

# Wettable phosphorylcholine-containing polymers useful in blood filtration

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The use of phosphorylcholine (PC)-containing polymers has long been acknowledged as a method to improve the haemocompatibility of blood contacting devices. Such polymers were investigated for coating leukocyte filters, as a means of preserving precious platelet numbers and function. It was demonstrated that by use of such coated filters, the platelet recovery could be significantly increased by some 30%. This was however, balanced by a decrease in the leukocyte removal efficiency of the filter. More problematic however, was the poor critical wetting surface tension (CWST) of the filter ( $45 \text{ mNm}^{-1}$ ). This was due to the surface expression of the hydrophobic groups of the polymer in air. In order to obtain a filter that could be immediately wetted by the blood and hence remove the need for any detrimental priming of the filter, the PC polymer was modified in order to reduce its hydrophobic content. A series of new cross-linkable polymers was developed that contained other hydrophilic monomers, yet could film-form to produce a coating stable to fluid contact. These materials demonstrated the required wetting characteristics (a CWST of  $> 78 \text{ mNm}^{-1}$ ), whilst retaining the excellent blood-contacting properties.

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## 1. Introduction

The filtration of blood is necessary in order to remove donor leukocytes and thus reduce the adverse effects they cause transfusion recipients [1,2]. Many types of filtration device have been developed from a range of materials. Most common are filters composed of a mat of nonwoven fibers that separate the white cells from the other blood components on the basis of size. The filters are used only once and then disposed of, and are fabricated from materials such as polyethylene terephthalate fibers which are far from compatible with the blood. Indeed, some of the efficiency of the filter can be attributed to the fact that granulocytes in particular recognize the fibers as foreign and adhere to the surface [3]. The down side to this effect is that many other blood components become activated, in particular platelets, which are of great value to the transfusion patient. Hence, although filtration removes problematic leukocytes, the general condition of the blood is worsened and the level of platelets also reduced.

Many approaches have been studied in order to improve the leukocyte depleting properties of filters whilst retaining maximal platelet recovery. One strategy has been simply to coat the filter fibers with various polymer coatings in order to mask the thrombogenicity of the underlying substrate [4–6]. With this strategy in mind, one family of materials that has received a great deal of attention in recent years, and is indeed yielding many significant clinical results in blood contacting applications, is that based on PC-containing polymers [7].

Phosphorylcholine (PC) is the major phospholipid head-group found in the outer leaflet of biomembranes. Biomimetic synthetic polymers that contain this head-group have been shown to be haemocompatible in nature in a variety of tests [8–10]. For instance, significant reduction of platelet adhesion and activation has been demonstrated *in vivo* for PC-coated coronary stents [11]. Results such as these support the view that these materials may make ideal coatings for blood filtration materials, where platelet recovery and the general condition of the blood are of importance. Preliminary work using simple PC polymer coatings has supported this view, although issues concerning the immediate wettability of the coated filters was noted [12]. The work described here reports an extension of this initial investigation.

## 2. Materials and methods

### 2.1. Materials

The monomer 2-methacryloyloxyethylphosphorylcholine (MPC) was made and purified by the method described previously [13]. Poly(ethylene glycol) methacrylate (PEGMA, 550 Mw) was purchased from Inspec Ltd. (Bisomer 550) and all other monomers were purchased from the Aldrich Chemical Co. and used without further purification. These included lauryl methacrylate (LMA), n-butyl methacrylate (BMA), 2-hydroxypropyl methacrylate (HPMA), 3-(trimethoxysilyl)propyl methacrylate and N,N'-dimethylacrylamide

(NNDMA). The polymers described here are represented in terms of the weight percent content of each monomer in the reaction feed (e.g. MPC<sub>37</sub>LMA<sub>63</sub> contains 37 wt % MPC and 63 wt % LMA). Polymers were prepared using a monomer-starved free-radical polymerization technique detailed by us elsewhere [12, 14]. The materials were characterized by <sup>1</sup>H and <sup>13</sup>C NMR, elemental analysis and HPLC determination of residual monomer contents to ensure that the ratio of monomers combined in the feed were essentially that found in the final product.

