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# ENGINEERING DEVELOPMENT OF STEROID PROCESSES

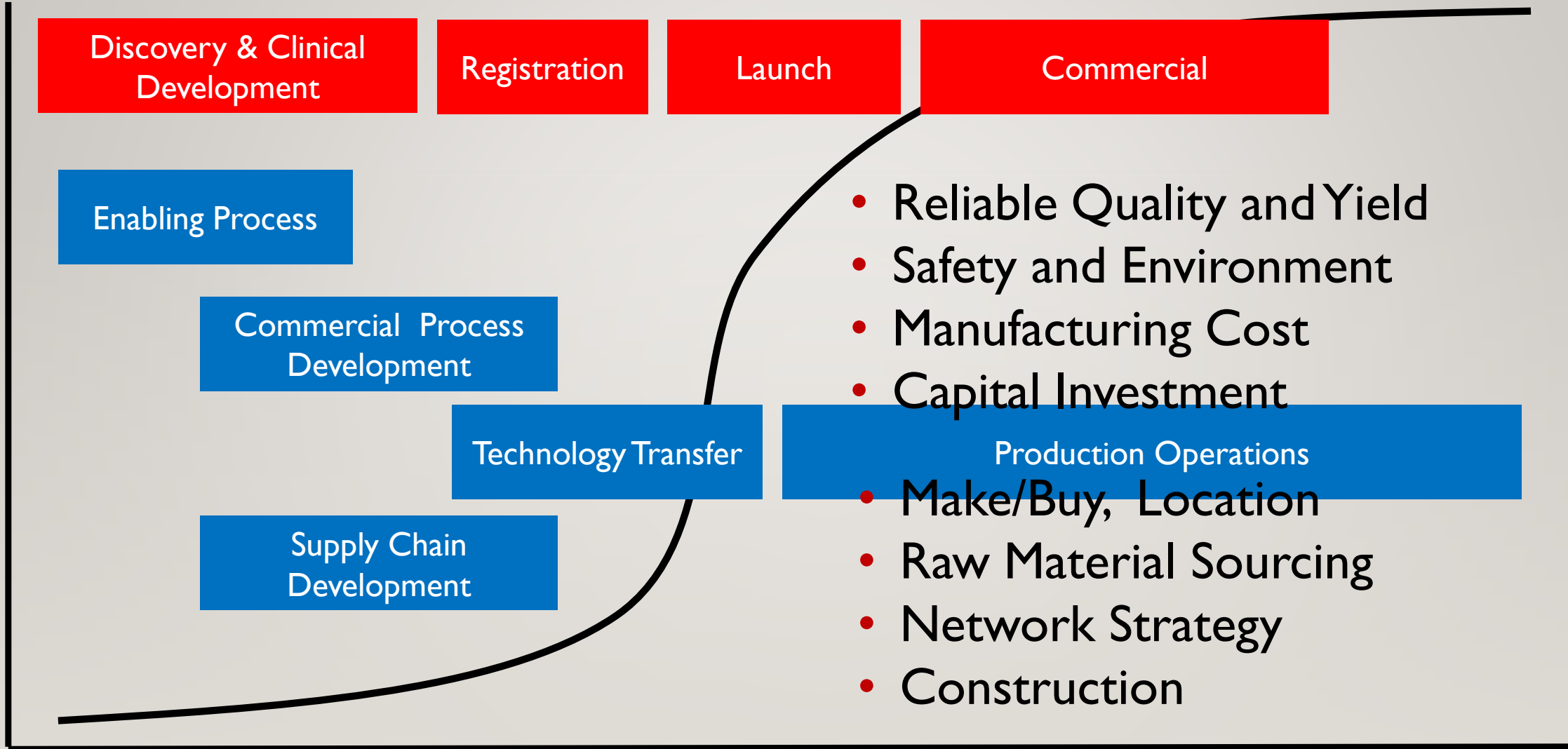
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BILL KOVATS

