Enablers of the successful scale up of industrial biotechnology processes

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Motivation for the research

- **Increasing importance of innovative technologies in the process industry**
  - **In particular, the replacement of conventional technologies with industrial biotechnology processes**
- **However, the scale up of innovative processing technologies is problematic**

Background (1)

- Successful scale up appears elusive across several applications within the process industries, including industrial biotechnology applications (Mitchell et al., 2000)
- A majority of literature tends to cover specific technologies and in almost all of the cases where scale up was not achieved, it was stated that the reason was an inability to model the process in question
- There is some literature suggesting that non-technical factors affect the success of scale up

Background (2)

- Individuals' judgement and experience must be relied upon in achieving predictable scale-up (McCabe, Smith and Harriott, 1993)
- Individuals' experience, training and judgement is important in designing, constructing and operating pilot plants (Palluzi, 1992)
- It is important to decide, from among the many, the chemical and physical mechanisms of greatest significance (Euzen, Trambouze and Wauquier, 1993)

Background (3)

- **Knowledge management process is recognised as the primary process through which organisations innovate (Chakravarthy, McEvily, Doz and Rau, 2003)**
- **Knowledge required for innovation often pushes the boundaries of existing technical information - this makes integrating "experience-based, intuitive knowledge of the tacit kind" more important (Almeida, Phene and Grant, 2003)**

Research gaps

The following research gaps emerge:

- **Limited focus on process innovation (compared with product innovation)**
- **Lack of focus on the drivers that influence the testing and validation stage in the development of process technologies**
- **Limited exploration of the concept that individuals' experience, judgement, training and knowledge shape the scale up of new processes**

Initial research questions

- **Research questions for the initial stage of research were:**

  "What enables the successful scale up of new process technologies?"

  "In particular, what knowledge is required to support successful scale up in the process industries?"

  "Compared with conventional chemical processes, are there different or additional factors that need to be considered in the scale up of industrial biotechnology processes?"

Initial research methodology

- **The initial research questions were investigated by conducting interviews with nine members of six companies in the process industries**
  - **Structured and semi-structured interview questions**
- **Transcription and coding of interview responses**

Initial research findings

1. Several problems are encountered during scale up in the process industry
2. Knowledge is a critical enabler of successful scale up
3. Tradeoffs exist between batch versus continuous processing for scale up
4. Scaling up industrial biotechnology processes involves a unique set of enabling factors
5. There is disconnection between project management and knowledge management in scale up

Problems encountered in scale up

- **Fifteen problems were reported**
- **Leading problems were:**
  - **Poor mixing in reaction steps**
  - **Noise emission issues**
  - **Inaccurate measurements**
  - **Investment uncertainties (business decisions)**
  - **Unpredictability of mass transfer phenomena**
  - **Hot spots (unpredictability of heat transfer phenomena)**
  - **Process control tuning**
  - **Lack of pilot plant data**

Knowledge is a critical enabler

- **Results were unanimous; knowledge is a critical success factor**
  - **Problems occur in scale up because of a lack of knowledge**
- **The requisite knowledge for scale up is:**
  - **Explicit knowledge associated with theoretical design aspects of the pilot plants**
  - **Explicit and tacit knowledge for translating theory into representative pilot plants**
  - **Tacit knowledge based on experience**
  - **Knowledge for creating certain design parameters to be resilient to scale effects - such factors include reactor tube thickness and compressor performance**
- **Knowledge management systems for scale up are broken**
  - **One-directional**
  - **Revert back to the "experienced few", which is untenable**

Tradeoffs between batch and continuous trials

- Dilemmas exist in selecting batch versus continuous processes for scaling up new technologies
  - Batch trials are more accessible but can be unrepresentative
  - Shift from batch to continuous processing across industry sectors
- However, batch conversion steps are prevalent in industrial biotechnology applications
  - Tendency towards multiple smaller batches
- Potential conflict exists

Uniqueness of scaling up industrial biotechnology processes

- **A different set of considerations appear to govern scale up. In particular, knowledge is needed to address:**
  - **Tank size and mixing requirements**
  - **Temperature and pressure requirements**
  - **Catalyst tuning and removal of catalyst poisons**
  - **Variable feedstock compositions**
- **Although reported as sparse, knowledge based on prior scale up experience is still cited as an important enabler of scale up**
  - **Experience from other industries may be tapped but, on the whole, it was suggested that the required knowledge is not readily transferable**

Disconnection between knowledge management and project management

- **Project management skills were reported as lacking in scale up activities**
- **Interestingly, measures for successful scale up appear analogous with measures for successful capital projects**
- **However, acquiring, using or capturing knowledge (knowledge management) is not reflected in the measures of successful scale up**
  - **Despite the critical role of knowledge in achieving scale up**

Further research questions

- **Based on initial research findings and further discussions with members of industry, the further research questions are:**

  "What problems occur during the scale up of industrial biotechnology processes?"

  "What specific knowledge and skills are necessary to overcome the problems encountered during scale up?"

  "How are these knowledge and skills acquired?"

Further research methodology (1)

- A case study methodology will be employed to address the research questions
- Data will be primarily sourced from research interviews and if possible, from documented records
  - Interviews will contain structured and semi-structured questions
- The research interviews will be conducted with representatives of the following functions from the case study companies
  - R&D
  - Process Engineering
  - Operations
  - Project Management
  - Business

Further research methodology (2)

	Knowledge 1:	Skill 1:	.....	Knowledge n	Skill n
Problem 1: Poor mixing	What? How? When?	What? How? When?			
Problem 2: Noise emissions	What? How? When?	What? How? When?	→		
Problem 3: Inaccurate measurements	What? How? When?	What? How? When?			
.....	↓				
Problem n					

Further research methodology (3)

Process Industry Sector	Cases		
Industrial Biotechnology ↕	Company 1 ↔	Company 2 ↔	Company 3
Specialty Chemicals ↕	Company 1 ↔	Company 2 ↔	Company 3
Commodity Chemicals ↕	Company 1 ↔	Company 2 ↔	Company 3
Refining (oil)	Company 1 ↔	Company 2 ↔	Company 3

Proposed research outcomes (1)

- **To provide process maps and tools for streamlining the successful scale up of new industrial biotechnology processes**
  - **Necessary knowledge and skills**
  - **Optimal timing for applying the knowledge and skills**
  - **Means of obtaining the knowledge and skills**

Proposed research outcomes (2)

- **Technology developers with the knowledge and skills to overcome the challenges of successfully scaling up new processes from the lab to commercial production will have an advantage in achieving competitive operations in shorter timeframes**
- **Increased adoption of industrial biotechnology processes is expected to lead to environmental benefits**

Thank you

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