Enhancement of Distributed Manufacturing using expanded Process Intensification Concepts

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Distributed manufacturing definition

For the production of things, like cars and planes, it means making parts all over the world and using supply chain management concepts to bring it all together for final production. Labor costs are a key driver

For the production of chemical materials it means the efficient production of a smaller volume product at one site. There are usually multiple sites around the world where this is done. Shipping is often a key driver

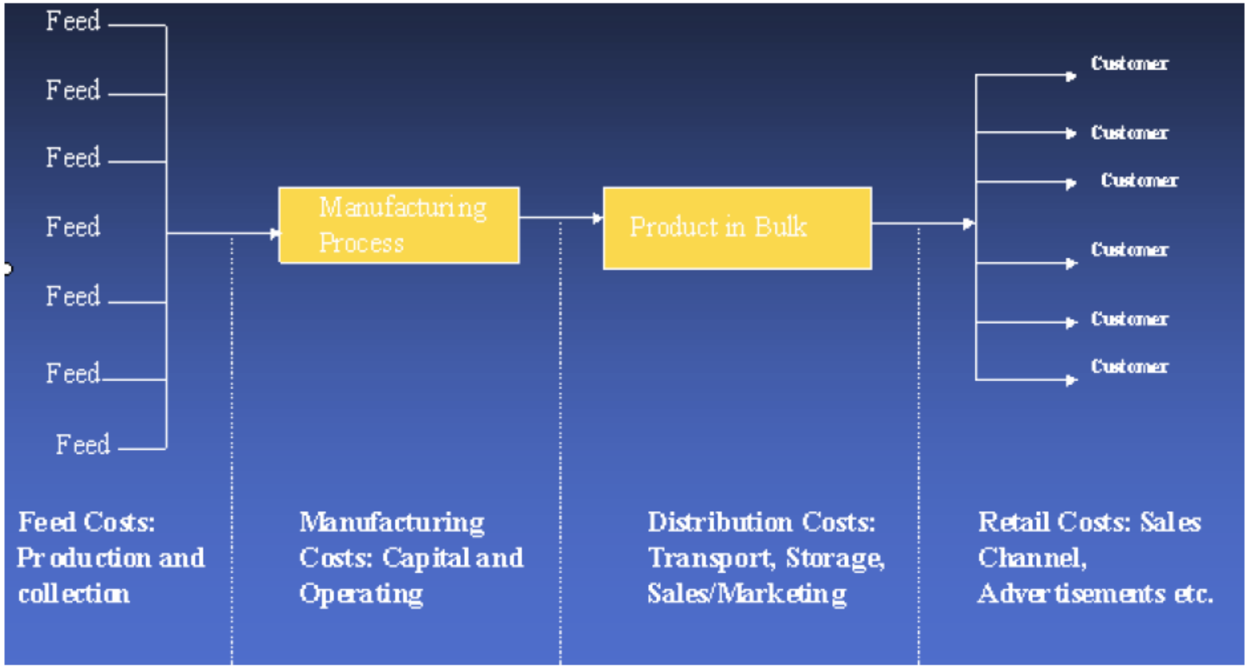
Reasons for distributed Chemical manufacturing

- High cost of shipping raw materials such as biomass; also the cost of shipping the product
- Safety of shipping and storing large volumes of reactive materials (usually not a cost driver)
- Regulatory issues related to the registration of materials of commerce; PMN's and REACH
- Energy and byproduct integration when some early processing is required before shipping

To be successful distributed manufacturing must reduce costs across the total value chain and in all areas including shipping, labor and energy

Value chain in the Chemical Industry

UOP
A Honeywell Company



Regulatory compliance issues can be an additional key cost that should be factored into the process design

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Problems with distributed Manufacturing

- **Economies of scale will make cost competitive production of large volume chemicals difficult for regional/local production facilities; must focus on efficient production process**
- Available infrastructure required for production
- Available technical production workforce
- Support staff such as QA/QC and maintenance
- Technology development (market development as well as process dev.) and system wide upgrades; use McDonalds type of approach

One approach to increasing process efficiency is process intensification (Concept developed to lower capital costs)