MAY 17, 2019



# MANUFACTURING DEVELOPMENT OVERVIEW





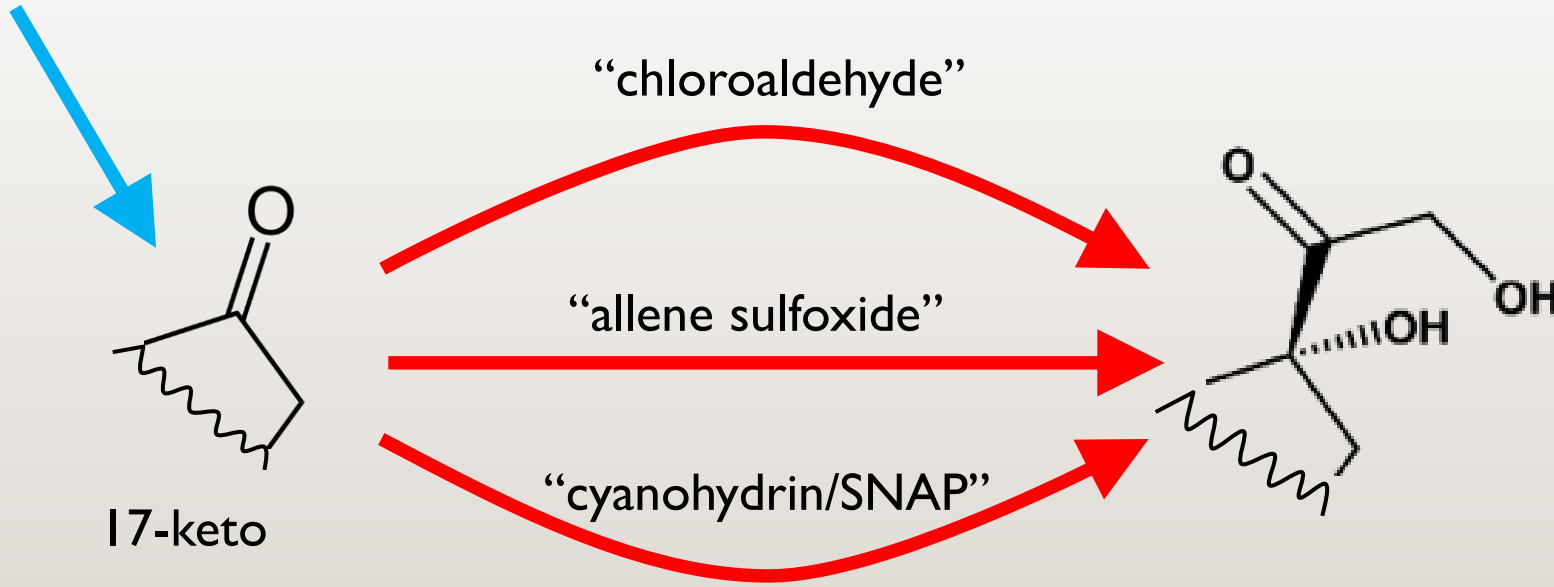
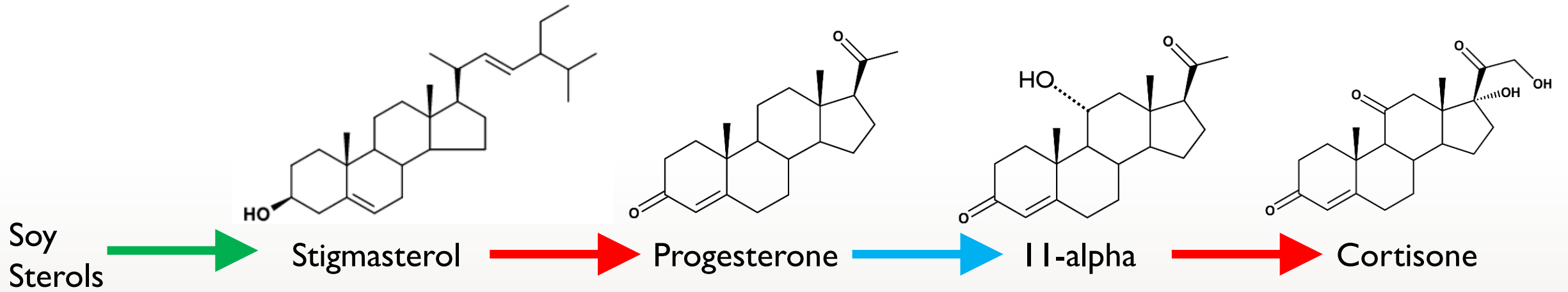
# PROCESS DEVELOPMENT SEQUENCE



