A QUICK GUIDE FOR MEMBRANE SELECTION IN TANGENTIAL FLOW FILTRATION

Ruth Ordóñez, Ph.D.
Downstream Application Specialist

CONTACT DETAILS

knowledgehub@bionet.com
www.bionet.com

The most common membrane modules used in the Biotech industry for Tangential Flow Filtration (TFF) are cassettes, hollow fiber and ceramic membranes. Each membrane type has certain characteristics *(see Table 1)* in terms of batch volume, sensibility to and with product type, and its own lifetime, that makes it more or less suitable for a specific broth or application.

When selecting the most suitable membrane module, we must focus on two main aspects. On one side, we have to characterize the suspension/ solution where our product of interest is contained in. On the other side, we need to define the application or filtration goal.

Membrane module	Advantages	Drawbacks
Ceramic	• Resistant to solvents • Extreme pH (0–14) • Long lifetime • High tolerance to suspended solids and viscosity	• Low m^2/volume • Fragile • High energy consumption • Not gentle for the product
Hollow fiber	• High m^2/volume • Very gentle with the product	• Low tolerance to suspended solids and viscosity • Short lifetime • More limited to solvents
Cassettes	• High m^2/volume • Higher fluxes than hollow fibers • High protein concentration	• Low tolerance to suspended solids and viscosity • Not gentle for the product • More limited to solvents

Table 1. Advantages and disadvantages of membrane modules

CHARACTERIZATION OF THE SUSPENSION/SOLUTION

The main parameters that we shall consider for this characterization of the suspension/solution are:

Shear rate sensitivity

Some cells and biomolecules exhibit low mechanical resistance and may be damaged by shear exposure. One way that we have in order to manipulate shear stress is to control the tangential flow over the membrane surface. Depending on the membrane type, tangential flow is translated into cross flow velocity for ceramic (2–5 m/s), shear rate for hollow fiber (2000–10000 s^{-1}) and cross flow feed for cassettes (4–35 L/min/m^2). The higher these values are, the more stress is applied to the product.

Hollow fiber is the preferred option if the product needs to be handled gently, by limiting the shear rate up to 2000–4000 s^{-1}.

pH

This parameter gains importance in the process of protein concentration, as it impacts in their solubility. If pH is not controlled, proteins can aggregate and precipitate on the membrane surface, enhancing fouling and reducing recovery yields. All the membranes modules can operate at normal pH ranges (pH 2–11) but if extreme pH is required (pH <2 or pH >11) ceramic membranes are the best option.

Viscosity and/or suspended solids content

The more viscous a broth is and/or the more suspended solids it has, the greater the pressure drop along the membrane is, which can limit the filtration process. In order to reduce the impact of pressure loss, all the membranes have different configuration possibilities to choose from. For example, in the case of multitubular membranes (ceramic and hollow fiber) for which several channel diameters are available, the higher the diameter the more viscosity and/ or suspended solid content is allowed. In the case of hollow fiber, apart from lumen diameter, membrane effective length has to be also bounded. In this case, selecting the shortest module makes sense for higher viscosities and/ or suspended solids content. Instead of channel diameter or membrane length, cassettes have screens with pass sections of different thickness. The thicker the section is, the more viscosity and solid content can be handled.

FILTRATION GOAL

On the other hand, the best way to define the application or filtration purpose is to pay attention to the location of the product of interest:

Biomass concentration

In this case the target product is the **biomass**. Either because we are interested in the whole microorganism/cell or because our biomolecule is intracellular, we will need to first collect all the biomass and then proceed to a subsequent lysate for the **biomolecules extraction**. In this case it is extremely important to keep the microorganism/cell without any damage until the end of concentration, to avoid undesired premature lysis.

Biomass clarification

In contrast to the previous case, the **product of interest** in this case is **extracellular**, so the biomass must be removed by filtration. In this scenario it is also important to treat the biomass gently to manage an easy-going broth without intracellular material.

Lysate clarification

In this application, treating the product gently is not as important as before because the target product is already "swimming" in the media. However, it is not the same to clarify a **lysate fraction** which has a lot of undesired compounds interacting with our desired component than clarifying an extracellular component (paragraph b). Normally, lysates have a larger fouling capacity and/or present more viscosity, what can complicate the filtration process.

Biomolecules concentration and diafiltration

This would be the cleanest stream compared to the previous ones. This application is where **cassettes** feels more comfortable, although special care has to be taken with the effect of shear stress over protein conformation, as some **proteins** are really affected by this factor. In that cases **hollow fiber** modules take advantage over the others.

DECISION TREE

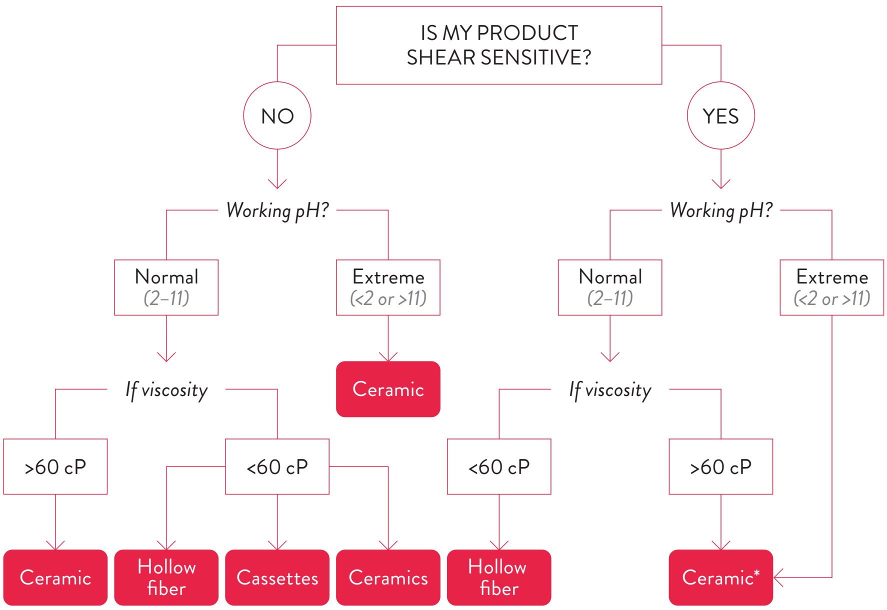
With all the previous information we are ready to build a decision tree that help us decide, from a theoretical point of view, the most recommended membrane type for the different filtration purposes and product characteristics. The heart of this decision tree is the **product sensitivity** to stress derived from the shear during filtration. In addition, we can also take the **viscosity** of the media as a key factor for final membrane screening *(see Figure 1)*.

Sometimes, however, despite making a theoretical study about the broth it is still not clear which membrane we should select. In all that cases, the most sensible way is to compare their performances at lab scale so that we can take a decision based on real experience.

At Bionet we have developed the **M1 TFF system**, an unique benchtop system for R&D, optimization and scale-up studies, since it allows technology screening and real **scalability**. This is possible due to the combination of technological **modularity** (i.e. flexibility) and the presence of leading technology that is also used in industrial environments. In terms of flexibility in the membrane selection space, the M1 TFF has:

- The possibility to work with the three different membrane technology types interchangeably (ceramic, hollow fiber and cassettes) in both the Microfiltration and Ultrafiltration ranges.
- The possibility to integrate membranes from the main leading vendors, also interchangeably.

Figure 1. Decision tree for membrane selection



(*) Too risky. Validate first at lab scale with cross flows between 2–3 m/s.

To get more information about this system, go to: **https://bionet.com/technology/m1-labscale-tangential-flow-filtration-system/**