Click Record

Ollscoil Teicneolaíochta an Atlantaigh
Atlantic Technological University

nibrt
National Institute for Bioprocessing Research and Training

Protein Purification
Lecture 1
Module Overview & Introduction to Bioprocessing

I'll be with you shortly

Robert Byrne
robert.byrne@associate.atu.ie

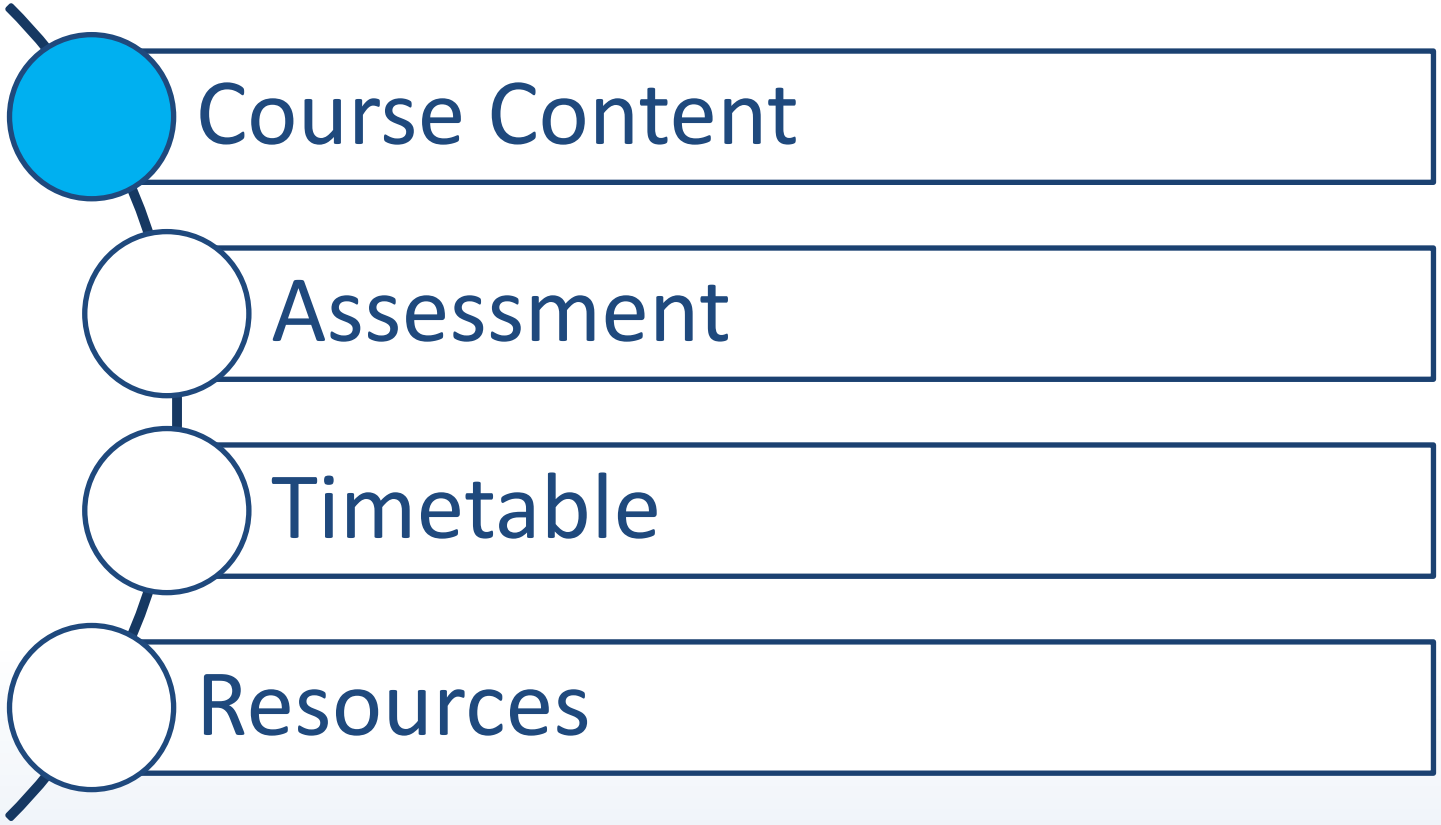
Intro

robert.byrne@nibrt.ie

What is This Lecture About?

- Brief Overview of Course Content
- Forms of Assessment
- Methods of Delivery
- Required Reading
- Questions

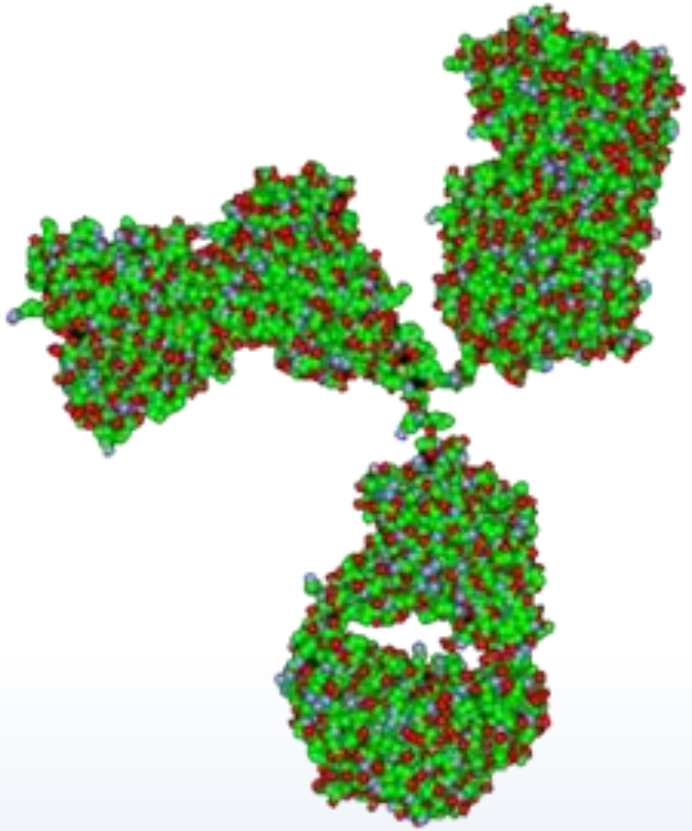
Topics



Semester 1
Jan 2025 – April 2025

Your subjects this semester:

