An Introduction to Cellular Agriculture – a new way to sustainable and ethical foods

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What is Cellular Agriculture? (1)

Cellular Agriculture = production of animal-sourced products <u>using cells rather than whole animals</u>

Examples of products: meat, egg whites, milk, vanilla, silk, leather etc

What is Cellular Agriculture? (2)

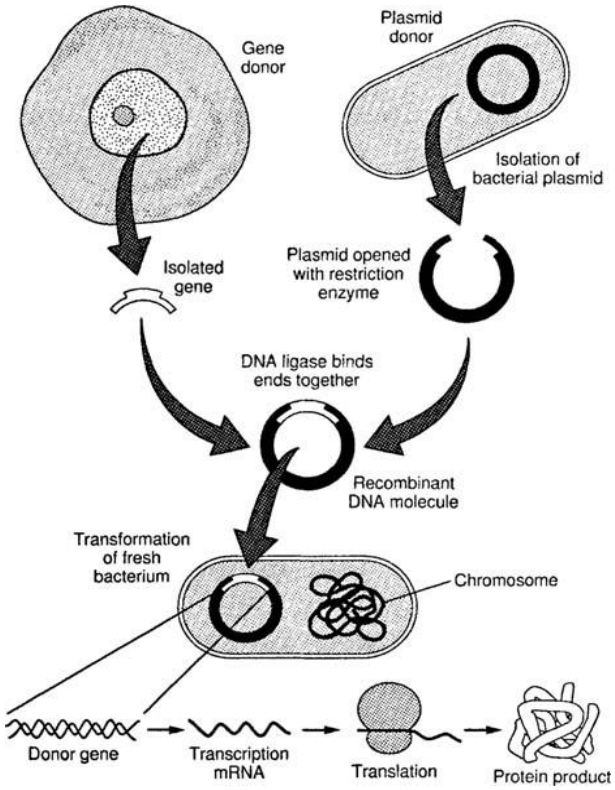
Sir Winston Churchill (1931)

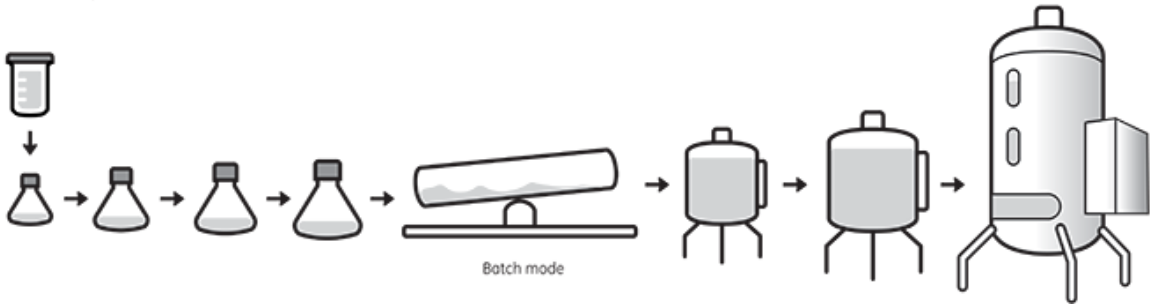
“We shall escape the absurdity of growing a whole chicken in order to eat the breast or wing, by growing these parts separately under a suitable medium”

Type of product: ACELLULAR

=> Are made of organic molecules like proteins or fats and don't contain live or whole cells

=> Are made using fermentation with recombinantly engineered host cells (bacteria, yeast, fungus, algae)

