Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

A Technique for Increasing Permeate Flux in Hemofiltration by Periodic Step Changes in Pressure

M. Defossez[a]; L. Ding[a]; M. Y. Jaffrin[a]; J. Mazaudier[a]
[a] URA CNRS 858 BIOMÉCANIQUE ET INSTRUMENTATION MÉDICALE, UNIVERSITÉ DE COMPIÈGNE, CÉDEX, FRANCE

To cite this Article Defossez, M. , Ding, L. , Jaffrin, M. Y. and Mazaudier, J.(1997) 'A Technique for Increasing Permeate Flux in Hemofiltration by Periodic Step Changes in Pressure', Separation Science and Technology, 32: 8, 1351 — 1369
To link to this Article: DOI: 10.1080/01496399708000965
URL: http://dx.doi.org/10.1080/01496399708000965

SEPARATION SCIENCE AND TECHNOLOGY, **32**(8), pp. 1351–1369, 1997

A Technique for Increasing Permeate Flux in Hemofiltration by Periodic Step Changes in Pressure

M. DEFOSSEZ, L. DING, M. Y. JAFFRIN,* and J. MAZAUDIER
URA CNRS 858
BIOMÉCANIQUE ET INSTRUMENTATION MÉDICALE
UNIVERSITÉ DE COMPIÈGNE
BP 529-60205-COMPIÈGNE CÉDEX, FRANCE

ABSTRACT

This paper describes a technique for increasing the ultrafiltration flux from blood in hemofiltration used for the treatment of end-stage renal failure. This technique is based on the principle that the filter transient response to a step change in transmembrane pressure ΔP_{step} from an unpolarized state to a highly polarized state can temporarily exceed the maximum UF flux J_{fp}, at plateau, reached in a stationary regime. We have demonstrated that the total filtrated volume can be appreciably improved by applying periodic stepped pressure increments and by appropriately choosing the kinetic parameters τ_1 duration of high-pressure phase (>80 kPa) and τ_2 duration of low-pressure phase (<10 kPa). This improvement occurs only if a backwash flow Q_{ret} around 3 cm^3/s is applied to the filter during t_2 in order to depolarize the membrane, and if τ_1 and τ_2 are close to 20 and 2 seconds, respectively, when the inlet flow Q_i is chosen in the range from 1.7 to 5.0 cm^3/s for a membrane area of 0.65 m^2. The relative gain G between the total filtrated volume obtained in a dynamic regime and the one obtained in a stationary regime can reach 60%. We have found that G mainly depends on ΔP_{step} and τ_1. This technique has been shown not to hemolyze the blood and to retain its efficiency over long periods.

Key Words. Ultrafiltration; Hemofiltration; Concentration polarization layer; Backwash

* To whom correspondence should be addressed.

INTRODUCTION

It is well known (1, 2) that ultrafiltration (UF) of proteins leads to the formation of a concentration polarization layer formed by macromolecules retained by the membrane. This phenomenon hinders the permeate flux because it adds another filtration resistance to that of the membrane (3) and it decreases the driving force TMP-$\Delta\pi$ by increasing the osmotic pressure $\Delta\pi$ at the membrane wall (4). The specific application of ultrafiltration considered in this paper is hemofiltration used in the treatment of end-stage chronic renal disease as an alternative to hemodialysis (5). Hemofiltration has the advantage of providing better hemodynamic stability and higher clearance of high molecular weight toxins than conventional hemodialysis. However, in order to provide adequate urea clearance, the permeate flux must represent a large fraction of the inlet blood flow in the hemofilter (typically 120 mL/min out of 300 mL/min for an adult). Since this inlet blood flow is limited by the patient arteriovenous fistula permitting blood access from a radial vein, it is important to develop techniques which augment the permeate flux at low tangential velocities. Chemical methods (like using surfactants) have been tested (6), but physical methods such as negative transmembrane pressure pulses or pulsed flows are more universal since they do not impose conditions on both solution and membrane (7, 8).

In the case of plasma separation from whole blood by microfiltration, our laboratory has proposed an efficient method for increasing permeate flux by superimposing pressure and flow pulsations at 1 Hz on the inlet blood flow of the plasma filter (9, 10). Plasma filtration flux enhancements of up to 200% were obtained because these pulsations were able to effectively perturb the red cell concentration polarization layer. However, when the same technique was used in ultrafiltration, results were disappointing. A possible explanation was that, in the case of ultrafiltration, the permeate flux was limited by a protein layer deposited on the membrane rather than by a red cell layer, and that this protein layer was more difficult to perturb than the red cell layer. This assumption was confirmed by another investigation in our laboratory (11, 12) in which the membrane was submitted to stepped transmembrane pressure increments from the unpolarized regime to a highly polarized one. This technique permits one to determine the time for the concentration polarization layer to establish itself by monitoring the instantaneous variation of permeate flux simultaneous with the pressure rise and in particular with the time necessary for the flux to decay to its equilibrium value.

In the case of a microfiltration membrane transmitting the proteins freely, the red cell concentration polarization layer takes 2 to 3 seconds

to become established (11). This explains why 1 Hz pressure pulsations are effective for enhancing the permeate flux: when the pressure increases rapidly, the permeate flux increases above the equilibrium limit before polarization concentration sets in. However, when an ultrafiltration membrane is used, the concentration polarization concentration layer, which in this case is formed of proteins, takes 30 to 60 seconds to build up (12). To adapt the pulsatile flow technique to ultrafiltration, it seems logical to use pulsations with periods of about 20 to 40 seconds. Thus, rather than using a pulsation generator based in a peristaltic pump, we propose to use a system which generates periodic pressure increments at a value of P_{max} for a duration of τ_1 separated by a return phase to the basal level of P_{min} for a duration of τ_2. According to our previous experience (12), the permeate flux reaches a peak during the high-pressure phase and decays toward its equilibrium level, according to

$$J_v(t) = J_{fp}(1 + \alpha e^{-t/\tau}) \tag{1}$$

where

$$\alpha = \frac{J_{fpeak} - J_{fp}}{J_{fp}} \tag{2}$$

But before equilibrium is reached, the pressure is reduced to P_{min} in order to phase out the concentration polarization layer. Thus the duration τ_2 must obey conflicting requirements; it must be long enough so that concentration polarization reverses itself and short enough to reduce the loss in permeate during this period. Optimization will then be necessary to find the best compromise.