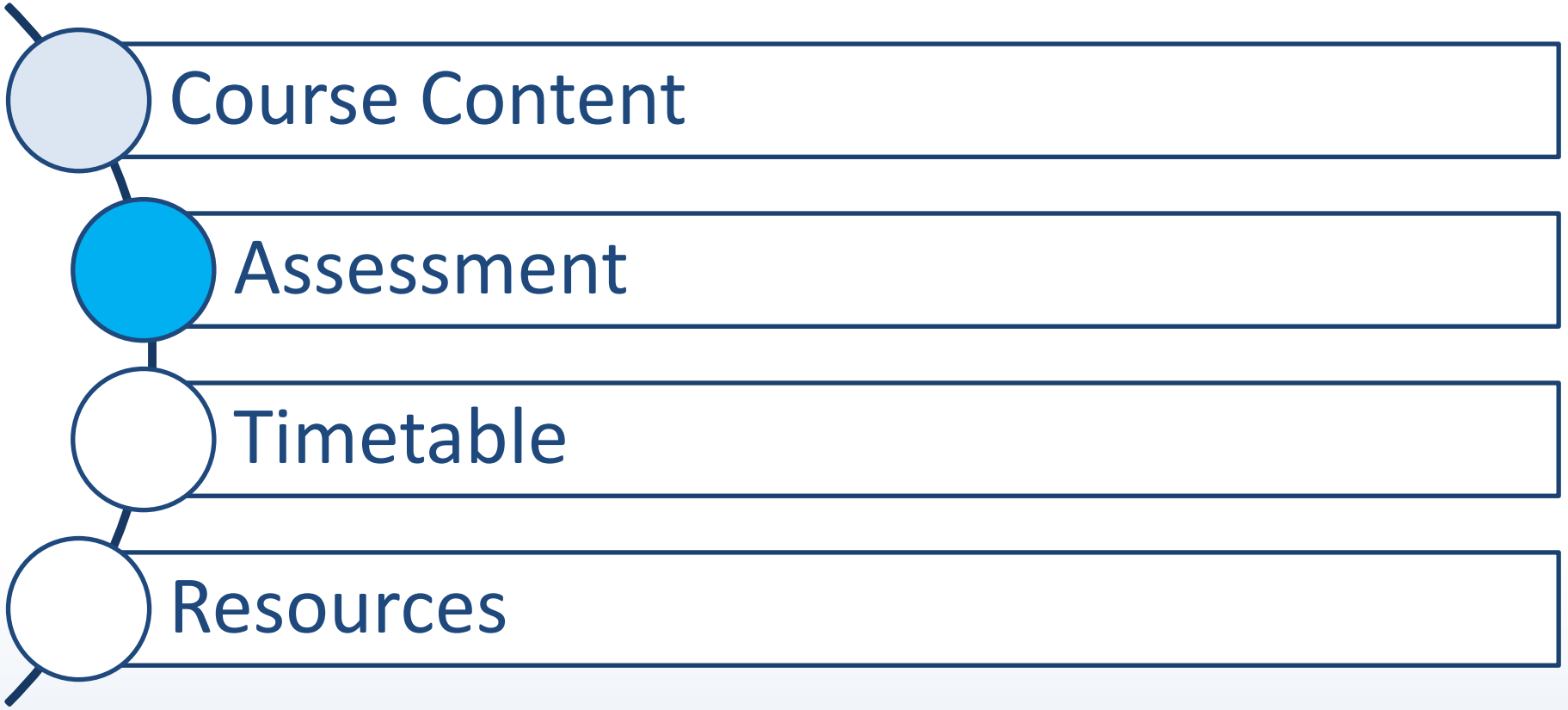
- Bio-Validation
  - Carl Bermingham
- Protein Purification
  - Robbie Byrne
  - Thursday 6pm – 7pm
- Bioanalytics
  - Maja Kristek



Course Content

1) Introduction to downstream processing (DSP) & protein purification.
2) The design and operation of an effective protein recovery and capture systems – centrifugation & filtration.
3) Theory and principle of chromatography for purification.
4) Chromatographic methods for purification.
5) Viral exclusion technologies for protein purification.
6) Quality control aspects of protein purification

Topics



Module Breakdown

- **Number of lectures**
  - 9 lectures
  - Start January 23rd 2025
  - Finish 28th April 2025 - Final Lecture is April 3rd
  - No lecture on an assessment week
  - No lecture during mid-term break
- **Assessment details**
  - Continuous assessments & Project (100%)

Assessment: Theory

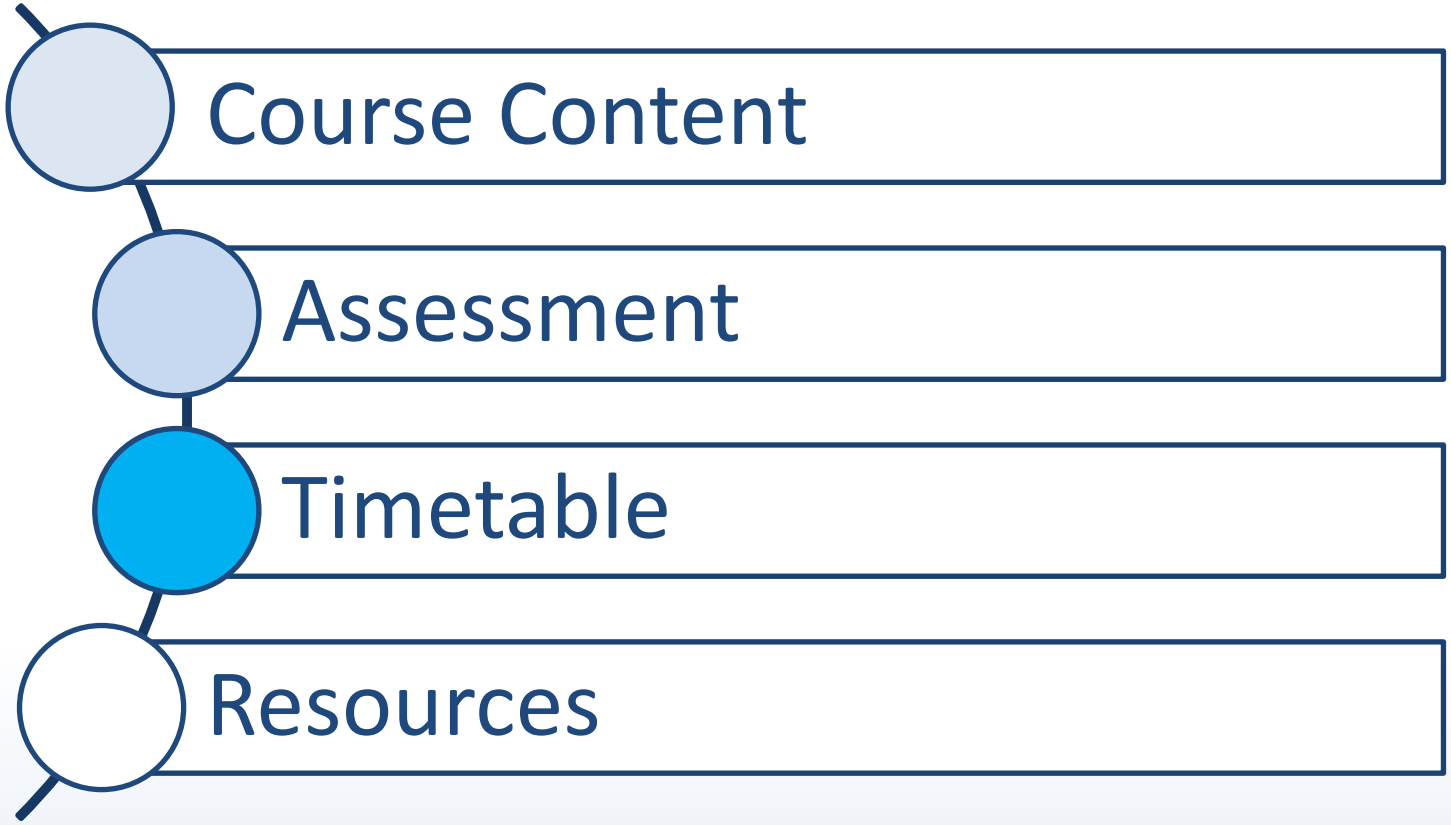
- **MCQ Multiple Choice Questions & LAQ Long answer Questions**
  - MCQ 1 - Week 5 (10%)
  - MCQ 2 – Week 10 (10%)
  - LAQ - Week 12 (30%). **50% of marks**

