Advances in Continuous Chemical Reactor Technology

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Commercial chemical reaction practice utilizes batch reactors, typically agitated and temperature controlled. Mixing is inefficient, so that reactant-containing liquid structures, often a millimeter or greater in size, do not interact efficiently, and so prevent rapid reaction. Diffusion rates of reactant molecules from the large liquid structures control overall reactor kinetic performance. This dynamic leads to long reaction times, allows slow reactions to produce impurities, and affords little or no control of product properties, particularly size and crystal structure. Even if otherwise acceptable, slow overall reaction rates limit efficiency of operation. A major drawback of legacy reactor equipment is its batch nature, requiring multiple reactors for scaleup and consequent loss of uniformity and reproducibility in reaction product characteristics. While continuous reaction schemes are possible with linked batch reactors, product control is limited by the slow reaction rates realized. Capital costs for high production throughputs are high for multiple batch or linked reactor systems. It should be noted that nanomaterial preparation by precipitation is often impossible in batch reactors.

Recent introduction of microreactors[1] addresses the need for examining novel fast chemistry by miniaturizing flow channels and reaction spaces, thus reducing diffusion dimensions. These units cannot be scaled up since flow paths dimensions cannot be much enlarged. Thus, scaleup requires use of many parallel microreactors, an expensive equipment cost issue, and one which demands that uniformity and reproducibility be questioned. In addition, precipitation reactions or the presence of solids in the reacting streams cause clogging. These microreactors are operated at low pressure, with resultant typical residence times of a few seconds to minutes.

Operation at elevated pressures, in the 5,000 to 25,000 psi range, would shorten residence time, minimize clogging problems and enable scaleup to the kilograms/minute range in a

single continuous reactor. Further, the kinetic energy in liquid streams at these pressures can be utilized to form nanostructures by stopping the high velocity streams in restricted reaction spaces, resulting in ultraturbulent mixing at the point of reaction.

Combinatorial parallel reaction development can be performed in microreactors, albeit with the disadvantage of low pressure, which limits the ability to control reaction kinetics and limits classes of reactions which can be utilized. Precipitations and suspension reactants are not permitted. Such experiments can define the parameter space in which a useful production reactor scheme can be sought.

Now, continuous chemical reactors (CCR) are available[2]. These enable ultraturbulent mixing of reactant streams, continuously. Reactant mixtures are highly pressurized, subjected to high shear in microchannels, and enter a microliter size reaction chamber at a velocity of several hundred feet/sec. Shear rates exceed 10^6 sec^{-1}, several orders of magnitude greater than high speed stirring in a batch reactor, or ten times that achieved in high-pressure homogenizers. Reactant-bearing liquid structures are reduced to nanometer scale, often approaching molecular size. Diffusion resistance becomes minimal, and reaction kinetics are rapid and exclude slow side reactions. Digital control of inlet streams ensure design stoichiometry and shear levels during processing.

A CCR consists of a high pressure mixing system capable of subjecting a reaction mixture to high pressure and shear, in a very restricted reaction zone. Control of flow and stoichiometry, coupled with ultraturbulent mixing to minimize diffusion resistance to reaction, allow continuous reaction with precise control of product characteristics.

A standard Microfluidizer® Materials Processor schematic is shown in Figure I; a laboratory Microfluidizer Processor is shown in Figure II. The reaction mixture is formed as a premix, then flows into an intensifier pump. The mixture is pressurized (up to 40000 psi), then conducted through microchannels (in which streamline flow minimizes mixing) to a microliter-size reaction zone in which the kinetic energy of the pressurized liquids is dissipated, causing ultraturbulent mixing.