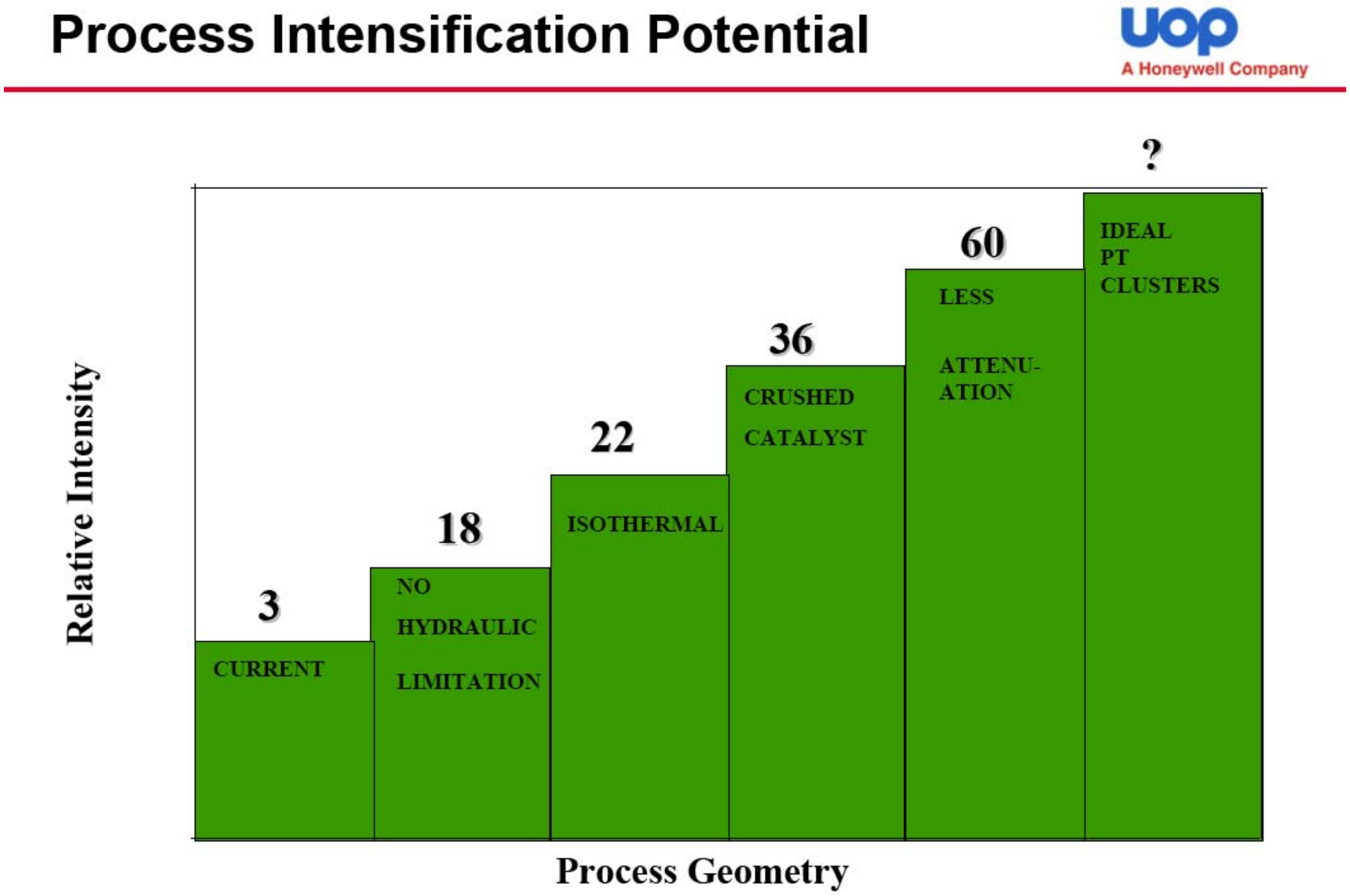
Find the barriers to production and remove them to intensify the process, usually new equipment designs to significantly increase production with lower capital costs; Not just optimization but a new processing approach

Will the broadened view of process intensification (new processing approach) have a significant impact on other processing costs?

