Process intensification – think small

With the availability of novel miniaturised technologies, process intensification can provide manufacturers with a new competitive advantage.

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Put simply, PI is the miniaturisation of unit operations

recent trip to Informex 2002 showed many Asian companies selling their specialty and fine chemicals to North American and Western European firms. Many manufacturing firms are pondering how they will stay competitive. How many more years will their division or company survive? How can they fill idle equipment? Since compliance with environmental and safety regulations is virtually non-existent in Asian countries, there is an uneven playing field. This is most pronounced in India and China. In manufacturing, these two costs - environmental and safety - are the 'big ticket' items. Central and Eastern European nations have cheap labour, but many have elected to meet EU environmental and safety regulations prior to admittance to the EU.

How can we even out the playing field? The answer lies in new technology and that new technology is Process Intensification.

The term 'Process Intensification' (PI) was originally coined at ICI (Imperial Chemical Industries) in the UK in the 1970s. Colin Ramshaw, currently a professor at the University of Newcastle (UK), is considered to be the father of PI. Put simply, PI is the miniaturisation of unit operations. This miniaturisation should accomplish the following:

- A reduction in energy use,
- A reduction in capital expenditures (through building lower-cost plants),
- A reduction in plant profile (height) and plant footprint (area),
- Environmental benefits, and
- Safety benefits (low volumes of hazardous or toxic compounds in process).

Approximately 20 per cent of the cost of a new plant is process equipment, with the balance being

structural steel, piping, conduit, wire and instrumentation. Smaller unit operations mean smaller size, less weight and less structural steel, piping, conduit and wire. This means lower-cost plants with smaller footprints. In addition, many plants are now amenable to skid-mounted construction, which can lower costs even further.

The Holl STT[™] Reactor

The heart of the chemical process industries is the reactor and, until recently, there was no process intensification technology available for reactors. A number of specialty reactors have appeared over the years, but none has had such far- and wide-reaching applications as the Spinning Tube in a Tube (STTTM). The Continuous Stirred Tank Reactor (CSTR) was first used over 300 years ago in the processing of gold ore. Since then, numerous specialised reactors have been developed, but all were volume-based - as was the CSTR. Recently however, Holl Technologies has developed a reactor that not only establishes a new paradigm but also provides process intensification. The Holl STTTM is simply a cylindrical rotor spinning in a cylindrical stator - the annular space being where the chemical reaction takes place (Figure 1).

Holl's STTTM Reactor achieves a paradigm leap by moving from a volume-based to an area-based reaction vessel. The STTTM eliminates:

- The large volumes of valuable liquids held up in a stirred tank reactor,
- The large amounts of power expended merely to recirculate large liquid volumes in stirred tanks (although only the shearing areas of the impeller blades impart most of the useful work for mass transfer),
- Long scale-up times for new processes from



Figure 1. The Holl Spinning Tube in a Tube (STT™) Reactor.

bench-top to commercial size (typically, three to five years are needed for scale-up),

- Unwanted side-products in reactions due to inadequate thermal control or hot-wall effects, and
- Fouled surfaces associated with stirred tank, tubular reactors and heat exchangers.

Holl's STT™ Reactor achieves a paradigm leap by moving from a volume-based to an area-based reaction vessel The STTTM can be used for liquid-liquid reactions, gas-liquid reactions, gas-gas reactions and solid-liquid reactions where the solid is carried in a liquid as a slurry.

It is a perfect process for polymerisation reactions. In CSTRs, the liquid adhering to the vessel wall can be up to 10°C hotter than the liquid mass in the rest of the vessel. These localised hot spots can cause the polymer to achieve much higher chain lengths (higher molecular weights) – potentially producing off-specification product that requires a further separation step to eliminate the long polymeric chain material. The STTTM has such high shear rates against the stator wall that hot spots do not exist. This also implies that higher heat transfer rates are possible, since the inside liquid heat transfer film coefficients are very thin and are continuously renewed along the inside vessel wall due to the high shear.

When the stator is made of glass, ultraviolet light can pass into the reaction chamber for photochemical reactions where UV light is the initiator. Photochlorinations and photo-brominations can easily be accomplished in the STT^{TM} . Polymerisations can also be initiated with UV light instead of costly chemical initiators.

Because of the high shear rates and levels of micro mixing achieved, phase transfer catalysts can,

in many cases, be completely eliminated – thus simplifying purification of the final product.

Other PI technologies

In manufacturing, the reactor's partner is the distillation column. Traditionally, columns have been bulky, large and limited by gravitational force. The Higee miniaturised spinning packed column changes all this. Invented by Dr Ramshaw well over a decade ago, the Higee is a High Gravity Rotating Contactor (Figure 2). Typical installations have been in the air-stripping of organics from wastewater. Future installations include various types of distillation and retrofits to existing columns.

With the availability of miniaturised reactors and distillation columns, process intensification is expected to go full-swing in the new millennium. Additional process intensification technologies now available include compact heat exchangers (CHEs), such as Alfa Laval's Compabloc[®] welded plate heat exchangers. These have very high surface areas per unit volume.

