

# Scale Up of Fermentation Process

## Scale Up of Fermentation Process: Principles

- Scale up of fermentation means increasing the size of a fermentation process from laboratory level to pilot scale and finally to industrial production scale while maintaining the same performance and product quality.

### Definition of Scale Up

- Scale up is the process of transferring fermentation from small-scale operation to large-scale production.
- It involves increasing the size of equipment and volume of production.
- The aim is to obtain the same results at industrial level as in laboratory scale.

### Need for Scale Up

- Laboratory fermentation produces only small quantities.
- Industrial production requires large amounts of product.
- Scale up helps convert research processes into commercial production.

### Basic Principles of Scale Up

Scale up is based on maintaining important process conditions similar at all scales.



#### 1. Maintaining Similar Environmental Conditions

- Temperature should remain suitable at all scales.
- pH should be maintained in the same range.
- Dissolved oxygen should remain adequate.
- Similar microbial growth conditions should be preserved.

## **2. Maintaining Similar Mixing Conditions**

- Proper mixing should be maintained in large reactors.
- Nutrients should remain uniformly distributed.
- Agitation should provide similar performance as small scale.

## **3. Maintaining Oxygen Transfer**

- Oxygen transfer should remain sufficient in large fermenters.
- Similar oxygen availability should be maintained.
- Mass transfer efficiency should be preserved.

## **4. Maintaining Sterility**

- Sterile conditions must be maintained during scale up.
- Risk of contamination increases in large systems.
- Proper sterilization becomes very important.

## **5. Maintaining Product Yield**

- Product quality and yield should remain similar after scale up.
- Large scale production should reproduce laboratory results.

## **Common Scale Up Criteria**

Scale up may be based on maintaining:

### **1. Constant Power Input**

- Power supplied per unit volume may be kept constant.

### **2. Constant Agitation Speed**

- Similar mixing intensity may be maintained.

### **3. Constant Oxygen Transfer Rate**

- Oxygen transfer capacity may be preserved.

### **4. Constant Tip Speed**

- Impeller tip speed may be maintained.

### **5. Constant Reynolds Number**

- Flow behavior may be kept similar.

## **Stages of Scale Up**

### **1. Laboratory Scale**

- Used for research and process development.

## 2. Pilot Scale

- Intermediate stage for testing scale-up performance.

## 3. Industrial Scale

- Full production level.

## Challenges in Scale Up

- Mixing becomes more difficult in large vessels.
- Heat transfer may change.
- Oxygen transfer may decrease.
- Foam formation may increase.

## Importance of Scale Up Principles

- They help achieve successful industrial production.
- They reduce process failures.
- They improve process efficiency.

## Scale Up of Fermentation Process: Theoretical Considerations

- Theoretical considerations are scientific and engineering factors that must be considered during scale up to maintain process performance.

## Definition of Theoretical Considerations

- These are calculations and principles used to guide scale up.
- They help predict behavior in large fermenters.
- They support proper reactor design.

## Important Theoretical Considerations

### 1. Geometric Similarity

- Fermenters at different scales should have similar shape.
- Height to diameter ratio may be maintained.
- Impeller design may remain proportionally similar.

#### Importance of Geometric Similarity

- It helps maintain similar flow patterns.
- It supports similar mixing behavior.

### 2. Kinematic Similarity

- Fluid motion should remain similar at different scales.

- Circulation patterns should be maintained.

### 3. Dynamic Similarity

- Forces acting in the system should remain similar.
- This includes inertial and viscous forces.

### 4. Oxygen Transfer Considerations

- Oxygen transfer rate is very important during scale up.
- Large reactors often have lower oxygen transfer.
- $k_L a$  is often used in theoretical analysis.

### 5. Heat Transfer Considerations

- Heat removal becomes harder in large reactors.
- Temperature control must be considered.

### 6. Power Consumption

- Agitation power changes with reactor size.
- Power requirement must be estimated.

### 7. Fluid Flow Behavior

- Flow patterns affect mixing and oxygen transfer.
- Reynolds number is often used to study flow behavior.

### 8. Mass Transfer Considerations

- Nutrient and oxygen transport must be maintained.
- Diffusion limitations may increase at larger scale.

## Mathematical Factors Used in Scale Up

- **Important theoretical parameters include:**
  - Reynolds number.
  - Power number.
  - Oxygen transfer coefficient.
  - Power per unit volume.
  - Impeller tip speed.

## Importance of Theoretical Considerations

- They reduce errors during scale up.
- They help predict large-scale performance.
- They improve reactor design.

## Scale Up of Fermentation Process: Techniques Used

- Different techniques are used to perform scale up depending on process requirements and engineering considerations.

### Definition of Scale Up Techniques

- Scale up techniques are methods used to transfer fermentation from small to large scale.
- They help maintain important process conditions.

### Common Scale Up Techniques

#### 1. Scale Up Based on Constant Power per Unit Volume

- Power input per unit volume is kept constant.
- This helps maintain similar mixing intensity.

##### Applications

- Commonly used in aerobic fermentations.
- Useful when mixing is very important.

#### 2. Scale Up Based on Constant Tip Speed

- Impeller tip speed is maintained constant.
- It helps control shear forces.

##### Applications

- Useful for shear-sensitive cells.
- Common in cell culture processes.

#### 3. Scale Up Based on Constant Oxygen Transfer

- Oxygen transfer rate is maintained.
- $k_La$  may be kept similar.

##### Applications

- Used in oxygen-demanding fermentations.

#### 4. Scale Up Based on Constant Agitation Speed

- Same impeller speed may be maintained.
- Helps preserve mixing conditions.

#### 5. Scale Up Based on Constant Reynolds Number

- Similar fluid flow regime is maintained.
- Useful for studying dynamic similarity.

#### 6. Empirical Scale Up



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