

Разработка биотехнологических процессов.

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Продукты, получаемые с помощью клеток

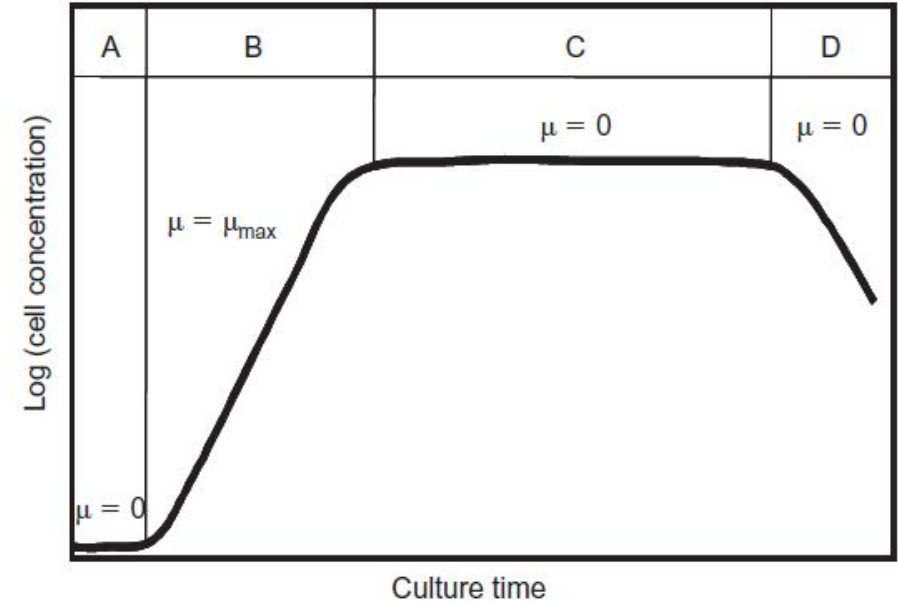
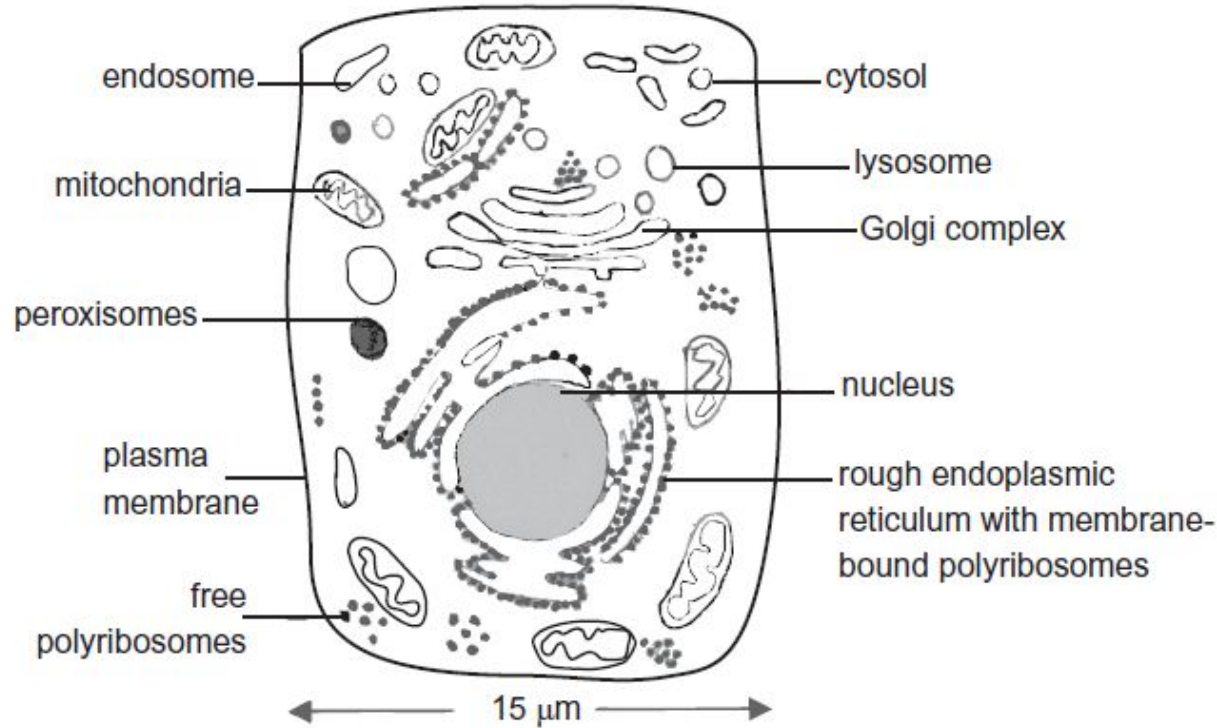
Product	Protein	Use	Cell	Approval year
Avonex [®]	β-Interferon	Multiple sclerosis	CHO	1996
BeneFix [®]	Factor IX	Hemophilia B	CHO	1997
Epogen [®]	Erythropoietin	Anemia	CHO	1989
Gonal-f [®]	Follicle-stimulating hormone	Female infertility	CHO	1995
Herceptin [®] / trastuzumab	mAb	Breast cancer	CHO	1998
Kogenate [®]	Factor VIII	Hemophilia A	BHK	1993
Simulect [®] / basiliximab	mAb	Acute transplanted kidney rejection	Murine myeloma	1998
Campath [®] / alemtuzumab	Humanized mAb	Leukemia	CHO	2001
Xolair [®] / omalizumab	Humanized mAb	Asthma	CHO	2003
Avastin [®] / bevacizumab	Humanized mAb	Colon or rectum carcinoma	CHO	2004