Process intensification approach

- Reduce the number of unit operations by combining steps like synthesis and separations
- Remove barriers to production such as heat and mass transfer; For example by using microreactors
- Improve process integration through the use of continuous processing
- Utilize new processing concepts based on enhanced control enabled by PAT e.g. reactive separations
- Use of enhanced catalyst operating environments

Find the barriers to production and remove them to intensify the process



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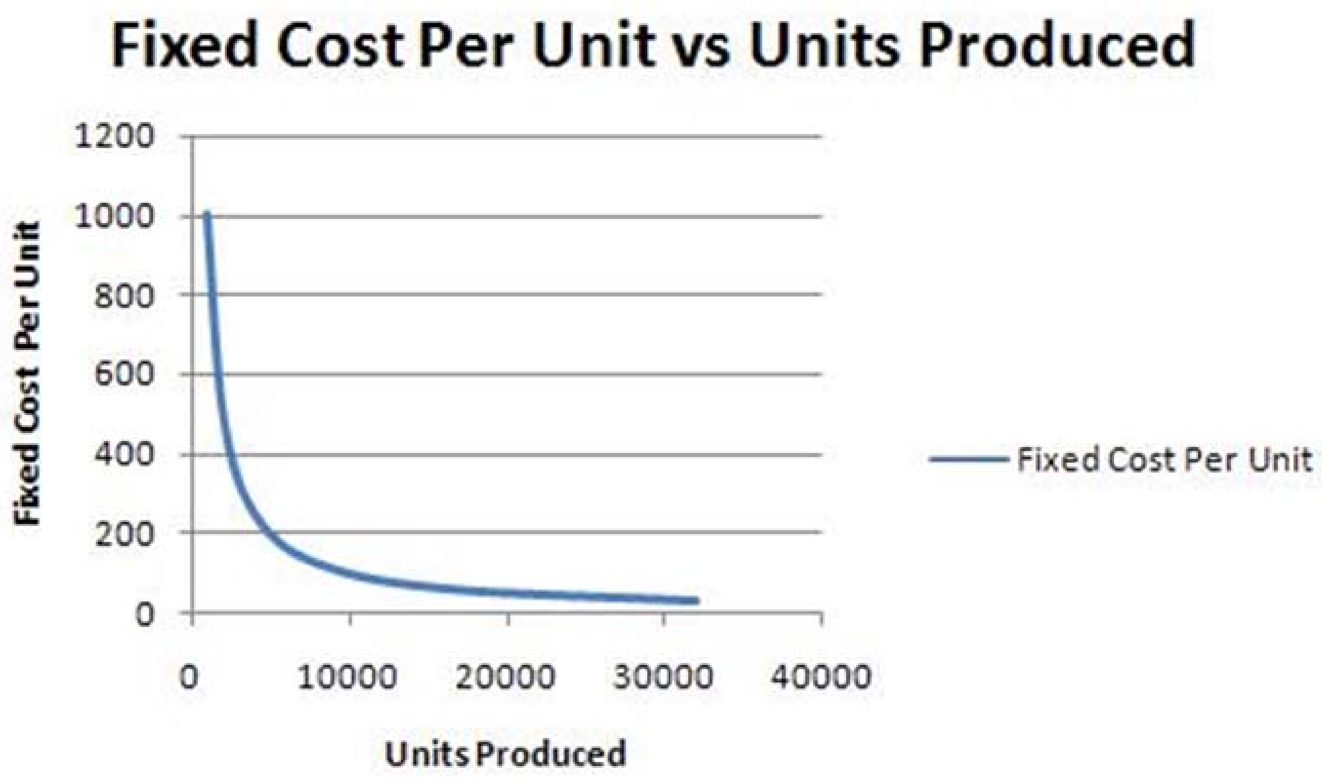
One of the key problems with the implementation of process intensification technology is the time/cost required to characterize process performance with new modes of operation

As mentioned earlier in the week, utilization of PAT in process development research can dramatically speed that step

The first issue with distributed production is competition with larger scale operations; Achieving efficient production at a small scale

