Review

A review of process intensification applied to solids handling

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ARTICLE INFO

ABSTRACT

Process intensification (PI) is a strategy aimed at transforming conventional chemical processes into more economical, productive and green processes. Its fundamental concept hinges upon the volume reduction of processing equipment resulting in enhanced mixing and heat/mass transfer as well as a multitude of other benefits. To date, the focus of PI has been on processes mainly involving gas/liquid systems. Solids handling applications have been more limited as fouling and blockages can occur due to large concentrations of solids in smaller equipment sizes. Appropriately designed equipment is therefore a key consideration for intensifying industrially-relevant solids handling processes.

In this review paper, we highlight a number of solid processing applications including precipitation, separation, granulation and milling, etc. where PI has been demonstrated. Much effort has been directed at reactive crystallization and precipitation in various intensified technologies, exploiting their enhanced mixing capabilities to produce uniformly distributed nano-particles. Generally, the objective in many of these processes has focused on transforming solids handling in batch processes into continuous ones with processing time reduction and improved energy efficiency. The review highlights the considerable opportunity for further development of multifunctional technologies in solids handling applications such as granulation and drying, the subject of a European Commission-funded HORIZON 2020 project.

1. Introduction

Process intensification (PI) is a concept that has evolved over the last three decades since it was first introduced to become diverse in its implementation and practice. For many, miniaturization remains the fundamental basis of PI, with microreactor being the most typical example. For others, PI is based on functional integration, with reactive distillation being a prominent example. Thus, the original definition of PI focusing on "*the physical miniaturization of process equipment while retaining throughput and performance*" [1] has been broadened to "*the development of innovative apparatus and techniques that offer drastic improvements in chemical manufacturing and processing, substantially decreasing equipment volume, energy consumption, or waste formation, and ultimately leading to cheaper, safer, sustainable technologies.*" [2]. The latter definition widens the PI concept to include processing techniques such as alternative energy input alongside novel equipment design for miniaturization.

Whilst the original idea of PI is based upon the significant reductions of equipment size (typically at least a ten-fold volume reduction) and the associated cost savings [3], several other potential

benefits related to business, process and environmental aspects can also be envisaged, as highlighted in Fig. 1. Where some of these processing benefits may be attained without a dramatic reduction in equipment size, this can be still be considered as the more modern interpretation of process intensification [2].

In terms of process safety, the reduction of plant size results in a smaller volume of toxic and flammable inventories within processes, thereby reducing the possibility of explosions. In addition, the lower number of unit operations can further simplify the process. PI is also capable of mitigating the risk of thermal runaway in highly exothermic chemical reactions by carrying out the process in the reactors. It offers greatly enhanced surface area to volume ratios for rapid removal of liberated heat e.g. in microreactors and spinning disc reactors [3–6].

PI equipment for reactions is designed with efficiency in productivity, selectivity and conversion of reactants in mind with important beneficial implications for the environmental awareness of such processes. With less by-product formation, fewer and more simplified downstream purification steps can be envisaged together with dramatically reduced net energy consumption [3,7]. On the basis of enhanced mixing and heat and mass transport rates, which have the potential to

Nomenclature

ACR	Coflore® agitated cell reactor
API	active pharmaceutical ingredient
ATR	Coflore® agitated tube reactor
CBR	compact bed reactor
CPR	catalytic plate reactor
CSD	crystal size distribution
CSTR	continuous stirred tank reactor
DIJ	dual impinging jet
EBR	TORBED Expanded Bed Reactor
EJAC	Elbow-Jet Air Classifier
FAME	fatty acid methyl ester
IS	impinging stream
MAFBR	membrane assisted fluidized bed reactor
MSB	magnetically-stabilized bed
MSFBR	magnetically-stabilized fluidized bed reactor
MVD	microwave-assisted vacuum drying
OBR	oscillatory baffled reactor
PDG	pneumatic dry granulation
PI	process intensification
RE	reactive extraction
RFB	rotating fluidized bed
RPB	rotating packed bed
RSSD	rotor-stator spinning disc
SCR	spinning cone reactor
SDR	spinning disc reactor
SSHE	scraped-surface heat exchanger
TCR	Taylor–Couette reactor
TSG	twin screw granulator
WSMM	wet-stirred media milling

reduce reaction times significantly, PI plants require less solvent and energy. This would result in further carbon emission mitigation. As an example, compact heat exchangers, such as welded or brazed plate units where approach temperature differences can be very small, can be very efficient.

Over the years since it was first conceptualized, the implementation of PI has evolved into two distinct classifications involving the development of equipment and methods. PI equipment includes reactive and non-reactive apparatus. The former includes spinning disc reactors (SDR), static mixer reactors, monolithic reactors, micro reactors, rotating packed beds (RPB) and jet impingement reactors. The latter includes intensive mixing devices and units for separation e.g. static mixers, rotor/stator mixers and rotating packed beds as well as heat transfer devices e.g. compact heat exchangers and microchannel heat exchangers. PI methods also include multifunctional reactors, hybrid separations and the usage of alternative energy sources such as microwaves, ultrasound, and other electric fields. Multifunctional reactors enhance chemical conversion and integrate reactions and downstream operations into a single unit. Examples include membrane reactors, reactive distillation, reactive crystallization, etc. [2]. Multifunctional systems need not be limited to those incorporating reactors.

Besides liquid/liquid and liquid/gas reactions, solids handling is also an important process in many industries such as pharmaceuticals, ceramics, and mineral processing. In the case of PI, solids can be considered as the literal "blockers" to the application of PI, as PI equipment based on the miniaturization concept (on spatial domain) sometimes has narrow channels (e.g. microreactors), which large solids would foul or cut-off channels completely [3]. It is therefore important to understand the challenges and limitations presented by solids handling within the fold of PI.

In this paper, a review of the development in PI technologies and techniques for solids handling is presented. To date, several of the PI technologies discussed in this paper have been successfully developed and commercialized e.g. rotating packed beds [8] and micro reactors [9]. Other PI technologies are still under development or at the prototyping stage. One way in which one may categorize the PI characteristics of processes, including many where the size reduction associated with what one might call 'ideal' PI examples is not present, is that of Van Gerven and Stankiewicz [10] where the PI approach is classified into spatial, thermodynamic, functional or temporal domains. In this paper, particularly in Table 1 which summarizes the PI equipment discussed, the applicable approaches are identified for each technology. The extent of intensification achieved for each of the technologies reviewed is also highlighted in Table 1 in qualitative and quantitative terms, depending on the availability of information.
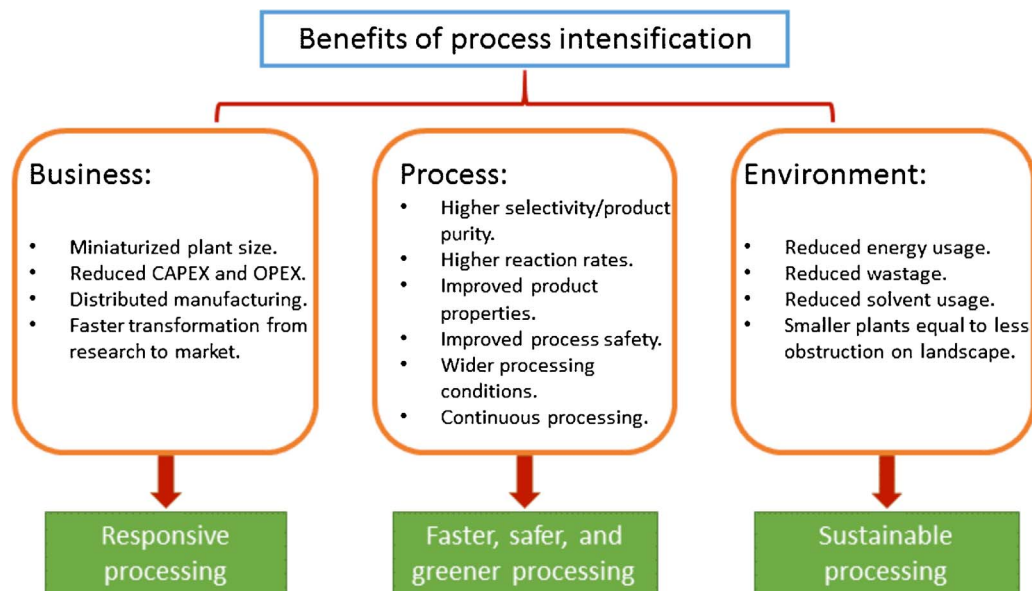

Fig. 1. Business, process, and, environmental benefits of process intensification [4].

Table 1
Summary of PI technologies/techniques for solids handling.

Technology/technique (listed alphabetically)	Associated process(es)	PI domain	Qualitative and quantitative comparison with conventional technologies[a]	Reference(s)
(Coflore) Agitated tube reactor (Coflore) Agitated cell reactor	• Mixing	Spatial and functional	• Enhanced mixing. • Capable of creating homogeneous, multiphase suspension. • Transforming batch to continuous.	[121–124]
Catalytic plate reactor	• Catalytic reaction	Spatial, thermodynamic, and functional	• Higher yield products (94%) [124]. • Enhanced catalyst activity. • Improvement in transverse temperature gradients compared to a tubular reactor.	[139–141]
Continuous flow microreactor	• Precipitation	Spatial and temporal	• Ability to control crystallization reactions. • Reduced residence time (one order of magnitude smaller than in the batch reaction) [50]. • Enhanced heat transfer coefficient (up to 35%) [48]. • Small particle size production (90% smaller than a stirred batch reactor) [50].	[46,47,49–51]
Consigma compact unit	• Granulation	Thermodynamic, functional, and temporal	• Multifunctional unit for continuous granulation. • Faster processing (up to 10×). • 40% savings on labour cost. • 60% reduction in equipment size. • 50% in energy saving.	[104,105]
Elbow-Jet Air Classifier	• Particle classification	Functional	• Simultaneous fine and coarse particle classification. • Capable of classifying particles of very small size range (0.5–10 μm).	[170]
Froth flotation devices	• Separation	Spatial and temporal	• Very rapid process (1 s vs. 300 s for batch) [93]. • Capable of fine particles (micro-scale) separation.	[93–95]
(CGS) Fluidized bed jet mill	• Milling	Spatial	• Capable of grinding fine particles (1–70 μm). • No contamination.	[136]
Fluidized bed with various modification	• Granulation • Drying	Spatial, thermodynamic, and temporal	• At optimum conditions, high drug uniformity in granules can be achieved. • Enhanced drying process with indirect heating.	[106,150,163,173]
Helix reactor	• Precipitation	Thermodynamic and temporal	• Enhanced mixing – plug flow with reduced pressured drop. • Capable of nanoscale crystal size production.	[56]
High-speed stirred ball mill	• Grinding	Functional	• Capable of ultra-fine particle grinding.	[137,138]
Impinging stream reactor	• Precipitation • Drying • Milling • Grinding	Spatial, functional, and temporal	• Enhanced heat and mass transfer due to direct contact of two opposing streams. • Excellent micro-mixing. • No external agitation required. • Capable of small crystal size production with narrow crystal size distribution (7.5–11.3 nm) [72].	[72,74,75,132,135,186,187]
Jameson Cell (froth flotation)	• Separation	Temporal	• Excellent for solids grinding (Trost Jet Mill). • ~100% particle-bubble contact probability. • Rapid mineral recovery (5–10 s).	[94]
Magnetically stabilized bed	• Separation	Functional	• High separation efficiency for magnetic particles (> 90%) [86].	[85,86,88]
Microfluidics	• Separation • Particle classification • Bioprocessing	Spatial and functional	• Fast and accurate separation of microparticles (efficiency over 95%) [89]. • Low fabrication coast and reagents. • Customized particle segregation possible (through gap size e.g. 5 microns).	[89–92,171,172]
Microwave	• Precipitation • Catalytic reaction • Drying	Thermodynamic, functional, and temporal	• Reduced crystallization time (decreased by ~60-fold than conventional evaporative crystallization) [57]. • Reduced particle size (70% smaller) [58]. • Reduced drying time (25–90% shorter than conventional drying) [177].	[57–60,166,177–183,211]
Micro-fluidized beds/packed beds	• Catalytic reaction • Granulation	Spatial, thermodynamic, functional, and temporal	• Increase in mass transfer coefficients (11–13 times). • Increase in reaction rate constants (5–7 times) [164]. • Increase in conversion (81%) [146]. • Rapid screening of reaction kinetics and granulation dynamics with small samples. • Save energy (23% lower than conventional method) [156]. • Small batch granulation is possible. • Granule size correlated with liquid flow rate and voltage. • Rapid pharmaceutical formulation development.	[115,116,145–147,150–162,164,165]
Oscillatory baffled reactor	• Precipitation	Spatial and temporal	• Transforming batch to continuous.	[36–42,44,45,144]

Table 1 (*continued*)

Technology/technique (listed alphabetically)	Associated process(es)	PI domain	Qualitative and quantitative comparison with conventional technologies[a]	Reference(s)
Plasma	• Catalytic reaction	Functional	• Reduced reaction time (80% shorter than CSTR) [41]. • Reduced volume for similar throughput (99.6% smaller than CSTR) [45]. • Greater crystal size control. • Uniform suspension of particles.	[195,196]
Pneumatic dry granulator	• Thermal processing • Granulation	Thermodynamic	• Overcoming the limitations of current technologies at industrial scale. • Good flowability. • Low cost.	[97,101,102]
Reactive extraction	• Catalytic reaction	Thermodynamic	• Huge cost savings esp. due to the integrated processes within a single equipment. • Improved product properties.	[168]
Reactive separation	• Catalytic reaction	Thermodynamic and functional	• Energy and capital costs reduction. • Reduction of waste emission.	[167]
Reflux classifier	• Particle classification	Thermodynamic	• High yield possible in mineral beneficiation.	[169]
Rotating fluidized bed	• Particle coating • Thermal processing	Spatial and temporal	• Sufficient particle residence time for coating. • Higher heat and mass transfer when particle size decreased (up to 3 times higher) [127]. • High mixing efficiency (mixing coefficient increased by 4 times) [130].	[128–130,190–192]
Rotating packed bed	• Precipitation • Bioprocessing	Spatial	• Rapid mixing (mixing time 0.01–0.1 ms) [27]. • Excellent control of particle size [27,28]. • Scaled-up to an annual capacity of 10,000 tons [27].	[27,28,203]
Rotor-stator spinning disc	• Separation	Spatial	• Enhanced particle entrapment (~100% with the reticulated foam).	[76]
Scraped-surface heat exchanger	• Mixing	Thermodynamic	• Simultaneous mixing (mass), heat transfer enhancements, and fouling remediation.	[125,126]
Screw conveyor/mixer	• Drying • Precipitation • Thermal processing	Thermodynamic	• Cost- and energy-efficient drying.	[175,176]
Spinning cone reactor	• Precipitation	Spatial	• Reduced particle size by 50–90% than in the batch run [26].	[26,189]
Spinning disc reactor	• Precipitation • Catalytic reaction • Bioprocessing	Spatial, thermodynamic, and temporal	• Controlled and reduced particle size by 70% than conventional technology [14,16,18–20,24]. • Enhanced heat and mass transfer in wavy film (5–9 times higher than in smooth film) [21,23]. • Increased selectivity (up to 75%) [143]. • 15% lower power dissipation than conventional reactor [15].	[14–21,23,24,143,199–202,204]
Taylor–Couette reactor	• Crystallization • Mixing • Granulation	Spatial and thermodynamic	• A faster crystallizer (3–5 times faster than conventional stirred tank crystallizer) [30–34]. • Ideal plug flow properties. • No detectable damage to particles.	[30–34,99,100,117–120]
TORBED reactor	• Separation • Drying • Thermal processing	Spatial and functional	• Ability to process different shapes of fine particles. • Capable of fluidizing fine particles (< 50 μm diameter) [82]. • Convenient drying processing of sludge.	[82,174,193,194]
Turboscrubber	• Separation	Spatial and thermodynamic	• 100% non-clogging operation (no-maintenance). • High mass and heat transfer rates. • High efficiency sub-micron particulate abatement.	[96]
Twin screw granulator	• Granulation	Spatial, thermodynamic, and temporal	• Transforming batch granulation to continuous. • Very short residence times (a few seconds, batch granulators: a few minutes). • All particles experience all the granulation steps (in batch granulators, powders tend to stay in the bulk form).	[109,111–114]
Ultrasound	• Precipitation • Drying	Thermodynamic and functional	• Reduced particle size (~75% smaller than conventional method) [61]. • Reduced drying time (reduced 30–50% time) [185].	[61,62,67,68,184,185,205–210]

Table 1 (*continued*)

Technology/technique (listed alphabetically)	Associated process(es)	PI domain	Qualitative and quantitative comparison with conventional technologies[a]	Reference(s)
Vertical thin film dryer	• Drying	Spatial and thermodynamic	• Saving more than 92% of energy than conventional method [62]. Antifouling in the reactor. • Continuous drying. • Compact equipment. • High thermal efficiency. • Flexible heating source.	[188]
Vortex reactor	• Separation	Spatial	• Excellent gas–solid separation (~100%).	[78–80]
Wet-stirred media milling	• Milling	Spatial and temporal	• Nanoparticle production (down to sub 100 μm). • Rapid process and eliminates the use of solvents (eco-friendly).	[133,134]

[a] When compared to standard equipment such as CSTRs and straight tube reactors (and to standard batch processing where applicable).

2. Process intensification in solids handling

Notwithstanding the limitations imposed by the presence of solids when PI is being considered, there are a substantial number of PI based unit operations where the processing of solids has been applied. In other cases, there are considerable opportunities for intensification by existing PI equipment or those under development. In the following sections, the processes across a range of sectors where PI might be applicable and has been demonstrated in some cases are described and discussed. The range of PI technologies/techniques related to solids handling, categorized into distinct processes is summarized in Fig. 2.

2.1. Precipitation/crystallization

Precipitation/crystallization is the generation of solid particles from solution. The solubility rules for common ionic solids can be used to determine if a reaction could form a precipitate. Good control of operating parameters such as temperature and mixing intensity can affect the desired particle characteristics. For instance, the formation of small particles with narrow size distribution is governed by nucleation/growth kinetics and residence time distribution of the processing mixture, which are the direct results of the fluid dynamics [11]. Precipitation and crystallization can be achieved by using different PI technologies and methods, such as the spinning disc reactor (SDR), spinning cone reactor (SCR), rotating packed bed (RPB), Taylor–Couette reactor (TCR), oscillatory baffled reactor (OBR), continuous flow microreactor, Helix reactor, microwave applicator, ultrasound applicator, and dual impinging jet (DIJ) mixers. The common feature of this equipment is the high shear or mixing rates which can be achieved, generating exceedingly high supersaturations. In turn this allows very fine crystals to be grown.