Laboratory → Pilot Plant → Production



# STEROID TREE (ABRIDGED)



## Process Key:

- **Chemical**
- **Biological**
- **Physical**



# CHEMICAL REACTION ENGINEERING



Substrate



Reagents



Solvents



Thermodynamics  
Reaction Kinetics  
Heat Transfer  
Fluid Dynamics



# CHEMICAL REACTION ENGINEERING



## Challenges

- Energetic Reactions
- Toxic Materials
- Gas/Liquid Operations
- Cryogenic
- Mixing
- Corrosion

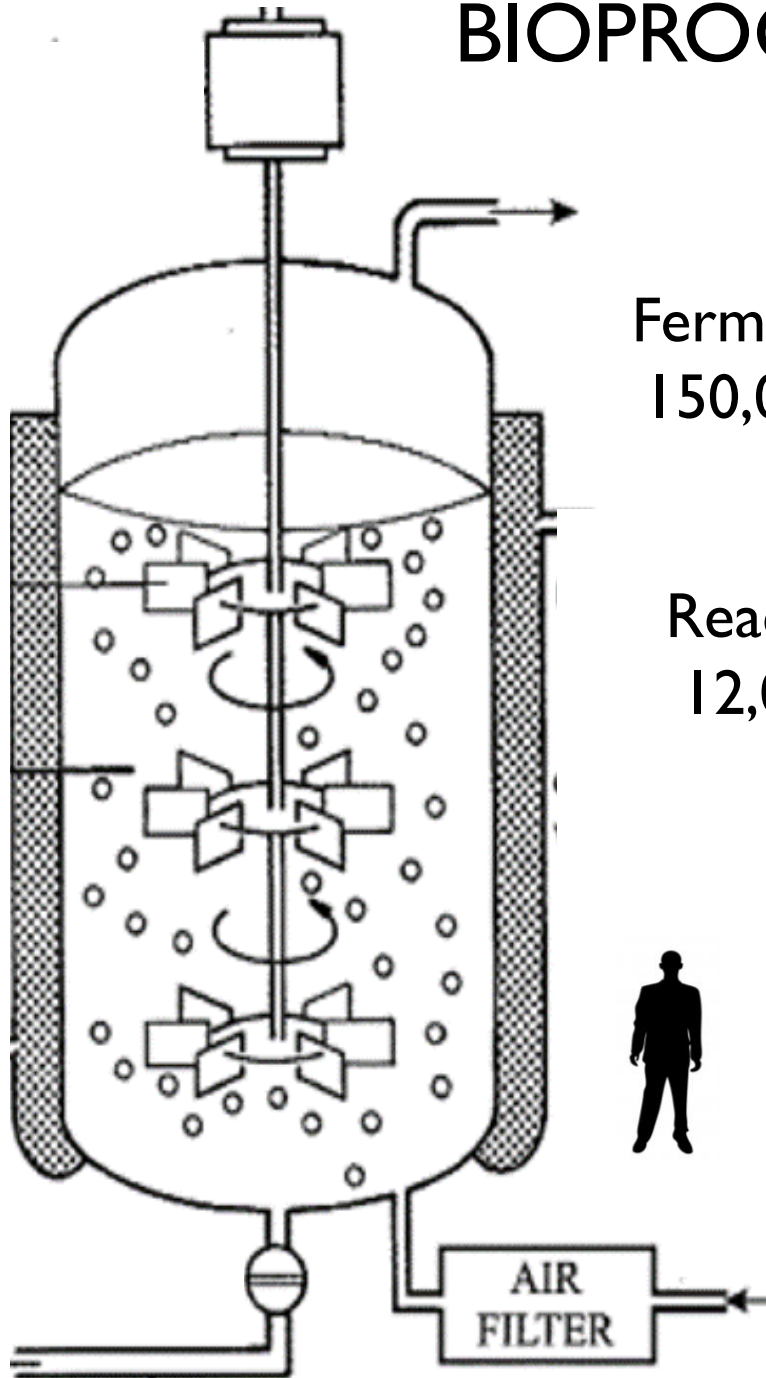
## Examples

- Ozonolysis, Chlorine, Osmium
- Cyanide, Hydrogen, n-Butyl Lithium, Acetylene

## Solutions

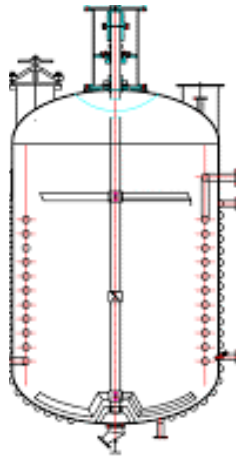
- Multipurpose or Dedicated Workcenters
- Cubicles
- B-335
- Automation
- Flow Reactors