Figure 1. Micrfluidizer Processor Schematics

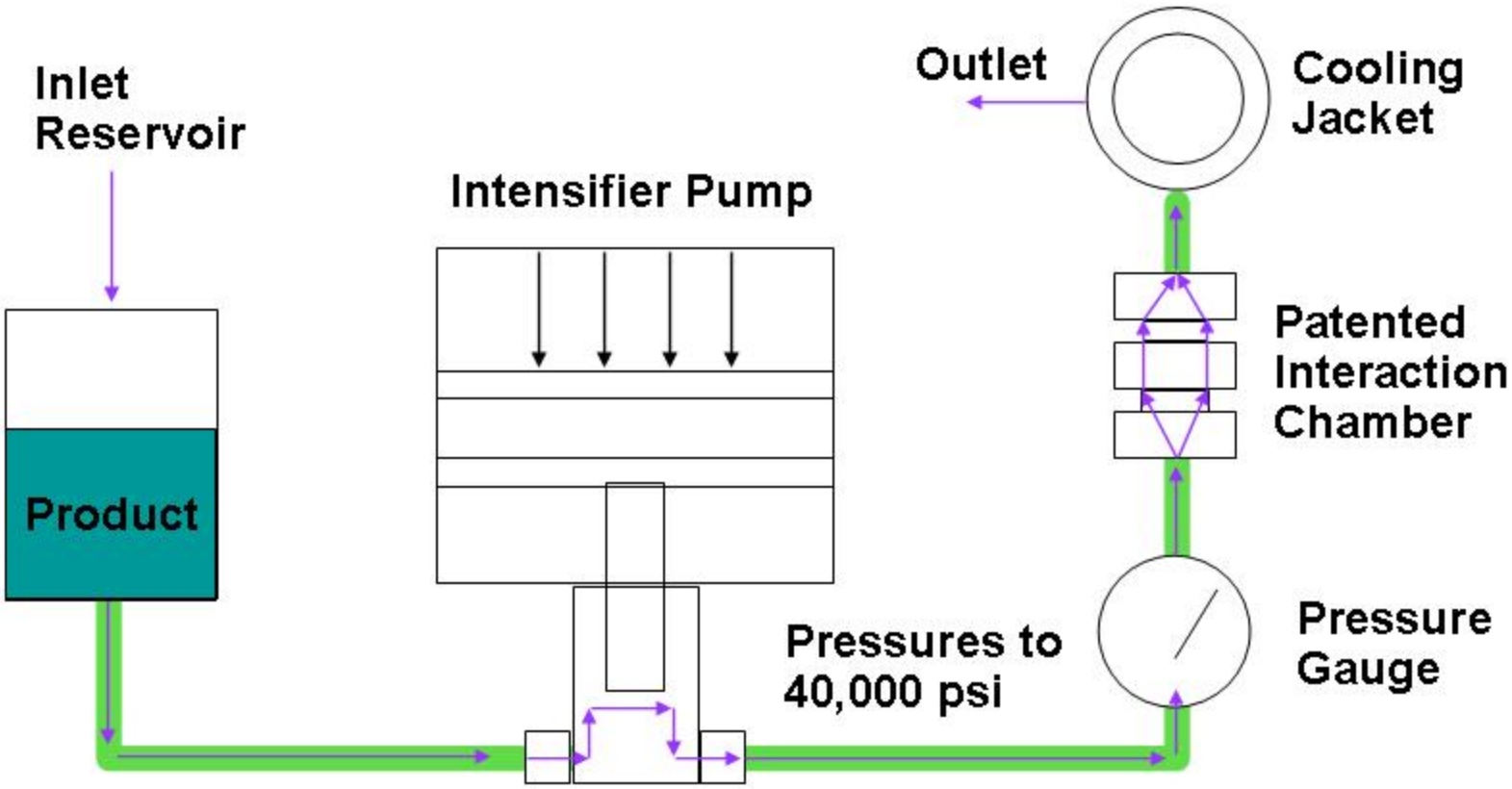


Figure II. Laboratory Microfluidizer® Processor

The delay time between pump and reaction zone is 0.1 to 1 second. For slower reactions this delay and a controlled premix storage time may be practical. Serial treatment in Microfluidizer Processors and the use of an online accumulator can maintain continuous operation.

For fast reactions, (95% completion in 1 – 5 seconds) premix storage is not acceptable. By using metered coaxial feed of reactants into a Microfluidizer® Processor, the delay time prior to reaching the reaction zone will usually be short enough to allow continuous one-pass operation with high yield and full control of reaction product size, size distribution, purity and phase identity. Even if some reaction products form en route to the ultraturbulent reaction zone, this can be minimized by appropriate choice of upstream channel size, to maintain streamline flow of large liquid structures prior to reaction. Further, for precipitated reaction products significant remodeling of freshly formed solids can occur in the ultraturbulent reaction chamber. A schematic drawing of such a system is shown in Figure III.

