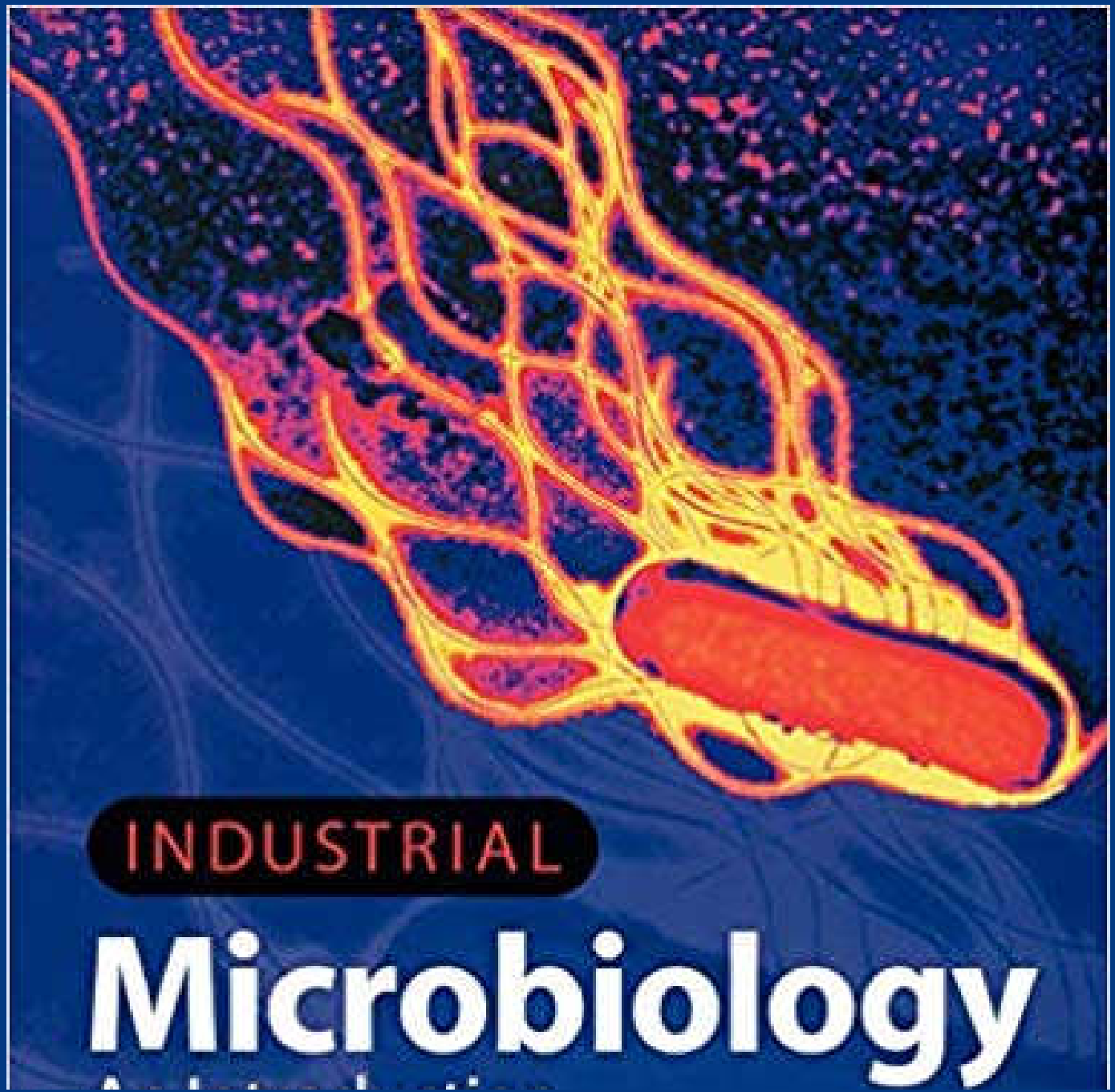