## 2.2. Coating of filter materials

Sections of leukocyte filter (10 cm<sup>2</sup>, Pall non-woven PET fibers No. B-1358M) were dipped into the appropriate polymer solution for between 5–10 s in order to ensure complete penetration into the filter mat. The material was then removed and allowed to drip-dry in a fumehood overnight, or in the case where the polymer was the cross-linkable type, for at least 2 h before curing in an oven overnight at 70 °C.

## 2.3. Filtration experiments

Blood filtration experiments were carried out using platelet rich plasma (PRP). The filter material under study was cut into three 8 cm diameter circles and each fitted into a separate polycarbonate filter holder fitted with a rubber “O” ring to ensure a tight seal. Care was taken to avoid over-tightening the holder in order to avoid shearing the fibers and thus damaging the filter mat. The PRP was fed by gravity from a blood bag reservoir, *via* a 29 cm PVC tube and into the filter housing. The filtered PRP was collected from the underside of the filter holder using a bijou and the platelet count determined using a Coulter Counter.

## 2.4. Blood contact SEM and fibrinogen adhesion assay

Each sample of filter material was placed in a test tube to which 4 ml of citrated whole blood, collected less than 2 h previously, was added. The tubes were placed on roller mixers for 45–60 min at room temperature. The blood was decanted from each tube and 4 ml of phosphate buffered saline (Inverclyde Biologicals) was added. The samples were washed using a DiaCent 2000 cell washer with a program of 4 washes with phosphate buffered saline (PBS), and then transferred to clean tubes. 4 ml of glutaraldehyde (Sigma), diluted in PBS to 2%, was added to each tube and the tubes placed on roller mixers for 10–15 min at room temperature. The glutaraldehyde solution was decanted from each tube, replaced with PBS and the samples washed as described above. The samples were then rinsed by hand in distilled water, and placed in clean tubes that were left overnight in a desiccator. Samples were attached to aluminum mounts using double-sided sticky carbon discs, and sputter coated with gold using a Polaron SC502 Sputter Coater. Inspection of the samples was carried out within 36 h of preparation using a Hitachi S-3500N SEM.

For fibrinogen adsorption determination, an enzyme-linked immuno-sorbent assay (ELISA) was used as

previously described [15]. PET strips (30 mm × 9 mm) were dip-coated from ethanolic solution with a 10 mg ml<sup>-1</sup> solution of the polymer under study. Where the polymer was of the cross-linkable type, the coated strip was cured in an oven at 70 °C overnight to induce crosslinking. The sample was then subjected to the assay (*n* = 7 for each coating), where the result was compared to uncoated PET as a control.

## 2.5. Contact angle and critical wetting surface tension determination

Wettability of the polymeric coatings was assessed by a number of techniques. For contact angle measurements, 22 mm<sup>2</sup> glass cover slips were dip-coated into solutions of the various polymers in propan-2-ol at 10 mg ml<sup>-1</sup>, and a withdrawal speed of 3 mm sec<sup>-1</sup>. If the polymers were of the cross-linkable type, the cover slips were placed in an oven at 70 °C overnight to cure before being analyzed. The dynamic contact angle profile was determined using a Cahn DCA with ultrapure water (Romil) as wetting medium, and a stage speed of 157 μm sec<sup>-1</sup> unless otherwise stated. A minimum of 3 consecutive cycles was normally performed in order to determine hysteresis effects due to reorientation.

Static contact angles were determined on coated glass slides by careful placement of a 10 μl drop of ultrapure water (Romil) onto the surface. The side profile of the resulting drop was imaged by a JVC TK-1280E video camera fitted with a Navitor Zoom 6000II lens and connected to a JVC BM 1400PN monitor with Hitachi VY-300 video printer, and a hard-copy of the video image taken. The contact angle of the fluid and the surface was measured at each side of the drop profile and an average taken. A minimum of five drops taken at random across the coating was imaged per sample.

Critical wetting surface tension (CWST) was determined using a technique reported in detail by us in a similar study [12]. It involved the use of a range of solutions of surface tensions varying from 38.43 to 78.33 mNm<sup>-1</sup>. A drop of each solution was tested sequentially on a different area of the filter for a 10 min period, to see if it wetted through the pores or remained as a distinct droplet at the surface. The CWST for the filter was quoted as the average of the two solutions that sat at the boundary between wetting and non-wetting.