# BIOPROCESS ENGINEERING



Fermentor  
150,000 L

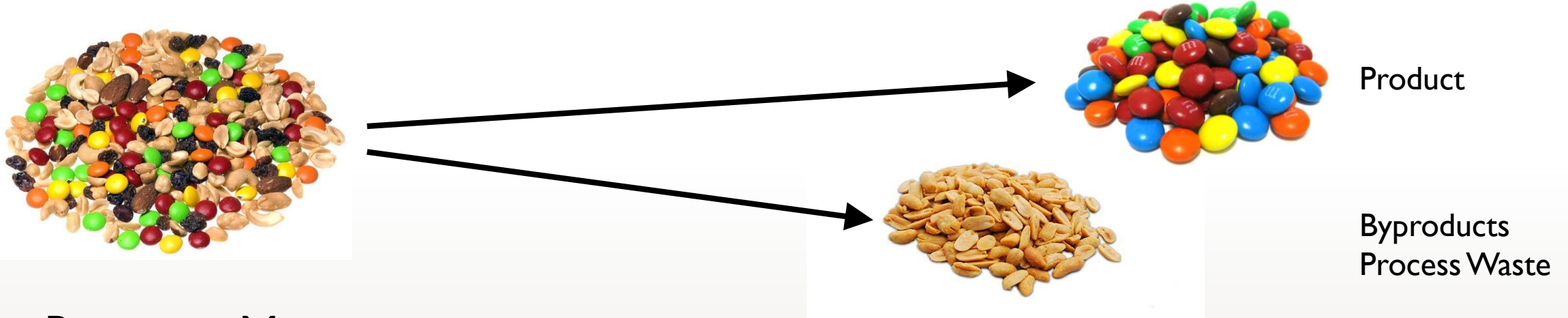
Reactor  
12,000 L



- Enzyme catalyzed modification of substrates
- Enzymes produced by growing microorganisms
- Selection and mutation → Genetic Engineering
  
- Large Scale, Aqueous, Dilute, Long Cycle, Variable
- Oxygen, pH, Temperature, Nutrients, Feed Rate, Sterility, Mixing, Foam
- Much development at pilot plant scale (100 L) vs Lab Scale (1 L)