- **Mini Project (ca. 5000 words)**
  - Can be suggested by the student or assigned by the lecturer.
  - Assigned / agreed by end of week 2/3 of course.
  - Optional - Outline of project plan due end of week 6

Final report due **24th April -2025**	**40% of marks**
• *Introduction / Background / References*	***5%***
• *Analysis / Discussion / Conclusions*	***15%***
• *Main body of report content*	***20%***

- Recorded project presentation – ***Mandatory - 10% of*** **marks (28th April 2025)**

Topics



Timetable 2025

Lecturer Name: Carl Bermingham			Lecturer Name: Robbie Byrne	Lecturer Name: Maja Kristek
Module Title: Bio-validation			Module Title: Protein Purification	Module Title: Bioanalytics
Week Number	Dates	Lecture Day & Time	Lecture Details Thursday 6pm – 7pm	Lecture Details
1	W/C Jan 20th	Lecture 1 and Course Overview	Lecture 1 and Course Overview	Lecture 1 and Course Overview
2	W/C Jan 27th	Lecture 2	Lecture 2: DSP Protein Recovery – Harvest	Lecture 2
3	W/C Feb 3rd	Lecture 3	Lecture 3: Filtration	Lecture 3
4	W/C Feb 10th	MCQ 1 10%	Lecture 4: Protein Biochemistry and Protein Handling	Lecture 4
5	W/C Feb 17th	Lecture 4	MCQ 1 10%	MCQ 1 (10%)
6	W/C Feb 24th	Lecture 5	Lecture 5: Principles of Chromatography	Lecture 5
7	W/C Mar 3rd	Lecture 6	Lecture 6: Modes of Chromatography	Lecture 6
8	W/C Mar 10th	MCQ 2 10%	Lecture 7: Process-Scale Chromatography	Lecture 7
9	W/C Mar 17th	Lecture 7	Lecture 8: Viral Clearance	MCQ 2 10%
10	W/C Mar 24th	Lecture 8	MCQ 2 10%	Lecture 8
11	W/C Mar 31st	Lecture 9	Lecture 9: QA and QC Aspects of Purification	Lecture 9
			Easter Break	
12	W/C April 14th	LAQ 30%	LAQ 30% **April 17th**	LAQ 30%
13	W/C Apr 21st	Project reports due (40%)	Project reports due (40%)	Project reports due (40%)
14	Apr 28th	Project Presentations Due (10%)	Project Presentations Due (10%)	Project Presentations Due (10%)

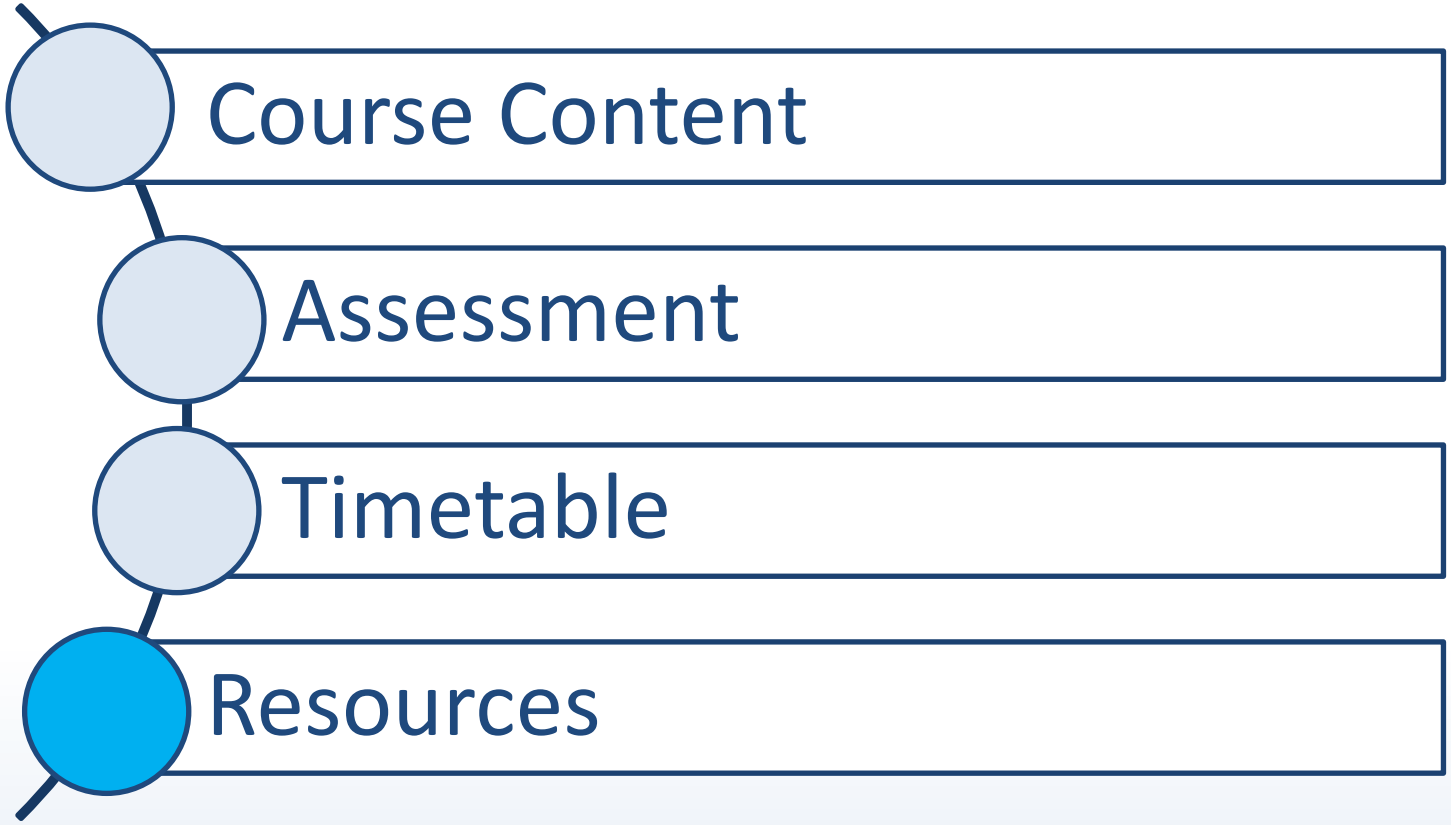
Course Delivery

- **Lecturer Course Notes.**
  - Available on Moodle in blocks at regular intervals.
  - Will be in pdf format with embedded slides.
  - Aim to cover all material by end week 11 of the course.
- **Live or recorded lectures** - live lectures to take place each **Thursday at 6PM** (IRE time) unless otherwise advised.
  - These online lectures will be in tutorial format.
  - Will utilise supplemental slide material to support course notes where relevant.