However, it was found that the values of τ_2 necessary to obtain a stable and periodic operation are so large so that they lead to a low time-averaged permeate flux. In order to reduce the duration of τ_2 while obtaining satisfactory reduction in concentration polarization, we modified the circuit to induce a short retrofiltration phase (backwash) during the phase τ_2 by means of a peristaltic pump.

It may be noted that in the ultrafiltration of protein solutions, there may be a natural backfiltration flux in the downstream part of the filter, provoked by the high osmotic pressure induced by the high concentration in protein in the bulk and on the membrane surface (13). It disrupts the polarization layer, causing the proteins concentrated at the surface membrane to diffuse in the bulk, but this phenomenon is slow, and mechanically imposed backfiltration is preferable.

The purpose of this paper is to describe this technique and the investigation leading to optimal operating parameters which are τ_1, τ_2, Q_{ret} the backfiltration flow rate, and the pressure step increment ΔP_{step} defined

by

$$\Delta P_{step} = P_{max} - P_{min} \tag{3}$$

The aim is to find the set of parameters for which the gain in net filtration is maximum.

The filtration gain in percent will be given by

$$G = \frac{V_{fdyn} - V_{fp}}{V_{fp}} \times 100 \tag{4}$$

First, we will describe the experimental set-up and protocol. Then we will present and discuss the results, and we will show that they are very sensitive to the compliance of the system. Finally, we shall present a model which permits τ_1 to be chosen according to the other parameters and to forecast approximatively the gain in filtration G.

MATERIALS AND METHODS

Set-up

The experimental set-up is shown on Fig. 1a. It permits tests in a dynamic regime without or with backwash. If the backwash is not used, the part of circuit included in the dotted line rectangle is omitted (or simply disconnected). Because the high-pressure period τ_1 and the low-pressure one τ_2 must be set accurately, the system is monitored by a microcomputer PC-AT which controls the two electrovalves while simultaneously recording the experimental values (pressures and flux) with respect to time.

Five liters of bovine blood (fresh from the slaughterhouse of Compiègne) were mixed with 700 mL of CPD (citrate phosphate dextrose) and diluted with a 9% saline solution in order to adjust the hematocrit at 25%. The protein concentration was in the range of 26 to 49 g/L depending on the animal sacrificed.

The filter "F 40" is a hollow fiber hemofilter made by Fresenius Company, Germany. It is constituted of 4500 hollow fibers in polysulfone PS 600 with inner diameters equal to 200 μm. Its membrane cut-off is 30,000 Da, its length 23 cm, and its membrane area 0.65 m^2.

The peristaltic pumps P1 and P2 used in the main circuit (filtration circuit) and the backwash circuit are Masterflex 6–600 rpm, made in France, with mounted head no. 7015/20 (for a silicone tube with an inner diameter equal to 4.8 mm) and no. 7016/20 (for a silicone tube with an inner diameter equal to 3.1 mm), respectively. The electromagnetic flowmeters are model EP 604 made by Carolina Medical Electronics Inc., USA. The pressure transducers are model DP 15 made by Validyne, USA,

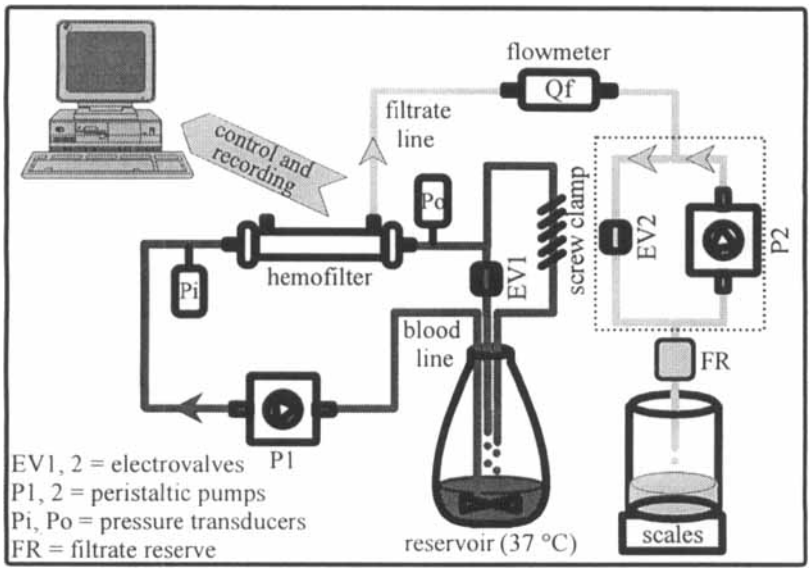


FIG. 1a Experimental set-up for periodic step changes in pressure synchronized with short periods of backwash.

mounted with a membrane no. 42 with a 0–140 kPa range. The scale is an electronic model made by Sartorius, Germany, with a 0–3.1 kg range. The tube pinch electrovalves EV1 and EV2 are made by Bürkert, Germany; EV1 is a NC type (normally closed) and EV2 is a NO type (normally open). The circuit tubing has an inner diameter equal to 4 mm and is made of semirigid silicone to avoid size variation as much as possible.

Experimental Protocol

The blood in the reservoir is homogenized by a stirrer and thermostated at 37°C. The preliminary step needed for the experiments is to determine the accurate value of J_{fp} as a function of the inlet flow Q_i because it strongly influences the value of the filtration gain G and the transmembrane pressure P_p at which it appears. The sequence of filtration and backwash in the dynamic regime is given on Fig. 1b.