## 3. Results and discussion

### 3.1. Bovine blood filtration

Initial evaluation of the platelet preservation properties of PC-containing polymers was performed by comparison of the filtration efficiency of uncoated *versus* coated commercial non-woven leukocyte material. Citrated bovine blood was passed through 3 filters of each type and the numbers of both platelets and white blood cells determined and compared to the unfiltered blood. Fig. 1 shows the comparison of these cell counts for the uncoated natural filter with the same material coated with two different concentrations of a well-characterized PC copolymer, MPC<sub>37</sub>LMA<sub>63</sub> described by us in detail previously [8, 12]. Clearly, platelet recovery was vastly improved by use of the coated filter, the higher

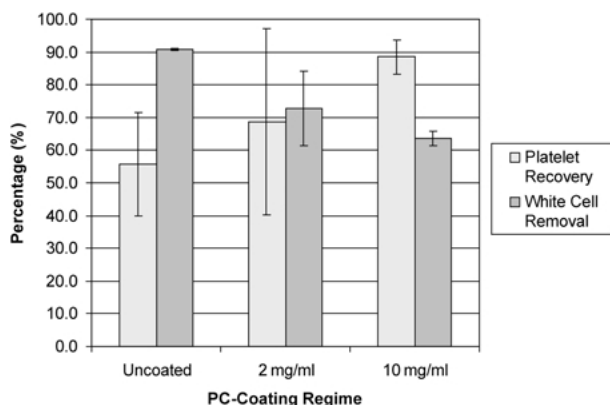


Figure 1 Effect of PC coating at two different concentrations on filter performance.

concentration yielding the best results (an increase of some 30%,  $p = 0.027$  by Student's  $t$ -test). The lower concentration coating also produced an average increase in platelet recovery, but the higher variability of the data meant that this was not statistically significant compared to the uncoated filter. The variability was probably due to inadequate coating of the filter fibers at such low polymer concentrations. Concomitantly, the number of white cells that was found to pass through the filter was also found to increase for the coated material. This may not be totally unexpected, as some of the filters natural efficiency is derived from the interaction and adhesion of white cells to the filtration material. The PC-coating reduced this level of cellular interaction and hence the leukocyte depleting properties. It is thought however, it may be possible to compensate for loss of filtration efficiency by control over the packing density of the fiber mat such that white cell removal becomes predominantly a size-related phenomenon.

Whilst the effect of PC-coating on platelet recover was encouraging, it was another feature of the filter's performance that proved to be of more concern. When blood comes into contact with the filter mat, it is a prerequisite that the blood should wet the fibers spontaneously and flow through the fiber mat freely under the influence of gravity. It was found that once coated, it was necessary to "prime" the filter by squeezing the blood bag in order to encourage the blood to wet through the fiber mat. This type of "priming" process is thought to be detrimental and may lead to activation of some of the components and general deterioration of the condition of the blood. This observation was not in keeping with the known hydrophilicity of PC-containing polymer systems [7]. It has also been reported however, that PC-polymers may undergo reorientation of the chemical groups at the surface of the material in order to minimize interfacial free energy [16,17]. Indeed, a study of the dynamic contact angle for coatings of the simple copolymer MPC<sub>37</sub>LMA<sub>63</sub> showed that the initial contact angle was very high (*ca.*110°), yet after a brief immersion in water, the coating became very wettable with low contact angles [12,17]. In this study, the same effect was observed in that the blood was unable to wet the initially hydrophobic coating, but once exposure to the aqueous environment had reoriented the PC groups to the surface,

the coating was able to significantly reduce cellular interaction with the substrate.

Whilst maximizing platelet recovery is a target attribute required of the modified filter, this cannot be at the expense of other key properties such as the need for the filter to be immediately wetted by the blood. The remainder of this paper describes the strategies adopted in order to modify the characteristics of the coating polymer systems in order to achieve a spontaneously wettable surface coating whilst retaining its haemocompatibility.

