

concentration is now limited by either the discharge pressure of the pump (around 20

[0002] During concentration of a protein solution, for example, the final
to increase the distance between the screen and the membrane surface.

"suspended" screen consisting of a coarse screen placed between nonwoven spacers
coarse screen and a fine screen. Additionally, some cassettes are available with a
feed streams with low and high viscosity. Cassettes are available generally with a

[0003] The TFF devices are available with different screens to accommodate
pressure drop down the channels between the feed port(s) and the retentate port(s).
of enhanced wall shear stress and eddy promotion. However, they also increase the
The screens are turbulence generators that increase the mass transfer rate because
modules that significantly influence the mass transfer performance and pressure drop.

[0004] Membrane spacers such as screens are an essential part of TFF
becomes higher.

normalized for membrane area it passes through, decreases as solution viscosity
increase of solution viscosity; meanwhile, flux, which is defined by the volume flow
drop from the feed side to the retentate side of the TFF cassettes increases with the
retentate end of the channel. During concentration of a protein solution, the pressure
channel between two membranes causes a pressure drop from the feed to the
macromolecules are retained to the retentate side. The feed flow along the length of
stream through the membrane surface to the filtration side. Particles and
surface of the membrane. An applied pressure serves to force a portion of the feed
macromolecules or proteins. In TFF, the protein fluid is pumped tangentially along the
the clarification, concentration and purification of fluid streams containing

[0005] Membrane-based tangential flow filtration (TFF) cassettes are used for
Background of the invention

viscosity fluids.

(TFF). More particularly, it relates to a feed screen for a TFF device used with high

[0006] The present invention relates to a device for tangential flow filtration
incorporated by reference herein in its entirety.

Patent Application No. 61/528,885, filing date December 8, 2011, of which is

[0007] The present application claims the benefit of priority of U.S. Provisional

HIGH VISCOSITY TFF DEVICE DESIGN

least 20.8 micrometer (5 mil) to 503.5 micrometer (8 mil) above the height of the first rim attached to an outer periphery of the screen, wherein the rim is of a height of at least 20.8 micrometer (5 mil) and the screen having one or more features selected from the group consisting of a width and a thickness between a first upper surface and a second lower surface.

[0012] It is an object of the present invention to provide a screen having a length, as the fibers in the screen.

the effective channel height is also affected by the hardness of the membrane as well as the overmolded screen. Since the screen is embossed into the surface of the membrane, on the overmolded screen or by using a thicker nonwoven as a spacer in a non-circular diameter fiber in the screen, by increasing the thickness of the molded border or rim of the channel hydraulic resistance. One can increase the channel height by using a larger decrease the channel pressure drop by increasing the channel height or reducing the For a given channel length and width (relatively fixed by the cassette design), one can

[0011] A device for the tangential filtration of liquids at high viscosities is taught, better handle high viscosity streams.

[0010] The present invention provides an improved design of TFF devices to Summary of Invention

while maintaining a relatively high mass transfer rate.

viscosities, there is a need to provide a cassette with reduced channel pressure drop

[0009] In order to allow operation to higher concentrations and higher transfer at the high concentration.

"suspended screen design containing a gap," but they also suffer from lower mass pressure drop. Some have a slightly lower pressure drop due to the use of a solutions using a coarse mesh screen. Most have a performance that has a high

[0008] Some of these devices appear to be capable of handling high viscosity severely reduced due to the open-channel nature from the nonwoven spacers.

due to the open channel formed by the nonwoven spacer, the mass transfer rate is While the suspended screen device does have a substantially lower pressure drop performance between the coarse screen devices and the suspended screen devices.

[0007] With the current cassette designs, there is a large difference in concentrations, say greater than 500 or 520 g/L.

component in the system, say 80 or 90 psi. As a result, it is difficult to obtain high final psi for a peristaltic pump), or the pressure rating of the cassette or some other

a twill weave design of two under and one over in the warp direction.