Часто используемые клеточные линии

Cell line	Source	Applications
COS	Monkey	Transient expression Production of recombinant viruses
HEK-293	Human	Transient and stable expression Production of recombinant viruses
BHK-21	Hamster	Transient and stable expression Vaccine production
CHO.K1, CHO dhfr- Hybridomas, NS0, SP2/0	Hamster Mouse	Transient and stable expression Stable expression Monoclonal antibodies production
MDCK	Dog	Stable expression Vaccines production
Per.C6™	Human	Stable expression Production of recombinant viruses and vaccines
Vero Sf9, Sf21	Monkey Insect	Vaccine production Production of recombinant proteins and baculoviruses
Tn-368, High-Five® BTI-TN-5B1-4	Insect	Recombinant protein production

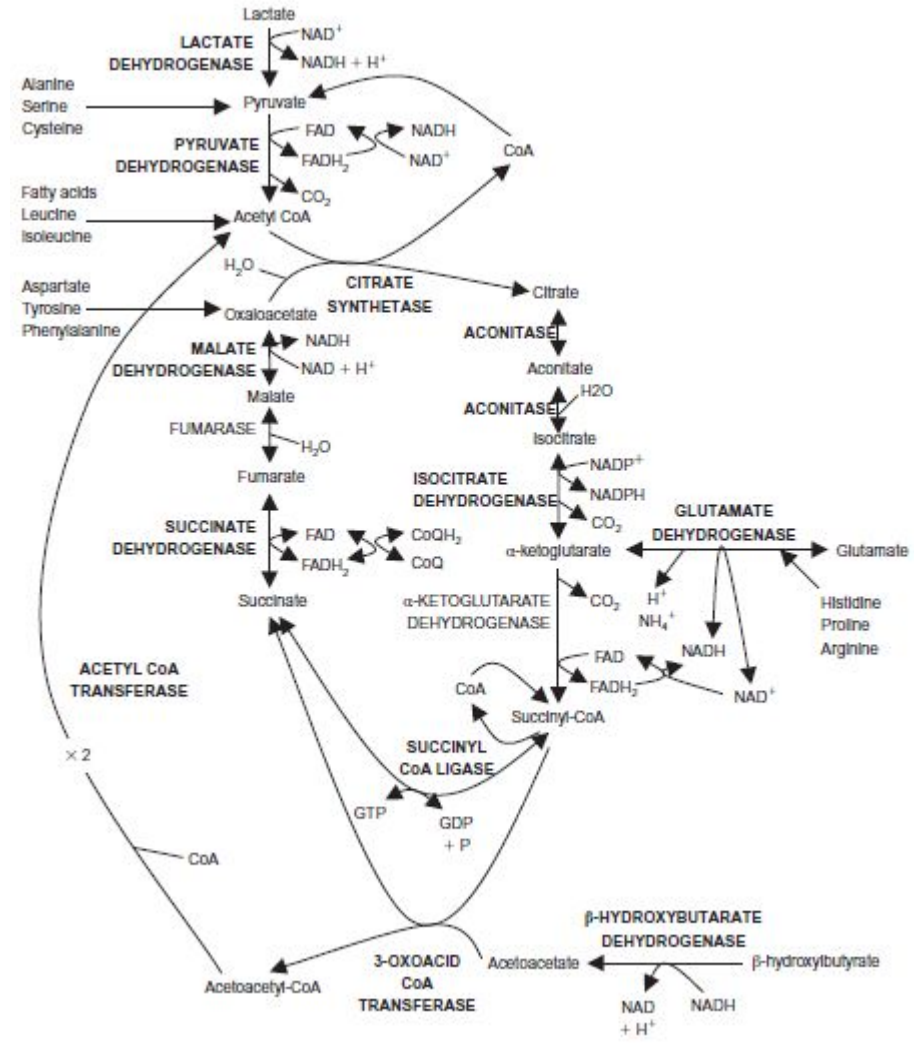
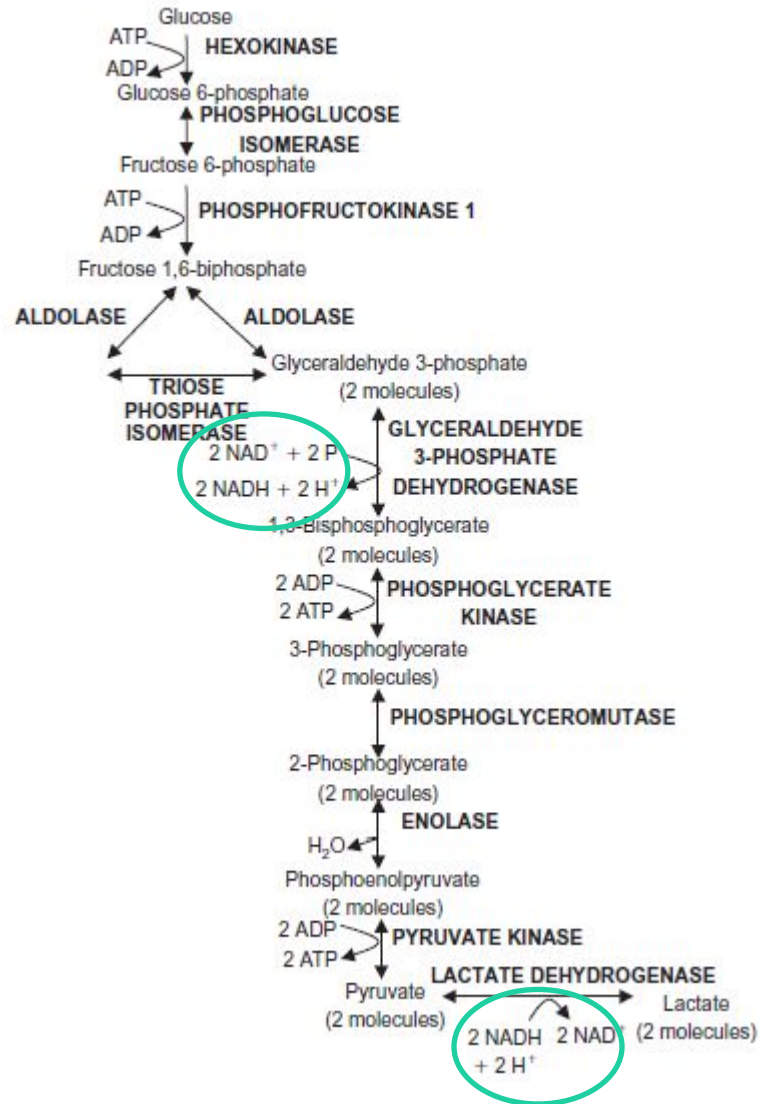