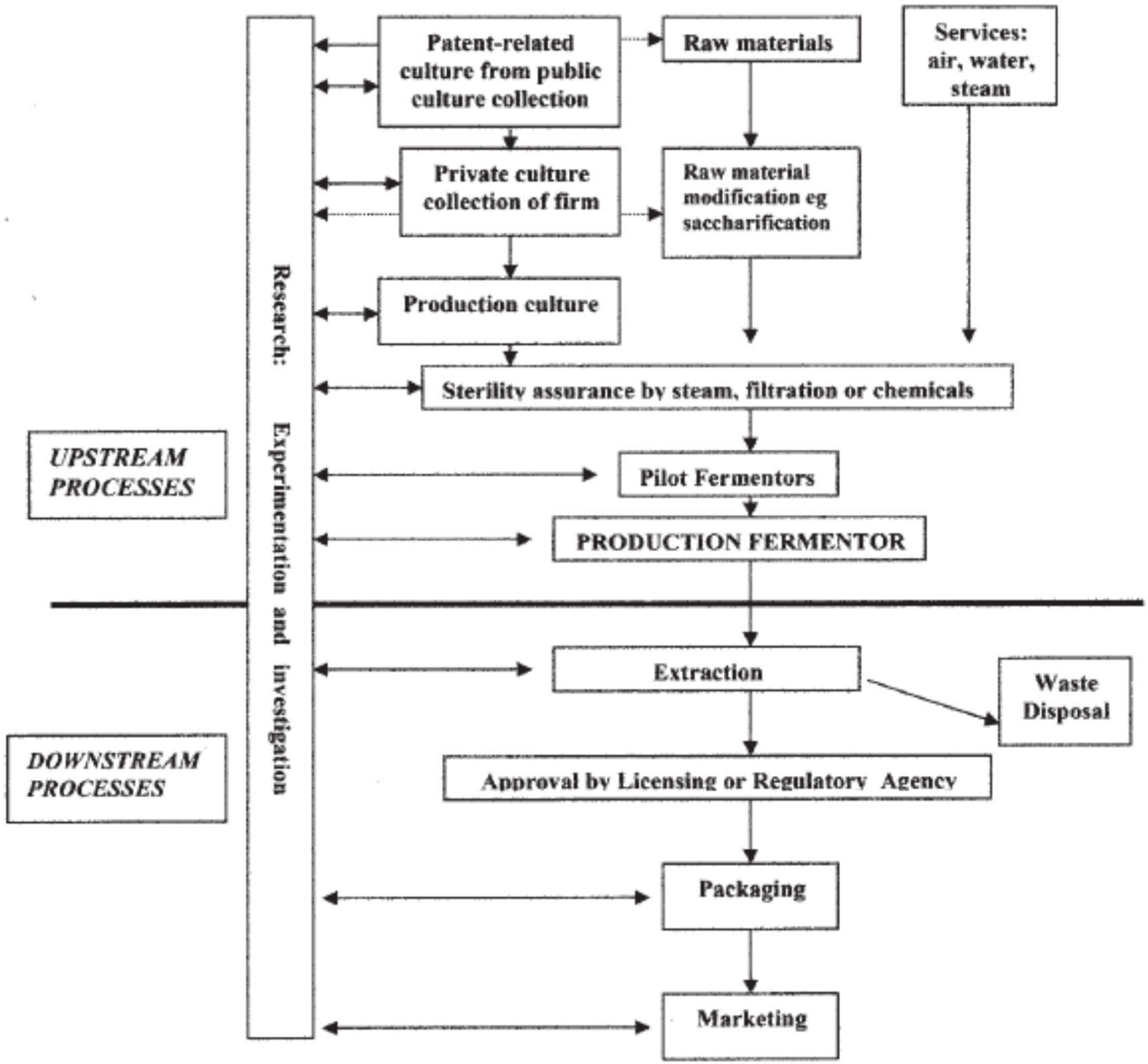
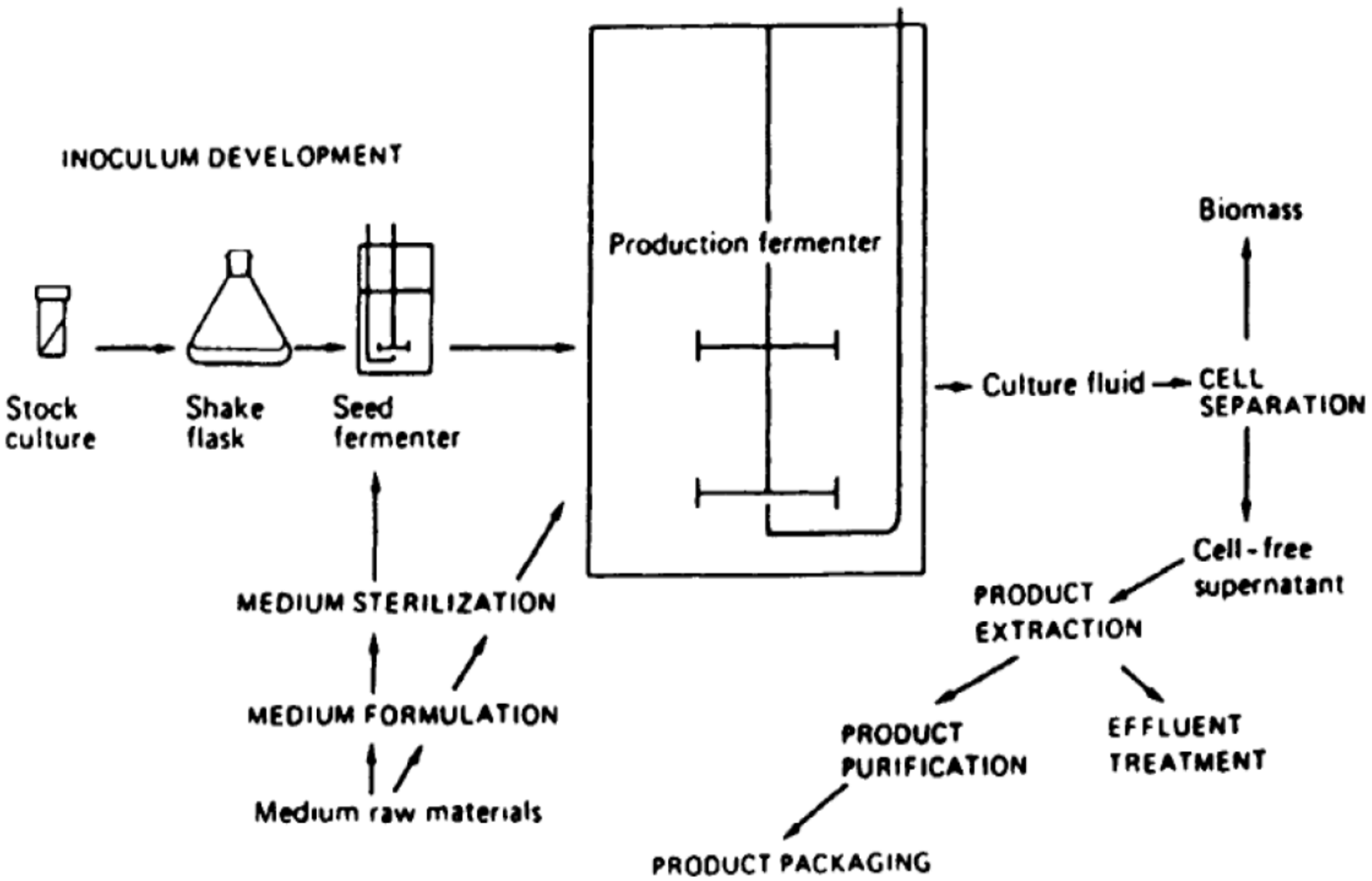
