

Filter Sizing Methods

■ For normal flow filtration (NFF) applications

Filtration Systems for normal flow filtration (NFF) processing applications generally consist of a series of filter cartridges, with each cartridge in the series protecting and extending the life of the next filter cartridge. Choosing the correct type and combination of filter cartridges for each application will lead to an optimized filtration train and reduced overall filtration costs. Due to many different types of feed solutions and filter types, choosing the best filter train offers a unique challenge.

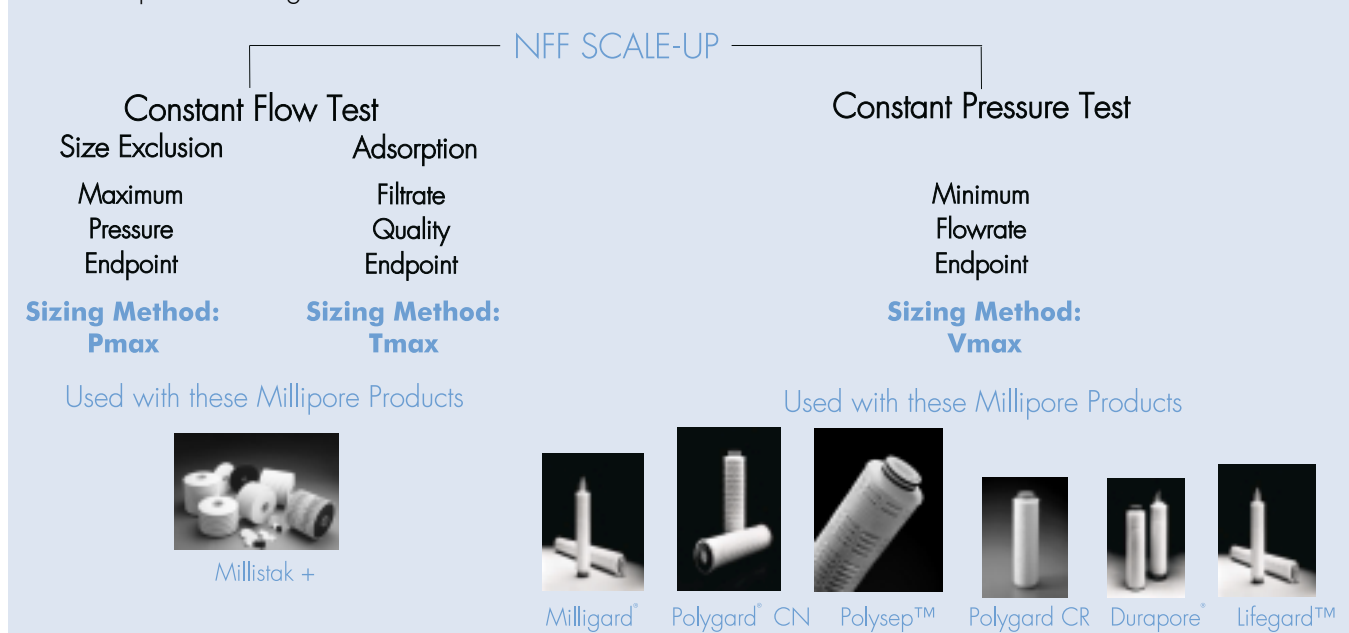
Feed solutions, such as LVP's, water, and buffers, exhibit very predictable behavior. Millipore has significant experience in these applications and has developed a selection guide to

help select the correct filter for a specific application. For other feed solutions that are not as predictable such as cell cultures, lysates, and plasma, trials must be conducted to accurately predict filter performance.

Millipore uses Vmax™, a constant pressure test, for the selection and sizing of filters with unpredictable feed solutions. While Vmax is the preferred sizing technique for the majority of Millipore products, recent work indicates that when using a charged adsorptive depth filter such as the Millistak+™, a constant flow test provides a more accurate result. Based on this work, Millipore has developed two constant flow sizing techniques, Pmax™ and Tmax™, that can be used for selecting and sizing Millistak+ depth filters. When distinguishing among Vmax, Pmax, and Tmax, the type of particle-filter media interaction that occurs during the filtration step determines which sizing method to use. This application brief will explain each of these sizing techniques and discuss how to use each method with the appropriate filter materials.