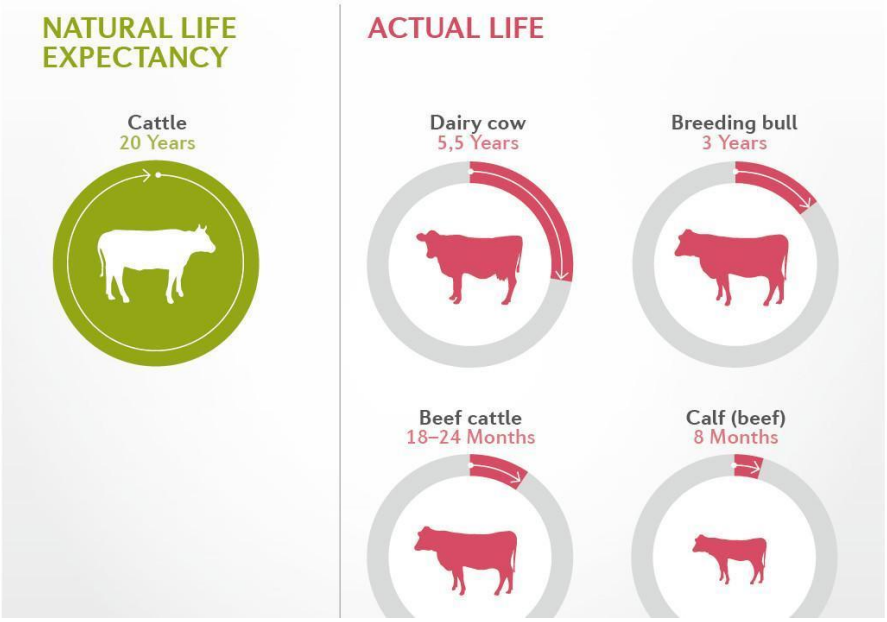




Example of acellular products: *Milk*

Traditional Animal Agriculture

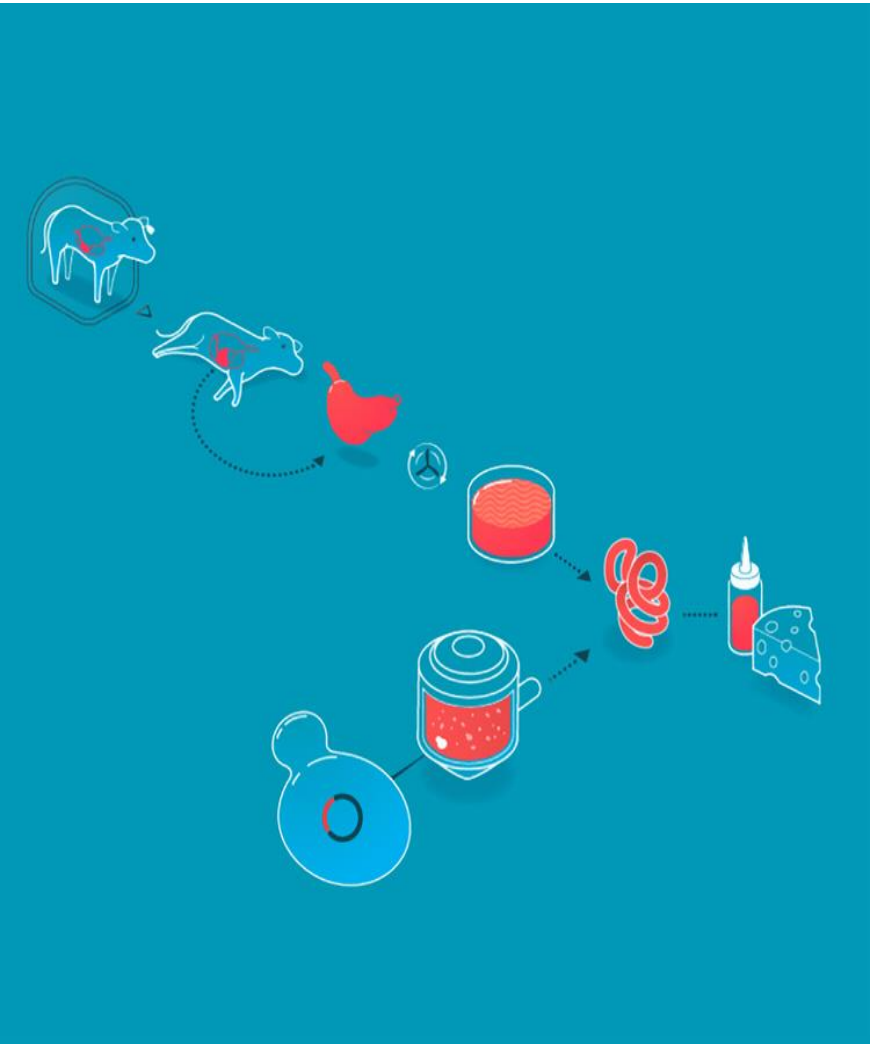
- Mother cows kept in a continuous lactating state



Cellular Agriculture

- **Casein** (a milk protein)
- Formulation with other milk components like **fats**, **vitamins**

Example of acellular products: *Rennet*



- **Rennet** is a mixture of enzymes that turns milk into curds and whey when making **cheese**.

- **Traditionally, RENNET was extracted from the inner lining of the 4th stomach of calves => calf slaughter**

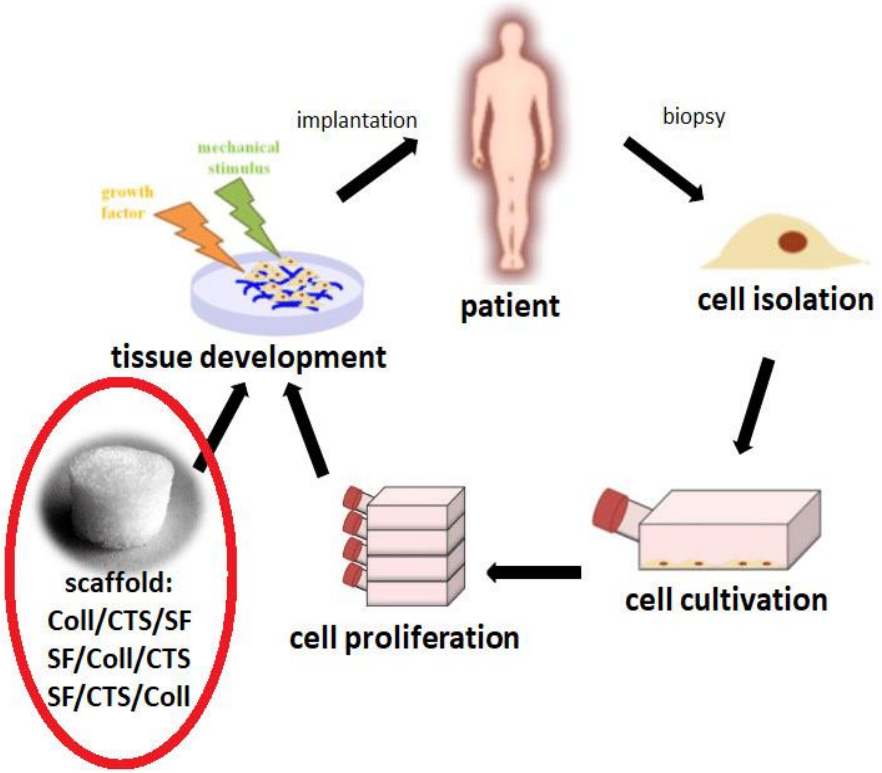
- Today, the majority of cheesemaking uses rennet enzymes produced by fermentation and recombinant technology.
- In 1990, the FDA approved the first engineered bacteria for production of rennet
- Rennet harvested from cell cultures is **purer, more consistent, and cheaper** than animal-derived rennet.

Type of product: CELLULAR (1)

⇒ Are made of actual whole and live cells

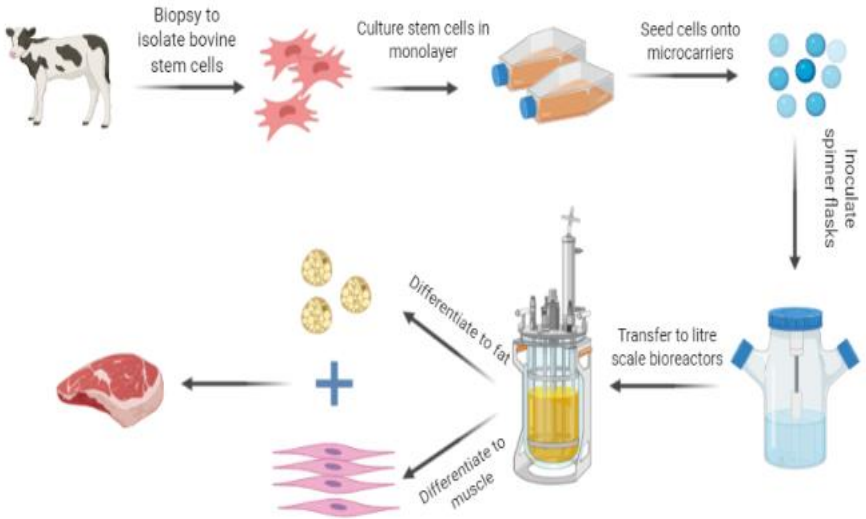
⇒ Are produced using Tissue Engineering Techniques

Type of product: CELLULAR (2)



TISSUE ENGINEERING

THERAPIES vs FOOD



Cultured Meat

Cultivated meat (*i.e.* cell-based meat, cultured meat, clean meat, lab-grown meat, synthetic meat)

- It is **genuine animal meat.**
- **It doesn't require animal slaughter.**
- It is produced in a **controlled environment** (*e.g*. bioreactor).
- Same **composition** as animal-based meat.
- Same **cell types**: muscle, fat, connective cells.
- Same **taste and nutritional profile** of animal meat.
- It can be **tailored for improved nutrition** (*e.g*. omega-3-oils, good fats).