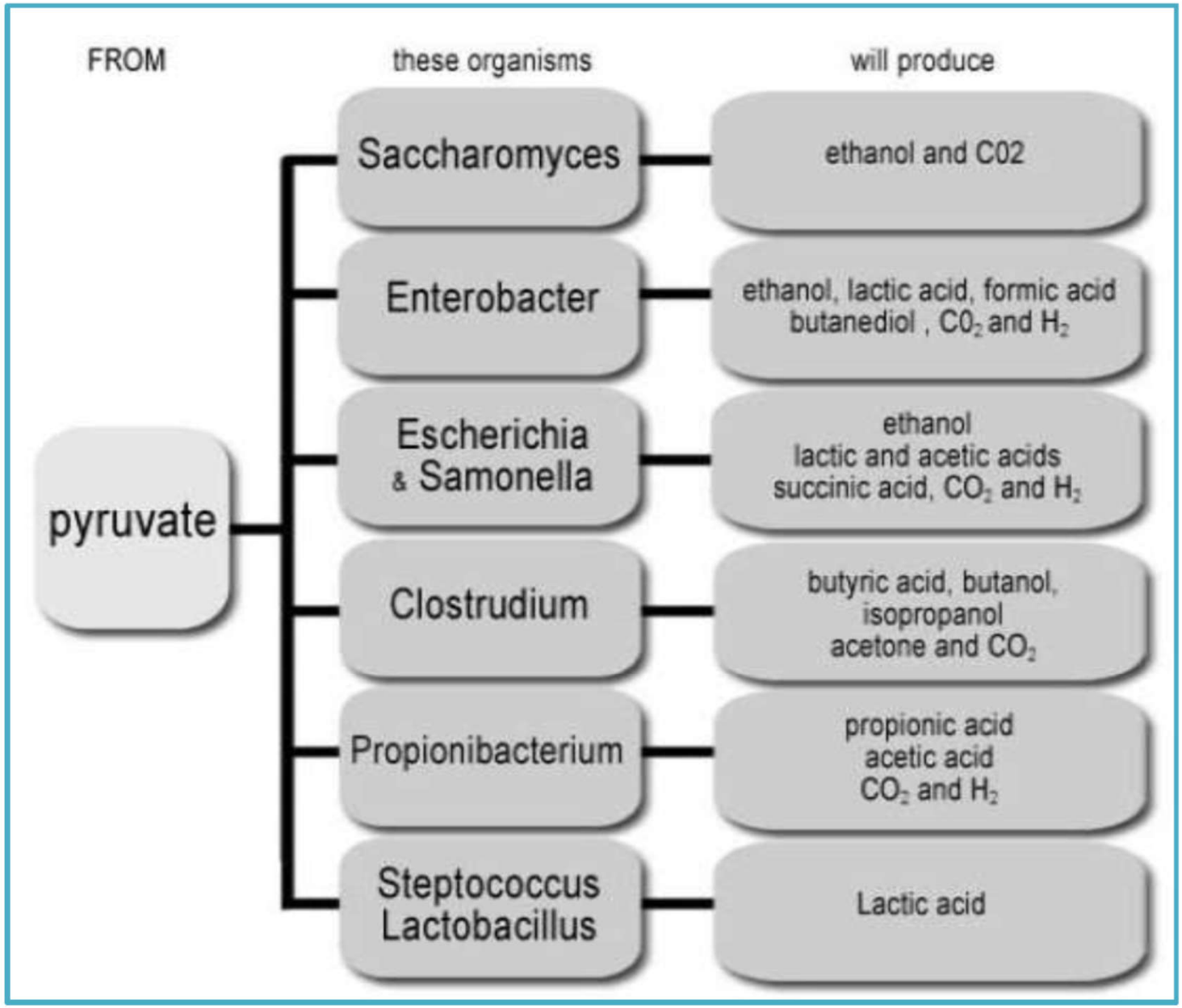

