

# Downstream processing

Instrumentation through innovation

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SPECIAL  
POINTS OF  
INTEREST:

Perfusion chromatography

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- Membrane electrophoreses

## A bio-technology news letter

In any reaction engineering process, the separation of useful products from the rest of the media is of utmost importance. Bio-engineering process is no exceptions for this general rule. Always the down stream processing is the rate-limiting step. At the same time product cost is also dictated by the process. The purity of the product, the waste dispersal methodology and the over all process efficiency are the factors that contribute to the successes of Bioprocesses.

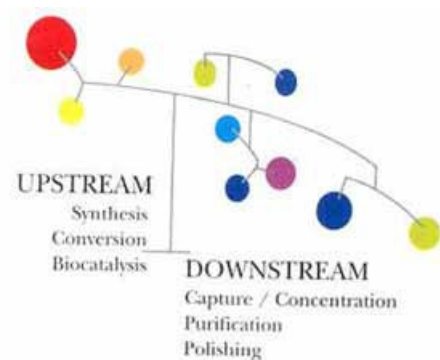
Cell culture has achieved remarkable up-stream efficiencies, to the tune of thirty or better times cell density, ten time higher cellular productivity and fermentation times spans that are three or more times longer. During this span the protein titers have increased from about 10 mg/lit to several grams per liter quantities

At the same time the down stream processes are not developed to the same extent. The researcher is tied down to the age-old practices of protein separation etc that consume time and money. Also the waste disposals pose bigger problems due to stringent laws of environmental protection agencies/ Govt. bodies. The same old time tested methods which are reliable but time consuming are to be revisited and revitalized. Same amount of effort is to be put to reshape the technology for the modern requirements.

At the same time the industrial Bio-processing, (i.e.) extraction, precipitation crystallizations of technical enzymes is vastly improved.

If these processing steps, with the needed modifications are employed, bioprocess will be better off.

All the big players of the field of separation, Zeroed to the twin technologies of (a) membrane electrophoreses or cross flow filtration with electrodes to facilitate charge separation, & secondly crystallization. It appears membrane separation may ultimately succeed since what is tackled in the process is, the impurities are held up at the membrane through adsorption. Since selective adsorption of the impurities that are a minor constituents is more practical and can simultaneously treat large volumes



Similarly absorbers are currently used to separate the process that is known as polishing step. At present DNA, Viruses-endo-toxins, residual protein A and even protein aggregates are separated by adsorption. At the end of several repeated uses the systems can be discarded since regeneration and validations technologies are cumbersome and do not work out economical.

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Most of the separation technologies adapted by the bioengineering is three decades old. Even FDA is encouraging drug manufactures to adapt new process analytic technology (PAT). However the chromatography systems are not ready to take over, HPLC based analytical platform for process chromatography though offers solution is yet to prove commercial viability. Some research in the field of resins for high productivity is going on Introduction of UNO sphere, high flow rate, high capacity resin by Bio-rod, greatly, appreciated by one and all.

Biorad had also developed ceramic hydroxyapatite and ceramic fluoroapatite (CHT and CFT), which are more resistant to pH with longer, resins lifetime. It is likely that Biorad will introduce profanity resin line ...

**"Profanity 1 MAC"** This can be used for protein and Virus purification.

GE Healthcare has introduced a new high capacity quaternary ammonium anion exchange resin under trade name capcto™ Q. This resin has a rigid matrix and can with stand wider flow velocities, bed heights and sample viscosities. This will help in achieving lower processing times and bigger columns with longer bed heights, less dilution and high flows, ideal for production processing.

The market growth is driven by the biotherapeutics proteins. Monoclonal antibodies are growing at the rate of 25-28% per year. This simulates all the segments of bioprocesses including fermentation and chromatography separations.

In fact now more customers are aware that purification is the real bottleneck. Research in identifying and reducing the process bottlenecks and processing time is being promoted in a big way by funding agencies and Government bodies.

Presently perfusion chromatography is being used for separation of protein. Rigid porous 50-micron particles with high throughput and resolution are employed in perfusion chromatography. Most of the customers need better resin that have higher capacity and higher throughput.



A Word of caution is to be remembered in the field of separations. Simply increasing capacities will not achieve higher through puts. Parameter optimization is an art of compromise and only when all right choices are made the productivity will improve.

**In our next issue:**  
Making drug discovery a career

We also offer projects for biotechnology students in reactor design, process control, fermentation, DSP,



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