The spinning disc reactor technology imposes high centrifugal acceleration to liquids flowing on its surface as shown in Fig. 3. The fluid, which is typically supplied at or near the centre of the spinning disc, is rapidly accelerated to the local angular velocity of the disc surface and forms an extremely thin wavy film (typically ranging from 50 to 500 μm) with high surface area to volume ratio (typically up to 30,000 m^2/m^3), even on scale up [12]. The SDR has the ability of achieving high supersaturation levels by rapid micromixing in the thin film [13,14], which makes it suitable for precipitation. The reactive-precipitation process in an SDR has been explored in various earlier studies [14–21]. Cafiero et al. [15] reported that it was possible to produce a very high specific number of crystals ($4 \times 10^9/cm^3$) in an SDR with a much lower power dissipation (115 W/kg) than the conventional continuous-flow stirred tank reactor (100 kW/kg with $2–4 \times 10^8/cm^3$ crystals). The variation of operation and reactor design parameters, such as the initial supersaturation, rotational speed, surface structure of the disc, and the disc diameter, influences the precipitation in the SDR. Khan and Rathod [16] utilized the SDR for the continuous preparation of curcumin nanoparticles via solvent–nonsolvent (S–NS) precipitation. By increasing the operational parameters such as disc speed, disc size, and non-solvent flow rate, the average curcumin nanoparticles size can be reduced almost 30%, which also benefits from the low concentration of curcumin in the solvent. However, the particle size was increased with increasing the flow rate of the reactants which was also demonstrated by Tai et al. [17]. The studies by Jacobsen and Hinrichsen [14] and Dehkordi and Vafaeimanesh [18] presented the influence of parameters on the precipitation of barium sulphate in an SDR. They demonstrated the advantages of controllable particle size and distribution, ranging from micrometres down to smaller than 100 nm, as well as fouling or blocking remediation in an SDR by varying operating parameters, such as disc rotational speed, initial supersaturation, and design parameters (i.e. the disc diameter, the feed location, and the surface structure of the disc). Reactive precipitation of TiO_2 in an SDR was investigated by Mohammadi et al. [19] for a wide range of physical and operational parameters. The SDR generated small
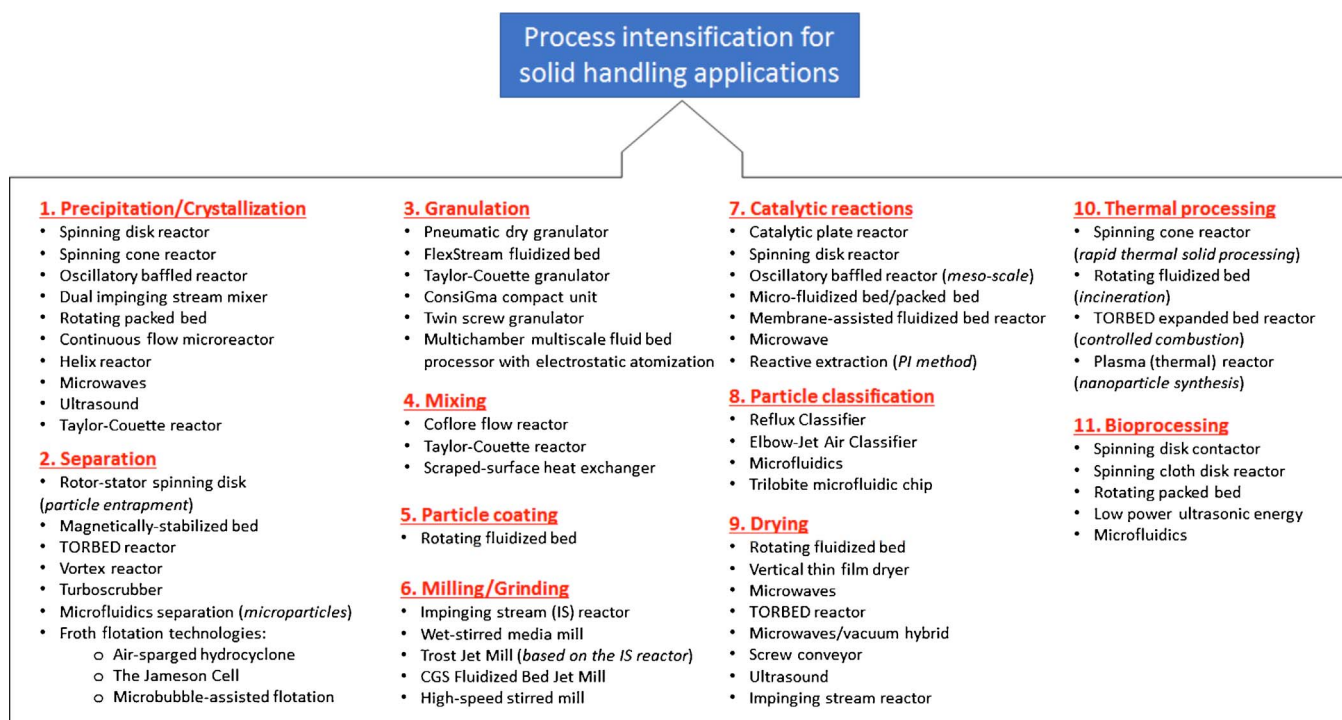
Process intensification for solid handling applications

1. Precipitation/Crystallization
- Spinning disk reactor
- Spinning cone reactor
- Oscillatory baffled reactor
- Dual impinging stream mixer
- Rotating packed bed
- Continuous flow microreactor
- Helix reactor
- Microwaves
- Ultrasound
- Taylor-Couette reactor

2. Separation
- Rotor-stator spinning disk (*particle entrapment*)
- Magnetically-stabilized bed
- TORBED reactor
- Vortex reactor
- Turboscrubber
- Microfluidics separation (*microparticles*)
- Froth flotation technologies:
  - Air-sparged hydrocyclone
  - The Jameson Cell
  - Microbubble-assisted flotation

3. Granulation
- Pneumatic dry granulator
- FlexStream fluidized bed
- Taylor-Couette granulator
- ConsiGma compact unit
- Twin screw granulator
- Multichamber multiscale fluid bed processor with electrostatic atomization

4. Mixing
- Coflore flow reactor
- Taylor-Couette reactor
- Scraped-surface heat exchanger

5. Particle coating
- Rotating fluidized bed

6. Milling/Grinding
- Impinging stream (IS) reactor
- Wet-stirred media mill
- Trost Jet Mill (*based on the IS reactor*)
- CGS Fluidized Bed Jet Mill
- High-speed stirred mill

7. Catalytic reactions
- Catalytic plate reactor
- Spinning disk reactor
- Oscillatory baffled reactor (*meso-scale*)
- Micro-fluidized bed/packed bed
- Membrane-assisted fluidized bed reactor
- Microwave
- Reactive extraction (*PI method*)

8. Particle classification
- Reflux Classifier
- Elbow-Jet Air Classifier
- Microfluidics
- Trilobite microfluidic chip

9. Drying
- Rotating fluidized bed
- Vertical thin film dryer
- Microwaves
- TORBED reactor
- Microwaves/vacuum hybrid
- Screw conveyor
- Ultrasound
- Impinging stream reactor

10. Thermal processing
- Spinning cone reactor (*rapid thermal solid processing*)
- Rotating fluidized bed (*incineration*)
- TORBED expanded bed reactor (*controlled combustion*)
- Plasma (thermal) reactor (*nanoparticle synthesis*)

11. Bioprocessing
- Spinning disk contactor
- Spinning cloth disk reactor
- Rotating packed bed
- Low power ultrasonic energy
- Microfluidics

Fig. 2. State-of-the-art of intensified technologies/methods for processes related to solid handling applications.
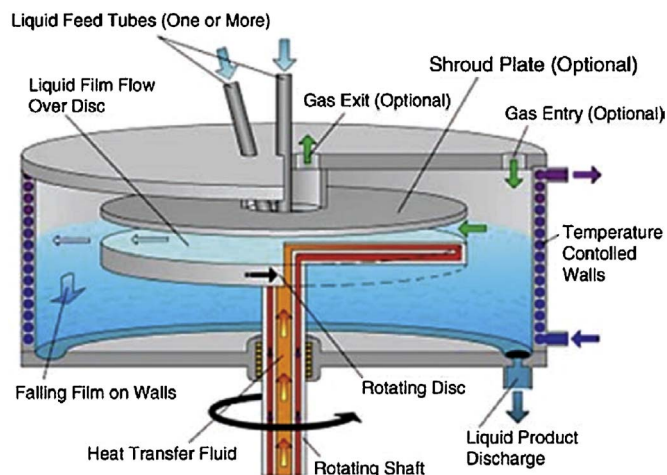

Fig. 3. Schematic of a typical SDR [25].

particles of the order of less than 1 nm with narrower distribution at higher disc rotational speeds and higher flowrates on grooved disks (Fig. 4). These particles were typically about 2–3 orders of magnitude smaller than those obtained from conventional stirred reactors. Fouling was avoided in this process by careful selection of the operating conditions; a low water to precursor ratio below 6:1 was especially detrimental in controlling particle agglomeration and preventing clumps on the disc surface [22]. Fig. 5 shows the severe fouling in SDR at low ratio of water/TTIP (titanium tetra isopropoxide). De Caprariis et al. [20] performed experimental and numerical investigations of the reactive precipitation in an SDR. Both experimental and numerical studies showed the inverse proportion of the size of nanoparticles and disc speed. The size of nanoparticles decreased from 350 nm to 78 nm as the rotational speed of the disc increasing from 58 rad/s to 147 rad/s. In the investigation of continuous production of superparamagnetic Fe_3O_4 nanoparticle by Chin et al. [21], the SDR was demonstrated to be an efficient reactor which presented advantages such as rapid mixing and effective heat and mass transfer for coating

surfactants onto the nanoparticles. Indeed, Aoune and Ramshaw [23] also demonstrated the SDR has the advantages of higher heat and mass transfer in wavy films compared to the Higbie model for smooth film flow. The heat transfer in the wavy film was 5 times higher and the mass transfer in the wavy film was almost 9 times higher than in the smooth film. The SDR is also capable of producing fine crystals with low risk of fouling or plugging. Oxley et al. [24] presented the results of using a continuous SDR for the recrystallization of an active pharmaceutical ingredient (API) in a solvent/antisolvent crystallization process. The SDR was capable of forming particles with a narrow particle size distribution and a mean particle size of around 3 μm, representing a drastic improvement on the conventionally processed product (Fig. 6).
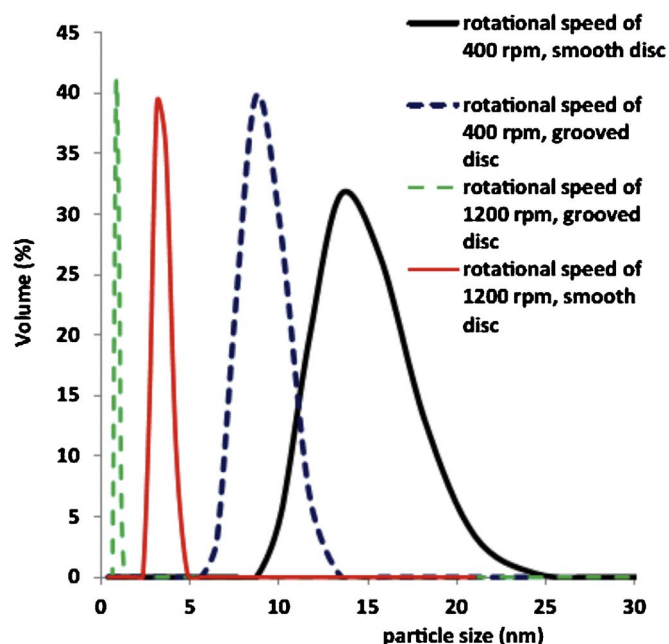

Fig. 4. Effect of SDR processing on TiO_2 particle size distribution [19].

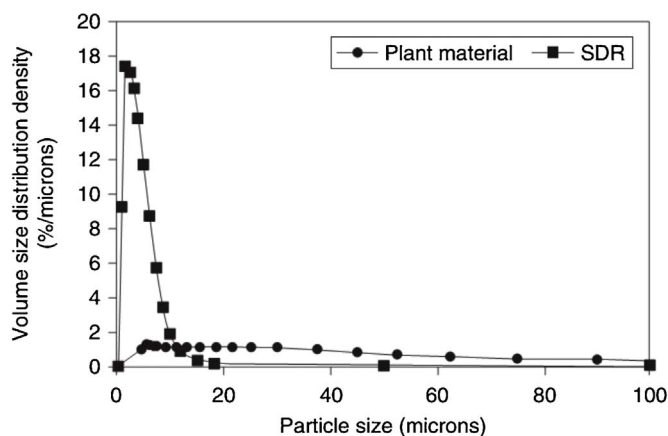**Fig. 5.** Severe fouling in SDR at low ratio of water/TTIP = 4 [22].

Fig. 6. Recrystallization of an API, comparison of particle size distributions [24].

Fig. 7. The spinning cone concept [26].

In order to overcome potential fouling of the disc surface, the authors employed a Teflon coated disc surface [24].

The concept of a spinning cone reactor (SCR) (Fig. 7) is similar to that of an SDR except that the surface is in the form of cone and the centrifugal force imposed on the flowing liquid is not aligned to the cone surface as it is in an SDR. Hetherington et al. [26] used an SCR for the precipitation of barium sulphate. Smaller crystal sizes were consistently obtained in the SCR than in batch processing. At a supersaturation of 500 and the rotational speed of 6000 rpm, the crystal size of a Sauter mean diameter of 3.2 μm was found using the SCR comparing to 6.85 μm from the batch runs. The particle size in SCR (0.1–1 μm) was found to be smaller than in the batch run (1–10 μm) with increasing cone rotational speed to 8000 rpm.

The rotating packed bed (RPB) is another piece of intensified equipment that is based on the high centrifugal acceleration technique. In contrast to spinning disks or cones, it consists of an enclosed volume packed with structured packings of higher specific surface area compared to conventional packed bed devices. Sketches of two counter-current RPB configurations are presented in Fig. 8. In the context of solids processing, the RPB technology has been exploited for its rapid micromixing characteristic (0.01–0.1 ms, [27]) in the production of nanoparticles. A new method called high-gravity reactive precipitation (HGRP) was used by Chen et al. [28] and Chen and Shao [27] in the RPB for the manufacture of $CaCO_3$ nanoparticles. They demonstrated the advantages and industrial potential of RPB by synthesizing $CaCO_3$, $Al(OH)_3$ and $SrCO_3$ nanoparticles in RPB, scaled-up to an annual capacity of 10,000 tons. Based on their study, the RPB could control and adjust $CaCO_3$ particle size in the range of 17–36 nm by varying the operating parameters, such as rotating speed, fluid flow rates, and reactant concentrations.

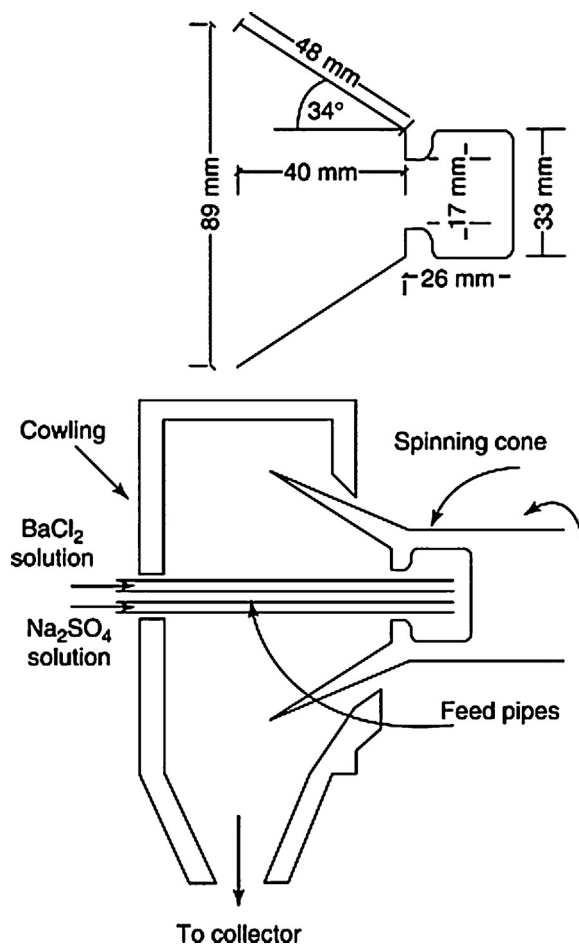Taylor–Couette flow, which is the flow between two concentric cylinders, has long been a subject of interest in fluid mechanics (Fig. 9). The fluid in the gap between the two differentially rotating cylinders exhibits a series of instabilities, in both the laminar and turbulent regimes, as the rotational velocity of the cylinder is increased. A Taylor–Couette reactor (TCR) is used in several crystallization studies [30–33]. The residence time in TCR was reported to be 3–5 times faster than in the conventional stirred tank crystallizer. The size distribution of crystal product was much narrower in TCR (size distribution coefficient, 0.45) when compared to the conventional stirred tank crystallizer (size distribution coefficient, 0.8) [33].

An oscillatory baffled reactor (OBR) consists of a tube fitted with a series of equally spaced baffles, commonly orifice type (Fig. 10b). It is a form of plug flow reactor. Fluid inside the reactor is oscillated via diaphragms, bellows or pistons placed at one or both ends of the tube. This results enhanced fluid mixing as well as the heat and mass transfer. OBRs can be classified based on tube diameter: conventional OBR (> 12 mm) and meso-OBR (< 5.0 mm). OBRs, both conventional and meso-scale typically operate at low net flowrates whilst maintaining plug flow. Meso-scale OBR on the other hand enables the use of small volume of chemicals. It is a viable process screening platform as well as to optimize process conditions [35]. Established applications of OBRs include biodiesel productions [36], bioprocessing [37], saponification [38], and mass transfer (ozone-water dissolution) [39]. McGlone et al. [40] were one of the first teams to investigate the efficacy of continuous crystallization of APIs in OBRs, which would convert the traditional batch mode – which is slow, into the more efficient continuous mode. Lawton et al. [41] investigated continuous crystallization of APIs in an OBR and have found that the processing times were on average 80% shorter than batch processing. Abernethy et al. [42,43] carried out L-glutamic acid crystallization in a meso-OBR and achieved a narrow CSD
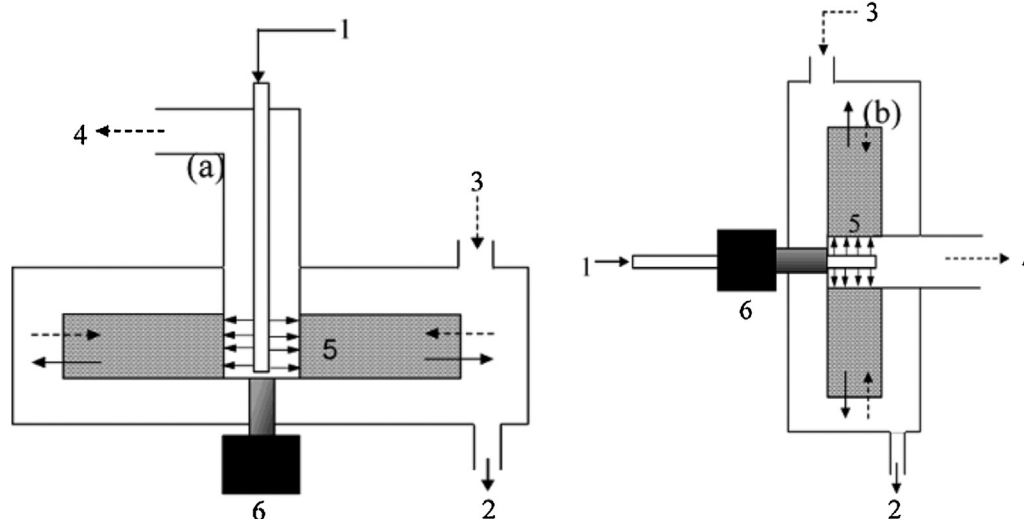
Fig. 8. Schematic of a rotating packed bed: (a) horizontal-axis RPB, (b) vertical-axis RPB. *Legend*: 1, liquid feed inlet; 2, liquid outlet; 3, vapour inlet; 4, vapour outlet; 5, packing; 6, motor [29].
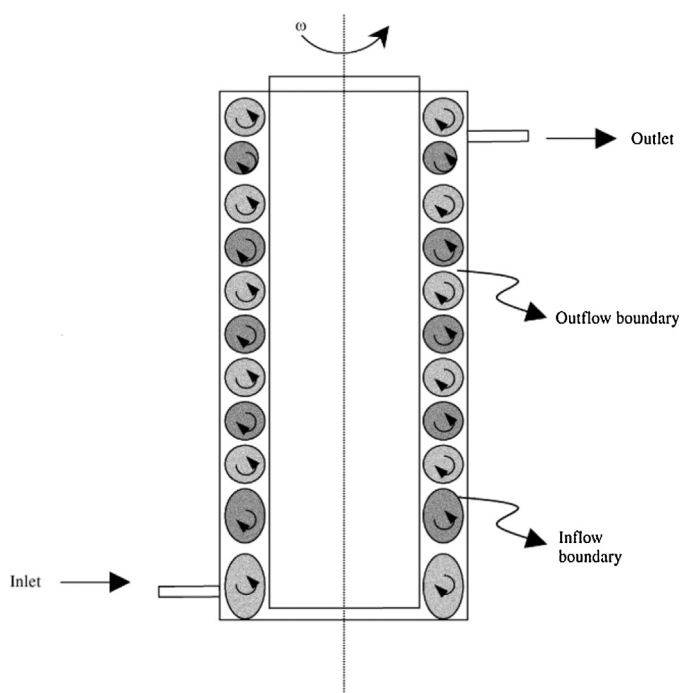

Fig. 9. The Taylor–Couette reactor [34].

with a critical particle size of approximately 20 μm. These studies concluded that OBRs are beneficial for crystallization due to their enhanced mixing, enhanced heat transfer, and plug flow – all of which resulted in better distribution of supersaturation, additives and impurities, more uniform CSDs, faster cooling rates, better temperature control, and consistent product properties. In addition, greater crystal morphology control (via experimental conditions e.g. oscillation frequency) resulted in a more uniform crystal shape and size due to the uniform mixing environment within the OBRs. This led to the improved particle flow characteristics and filtration [44]. A demonstrator OBR crystallizer was installed in the Sanofi plant at Haverhill, UK for the synthesis of an API in 2007. The volume of the crystallizer was 99.6% smaller than CSTRs of similar throughput [45], which was an impressive size reduction factor. At the time of writing, no further updates are available to indicate whether this demonstrator has been up-scaled to industrial size.