Строение и рост клеток

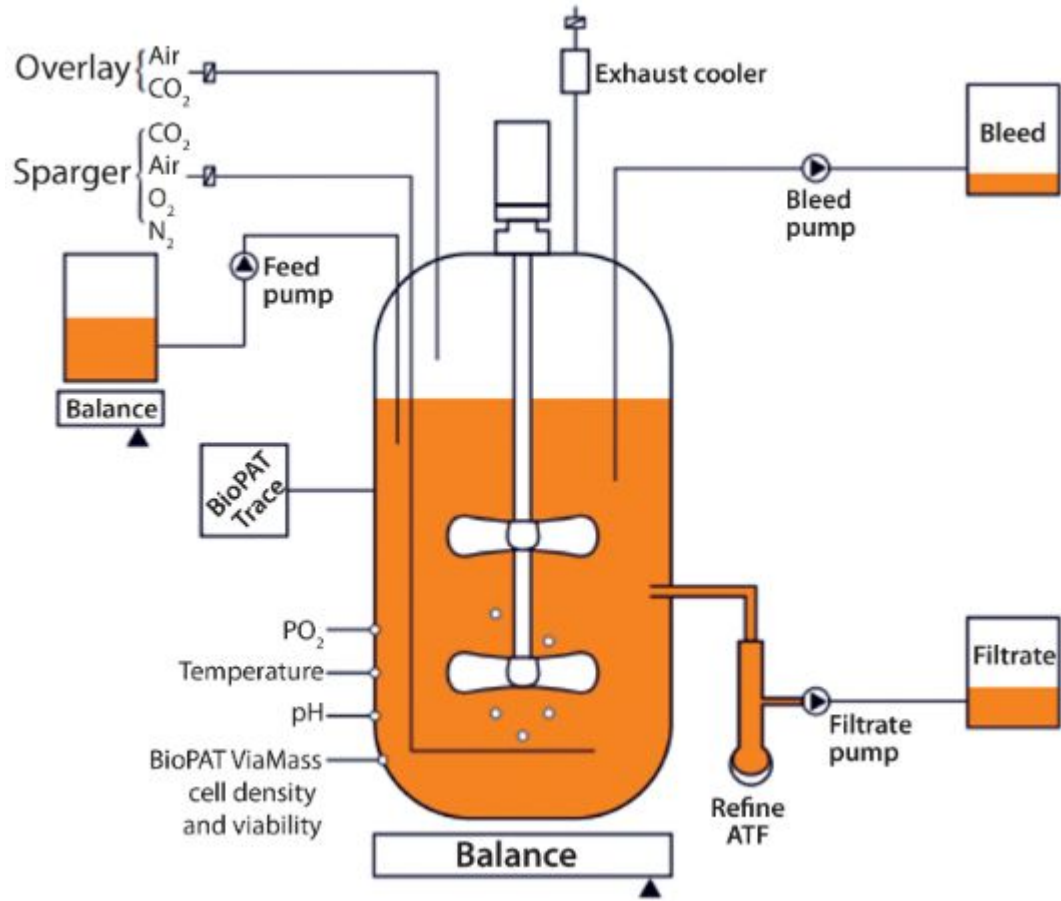


- A – лаг-фаза (адаптация)
- B – лог-фаза (экспоненциальный рост)
- C – стат-фаза
- D – фаза гибели