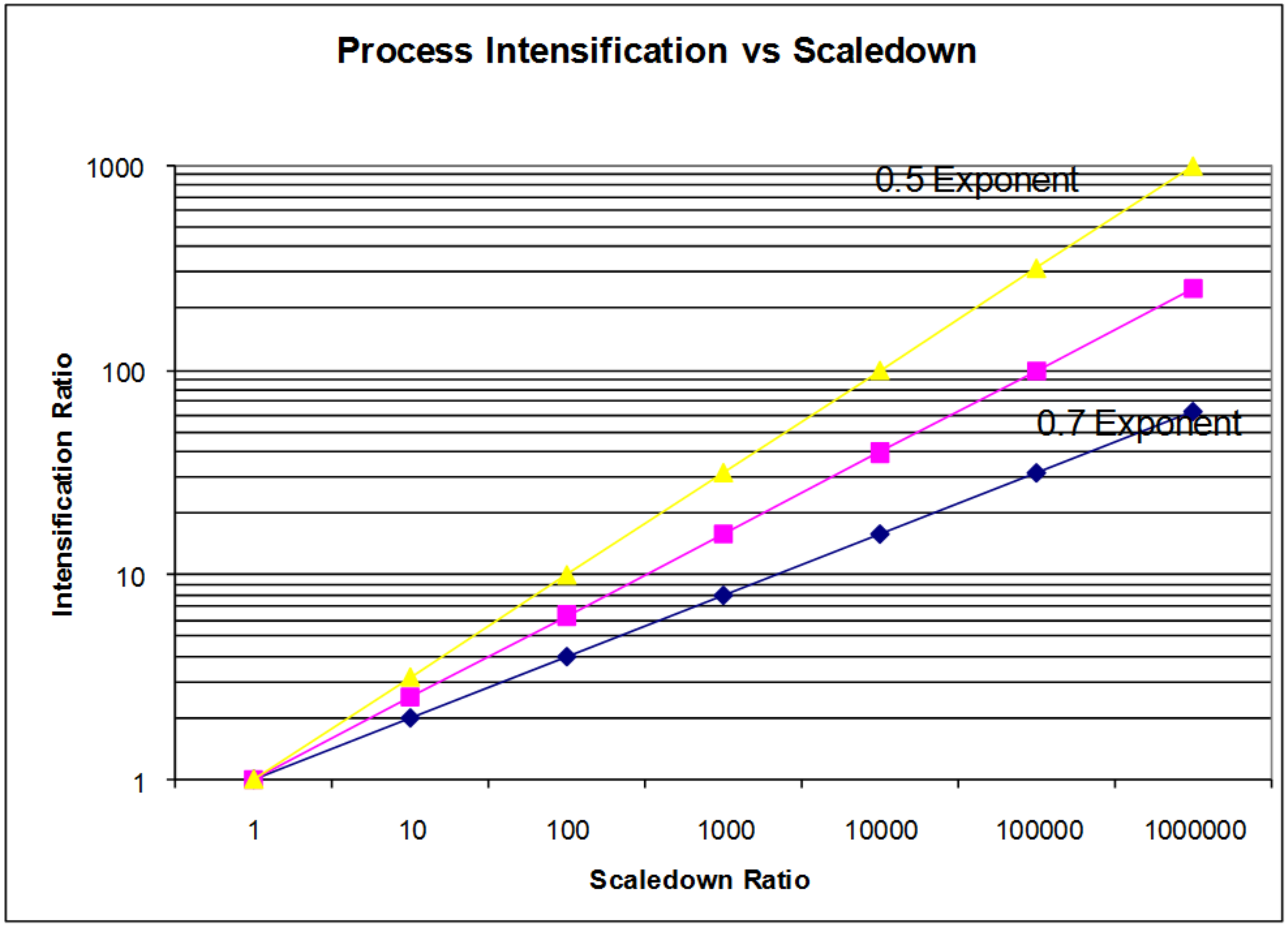
A general misconception is that if capital costs are not significantly lower then distributed, smaller volume, processing will not be competitive

General Curve for Economy of Scale; For large volume chemical production the factor is often 0.6 increase in cost per unit of production



http://www.wikinvest.com/wiki/Economies_of_scale

Indicates that a distributed process with a production volume 1000 times less than a conventional reactor will need an intensification factor of 16 (capital cost per pound of a 100 K pound plant needs to be 16 times lower than the volume ratio to equal the capital cost per pound of a 100 million pound plant)



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However, capital is not the only issue when comparing cost

Costs for a co-product distributed methanol/ power production process compared to bulk production. Should be intensified by 3-4 since it is 25 time smaller, not the case.