The term microreactor refers to a reactor with small channels of size

(depth/width) in the order of micrometres. Microreactors usually contain micro-machined or chemically etched channels (10–100 μm in diameter) and support chemical reactions in millilitre/microliter scale. Microreactors can efficiently control the process parameters associated with nanoparticle generation e.g. temperature, flow mixing, and continuous-flow operation. It also possible to continuously vary the composition of the reaction mixture because the smaller reaction volume is often sufficient to lower the polydispersity of particles [46]. Continuous processing presents many advantages compared to batch processing such as rapid heat transfer, better control of selectivity and efficient handling of safety issues [47–49]. These factors make the combination of continuous flow and microreactor an efficient technology for process intensification, especially in particle processing. McCarthy et al. [50] used a continuous flow microreactor with 4 channels for the crystallization of barium sulphate. The maximum mass production rate of one of the best channels was found to be 2.59 mg/s. They observed that the average particle size formed in the microreactor was 0.2 μm compared with 3 μm in a stirred batch reactor and formed when conversion was within the range of 30–40%. A continuous flow microreactor with an internal diameter of 0.8 mm and a length of 200 cm was used in the study of Appalakutti et al. [51] for copper chromite nanoparticle production. Particle size was found to be 15% smaller than in conventional co-precipitation method, since the residence time in the microreactor was decreased one order of magnitude in comparison to a batch process. Fouling and clogging need to be dealt and reduced in the microreactor. In a review of solid handling in microreactor by Wu and Kuhn [52], the authors mentioned the clogging phenomena could be affected by the channel design of microreactors. Surface modification and curvature of the channel have effects on the growth of particulate matter. Chen et al. [53] and Marcati et al. [54] used the similar plug-based microfluidic system to prevent clogging in microreactors as reviewed by Hartman [55]. Microreactor clogging can be eliminated by dispersing droplets in a carrier fluid in protein crystallization [53] and dispersing polymer products to contact with the microreactor walls [54].

A helical micro-reactor called the "Helix reactor" has been developed by TNO in The Netherlands as a contender for straight tube reactors. The helical configuration improves radial mixing and inhibits turbulence, which results in a near plug flow characteristic with a small pressure drop [56]. It was tested for the precipitation of calcium carbonate ($CaCO_3$), which showed a desirable morphology (smaller size) of precipitates as shown in Fig. 11b (right), compared to agglomerates typically formed in straight reactors, shown in Fig. 11b (left). This could be attributed to the enhanced mixing in the reactor.
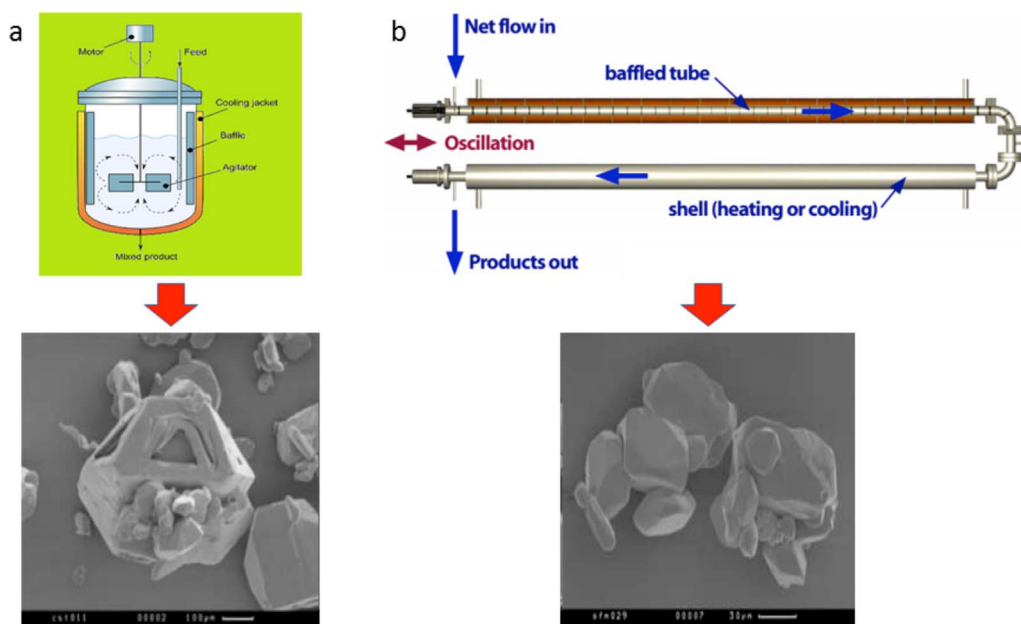
Fig. 10. Greater crystal morphological control is possible in continuous OBRs: (a) the traditional CSTR, (b) OBR [44].

Microwave processing is an example of the use of electric field for process intensification that has found widespread application in industry. Microwaves that correspond to wavelengths of 1 mm to 1 m and frequency from 1 to 30 GHz are typically assigned to industrial and scientific microwave heating and drying. Compounds with dielectric elements such as water can be heated easily by microwave irradiation (Fig. 12). The penetration depth of microwaves is highly dependent on the material property. Microwave-assisted evaporative crystallization was applied by Pinard and Aslan [57] to glycine molecules. They presented a technology called metal-assisted and microwave-accelerated evaporative crystallization (MA-MAEC), which was based on the combined use of metal nanostructures and microwave heating. Microwaves created a temperature gradient between the solvent and the nanostructures, which accelerated mass transfer and thereby, nucleation. It was reported that the use of microwaves decreased crystallization time by ~ 60-fold compared to the conventional evaporative crystallization. In a study by Radacsi et al. [58], niflumic acid was crystallized by microwave irradiation (injecting the solution in a single-mode microwave) and compared with conventional conductive heating (on top of a hot plate) [58]. Microwave irradiation increased the evaporation rate (corresponding to 166 s at 120 °C and 70 s at 180 °C in conventional heating and 43 s at 150 W power and 21 s at 300 W power in microwave heating) which led to reduced product size (about 70% smaller in size) since the crystal size increased approximately linearly with increasing crystallization time. They also reported that crystal form was not altered during the microwave-assisted crystallization
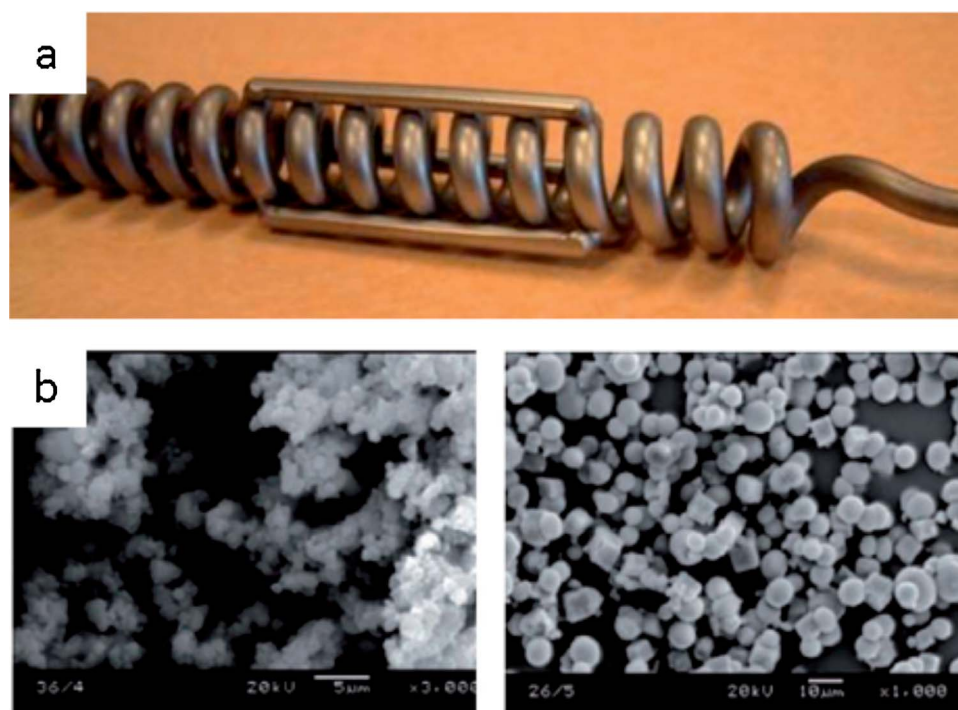

Fig. 11. (a) The TNO Helix reactor, (b) the precipitation of $CaCO_3$ particles in a straight tube (left) and in a Helix tube (right) [56].
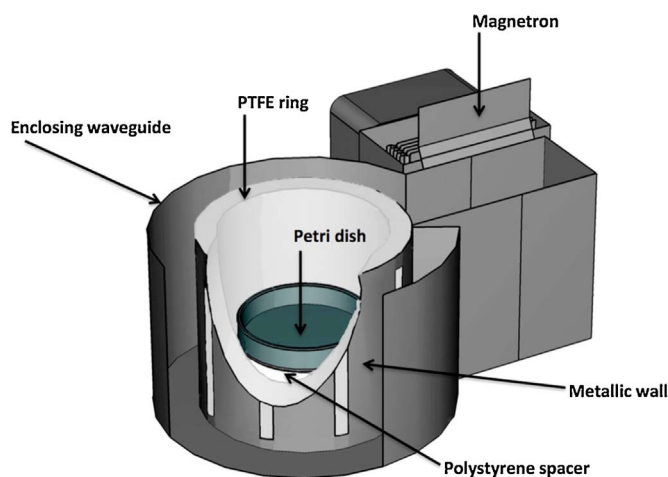
Fig. 12. Schematic of microwave irradiation used in Radacsi et al. [58].

which was verified by X-ray diffraction. This was probably due to the fast solvent evaporation in microwave heating. Microwaves were used by Kahrilas et al. [59] in a one-step microwave-assisted synthesis (AgNO$_3$ and aqueous extracts of various citrus fruits) of silver nanoparticles. Microwave operating parameters (time, temperature and pressure) were controlled. Synthesis of silver nanoparticles with a mean diameter of 7.36 ± 8.06 nm by reducing Ag$^+$ ions from silver nitrate using microwave and the orange peel extract were confirmed in the study. Pal et al. [60] also demonstrated the synthesis of silver nanoparticles by using microwave irradiation of silver nitrate solution in an ethanolic medium in microwave oven. By using polyvinylpyrrolidone (PVP) as a stabilizing agent, nanoparticles with 10 ± 5 nm diameter were obtained within 5 s of microwave irradiation.

Another PI technology that can be used in precipitation and crystallization is ultrasound. Ultrasound technology involves the use of sound waves that are beyond the frequencies detectable by the human ear. The frequency of ultrasound is normally considered to be between 20 kHz and 500 MHz [4]. Ultrasonication is the irradiation of a liquid, solid or gas with ultrasound waves resulting in the agitation of particles (Fig. 13). An ultrasound-assisted process was used by Bhanvase et al. [61] for the preparation of sodium zinc molybdate nanoparticles. Ultrasonic irradiation caused rapid nucleation and restricted the growth of nanoparticles. The average particle size was found to be lower by using ultrasonication (78.3 nm) than the conventional method (glass vessel with constant speed magnetic stirrer by means of continuous heating, average particle size = 340.2 nm). The ultrasonic-assisted precipitation method was also found to be more energy efficient than the conventional synthesis approach, saving more
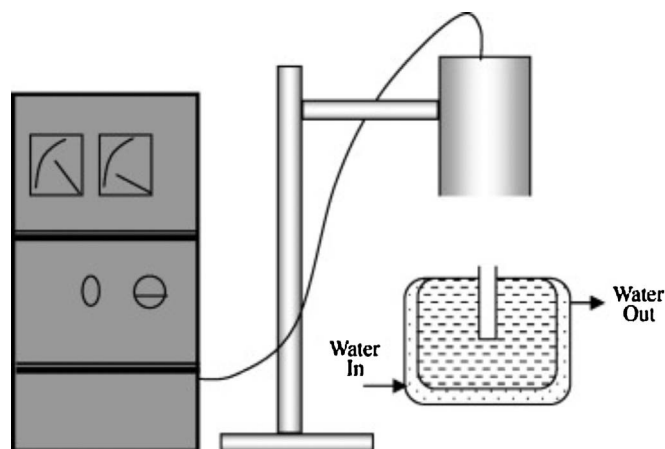

Fig. 13. Ultrasonic equipment used in Pinjari and Pandit [62].

than 92% of energy [62]. Jamshidi et al. [63] investigated the effect of ultrasound parameters on sonocrystallization in a microreactor. The mean size of the crystals decreased from 35 μm to 25 μm by increasing the ultrasound duty cycle from 500 to 6000 ultrasound cycles over the 2-s time interval. Rossi et al. [64] also used ultrasound in a microfluidic reactor for continuous flow sonocrystallization of adipic acid. It was found that the ultrasound was able to provide crystals with a very small mean size (ca. 15 μm) at high production rates (up to 20%). Jiang et al. [65] used indirect ultrasonication-assisted slug-flow crystallizer with an ultrasonication probe to generate crystals using L-asparagine monohydrate as the solute. They reported that the use of ultrasonication could avoid the potential for sample contamination. The ultrasonication probe produced a narrower product crystal size distribution (about 30% smaller) than in an ultrasonication bath process [66]. Ultrasonic vibration was used by Zhang et al. [67] for inducing the cavitation and acoustic streaming which mainly contributed to obtaining fine and spherical α-Mg particles. The solid volume fraction and average particle size were found to be increased when reducing the liquidus temperature of ultrasonic vibration in the study (Fig. 14). One particular advantage of processing under ultrasonic conditions in the presence of solids is the propensity for fouling to be controlled. This technology can effectively serve the dual purpose of intensification and displacement of the solid formed. This opens up the possibility for ultrasound technology to be combined with miniaturized equipment where solid blockages can cause major processing problems as has been highlighted by Benzinger et al. [68] who investigated the use of ultrasonic power to reduce fouling in microchannels. Their experiments utilized calcium nitrate/sodium hydrogen carbonate reactants, pumped through the channels of a microstructured device with increased operating temperature. This temperature caused precipitation of solid calcium carbonate on the surface, resulting in a reduced heat transfer coefficient. An ultrasonic pulse of 1 min broke up the fouling layer and the heat transfer coefficient reached its starting value. This study opened up the possibilities of sonification in diminishing fouling in microchannels. Hou et al. [69] designed an ultrasonic assisted direct contact membrane distillation hybrid process and tested the influence of ultrasonic irradiation on membrane fouling mitigation. With calcium ions in the feed, severe permeate flux decline through the membrane was found to be higher than 20% since the humic acid (HA) solution aggravated on the membrane surface. If ultrasonic irradiation was added in the process, most of the membrane pores remained open and clean and the relative permeate flux was maintained about 94%. Kan et al. [70] also used ultrasound for the cleaning of polytetrafluoroethylene (PTFE) membrane fouled by a pre-coagulated humic acid–bentonite mixture. It was reported that the flux recovery reached 45% with the help of ultrasonic cleaning.

The impinging stream (IS) reactor is based on two solid-in-gas suspension streams (recently, it has been expanded into liquid-in-gas streams) to flow in opposite direction at a high velocity and impinge against one another, yielding extremely high relative velocities at the instant of impingement [71]. This means that the IS reactor does not involve external agitation but instead, agitation occurs via direct contact of the reacting streams. Due to this effect, heat and mass transfers are greatly enhanced. The original concept for the impinging stream is depicted in Fig. 15. Fan et al. [72] recently attempted to combine an IS reactor with a rotating packed bed in the continuous preparation of Fe$_3$O$_4$ nanoparticles in the pilot plant scale. Their set-up was able to produce small nanoparticle size range (7.5–11.3 nm), which was highly desirable. They concluded that scale-up to industrial scale was indeed feasible, and highlighted the micro mixing characteristic of IS reactors.

The dual impinging jet (DIJ) mixers, based on the impinging stream concept, have been demonstrated to produce small crystals with narrow crystal size distribution in reactive and antisolvent crystallization, attributed to the enhanced mixing. Jiang et al. [74] recently investigated the production of a drug compound via the combination of
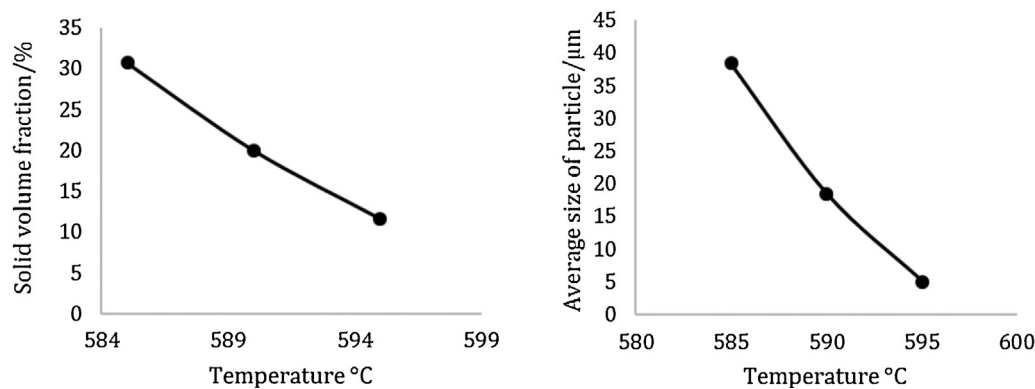
Fig. 14. Influence of ultrasonic vibration temperature on solid volume fraction and average size [67].

cooling and antisolvent crystallization in a DIJ mixer with a varying jet velocity (1–15 m/s). It was found that as the inlet velocity of the DIJ mixer increased, the mean crystal size decreased, the CSD narrowed, and the CSD changed into unimodal from bimodal. The impinging stream method in general is advantageous compared to competing technologies and has been demonstrated to be versatile e.g. applicable for drying, grinding, and milling – as reported in subsequent sections of this paper. In its miniaturized form, the IS method also shows the ability to prevent fouling. It was found that in impinging jet mixers, the induced mixing energy was sufficient to prevent particle agglomeration. Although not appropriate in all applications, particle–wall contact could be avoided by encapsulating precipitated particles in droplets of a liquid that is immiscible in the surrounding fluid. This had been demonstrated for the synthesis of colloidal cadmium selenide nanoparticles. Electric fields have also been used to inhibit particle fouling and although not elaborated here, the use of externally-applied magnetic fields to inhibit scaling has been successfully used in many systems whereby calcium carbonate in particular can build up a thick film [75].