[0012] It is a further object of the present invention to provide a feed screen with wherein the screen has a twill weave design.

[0014] It is an additional object of the present invention to provide a feed screen of the screen.

20.8 micrometer (5 mil) above the height of the first and second surfaces on each side attached to an outer periphery of the screen, wherein the rim is of a height of at least

[0013] It is another object of the present invention to provide a screen has a rim the screen from about 10.8 to about 50 microm.

of from -10 degrees or greater than +10 degrees to 100 degrees and a mesh count in micrometer to 360 micrometer, an orientation of the warp of the screen to flow direction

and second surfaces on each side of the screen, a fiber diameter of greater than 512 the rim is of a height of at least 20.8 micrometer (5 mil) above the height of the first

degrees; a combination of a rim attached to an outer periphery of the screen, wherein the screen to flow direction of from -10 degrees or greater than +10 degrees to 100

of greater than 512 micrometer to 360 micrometer; and an orientation of the warp of the height of the first and second surfaces on each side of the screen, a fiber diameter

of the screen, wherein the rim is of a height of at least 20.8 micrometer (5 mil) above micrometer to 360 micrometer; a combination of a rim attached to an outer periphery

and second surfaces on each side of the screen, a fiber diameter of greater than 512 the rim is of a height of at least 20.8 micrometer (5 mil) above the height of the first

pattern; a combination of a rim attached to an outer periphery of the screen, wherein fiber diameter of greater than 512 micrometer to 360 micrometer and a twill weave

mil) above the height of the first and second surfaces on each side of the screen, a periphery of the screen, wherein the rim is of a height of at least 20.8 micrometer (5

than 512 micrometer to 360 micrometer; a combination of a rim attached to an outer first and second surfaces on each side of the screen and a fiber diameter of greater

at least 20.8 micrometer (5 mil) to 503.5 micrometer (8 mil) above the height of the of a rim attached to an outer periphery of the screen, wherein the rim is of a height of

degrees; a mesh count in the screen from about 10.8 to about 50 microm; a combination screen to flow direction of from -10 degrees or greater than +10 degrees to 100

of greater than 512 micrometer to 360 micrometer; an orientation of the warp of the and second surfaces on each side of the screen; a twill weave design; a fiber diameter

wherein the screen has a mesh count from about 10.8 to about 50 n/cm.

[0053] It is an additional object of the present invention to provide a feed screen and polyethylene terephthalate.

wherein the screen material is selected from the group consisting of polypropylene

[0055] It is a further object of the present invention to provide a feed screen degrees.

screen to flow direction of from -10 degrees or greater than +10 degrees to 100 degrees greater than 512 micrometer to 360 micrometer; and an orientation of the warp of the height of the first and second surfaces on each side of the screen, a fiber diameter of screen, wherein the rim is of a height of at least 20.8 micrometer (5 mil) above the wherein the screen has a combination of a rim attached to an outer periphery of the

[0057] It is another object of the present invention to provide a feed screen of greater than 512 micrometer to 360 micrometer.

height of the first and second surfaces on each side of the screen, and a fiber diameter screen, wherein the rim is of a height of at least 20.8 micrometer (5 mil) above the wherein the screen has a combination of a rim attached to an outer periphery of the

[0059] It is an additional object of the present invention to provide a feed screen greater than 512 micrometer to 360 micrometer and a twill weave pattern.

height of the first and second surfaces on each side of the screen, a fiber diameter of screen, wherein the rim is of a height of at least 20.8 micrometer (5 mil) above the wherein the screen has a combination of a rim attached to an outer periphery of the

[0061] It is another object of the present invention to provide a feed screen of greater than 512 micrometer to 360 micrometer.

height of the first and second surfaces on each side of the screen and a fiber diameter screen, wherein the rim is of a height of at least 20.8 micrometer (5 mil) above the wherein the screen has a combination of a rim attached to an outer periphery of the

[0063] It is a further object of the present invention to provide a feed screen from -10 degrees or greater than +10 degrees to 100 degrees.

wherein the screen has an orientation of the warp of the screen to flow direction of

[0065] It is an additional object of the present invention to provide a feed screen having a fiber diameter of greater than 512 micrometer to 360 micrometer.