In the field of heat transfer, the Klarex self-cleaning heat exchanger technology from the The Netherlands has reduced installed surface areas by approximately one-fifth. Since the Klarex units are self-cleaning, there is no need to oversize an installation in order to compensate for pluggage. The technology features a 'shell and tube' heat exchanger in the vertical position; although it was originally designed for the petrochemical industry, it can easily be adapted to the pharmaceutical and fine chemical industries. Chopped wire of the same metallurgy as the heat exchanger is circulated through the unit, scouring the tubes clean. That is, if the heat exchanger tubes are made of 316 stainless steel, then the chopped wire is also made of 316 stainless steel. The wire exits the unit and flows back to the inlet through an external downcomer. In a smaller size, this technology can be used as a reaction system.

With reactors, columns, extractors and heat exchangers all offering a PI alternative, the

Figure 2. Internal schematic of the Higee High Gravity Rotating Contactor.



Innovations in Pharmaceutical Technology

practicality and cost-effectiveness of process intensification has become a reality.

Macro- and microchemical plants

For the future, the biggest change we will see in process intensification will be a switch from batch to continuous processes. We believe that tabletop miniature plants will replace expensive batch plants at greatly reduced costs. As plants become smaller, two types of plant will emerge - the 'macrochemical' and the 'microchemical'. With microchemical plants, instead of using cooling towers, cooling will be accomplished by thermoelectric (Peltier) modules, such as those produced by Tellurex Corporation (Traverse City, Michigan, USA). These same modules can also be used for heating, along with other electric resistance heating devices. In microchemical plants, Ranque-Hilsch Vortex Tubes will be used as another method of cooling, since they only require compressed air to operate. ARTX Ltd and EXAIR Corporation (both of Cincinnati, Ohio, USA) produce these miniature-cooling devices. (Ranque-Hilsch Vortex Tubes are something of an engineering wonder, in that they take in compressed air in the middle of the tube, and then emit hot air from one end and cold air from the other (Figure 3)).

We believe that tabletop miniature plants will replace expensive batch plants at greatly reduced costs

Another new technology unveiled at Informex 2002 was the intensified hydrogenation technology developed by Härröd Research (Göteberg, Sweden) (Figure 4). This technology performs hydrogenation reactions at critical pressures and in a continuous liquid-liquid system. (Hydrogenation reactions have typically been performed in batch gas-liquid systems.) The new technology eliminates the mass transfer issues (difficulty of getting gaseous

Figure 3. The Ranque-Hilsch Vortex Tube. Compressed air is taken in at the middle of the tube, and hot air is then emitted from one end of the tube and cold air from the other



Figure 4. Schematic of the intensified hydrogenation technology developed by Härröd Research (Göteberg, Sweden).



hydrogen to dissolve in organic chemical compounds) and heat transfer issues (removing the heat from the highly exothermic chemical reactions) normally associated with hydrogenation reactions.

Using a carrier such as liquid propane or dimethylether, the hydrogen remains a liquid at critical pressures and liquid-liquid chemical reactions occur very quickly. In addition, heat is very easy to remove. The plant has a very small reactor and the company claims its installed cost is one-fourth of that of traditional hydrogenation processes.

Leonard Parker Pool, founder of Air Products and Chemicals in 1940, had a revolutionary concept for selling oxygen and nitrogen whereby onsite plants were installed at the client's facility. This concept can be expected to now be used for things such as hydrogen peroxide, polystyrene and PET – chemical companies will again maintain small chemical plants at their clients' sites.

A commitment to PI

Management must make a commitment to the change to process intensification. People that embrace PI will be regarded as forward-thinking, whereas those that don't will be seen as dinosaurs. Where will the cutbacks in staff begin when another round of downsizing takes place? Pharmaceutical and chemical companies that outsource the production of new compounds will be reluctant to accept traditional technology. Toll processors will be required to provide intensified technology - not as an alternative but as the norm. Firms that outsource may eventually scale up a new technology in their own plant. PI can dramatically reduce the time-line for plant completion and start-up - providing earlier product entry to the marketplace. Validation of an identical scaled-up continuous pharmaceutical process should also be much faster.



Rocky C. Costello, PE, is a licensed professional chemical engineer. He received his bachelors degree from Youngstown State University (Youngstown, Ohio, USA) and then did some graduate work at Manhattan College in The Bronx. He worked in polymers for Owens-Corning Fiberglass, and later spent over 15 years with Stauffer

Chemical in both specialty and basic chemicals. At Stauffer, he worked in the corporate engineering centre and was later appointed one of the youngest Plant Managers in the history of the company. His group at Stauffer was subsequently purchased by Rhodia. Mr Costello is currently President of R.C. Costello & Associates, Inc – an engineering firm specialising in process intensification and process safety, with offices in Redondo Beach, California, and The Woodlands, Texas. He holds patents in waste processing and colloidal separations.