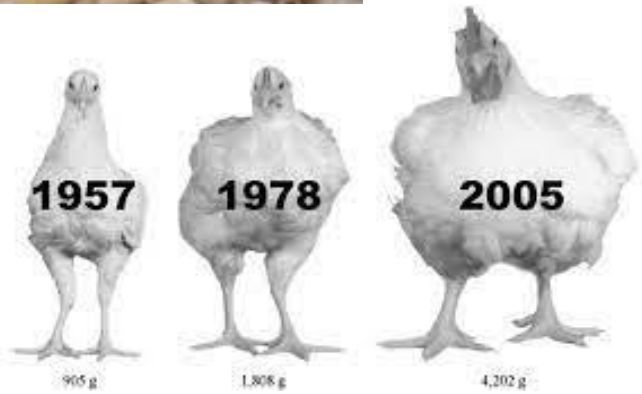
Why is this concept needed? (1)

Traditional animal agriculture

Why is this concept needed? (2)

Intensive animal agriculture

- Ethical concerns about animal welfare
- Animal overcrowding
- Use of antibiotics => superbugs
- Deforestation
- Loss of biodiversity
- **Not sustainable**
- **Unable to feed the growing population**



What if we could produce foods that…

- Don’t harm the animals
- Don’t damage the environment (doesn’t require deforestation; doesn’t cause loss of biodiversity)
- Don’t require antibiotics
- Need less natural resources (land, water)
- Produce less green house gas emissions
- Are more sustainable

World's first proof-of-concepts

2013 Prof Mark Post
World's First Cell-based Burger Patty

2016 Memphis Meats
World's First Cell-based Meatball

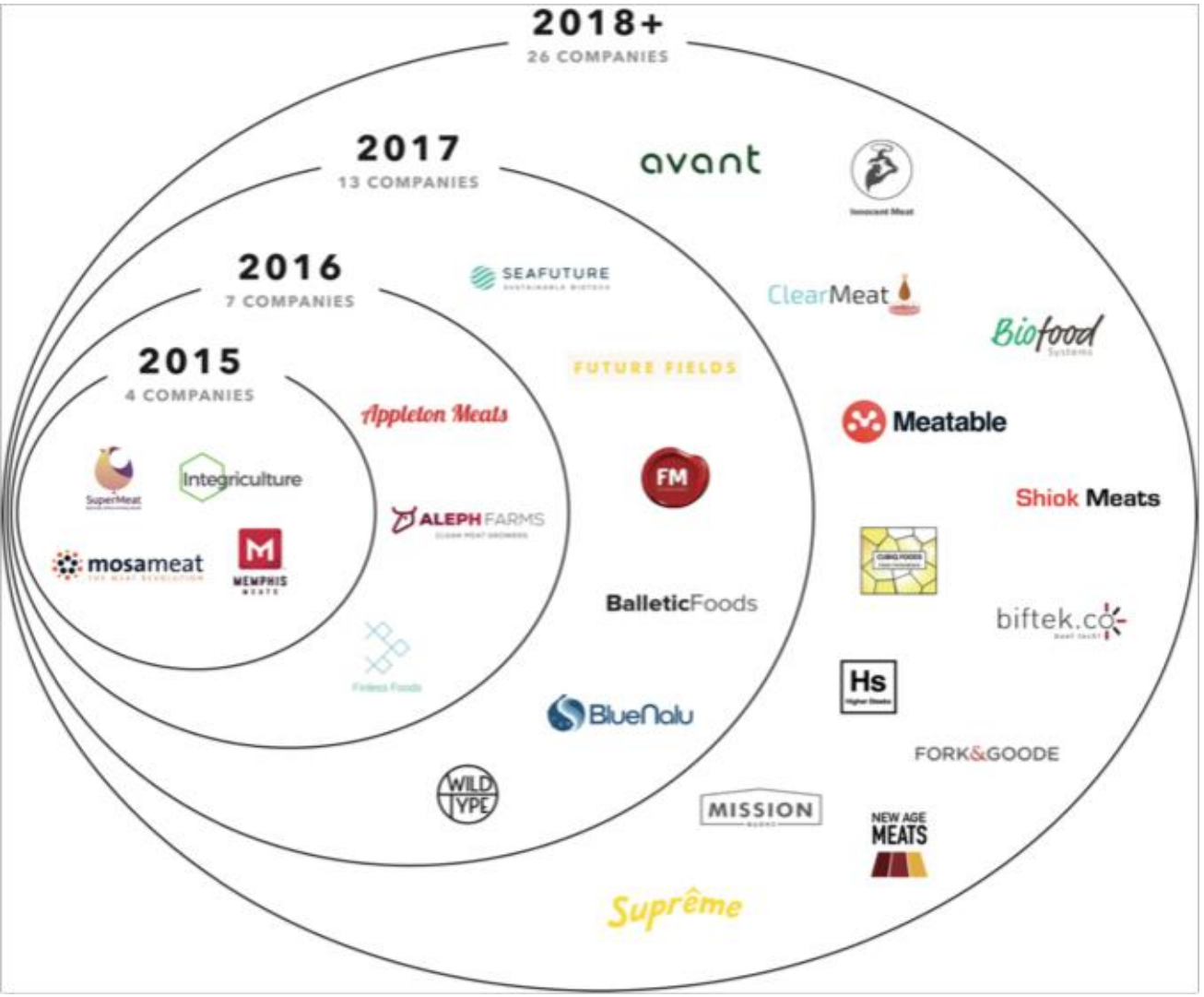
2017
Finless Foods
World's First Cell-based Fish