In summary, in precipitation/crystallization, the SDR is a good option. It can produce particles 2–3 orders of magnitude smaller than those obtained from conventional stirred reactors while consuming 15% lower energy. Where appropriate, fouling mitigation strategies involving, for instance, disc surfaces coated with a non-stick layer can be envisaged. The use of microwaves is also beneficial and can decrease crystallization time by ~60-fold compared to the conventional eva-

porative crystallization when generating particles. Ultrasound is another method applicable to precipitation and crystallization. With the assistance of ultrasound, the consumption of energy can be reduced by more than 92% compared to conventional methods. Ultrasound can also prevent fouling inside the reactor. Other technologies and methods, such as the OBR, RPB, and microreactor, also show capabilities in precipitation/crystallization. OBR and RPB are reported to have the ability of scaling up to industrial size.

2.2. Separation

After reactions, separation processes are the most important unit operations in chemical industry and include distillation, stripping, absorption, extraction, evaporation, crystallization, and so on. Intensification of separation processes typically involve 'active' methods e.g. rotation (HiGee distillation) and electromagnetic fields. In this section, intensified separation equipment involving solids handling are described, which include the rotor-stator spinning disc (RSSD), vortex reactor, TORBED reactor, magnetically stabilized bed, froth flotation, microfluidics separation, and Turboscrubber.

A rotor-stator spinning disc (RSSD) contains a rotating disc (rotor) located between two static disks (stators), and is a variant of the thin film SDR (Fig. 16). Small channels which are a few millimetres in height are formed between the rotor and stators. The spinning disc normally rotates at around 1000 rpm and generates high shear thin films. van
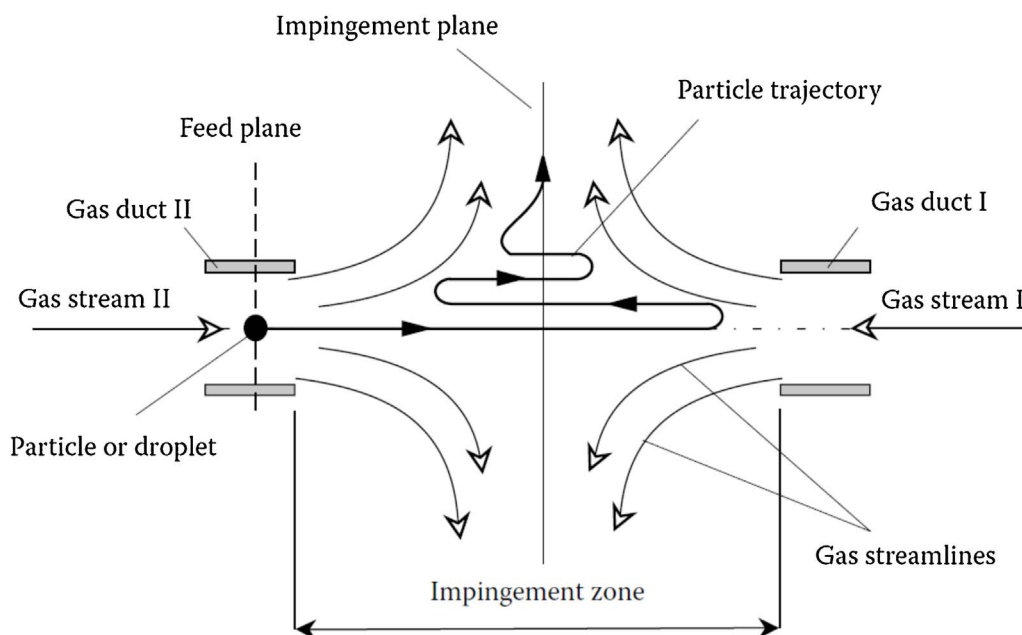

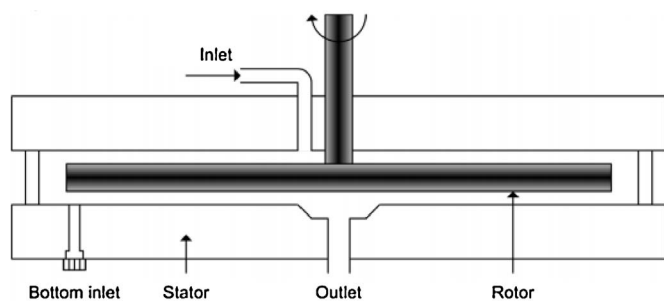**Fig. 15.** The original concept of the impinging stream process [73].

Fig. 16. Rotor-stator SDR equipment [77].

Eeten et al. [76] used a novel type of RSSD for the entrapment of solid particles. In their experiments, the volume between two rotors was filled with a reticulated carbon foam which was found to improve the particle containment in the reactor. The study found that the reticulated carbon foam played an important role in the particle entrapment. Particles with diameters down to 18 μm could be completely entrapped in the gaps, filled with the foam.

The vortex reactor, which can also be called a rotating fluidized bed reactor in static configuration, shares the same working concept as the conventional rotating fluidized bed reactor. However, it contains a static fluidization chamber where the rotating motion of fluid comes from the tangential injection of fluidizing gas through multiple slots on the wall of the chamber. Fig. 17 shows the configuration of vortex reactor. The fluidizing gas is forced to leave the chamber via a chimney located in the centre of the chamber. The centrifugal forces make the vortex reactor an effective device in gas–solid separation. The relatively small bed thickness and high gas flowrate also lead the gas–solid contact time to be very short. Gas that is being injected into the chamber exerts both radial and tangential forces which results in radial and tangential motion of the gas, leading to bi-directional fluidization of the bed. De Wilde and de Broqueville [78] carried out gas–solid separation by using a vortex reactor for two different types of particles, polymer particles, and salt particles. The solid accumulation in the vicinity of the gas inlet slots led to the non-uniform distribution of the gas flow, which caused "slugging" until complete separation of solid particles took place. Dutta et al. [79] performed a numerical study of a vortex reactor. Compared with the experiments of De Wilde and de
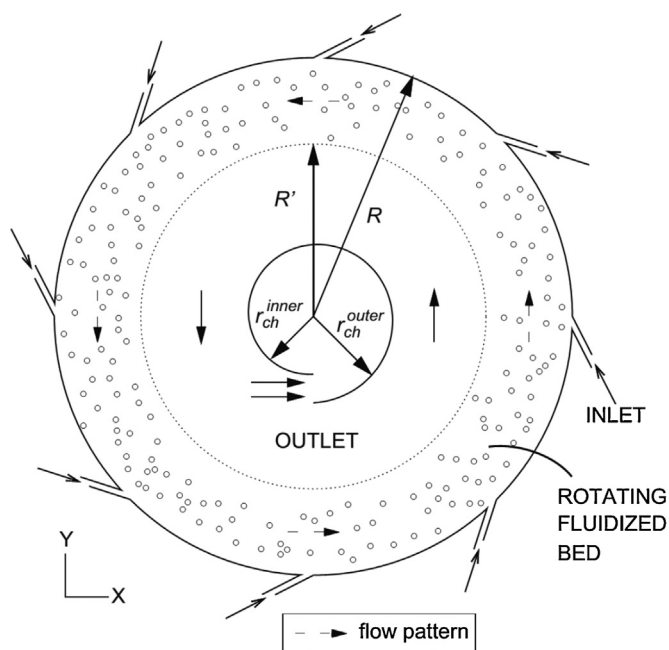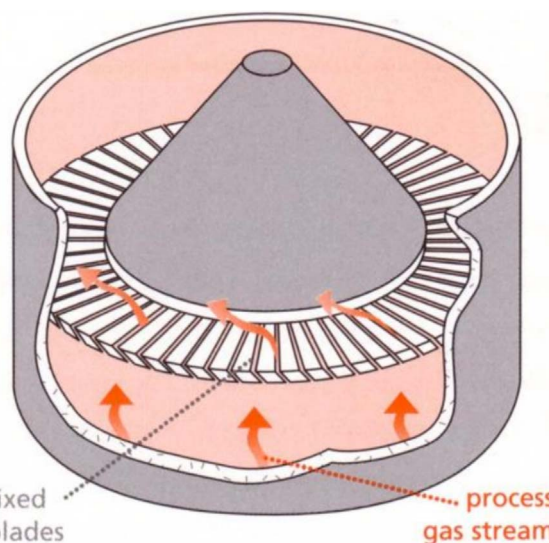

Fig. 18. TORBED™ Compact Bed reactor [83].

Broqueville [78], they reported that the efficient gas–solid separation was due to the fact that the solid particles did not leave the chamber through the chimney but instead, kept rotating in the chamber. Kang et al. [80] tested the capability of a swirling fluidized-bed reactor for pyrolysis in recycling of polystyrene plastic (PSP) wastes. The reactor used in this study was not a typical vortex reactor – the swirling flow pattern (vortex flow pattern) was formed by injecting a swirling gas (secondary) tangentially into the reactor at the wall of the reactor. The waste PSP was effectively decomposed thermally by the swirling motion in the reactor, which gave further evidence of the excellent separation in the vortex reactor.

The TORBED reactor, a swirling fluidized bed reactor which employs the concept of vortex reactor with a fixed and angled blade in the reactor (Fig. 18), is a technology developed by Torftech in 1980 which can be used for processing a wide range of materials, such as food, catalysts and toxic waste. It is widely used in Europe, Australia, North America, New Zealand, and Japan [81] because of its capability in dealing with different shapes of extremely fine particles (< 50 μm diameter) and facilitating easy gas recirculation. There are two types of TORBED reactor: the TORBED Compact Bed Reactor (CBR) (Fig. 18) and the TORBED Expanded Bed Reactor (EBR) (Fig. 19). Dodson [82] used the TORBED EBR to thermally treat sediments contaminated with polycyclic aromatic hydrocarbons (PAHs). By using an EBR, the PAH destruction efficiency was found to be 99.99% and no residual PAHs were detected in the emissions from the cyclone. About 20% of the particles not captured in the emission indicated a need for additional emission equipment downstream of the cyclone.

Magnetic fields can be used to augment classical fluidization technology, intensifying the process. The movement of magnetic solids can be controlled by an externally applied magnetic field. A magnetically stabilized bed (MSB) is a fluidized bed of magnetizable particles subjected to a spatially uniform and time invariant magnetic field oriented axially with a fluidizing flow. The particles with different density can be easily separated in a MSB. The ability to control solid movement in reactors attests to the advantage of a magnetically stabilized bed (MSB). The conventional air separation method by using air as the separation medium with a magnetic tracer has low separation efficiencies with the proportion of misplaced magnetite being above 40% [85]. In the study of Luo and Chen [86], their MSB used a mixture of magnetite powder and fine coal of 0.45–0.9 mm as solid media – it had excellent fluidizing performance and bed density stability. It could separate the coal efficiently, with the partition coefficient (the ratio of the concentrations of the non-ionized compound in organic and aqueous phases at equilibrium [87]) reaching > 90%. Zhou et al.
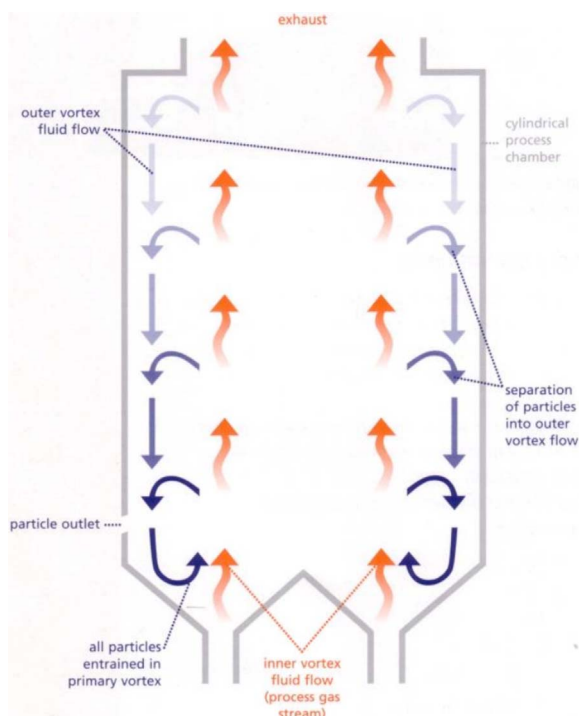

Fig. 17. A schematic of a vortex reactor [79].

Fig. 19. The principles of the expanded TORBED™ reactor [84].

[88] developed a magnetically-stabilized fluidized bed reactor for biodiesel production based upon immobilized *Rhizopus oryzae* lipase in magnetic chitosan microspheres (MCMs). In their study, the microspheres could be rapidly and easily separated from the reaction system. The productivity of the MCMs-immobilized lipase was still 80% with magnetically stabilization compared to 58% without magnetic stabilization after 6 repeated-batch cycles. It can be concluded that a magnetic field has some advantage in the separation. However, this technology requires magnetic particles inside the reactor.

Microfluidics has undergone rapid development in recent years. Various techniques related to microfluidics have been established for fast and accurate separation of microparticles. Warkiani et al. [89] developed a membrane-less microfiltration platform for cell separation (Fig. 20). The separation efficiency of the inertial microfiltration system for CHO and yeast cells was over 95% at a flow rate of 6 mL/min for a single chip and remained above 90% for various cell lines at different concentrations during 10 days of processing. Kumar et al. [90] used a novel inertial microfluidics (IMF) based procedure to separate cementitious powders. This IMF based procedure was able to separate mineral particles based on particle size. The smaller particles ($< 4 \, \mu m$) accumulated in the outer channel outlets, while the larger particles ($\geq 4 \, \mu m$) migrated close to the inner channel outlets. These results were in excellent agreement with other researchers' results [91,92]. Microfluidics can contribute to small reactors with lower fabrication cost and benefits in terms of reduced cost of reagents.
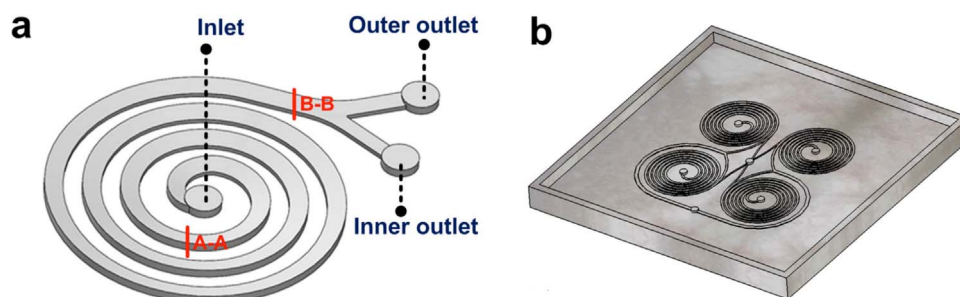
Froth flotation is a method for physically separating particles based on the differences in the ability of air bubbles to selectively adhere to specific mineral surfaces in a mineral/water slurry (i.e. hydrophobicity). Van Denventer [93] tested an air-sparged hydrocyclone (ASH) used for intensifying pyrite (iron sulphide, FeS_2) recovery from ores. They achieved a high (85–93%) pyrite recovery with a residence time of ~ 1 s, which was extremely rapid compared to batch flotation with a similar throughput (300 s). A modified ASH, the "Jameson Cell", is a highly intensified froth flotation cell. Its unique design allows for high intensity mixing between slurry and air, which results in the generation of a dense foam of fine bubbles and maximizing particle-bubble interaction ($\sim 100\%$ contact probability). The ability of the Jameson Cell in recovering minerals rapidly (within 5–10 s) rendered it being employed in base/precious metals, coal, oil sands, solvent extraction and mineral industries [94]. Microbubble-assisted flotation was recently investigated to enhance fine particle separation process. Microbubbles are classified as bubbles having the diameter range of 1–100 μm. Parmar and Majumder [95] recently studied the dispersion characteristics of microbubble-suspension flow (Fig. 21). After in-depth parametric studies, they recommended this technology due to its promising enhancement of the mineral beneficiation process. Their studies also established the basis for microbubble-flotation kinetics to aid further research on the technology.

The "Turboscrubber", developed by Osprey Corp. and FTL Technologies, is a high efficiency turbulent bed gas scrubbing technology. The Turboscrubber system uses different hollow plastic elements of varying shape to generate a three-phase fluidized bed whereby, increased Reynolds numbers (hence, turbulence) in the gaseous phase and the liquid phase provoke an intense enhancement of turbulent action which in turn leads to substantial increases in overall mass and heat transfer coefficients and interphasic surface renewal rates. There is therefore a high potential for very fine (sub-micron) particulate abatement from the gas streams. It is also inherently non-clogging so able to operate without fouling even when handling fluid streams with high solid contents and sticky substances. Some examples include Cl_2 abatement/metallic chlorides fume removal in gold smelting plant (Switzerland) and HCl abatement/SiO_2 fine particulate ($< 0.5 \, \mu m$) removal in fibre optic manufacture (UK). There is a potential for heat recovery from gas streams with high moisture contents and relatively low dew point temperatures e.g. 0.1 kg/kg dry gas, $> 52 \,^\circ$C dew point [96].

In summary, in larger particle separation (millimetre scale), the vortex reactor and the Magnetically Stabilized Bed (MSB) can provide very good results, up to 100% separation efficiency. However, the MSB use imposes limits on the reactants and vortex reactor is mainly used in gas–solid separation. Magnetizable particles are required which restrains the usage of the MSB in industry. The RSSD, TORBED, microfluidics, and Turboscrubber show excellent outcomes in smaller particle separations (micrometre scale). However, the RSSD requires a medium inside the reactor for separation and this necessitates further separation of particles from this medium. Microfluidics is a rapid developing method in separation which has high separation efficiency

Fig. 20. (a) Schematic of a trapezoidal cross-section spiral microchannel. (b) Schematic 3D drawing of a high throughput module consisting of four spirals connected together [89].
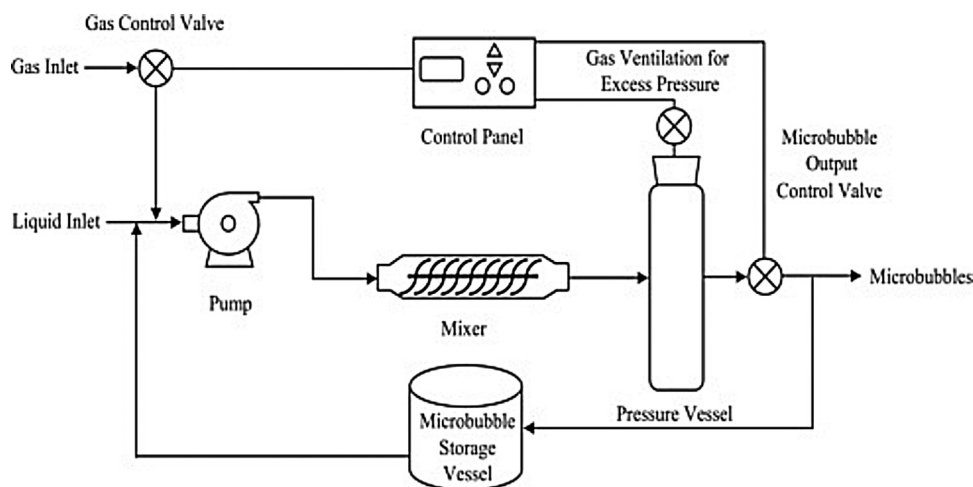
Fig. 21. Schematic representation of the microbubble generation technique [95].

and low cost but at the small scale. The Turboscrubber is a commercial product with a high potential for very fine (sub-micron) particulate abatement from a gas stream. So, for industrial use, it may be good option.

2.3. Granulation

Granulation is an important process step in agrichemicals, pharmaceuticals, foods, chemicals, and minerals. Granulation is the process of particle enlargement through agglomeration. Based on the method used to facilitate agglomeration, granulation techniques can be categorized as being either dry or wet. Dry granulation employs mechanical compression (slugging) or (roller) compaction to facilitate the agglomeration of dry powder particles, whilst wet granulation employs a granulation liquid (termed the "binder/solvent") to facilitate agglomeration by the formation of wet mass via adhesion. Wet granulation is the more prominently applied technique due to the capability of customizing the characteristics of the finished granule products compared to the dry method, despite it being technically more complex

[97]. The Taylor–Couette reactor has also been highlighted as a potential technology for efficient wet granulation [98–100].