Гликолиз и ЦТК

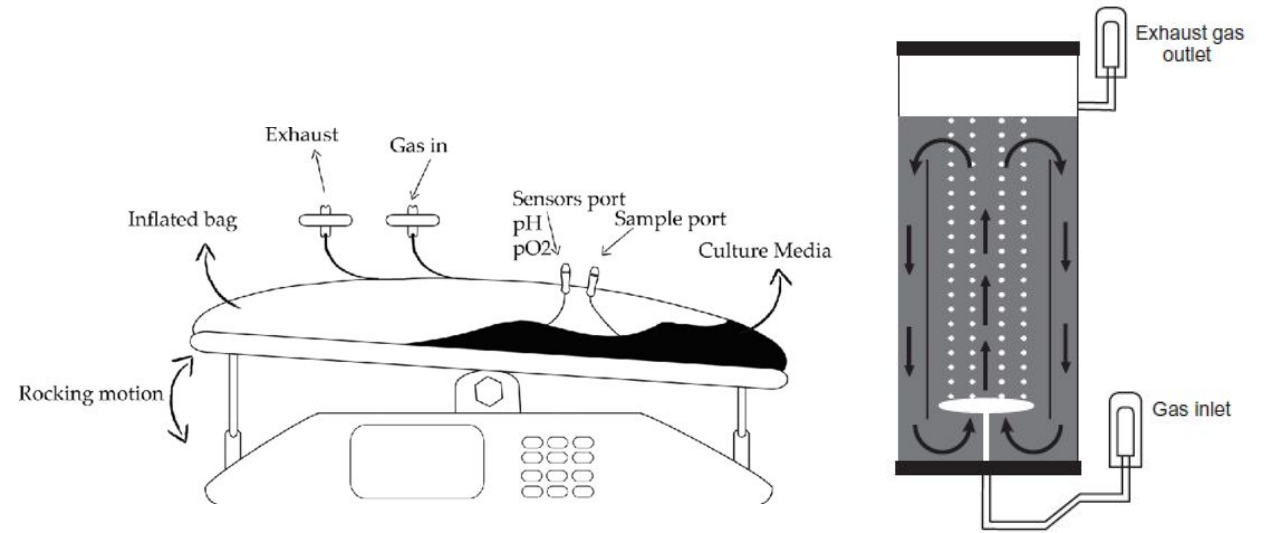
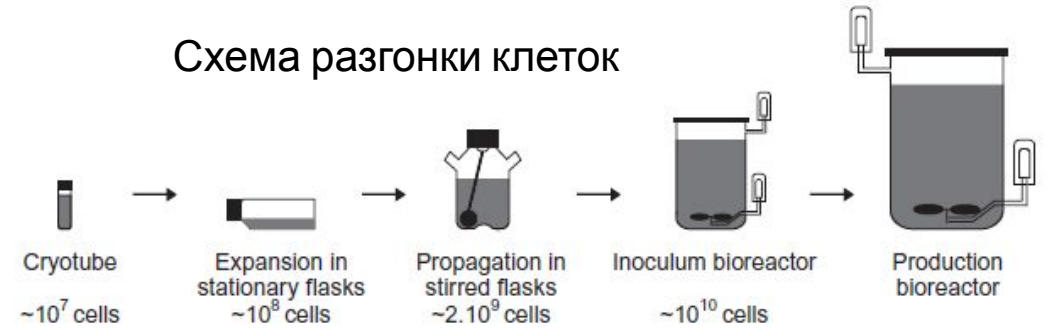


Types of bioreactors



Bioreactor with perfusion system

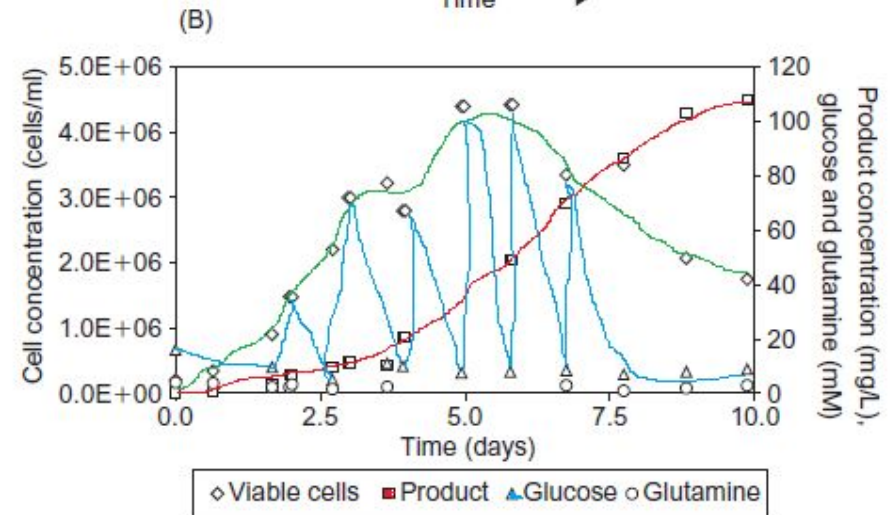
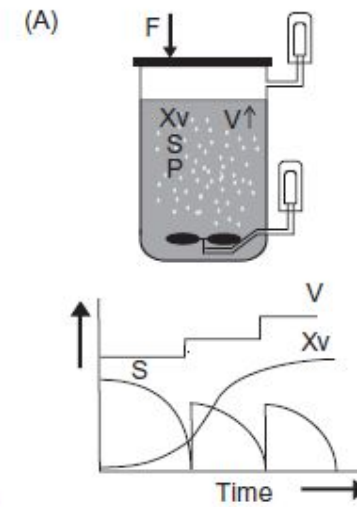
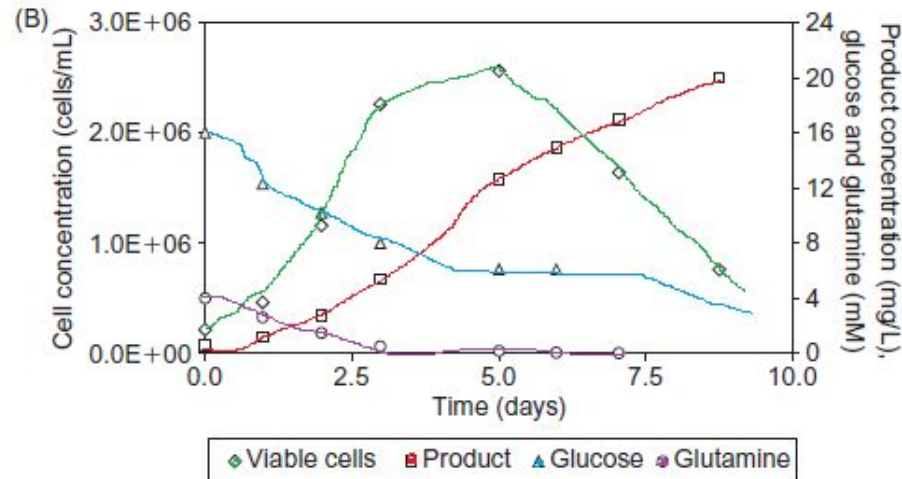
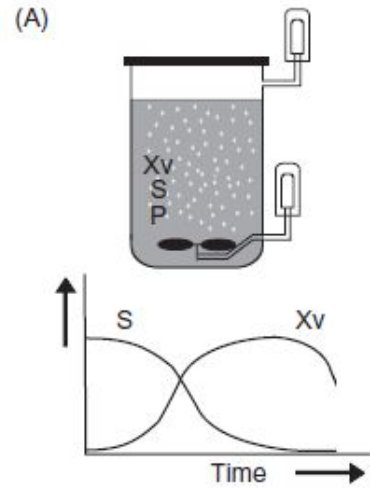
Cell expansion scheme