2019
Shiok Meats
World's First Cell-based Shrimp Dumpling

2020
Higher Steaks
World's First Cell-based Bacon

1st approved Cultivated meat product in Singapore

Industry landscape



2022: over 80 start-ups worldwide

multus media

Better Dairy

HOXTON FARMS

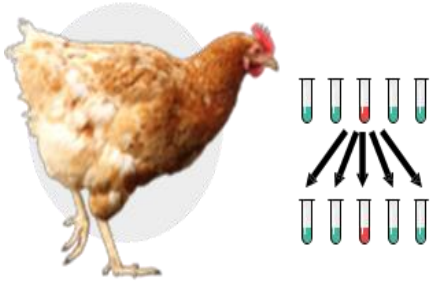
Hs Higher Steaks

ivy farm technologies

Cultured Meat: production flow

SAMPLE

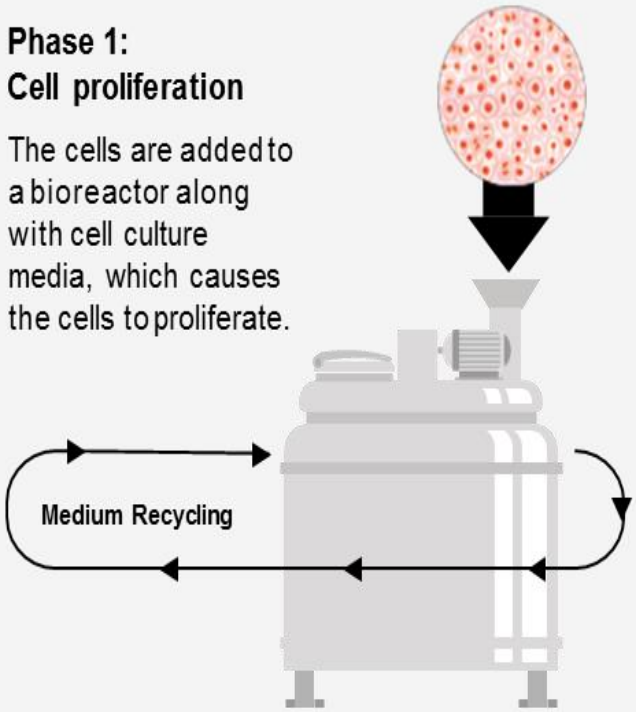
A small sample of cells is obtained from an animal.



CELL STARTER CULTURE

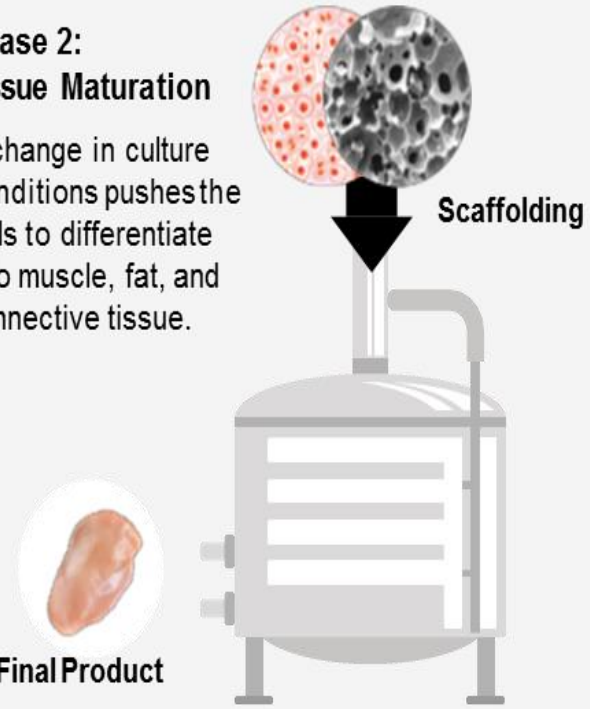
Phase 1:
Cell proliferation

The cells are added to a bioreactor along with cell culture media, which causes the cells to proliferate.



Phase 2:
Tissue Maturation

A change in culture conditions pushes the cells to differentiate into muscle, fat, and connective tissue.



CELLS AT MATURATION

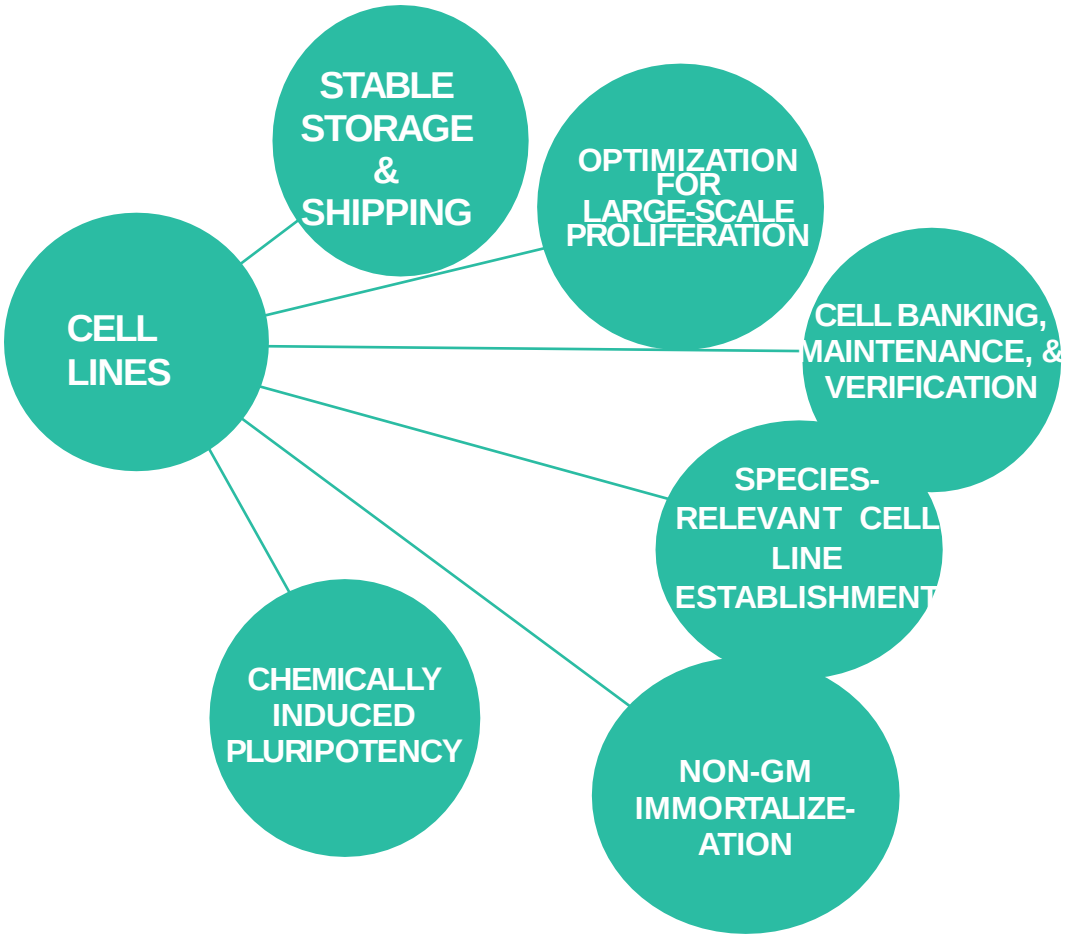
Primarily muscle, fat, and connective tissue.