Recommended reading material from course textbook.

- Supplemental reading from course textbook as relevant.
- Relevant articles posted on Moodle.

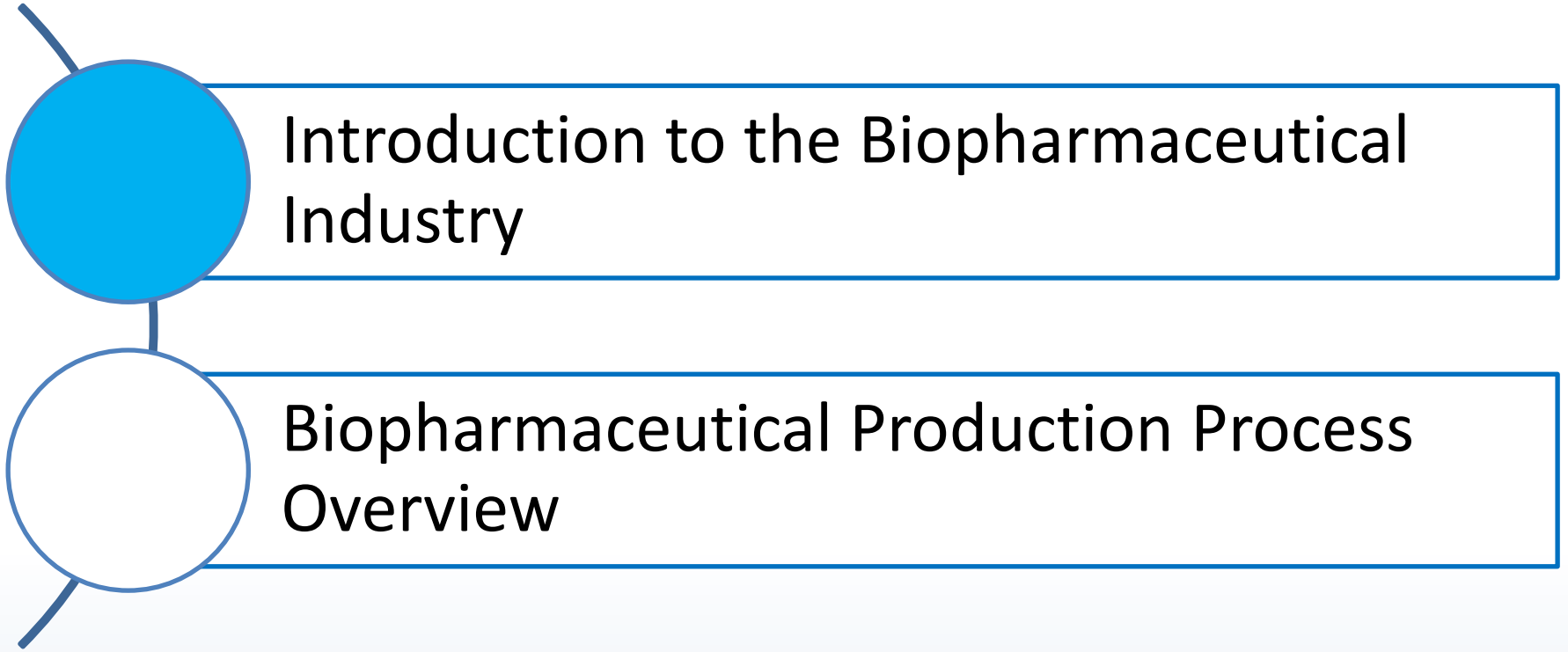
Topics



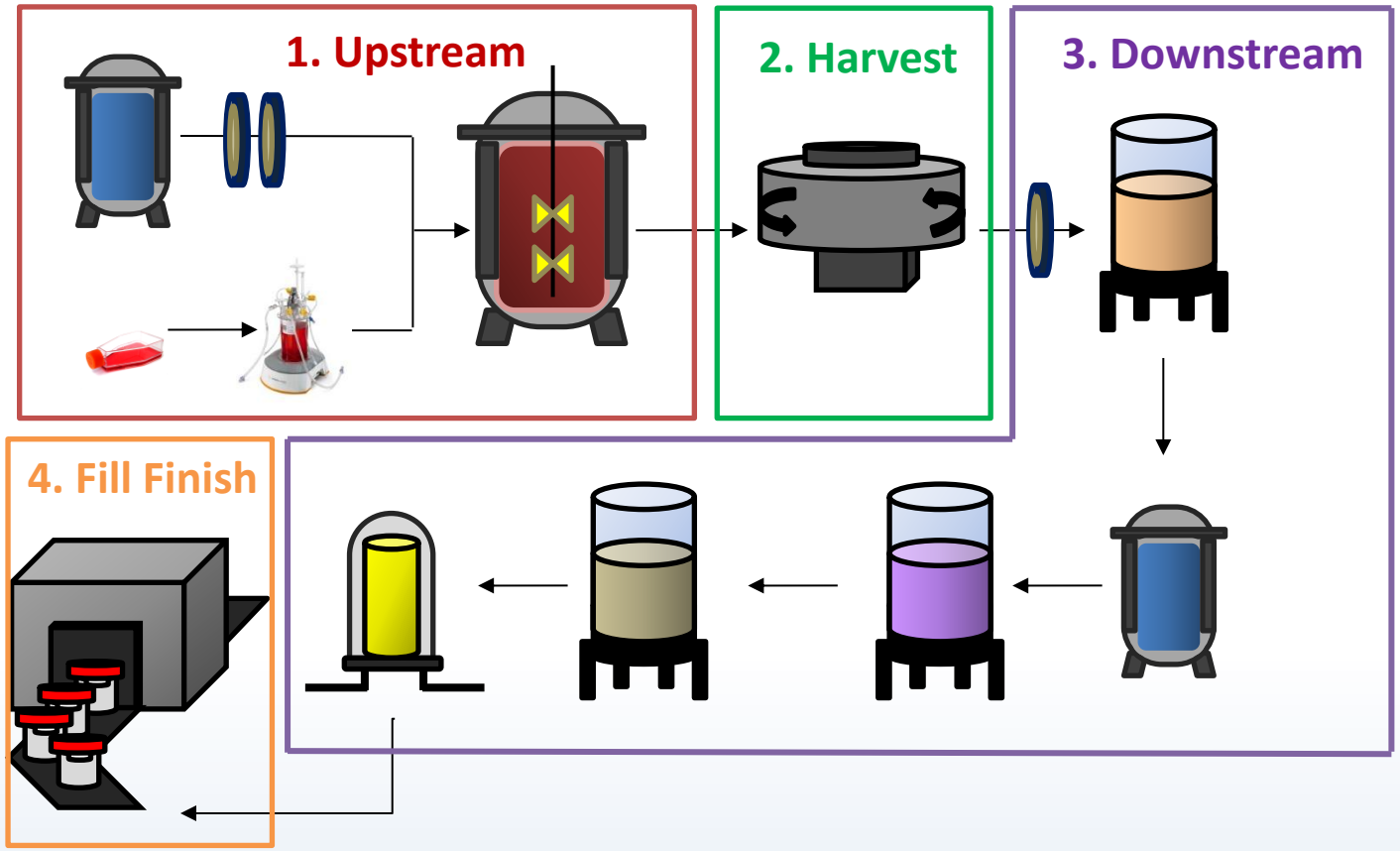
Every week you will receive…

- Live lecture (link provided on main course page)
- Lecture notes (pdf)
- Relevant reading material
- Links to websites
- Link to recorded live lecture

Topics

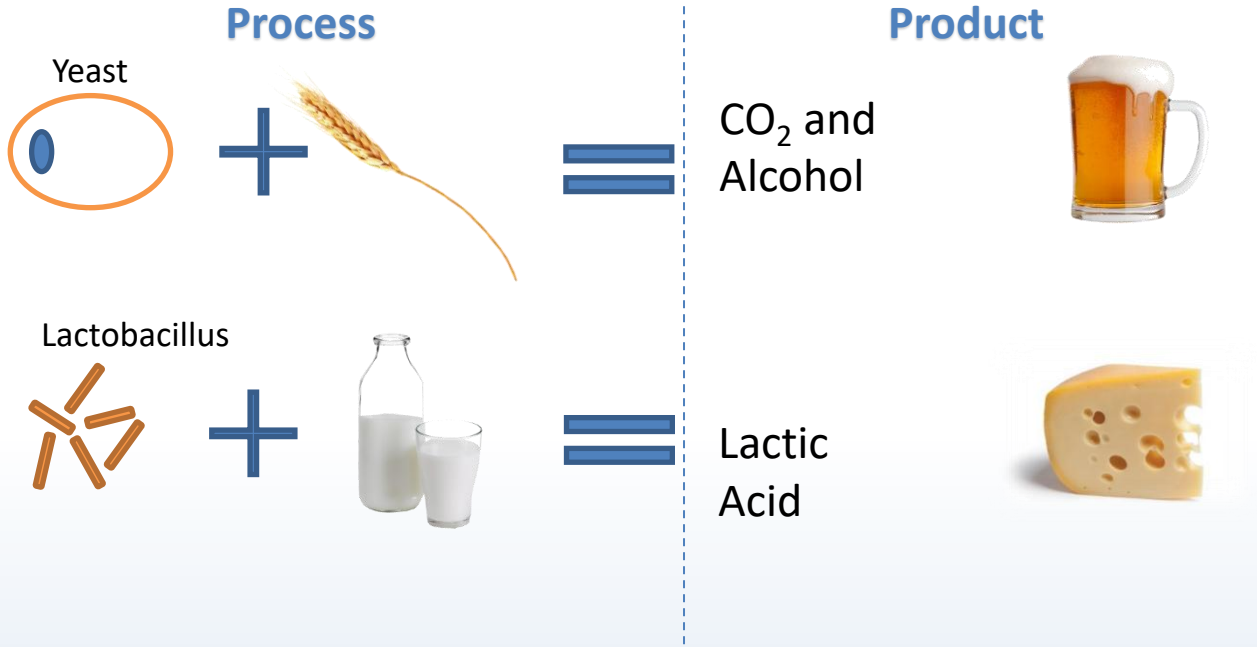