### 3.2. Polymer system modifications

In order that the coating would be spontaneously wettable, it seemed sensible to reduce the level of hydrophobic component within the polymer, with a concomitant increase in the hydrophilic portion. This, of course, has its own consequences, as the stability of the coating is derived from the strong physi-adsorption between the hydrophobic domains in the polymer and the substrate surface [8, 18]. Indeed, increasing the hydrophilicity too far would render the polymer water-soluble and hence useless as a permanent coating. We have previously described a variant PC-polymer family, based upon the simple methacrylate copolymers already mentioned, that contains a cross-linking system consisting of trimethoxysilyl and hydroxyl-groups [15]. In this instance, the polymer not only forms coherent physi-adsorbed coatings but can also be thermally post-crosslinked for additional stability.

The most obvious strategy was therefore to replace a proportion of the LMA component in the crosslinkable polymers with MPC in an attempt to mask the expression of the hydrophobe at the surface when in air. Table I demonstrates this effect using a series of high-MPC containing cross-linkable polymers. Interestingly, even comparatively low levels of LMA were sufficient to dominate the surface characteristics in air, causing severe hysteresis in the dynamic contact angle profile of the coating. When the level of hydrophobe was dropped below 10 wt%, the film-forming properties of the polymer became very poor, resulting in incoherent powdery coatings due to an increase in the glass transition temperature of the material. Thus, although MPC itself is an extremely hydrophilic monomer, very high levels of this material in polymers designed for coating applications were in general precluded due to the effects of its crystalline nature upon film-formation.

Other studies by us have shown that the levels of MPC in these methacrylate polymers could be greatly reduced

TABLE I Advancing contact angle variation for a polymer coating series with increasing amounts of PC

Polymer formulae	Advancing contact angle ( $\theta_A$ )°
MPC <sub>30</sub> LMA <sub>50</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	108 ± 6
MPC <sub>40</sub> LMA <sub>40</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	106 ± 6
MPC <sub>50</sub> LMA <sub>20</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	113 ± 8
†MPC <sub>70</sub> LMA <sub>10</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	110 ± 15

† Denotes poor coating achieved.

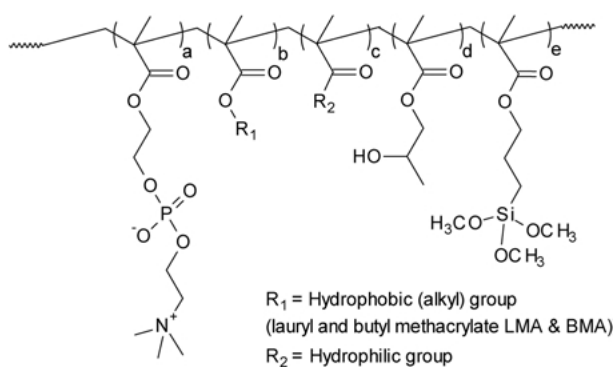


Figure 2 Generalized chemical structure of modified PC polymers evaluated for filter coating applications.

whilst still maintaining an acceptable degree of biocompatibility [19]. Indeed, in many previously described systems, surface reorientation effects ensure a PC-rich interface in aqueous environments [10, 15]. Here it was decided to fix on a constant level of MPC of 25 wt %, as this was more than adequate to ensure a biocompatible surface for these coating materials. The cross-linking system was also fixed at 15 wt % hydroxypropyl methacrylate and 5 wt % trimethoxysilyl methacrylate, to guarantee a stable surface coating, regardless of hydrophilic monomer content. The remaining 55 wt % of the polymer formulation was split between differing ratios of hydrophobic/hydrophilic monomer combinations (Fig. 2). A balance between these monomers was sought in order to obtain both good film-forming properties and spontaneous wettability. Two readily obtainable hydrophilic monomers were chosen for study: *N,N'*-dimethylacrylamide (NNDMA) and methoxy(polyethyleneglycol) methacrylate (550 Mw PEG, MPEGMA). Both monomers were shown to incorporate within the methacrylate systems with good conversion.