First, let us consider the stationary regime, when the electrovalves are in their normal position and the backwash circuit is disconnected. The blood flows in a closed circuit in order to keep the reservoir concentration constant, which means that both retentate and filtrate return to the reser-

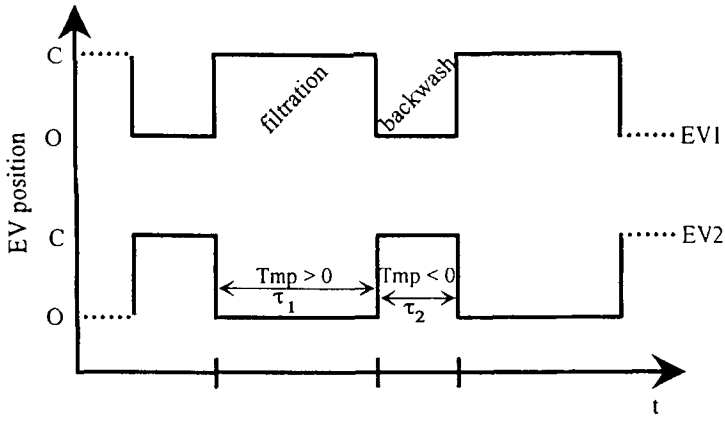


FIG. 1b Sequence of valve opening and closing.

voir. It can be seen in Fig. 1a that the retentate outlet of the filter is separated into two lines: one is a free line with no hydraulic resistance and the other is a high-resistance line on which a screw clamp imposes a hydraulic resistance and therefore the transmembrane pressure. Since EV1 is of the NC type, the retentate must flow through the high-resistance line in which the screw clamp is adjusted to make the transmembrane pressure higher than P_p and the filtration flux equal to its maximum J_{fp}.

Second, let us consider the dynamic regime without backwash when only valve EV1 is active. Then the blood will flow alternatively through the high-resistance line and the free line, creating step changes in transmembrane pressure from 10 to 100 kPa. Therefore, the response in filtration of the filter will follow the increments of pressure with a tiny phase shift. It will be seen later that applying periodic increments of pressure is not sufficient to improve the filtration rate.

Finally, let us consider the dynamic regime with periodic backwash, i.e., both EV1 and EV2 are active and the backwash circuit is operational. On Fig. 1b we can see that the electrovalves work with a 180° phase shift. During the interval τ_1, the transmembrane pressure is higher than P_p since EV1 is closed, and the backwash circuit is not active since it runs in an open loop. During the interval τ_2, the retentate flows through the free line since EV1 is open, and the backwash circuit is active since EV2 is closed; then the peristaltic pump P2 provides a backfiltration flow Q_{ret}. The values of τ_1, τ_2, Q_{ret}, and P_p will govern the efficiency of this technique. Figure 2 schematizes the response of the UF flux to the step changes in pressure.

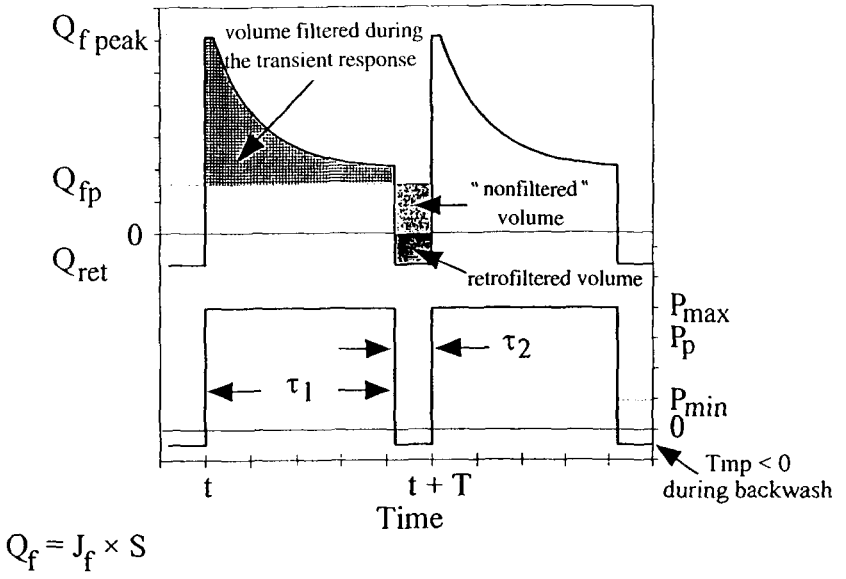


FIG. 2 Schematic of filtration response to step changes in pressure.

RESULTS

Comparison of Permeate Fluxes Without and With Backwash

It is found that when the membrane is subjected to sudden pressure increments, the UF rate is not improved because the polarization layer is not disturbed enough by the step changes in pressure. Furthermore, the time needed for depolarization when the transmembrane pressure is low is much higher than τ_2, at least 60 seconds, whereas τ_2 must be less than 5 seconds in order to expect a positive filtration gain G. Therefore, it is not very interesting to describe experiments without backwash, but examination of differences between experiments without and with backwash will give useful information.