Fat Cell

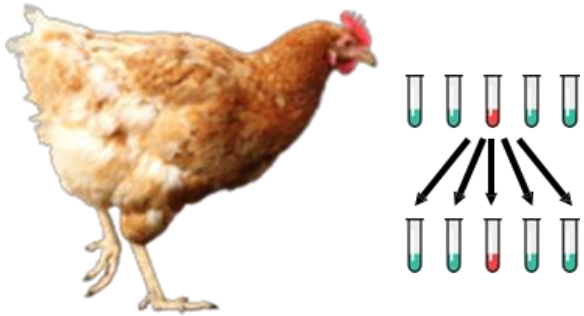
Muscle Cell

Fibroblast Cell

Cell line development



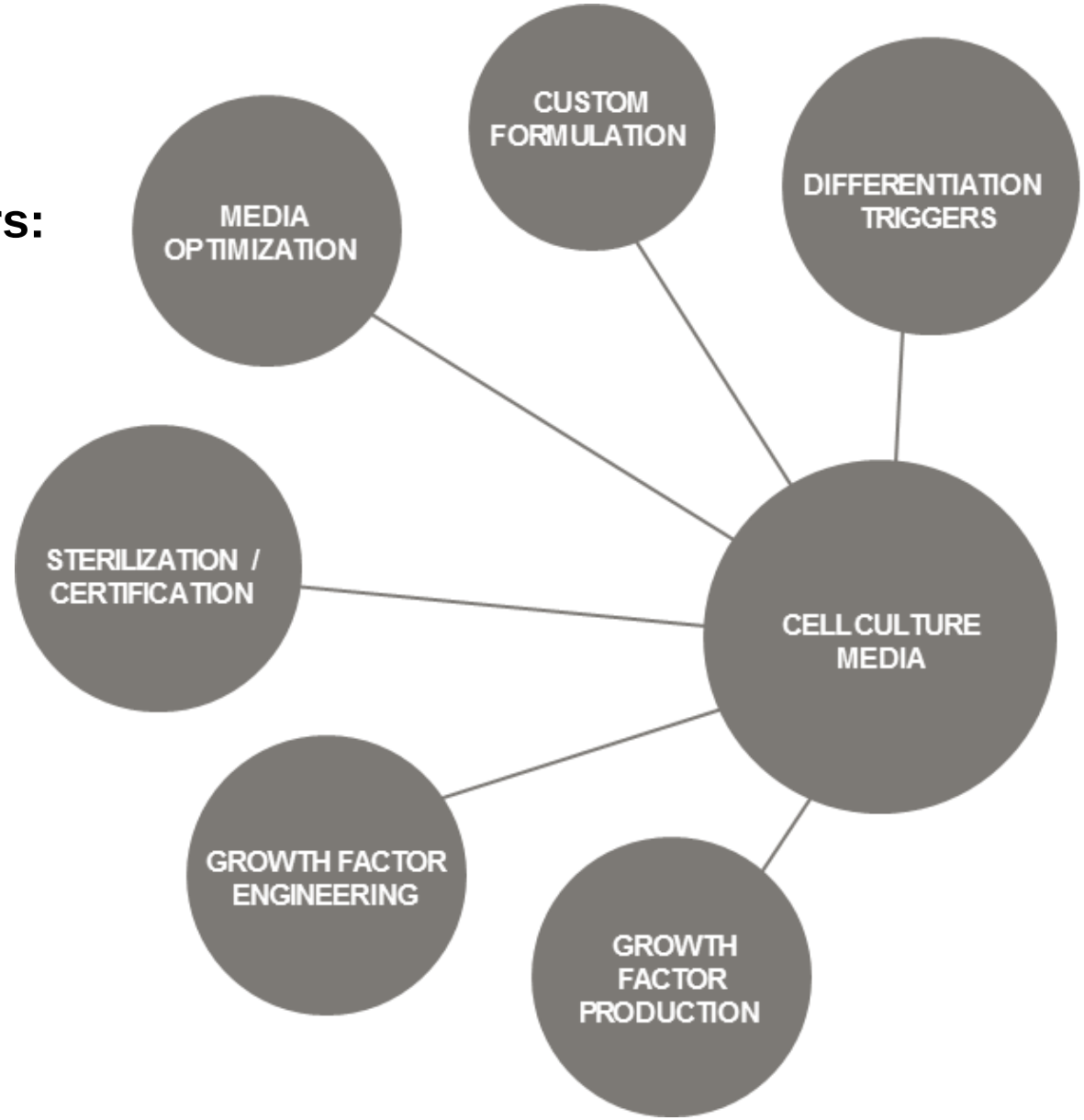
- Isolated cells may be pluripotent (iPSC, ESC), multipotent, or specialized adult stem cells.
- Require detailed characterization (genomic, transcriptional, phenotypic) of starting cells.
- Multi-generation stability is a necessity.



Cell culture media

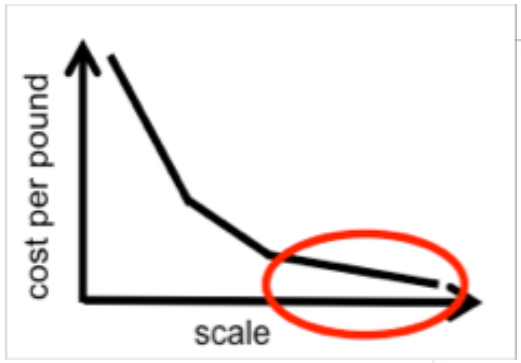
Key drivers and parameters:

- ❑ Cost vs. performance
- ❑ Differentiation efficiency
- ❑ Serum-free and animal-origin-free
- ❑ Concentrated feeds
- ❑ Component stability
- ❑ Oxygen carrying capacity and viscosity suitable for perfusion through thick tissues



Cost

$400/L



<<$1/L

COST – a major challenge

Culture media composition

Most cell culture media components can be sourced as common food ingredients

INORGANIC SALTS

Calcium chloride, sodium chloride, magnesium sulfate, ferric nitrate, magnesium chloride, cupric sulfate, ferrous sulfate, potassium chloride, sodium hydrogen phosphate

AMINO ACIDS

Alanine, glycine, leucine, aspartic acid, proline, valine, threonine, etc.