INDUSTRIAL
Microbiology

Table 19.3 A selected list of important microorganisms and their products

Microorganism	*Product*
Algae	
Chlorella sorokiniana	Single-cell protein
Spirulina maxima	Single-cell protein
Bacteria	
Acetobacter aceti	Acetic acid
Acetobacter woodii	Acetic acid
Bacillus subtilis	Bacitracin
B. brevis	Gramicidin
B. thuringiensis	Endotoxin
Clostridium aceticum	Acetic acid
Methylophilus methylotrophus	Glutamic acid
Pseudomonas denitrificans	Vitamin B_{12}
Actinomycetes	
Streptomyces aureofaciens	Tetracycline
S. griseus	Streptomycin
S. tradiae	Neomycin
Nocardia mediterranei	Rifamycin
Micromonospora purpurea	Gentamycin
Fungi	
Aspergillus niger	Citric acid
A. oryzae	Amylase, cellulase, single-cell protein
Candida lipolytica	Lipase
C. utilis	Single–cell protein
Penicillium chrysogenum	Penicillin
Saccharomyces cerevisiae	Ethanol, wine, single-cell protein
S. lipolytica	Citric acid, single-cell protein
Rhizopus nigricans	Steroids
Gibberella fujikuroi	Gibberellin
Trichoderma viride	Cellulase


