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The V_{max} Nomograph

A Quick Reference Tool to Estimate Filter Sizing

The V_{max} technique has been widely used to successfully describe many of the filtration processes in the biopharmaceutical industry. This document provides a quick reference chart to estimate filter sizing requirements given knowledge of typical performance parameters for an application.

Contributions to filter sizing arise from both filter capacity limitations (V_{max}) and flow-time (J_i, t_B) considerations. Scale down filtration studies using data on Volume vs. time, lead to the calculation of the sizing parameters V_{max} and J_i. These parameters, along with the design requirements (V_B and t_B), allow us to estimate filter sizing for a given application.

V_{max} Equation 1

$$\frac{A_{min}}{V_B} = \underbrace{\frac{1}{V_{max}}}_{\text{Capacity}} + \underbrace{\frac{1}{J_i \times t_B}}_{\text{Flow-time}} \quad (1)$$

Key to Equations

A	filtration area (mm^2)
V	process volume (L)
V_{max}	maximum capacity (normalized) that can be filtered at time infinity (L/m^2)
J_i	initial volumetric (normalized) flow rate (L/m^2 min.)
t_B	process time (min.)

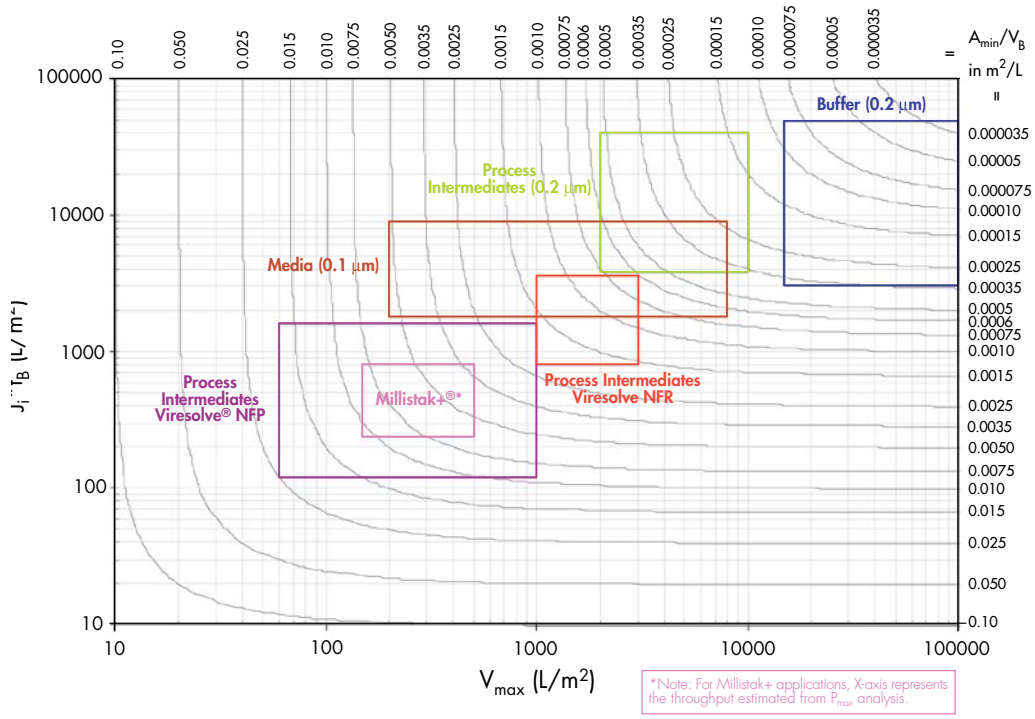
Frequently, we need to 'ball-park' the area requirements for a typical process step, or assess the impact of process (V_{max}, J_i) or design (V_B, t_B) parameters on filter sizing. The nomograph in Figure 1 is a handy reference chart, with an ability to rapidly estimate filter area requirements for various capacity, flow, time combinations.

The nomograph represents a family of constant A_{min}/V_B curves, which cover the range typically encountered in filtration applications. The X – Y axes for the nomograph are V_{max} and J_i t_B respectively.

Application experience allow for a better estimation of sizing parameters such as V_{max} or J_i; once these parameters are chosen, an estimate of the specific area for the application ie: A_{min}/V_{Batch} may be determined from the nomograph.

Note: the areas designated A_{min} is the minimum area required to complete filtration at the base conditions (time, volume, pressure) and does not include safety factors to account for process variability or process expansion.