Introduction to the Biopharmaceutical Industry
Biopharmaceutical Production Process Overview

Overview of Bioprocessing



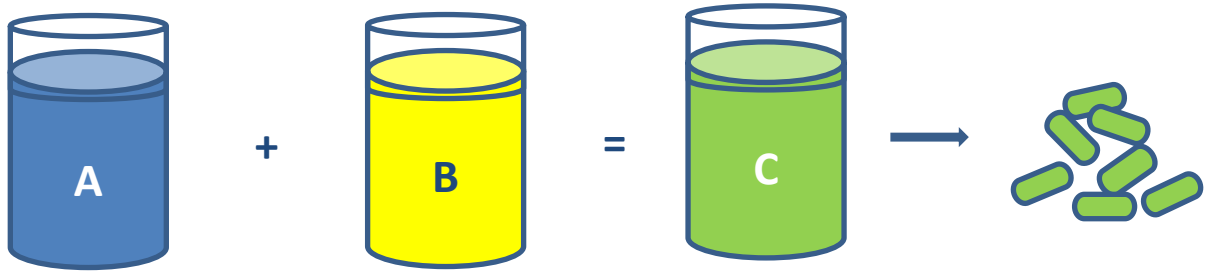
What is Bioprocessing?

Bioprocessing uses organisms or biologically derived macromolecules to carry out enzymatic reactions or to manufacture products.



Pharmaceutical -v- Biopharmaceutical

- Traditional Pharmaceutical:



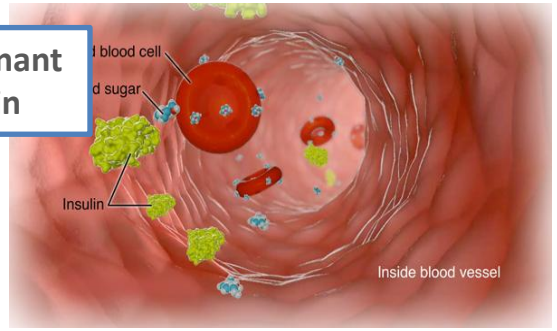
- Biopharmaceutical:

What are Biopharmaceuticals/Biologics?