# PHYSICAL PROCESSES: SEPARATIONS



- Reaction Mixture
- Fermentation Beer
- Soy Sterols
- Mixed Solvent

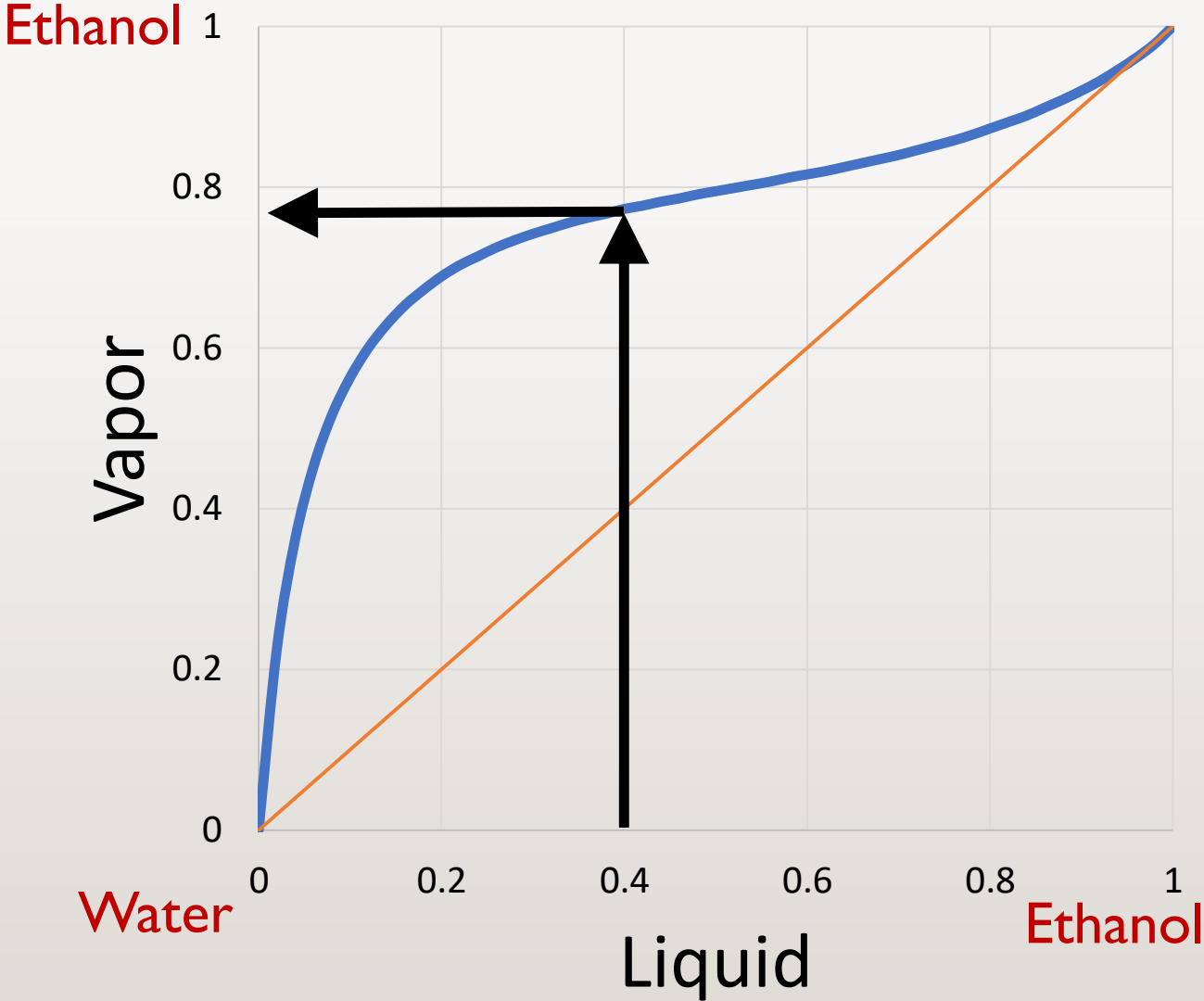
- Liquid Extraction
- Distillation
- Crystallization
- Filtration
- Drying