2.3.1. Dry granulation

Literature highlights only one main technology which has recently been applied to dry granulation processing: the pneumatic dry granulator (PDG).

2.3.1.1. Pneumatic dry granulator. The PDG (Fig. 22) produces granules from powder particles by firstly applying mild compacting force via a roller compactor to produce a mixture of fine particles and granules. Granules outside the intended size range are then separated from the mix in a fractioning chamber by entraining them in a gas stream (a pneumatic system). The entrained particles subsequently pass through devices, for example a cyclone, and are immediately returned to the compactor for re-processing or stored for later treatment [101]. The first PDG was set up in Excella GmbH (Germany) as a demonstration project for tablet production in 2010 [102]. The equipment was capable of processing up to 60 kg/h, equivalent to 1 ton/day. It has been
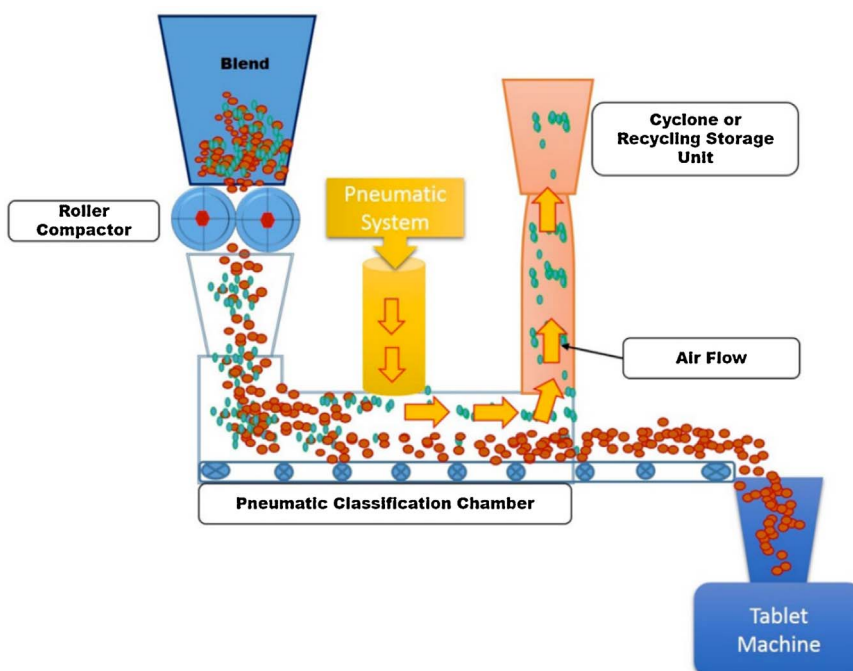

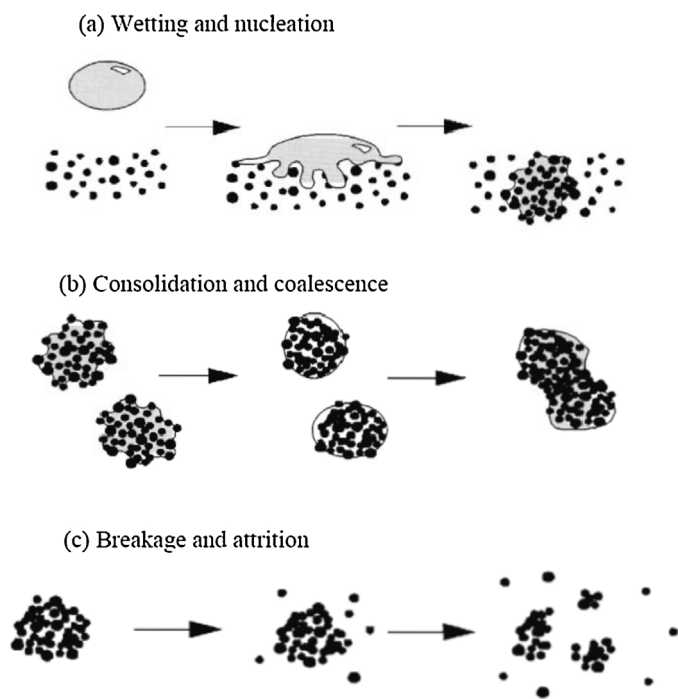Fig. 22. Pneumatic dry granulation (PDG) process [97].

(a) Wetting and nucleation

(b) Consolidation and coalescence

(c) Breakage and attrition

Fig. 23. The mechanism of wet granulation can be generalized into the stages: (a) wetting and nucleation, (b) consolidation and coalescence and (c) breakage and attrition [103].

reported to produce good flowability, and porous and highly compressible granules. This technology also allows for faster processing speed, reduced cost, little or no wastage and low dust exposure because of the enclosed design of the PDG equipment. However, the technology suffers from some issues relating to the quality of the recycled granules, its suitability for low dose formulations and friability [97].

2.3.2. Wet granulation

In wet granulation, the granules are produced by wet massing the formulation i.e. inactive excipients and active ingredients with granulation liquid, with or without a binder. Wet granulation for particle enlargement is a relatively complex process, which can be visualized with the assistance of Fig. 23. The liquid binder is first added to the premixed powder bed by pouring or spraying directly onto the bed. It can also be a solid binder, which is melted via heating the vessel to the melting point of the solid binder, a process known as "hot melt granulation". The liquid binder is distributed in the agitated powder bed and the wetted particles will form nuclei that are deformed and densified when colliding with the vessel wall, the blade, and with the

neighbouring particles. The densification process will force the liquid to migrate to the nucleus surface, which allows for coalescence and binding with other particles to form a larger aggregate. Breakage also occurs when the collision force exceeds the critical value a granule can withstand. The wet granulation process therefore can generally be classified into three steps: (a) wetting and nucleation, (b) consolidation and coalescence and (c) breakage and attrition [103].

A generalized industrial process of wet granulation is described in Fig. 24. Up until now, fluidized bed granulators and high shear mixer-granulators have dominated the scene – these equipments are often operated in batch mode. The former is an option to produce more porous granules whereas the latter produces more dense and uniform granules [103].

The following subsections discuss some other equipment options: the ConsiGma unit, the FlexStream fluidized bed and the twin screw granulator (TSG). These are designed to provide continuous granulation to reduce time-to-market and to increase the cost-effectiveness in production. All the technologies described can be considered PI, mainly due to their energy saving feature, faster processing and the reduction in solvent use.

2.3.2.1. ConsiGma compact unit. The ConsiGma continuous high shear granulation and drying system developed by GEA Group is a novel platform that can transfer powder into coated tablets in development, pilot, clinical and production volumes in a single compact unit. The system can perform dosing and mixing of raw materials, wet or dry granulation, drying, tableting and quality control – all in one production line. By producing granules continuously, batch sizes are determined by how long the machine is run. Because of ConsiGma's innovative design, the amount of waste produced during start-up and shut down is significantly reduced compared with conventional methods. Quality is measured throughout the process – therefore, it drastically reduces the cost per tablet. After multiple tests, it was concluded that the unit would provide (relative to the traditional methods): 10 times faster processing, 40% savings on labour, 60% reduction in equipment size, 50% energy savings based on reduction in installed power/heat recovery and 0.5–5.0% yield improvement [104]. Fig. 25 shows a ConsiGma unit installed at Pfizer Lab in Groton, United States for the research into on-demand tablet production [105].

2.3.2.2. FlexStream fluidized bed processor. The FlexStream fluidized bed processor developed by GEA Group is an industrial application of a fluidized bed in its static configuration with a side-spray for granulation. Wong et al. [106] employed the FlexStream™ fluidized bed for high-speed granulation in the production of chlorpheniramine maleate, used as a drug in the pharmaceutical industry (Fig. 26). They carried out extensive parametric studies on design and experimental conditions. At optimum conditions, high drug uniformity – a desirable
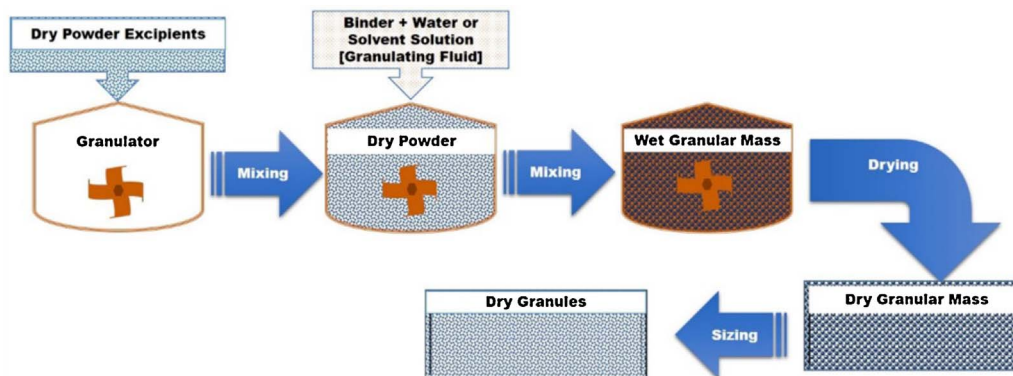

Fig. 24. Schematic diagram of the conventional wet granulation process [97].

Fig. 25. A ConsiGma unit in Pfizer Lab at Groton, United States for the investigation into on-demand tablet production [105].

characteristic, was observed in granules.

2.3.2.3. Twin screw granulator (TSG). Wet granulation can be carried out in twin screw granulators (TSG – Fig. 27a) as reported in reviews of the subject [107,108]. The TSG is often divided into different zones for feeding (usually from external feeders), wetting (from liquid injector port), mixing, homogenization and discharging the product. These are arranged in series to link each granulation step. This provides a greater opportunity for controlling product granule properties such as size, density, friability and compressibility – this has so far been difficult to achieve using current granulation technologies [109].

According to Vervaet and Remon [110], the TSG is popular because of its flexibilities, namely in feed/liquid injector port locations, and screw configurations that give different mixing and compounding
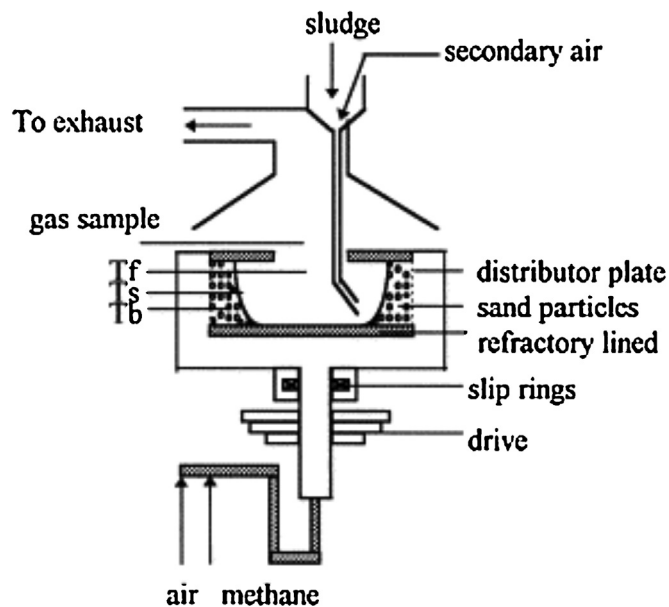

Fig. 26. The schematic diagram of the RFB combustor [106].

effects as well as temperature control via a heating/cooling jacket around the barrel. In addition, the screws are inherently self-wiping, which minimizes the accumulation and possible degradation of materials. This keeps the surface of the screws clean. Kumar et al. [111] reiterates that the TSG is an important development in transforming the current batch mode granulation in pharmaceutical industry into continuous mode. One of the key factors is the very short residence time in a TSG (only minutes from start to finish). TSG also offers a wide range of throughputs and an excellent mixing of formulations compared to

alternative wet granulation methods. Another advantage is that TSGs can be used to scale up batch granulation simply by operating the equipment for longer time periods. This eliminates scaling-up hurdles. Liquid to solid ratios used in the TSG (typically 0.2–0.4) are relatively small compared to other techniques – this would negate or lower the load of downstream drying of granules as well as preventing over-wetting of the agglomerates [112–114].

2.3.2.4. Multichamber multiscale fluid bed processor with electrostatic atomization. Small batch granulation is becoming a huge interest in pharmaceutical industry because it enables faster drug development and shorter time-to-market [115]. The multichamber micro-fluidized bed processor with electrostatic atomization has been used by Kivikero et al. [116] to granulate small batches (20–50 g) of a common tablet filler, alpha-lactose monohydrate. In their set-up, electrostatic nozzle was used to spray highly charged droplets of granulation liquid. The advantage of this was that the droplet size can be controlled via changing the electric field and the granulation liquid feeding rate. Their results were still preliminary i.e. more pharmaceutical materials needed to be tested. However, it already showed that granule size was proportionally correlated with liquid flow rate and atomization voltage. They encountered difficulty in producing narrow granule size distributions, which needed to be rectified for the technology to be viable.

2.3.3. Taylor–Couette granulator

Taylor–Couette flow, which is the flow between two concentric cylinders, has long been a subject of interest in fluid mechanics. The Taylor–Couette reactor (TCR), which is based on this flow regime, can be used as granulator for solid particles, as well as for mixing (see Section 2.4). Wang et al. [98] reported the aggregate of latex sphere particles in the TCR by both numerical and experimental study. The mean size of aggregations increased with increasing rotation speed of the cylinder in laminar flow regimes. Conway et al. [99] and Krishnaraj and Nott [100] used the TCR for the study of granular flow. They found some unexpected behaviours that emerged when the device was used for granular materials, such as the formation of a single toroidal vortex that spans the entire cell in solid granulation which was not seen in fluid material. In contrast to the traditional Taylor instability in fluids, the vortices in the granular materials (with or without gas fluidization) developed in a manner consistent with the primary Taylor instability in fluids, while the vortices remained the same size associated with the traditional Taylor instability. They concluded that the potential is high for the TCR to be developed as a granulation device.

2.3.4. Summary

Granulation is an important processing step especially in pharmaceutical processing. The twin screw granulator is regarded as the technology to transform pharmaceutical processing based on its advantages compared to common granulation equipment: the residence time in a TSG is a few seconds (in batch granulators: a few minutes). In addition, all particles experience all the granulation steps and stay in the active granulation zones for a longer fraction of the total processing time, as opposed to particles in batch granulators, which tend to exist in the bulk of the powder bed.

2.4. Mixing

Mixing is the process of bringing different elements into a system to induce uniformity. It is a particularly important process in chemical engineering, which can be intensified by different methods and technologies, such as Taylor–Couette reactor (TCR), Coflore flow reactor, and scraped-surface heat exchanger (SSHE). Other high intensity mixing devices such as the SDR, OBR and the RPB have been described in earlier sections.

The Taylor–Couette reactor (TCR), based on the properties of Taylor
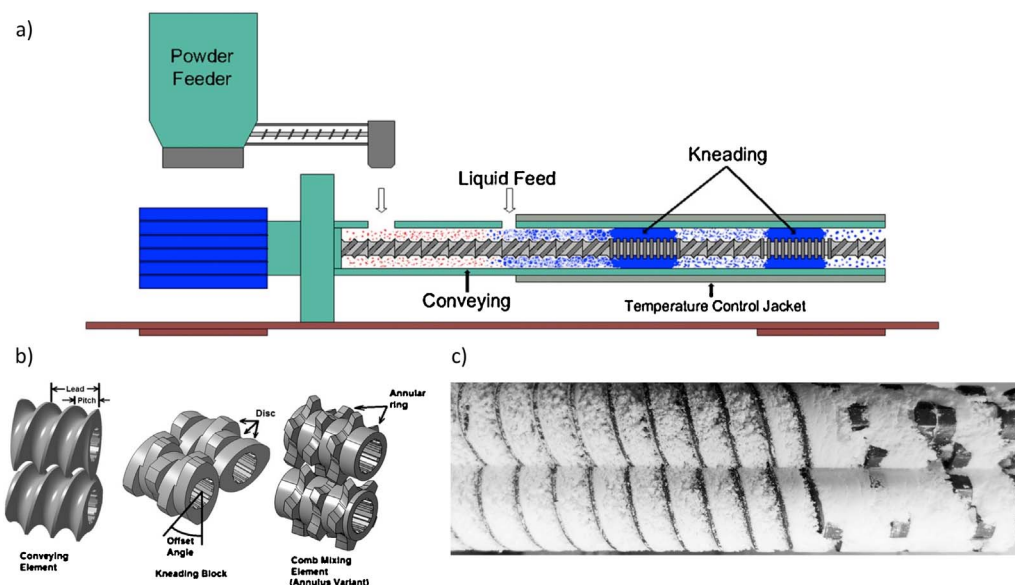
Fig. 27. (a) The components of a typical twin screw granulation module, (b) the three different screw elements, (c) wet granulation in TSG of microcrystalline cellulose/lactose monohydrate [107,108].

vortex flow – leads to a residence time distribution similar to the plug-flow reactor with good mixing. Each vortex can be treated as a well-mixed batch vessel and no intermixing over the cell boundary can be observed [117]. It has the advantages of efficient heat transfer and low hydrodynamic shear rates in the liquid phase. According to Kataoka et al. [117] who investigated mixing in Taylor–Couette flow, the TCR with axial flow has the ideal plug flow property in a range of rotating speeds of the inner cylinder ($0 < Re < 90$ for the geometry $d/R_i = 0.333$). Once the rotating speed exceeds a certain value ($Re = 90$ in this study), a new type of mixing appears in the Taylor vortices, which makes the Taylor–Couette flow deviate from ideal plug flow behaviour. A modified reactor with ribbed rotor constructed [118,119] enhanced micromixing whilst reduced macromixing simul-

taneously – this could be due to the bypassing of weakly mixed tracer being promoted more in the higher axial flow (depicted in Fig. 28). Sczechowski et al. [120] utilized a similar design as a novel photo-catalysis reactor for photocatalytic organic decomposition reactions in water. Fluid mixing based on the complex vortex motion in a range of rotational speeds (2–300 rpm) of the TCR provided controlled periodic illumination, which was essential to heterogeneous photocatalysis and high photoefficiencies. The photoefficiency in the TCR was increased by nearly a factor of three. Giordano et al. [34] reported that the TCR could be used for suspension of particles because of its low shear-rate but effective mixing characteristic in the fluid. They reported that the TCR can be used for transporting and processing solids through the annular section. The rotation of the cylinder could suspend the particles
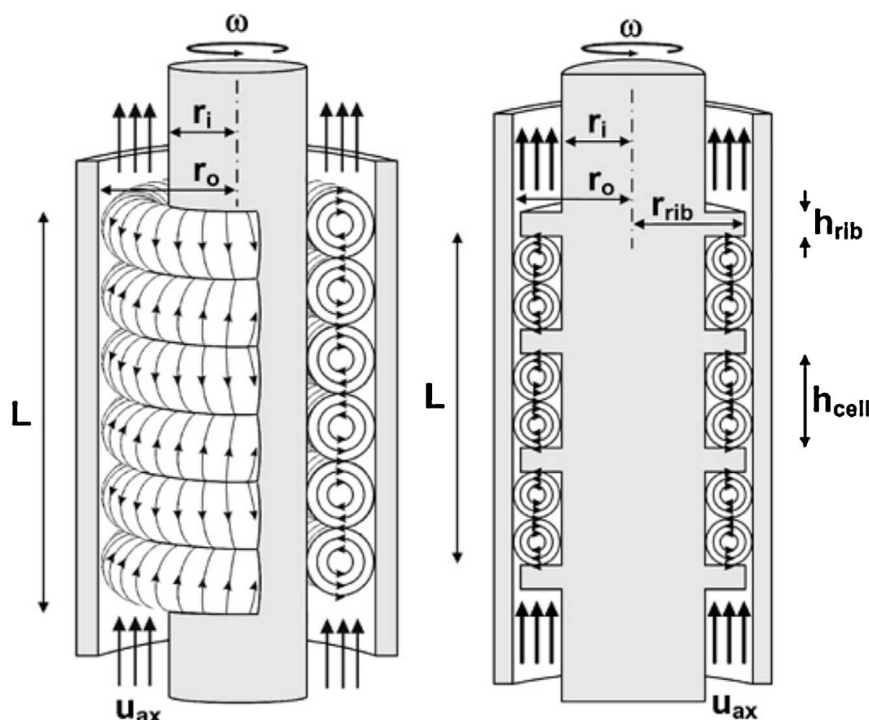

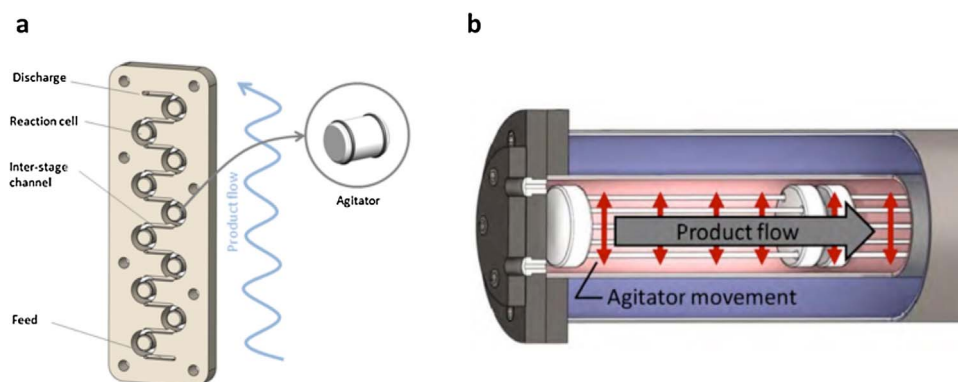**Fig. 28.** Ribbed Taylor–Couette reactor [118,119].

a

b

Fig. 29. Two variants of Coflore flow reactors: (a) agitated cell reactor (ACR), (b) agitated tube reactor (ATR) [122,123].

by the moving vortices or by the upstream by-pass. A gentle vortex agitation (even at high rotation rate, 3000 rpm in their case) was observed to cause no detectable damage to the suspended particles.