SIZING METHOD	METHOD
Volume Endpoint	Vmax
Pressure Endpoint	Pmax
Turbidity Endpoint (<i>Indicates filtrate quality</i>)	Tmax

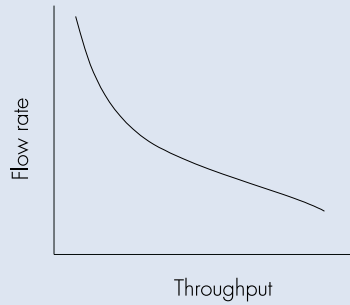
The roadmap to NFF sizing can be described as follows:



The first decision encountered in NFF is the type of test to perform. Shown here are the behaviors observed in the different tests and the types of filters that each test would typically be used for.

Constant Pressure Test: Size Exclusion

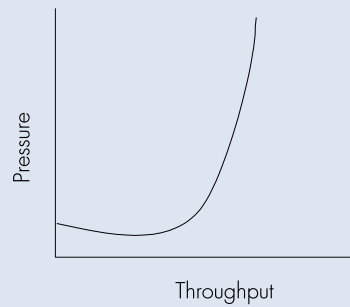
- Size Exclusion is primary mechanism of particle retention
- Measure decrease in flow as a function of throughput
- Endpoint determined by flowrate or volume
- Vmax method



Milligard

Constant Flow Test: Size Exclusion

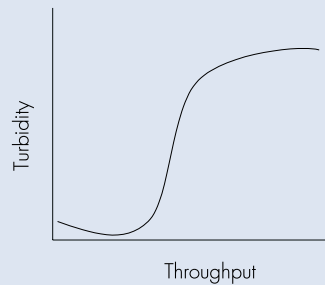
- Size Exclusion is primary method of particle retention
- Measure increase in pressure as a function of throughput
- Endpoint determined by pressure loss
- Pmax method



Millistak+

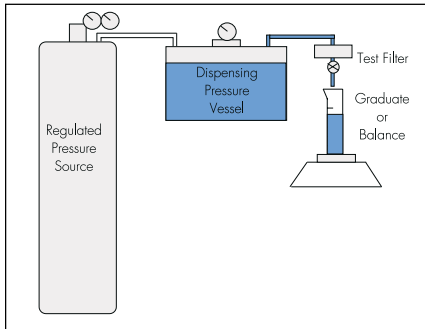
Constant Flow Test: Adsorption

- Adsorption is method of particle retention
- Measure decrease in filtrate quality as a function of throughput
- Endpoint determined by desired filtrate quality
- Tmax method

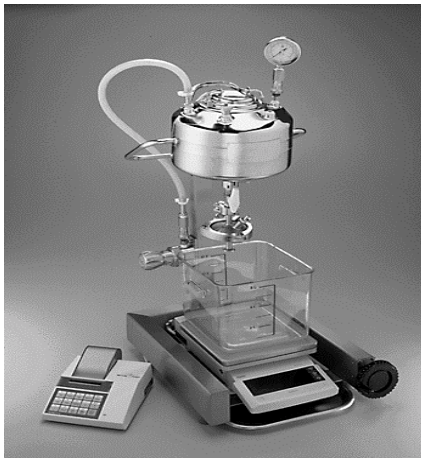


Millistak+

Constant Pressure: Vmax



Vmax Setup



Vmax Test Stand, Catalogue No. MSDVMAX01

Vmax is the preferred test method for a constant pressure test. In a Vmax test, the challenge solution is filtered through the test device and cumulative volume is recorded as a function of time (typically for 10 minutes) at a selected differential pressure, usually 5-10 PSID. If a linear plot of t/v vs t is obtained, it is assumed the solution follows the gradual pore-plugging model. Vmax can then be calculated as the inverse slope of this graph. Vmax represents the maximum volume of fluid that will pass through a filter before it is completely plugged. The advantages of this method are the smaller volumes of process fluid required and short testing times compared to traditional flow decay testing. These advantages over traditional flow decay testing help facilitate fast and efficient filter media selection. The disadvantage to Vmax is

that it does not accurately predict sizing when the fluid being tested does not follow the gradual pore-plugging model.