In Fig. 3 we can see that the main difference between the two cases is that without backwash the UF flux tends to the steady-state plateau at the end of each pressure step, whereas with backwash it stabilizes at a value higher than J_{fp}. This indicates that the polarization layer has been disturbed by the backwash. For this example, the filtration gain is about 10%. We notice that the periodic state is established after about 150 sec-

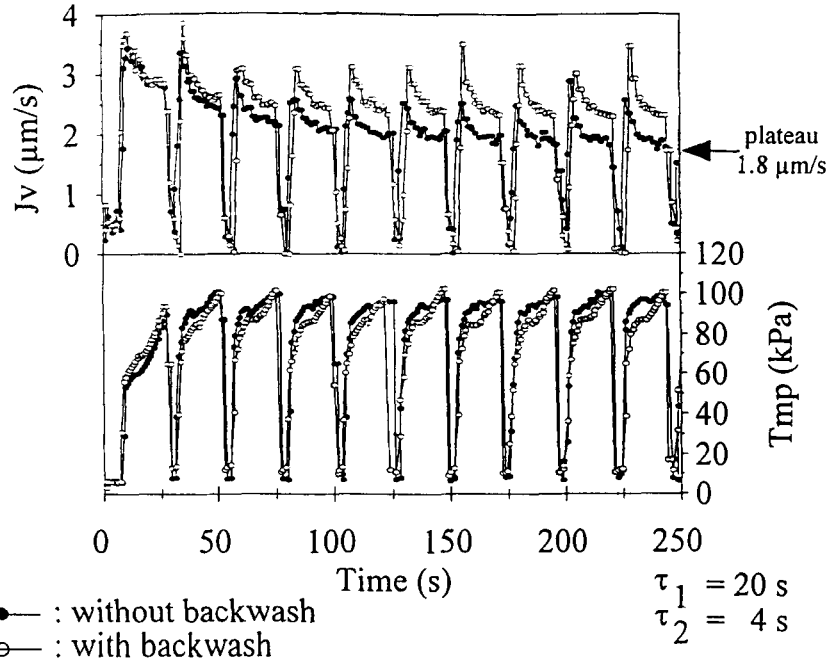


FIG. 3 Permeate flux and transmembrane pressure variation with time during stepped pressure increments without and with backwash. With backwash, pressure and UF flux are incorrect during interval τ_2.

onds. All the calculations are therefore made after this time, for otherwise the results would be artificially improved. Another observation is that with backwash, the pressures and the UF flux recorded during the interval τ_2 are incorrect because they must be negative. The reason is that we did not put a pressure transducer on the filtrate line, and the UF flux is measured with an electronic scale which cannot measure the backfiltered volume but is more accurate than an electromagnetic flowmeter. This is not important since the data obtained during this phase are unnecessary for our analysis.

In Fig. 4 the results of the comparison between the cases without and with backwash are summarized for $\tau_1 = 10$ seconds. Note that we did not make any experiment with $\tau_2 > 5$ seconds because the backfiltered volume would be too large and the consecutive hydraulic pressure would damage the filter. It is seen that for $\tau_2 = 1$ second the backwash has no effect due to the fact that the size variation of the filtrate circuit absorbs

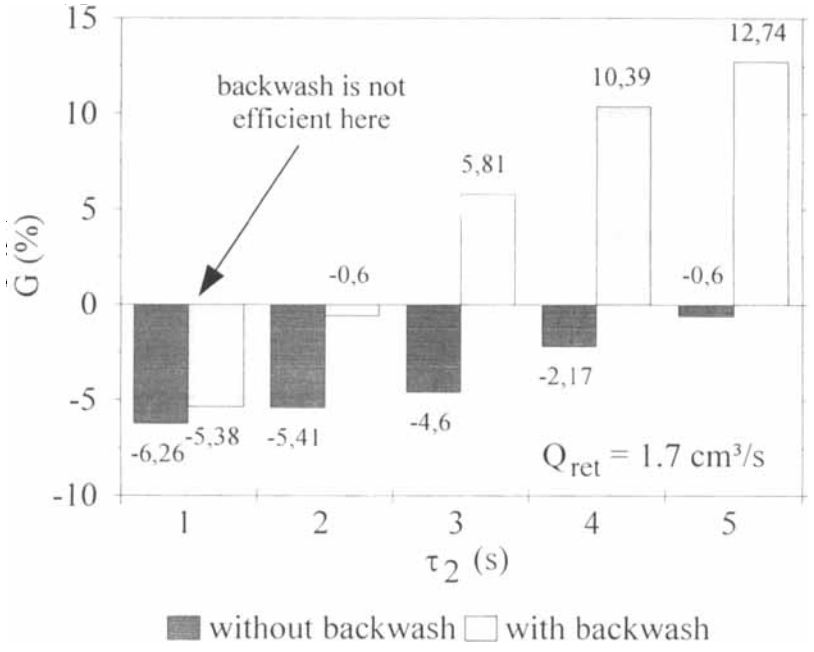


FIG. 4 Gain in filtration obtained without and with backwash for various values of τ_2 and $\tau_1 = 10$ s.

a part of the retrofiltered volume and the protein layer has not had enough time to diffuse into the bulk fluid. Furthermore, the backfiltration optimal τ_2 seems to be around 5 seconds.

In the case with backwash, a backfiltration volume V_{ret} is returned periodically to the filter in order to depolarize the membrane. Since Q_{ret} is set constant by the peristaltic pump, it is given by

$$V_{ret} = Q_{ret} \times \tau_2 \tag{5}$$

Actually, Eq. (5) does not give the exact backfiltered volume because the size variation of the backwash circuit absorbs from 5 to 15 mL of filtrate, and therefore the amount of filtrate which really returns inside the fibers is less than V_{ret}. So, the size variation can dramatically decrease the efficiency of this technique if V_{ret} is low. Unfortunately it is impossible to avoid this size variation because it is induced by air bubbles trapped between the fibers, and the filter design does not permit total evacuation of these bubbles.

For those experiments, the dependent parameters are P_p, τ, and α since $P_p = P_p(Q_i)$, $\tau = \tau(Q_i)$, and $\alpha = \alpha(\Delta P_{step})$. Other adjustable parameters are τ_1, τ_2, and Q_{ret}. Note that ΔP_{step} is not an adjustable parameter since J_{fpeak} depends on it (11). So, it is obvious that the higher ΔP_{step} is, the higher α will be, and therefore the higher will be the improvement in ultrafiltration during the transient. In practice, α has been set in the range 0.6 to 1.2 for ΔP_{step} from to 110 kPa, respectively.