		Conventional US	Large Middle East	Distributed	
Capacity	*Tons/day*	2326	5000	195	Capacity ~25 X less
Capital Charge	*MM US$*	0	490	35	Capital ~14 X less
Methanol Production Cost	*$/gal*	0.53	0.15	1	
ROI	*$/gal*	0	0.12	0.22	
Power credit	*$/gal*	0	0	-0.62	
Shipping/ Storage/ Insurance	*$/gal*	0.14	0.26	0.1	
Total	*$/gal*	0.67	0.53	0.7	
	$/Mton	**224**	**178**	**235**	

Koch, VandenBussche, and Chrisman, Eds., “Micro-Instrumentation for High Throughput Experimentation and Process Intensification – A Tool for PAT”

BEST Energies has a similar approach for a co-product biochar/energy process for biomass processing

- It is not cost effective to transport the biomass (manure) more than about 30-50 km.
- In rural US burner gas substitution is most cost effective energy product if a user is available
- Continuous process enables integration of raw material drying and reactor heating & lower labor costs
- Process can shift ratio of biochar/energy for market demand variations for a 25-30% internal rate of return

The project was supported by the Small Business Innovation Research program of the U.S. Department of Agriculture, grant number 2008-33610-18876

Comparison of batch versus microreactor production of biodiesel for small distributed plant. Note plant size as construction costs can be 80% of capital cost

Production of biodiesel	Batch plant	Microreactor plant	Comments
Plant output (tons/yr)	20 000	20 000	
Reactor volume (m^3)	10	2.4×10^{-3}	4167x smaller
Plant footprint (m^2)	149	60	60% smaller
Surface area to volume ratio (m^2/m^3)	14.9	2.5×10^4	1678x higher
Productivity ($kg/h/m^3$)	250	10.4×10^5	4167x higher
Energy input (kJ per kg)	7.1	0.4	18x lower
Mass transfer coefficient $k_l a$ (s^{-1})	10^{-2} – 10	10-100	10^4 higher
Heat transfer coefficient (kJ/m^3)	628	2.86×10^6	4554x higher
Mixing efficiency (Re)	7×10^5	10	7×10^4 higher
Capital cost (Rm)	8.6	6.5	24.4% saving
Manufacturing costs (R/L)	6.60	5.87	11.1% saving