### 3.3. Surface wetting characteristics

The first consideration was that of the effect of crosslinking within the system on the orientation effects of the hydrophilic groups. It can be seen from the dynamic contact angle (DCA) trace shown in Fig. 3(a) that the initially hydrophobic surface nature of MPC<sub>37</sub>LMA<sub>63</sub> ( $\theta_A$  1st cycle  $\sim 105 \pm 3^\circ$ ) was changed in character once exposed to water ( $\theta_A$  2nd cycle  $\sim 30 \pm 10^\circ$ ); this occurred within one cycle, i.e. instantaneously upon exposure to water. With the cross-linked polymer coating MPC<sub>30</sub>LMA<sub>50</sub>HPMA<sub>15</sub>TSMA<sub>5</sub> the situation was somewhat different (Fig. 3(b)). The initial contact angle cycle showed the surface to be slightly more hydrophobic in nature than the simple copolymer system; the main difference however, being that the surface did not demonstrate the instant reorientation to a hydrophilic character. Certainly, at the stage speed selected for the experiment, the initial few millimeters of the sample mirrored that of a wettable surface, as the water associated with the sample upon its initial immersion drained under gravity to the lower portions of the glass slide. Once this “pre-wetted” area had been passed, the contact angle once more reverted to a value similar to

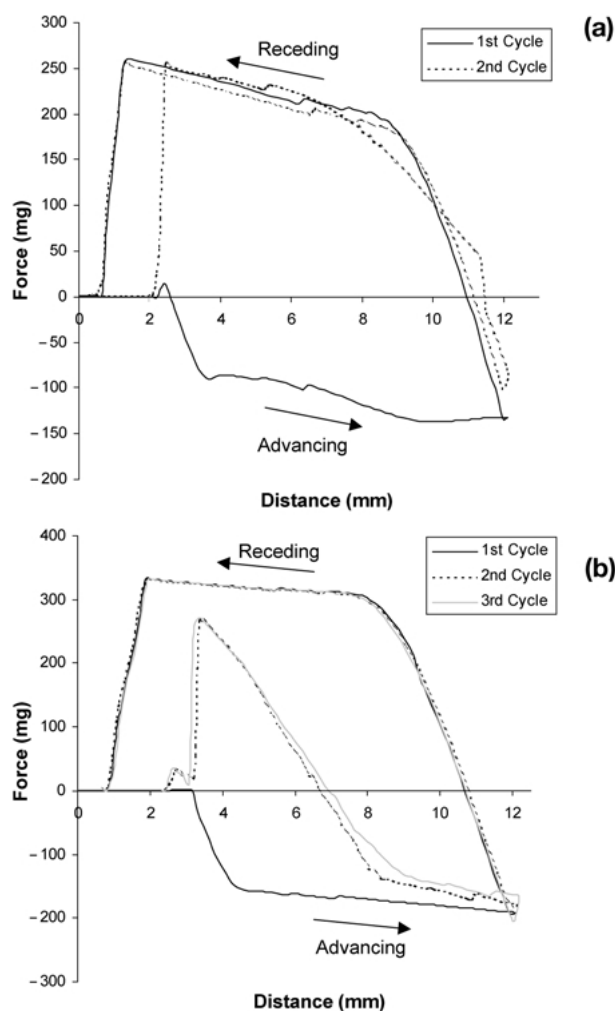


Figure 3 Dynamic contact angle traces for (a) MPC<sub>37</sub>LMA<sub>63</sub> and (b) MPC<sub>30</sub>LMA<sub>50</sub>HPMA<sub>15</sub>TSMA<sub>5</sub>.

that prior to immersion (i.e. the surface had remained substantially unchanged in character from that of the initial hydrophobic surface). This observation could be substantiated by performing a one-dip cycle with a dwell time of several minutes to allow time for the water film to evaporate from the surface of the slide. Upon immersion during a second cycle, a profile somewhat similar to that of the first was obtained. Thus, it would seem that for the cross-linked system MPC<sub>30</sub>LMA<sub>50</sub>HPMA<sub>15</sub>TSMA<sub>5</sub>, the surface orientation times are increased, as the mobility of the polymer chains particularly at the surface interface, are significantly reduced by the inter-chain cross-links.

