XPURE
innovative continuous chromatography

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Designing a Chromatography Process

There are quite a few excellent textbooks that cover the design of separation processes, this also applies to adsorption chromatography processes, the subject of this blog. The majority of these books, however, deal with the design process from a rather academic approach. Most of the time, too little attention is paid to the specific product requirements and market or client specifications to be complied with.

Moreover, most often the design information is not readily available.

The reality is a bit more complicated and the majority of information required for designing an SMB operation has to be derived from column tests, estimated or correlated.

BASICS OF DESIGN PROCEDURE

Any design procedure is an iterative process, it starts with some essential considerations

1. Can the (target) product be purified
2. Is it feasible and thus easier, to design an adsorption process for removal of impurities
3. Is fractionation a better alternative when dealing with poor binding properties of either the target molecule or impurities
4. Is conversion of the target molecule the case, for example dealing with acidification of organic acid conjugates.

Next items to thoroughly think about are feed properties, process capacity, and product requirements.

1. Plant factor. A continuous adsorption process should be designed as full continuous 24h/day. If the upstream process is a (semi-)batch process, one should base the design capacity on a time-average feed production rate
2. Maximum feed capacity, it is noted that a continuous adsorption process can be easily be downrated by simply slowing down the cycle time and related feed, wash and buffer consumption rates. So it’s best to design and configure a system based on the maximum (future) expected feed capacity
3. Feed properties, like density, viscosity, stability, particulates, and temperature. Mass transfer kinetics are influenced by temperature and viscosity, and also by flow velocity in the resin bed. Particulates may disturb the bed stability and flow

distribution and should, therefore, be avoided

4. Last but certainly not least, requirements like product purity, yield and concentration are of tremendous influence on the design. Concentration has a substantial effect on further downstream process costs, e.g. evaporation/crystallisation and drying.
   In general, in case it is required to attain purity levels beyond 98% the costs of processing will exponentially grow

SEQUENCE OF THE DESIGN PROCEDURE

Iterating to an optimal process design, it is important to look at:

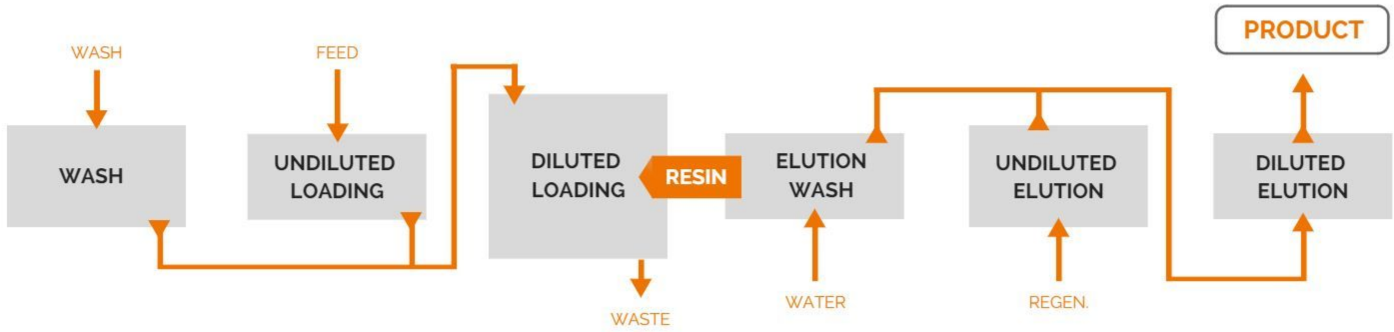
1. Process chemistry, this is the resultant of combining feed and buffer (eluent) properties, with an appropriate resin, having the best adsorption performance
2. Process parameters are resin adsorption capacity and other resin manufacturer data, flow velocity, pressure drop (in particular the packed resin bed), equilibrium behaviour between the target molecule and the resin particle.
3. Kinetic parameters, these can be derived from literature or column tests. In the process model calculations, a 2-film model featuring diffusion from bulk to film, respectively from liquid film to stationary phase film has been applied. The model also contains correlations from published experimental data

For 2 and 3 most of the time good and reliable information can be obtained by column tests. Often an industrial scale batch chromatography process already is in place which data could be of tremendous value when it is considered to change to a continuous process.