The Coflore flow reactors, developed by AM Technology (AMT), are advanced tubular reactors. The principal design employs a patented mixing technology whereby freely moving agitators with the reactor promote mixing when the reactor body is subjected to lateral shaking. This generates intense mixing without the need for rotating shafts, mixing baffles, or mechanical seals. The Coflore flow reactors provide excellent mixing performance with homogeneous fluids, immiscible liquids, slurries and gas/liquid mixtures with zero back mixing between reaction stages – this is an ideal plug flow condition [121]. The relatively simple geometry and excellent mixing throughout the Coflore reactors enable an effective means of keeping multiphase mixtures suspended and well dispersed in order to maintain an orderly flow through the reactors. Centrifugal separation (between two-phase reactants) is also eliminated [121]. The Coflore agitated tube reactor (ATR) was designed for homogeneous and multi-phase fluid mixing. Fig. 29 shows the two variants developed by AMT. Jones et al. [122] investigated an oxidation reaction catalysed by D-amino acid oxidase operated under benchtop batch mode in an ACR, and the subsequent scale-up in multi-litre continuous production in an ATR. The success of this continuous mode was an important milestone for the previously un-scalable process.

Browne et al. [124] demonstrated the efficacy of industrial-scale ACR tubes in the continuous production of a slurry, N-iodomorpholine, via the reaction of morpholine with iodine. The common batch mode in industry often resulted in a 90% yield. The continuous tests in the ACR resulted in a higher yield – 94%. They also noted the very little manual handling required (i.e. reagent stocking and waste removal), which was beneficial for continuous processing.

The scraped-surface heat exchanger (SSHE) is a mechanically-assisted heat exchanger (a form of shell and tube unit) where the heat transfer surface (typically the inner surface of the shell) is periodically scraped by a moving element (Fig. 30). This prevents fouling and enhances mixing as well as heat transfer. Solano et al. [125] evaluated its performance and found that it promoted high flow mixing due to the macroscopic displacements of flow, which was induced by the insert
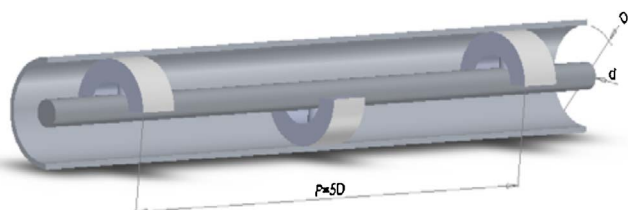

Fig. 30. Geometry of the scraped-surface heat exchanger showing a tube with a scraping rod inserted. Semi-circular elements are mounted on the rod with a pitch, $P = 5D$ with D being the inner diameter of the tube [125].

device motion. Boodhoo et al. [126] investigated this technique as a continuous transportation method for solid biomass of different densities. It was found that without reciprocating and rotating action of the scrapers, the biomass flow separated into a slow-moving bulk phase and a faster moving suspended phase which demonstrated the reciprocating scrapers' advantage in enhancing biomass mixing. The scrapers would clean the inner surface of a reactor tube where viscous oils are formed and deposited. The authors envisaged that the technology could be a step forward in the development of a continuous, large scale process for the microwave-assisted decomposition of solid biomass to produce bio oils.

In summary, in the process of mixing, the TCR and Coflore flow reactors both show excellent mixing abilities since ideal plug flow is present in both reactors. The TCR is a novel PI module with good mixing and no detectable damage to suspended particles. The Coflore flow reactor has already been developed to an industrial scale product which would be a good option for mixing processes.

2.5. Particle coating

Coating of particles is an important unit operation, especially in the pharmaceutical industry. A rotating fluidized bed (RFB) reactor, which is used in particle coating, shares a similar concept with the rotating packed bed that utilizes centrifugal force which can be varied by adjusting the rotational speed of the bed. RFB consists of a cylindrical vessel that rotates along the central axis of the facility with fluid injected into the chamber at multiple slots. RFB has higher heat and mass transfer as the particle size decreases (up to 3 times higher when particle size decreases 50%) [127]. The rotational movement forces the particles to the cylinder wall to form a fluidized annular region. Eliaers et al. [128] designed and built a vortex chamber that could generate a strong high-gravity field and thus a sufficiently high particle residence time. In the test, the gas–solid mass and heat transfer as well as the shearing in the particle bed were intensified by increasing the gas flow rate. The pressure of the coating solution had little effect on agglomeration but a large effect on the overall coating efficiency. By increasing the pressure from 1.5 to 3 bar, agglomeration barely increased while the overall coating efficiency increased by more than 30%. A more advanced version of the RFB system (Fig. 31) was developed by Watano et al. [129] for fine particle coating. It contained a plenum chamber and a porous cylindrical air distributor. It achieved uniformly coated surface of individual corn starch particles with prolonged drug release properties (80% drug release took 10 min at 9% coating level, while 80% release occurred after just 1 min without coating) – which was a desired effect. The problem of over-wetting in the RFB granulator resulting in poor particle mixing in the rotational axis direction was addressed by Nakamura et al. [130]. An air distributor was installed in the RFB to prevent large agglomerates generated in the conventional RFB and resulted in an improved particle mixing in the rotational axis
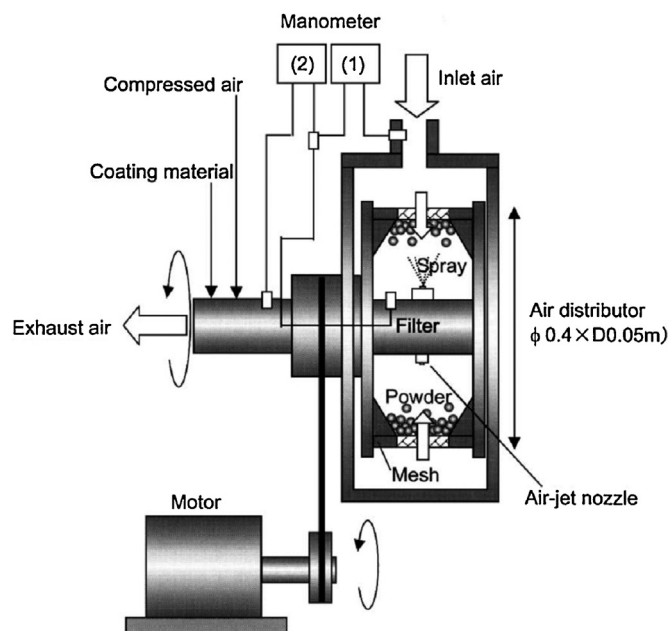
Fig. 31. Schematic of the novel rotating fluid bed granulator [129].

direction.

2.6. Milling/grinding

Milling is the de-agglomeration of particles and dispersing them in a liquid medium. To keep them from reforming into large clumps after they have been milled, there is a need to have the right formulation so that the particles are coated. The paints, inks, cosmetics, and coatings industries use this technique because their products are more likely to create agglomerates [131]. Grinding is more often used to refer to the process of taking a particle and shearing it down to actually reduce the size. Pharmaceuticals, agrochemistry, metals and electronics are some of the industries that are more likely to use this technique. The reduction of particles down to nano-scale can produce more durable products that have a longer life, and on occasion, a byproduct [131].

Notably, due to its intense stream-impinging characteristic, the IS reactor is considered to be a promising intensified technology for milling. Tamir [132] has extensively reviewed the use of IS as reactors and dryers as well as milling devices. Some of the reported applications include compact IS calciners, solid pigment production, and milling/roasting/reduction of iron oxide depleted ores.

Wet stirred media milling (WSMM) has also been proven to be an attractive milling technology in nanoparticle production. WSMM comprises of mechanical attrition of particles (usually drug particles in pharmaceutical industry) by using milling beads. Stabilizers are often added to prevent aggregation of the milled particles as well as to prevent particle growth i.e. ripening during storage [133]. The process is very fast and eliminates the use of organic solvent – hence it is eco-friendly but reported to be highly expensive and energy-intensive. Recently, Li et al. [134] produced sub-100 nm drug particles by using small beads in WSMM. They developed a novel methodology that enabled them to further intensify and optimize the process – faster reaction rate, reduced energy consumption and keeping the bead contamination low (Fig. 32).

Gas-in-solid impinging stream reactor was initially used for grinding of solids after its inception (another early application was for coal gasification). The strong collisions between particles in the impingement zone effectively crush particles. The "Trost Jet Mill" is a well-known IS pulverizer, which has been successfully applied in mineral processing [135]. Netzsch in Germany markets the "CGS" fluidized bed jet mill, capable of fine grinding all kinds of dry products with no contamination [136].

High speed stirred ball mills are used for ultra-fine grinding (typically < 2 μm). These mills are based on grinding using loose, moving grinding media which are moved by rotation of an axial stirring device. Bernhardt et al. [137] investigated wet ultra-fine grinding of limestone with the addition of surfactant for the control of feed viscosity. Their investigation involved parametric evaluations e.g. solid and surfactant concentrations and their effects upon energy consumption. Their studies also indicated that more research was needed to understand the energy efficiency of the mills. Recently, Shakhova et al. [138] added organic compounds as grinding aids into the mills to reduce the energy consumption in ultra-fine clinker grinding. The compounds were also found to increase the mobility of fine powder during its transportation through pipes, into silos and bins.
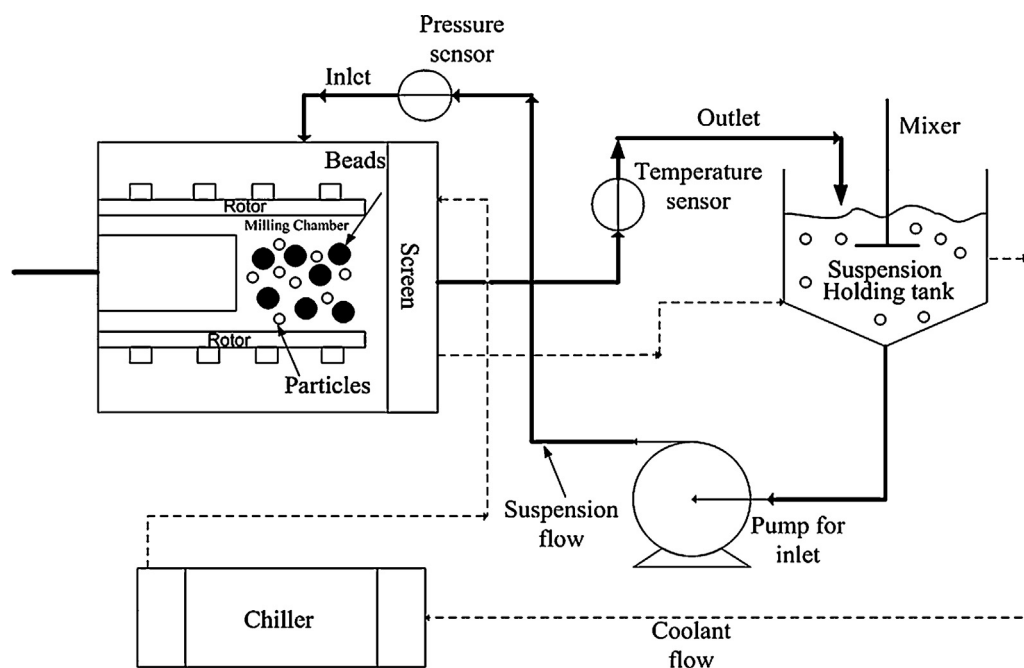

Fig. 32. Schematic of a wet stirred media mill with recirculation mode of operation [134].
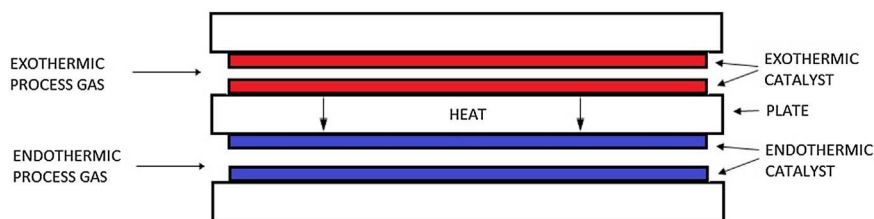
Fig. 33. A pair of adjacent channels in the catalytic plate reactor [3].

For milling and grinding-related PI technologies, the impinging stream reactor stands out as the technology of choice given its positive reception in industries due to its practicalities. The other technologies described here are still in the experimental/assessment stage.

2.7. Catalytic reactions

Catalytic processes are widely employed across the chemical and related industries to increase reaction rates. Intimate contact between the catalyst and the fluid is key in maximizing the full benefits of any catalytic process. Intensification often involves deploying techniques to enable good mixing and to separate the catalyst, preferably in situ or via immobilization in order to minimize downstream separation effort and cost. Whilst many of the technologies described already have been applied to catalytic processes, there are a few novel concepts such as the catalytic plate reactor (CPR). The CPR offers a route for direct heat supply from an exothermic reaction to an endothermic reaction, which is vital in intensifying many important chemical processes. The catalytic plate concept in a reactor involves a series of metal plates coated on one or both sides with thin catalyst layers (Fig. 33). The CPR can be applied in steam reforming, hydrogenation and hydrocarbon cracking. Sigurdsson and Kær [139] used reactant bypass flow in a CPR for hydrogen production and studied the pressure drop and flow maldistribution in the CPR with a coated wire mesh catalyst. The ratio of wire mesh catalyst width to reactor width had an effect on the bypass flow which could influence the reactor's performance. If the ratio was 0.97, about 25% of the total mass flow in the channel could be expected to flow in the bypass channel. Zanfir and Gavriilidis [140] also presented a series of numerical investigations on the influence of parameters, such as catalyst loading and wall thermal conductivity – for catalytic ethane dehydrogenation in a CPR. Catalyst loading was found to be a key parameter since the variation of it could lead to hot spots or insufficient reactant conversion. Thermal conductivity variations were also found to give rise to hot spots and caused poor heat transport along the axial direction of the plate. Steam reforming of methane with methane catalytic combustion was also performed in a catalytic plate reactor (CPR) by Zanfir and Gavriilidis [141]. Due to the factors of heat from a suitable amount of fuel, catalyst activity in the combustion channel and heat transfer increase based on the short distance between the heat source and heat sink, the CPR gave an important improvement in transverse temperature gradients in comparison to the conventional tubular reformers. They also suggested that a CPR which was properly designed with flowrates, channel heights, catalyst loadings and thickness would present enhancements in steam reforming.

Vicevic et al. [142] tested the viability of the SDR for performing catalytic reactions. Silica-supported zinc triflate (Zn(CF$_3$SO$_3$)$_2$) catalyst was immobilized on the surface of the SDR. The SDR was found to be capable of using the catalyst more efficiently and exhibited a faster reaction rate (2-fold increase), which led to a rise in selectivity towards campholenic aldehyde from 0 to 75%, compared to the conventional batch stirred tank vessel. The intense mixing mechanism within the thin film in a SDR and the short residence times were responsible for the enhancement observed.

Eze et al. [143] have demonstrated that at certain oscillation conditions within a meso-OBR (8 mm amplitude, 4.5 Hz frequency, oscillatory Re = 2400), a uniform suspension of catalyst particles could be achieved. They applied this technique in suspending PrSO$_3$H-SBA-15 catalyst powder (Fig. 34) and carried out continuous esterification of an organic acid, hexanoic acid, an important prototype reaction for biofuel synthesis – this highlights the potential of OBRs for continuous, heterogeneously catalysed liquid phase transformations.

Losey et al. [144] carried out pioneering work on micro-packed beds. The rate of gas–liquid mass transfer in their study (5–15 s^{-1}) was found to be more than a 100-fold increase compared with values reported for traditional multiphase packed-bed reactors (0.01–0.08 s^{-1}). Al-Rifai et al. [145] studied gas–liquid hydrodynamics in a micro-packed bed reactor during benzyl alcohol oxidation on a catalyst. With wet catalyst, the micro fluidized bed experienced an enhanced external mass transfer which improved benzaldehyde selectivity and reactant conversion. A selectivity to benzaldehyde was found to reach a maximum of 93% compared with a conventional stirred glass reactor, while the conversion could be increased to 81%. Tadepalli et al. [146] used a laboratory semi-batch reactor (25 mL) and a packed-bed microreactor (775 mm ID) for the kinetic study of hydrogenation reactions. Under similar conditions, the mass transfer coefficients in the micro-packed bed reactor were two orders of magnitudes higher than those of the semi-batch reactor. The most important commercial example is by Velocys technology who developed micro-packed bed for the Fischer–Tropsch synthesis using highly active proprietary catalyst for small scale gas-to-liquids (GTL) and biomass-to-liquids (BTL) applications which is not economically viable using conventional technology [147]. The technology success is based on ability of microchannels to remove high heat flux efficiently enabling up to 95% CO$_2$ conversion per pass [148].