For very fast reactions (95% completion in less than 1 second), where exposure of reactants prior to reacting the ultraturbulent zone would lead to non-uniform reaction conditions and unacceptable variations of product characteristics, a direct interaction Microfluidizer Mixer/Reactor (MMR) is able to introduce two or more independent, pressurized streams which are forced to collide at high velocity in a microliter-size reaction chamber, with shear levels exceeding 10^6 $sec^{-1.}$ Reacting molecules interact at the nanometer scale and precipitation reactions produce nanoparticles, uniformly and continuously.

A schematic drawing of an MMR is shown in Figure IV and a schematic drawing of a direct interaction chamber is shown in Figure V. A laboratory MMR System is shown in Figure VI. Figure VII shows a Microfluidizer Processor, configured to operate as a high throughput MMR.

Figure III - Coaxial Feed MMR Schematic

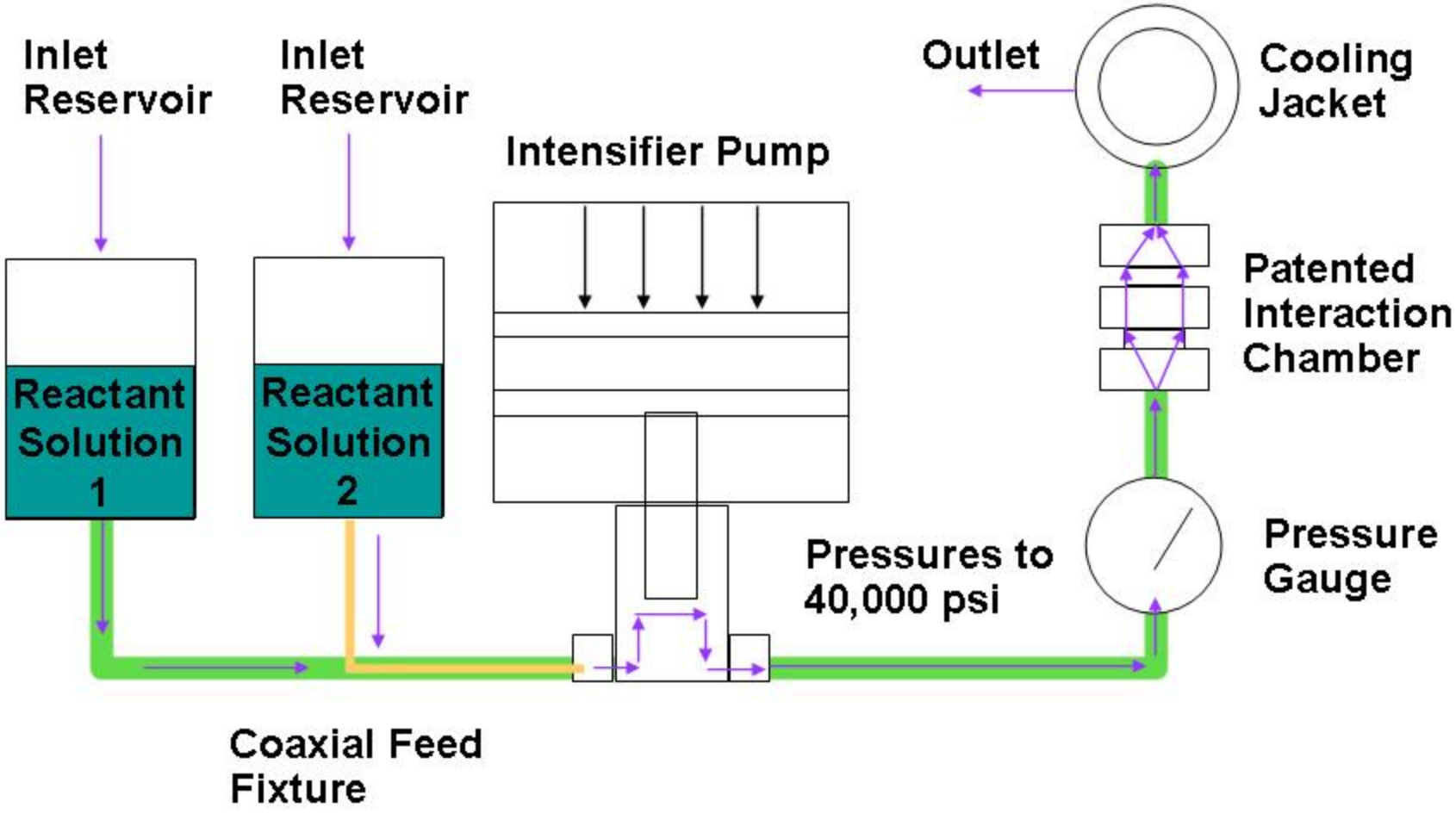
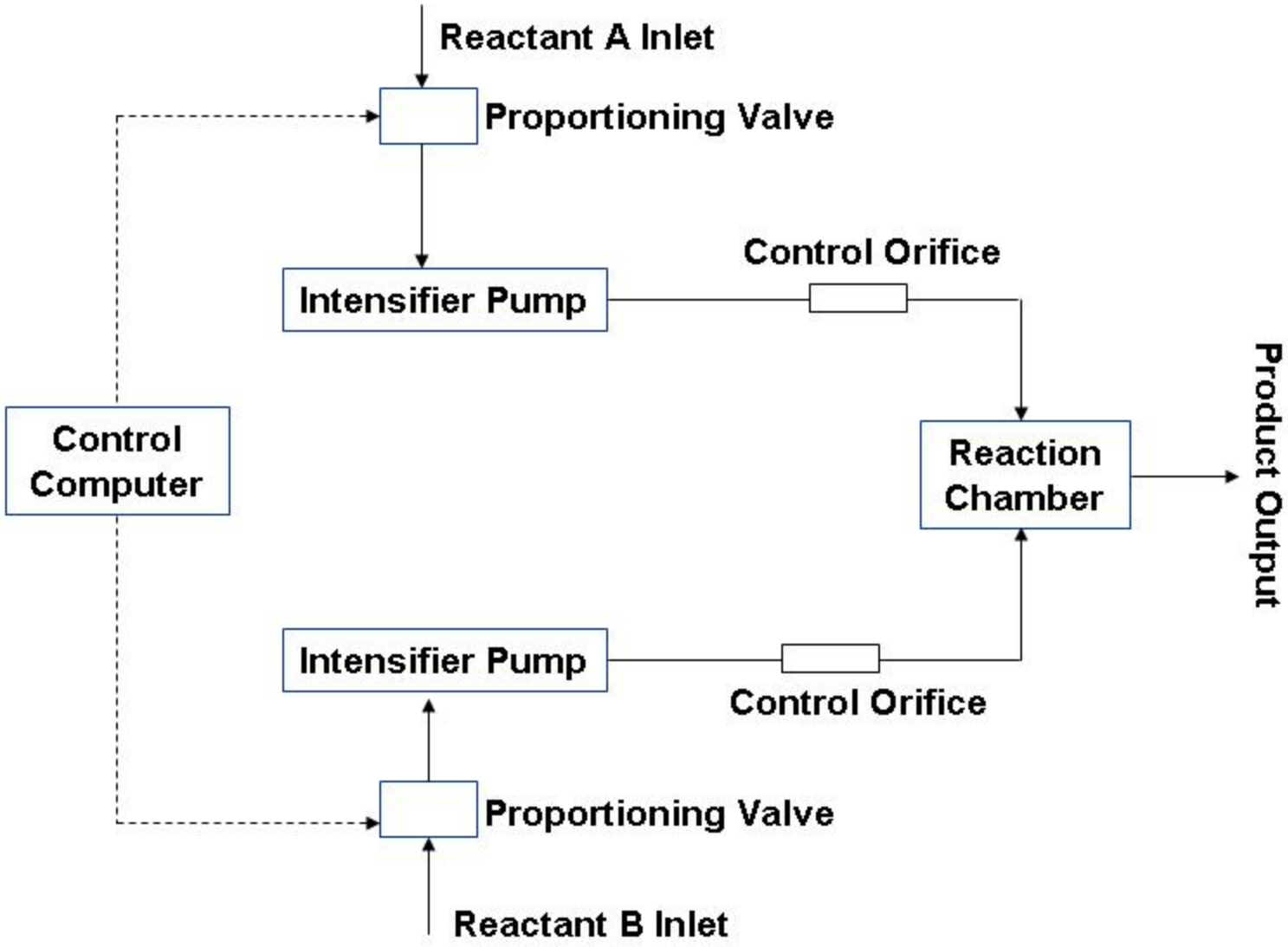
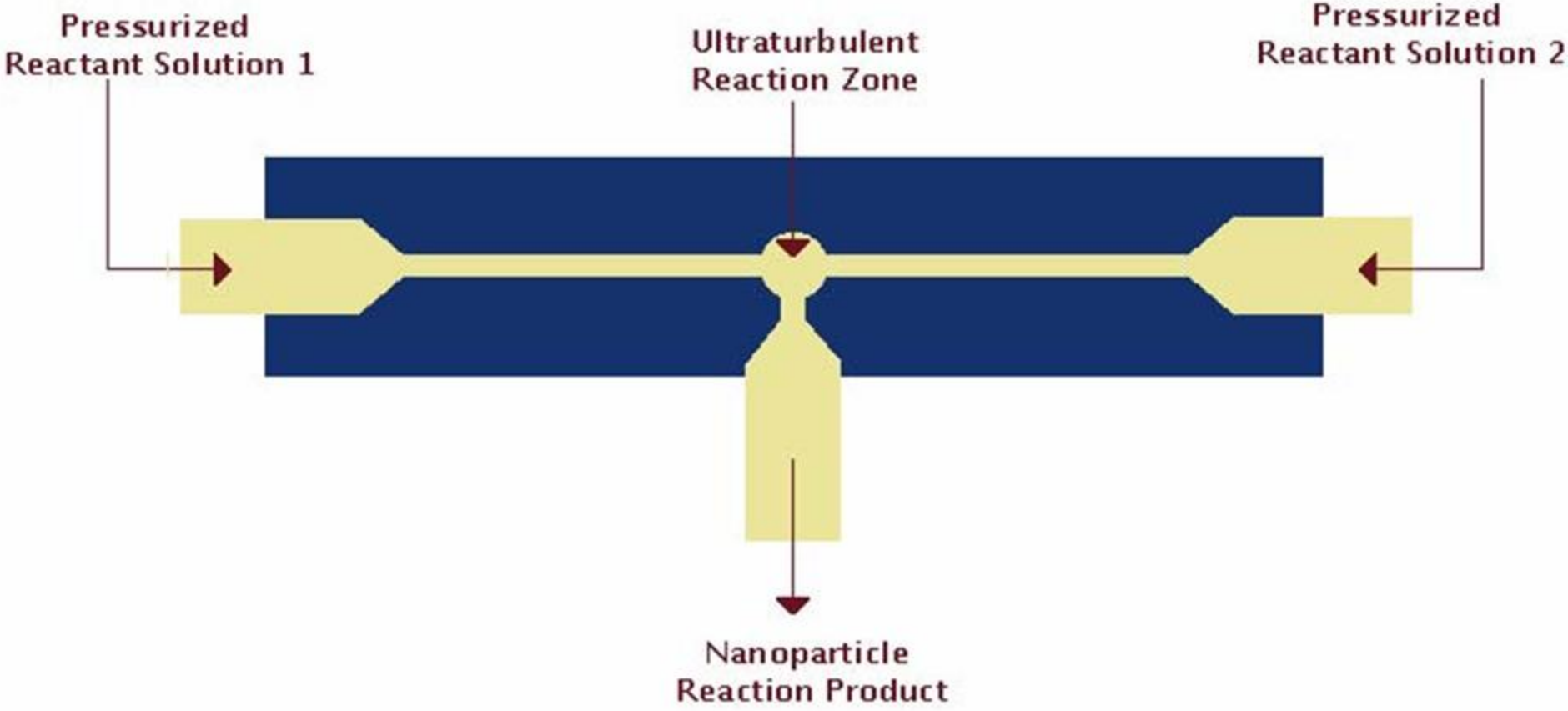