τ_1 is selected by estimating how long the transient UF flux may be effectively exploited. It is obvious that τ_1 must be larger than τ_2 and smaller than 40 seconds for physical reasons (packing of the polarization layer, drastic increase of transmembrane pressure, . . .). τ_2 is selected by determining by what value the depolarization time may be reduced when a backwash is applied. Equation (5) also induces a constraint on both τ_2 and Q_{ret} because V_{ret} must not be too large, otherwise the hydraulic pressure increases dramatically and the filter might burst. In practice, V_{ret} has always been set below 5 $cm^3/s \times 5$ s = 25 cm^3. However, τ_2 must be large enough to give the proteins of the polarization layer time to diffuse in the bulk fluid, and Q_{ret} has to be as large as possible in order to fill quickly the volume due to the size variation of the backwash circuit.

Because the aim of this study was to find the region where G is maximum, we have never set α at a value above 1.2. By doing so, the maximum of the transmembrane pressure always stabilized below 140 kPa. This is important in order to avoid too large a stress on the system. In spite of this limitation, in many cases we have obtained very good results, as can be seen in Figs. 5(a–c) and 6(a–c).

In Fig. 5(a) the low values of G are due to an error made during the experiment. Indeed, at the beginning of the test, P_{max} was set at about 100 kPa but after several cycles [τ_1, τ_2] the transmembrane pressure during τ_1 was close to 160 kPa, which is much beyond the acceptable system limit. In order to avoid destruction of the filter, P_{max} was changed by slightly unscrewing the screw clamp. Unfortunately, the pressure is very sensitive to any change in the hydraulic resistance, and the value of P_{max} dropped to 40 kPa whereas P_p was 27 kPa. Therefore, ΔP_{step} also dropped from 73 to 13 kPa and α was then only 0.6. Nevertheless, this error has shown that α is a very important parameter which strongly influences the efficiency of the technique.

For Figs. 5(a–c) we worked with $\tau_1 = 10$ seconds and $\tau_2 = 1$, 2, 3, and 4 seconds. It can be seen that the maximum of G is always obtained when τ_2 is equal to 2 or 3 seconds. Actually, τ_2 has to be greater than 1 second because of the delay needed to saturate the size variation of the backwash circuit. But at the same time, τ_2 has to be minimum in order to minimize the loss of permeate flux during τ_2. Interestingly, we can see that appar-

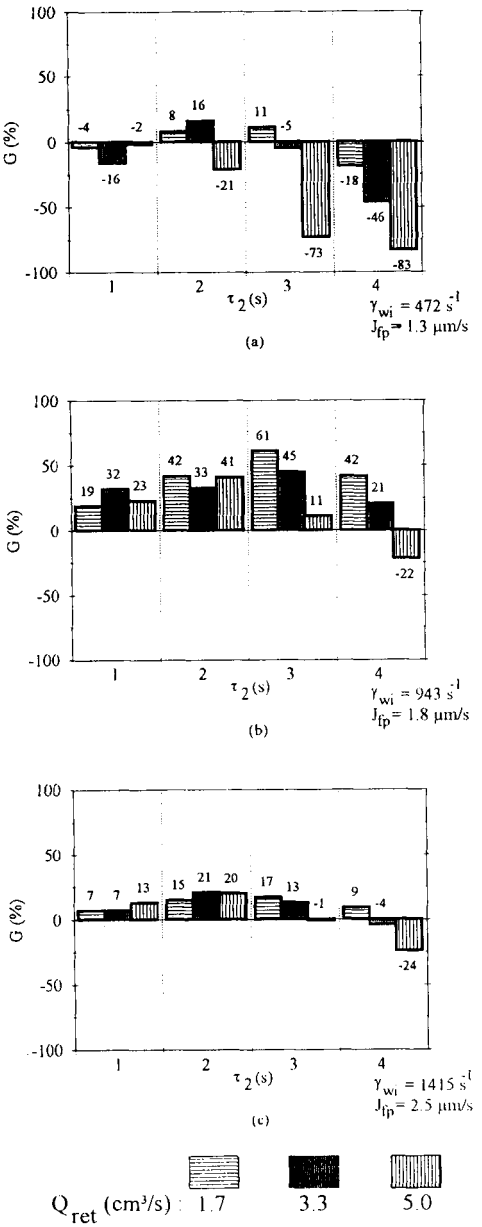


FIG. 5 Gain in filtration for $\tau_1 = 10$ s as a function of τ_2 and Q_{ret} (bovine blood: 25% Hct; $C_p = 48$ g/L for a, b, c).

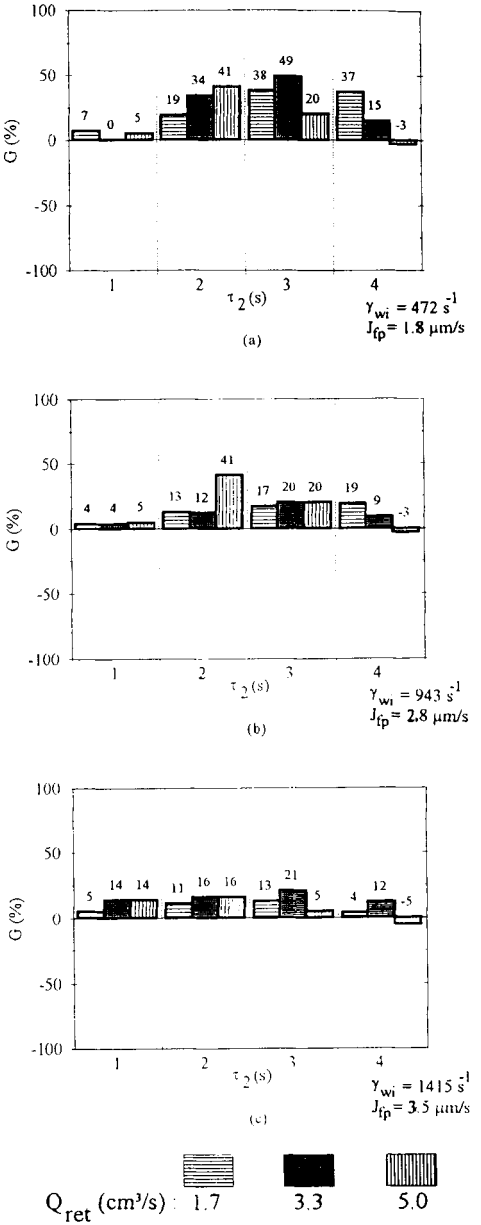


FIG. 6 Gain in filtration for $\tau_1 = 20$ s as a function of τ_2 and Q_{ret} (bovine blood: 25% Hct; $C_p = 26$ g/L for a, b, c).