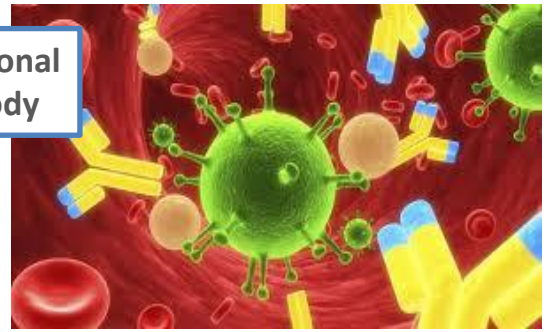
"A biological medicine is a medicine that contains one or more active substances made by or derived from a biological source"

-European Medicines Agency

Recombinant Protein

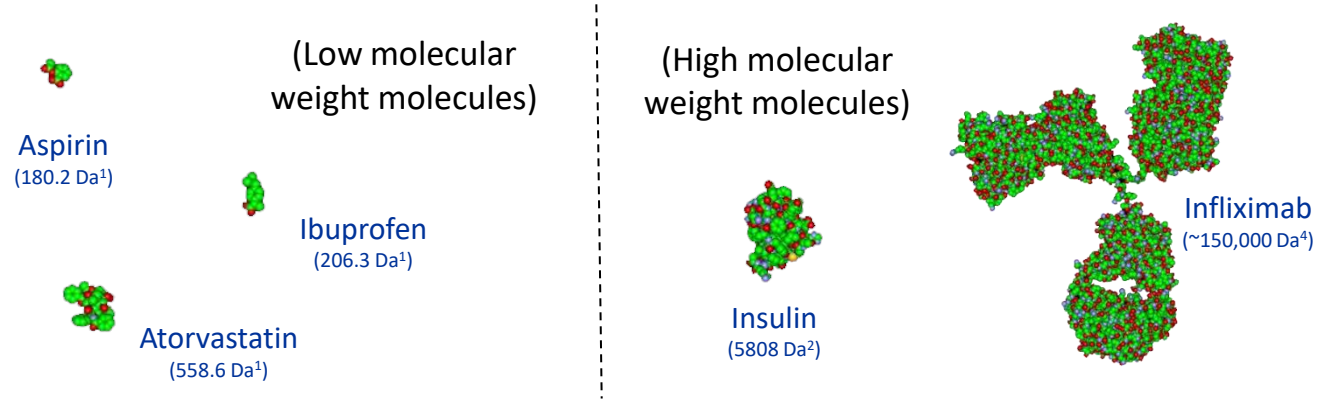


Monoclonal Antibody



They are not chemically synthesised

Pharmaceutical -v- Biopharmaceutical



Chemical (small molecules)	Biological (large molecules)
Less complex production process	Complex production process
Product robust; Can be taken as tablet	**Fragile product**; would be destroyed in the gastrointestinal system, administered by injection
Low risk of product degradation or contamination	High risk of product degradation or contamination
Process is well defined and losses are low	High process variability and losses; 30% and up
Simple analytical techniques used	Complex analytical techniques required

So Why Biologics?

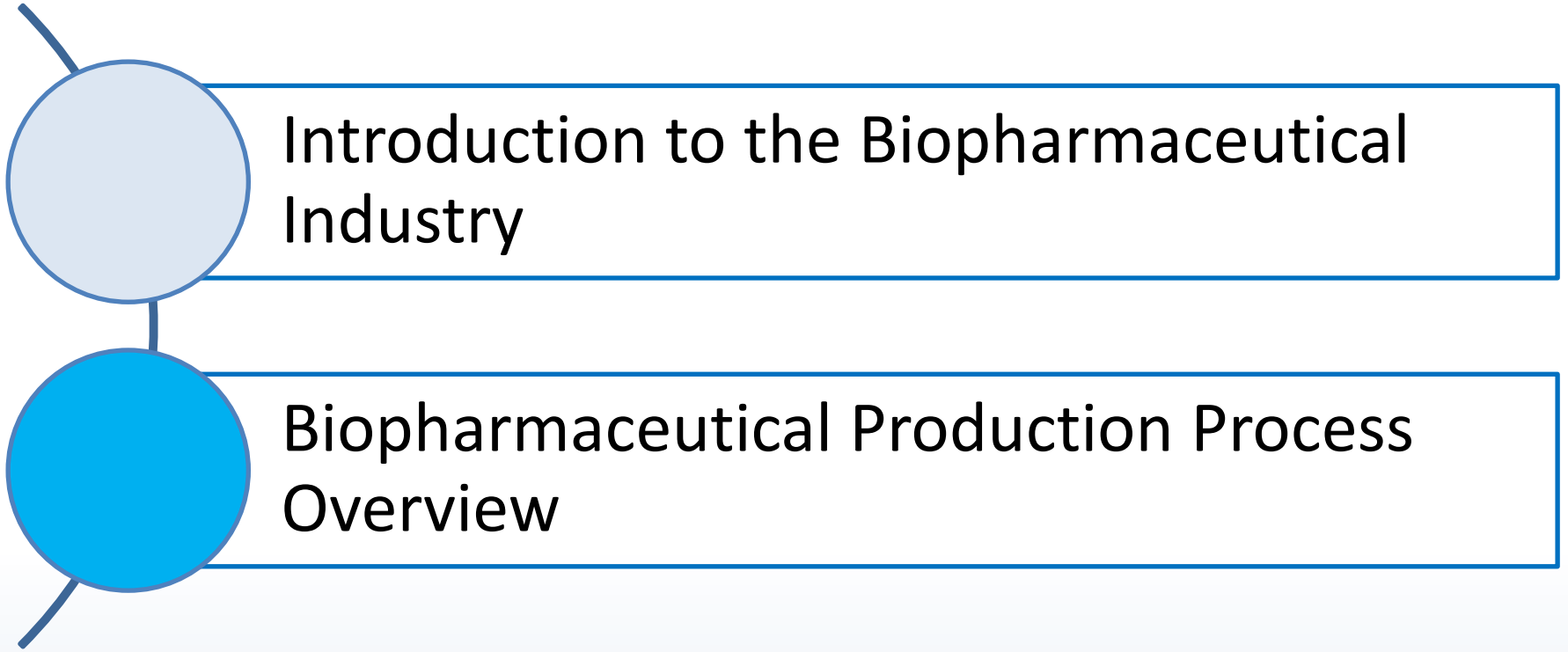
- Small molecule drugs often **lack specificity** which can cause off-target interactions and side-effects
- Biologics can be engineered to **bind with extreme precision** resulting in less side effects and lower toxicity
- Biologics **can target complex molecular processes** that small molecules cannot – can treat diseases such as cancer or autoimmune diseases