PROCESS DESIGN

A conceptual SMB configuration contains a number of zones. A zone is defined as a part of the overall process flow diagram in which the flows through all applicable columns are equal.
The conceptual configuration displays these zones in terms of a block diagram with the interconnections between the zones.
The figure below shows an elementary conceptual design for the most simple bind & elute chromatography system. It contains 4 zones:

1. Adsorption
2. Elution
3. Adsorption wash
4. Elution rinse



In the conceptual design phase, the following zone may be considered

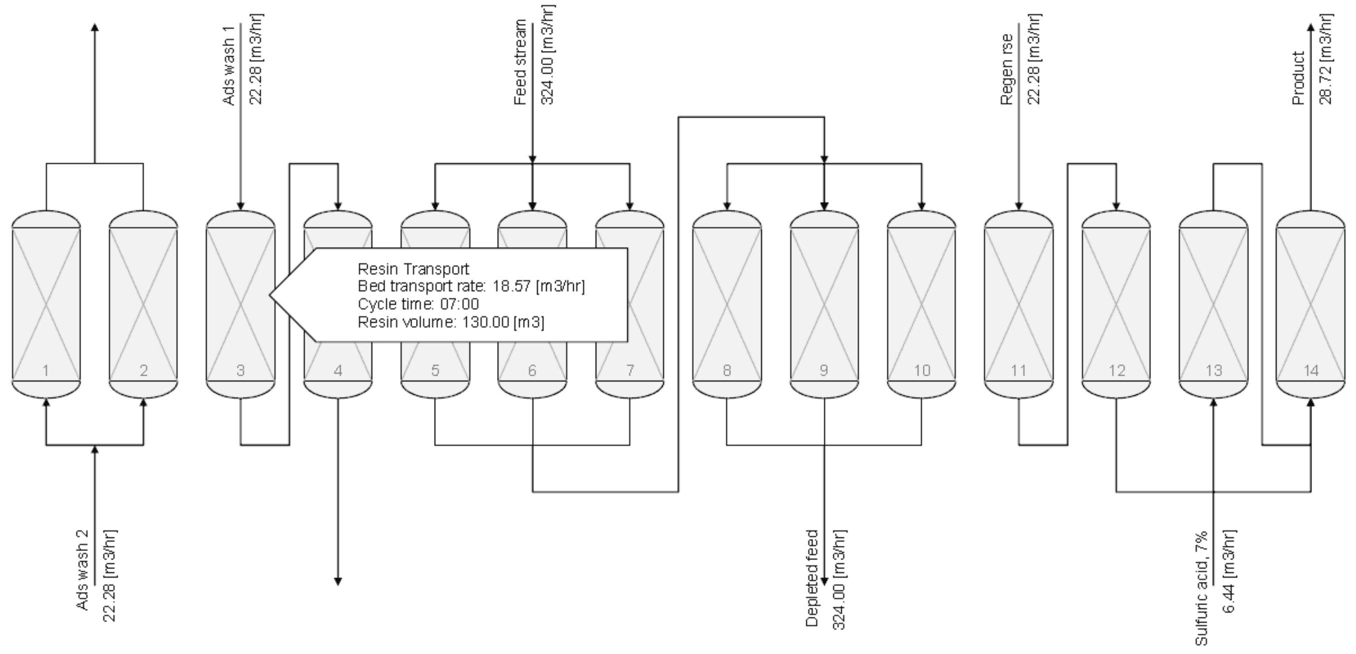
- To apply diluted adsorption section (same applies to elution zone). The advantage of adsorption wash recycle is that entrained feed liquor will be recovered and moreover it saves an additional side-stream. It should be noted that the sorption isotherm must show adequate binding capacity in the lower feed concentration regime to make diluted adsorption advantageous.
- Entrainment rejection (upstream) adjacent to either adsorption or elution zone. This enhances the depleted feed or the elute (often containing the product) effluent concentration
- Regeneration zone. This may be necessary to bring back the IX resin into the adsorption condition. Or, in other cases, to remove residual impurities after the elution.
- Equilibration zone. After a regeneration or elution, the equilibration buffer brings the chromatography resin into the right condition to resume adsorption
- Upflow wash zone in case the feed solution contains particulates. An upflow wash should, therefore, be considered after the adsorption wash step.

An SMB configuration displays how the sequence of process steps is included in the SMB process cycle. The concept doesn't specify the number of columns (per zone) yet. This is one of the essential parameters that needs to be iterated in the detailed design process further on.

This iterative process concludes with a detailed design featuring:

- Performance indicators: yield, purity, and recovery
- Hydraulic indicators like pressure drop and flow velocities in both resin vessels and connecting piping.

To conclude the figure below shows a typical process flow diagram for a bind and elute IX-chromatography system. It features a diluted regeneration zone as well as additional upwash to remove any particulates that may be trapped in the feed adsorption zone.



XENDO

XPure Designer™
Version 0.20 (July 2014)

End user :	Client-end user
Project :	Exemplary
Date :	<Date of this paper>
Version :	1.00
Designer :	PdW

Column length :	1.80 [m]
Column diameter :	2.60 [m]
Bed height :	1.75 [m]
Bed volume :	9.29 [m3]
Total resin volume :	130.00 [m3]