[0067] It is another object of the present invention to provide a feed screen

method.

Figure 14 shows mass transfer coefficient of TFF devices designed with inventive

Figure 13 shows flux vs. concentration of TFF devices designed with inventive method.

inventive method.

Figure 12 shows pressure drop vs. concentration of TFF devices designed with orientations of TFF cassettes including those of the present invention.

Figure 11 shows mass transfer coefficient of TFF cassettes of different screen of TFF cassettes including those of the present invention.

orientations flux vs. concentration of TFF cassettes using different screen orientations

Figure 10 shows flux vs. concentration of TFF cassettes using different screen screen orientate of TFF cassettes including those of the present invention.

Figure 9 shows pressure drop vs. concentration of TFF cassettes using different C+3 screen of the present invention.

Figure 8 shows flux vs. concentration of TFF cassettes using PET C screen and PET and PET C+3 screen of the present invention.

Figure 7 shows pressure drop vs. concentration of TFF cassettes using PET C screen screen of the present invention.

Figure 6 shows flux vs. the concentration of TFF cassettes using C screen vs. C+3 C+3 screen of the present invention.

Figure 5 shows pressure drop vs. concentration of TFF cassettes using C screen vs. 4A.

Figure 4B shows a cross-sectional view taken on lines 4A of the feed screen of Figure invention with rim border.

Figure 4A shows a planar top down view of a feed screen according to the present including those of the present invention.

Figure 3 shows mass transfer coefficient of TFF cassettes of different feed screens of TFF cassettes including those of the present invention.

Figure 2 shows flux vs. the concentration of feed stream BgC of different feed screens gamma globulin (BgC).

invention using different feed screens vs. the concentration of feed stream bovine

Figure 1 shows pressure drop of TFF cassettes including those of the present [0054]

Brief Description of Drawings

μΕΙΣΙΝ·

of a thermoplastic so it can be overlaid to a thermoplastic outer film as described
similar materials would also be acceptable. It is preferred that the screen be made
screen such as polypropylene or polyethylene terephthalate. Other materials having

[0050] The present invention also includes using a material that is hard for the and thus influence the pressure drop and mass transfer.

changing the orientation of the screens, it will affect the fluid dynamics in the channel. The weave pattern of the screens is preferably a twill weave (over two, under one). By ± 10 degrees from the flow direction or greater than 10 degrees up to about 100 degrees. The screens are oriented at an angle to the tangential flow preferably about

[0058] The present invention also includes changing the orientation of the and the rim height is determined by the feed screen mold.

increased rim height of the feed screen is provided to reduce the pressure drop in the

[0051] In some embodiments according to the invention, a design for the like:

diameter, mesh opening size, mesh count, weave pattern, screen thickness, and the sand pressure drop. It includes inserting a new screen which has new features in mesh screen, which is known to have a significant influence on both the mass transfer rate

[0058] The major part of the invention is focused on the new design of the feed as the fibers in the screen.

the effective channel height is also affected by the hardness of the membrane as well overmolded screen. Since the screen is embossed into the surface of the membrane, on the overmolded screen or by using a thicker nonwoven as a spacer in a non-diameter fiber in the screen, by increasing the thickness of the molded border or film channel hydraulic resistance. One can increase the channel height by using a larger decrease the channel pressure drop by increasing the channel height or reducing the given channel length and width (relatively fixed by the cassette design), one can

[0052] Several approaches are possible under the present invention. For a detailed description of the Preferred Embodiments

coefficient of 114 cassettes including those of the present invention.