Vmax Sizing Method Summary Advantages

- experimentally determine filter/fluid performance
- provides basis for filter train selection
- allows for rapid testing relative to traditional flow decay
- requires smaller process fluid volume

Disadvantages

- only applies to Gradual Pore Blocking mechanism

Uses

- Milligard, Polysep, Lifegard, Polygard-CN, Durapore

Vmax Sizing Spreadsheet

Millipore has a sizing spreadsheet available to assist with Vmax calculations.

- Plots Data
- Sizing Calculations
- Sizing Recommendations
- Report of data analysis

Examples of spreadsheet output:

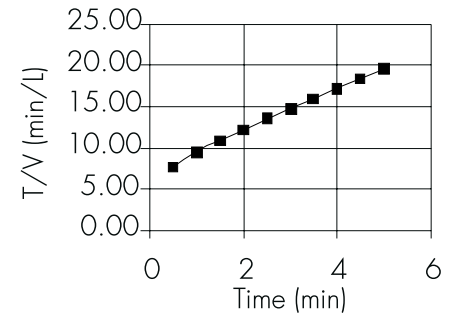
1. Typical Vmax Data

Time (min)	Volume (L)	Time/Volume (min/L)
0.5	.065	7.7
1.0	.106	9.4
1.5	.138	10.9
2.0	.164	12.2
2.5	.185	13.5
3.0	.203	14.8
3.5	.219	16.0
4.0	.232	17.2
4.5	.245	18.4
5.0	.256	19.5

2. Vmax Calculations

Slope: 2.45 L ⁻¹
Intercept: 7.20 min/L
Corr.Coefficient: .999
Vmax: .408 L

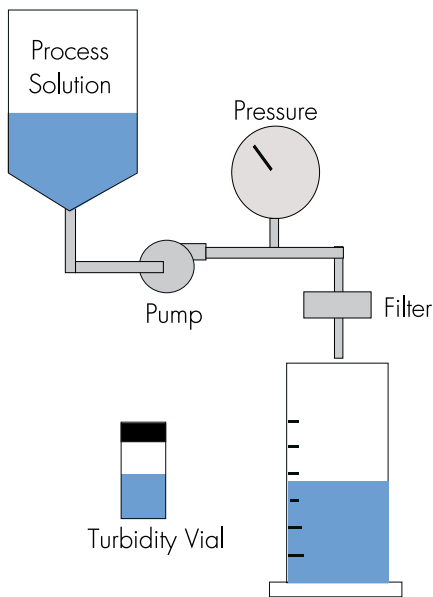
3. Vmax Graph



Constant Flow: Pmax

When a constant flow test is performed and size exclusion is the primary method of particle removal, Pmax is the preferred test method. The capacity of the filter is determined by a pressure endpoint. The Pmax sizing method involves determining the filter resistance to flow as a function of throughput. Based on these two parameters, filter sizing can then be easily calculated in the Pmax sizing spreadsheet. The advantages to this method are that it provides a basis for filter train selection and is independent of plugging model. The main disadvantage to this method is that it requires potentially longer test times and larger test fluid volumes.

Constant Flow Test



Pmax Sizing Tool Summary

Advantages

- experimentally determine filter/fluid performance
- provides basis for filter train selection
- independent of plugging model