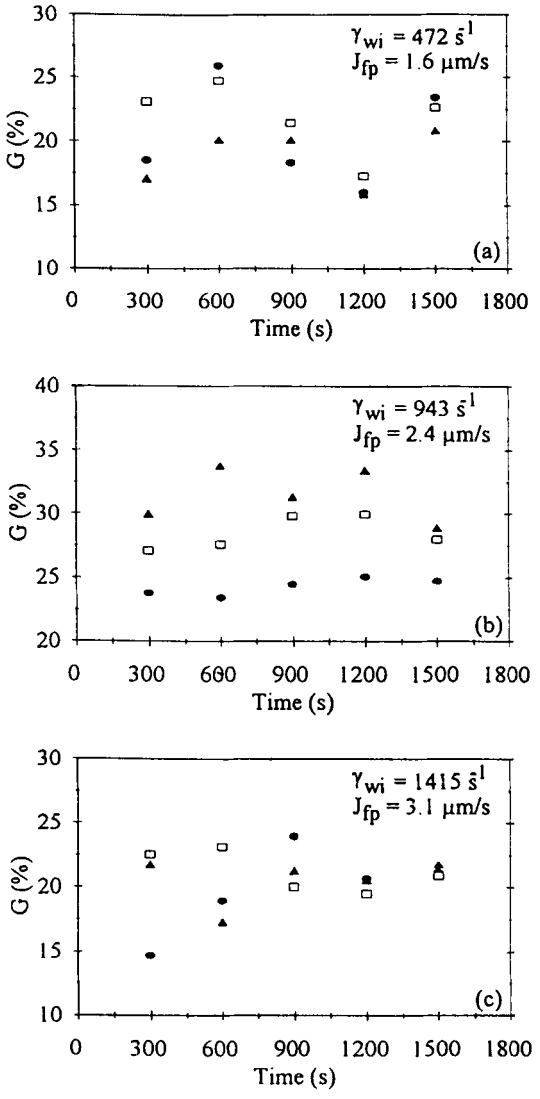
ently there is no systematic connection between G and Q_{ret}. This can be explained by the fact that the size variation of the backwash circuit absorbs a certain quantity of filtrate which depends on several parameters like the volume of the bubbles trapped between the fibers, the membrane resistance, and the pressure of the filtrate side. So the volume which has really backfiltered is very difficult to evaluate. However, it seems that with a Q_{ret} of 3.3 cm^3/s the membrane depolarization is sufficient to stabilize the flux. This is a good compromise when the transmembrane pressure rises with time when Q_{ret} is 1.7 cm^3/s, and the pressure in the backwash circuit is very high when Q_{ret} is 5.0 cm^3/s.

In Figs. 6(a–c) we have worked with $\tau_1 = 20$ seconds and $\tau_2 = 1$, 2, 3, and 4 seconds. The remarks about G remain valid. Unfortunately, we cannot make comparisons with the case $\tau_1 = 10$ seconds because our experiments lasted only 1 day for each τ_1, and the blood had to be replaced since it degrades rapidly. Anyway, even if we had the same fluid for each experiment, it would be very difficult to keep the experimental conditions constant due to the size variation of the circuit. Indeed, it depends on many inaccessible parameters like the air trapped between the hollow fibers. However, this difficulty does not really matter since we are looking for the value of τ_2 for which G is maximum. We can see that the values of G are of the same order in Figs. 5(a–c) and Figs. 6(a–c); this indicates that the adjustment of τ_1 is not critical. This last point, which is important for the efficiency of the technique, will be explained in the Discussion.

Long-Term Testing

It is essential to test the technique of periodic increments of transmembrane pressure over a long period of time, because a clinical hemofiltration session takes around 3 hours. Therefore, our runs were 30 minutes each in order to check whether G remains high or if some adsorption phenomena reduce the benefit of this technique. Furthermore, the system must be stabilized to validate the process, and therefore we have not tried to obtain the highest G in order to avoid excessive pressures. This is why τ_1 and τ_2 have been chosen as equal to 10 and 2 seconds, respectively, which guarantees good depolarization when Q_{ret} is larger than 1.7 cm^3/s.

In Figs. 7(a–c) we have drawn the gain in filtration as a function of time. Each point is the mean value of G calculated for a time lapse of 300 seconds. We can see that G is between 15 and 35%, and that the system is stabilized because there is no decline with time. Let us point out that this technique could provide better results if the pressure was not limited by the hollow fiber resistance. Furthermore, this shows that concentration polarization is reversible and that, for a short running period, the membrane properties remain constant.



(τ_1 = 10 s, and τ_2 = 2 s for those experiments)

Q_{ret} (cm³/s): • 1.7 ▲ 3.3 □ 5.0

FIG. 7 Long-term testing for τ_1 = 10 s and τ_2 = 2 s (bovine blood: 25% Hct; C_p = 38 g/L for a, b, c).

DISCUSSION

A calculation can be made by neglecting the size variation of the backwash circuit and considering that the backwash parameters have been chosen so that the membrane is fully depolarized. Therefore, the theoretical value of flux increment is overestimated. But the aim of the modeling is not to give accurate values of the gain in filtration G but to determine the range of experimental parameters which improve the UF rate.