Wave bioreactor

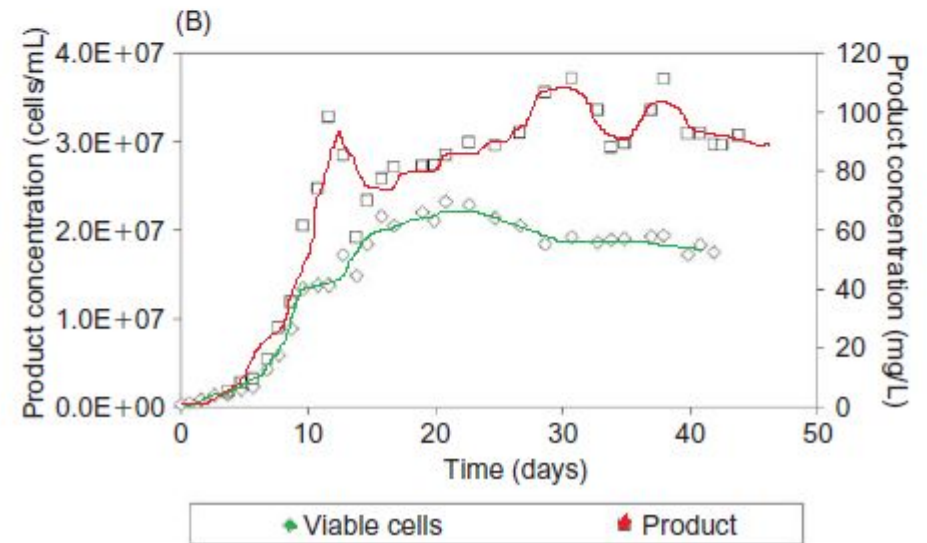
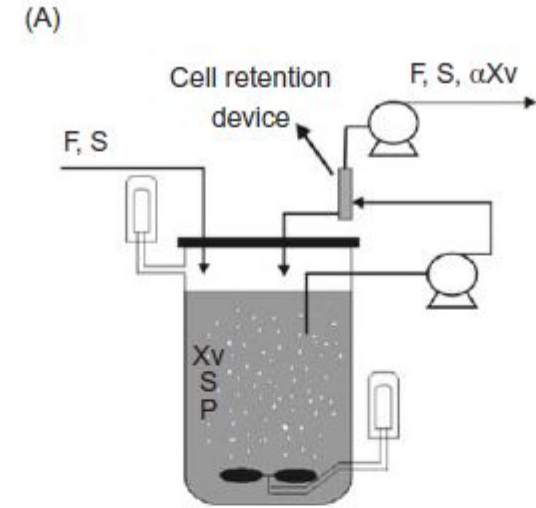
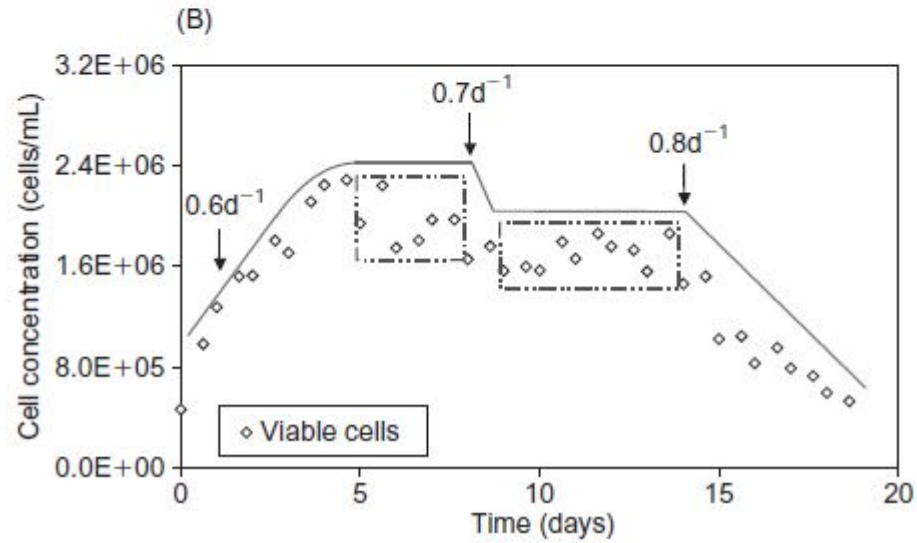
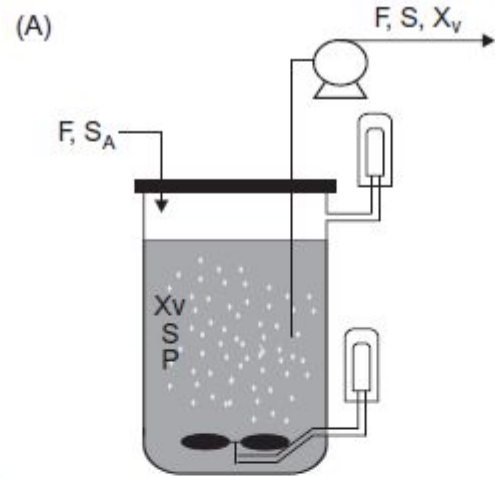
Airlift bioreactor