Figure 12 shows the ratio of pressure drop at 500 g/L concentration to mass transfer

corresponding to a half of the final screen 5 with rim design are made and placed on molded piece on both sides of screen 5. To form such an outer rim 10, two molds each both sides of the screen as desired. Preferably, rim 10 is formed as one injection-injection molded to the edge of the screen 5. The rim 10 may be formed on one or inner side of the rim 10 to the outer side of the screen 5. Preferably, the rim 10 is

[0033] The molded rim height 14 is formed by the molding or bonding of an on each side of the screen 5.

the thickness 16 of the screen 5. As shown the rim 10 has a height 14 of equal amount preferably bonded to each other and the rim 10 preferably has a height 14 greater than feed and retentate ports 4, 6. As shown in Figure 4B, the rim 10 and screen 5 are screen the permeate ports 8 are also sealed off by the rim from the screen 5 and the rim 10 is formed around the outer periphery of the screen 5. As shown for a TFF feed be used for a TFF device having feed port 4, retentate port 6 and permeate port 8. A outer periphery as will be described below in more detail. As shown, the screen 5 is to invention. As shown in Figure 4A the screen has an outer rim formed and joined to its

[0035] Figures 4A and 4B show a screen with the rim height detail of the present of 25.4 millimeter (an inch) to 81.000 of 25.4 millimeter (an inch) on each side.

mesh count varies from 50 to 10.6 microm. The rim height of screens varies from 21.000

[0037] The range of mesh diameter varies from 21.2 to 360 micrometer, and the in Table 1.

transfer as demonstrated by the pressure drop/mass transfer coefficient ratios shown attributed to a unique and surprising relationship between permeability and mass mass transfer coefficient. In this way, novel materials with improved performance overmolded rim height can further reduce the pressure drop while maintaining a high changing the screen. The unique combination of an improved screen with the a factor of 5, with a mass transfer coefficient 17% higher than achieved by simply of 25.4 millimeter (an inch), provides improved permeability of the device by more than coefficient (k) by 30%. The use of a rim height in the overmolded screen of 3.21000 screen design improves permeability by a factor of 5, but reduces the mass transfer. Conversion of the coarse screen to a screen of the present invention with special screens are changed to improve permeability at the expense of mass transfer, pressure drop and less reduced mass transfer even at high viscosities. Typically, screen and improved screen design provides a TFF device with significantly reduced

[0030] The combination of overmolded rim height above the surface of the

may also be done on the retentate side instead of on the filtrate side or on both sides recycled to the filtrate layer inlet port to effect tangential flow on the filtrate side. This inlet ports and one or more filtrate outlet ports can be formed so that some filtrate is stream is removed through the one or more filtrate ports. If desired, one or more filtrate is removed from the device through the one or more retentate ports and the filtrate stream or is retained by a membrane to form a retentate stream. The retentate stream the feed screen layer(s) and either passes through a membrane to form a filtrate incoming fluid feed to the apparatus enters at least one feed channel, passes through invention, the feed port, retentate port and filtrate port are arranged so that the

[0038] In a tangential flow filtration apparatus using the screen of the present the major surfaces of the screen.

rim, preferably a thermoplastic rim that extends above at least one, preferably both of formed in the following manner: a screen, preferably a feed screen is formed with a

[0037] A module using a screen according to the present invention is typically density and high density polyethylene, polypropylene and EVA copolymers.

molding. Preferred thermoplastics include low density, linear low density, medium elastomer so as to allow for its use in the preferred method of this invention, injection

[0036] It is preferred that the material be a thermoplastic or thermoplastic cell foamed urethanes, and rubbers, either natural or synthetic.