During τ_1, the UF flux is governed by Eq. (1), and during τ_2 it may be written as

$$J_v(t) = \frac{-Q_{ret}}{S} \tag{6}$$

Therefore, the total theoretically filtered volume collected during a period $T\ (= \tau_1 + \tau_2)$ is given by using Eqs. (1) and (6):

$$V_{fdyn} = S \times \int_0^T J_v(t)dt = SJ_{fp}(\tau_1 - \alpha\tau e^{-\tau_1/\tau} + \alpha\tau) - Q_{ret}\tau_2 \tag{7}$$

while for the same period the total volume collected in the stationary regime is

$$V_{fp} = SJ_{fp}T = SJ_{fp}(\tau_1 + \tau_2) \tag{8}$$

From Eq. (7) it is obvious that the smaller τ_2, the higher V_{fdyn} will be. But Eq. (7) does not take into account the time needed by the polarization layer to diffuse in the bulk fluid, nor the time needed to saturate the size variation of the backwash circuit. Experimental results have shown that τ_2 must be larger than 2 seconds. However, it is possible to determinate a lower limit for τ_1 and an upper limit for τ_2 by stating that, in order to have a positive gain, V_{fdyn} must be larger than V_{fp}. On using Eqs. (7) and (8) we obtain

$$SJ_{fp}\alpha\tau(1 - e^{-\tau_1/\tau}) - Q_{ret}\tau_2 > SJ_{fp}\tau_2$$

which requires

$$\tau_1 > \ln\left[\frac{\alpha\tau J_{fp}}{\alpha\tau J_{fp} - \left(J_{fp} + \frac{Q_{ret}}{S}\right)\tau_2}\right] \tag{9}$$

together with the condition that the denominator inside the logarithm be positive:

$$\tau_2 < \frac{\alpha\tau J_{fp}}{J_{fp} + \frac{Q_{ret}}{S}} \tag{10}$$

Let us apply Conditions (9) and (10) to a specific example. Using blood at 25% hematocrit, $C_p = 30$ g/L, an inlet blood flow of 3.3 cm^3/s, $Q_{ret} = 1.7$ cm^3/s, and $S = 0.65$ m^2 we have found experimentally that $J_{fp} = 2.6$ μm/s, $\alpha = 0.5$, and $\tau = 50$ seconds. Equation (10) yields $\tau_2 < 12.5$ seconds.

This condition on τ_2 is not compatible with experimental constraints, because applying a backwash for more than 5 seconds will generate very high negative transmembrane pressures. Actually, the value of τ_2 depends on the diffusivity of the particles in the concentration polarization layer, on the efficiency of the backwash, and on the circuit size variation at the same time. Therefore it is almost impossible to optimize τ_2 theoretically, and the optimum value for τ_2 must result from a compromise in order to ensure both that the depolarization is complete and that the experimental constraints are respected. For our experimental set-up, we have found that τ_2 must be between 2 and 3 seconds. Putting $\tau_2 = 3$ seconds in Eq. (9) leads to $\tau_1 > 13.8$ seconds. The condition on τ_1 is consistent with the fact that, for this example, the transient flux returns to the plateau in about 195 seconds [given by $\tau \ln(100\alpha)$], but we shall see below that there is a much more accurate way to determine τ_1.

So, τ_2 is not really an adjustable parameter since its optimum value is almost the same for all runs. Because the efficiency of the depolarization depends on V_{ret}, then Q_{ret} is strongly linked with τ_2 and must be found by a compromise. Consequently, τ_1 is the only controllable parameter whose determination is useful theoretically. According to Eq. (4), G is maximum when

$$\frac{d\left(\frac{V_{fdyn}}{V_{fp}}\right)}{d\tau_1} = 0 \tag{11}$$

using Eq. (7), the calculation gives

$$\alpha J_{fp} e^{-\tau_1/\tau}(\tau_1 + \tau_2 + \tau) + \left(J_{fp} + \frac{Q_{ret}}{S}\right)\tau_2 - \alpha J_{fp}\tau = 0 \tag{12}$$

With the data of the previous example, Eq. (12) gives $\tau_1 = 49.8$ seconds. Fitting this result in Eqs. (7) and (8), Eq. (4) gives $G = +18.5\%$. Actually, since V_{ret} is overestimated, G could be slightly higher if the depolarization process is efficient. Furthermore, τ_1 must be chosen as less than 40 sec-

onds to avoid leaving the system working too long at high pressure, i.e., it is better not to have the highest G gain in order to work safely.

It is useful to plot G as a function of τ_1 for several values of α. In Fig. 8 we can see that G can theoretically reach very high values (>80%) according to α, but for a biological fluid like blood, $\alpha = 1.2$ seems to be a maximum. Otherwise blood may be damaged because ΔP_{step} becomes too large. We can also see that around the maximum of G, a small variation of τ_1 does not change G much. So the adjustment of τ_1 is not critical. That means that the technique of step changes in pressure may be stable in spite of the dynamic regime, and therefore it may be easily automated.