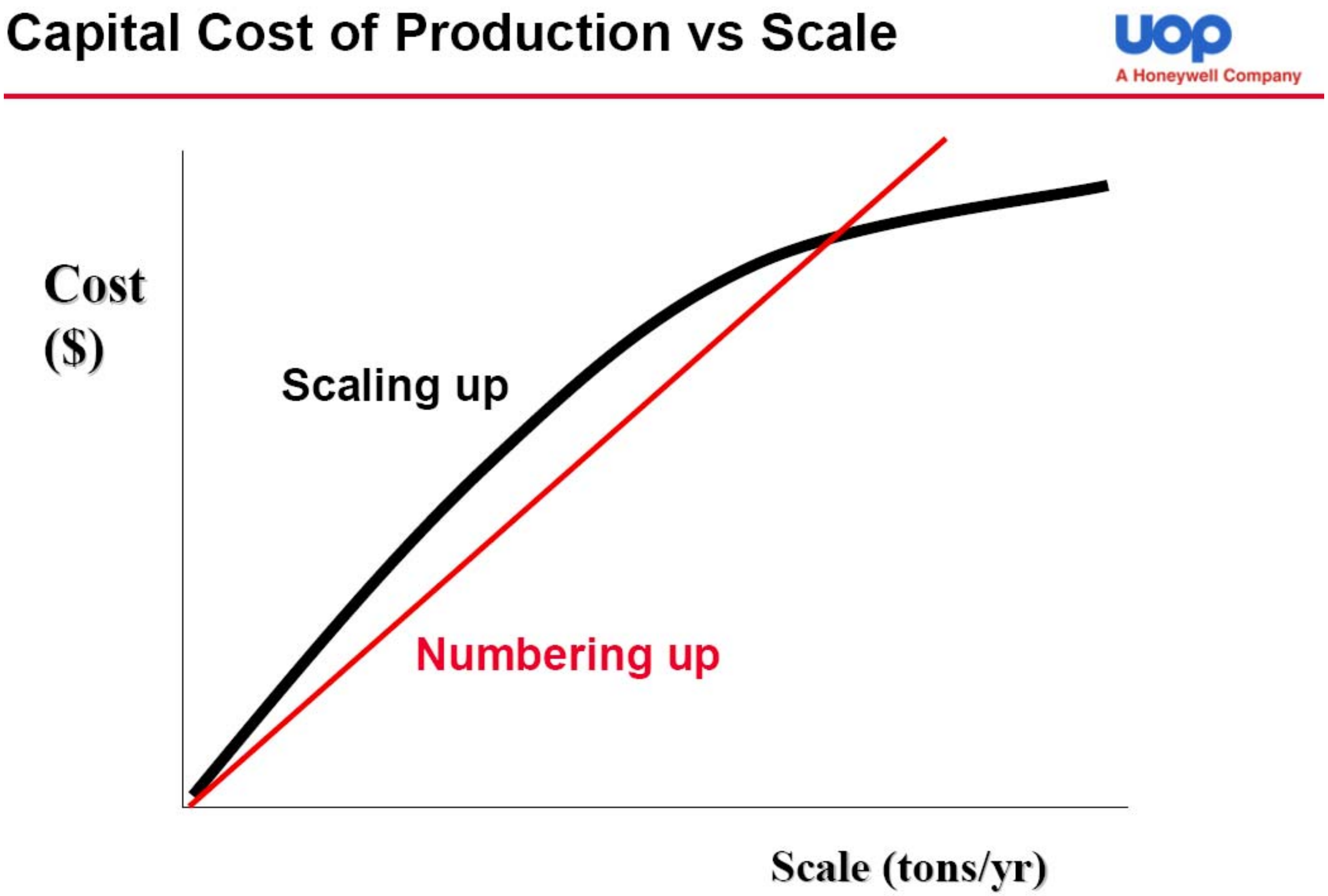
http://researchspace.csir.co.za/dspace/bitstream/10204/2680/1/Buddoo_P_2008.pdf, S R BUDDOO, N SIYAKATSHANA, AND B PONGOMA ,CSIR Biosciences

The three previous examples demonstrate that distributed continuous manufacturing can be made cost competitive even though capital cost may be higher

Capital costs should be minimized with process intensification concepts. In addition the previous data indicates that costs other than capital may also be lowered with process intensification

Since capital costs are always a concern with microreactor scaleup the next section is a little closer look at the issue

Microreactors do not achieve significant economies of scale compared to batch reactors but intensification factors are sufficient to keep capital costs reasonable.



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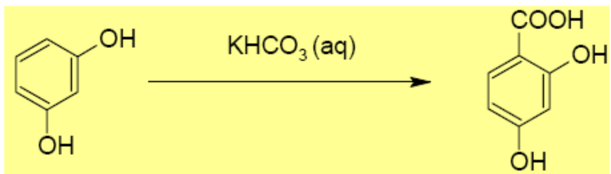
Several examples of potential intensification factors possible with microreactors were given in a presentation in 2006

This is one example

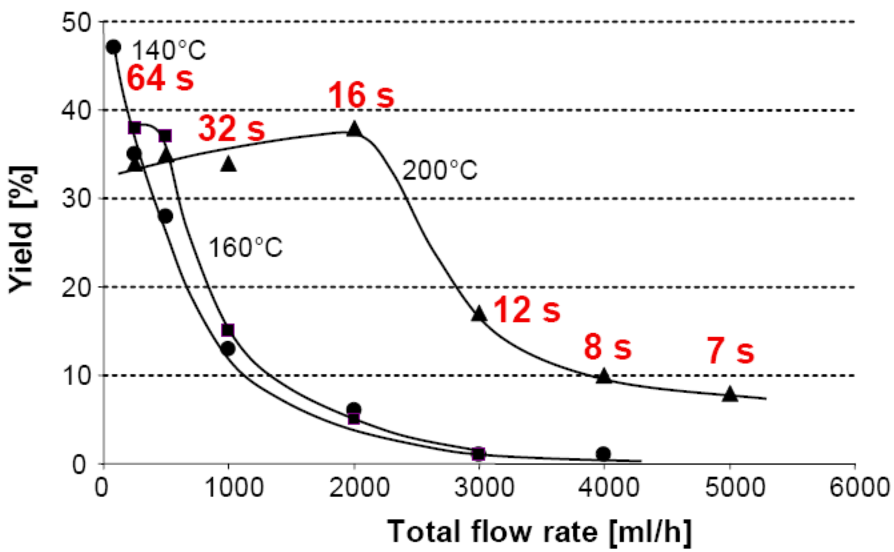
TU/e technische universiteit eindhoven IMM