Patent-related culture from public culture collection
Raw materials
Services: air, water, steam
Private culture collection of firm
Raw material modification eg saccharification
Production culture
Sterility assurance by steam, filtration or chemicals
Research: Experimentation and investigation
UPSTREAM PROCESSES
Pilot Fermentors
PRODUCTION FERMENTOR
Extraction
Waste Disposal
DOWNSTREAM PROCESSES
Approval by Licensing or Regulatory Agency
Packaging
Marketing


INOCULUM DEVELOPMENT
Stock culture
Shake flask
Seed fermenter
Production fermenter
Biomass
Culture fluid
CELL SEPARATION
Cell-free supernatant
MEDIUM STERILIZATION
PRODUCT EXTRACTION
MEDIUM FORMULATION
PRODUCT PURIFICATION
EFFLUENT TREATMENT
Medium raw materials
PRODUCT PACKAGING


FROM
these organisms
will produce
pyruvate
Saccharomyces
ethanol and C02
Enterobacter
ethanol, lactic acid, formic acid
butanediol , $C0_2$ and H_2
Escherichia
& Samonella
ethanol
lactic and acetic acids
succinic acid, CO_2 and H_2
Clostrudium
butyric acid, butanol,
isopropanol
acetone and CO_2
Propionibacterium
propionic acid
acetic acid
CO_2 and H_2
Steptococcus
Lactobacillus
Lactic acid

Requirements for industrially useful microorganisms

- To be used in industrial microbiology microorganism must be
  - Grow in simple media: preferably not require growth factors
  - Grow vigorously and rapidly
  - Produce the desired product in short time possible
  - Its end products should not include toxic and other undesirable materials
  - The organism should have a reasonable genetic, and hence physiological stability.
  - The organism should lend itself to a suitable method of product harvest at the end of the fermentation.
  - Wherever possible, organisms which have physiological requirements which protect them against competition from contaminants should be used.
  - The organism should be reasonably resistant to predators
  - the organism should not be too highly demanding of oxygen
  - organism should be easily amenable to genetic manipulation to enable the establishment of strains with more acceptable properties.

Fermentation

- The basic principle involved in the industrial fermentation technology is that organisms are grown under suitable conditions, by providing raw materials meeting all the necessary requirements such as carbon, nitrogen, salts, trace elements and vitamins.

- The end products formed as a result of their metabolism during their life span are released into the media, which are extracted for use by human being and that have a high commercial value.

What is fermentation techniques (1)?

Techniques for large-scale production of microbial products. It must both provide an optimum environment for the microbial synthesis of the desired product and be economically feasible on a large scale. They can be divided into surface (emersion) and submersion techniques. The latter may be run in batch, fed batch, continuous reactors

In the surface techniques, the microorganisms are cultivated on the surface of a liquid or solid substrate. These techniques are very complicated and rarely used in industry

In the submersion processes, the microorganisms grow in a liquid medium. Except in traditional beer and wine fermentation, the medium is held in fermenters and stirred to obtain a homogeneous distribution of cells and medium. Most processes are aerobic, and for these the medium must be vigorously aerated. All important industrial processes (production of biomass and protein, antibiotics, enzymes and sewage treatment) are carried out by submersion processes.

Fermentation

- **Definition**
  - *i. by biochemist*
    - i. anaerobic process that generate energy by the breakdown of organic compounds.
    - ii. Any process that generate bacterial metabolites as end products: lactic acid, enzymes, ethanol, butanol, and acetone.
  - ii. *by indusrial users*
    - i. Any aerobic process that produces microorganisms (biomass)as the end product.
    - ii. Biotransformation--transformation of a compound by microbial cells

- Industrial biotechnology, application of modern biotechnology for industrial production, is always referring to Fermentation technology.
  - Less waste generation
  - Reduced energy consumption

- Fermentation biotechnology involves partnership between
  - **Molecular biologists** ; responsible for isolating, characterising, modifying and creating effectively expression of industry desirable genes
  - **Biochemical engineers** ; to ensure that the GE of microorganisms can be grown in large quantities under the conditions that give optimal product yeild.

FERMENTER(bioreactor)

- Closed container with adequate arrangement for aeration, agitation, temperature and pH control, and drain or overflow vent to remove the waste biomass of cultured microorganisms along-with their products.
- Is a device in which a substrate of low value is utilized by living cells or enzymes to generate a product of higher value.
- Extensively used for food processing, fermentation, waste treatment, etc.