elastomers such Santoprene® polymer, EPDM rubber, thermosets such as cross polyacrylonitrile, polyvinylidene fluoride (PVDF), and blends thereof, thermoplastic polysulfone, polyethersulfone, polysulfone, polyphenylsulfone, PVC, polyamides such as nylon, polyesters, acrylonitrile-butadienestyrene (ABS), and metallocene copolymers, PEA, MEA, polycarbonate, vinyl copolymers such as thermoplastics, such as polyethylene, polypropylene, EVA copolymers, alpha olefins

[0035] Suitable materials for the rim 10 include but are not limited to opening of the rim 10 or by melt bonding the screen 5 into the rim 10

mechanical retention of the screen 5 such as by a press fit of the screen 5 within the screen 5 attached to the opening in the rim by various means such as adhesives or a

[0034] Alternatively, if desired, the rim portion 10 may be pre-molded and the mold with the rim material, thus forming the desired rim 10 in place on the screen 5.

other selected material is then injected into either one or both mold pieces and fills the opposite sides of feed screen in alignment with each other. Molten thermoplastic or

bovine gamma globulin (BGG) to the mass transfer coefficient is < 2.5 is preferred. good mass transfer performance. A device where the ratio of pressure drop at 500 g/L pressure drop from the feed ports to the retentate ports and in the meanwhile, remain

[0040] In various embodiments, the claimed features are useful to reduce the

height (predicted) increased rim mesh count and diameter, smaller with larger mesh with D3 screen inventive Device	53	18	1.4
height increased rim mesh count and diameter, smaller with larger mesh with D5 screen inventive Device	43	55.3	1.8
rim height only with increased with C screen inventive Device	20	53.4	1.5
with D3 screen Standard Device	24.8	50.7	5.8
with D5 screen Standard Device	25.2	53.1	5.7
with C screen Standard Device	117	58.2	4.0
Hydrasart Sartorius	27.8	50.8	5.8
Device (psi) cross flow rate (BGG) and 8 GMH gamma globulin 500 g/L bovine Pressure Drop at		(GMH) Coefficient K Mass Transfer	Transfer Coefficient Drop to Mass Ratio of Pressure

5.

compared to the prior art. Screen characteristics (A, C, D5 and D3) are listed in Table

[0039] Table 1. Pressure drop vs. Mass transfer coefficient for inventive method transmembrane pressure within the device.

to increase tangential flow efficiency of the device. By doing so, one may control the

respectively. The performances are shown in Figures 2 and 6.

transfer coefficients for devices with C screen and C+3 screen are 58.2 and 53.4, decrease of almost 80% pressure drop and also flux decreased about 50%. The mass membrane. Results show that increased rim height of feed screen gives rise to C+3 screen are shown for comparison. All cassettes are using Ultracel® 30KD screen, is used to replace standard C screen, and the results for both C screen and increased rim height of 88.8 micrometer (3.5\1000 inch) of each side, or the "C+3 of a C screen is 20.8 micrometer (5\1000 inch) of each side. The C screen with an in Figures 4A and 4B and discussed above. The standard current standard rim height Feed screen with an increased rim height is used in the TFF cassettes as shown [0044] Example 5: influence of feed screen with different rim height.

[0043] The performances of different screens are shown in Figure 1-3.

D3	280	38	10.8	380	110	842	0.402	0.22
D5	200	38	15.5	340	180	810	0.458	0.25
C	320	35	18.5	510	180	212	0.381	0.28
A	581	34	50	512	152	450	0.588	0.81
screen	micron opening Mesh	% Area Open	micron Count Mesh	micron Diameter Wire	g/m ² Weight Basis	micron Thickness	g/cm ³ density Bulk	fraction Void Avg

Table 1

[0045] Table 5: Comparison of Physical Properties A, C, D5 and D3 screens of 30KD 0.11m² TFF devices.

comparison of D5, D3, A, C screens are shown in Table 5. All cassettes are Ultracel® under one) and the material used for all the screens is polypropylene (PP). The traditional screens. The weave pattern of D5 and D3 screens are twill weave (over two diameter, less mesh count, greater mesh opening, and larger screen thickness than cassettes. The new screen herein called the D5 and D3 screens have a larger wire accommodate feed streams with high viscosity, a new screen is introduced in the TFF

A screen and C screen are currently used in Pellicon® 3 cassettes. To

[0041] Example 1: Comparison of different feed screen.