This model is based on the polarization time constant τ of Eq. (1). It does not take into account the efficiency of the backwash which depends on nonaccessible parameters like the size variation or the diffusivity of the protein layer. Furthermore, it considers that τ_1 is the sole adjustable parameter; this is true in practice because τ_2 and Q_{ret} are fixed for all cases in order to optimize the backwash. Since τ_1 is very easy to change, an automatic procedure may be implemented with the technique of step changes in pressure synchronized with periodic backwash periods in order to set the best value for τ_1 in real time. This may be useful to ensure high

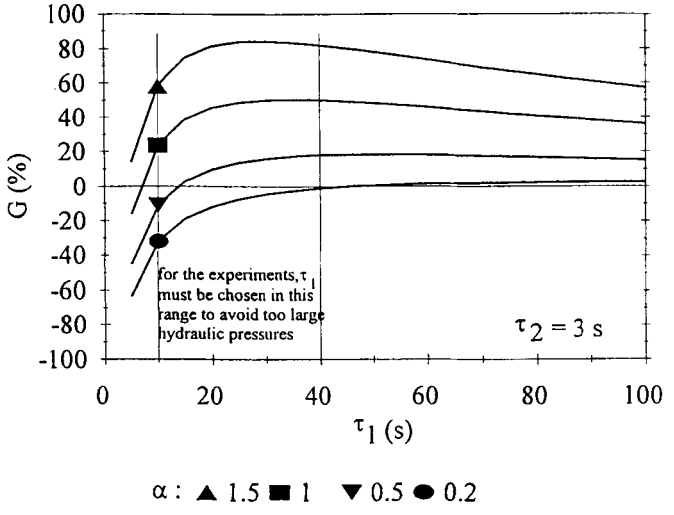


FIG. 8 Calculated gain as a function of τ_1 for $Q_i = 3.3$ cm^3/s, $J_{fp} = 2.6$ μm/s, $Q_{ret} = 1.7$ cm^3/s, and $\tau_2 = 3$ s.

efficiency not only in hemofiltration but more generally for all UF system when the membrane permeability decreases with time.

Finally, we have verified that this technique does not hemolyze blood, as is the case in hemofiltration.

SYMBOLS

C_p	bulk protein concentration (g/L)
EVi	Electrovalve i (—)
G	gain in filtration (%)
Hct	hematocrit (%)
J_{fp}	filtration flux at plateau (m/s)
J_{fpeak}	peak of filtration flux (m/s)
J_v	filtration flux (m/s)
P_1	main peristaltic pump (—)
P_2	backwash circuit peristaltic pump (—)
P_{max}	maximum transmembrane pressure (Pa)
P_{min}	minimum transmembrane pressure (Pa)
P_p	transmembrane pressure at onset of plateau (Pa)
Q_{ret}	backfiltered flow rate (cm^3/s)
S	membrane surface (m^2)
t	time (s)
T	period of a stepped pressure increment (s)
TMP	transmembrane pressure (Pa)
UF	ultrafiltration (—)
V_{fdyn}	volume of permeate filtered during T in dynamic regime (m^3)
V_{fp}	volume of permeate filtered at the plateau during T in steady-state regime (m^3)
V_{ret}	volume retrofiltered during T (m^3)
α	relative difference between peak flux and plateau flux (adim)
Δp	osmotic pressure difference at the membrane–solution interface (Pa)
ΔP_{step}	maximum and minimum transmembrane pressure difference (Pa)
τ	time constant of exponential decay (s)
τ_1	high-pressure duration (s)
τ_2	low-pressure duration (also backwash duration) (s)

REFERENCES

1. W. F. Blatt, A. Dravid, A. S. Michaels, and L. Nelsen, "Solute Polarization and Cake Formation in Membrane Ultrafiltration: Causes, Consequences, and Control Tech-

nique," in *Membrane Science and Technology* (F. E. Flinn, Ed.), Plenum, New York, NY, 1970.
2. M. C. Porter, "Concentration Polarization with Membrane Ultrafiltration," *Ind. Eng. Chem. Prod. Res. Dev.*, *2*, 234 (1970).
3. G. B. Van Den Berg and C. A. Smolders, "Flux Decline in Ultrafiltration Processes," *Desalination*, *77*, 101–133 (1990).
4. V. L. Vilker, "The Osmotic Pressure of Concentrated Protein and Lipoprotein Solutions and Its Significance to Ultrafiltration," *J. Membr. Sci.*, *20*, 63–77 (1984).
5. L. W. Henderson, C. K. Colton, and C. A. Ford, "Kinetics of Hemodiafiltration. II. Clinical Characterization of a New Blood Cleansing Modality," *J. Lab. Clin. Med.*, *85*, 372–390 (1975).
6. V. Chen, A. G. Fane, and C. J. D. Fell, "The Use of Anionic Surfactants for Reducing Fouling of Ultrafiltration Membranes: Their Effects and Optimization," *J. Membr. Sci.*, *67*, 249–261 (1992).
7. S. M. Finnigan and J. A. Howell, "The Effect of Pulsed Flow on Ultrafiltration Fluxes in a Baffled Tubular Membrane System," *Desalination*. *79*, 181–202 (1990).
8. V. G. J. Rodgers and R. E. Sparks, "Effect of Transmembrane Pressure Pulsing on Concentration Polarization," *J. Membr. Sci.*, *68*, 149–168 (1992).
9. M. Y. Jaffrin, B. B. Gupta, R. L. Cannon, and L. H. Ding, "Enhancement of Plasma Filtration in Hollow Fiber Filters by Pulsatile Blood Flow," *Life Support Syst.*, *2(Suppl.)*, 207–210 (1984).
10. L. H. Ding, J. M. Laurent, and M. Y. Jaffrin, "Dynamic Filtration of Blood: A New Concept for Enhancing Plasma Filtration," *Int. J. Artif. Organs*, *14*, 365–370 (1991).
11. M. Y. Jaffrin, L. H. Ding, M. Defossez, and J. M. Laurent, "Interpretation of Transient Ultrafiltration and Microfiltration of Blood and Protein Solutions," *Chem. Eng. Sci.*, *50*, 906–915 (1995).
12. L. H. Ding, M. Y. Jaffrin, and M. Defossez, "Concentration Polarization Formation in Ultrafiltration of Blood and Plasma," *J. Membr. Sci.*, *84*, 293–301 (1993).
13. M. Defossez, L. H. Ding, M. Y. Jaffrin, and M. Fauchet, "Scintigraphic Study of Local Membrane Phenomena Limiting the Ultrafiltration Flux in a Hollow Fiber Hemofilter," *J. Colloid Interface Sci.*, *177*, 179–191 (1996).

Received by editor March 27, 1996
Revision received September 16, 1996