Small molecules

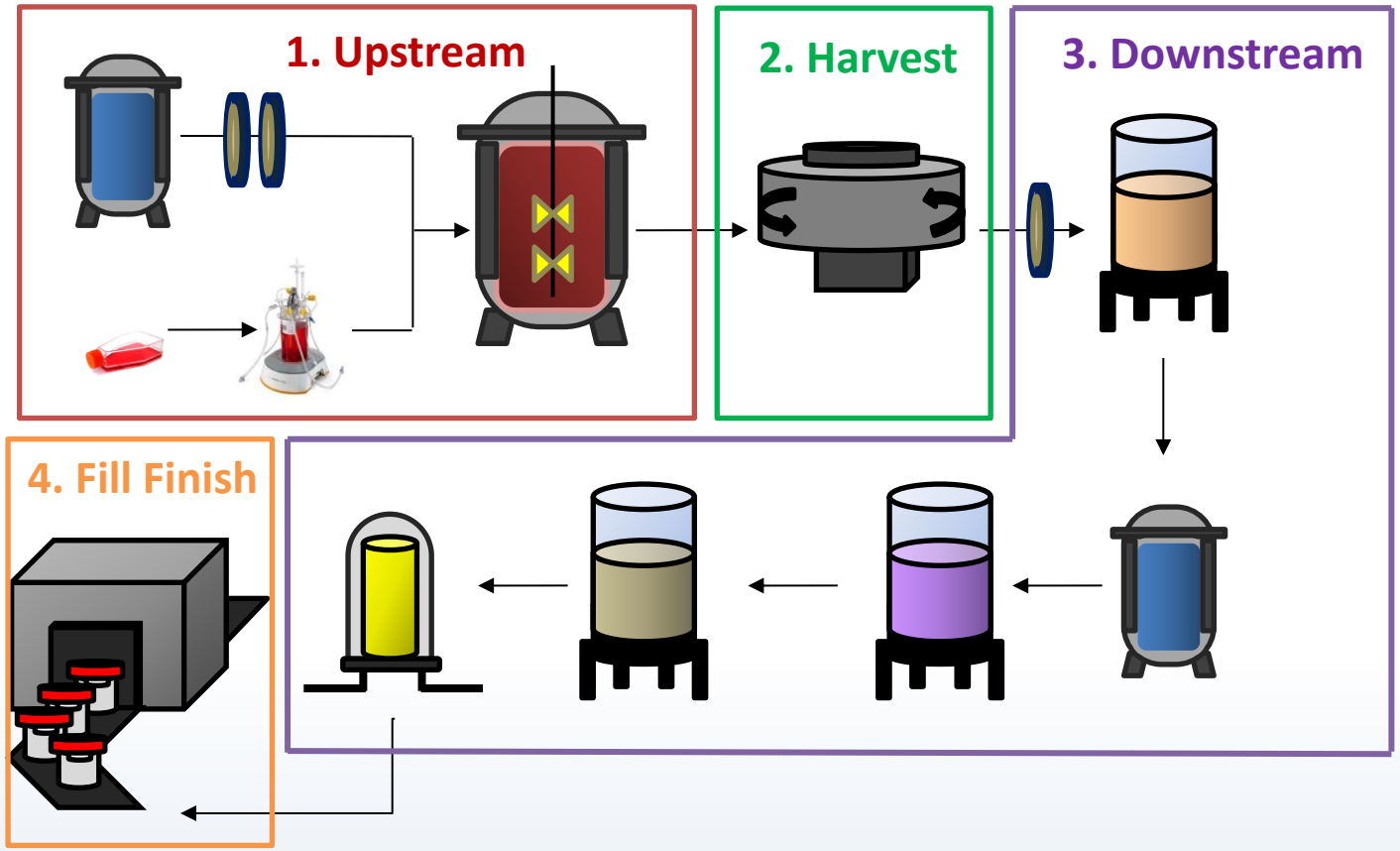
VS.

Biologics

Topics

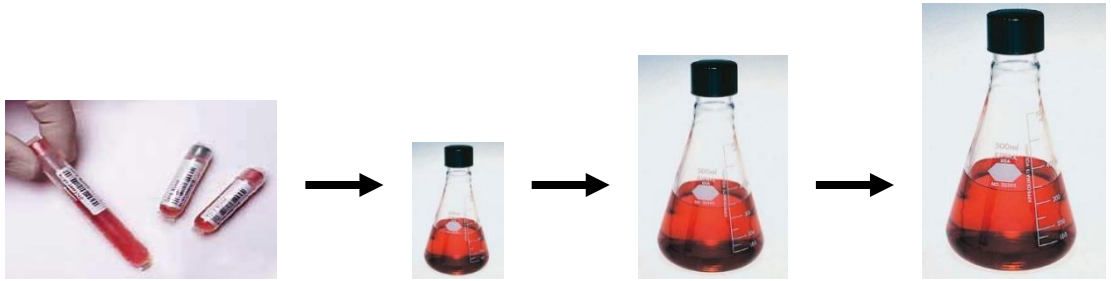

Introduction to the Biopharmaceutical Industry
Biopharmaceutical Production Process Overview

Overview of Bioprocessing



Upstream: Cell Culture

- Thaw vial of cells from working cell bank
- Expand culture to desired production volume
- Maximise product expression



Frozen cells cultured thawed and cultured in flasks of increasing volume

Shake flasks inoculated into benchtop bioreactors

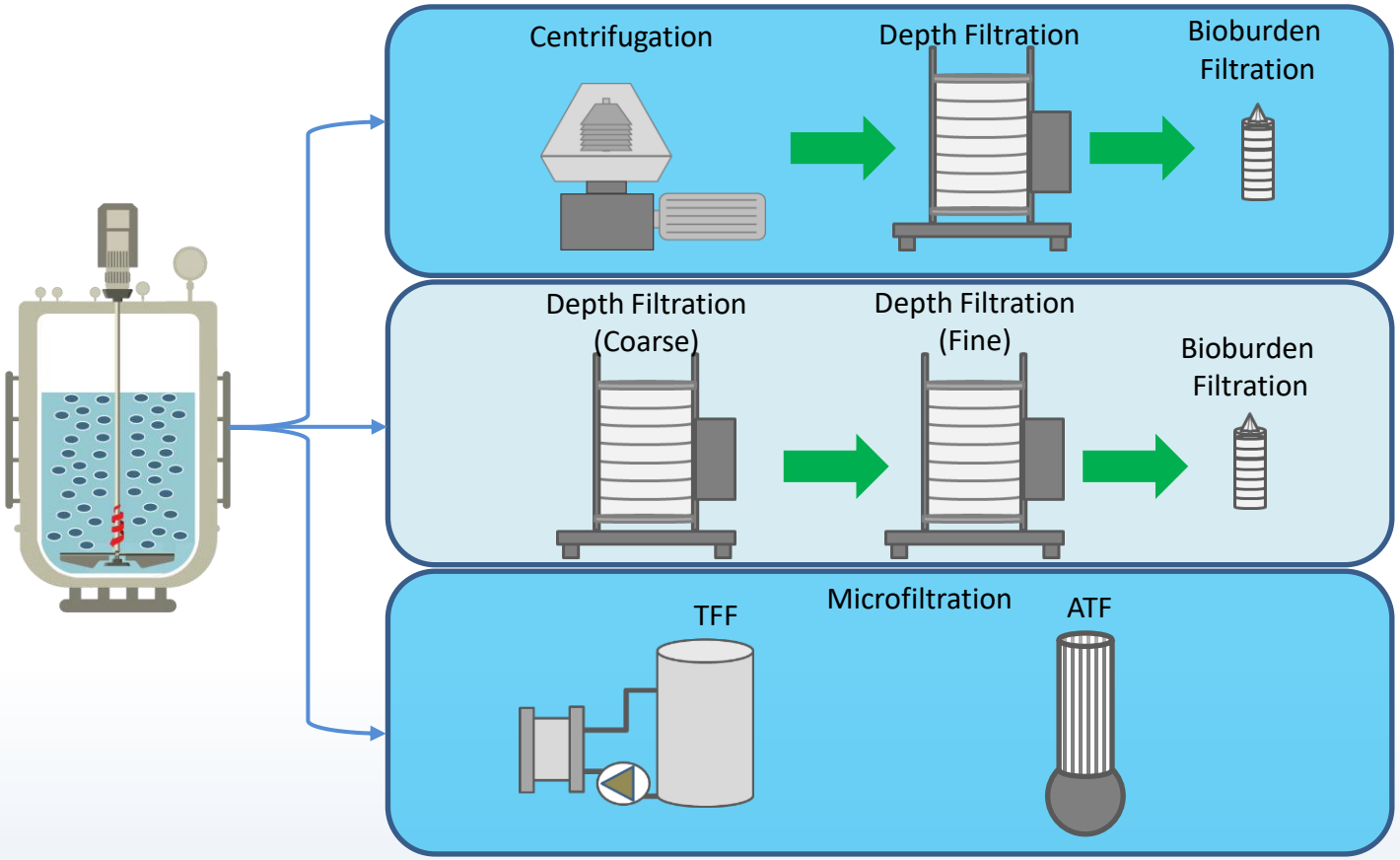
Cells inoculated into a series of larger bioreactors