Disadvantages

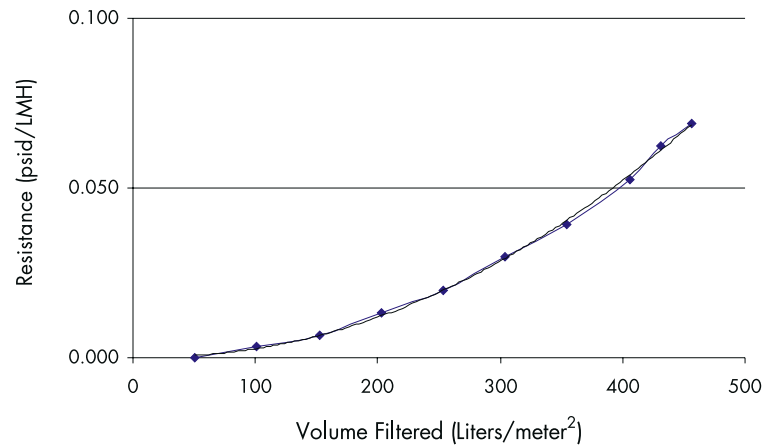
- requires longer test times close to process time

Uses

- Polygard CR
- Millistak+

Examples of spreadsheet output

1. Plot of resistance vs. throughput



2. Sizing information

Cartridge Selected	# Cartridges Required	Housing Sized Selected	# Housings Required	Calculated Safety Factor
16 Stack - 16 in	3	3 High	1.0	1.3

Pmax Sizing Spreadsheet

Millipore has a sizing spreadsheet available to assist with Pmax calculations.

- Plots Data
- Sizing Calculations
- Sizing Recommendations
- Reporting features

Constant Flow and Adsorption: Tmax

When a constant flow test is being performed and adsorption is the primary method of particle removal, Tmax is the preferred test method. Typically, these applications will have a large population of small particles. The small particles do not block the filter pores and are retained due to an electrostatic attraction to the charged areas on the filter. When there are no more active adsorptive sites available, particles smaller than the nominal micron rating of the filter can then readily pass through into the filtrate, decreasing filtrate quality. This filtrate quality change is measured using turbidity. The Tmax method involves measuring turbidity as a function of throughput, selecting the desired endpoint for filtrate quality, and then determining process parameters. The advantages to this method are that it provides a basis for filter train selection and allows sizing to be done when adsorption is the primary method of particle retention. The disadvantage is that the method requires potentially longer test times and large test fluid volumes. It would be primarily used in Millistak+ applications such as cell debris removal after a centrifuge or after a TFF clarification step.

Tmax Sizing Summary

Advantages

- experimentally determine filter/fluid performance
- provides basis for filter train selection
- independent of plugging model

Disadvantages

- requires longer test times close to process time

Uses

- Millistak+ applications
 - After TFF Filtration
 - After centrifuge

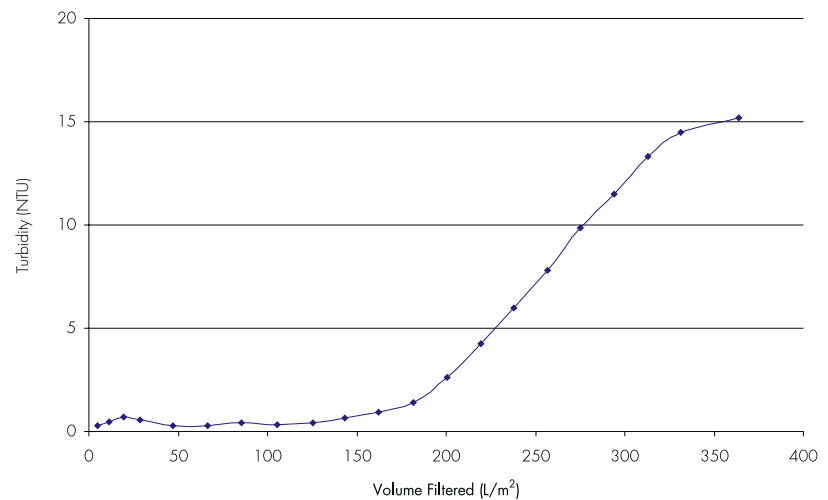
Millipore has a sizing spreadsheet available to assist with Tmax calculations.