This slower orientation time observed for the cross-linked system could be overcome by increasing the ratio of hydrophilic to hydrophobic content in the polymer. For the system MPC<sub>40</sub>LMA<sub>40</sub>HPMA<sub>15</sub>TSMA<sub>5</sub> the amount of MPC was increased by 10 wt % and LMA concomitantly decreased by 10%. The DCA revealed no change in the advancing angle in the first cycle ( $106 \pm 6^\circ$ ), but the second cycle indicated complete reorientation to a hydrophilic surface ( $\theta_A$   $26 \pm 11^\circ$ ), the trace being very much the same as that obtained for the non-cross-linked system in Fig. 3(a). Thus, when the critical balance between hydrophilic and hydrophobic content is exceeded, the reduction in chain mobility introduced by the cross-linking cannot prevent the rapid surface orientation of sufficient groups to render the

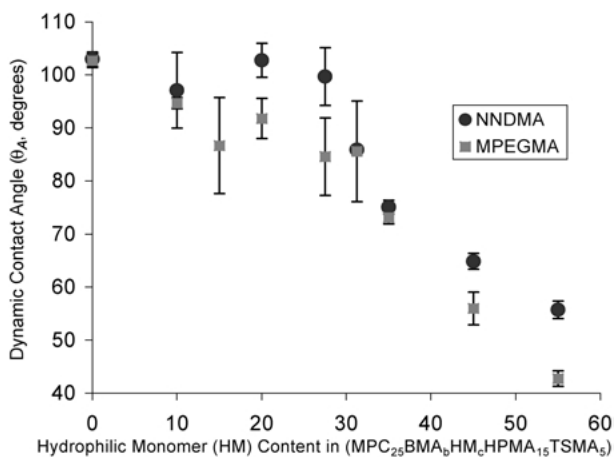


Figure 4 Effect of hydrophilic:hydrophobic monomer ratio on the advancing contact angles of PC copolymer coatings.

surface wettable. The objective of this study however, was to obtain a stable cross-linked coating formulation in which the hydrophilic groups were expressed at the air interface in the first instance, would not require time to reorientate, and would therefore be instantly wettable. This would intuitively require a significant reduction in the hydrophobic component of the polymer coating.

Coatings were therefore evaluated in which the hydrophobe:hydrophile ratios (HB:HP) were varied within the system and the DCA measured over a number of cycles. The hydrophobe was fixed as BMA for convenience, as a study had shown little difference between the contact angles produced by equivalent weight percents of butyl methacrylate compared to LMA (data not shown). Fig. 4 shows the effect of HB:HP on first cycle advancing angle ( $\theta_A$ ) for both NNDMA and MPEGMA polymer coatings. Clearly, any inclusion of hydrophobe affected the initial advancing angle value; within the compositions studied, the hydrophobe was seen to manifest itself and thus largely dictate the nature of the surface-air interface, as anticipated if the interfacial free energy is to be minimized. Indeed, for both hydrophilic monomers under study, it was only at a level of approximately 20 wt% or less of hydrophobic component, that the hydrophilic moieties were beginning to be expressed at the surface and able to influence the value of the initial advancing angle. As demonstrated in Fig. 4, the lowest values for  $\theta_A$  (and thus best wetting characteristics) were obtained when no hydrophobe was present at all, the film-forming properties being aided by the hydrophilic comonomer and stability attained purely from the cross-linking moieties.

When the DCA was performed for the range of polymers described in Fig. 4, trace profiles varying somewhere between that obtained for the first and second cycles in Fig. 3(a) were generally obtained. For the MPC<sub>25</sub>BMA<sub>35</sub>NNDMA<sub>20</sub>HPMA<sub>15</sub>TSMA<sub>5</sub> system however, it was noted that the first cycle was always characterized by a jagged saw-tooth pattern on the advancing stage (Fig. 5(a)). This phenomenon has been reported before for other polymer systems, and is characteristic of water advancing over a hydrophobic surface that experiences rapid rearrangement to a hydrophilic interface [20]. The water has an affinity for