VITAMINS

Biotin, riboflavin, folic acid, citric acid, thiamine, pyroxidine, vitamin B12, pyroxidal, etc.

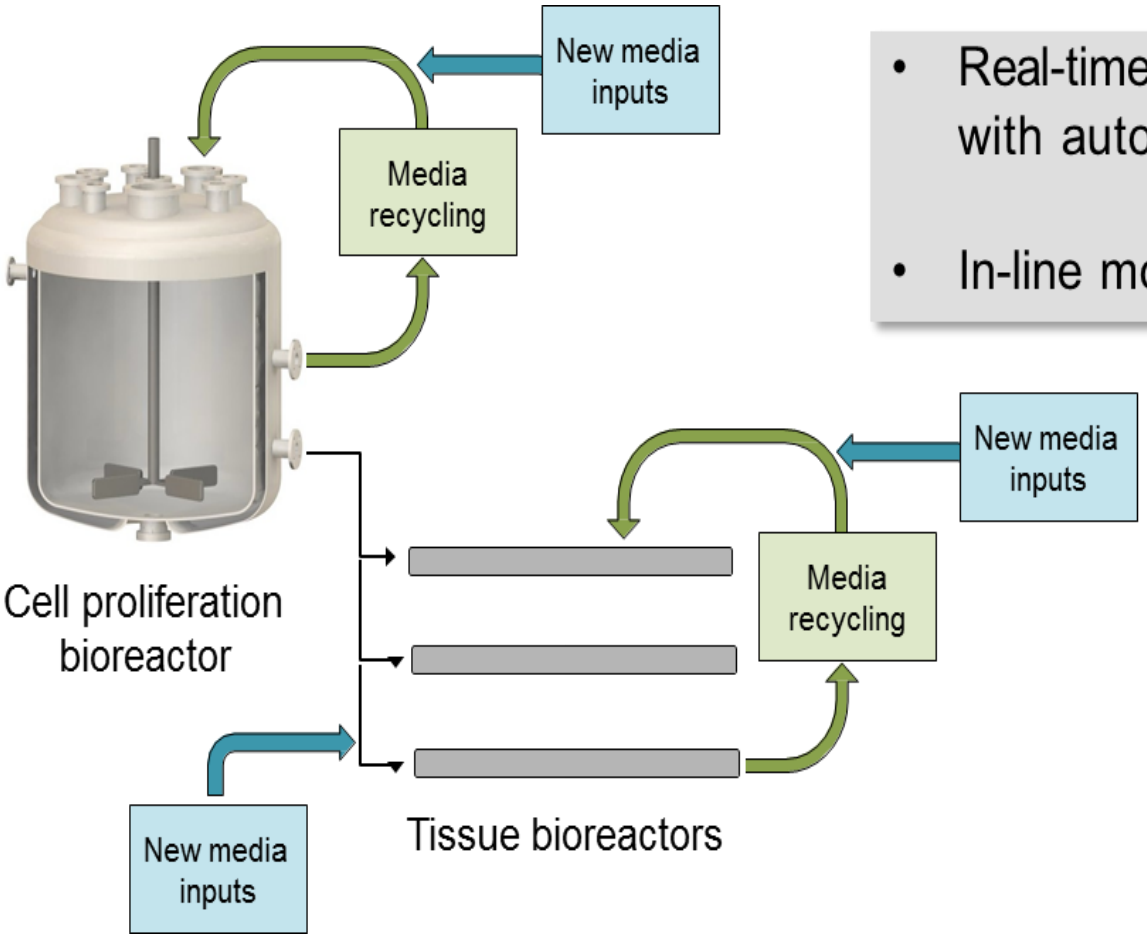
PROTEINS

Insulin, transferrin, FGF-2, TGF-beta, etc.

OTHER NUTRIENTS

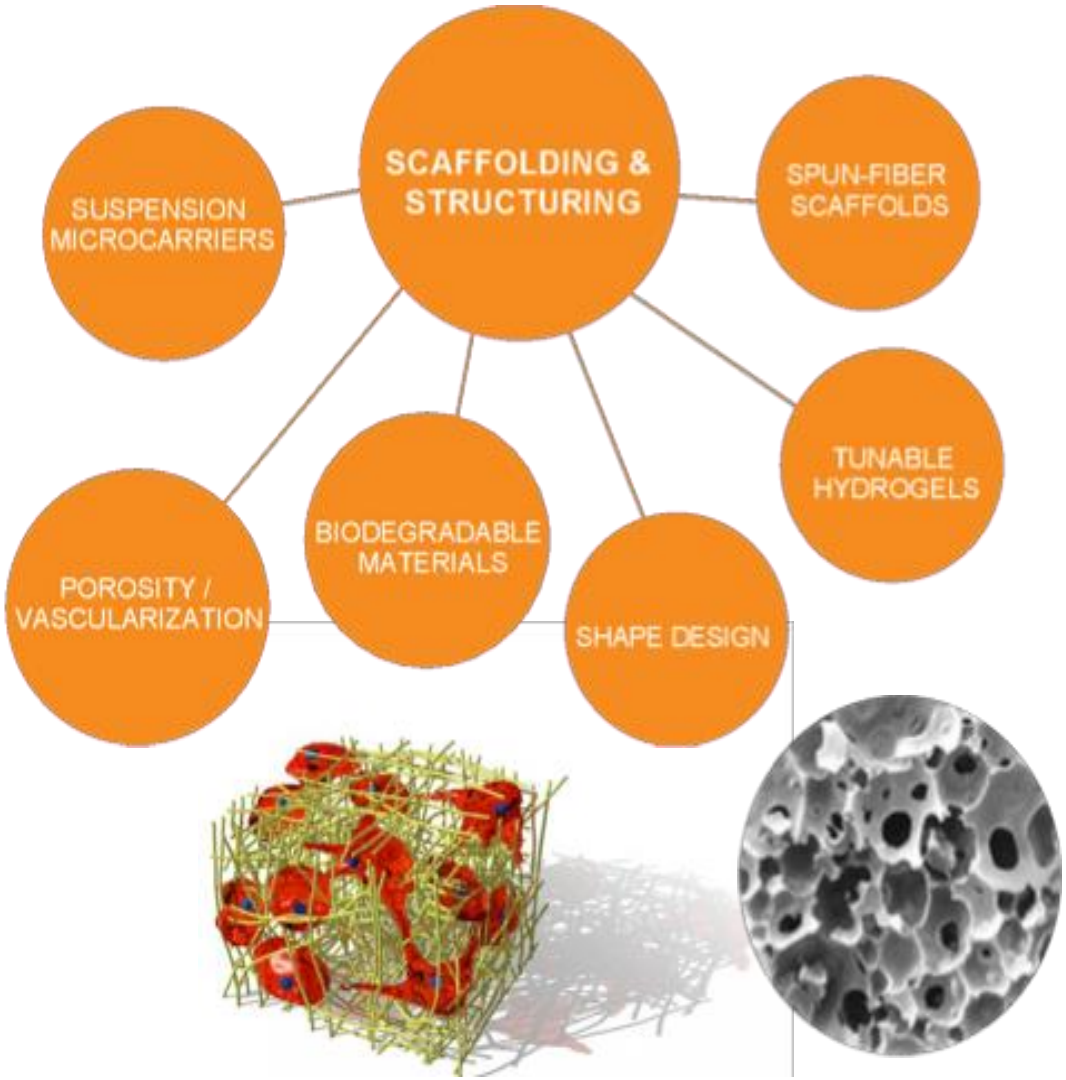
Glucose, HEPES (buffer), linoleic acid, lipoic acid, sodium pyruvate, etc.