OC Batch & Fed-batch





Continuous process

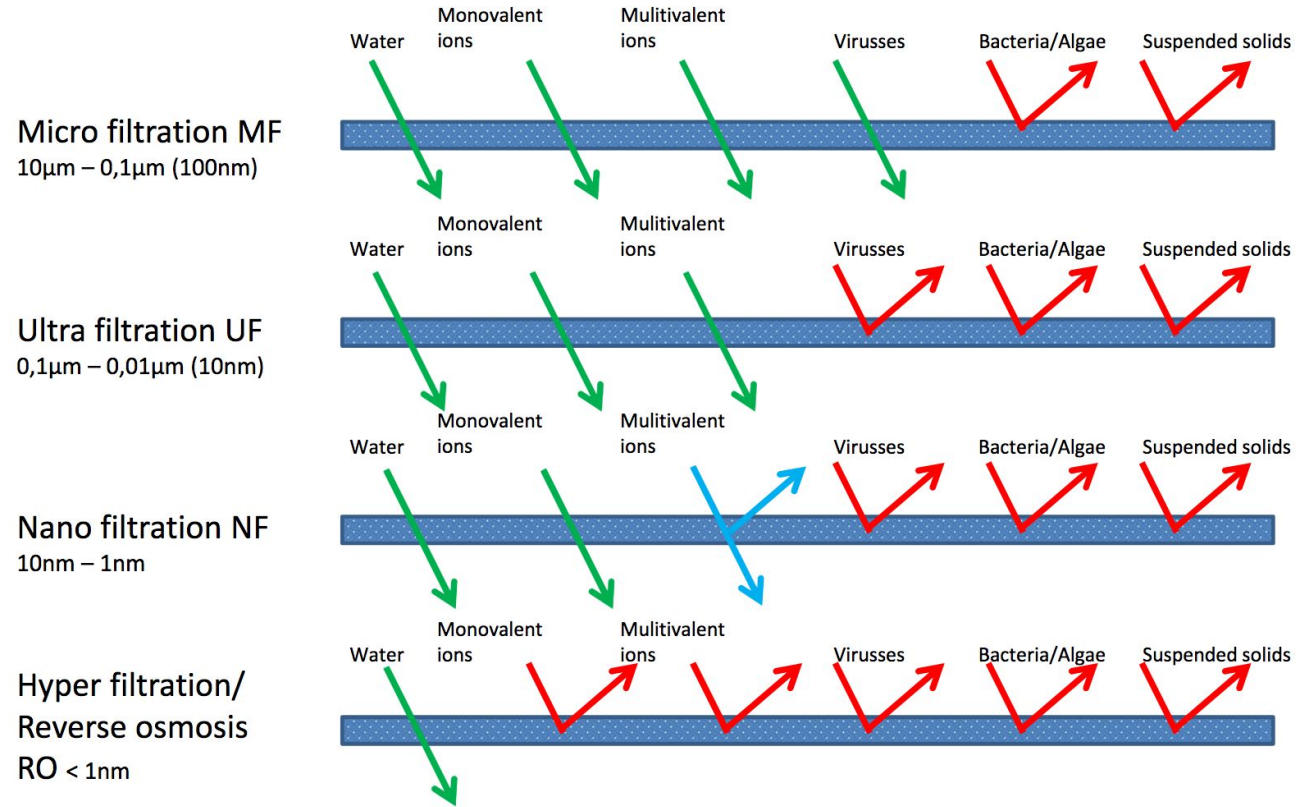




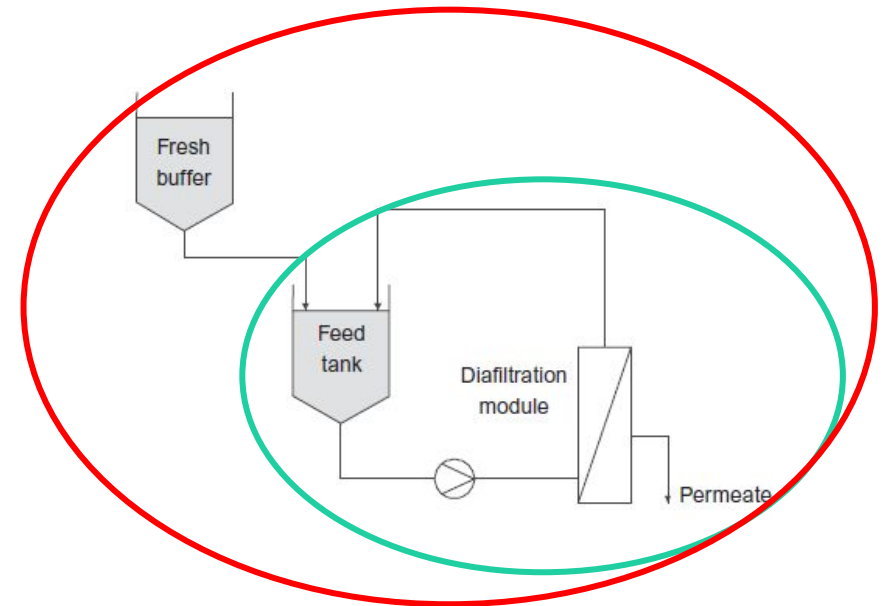
Методы очистки белков

Principle of separation	Technique	Capacity	Yield	Resolution	Cost
Solubility	Liquid-liquid extraction	High	High	Low	Low
	Fractional precipitation	High	High	Low	Low
Size	Microfiltration, ultrafiltration, dialysis	High	Medium	Low	Low
	Molecular exclusion chromatography	Medium-low	High	Medium-low	Medium
Electrical charge	SDS-PAGE	Very low	High	High	Medium
	Electrofocusing	Very low	High	High	Medium
	Ion exchange chromatography	Medium	Medium	Medium	Medium
Specific interaction with ligands	Affinity chromatography	Medium-low	Low	Very high	High
Surface hydrophobicity	Reverse phase chromatography	Medium	Medium	High	High
	Hydrophobic interaction chromatography	Medium	Medium	Medium	Medium