KOLBE-SCHMITT SYNTHESIS: HIGH p,T-PROCESSING



V. Hessel, C. Hofmann, P. Löb, J. Löhndorf, H. Löwe, A. Ziogas
Org. Proc. Res. Dev. **9**, 4 (2005) 479-489

High p,T



- **Pressure: 40-70 bar**
- **Temperature: 100-220°C**
- **Reaction time: 4 – 390 s**

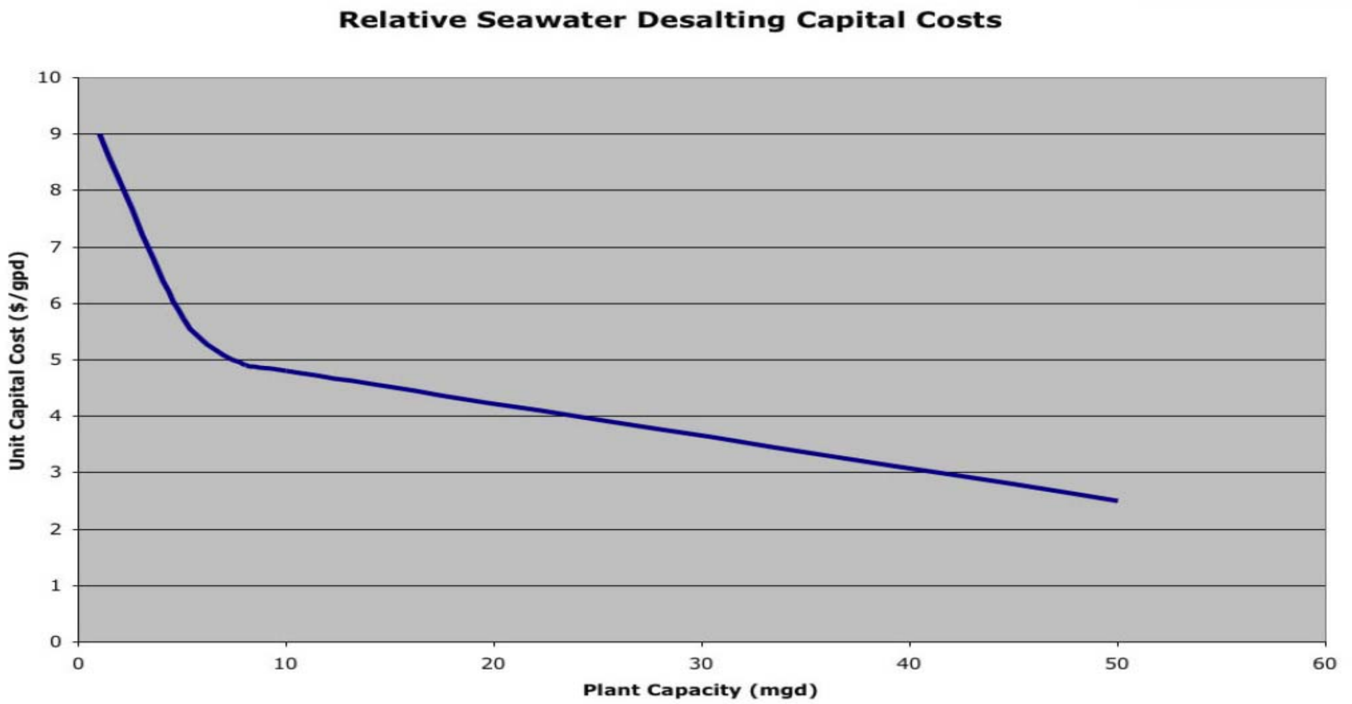
→ **Reduction of reaction time by ~2000**