Media recycling will likely be necessary in some form



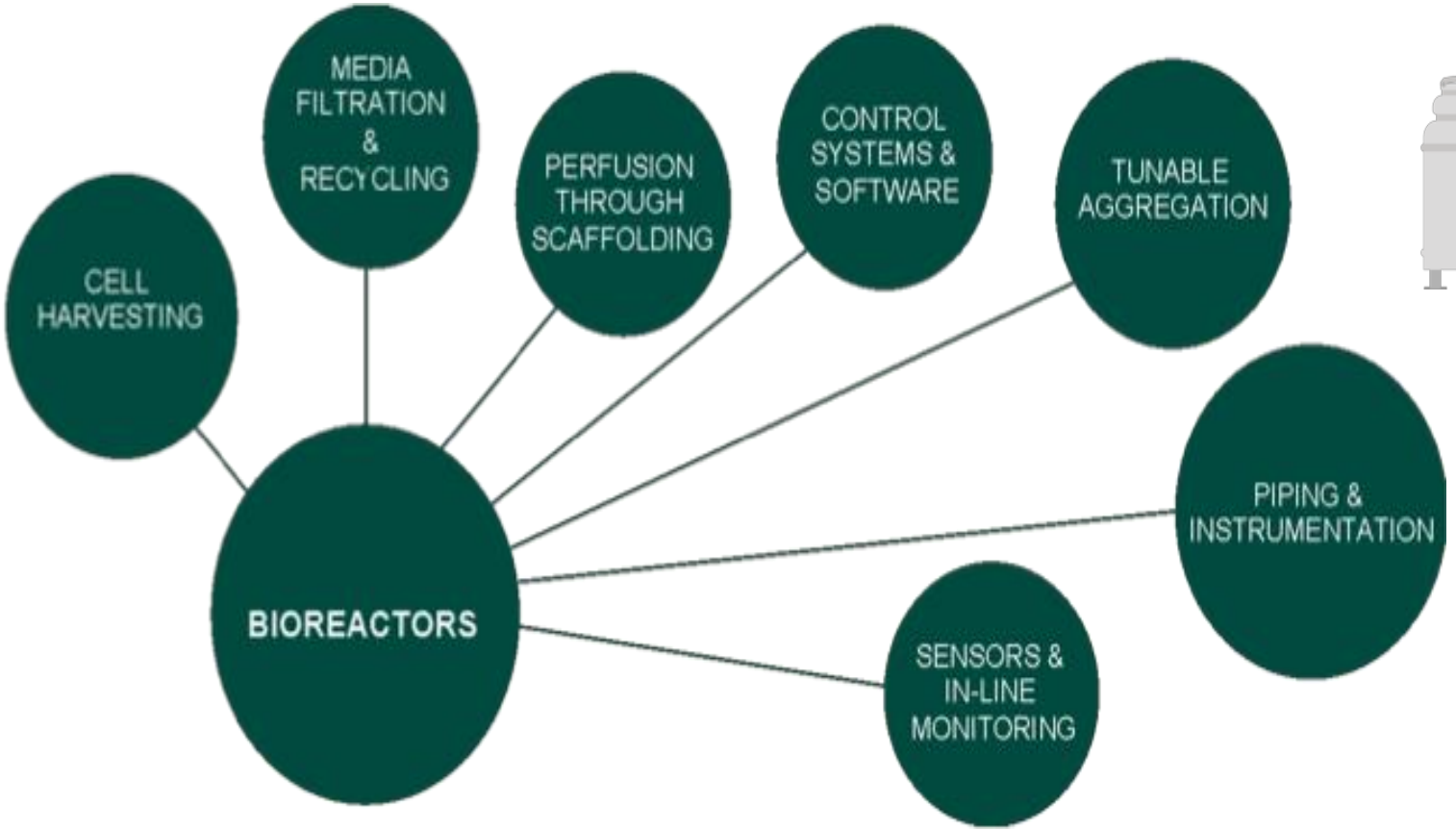
- Real-time analysis of media composition with automated input adjustments
- In-line monitoring of cell morphology

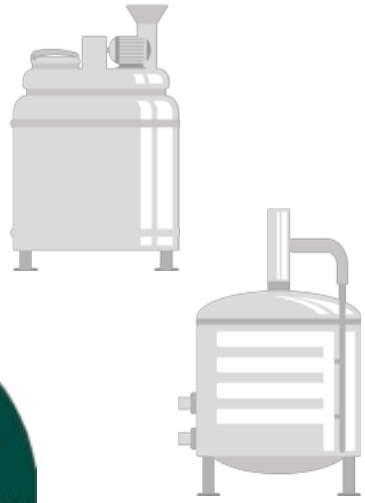
Biomaterials for scaffolds



- Materials may biodegrade and be replaced by the cells' own secreted ECM.
- Alternatively, edible scaffolds can be used. Food materials like alginate are common in tissue engineering.
- Porosity is a key trait for ensuring nutrient access to cells in thick tissues.
- Some processes use microcarriers for growth in suspension culture.