**20% Combining**  
**80% Separating**

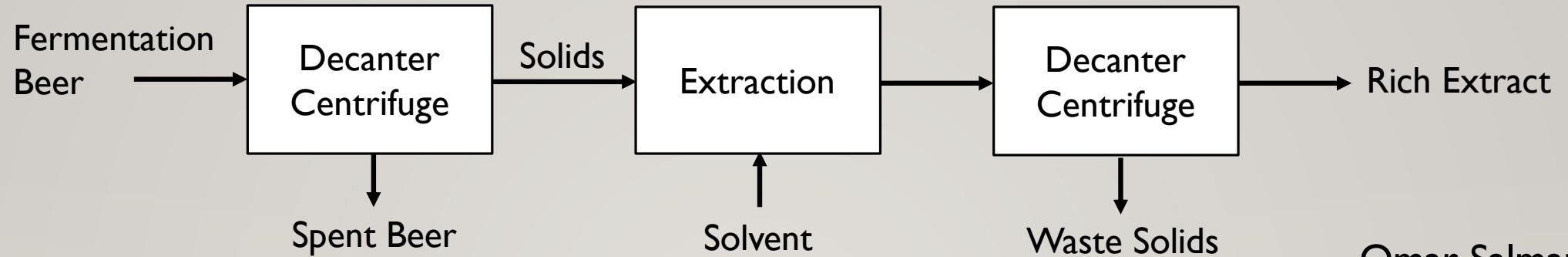


# PHASE EQUILIBRIA: THE KEY TO SEPARATIONS

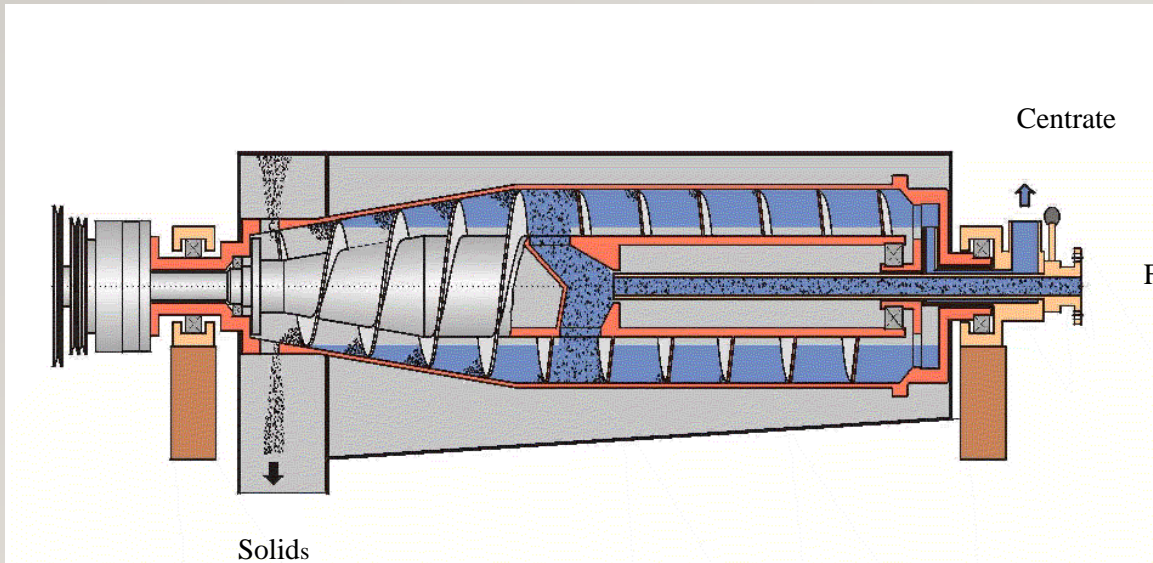
Extraction	Distillation	Crystal- lization
Liquid	Vapor	Liquid
Liquid	Liquid	Solid