→ **Increase in space-time yield by factor 440**

→ **Increase in productivity by factor 4**

V. Hessel, CPAC Rome meeting, 2006

In addition, experience should reduce the cost of microreactor plants just as has been seen with the scale-up of RO based seawater desalting plants that use the numbering up concept



Capital costs don’t preclude competitive production in smaller volume processes

http://texaswater.tamu.edu/readings/desal/DesalTechtrends.pdf

We don’t tend to think of fine chemicals and pharma production as distributed manufacturing but it is an area where efficient production of small volumes is important

We have seen that process intensification can help reduce shipping and energy costs.

Will the broadened view of process intensification (new processing approach) needed for distributed manufacturing help in this area?

Several small volume processes were studied to understand costs or barriers to cost reduction

- Labor costs were usually the largest cost except in the few cases where exotic starting materials were used and then labor was the second largest cost
- Capital costs were not significant
- Regulatory costs add to the labor costs, QA/QC and cleaning

Kralisch, Krtschil, Roberge, Hessel and Schmalz, Ch. 13, Micro process Engineering, Vol. 3

High labor costs have become a significant driver in the production of multi-step specialty chemicals and pharmaceutical compounds

This has driven the adoption of distributed production concepts much like in the auto case where out-sourcing is used to reduce labor costs

To lower labor costs; one pharma company's approach is to reduce the number of "touches"; defined as moving material from one discrete operation to another

- Reduce the number of unit operations by combining steps like synthesis and separations
- Improve process integration through the use of continuous processing enabled by PAT
- Evaluate new processing concepts like SMB for protein purification
- Use enhanced catalysts like enzymes

Very similar to process intensification

Can new processing concepts envisioned in a broadened view of process intensification (new processing approaches) have a significant impact on labor and other costs important in this area?

In the study mentioned earlier on small volume processes, several aspects reduced labor costs

- Continuous processing and process intensification reduced labor costs by a factor of **10** in one example (operation in novel process windows)
- QA/QC and change over and cleaning costs are reduced with continuous production
- Expensive raw material costs are lower with higher efficiency processing
- It also lowered capital cost but this had no real impact on total costs

Kralisch, Krtschil, Roberge, Hessel and Schmalz, Ch. 13, Micro process Engineering, Vol. 3

New catalyst technology can further intensify small scale processing

- Enhanced (almost quantitative) yield from enzymatic reactions under flow conditions
- Enhanced yield from metal catalyzed reactions with less contamination; 65% batch vs. 99.9%; flow synthesis of imines.
- Quantitative conversions reduce expensive raw material losses, key cost for multistep

Watts, CPAC Rome meeting 2008

The production and immediate use of intermediates may not require registration under REACH regulations

In the case of multistep continuous processes, a strong case can be made that the intermediates are fully controlled and do not need registration; This can be significant when 2 or more new intermediates are required

If registration is required the cost may be about 1.5 million Euros per compound plus the time for registration process

http://www.engineerlive.com/Chemical-Engineer/Safety_in_the_plant/Stem_cell_based_chemical_testing_cuts_cost_of_Reach_regulations/16841/

Continuous production also opens the door for additional concentration and purification approaches as well as more intensification; PAT should enable the utilization of these

- Membrane concentration is more compatible with continuous production
- SMB for material purification is more compatible with continuous production
- Reactive separations are more compatible with continuous processing

For Protein therapeutics separations and concentration may be 80% of capital cost and the majority of the processing time

Finally, PAT can enable the development and use of process intensification

- PAT should speed the characterization, development and introduction of intensified material processing (the key problem)
- PAT enables enhanced process control strategies
- PAT facilitates operation within the “design space” envisioned in the Quality by Design program from the US FDA which will reduce labor costs related to QA/QC and produce higher quality product

Conclusions

The utilization of new processing concepts, many of which are envisioned for process intensification and are enabled by PAT, will not only lower capital costs, but can also reduce other production associated costs such as labor, regulatory compliance, energy, environmental, and transportation.

The reduced costs enables distributed smaller volume production to be cost competitive