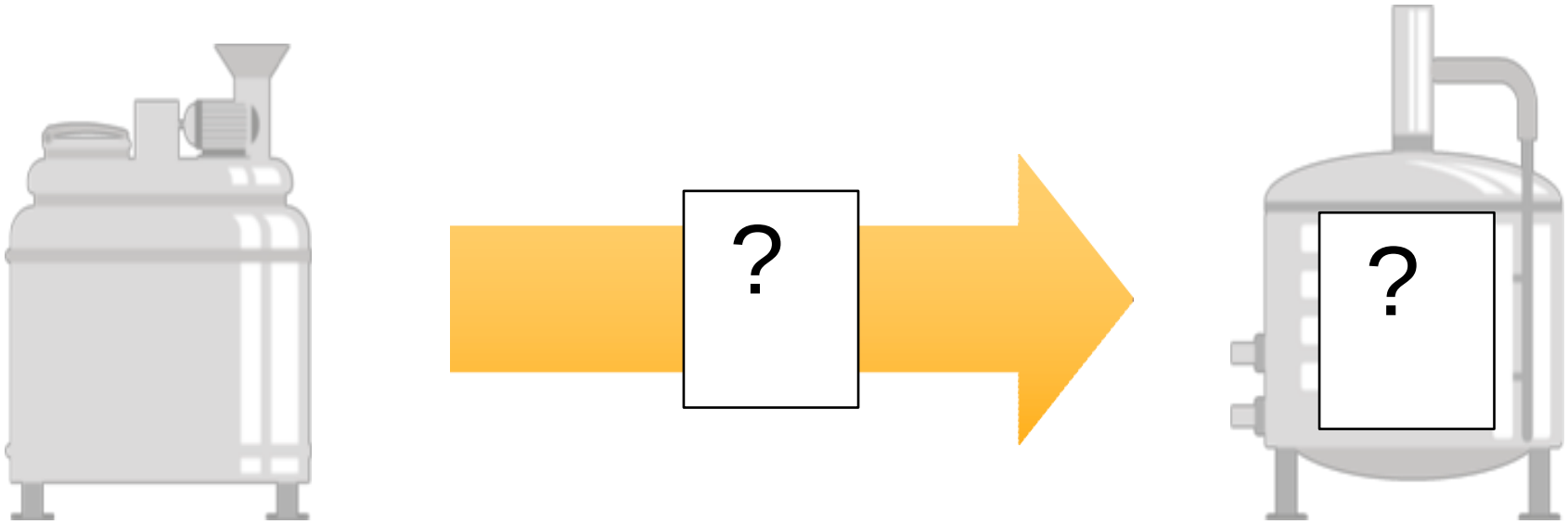
Bioreactors





Systems for integrated continuous bioprocessing and closed containment have been developed for both biopharma and food ingredients, but adapting these may not be sufficient.

Bioreactors

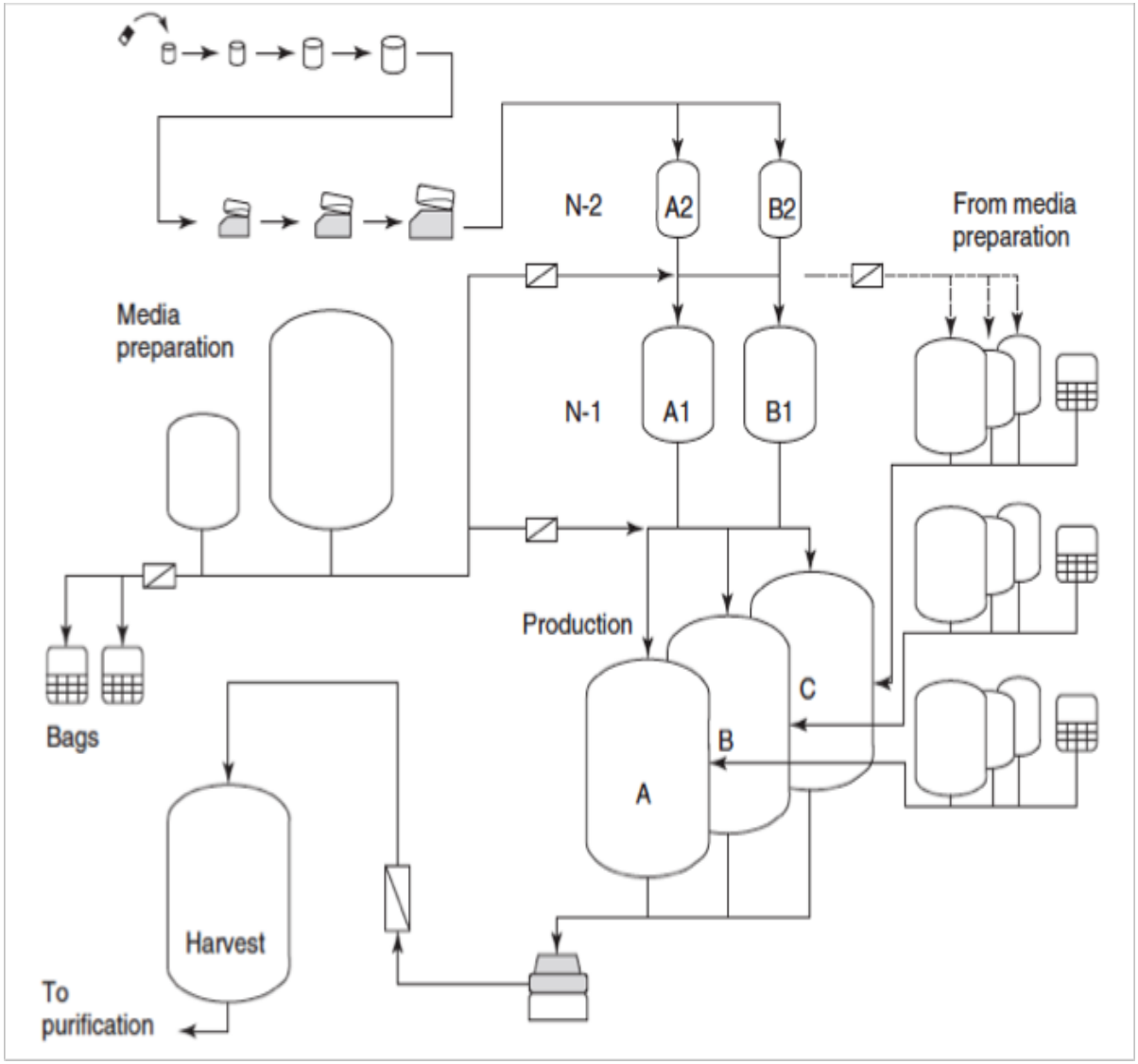


Proliferation

Differentiation

Bioprocesses

- Which stages could be single-use?
- Which stages could be batch processes?
- …semi-continuous? (Operational for how long?)
- …continuous?




ANY
QUESTIONS?