30KD Biomax®	C+3	1.0	30KD Ultracel®	C+3	8.0
		1.0			0.0
		1.8			2.0
		5.3			1.0
		5.1			1.4
		5.1			1.0
	C	3.0		C	13.0
		2.0			14.4
		3.0			13.8
		8.0			15.0
		2.0			14.1
		4.0			11.4
Membrane	2 screens Feed	water (psi) PB Test –	Membrane	2 screens Feed	water (psi) PB Test –

Ultracel® 30KD membranes using C and C+3 screen.

[0047] Table 3: water pressure drop of TFF devices for Biomax® 30KD and method to reduce pressure drop when handling high viscosity feed stock.

different screens validates that increase screen rim height is an effective and practical are shown in Table 3. The pressure drop of water for both membrane devices using of Ultracel® 30KD and Biomax® 30KD membranes using C screen and C+3 screen drop which works on different membranes. The hydraulics tests of micro TFF devices

An increase of the rim height of feed screen can significantly lower the pressure

[0048] Example 4: Increased rim height works on different membranes.

All cassettes are using Biomax® 30KD membrane.

for devices with PET C screen and PET C+3 screen are 11.1 and 12.2, respectively. performance with PB screens, shown in Figure 7 and 8. The mass transfer coefficients that an increased rim height of PET screens has a similar effect on TFF device screens with different rim heights are evaluated in the TFF cassettes. Results show materials. Instead of polypropylene (PB) screens, Polyethylene terephthalate (PET)

The effect of different rim height screens is applicable for screens of different materials.

[0049] Example 3: Increased rim height works on feed screens of different

PP screen material and 10 degree screen orientation, shown in Figures 15 to 18. All predictions are based on Ultrasel® 30KD membrane transfer. Predicted performance of such devices using Ultrasel® 30KD membranes is provides a UF device with significantly reduced pressure drop and less reduced mass

The combination of rim height, screen design and optimized screen orientation
Orientation

[0049] Example 8: Predicted performance of Screen, Rim Height and Screen in Figure 9 to 11.

the flow direction of -10°, 10°, 35°, 42°, 60°, and 100° are chosen. Results are shown evaluated using Biomax® 30KD membrane and C+3 feed screen. Angles relative to channel and thus influence dissipating energy. Effects of feed screen orientation are the orientation of screen relative to flow direction will influence the obstruction to the

The weave pattern of feed screen is twill weave (over two under one). Changing
[0048] Example 8: effects of feed screen orientation

flow direction is -10° 10° 55° 42° 60 or 100 degrees:

2) The feed screen of claim 1 wherein the orientation of the warp of the screen is 50 n/cm.

4) The feed screen of claim 1 wherein the screen has a mesh count from 100 to 200 and the screen is made of a material selected from the group consisting of polypropylene and polyethylene terephthalate.

3) The feed screen of claim 1 wherein the screen material is selected from the group consisting of: one over and one under in the warp direction.

5) The feed screen of claim 1 wherein the screen has a twill weave design of two on each side of the screen.

of at least 88.9 micrometers (3.5 mil) above the height of the first and second surfaces has a rim attached to an outer periphery of the screen, wherein the rim is of a height open area of mesh of the screen is 30 percent to 30 percent, and wherein the screen

(p) a fiber diameter of 340 micrometers to 360 micrometers, wherein an angle is from +10 degrees to 100 degrees; or

(a) an orientation of the warp of the screen to flow direction of -10 degrees, wherein the screen is characterized by a twill weave design in combination with:

(f) A feed screen for a tangential flow device comprising a screen having a length,

MPST MG C/SIW:

CLAIMS