Intensified fluidized beds can be used in catalytic reaction and testing applications. Hao et al. [149] studied fluidization characteristics of an aerogel Co/Al$_2$O$_3$ catalyst in a MSFBR. It was reported that channelling, large agglomerates and bubbles were eliminated in the MSFBR with improved fluidization quality of the catalyst. Performance of CH$_4$–CO$_2$ catalytic reforming in the MSFBR also was found to be better than in the conventional fluidized bed. The initial conversion of CH$_4$ in the MSFBR was 7.6% and 24.3% higher than in a conventional fluidized bed reactor and a fixed bed reactor, respectively. A micro-fluidized bed is a relatively new concept in chemical engineering field with potential applications in a micro process and micro fluidics context. The main difference with macroscopic counterparts is the importance of surface forces and inevitable wall effects which puts the
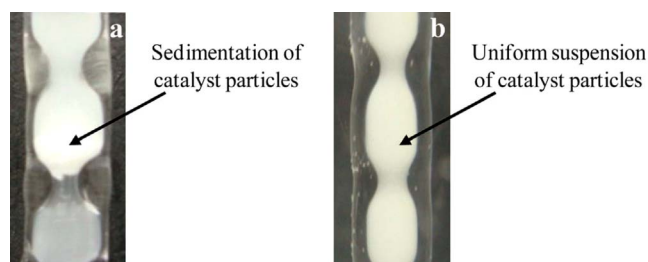

Fig. 34. (a) PrSO$_3$H-SBA-15 catalyst powder sedimented in a meso-OBR without oscillatory flow, (b) uniform suspension was achieved under certain conditions [143].

upper boundary between micro and macro-scale fluidization at 1 cm with a stricter limit at 1 mm in line with general [150–155]. Doroodchi et al. [156] studied mixing using ~98 μm diameter borosilicate particles by a sodium iodide flow in a 1.2 mm diameter capillary. The micro-fluidized bed was shown to reduce the mixing time to less than an eighth of that in the absence of particles. Similarly, Zivkovic et al. [157] determined up to four times greater mixing quality than those in the particle-free 400 μm × 175 μm microfluidics PDMS channel. Mixing efficiency is affected strongly by bed voidage with the optimal operating voidage at around 0.8. Yang et al. [158] used micro-fluidized bed reactors for the photocatalytic degradation of methylene blue. They found that when the inner wall of the fluidized bed was coated with a catalyst, the mass transfer coefficient increased by 11–13 times and the apparent reaction rate constant increased by 4.9 times compared to without coating. If the inner wall of the fluidized bed and the particles inside were both coated with catalyst, the degradation ratios were 5–35% higher than the case without coating. The best performance of a micro-fluidized bed photocatalytic reactor at a bed voidage of 0.75 is similar to above mentioned study. Pereiro et al. [159] used a type of hybrid fluidized bed which offers significant increase in surface area per unit volume with excellent mixing ability to develop fast, portable and low cost method to specifically capture and detect infectious bacteria. Recently, Li et al. [160] suggested a compact system for CO_2 capture based on micro-fluidized bed reactor. Their system presented 8% lower adsorbent attrition, 35% larger breakthrough time, and a 17% shorter saturation adsorption time than in the conventional fluidized bed.

Dang et al. [161] used a membrane assisted micro-structured fluidized bed for the study of solids holdup distribution and solid circulation. The micro-structured fluidized bed improved the solid circulation compared to the work of De Jong et al. [162] who used a large size fluidized bed when great care was paid to the extraction velocity. Dead zones inside the reactor could decrease the solid mixing and heat/mass transfer. In comparison with De Jong et al. [162], the dead zones observed in the micro-structured reactor kept moving while they were observed near the membrane wall in the large reactor. Yu et al. [155] decomposed $CaCO_3$ powders in a micro fluidized bed reactor. In their experiment, the apparent activation energy to decompose the powders was 142.73 kJ/mol, which was obviously lower than thermogravimetry-measured result using the Flynn–Wall–Ozawa meth-

od (184.31 kJ/mol). These results demonstrated that the micro fluidized bed reactors are reliable and rapid tools for gas–solid reactions.

A membrane assisted fluidized bed reactor (MAFBR) is a fluidized bed reactor with insertion of membranes, as shown in Fig. 35. Prasad and Elnashaie [163] investigated a novel membrane-assisted fluidized bed reformer for the production of hydrogen. Powdered catalyst particles were used to overcome the traditional diffusion limitation of the catalyst pellets. With membrane assistance, the hydrogen yield in the fluidized bed was 7 times higher than the industrial fixed-bed reactor, which was an important indication of its efficiency.

Microwaves can be used for selective heating in heterogeneous catalytic reactions involving gas–solid systems. Roussy et al. [165] investigated the selective heating of a catalyst particle in a low temperature gas phase environment using microwave technique. Microwave heating resulted in higher hydrocarbons selectivity and reduction of oxidation products compared to conventional oven heating.

Reactive separation (e.g. reactive crystallization, reactive distillation, reactive extraction, etc.) is fundamentally based upon integrating separation and reaction into a single equipment. This presents several benefits, namely: energy and capital costs reduction, increase of reaction yield and reduction of waste emission [166]. Of particular interest is the reactive extraction (RE) process – Shuit et al. [167] experimentally investigated the in situ extraction, esterification, and transesterification of *Jathropa curcas* L. seeds in producing FAME (fatty acid methyl ester) – a primer for biodiesel production. Their results have proven the huge cost savings associated with the RE method.

Among the range of PI technologies and methods combined with catalysis reactions that have been described and discussed, catalyst-coated micro-packed beds and fluidized bed variants, such as the micro-fluidized bed, MSBR, and MAFBR show promising potential for intensification based on the higher mass transfer coefficient and reaction rate. The CPR, SDR, and microwave irradiation also offer distinct advantages such as fast reaction time and high selectivity, compared with conventional technologies when dealing with catalytic reactions.

2.8. Particle classification

Gravity separation is an industrial method of separating different components via gravitational force, based on density differentials. A "Reflux Classifier" consists of parallel inclined channels above a conventional fluidized bed. Macpherson et al. [168] investigated the combination of vibration and sand as the dense medium for density-based separation in the Reflux Classifier (gas-fluidized) with promising results for coal separations i.e. 80% yield in beneficiation. The technology is deemed promising for the beneficiation of minerals (the concentration of valuable ore constituents via physical separation).

Matsubo Corporation in Japan has developed an air classifier that enables simultaneous multiple size classification of fine dry powder. The device is called an "Elbow-Jet Air Classifier" (EJAC), the operation of which is based on the Coanda effect (Fig. 36). The EJAC works on the principle that the trajectory of a particle in an air stream is a function of the inertia and air resistance of the particle i.e. the particle diameter. It can simultaneously separate fine and coarse powders with the size range of 0.5–100 μm [169].

Trilobite Microsystems (Norway) have invented the Trilobite micro-fluidic chip, based on the hydrodynamics principle – suspended particles are continuously concentrated and/or separated as the liquid flow runs through the chip, which contains a field of micro-units. Fig. 37a shows the schematic and operation of the Trilobite chip. Inlet suspension (blue arrow) enters on top. The liquid flows into the chip and down the holes (green arrow), which is then collected at the outlet in the bottom layer. Particles that are larger than the gaps (Fig. 37b – showing 5 μm gaps) are carried with the flow through the separation field, and are collected at the outlet at the end of the chip (red arrow). Hønsvall et al. [170] utilized this technology to sort rigid microalgae
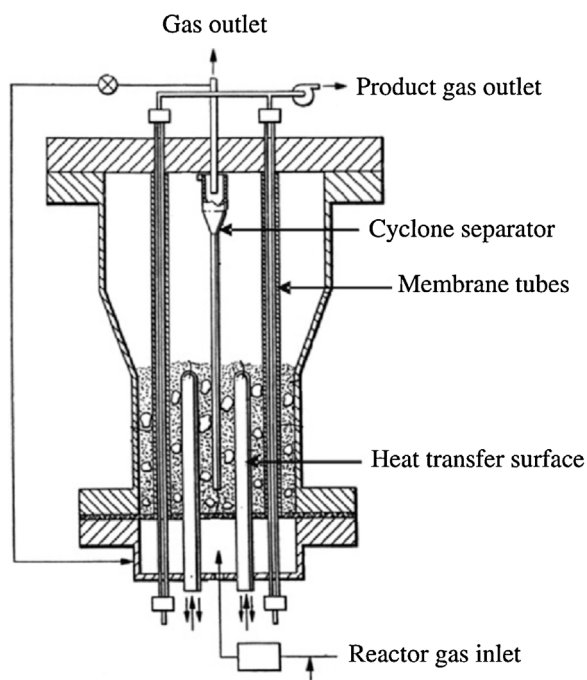

Fig. 35. Schematic representation of membrane assisted fluidized bed reactor [164].
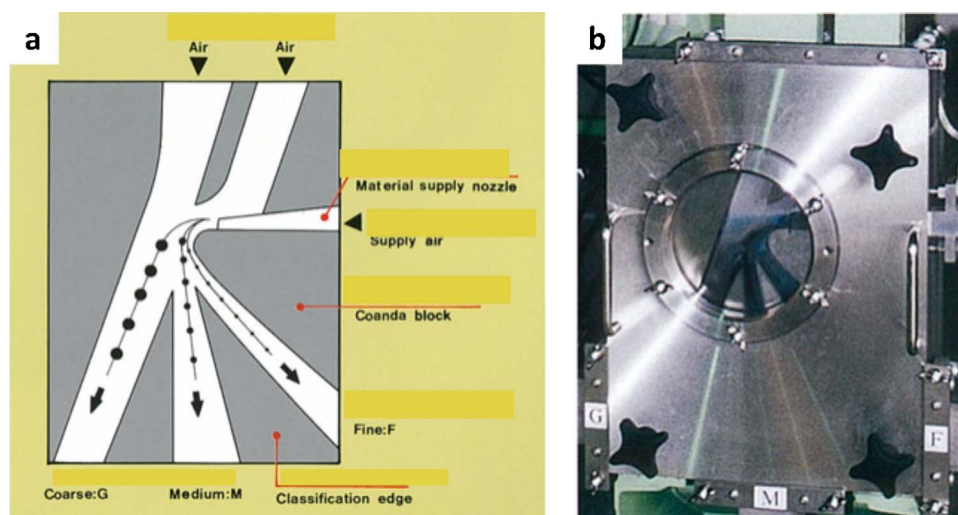
Fig. 36. Elbow-Jet Air Classifier: (a) the principal of particle classification is based on the Coanda effect, (b) the hardware [169].

according to size, which would be useful in harvesting microalgae. It was found that smaller sizes of microalgae can be returned into the incubator. For reference, a recent publication by Sajeesh and Sen [171] reviewed particle separation and sorting in microfluidic devices.

A few PI technologies have been developed for particle classification. The Reflux Classifier, Trilobite microfluidic chip, and Elbow-Jet Air Classifier all have high classification efficiency as reviewed. For industrial users, the Elbow-Jet Air Classifier, a commercial product for micrometre scale particle classification, is a better choice.

2.9. Drying

Drying is the removal of water or other solvent from solids, or a mixture of liquid and solids. The fluidized bed, TORBED, screw conveyor, microwave, ultrasound, impinging stream (IS) and vertical thin film dryer are the PI technologies and methods that can be used for solids drying.

The fluidized bed is a method that allows controlled, gentle and uniform drying of wet solids. Groenewold and Tsotsas [172] used the fluidized bed for the drying of γ-Al$_2$O$_3$ with particle diameters ranging from 50 to 1800 μm. The drying curves of different particle sizes (Fig. 38) illustrated that drying was intensified with indirect heating. It can be concluded that drying was successfully intensified by immersing heating elements in a fluidized bed reactor.

The TORBED reactor has also found uses in drying of slurries, sludges and biomass solids. As an example, a paper mill in Holland installed in 2004 a TORBED for drying paper sludge (55 wt.% moisture content) at a rate of 2 tons/h. By combining recycled low-grade waste heat (60 °C) elsewhere in the mill and primary hot air at 120 °C, the TORBED was able to reduce the moisture content down to 5 wt.%. Compared to other technologies, it enabled a more convenient processing – it coped with the sticky nature of the sludge through rapid 'skinning' of the particles [173].

Recently, drying has been investigated using screw conveyors. Osman et al. [174] used a steam-jacketed screw conveyor/mixer to dry low rank coal particles such as lignite and sub-bituminous coal (Fig. 39a). Although this study has yet to be completed, preliminary results have shown that the dryer technology was cost- and energy-efficient compared to competing technologies. The authors also conducted discrete element modelling (Fig. 39b), which indicated an excellent particle mixing in the dryer (in this case, at 7.5 rpm screw rotation and 300 m^3/h material throughput). Kaplan and Celik [175] carried out wood chip drying by using a similar technology and managed to reduce the moisture content from 60 to 27 wt.% under optimum conditions: 30 m^3/h drying air flow rate, 200 °C drying air temperature and co-current air/feed configuration.

Microwave drying is distinct from conventional drying. Heat is generated inside the product by absorbing energy from microwaves (as described in Section 2.1). One of the main advantages of microwave drying is the shorter drying time than conventional drying (up to 25–90% in food drying [176]). Uniform heating leading to uniform temperature distribution in the product, which is another important advantage of microwave drying, can be achieved with the inherently uniform distribution of the microwave field which has been studied by
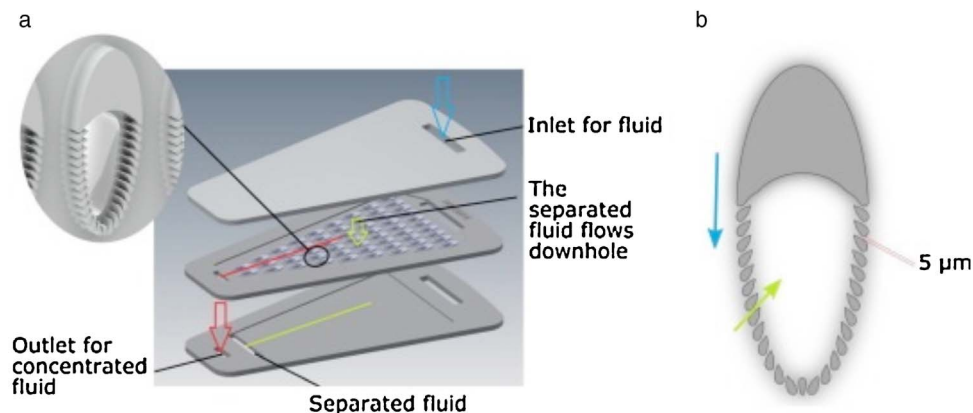

Fig. 37. The Trilobite microfluidic chip: (a) the schematic and operating principles, (b) a Trilobite unit with 5 μm gap between blades [170] (For interpretation of the references to colour in the text, the reader is referred to the web version of the article.).
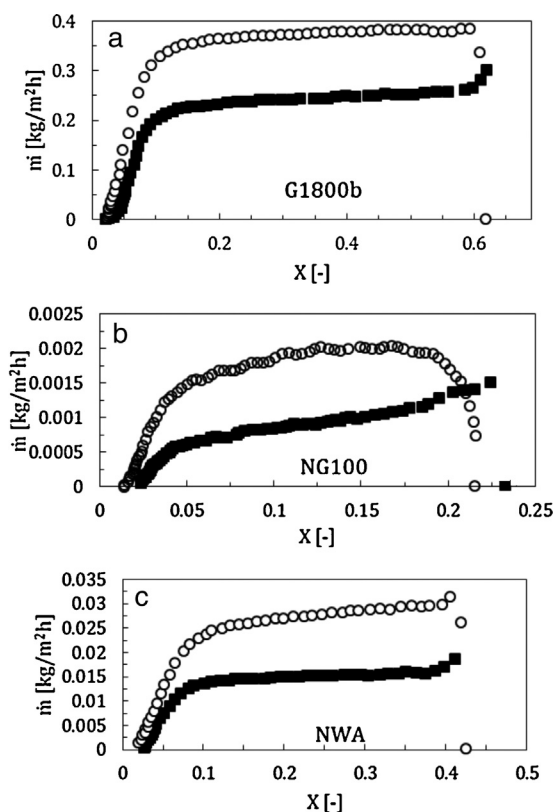
Fig. 38. Fluidized bed drying curves of three selected fractions without (full symbols) and with (empty symbols) indirect heating. (a) Gl800b (1820 μm, particle diameter); (b) NWA (255 μm, particle diameter); (c) NG 100 (49 μm, particle diameter); *X* represents moisture content [172].

several researchers [177–179], (although it does depend upon the properties of the material being dried), which can hardly be achieved in conventional drying. Microwave drying has been used to process pharmaceutical powders [180,181]. In these studies, microwave drying caused no thermal damage to the surface or interior of the powders. Microwaves have also been applied in hybrid drying processes, such as microwave-assisted vacuum drying (MVD) and microwave-assisted freeze-drying (MFD). MVD takes advantage of microwave heating with high energy efficiency by lowering the boiling point of water with the vacuum applied. MFD employs a microwave field as the heat source for sublimation in the freeze-drying process [182].

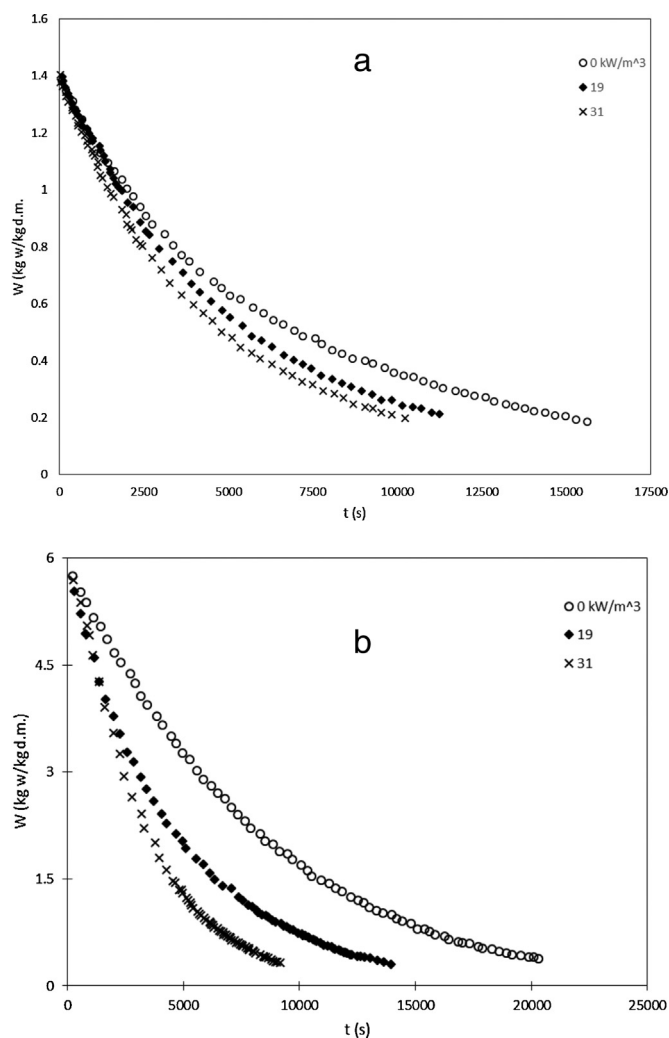Ultrasound can affect heat and mass transport processes, with

Fig. 40. Experimental drying kinetics of cassava (a) and apple (b) cubes, applying different ultrasonic powers [184].

different phenomenological effects observed in solid/liquid and solid/gas systems [176]. As reported by Cárcel et al. [183], in the solid/liquid system, the implosion of cavitation bubbles creates an external resistance at the outer solid–liquid interface. However, cavitation does not take place in gas or supercritical medium. In the solid/gas system, ultrasonication (used also in precipitation – see Section 2.1) can
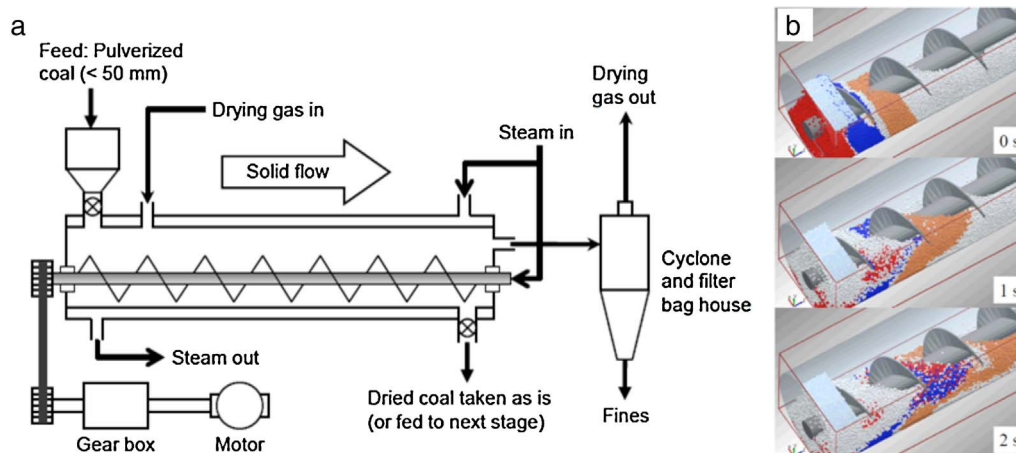

Fig. 39. (a) A steam-jacketed screw-conveyor dryer for drying of low rank coal, (b) particle mixing simulation in the dryer (time constant) – different colours correspond to different particle types [174]. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

significantly reduce the drying time by up to 32% in the case of cassava and 56% in the case of apple [184]. It was found (Fig. 40) that drying time was shortened with increasing ultrasound power.