# CENTRIFUGATION AND STERIOD EXTRACTION (CASE)

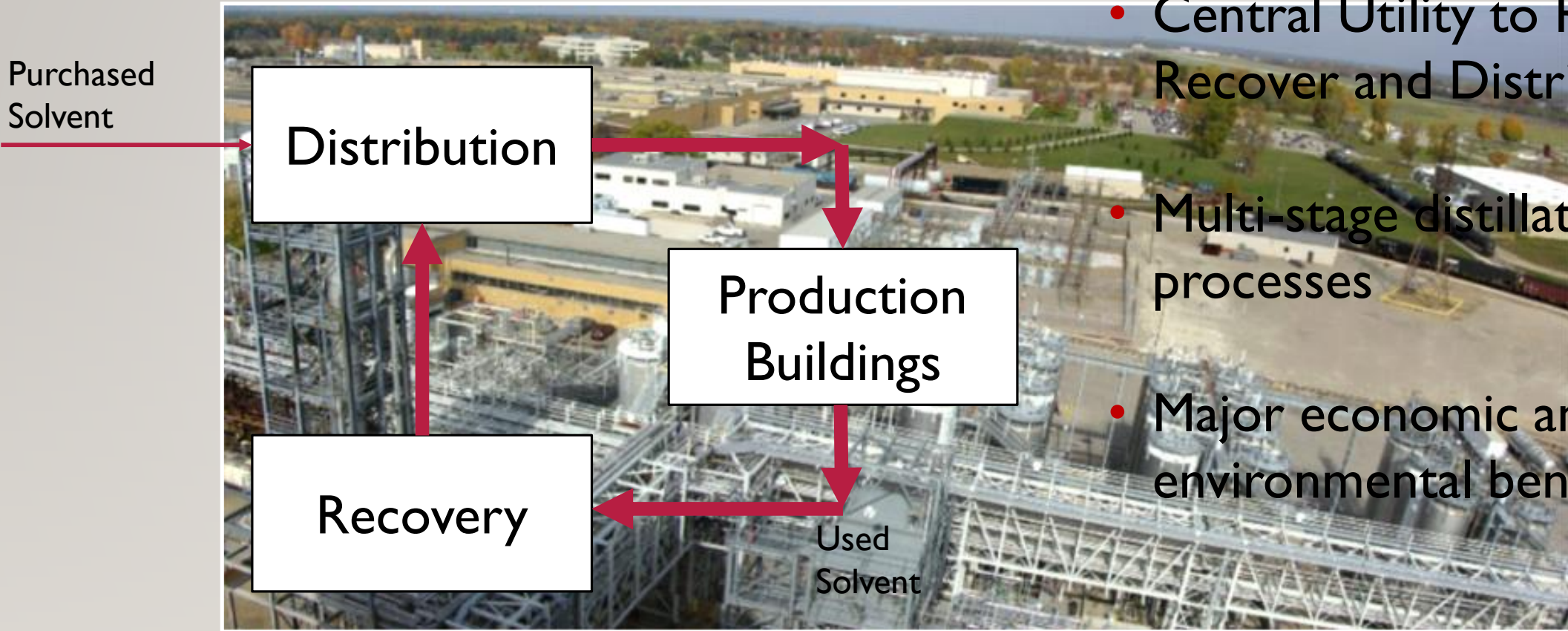


Omar Salman, 1990s



- Cost: Throughput Increase  
Materials Reduction
- Quality: Robust to Variable Beers
- EHS: Reduced Operator Exposure  
Reduced Air Emissions

# SOLVENT RECOVERY AND DISTRIBUTION



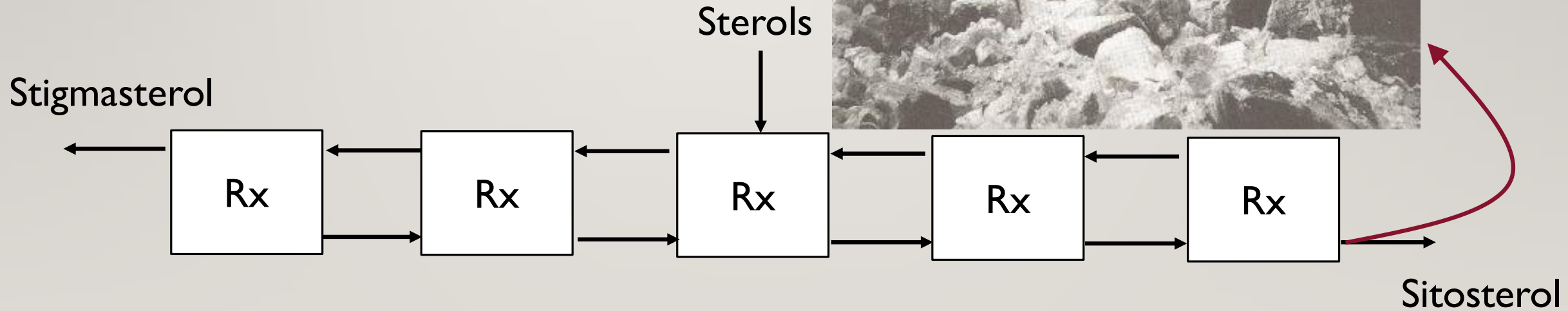
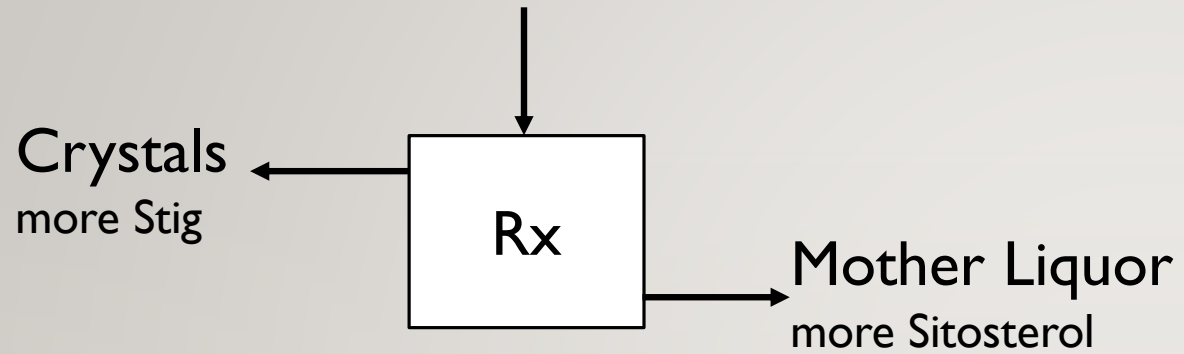
- Central Utility to Receive, Recover and Distribute
- Multi-stage distillation processes
- Major economic and environmental benefits