Goals of Upstream Processing

1. Start growing cells that produce the protein.
2. Grow enough cells to make enough product (‘scaling up’).
3. Keep cells healthy to ensure high quality protein product.
4. Maintain structural integrity of the protein.

Walsh, Gary. *Pharmaceutical biotechnology: concepts and applications*. John Wiley & Sons, 2007.

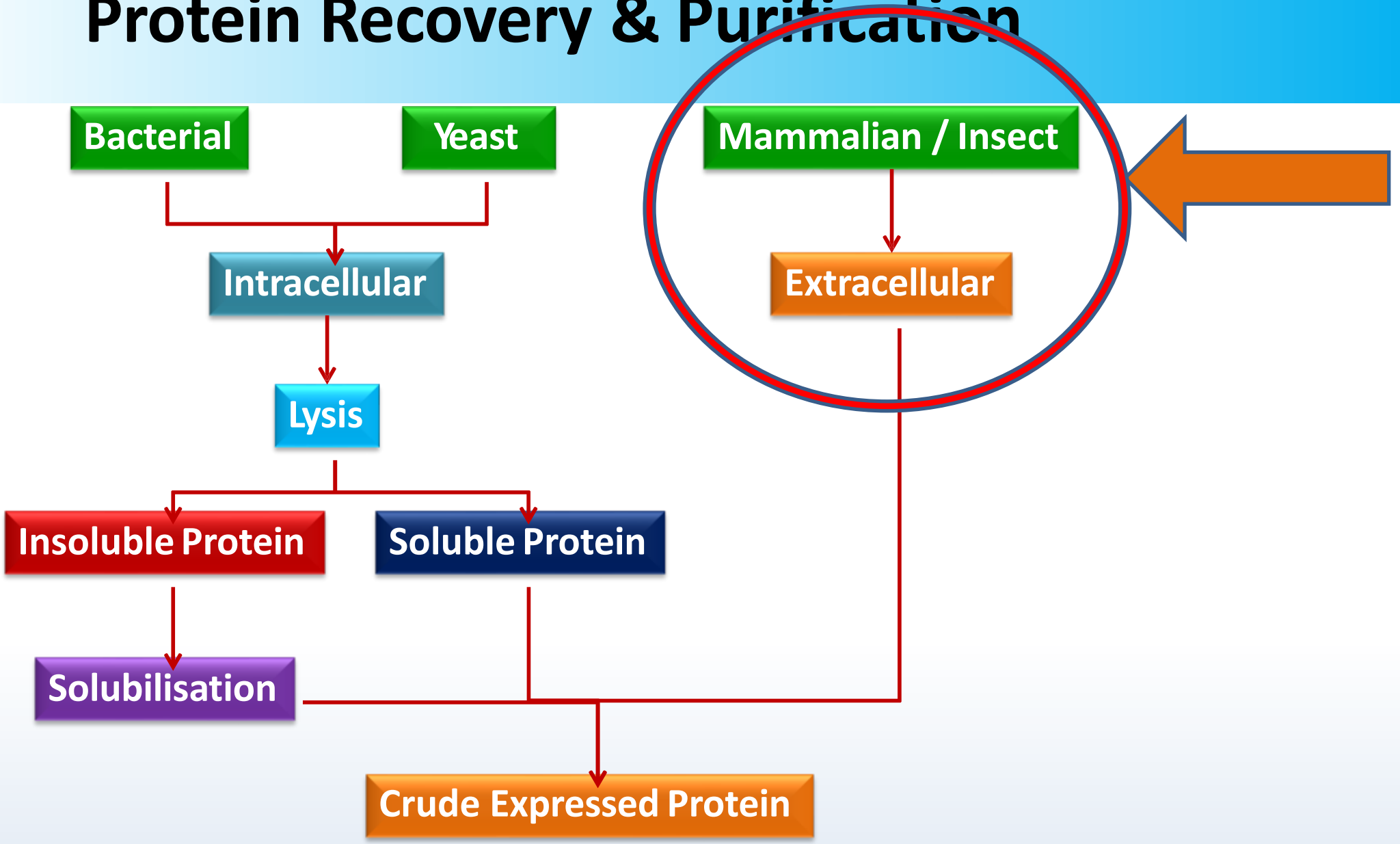
Harvest Options



Downstream Processing

- Biopharmaceutical downstream processing consists of those **operations required for the recovery of product** from the manufacturing process stream, concentration and purification, followed by product formulation and filling (*not covered here*)
- **Typical downstream processes include**:-
  - Harvest and protein extraction from cells where required
  - Cell separation - depth filtration and centrifugation
  - Product concentration and buffer exchange - tangential flow filtration (TFF) and diafiltration
  - Protein purification and polishing - chromatography
  - Viral reduction (if required)
  - *Lyophilisation of product*
  - *CIP and SIP of process equipment*

Protein Recovery & Purification



Goals of Downstream Processing

1. Concentrate the protein
2. Remove impurities
3. Inactivate and remove viruses
4. Maintain structural integrity of the protein

Ultrafiltration

Chromatography

Formulation and Filling

Formulation

- Adjust protein concentration, if necessary.
- Add excipients and/or stabilisers.

Filling

- Product is sterilised by filtration.
- Then aseptically filled into pre-sterilised containers.

Cannot be terminally sterilised

Lyophilisation can be performed for stabilisation and preservation.

Topics

- Introduction to the Biopharmaceutical Industry
- Biopharmaceutical Production Process Overview

Thank You