Figure IV. MMR System Schematic



MMR Nanomaterial Production System (Schematic)

Figure V



Separate high-pressure pumps (up to 30,000 psi) feed the reactant solutions, through shear-inducing microchannel passages, into an ultraturbulent reaction zone, of microliter size. Collision of the streams results in creation of nanometer-size liquid structures in which reaction occurs, resulting in uniform nanoparticles of precipitated reaction product.

Figure VI Laboratory MMR System (Multiple Stream Mixer/Reactor)

Figure VII. Production Microfluidizer/MMR (Multiple Stream Mixer Reactor) Processor

CCR technology can be adapted to multiplex a single high pressure stream to interact with multiple lower pressure streams of varying composition, on a continuous basis. Throughputs in the gram per minute range are achievable. Scaleup to 20 kg per minute can be based on the multiplex experimental results. CCR technology has been in wide commercial use for more than 15 years, in Microfluidizer Processors. The ability to attain linear scaleup, over a 100,000-fold throughput range, has been characteristic of this technology.

Applications

Table 1 shows the product classes which CCR technology can address. Table 2 shows current and proposed specific applications These can take advantage of the attributes shown below. Table 3 lists application programs which have been explored experimentally in Microfluidics' programs.

Advantages of CCR Technology

- Lower capital cost
- Continuous operation at high efficiency
- Control of stoichiometry
- Control of product purity, size, uniformity, phase purity
- Reliable scaleup

Characteristics of CCR's

- Flow rates to 20 gpm readily achieved
- Pressures applied to reactant mixtures up to 40000 psi
- Tested, trusted Microfluidizer Processors used. When needed, modifications are provided to reduce or eliminate interaction of reactants prior to reaching the ultraturbulent reaction zone.
    a. Coaxial feed at Microfluidizer Processor pump inlet
    b. Independent reactant feed to reaction chamber

Table 1 – Product Classes That May Utilize CCR Technology

- **Injectable drugs**
- **Catalysts**
- **Fine coatings**
- **Superconductors**
- **Fine grinding media (cmp)**
- **Pigments**
- **Ceramics**
- **Fine chemical manufacture (including API's)**

Table 2. New CCR Technology Applications

- High strength polymers reinforced with nanotubes
- Nanomaterials to enhance fabric conductivity, strength
- Better lubricants incorporating aligned nanotubes
- Nanotubes and nanoshells for medical therapeutics
- Computer memory using crossed nanotube geometry
- Nanotransistors, other high density electronic devices
- Field emission display components in large screens
- Nanoelectronic structures for future computer chips
- Nanoprinting materials to advance chip fabrication
- Quantum dots for medical diagnostic biolabels
- Photovoltaic cell components

Table 3. Experimental Programs

- Recrystallization of Active Pharmaceutical Ingredients (API's)
- Synthesis of API's
- Preparation of Catalysts and Catalyst Supports
  - Chemical reaction catalysts based on vanadium phosphate
  - Syngas partial oxidation catalysts
  - Cu-Al-Zn mixed oxide catalysts
  - Aluminum oxide catalyst support
  - Nano-crystalline zeolites for catalytic cracking
  - Activated carbon / metal catalysts
- Synthesis of mixed metal phosphate precursors of low thermal expansion ceramics
- Nutraceutical and cosmetic ingredient preparation

References

1. A.M. Thayer, Harnessing Microreactions, *Chemical & Engineering News*; May 30, 2005, p. 43-52
2. US Patent Numbers : 6,221,332 B1 and 6,159,442 - Multiple Stream High Pressure Mixer/Reactor and Use of Multiple Stream High Pressure Mixer/Reactor. European Patent No.: EP 1 011 856 B1 : Multiple Stream High Pressure Mixer/Reactor

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