Фильтрация



диафильтрация



ульфильтрация



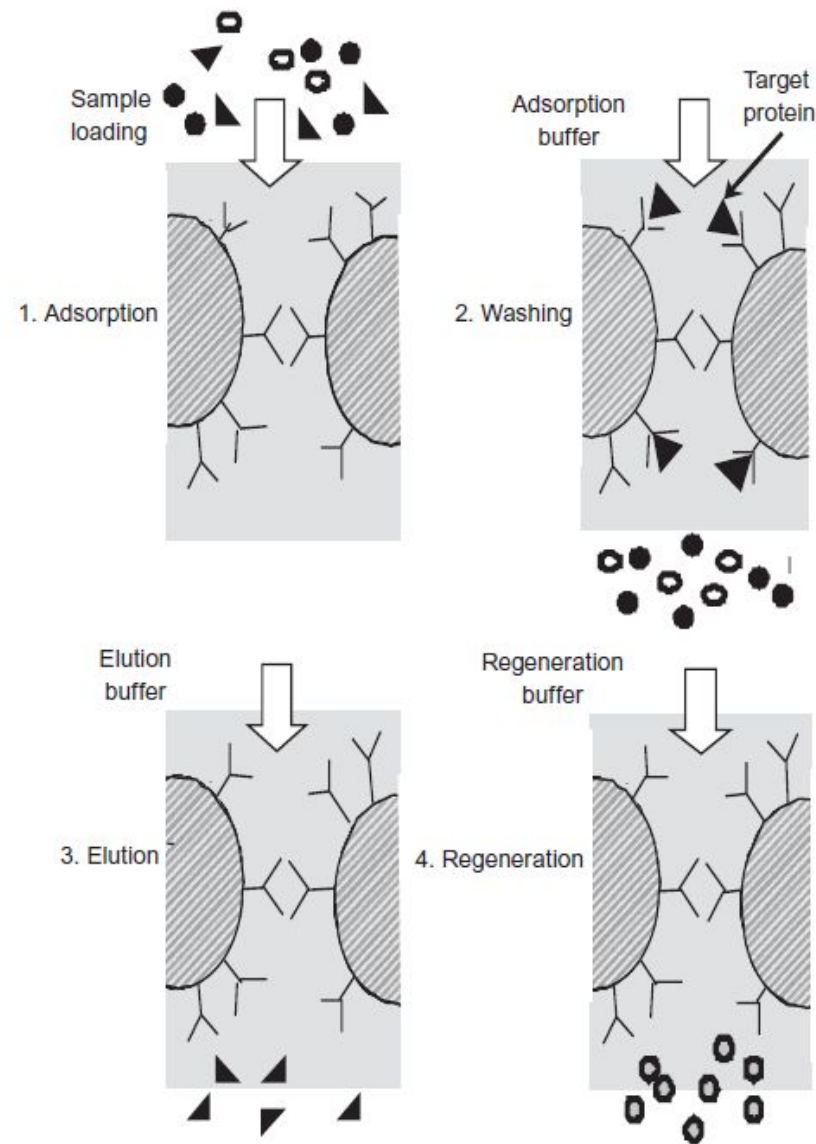
Хроматография

Аффинная хроматография

Хроматография гидрофобных взаимодействий

Обратно-фазовая хроматография

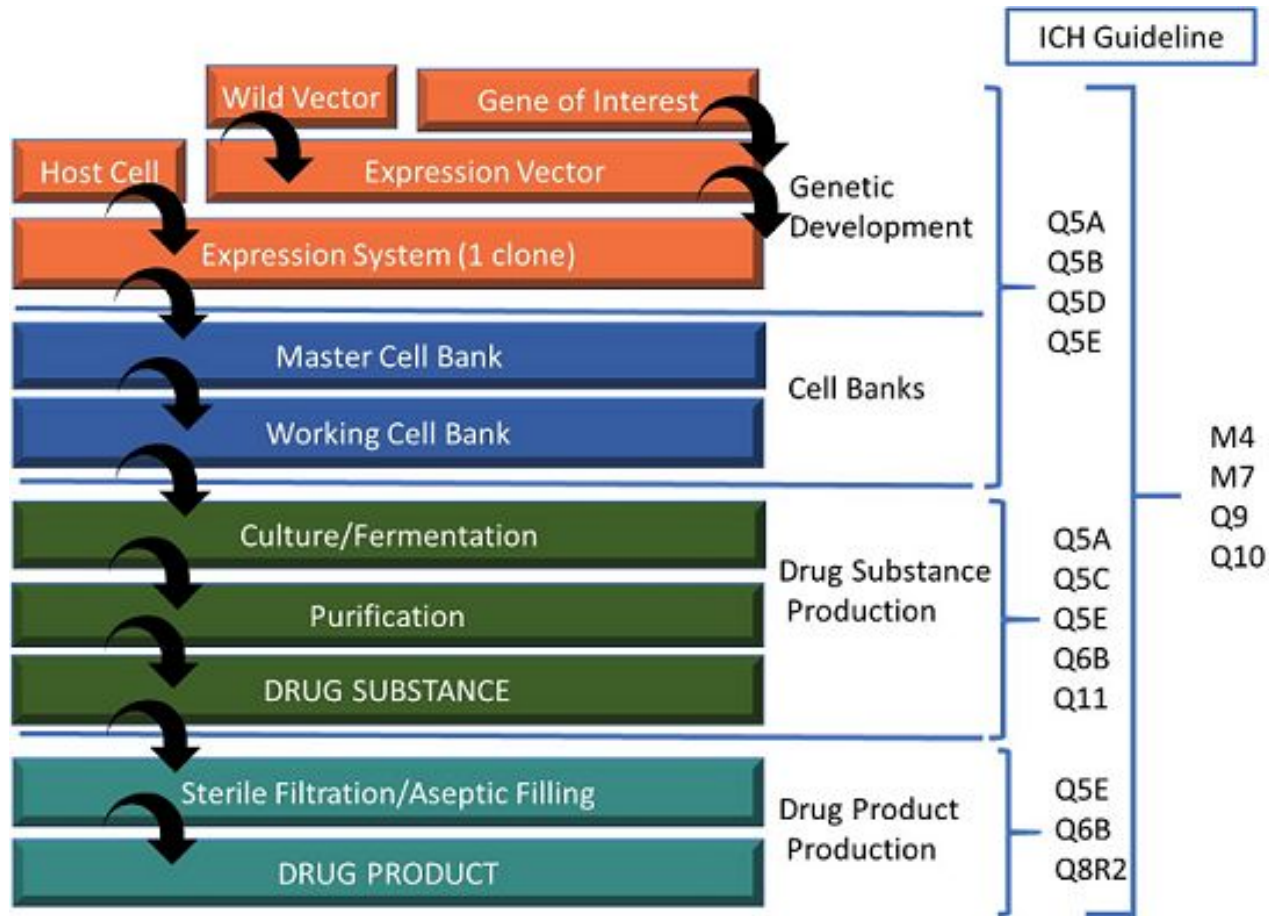
Ионообменная хроматография



Formula	Group
Strong anion exchangers	
$-\text{CH}_2\text{N}^+(\text{CH}_3)_3$	Trimethylaminomethyl (TAM)
$-\text{C}_2\text{H}_4\text{N}^+(\text{C}_2\text{H}_5)_3$	Triethylaminoethyl (TEAE)
$-\text{CH}_2\text{N}^+(\text{CH}_3)_3$	Quaternary amine (Q)
Weak anion exchangers	
$-\text{C}_2\text{H}_4\text{N}^+\text{H}_3$	Aminoethyl (AE)
$-\text{C}_2\text{H}_4\text{N}^+\text{H}(\text{C}_2\text{H}_5)_2$	Diethylaminoethyl (DEAE)
Strong cation exchangers	
$-\text{SO}_3^-$	Sulfonate (S)
$-\text{CH}_2\text{SO}_3^-$	Sulfomethyl (SM)
$-\text{C}_3\text{H}_6\text{SO}_3^-$	Sulfopropyl (SP)
Weak cation exchangers	
$-\text{COO}^-$	Carboxy (C)
$-\text{CH}_2\text{COO}^-$	Carboxymethyl (CM)



ICH Guidelines



- Q1:-Stability testing
- Q2:-Analytical validation
- Q3:-Impurities
- Q4:-Pharmacopoeias
- Q5:-Biotechnological products
- Q6:-Test procedures acceptance criteria
- Q7:-Good manufacturing practices
- Q8:-Pharmaceutical development
- Q9:-Quality risk management
- Q10:-Pharmaceutical quality system



Спасибо за внимание!