Tmax Sizing Spreadsheet

- Plots Data
- Sizing Calculations
- Sizing Recommendations

Examples of spreadsheet output

1. Graph of Typical Tmax Data



2. Output of sizing data

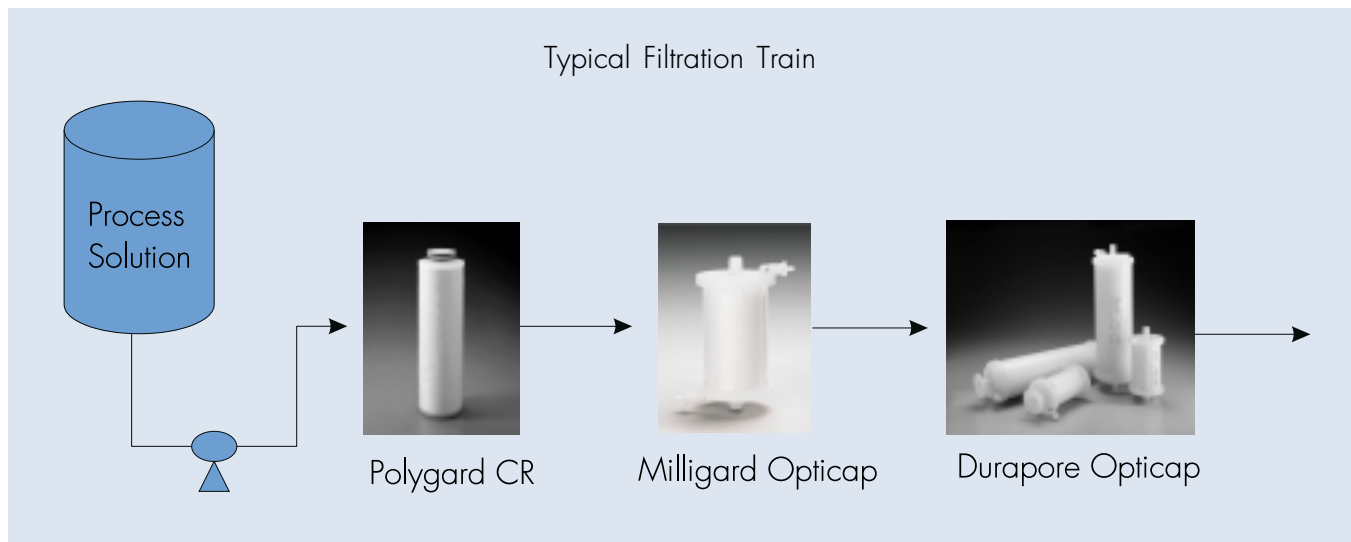
Cartridge Selected	# Cartridges Required	Housing Sized Selected	# Housings Required	Calculated Safety Factor
16 Stack - 16 in	3	3 High	1.0	1.3

Conclusion

When using any of the sizing tools discussed, considering a few key issues before testing will ensure a more useful test. The first issue is to understand the downstream goal of the filtration train. The overall objectives of the test can then be developed with this goal in mind. It is important to consider how the objectives will affect the test selection. If the goal of the test to protect a sterile 0.22 μm Durapore using a surface filter, a constant pressure test, such as Vmax, might be needed. However, if the objective is to

remove cell debris from a reactor process stream utilizing a depth filter, a constant flow test such as Pmax might be selected. Understanding the objective of the filtration allows the correct test to be used. Similarly, it is important to determine what the critical variables are in the separation so they can be accurately monitored. Once the test objectives and critical variables have been identified, developing a preliminary filtration plan can make the testing much more efficient and less cumbersome.

Using the Vmax, Pmax, and Tmax sizing tools in NFF can help produce a predictable initial design. It is important to note that while these methods are useful in obtaining preliminary sizing information, they are not a substitute for a well-designed process simulation at the pilot scale. When these sizing tools are combined with a pilot scale simulation, any application can be optimized.



To Place an Order or Receive Technical Assistance

For additional information call your nearest Millipore office. In the U.S. and Canada, call toll-free 1-800-MILLIPORE (1-800-645-5476). In the U.S., Canada and Puerto Rico, fax orders toll-free 1-800-MILLIFX (1-800-645-5439). On the Internet <http://www.millipore.com>, E-mail: tech_service@millipore.com

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