Figure 1: A Nomograph



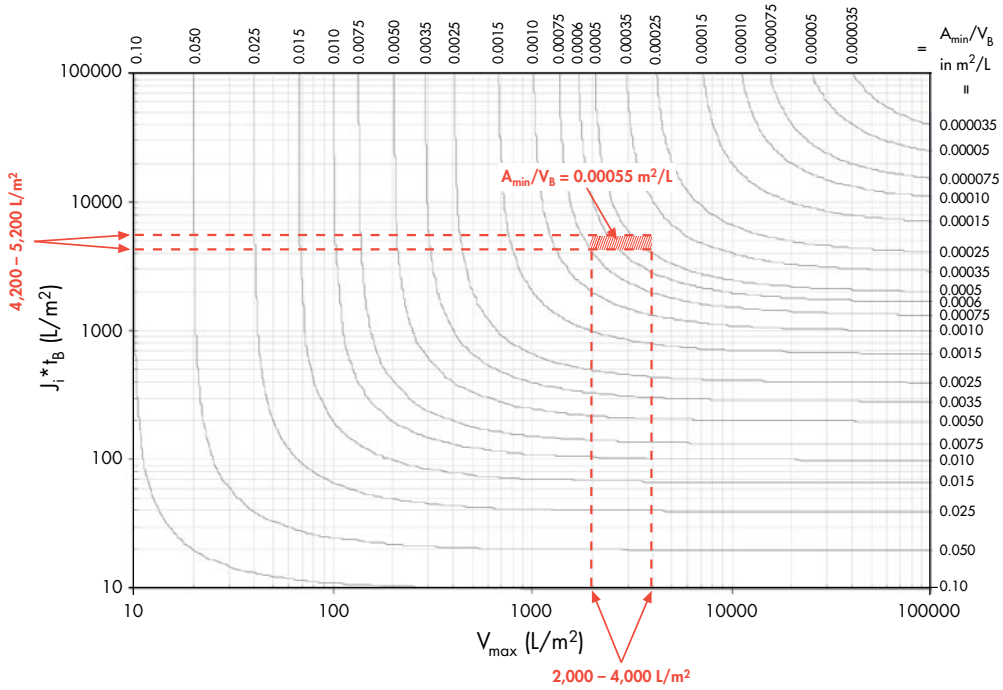
Example: Serum Free Media

Let us take the filtration of prefiltered serum free media through Durapore® 0.1 µm filters (CVVL).

- Typical filtration pressure for this application is 15 psi.
- Average normalized flux is known to be between 140 – 180 LMH/psi.
- Typical Vmax ranges between 2,000 – 4,000 L/m^2.
- Process time is assumed to be 2 hours for the initial estimate.
- $J_i \times t_B$ = 140 – 180 LMH/psi x 15 psi x 2h = 4,200 – 5,400 L/m^2.

Figure 2 shows the graphical method to interpolate the specific area requirements.

Figure 2: Example of Nomograph Use



*Proceed vertically up the V_{max} axis, at the appropriate V_{max} value (For this case 2,000 – 4,000 L/m^2) then do the same on the horizontal J_i*t_B axis (140 – 180 LMH/psi x 15 psi x 2h = 4,200 – 5,400 L/m^2). The specific area, A_{min}/V_B, may be determined from the location of the intersection point of these two lines on the A_{min}/V_B curves. For this case, the A_{min}/V_B may be estimated to be 0.00055 m^2/L. This implies that to filter a 10,000 L batch, the filtration area requirement may be calculated as:*

$$A_{min} = 10{,}000 \text{ L} \times (0.00055 \text{ m}^2/\text{L}) = 5.5 \text{ m}^2$$

which translates into a 3 x 30-inch cartridge configuration.

To facilitate the use of the nomograph, it is useful to review key sizing parameter ranges such as V_{max} and J_i for specific applications and filters. Table 1 summarizes parameters for a number of commonly encountered solutions:

Table 1: Recombinant Proteins

List of the typical streams encountered in recombinant protein processing with key sizing parameters.

Fluid Type	Prefiltration	Final Filtration	Final Filter Application	V_{max}, L/m²	J_i, LMH/psi
Serum Free Media	No Prefiltration	Durapore 0.1 µm PVDF filter (CVVL)	Sterile and mycoplasma reduction filtration	200 – 400	140 – 180
		Double-layer Millipore Express® SHR 0.1 µm PES filter (CVEP)	Sterile and mycoplasma reduction filtration	500 – 3,000	300 – 400
	Polysep® II 1.0 + 0.2+ 0.1 µm filter (CGW1)	Durapore 0.1 µm PVDF filter (CVVL)	Sterile and mycoplasma reduction filtration	2,000 – 4,000	140 – 180
		Millipore Express SHR 0.1 µm PES filter (CVEP)	Sterile and mycoplasma reduction filtration	2,000 – 8,000	300 – 400
		Durapore 0.1 mm PVDF filter (CVML)	Sterile and mycoplasma reduction filtration	800 – 1,000	80 – 90
		none		1,000 – 6,000	400 – 500
	Polysep II 1.0 + 0.2 + 0.1 µm filter (CGW3)	Durapore 0.22 µm PVDF filter (CVGL)	Sterile Filtration	5,000 – 10,000	250 – 300
Clarified CHO Cell Culture	Prostak® 0.65 µm MF Cassette (SK2P) or Centrifuge followed by Millistak+® HC (A1HC)	Durapore 0.22 µm PVDF filter (CVGL)	Sterile Filtration	1,500 – 3,000	250 – 300
		Double-layer Millipore Express SHC 0.5 + 0.2 µm PES filter (CHGE)	Sterile Filtration	2,000 – 5,000	650 – 700
Process Intermediates	No Prefiltration (Stream Dependent)	Durapore 0.22 µm PVDF filter (CVGL)	Sterile Filtration	2,000 – 4,000	250 – 300
		Double-layer Millipore Express SHC 0.5 + 0.2 µm PES filter (CHGE)	Sterile Filtration	4,000 – 10,000	650 – 700
		Viresolve NFR filter, > 50 nm (CZRV)	Large Virus Filtration	1,000 – 3,000	20 – 30
		Viresolve NFP filter, > 20 nm, (CVPV)	Small Virus Filtration	60 – 1,000	3 – 8
Buffers	No Prefiltration	Durapore 0.22 µm PVDF filter (CVGL)	Sterile Filtration	>>10,000	350
		Millipore Express SHF 0.2 µm PES filter (CGEP)	Sterile Filtration	>>10,000	800

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