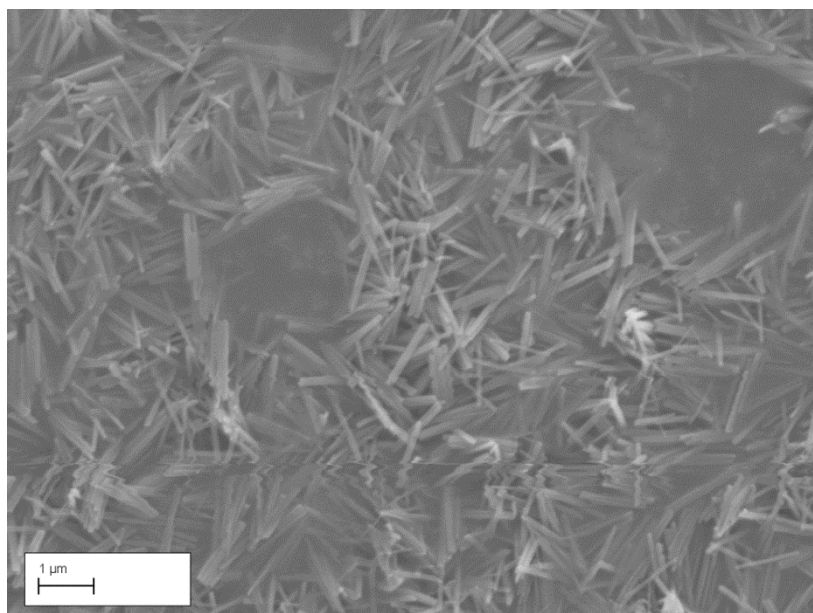
Experiment Number		28		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
0.5	2	8	3.374	8.32
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.318	5.54		50	9
Results				
APS (nm)			Particle Shape	
1273.4			Column-shaped	



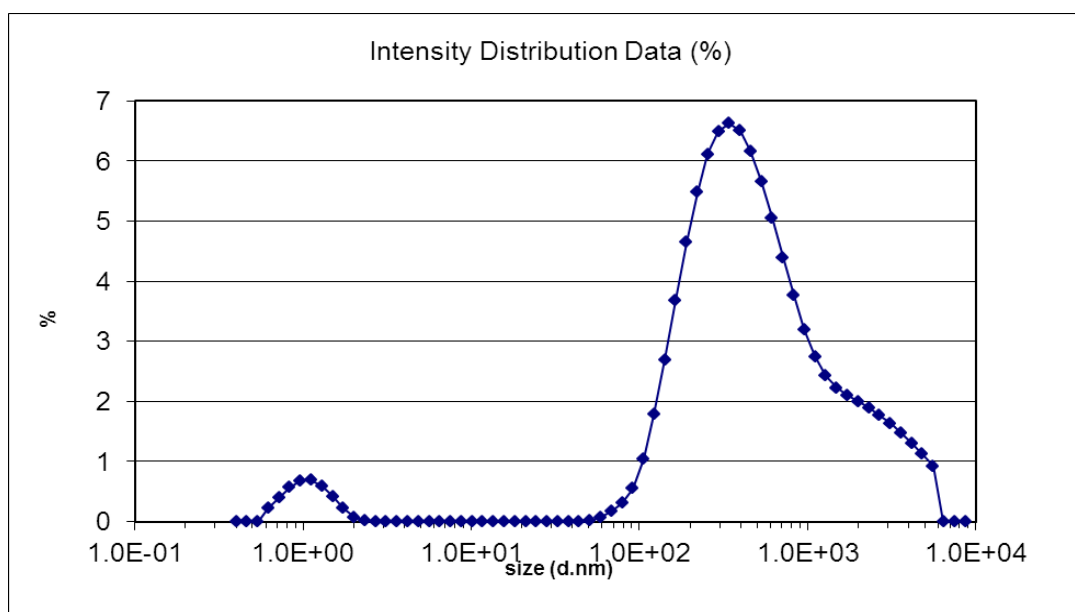
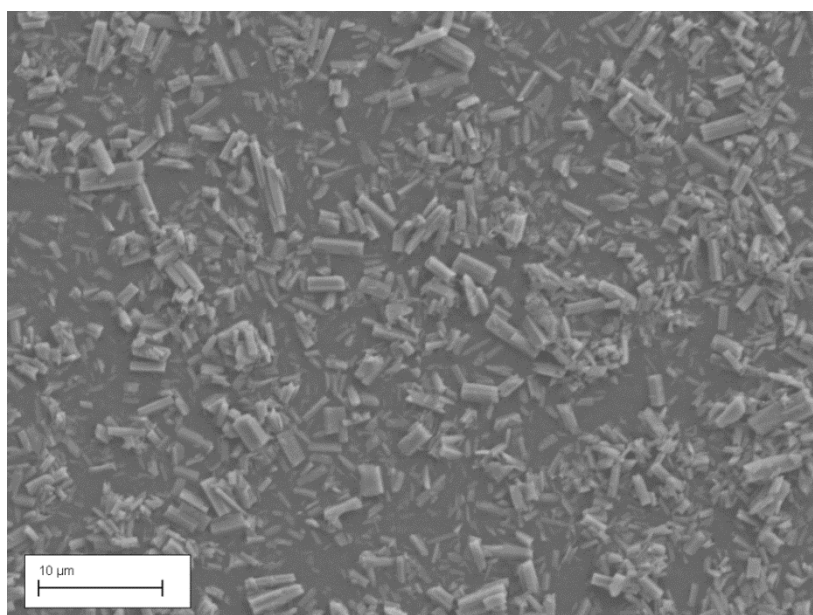
Experiment Number		29		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
0.5	2	20	3.374	3.374
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.318	2.21		50	22.6
Results				
APS (nm)			Particle Shape	
575.1			Rod-shaped	



Experiment Number		30		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
0.5	4	8	3.374	3.374
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.159	5.54		100	18
Results				
APS (nm)			Particle Shape	
441.8			Needle-shaped	



Experiment Number		31		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
4	4	20	3.374	3.374
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.159	2.21		800	362
Results				
APS (nm)			Particle Shape	
858.6			Rod-shaped	



Experiment Number		32		
Process variables and Chemical Composition				
Frequency (Hz)	Amplitude (mm)	Residence time (min)	Concentration of Iron (g/100 mL)	Concentration of Triazole (g/100 mL)
4	2	8	3.374	3.374
Dimensionless Numbers				
Strouhal Number	Reynolds Number		Oscillatory Reynolds Number	Velocity Ratio
0.318	5.54		400	72.2
Results				
APS (nm)			Particle Shape	
183.7			Needle-shaped	