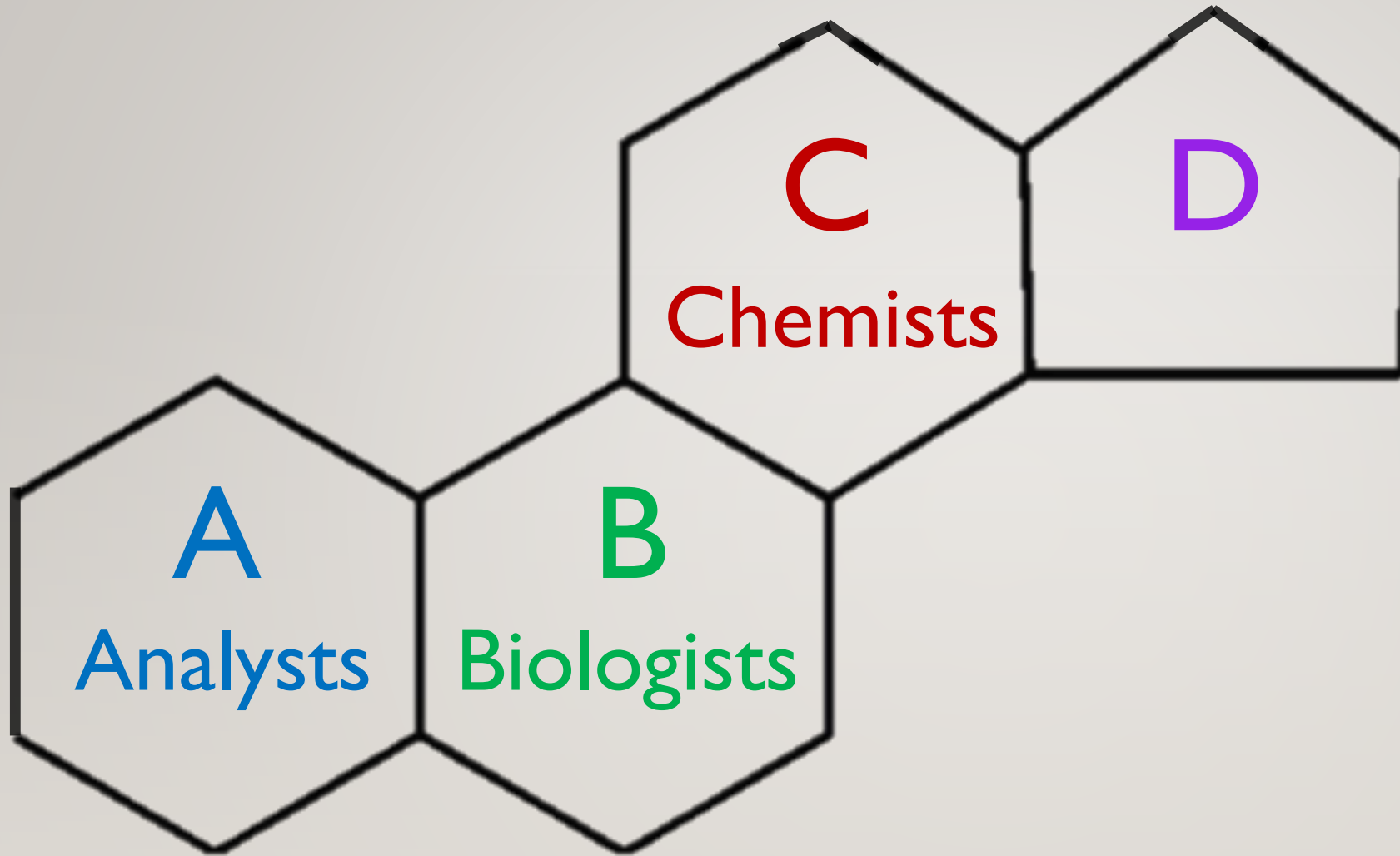




# STEROL SEPARATION (Late 1950s -- mid 1990s)

Sterols: 20/80 Stigmasterol/Sitosterol,





Darn  
Engineers