BIOREACTOR

❑A bioreactor should provide for the following:

- Agitation (for mixing of cells and medium),
- Aeration (aerobic fermenters); for O2 supply,
- Regulation of factors like temperature, pH, pressure, aeration, nutrient feeding, liquid level etc.,
- Sterilization and maintenance of sterility, and
- Withdrawal of cells/medium (for continuous fermenters).

✓Modern fermenters are usually integrated with computers for efficient process monitoring, data acquisition, etc.

Bioreactor

How a bioreactor differs from a chemical reactor ?

Both are agitated tanks

Bioreactor should be capable of being operated aseptically for number of days

Adequate aeration and agitation should be provided to meet the metabolic requirements which will vary from time to time

What is a Fermenter?

- Vessel or tank in which whole cells or cell-free enzymes transform raw materials into biochemical products and/or less undesirable by-products
- Also termed a Bioreactor

- The basic function of a fermenter is to provide a suitable environment in which an organism can efficiently produce a target product

BIOREACTOR

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- Withdrawal of cells/medium (for continuous fermenters).

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SIZE OF FERMENTERS(BIOREACTOR):

- The size of fermenters ranges from 1-2-liter laboratory fermenters to 5,00,000 liters or, occasionally, even more, fermenters of up to 1.2 million liters have been used.
- The size of the fermenter used depends on the process and how it is operated.

Bioreactor	Fermenter
• A bioreactor can be defined as an apparatus, such as a large fermentation chamber, for growing organisms such as bacteria or yeast that are used in the biotechnological manufacture of substances such as pharmaceuticals, antibodies, or vaccines, or for the bioconversion of organic waste.	• However a fermenter can be defined as an apparatus that maintains optimal conditions for the growth of microorganisms, used in large-scale fermentation and in the commercial production of antibiotics and hormones

BIOREACTOR VERSUS FERMENTOR

BIOREACTOR	FERMENTOR
An apparatus in which a biological reaction or process is carried out, especially on an industrial scale	A container in which fermentation takes place
Allows any type of biochemical reactions to occur	Only facilitate fermentation
A vessel that facilitates a biochemical reaction	A type of bioreactor
Various types of substrates can be used based on the desired reaction	Glucose or glucose-containing compounds are used
May use microorganisms or biochemically active substances such as enzymes or catalysts	Always uses microorganisms to carry out the reaction
Can use mammalian or insect cell populations	Use fungal or bacterial cell populations
Microorganisms are introduced	Microorganisms in the air are used
May use either aerobic or anaerobic conditions	Use anaerobic conditions
Volume can be up to several liters	Volume can be up to 2L
A preferable agitation RPM has to be maintained due to the presence of cells without cell walls	A considerable agitation RPM can be used since both bacteria and fungi have cell walls
Doubling time is long (14, 17 or 24 hours)	Doubling time is 20 mins
Can either be used to produce a cell mass or a particular metabolite	Used to produce a metabolite
Can produce secondary metabolites	Can only produce primary metabolites
Used in the production of medicines, pharmaceutical liquids, antibodies or vaccines	Used to produce lactic acid or ethanol
Tend to be infected by viruses	Generally not infected by viruses
Can be packed bed, fluidized bed, IVFR or Air lift bioreactor	Can be batch, fed batch or continuous

DESIGN OF FERMENTER

- A fermentation process requires a fermenter for successful production .
- Fermentor is the large vessel containing considerable quantities of nutrient media by maintaining favourable conditions.
- The design and nature of the fermentor varies depending upon the type of fermentation carried out. Invariably all the fermentors provide the following facilities for the process such as

  - contamination free environment,
  - specific temperature maintenance,
  - maintenance of agitation and aeration, pH control,
  - monitoring Dissolved Oxygen (DO),
  - ports for nutrient and reagent feeding (antifoam agents, alkali or acid),
  - ports for inoculation and sampling,
  - provide all aseptic conditions at the time of sample withdrawal and addition of innoculum
  - complete removal of broth from the tank and should be easy to clean
  - It should be designed in such away that it consumes less power, have less evaporation, can be used for long periods of operation

Fermenter: General Functions

What it should be capable of:

- Biomass concentration must remain high
- Maintain sterile conditions
- Efficient power consumption
- Effective agitation
- Heat removal
- Sampling facilities