The use of impinging stream (IS) technology in drying has been highlighted by Tamir [132]. They reported that the efficiency of the IS dryer was higher than common dryers e.g. spray, spouted bed and fluidized bed types. An example is the spray drying of aluminium sulphate in an IS spray dryer [185]. For this case, the pilot plant was able to produce an output of 2.78 kg dry product/s at a particle entrainment efficiency of 98–99%. Sathapornprasath et al. [186] investigated the drying of resin in an IS dryer and achieved a maximum evaporation rate of 110 kg-water/m^3 h with a residence time of only 2 s. With these very small residence times (of the order of seconds), only surface moisture is removed. Therefore, the IS dryer is an excellent alternative to flash dryers.

Buss-SMS-Canzler GmbH (Germany) invented the vertical thin film dryer (Fig. 41), which consists of a cylindrical, vertical body with heating jacket and a rotor inside of the shell, equipped with rows of pendulum blades all over the length of the dryer. The hinged blades spread the wet feed product in a thin film over the hot wall. The thickness of the layer is dependent on the clearance between the blade and the wall. A highly-agitated bow wave is formed in front of the rotor blades. The turbulence increases as the product passes through the clearance before entering a calming zone situated behind the blades. The volatile component then evaporates continuously. The product layer is typically less than a millimetre in thickness. The hinged pendulum blades are designed to give a minimum clearance with the dryer wall to prevent fouling of the heating surface by the product, but
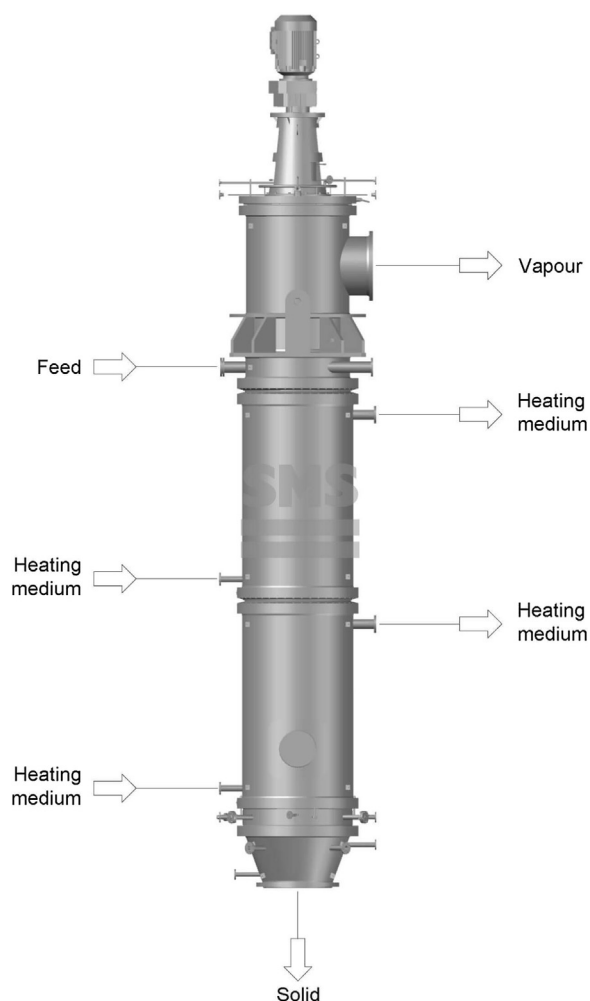
do not themselves the heated wall. The advantages of this dryer are high surface area (up to 60 m^2) in a compact unit and high thermal efficiency. The heating source is flexible: steam, warm water, thermal oil, or electrical heating [187].

In summary, the fluidized bed reactor, TORBED, screw conveyor, microwave, ultrasound, IS, and vertical thin film dryer are reviewed as the PI technologies and methods for drying. Screw conveyor and IS have higher drying efficiency than the conventional fluidized bed reactor. TORBED is a more convenient drying technology based on its design (Figs. 18 and 19). Microwaves and ultrasound are different from traditional drying methods and show advantages, such as shorter drying time and uniform drying (using microwaves). They will be a better option for drying if the materials to be dried meet the requirement of the methods.

2.10. Thermal processing

In addition to the solid handling processes discussed previously, applications for thermal solid processing that employ PI are compiled in this section, which include applications related to: the spinning cone reactor (SCR), rotating fluidized bed (RFB), and TORBED reactor as well as PI-supporting methods such as microwaves and plasma.

In the research of Wagenaar et al. [188], particle dynamics and gas-phase hydrodynamics in a SCR was studied as a first stage to understand the performance of the SCR which could be used for rapid thermal solid processing. The solids processing in the reactor was influenced by operational and physical parameters of the reactor, such as cone rotational speed, particle diameter, and cone top-angles. The residence time and shape of the trajectories of particles were independent of the particle diameter if the particles had diameters above 400 μm. However, the motion of particles less than 200 μm in diameter was highly influenced by the gas flow in the SCR since the viscous force became important compared to the mass inertia.

In the work of Taib et al. [189], a 200 mm diameter rotating fluid bed incinerator was designed and operated which is capable of burning large amounts of sewage sludge. They demonstrated the capability of the novel RFB technology in the incineration of sludge waste. They reported that different sets of hydrodynamic parameters could sustain the combustion, which proved that the bed hydrodynamics were critical for the incineration process. The RFB with a porous distributor plate and bed thickness of 33 mm had a uniform bed temperature and stable combustion which proved the good quality of the bed mixing. A novel spinning fluidized bed incinerator for the incineration of sludge was developed by the same team [190]. The spinning fluidized bed incinerator presented a high combustion intensity. In the study, it was pointed out that the rotating fluid bed combined with centrifugal sludge dewatering would result in further process integration and intensification on a sludge incineration plant. Wong et al. [191] designed and constructed a small-scale RFB for the investigation of the possibility of incineration of wool scouring sludges. In the cold test (the air flow and bed were not pre-heated), various operating parameters were tested for optimization for the second phase hot test (the air flow temperature was pre-heated to 850–1000 °C and bed temperature was pre-heated to a stable temperature of 700–800 °C) in the experiment to ensure complete fluidization and minimum particle elutriation. In the RFB, the efficient mixing in the turbulent fluid provided a good environment to increase the combustion efficiency even for a maximum moisture of up to 70%. Based on the CFD study, the gas combustion also benefited from the special advantage of swirling flow in the fluidized bed, which generated turbulence that promoted the mixing between particles and fluid.

The TORBED Expanded Bed Reactor (EBR) has also been applied for the controlled combustion of rice husk by Nehdi et al. [192]. The stationary angled blades of the EBR enabled the high velocity jets of process air to be introduced into the reactor chamber, which provided the combustion of rice husk. The TORBED reactor produced highly

Fig. 41. The vertical thin film dryer [187].

reactive rice husk ash (RHA) with lower carbon content and less grinding time than the conventional fluidized bed reactors. Compared with silica fume (SF) method, RHA production by using a TORBED reactor did not require superplasticizer and additional water, representing an important processing advantage. Hydrodynamic behaviour of the TORBED reactor was studied and compared with the conventional fluidized bed reactors [193]. The hydrodynamic behaviour of TORBED reactor was found to be capable of fluidizing fine particles below 30 μm, which were difficult in a conventional fluidized bed reactor.

Plasma, one of the four states of matter besides solid, liquid and gas, is defined as thermal plasma and non-thermal plasma. Plasma can be used for solid processing whereby energy is delivered to the solid particles, which are then evaporated and discharged from the plasma region. Fulcheri et al. [194] presented a new process for fullerenes production through a 3-phase thermal plasma to overcome the limitations of the standard arc process (such as the input carbon flowrate) for bulk production of fullerenes at an industrial scale. The plasma reactor could independently control the input carbon rate and obtain 3.5% yields of extractable fullerenes. Cold plasma was used by Vons et al. [195] for nanoparticle production. In their studies, plasma was generated by a dielectric barrier discharge. Nanoparticles were found to be successfully produced from acetylene, ferrocene and hexamethyldisiloxane by using argon and helium as carrier gasses.

2.11. Bioprocessing

Bioprocesses present unique challenges when considering intensification options. The relatively fragile and sensitive nature of micro-organisms and enzymes implies that many of the intensely turbulent and highly energetic PI techniques cannot be considered [196]. Many fermentation broths are also highly viscous and have high density cell cultures which require careful handling and specific operating conditions such as high oxygen transfer rates in aerobic fermentations to maintain their growth and viability. Cell/enzyme immobilization is routinely used in biotechnological applications for a number of reasons: to increase productivity, to allow repeated usage through a number of successive cycles and for ease of retention in the bioreactor, the latter being especially important in continuous operating mode. Although immobilization is advantageous in many respects, diffusional limitations in oxygen and nutrient transfer often negatively impacts on bioreactor productivity. The development of bioprocess intensification technologies has therefore focused on addressing these mass transfer limitations while taking the shear-sensitive nature of the organisms into account.

There are a number of documented examples in the literature where low to moderate centrifugal fields (typically 10–500 rpm) have been applied in biological processing [197]. Rotating disc contactors, for instance, which are similar to the spinning disc concept, except that they operate at much lower speeds of rotation (typically 10–20 revolutions per minute) have been extensively studied and applied in wastewater treatment [198] and whole cell fermentation processes [199,200]. The technology relies on the development of a biofilm of active micro-organisms on a number of vertical discs rotating about a horizontal axis as shown in Fig. 42 [200,201]. Under the rotational action, the biofilm is alternately submerged and covered by a thin liquid film, a set-up which enables enhancement of gas and liquid mass transfer even in high density cell cultures. In the fermentation processes, at least a 3-fold increase in volumetric productivity compared to free cell suspension in a typical stirred tank vessel has been reported.

There are examples where moderate centrifugal fields have been employed in bioprocessing. For instance, Boodhoo et al. [202] utilized the RPB as a bioreactor rotating at up to 550 rpm for the fermentation of *P. putida* KT2442 to produce polyhydroxyalkonates (PHA). After 24 h of fermentation in batch recirculation mode, the RPB with knitted wire mesh packing was able to sustain a biomass concentration of 0.5 g/l, total viable cell count of about 2×10^7 CFU and PHA yield of 6.2%. However, this performance was achieved under less than perfect temperature control even at the modest rotational speeds used. Generally, the design focus of RPBs is on intense mass transfer with little consideration given to heat transfer. Further research into improved RPB designs incorporating heat transfer surfaces within the rotating bed is needed to enable more diverse applications of the RPB technology, especially where good temperature control is key. The research did, however, highlight the potential for good oxygen transfer: bubbles as small as 0.36 mm in diameter were obtained at 1200 rpm as a result of the wire mesh filaments slicing the bubbles as they travel through the packing. If such operating conditions can be employed while maintaining good temperature control over long durations, there is scope for the RPB to further intensify fermentation processes. More recently, enzymatic hydrolysis of tributyrin on a spinning cloth disc reactor (SCDR) has been studied [203], with lipase enzyme immobilized on a woollen cloth fixed to the disc surface rotating at 400 rpm. The hydrolysis rate in the SCDR is up to 75% higher than in a conventional batch stirred tank with immobilized enzymes. Smaller emulsion droplet sizes and higher shear in the SCDR liquid film are responsible for the intensification achieved.

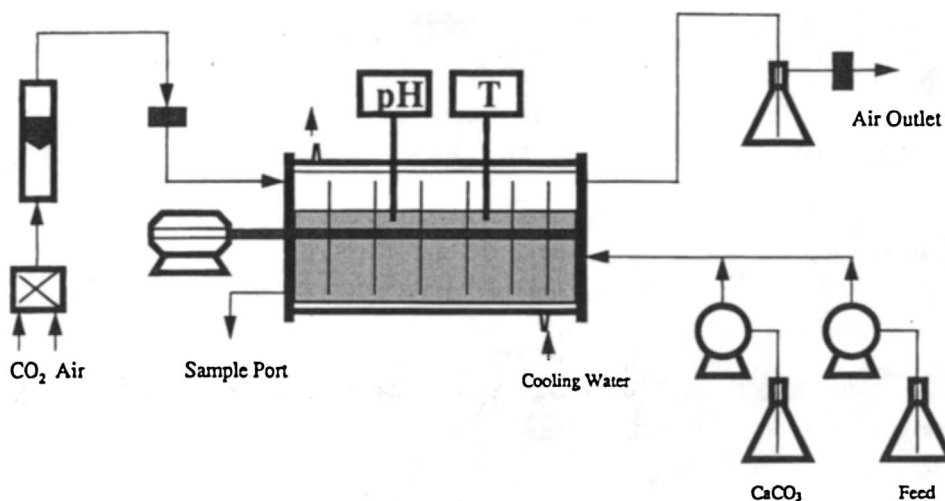The utilization of low power ultrasonic energy as a biological

Fig. 42. Schematic diagram of rotary biofilm contactor [200].

process enhancement technique has received much attention [204,205]. Although the use of high power ultrasound for cell rupture and intracellular metabolite recovery is well established in biotechnology, the effects of low power ultrasonication on cell biological responses are less clear. Trentin et al. [206] and Badgujar et al. [207] demonstrated enhanced activities in immobilized lipase under ultrasound-assisted conditions compared to conventional mixing methods. Some studies have indicated significant improvement in yield of secondary metabolites in bacterial, fungal and plant cell cultures suggesting improvements in intracellular and extracellular mass transfer of nutrients and oxygen [208,209]. These improvements have been explained by a thinning of the boundary layer around the cells from the pulsating action of ultrasonically-induced microbubbles of gas (extracellular enhancement) and by increased membrane permeability [205]. There may also be an ultrasonic effect on biological activity of the living cells [204].

Very recently, a review of bio-catalysed processing in microfluidic channels has highlighted that miniaturization technologies can be successfully exploited in bio-transformations, especially where integrated reaction-separation steps can be implemented [210]. The combination of miniaturization and immobilization of biocatalyst also offers the opportunity for intensification in transport and reaction processes as well as faster process development. Whilst the issue of blockages by solids remains a major challenge in many cases, it is possible nevertheless to control this problem by customized reactor design and operating conditions [210].

3. Concluding remarks and future perspectives

In this state-of-the-art review, technologies and techniques related to process intensification of solids handling have been described. A broad range of PI technologies and techniques have been classified into commonly encountered industrial processes for solids handling applications, including precipitation/crystallization, separation, granulation, mixing, particle classification, milling/grinding, catalytic reactions, particle coating, drying, thermal processing and bioprocessing applications. An overview of the reviewed technologies and methods is given in Table 1. Many papers highlight precipitation/crystallization to be perhaps the most common solids processing application to have been investigated for intensification, predominantly in continuous flow devices. The desirable features of intensified processing in precipitation/crystallization relate mostly to improved product properties (e.g. better control of particle size down to nanoscale range, narrower particle size distribution, and prevention of agglomerates) but also demonstrate other processing advantages such as improved energy efficiency and an increase in yield in continuous processing.

For separation processes, rotating equipment is dominant. For solid/gas, solid/liquid and solid/solid applications (e.g. mineral beneficiation), separation efficiency has been shown to be of the order of > 90% and fine particles down to sub-microns can be efficiently processed. Processing times have also been reduced to a few seconds.

Granulation is an important processing step in pharmaceutical and ceramic processes among others; it can involve a dry or the more common wet route. The mixing step in the granulation process is key and there are many ways to intensify this aspect in order to improve the process as highlighted by the range of technologies developed for the wet route. Ideally, batch granulation should be transformed into continuous processing for cost-effectiveness and reduction in time-to-market for new tablets. The ConsiGma unit is an all-in-one solution developed to achieve this goal. Another important development is the twin screw granulator, which allows for continuous granulation, customizable granule properties and reduction in solvent use.

Enhanced mixing has been the epitome of PI. Mixing is intricately linked to reactions and separation processes, with the focus of research having been on increasing micromixing efficiency and heat and mass transfer coefficients. Devices such as the Coflore, Taylor–Couette,

spinning disc reactor, and oscillatory baffled reactor offer great potential for uniformly good mixing. Mixing involving solids, either in suspension or in immobilized form, is commonly encountered in solid catalysed reactions and a multitude of intensified technologies such as catalytic plate reactors, micro-packed and micro-fluidized bed reactors have been evaluated for these catalysed reactions.

Particle classification or particle segregation based on physical size is another area of significant interest in solids handling applications. Novel intensified equipment includes the Elbow-Jet Air Classifier and microfluidic devices such as the Trilobite Chip, both of which could simultaneously segregate particles of multiple sizes – even down to the sub-microns scale.

Other processes related to solid handling, such as particle coating, milling/grinding, and drying, have also been reviewed. Although there have been some benefits from implementation of PI concepts, there appears to be scope for more advancement in these fields, especially in designing equipment that can incorporate a number of these functions (e.g. granulation/drying) in one unit. For bioprocessing applications, technologies giving mass and heat transfer enhancements have promising potential although the characteristically slow reactions and sensitive nature of micro-organisms/enzymes may require careful selection of operating conditions.

A common theme across many of the solids handling processes described in this review is the transformation from batch to continuous processing, which presents significant benefits especially in increasing the cost-effectiveness of processes. With nanotechnology demand increasing, PI equipment offers promising potentials to accommodate this need by focusing on the development of sustainable and effective production of smaller, high quality particles.

Future prospects for PI development in solids handling applications include:

(1) *Hybrid technologies*. Implementation of process intensification is moving increasingly towards continuous processing with some form of hybrid technology i.e. combining operations or processes into a single equipment to minimize the unit operation size, lower the energy use and cost, and reduce the operating time. For example, the screw conveyor dryer which involves hybrid mixing and drying is being developed for continuous processing as has been described in this paper. Future research should study the development and usage of these hybrid technologies.

(2) *Alternative energy sources*. Alternative energy sources such as magnetic field, microwave, and ultrasound also have an increasingly important part to play in achieving PI benefits, especially with regard to fouling remediation in solids processing applications. Plasma is also a promising technology which demonstrates advantages in dealing with small particles in a gas; hybrid technologies combining plasma as a source of energy with other PI devices can be envisaged in the future.

(3) *Novel techniques*. In addition to the PI technologies reviewed in this paper, other novel techniques have started to proliferate. At Newcastle University, we are investigating the feasibility of using heat pipe technology as a novel concept for energy-efficient drying of ceramic slurries and active pharmaceutical ingredients (API) [211]. Another example is 3D printing which offers exciting prospects for affordable and accessible manufacturing of miniaturized components with intricately designed internal structures which could be aimed at intensifying fluid dynamics [212–216].

(4) *Anti-fouling*. With PI involving miniaturization as a fundamental concept, fouling and blockages in the most extreme of conditions by solids entering or generated inside the spatial domain is a major concern. Whilst a few simple techniques have been highlighted in this paper for addressing fouling, there is considerable opportunity for further development in this area. For instance, future development of the 3D printing technology could be geared to the incorporation of surface-modifying structures [217] and dynami-

cally changeable structures [218] displaying anti-fouling properties for solids handling applications.

The prolific research in process intensification will continue for the foreseeable future. This engineering strategy will become a more robust subset of chemical engineering – driven by the need to offer greener, flexible and more efficient processing. With the growing demand for nanomaterials processing, process intensification will no doubt play a more prominent role in solids handling than ever before.

Acknowledgement

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