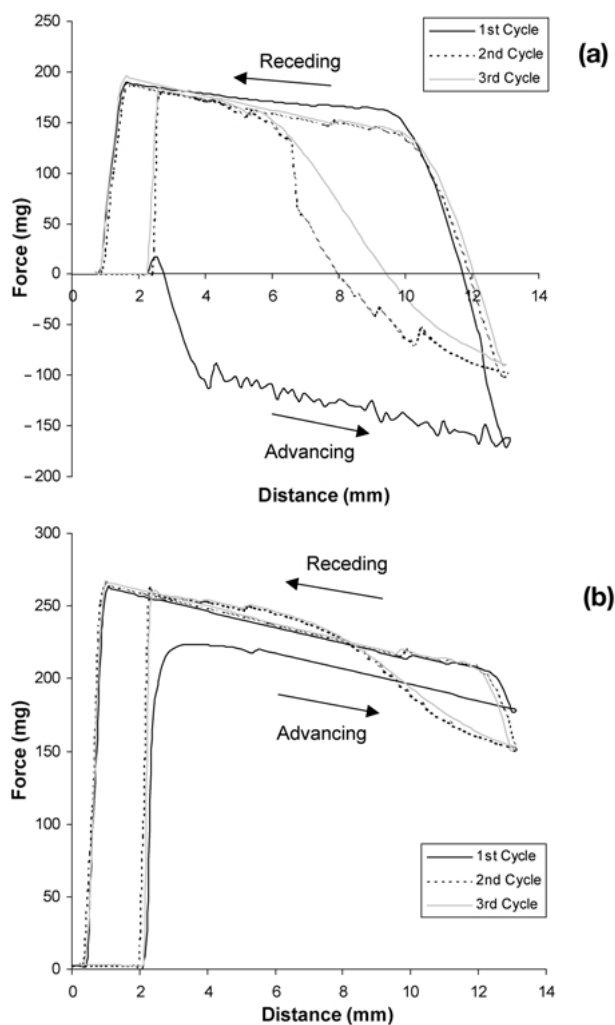


Figure 5 Dynamic contact angle traces for (a) MPC<sub>25</sub>BMA<sub>35</sub>NNDMA<sub>20</sub>PMA<sub>15</sub>TSMA<sub>5</sub> and (b) MPC<sub>30</sub>PEGMA<sub>55</sub>HPMA<sub>15</sub>TSMA<sub>5</sub>.

the wetted area but experienced resistance to movement over the next hydrophobic domain. Eventually, the force of immersion overcomes the resistance to the water advancement, and the water jumps to the next section of the sample, hydrating it instantly and the process is repeated. Hence, the advancing stage of the first cycle records the intermittent jumping of the water front as it progresses across the sample. This process was only seen to occur partially on the second cycle, as much of the surface had reoriented; on the third cycle, it had disappeared altogether, the surface being very wettable. It was interesting that this was the only polymer system for which this observation was made. The balance of hydrophilic and hydrophobic character coupled with the sample immersion speed (a known critical factor for this effect) must have been ideal for the effect to manifest itself in this sample. No detailed study on immersion speeds was undertaken here to study this effect further.

For the systems that contained no hydrophobic content at all, the DCA traces were very distinctive, displaying very little hysteresis, the advancing and receding traces closely paralleling one another. Fig. 5(b) illustrates a typical profile obtained for MPC<sub>25</sub>PEGMA<sub>55</sub>HPMA<sub>15</sub>TSMA<sub>5</sub>, and was similar to that obtained for the MPC<sub>25</sub>NNDMA<sub>55</sub>HPMA<sub>15</sub>TSMA<sub>5</sub>. In this case the advancing angle was  $43 \pm 2^\circ$ , and receding angle  $38 \pm 6^\circ$ . Only when the hydrophobic

content was reduced to zero was the instantly wettable surface obtained that was specifically sought for the leukocyte filtration application.

### 3.4. Aspects of coated filter performance

The first measure of filter performance was the determination of the critical wetting surface tension of the coated material. Table II summarizes the main findings for a small selection of the polymers studied. Clearly, whilst those filters coated with the simple MPC copolymer and cross-linked systems had an unacceptably low CWST value ( $45 \text{ mNm}^{-1}$ ), those filters coated with the PEGMA and NNDMA polymers possessed the necessary characteristics to enable blood to instantly wet through the surface of the filter ( $\text{CWST} > 78 \text{ mNm}^{-1}$ ). Comparison of the scanning electron micrographs of the non-woven filter surface pre- and post-coating demonstrated that a small degree of webbing between the PET fibers occurred upon coating the filter (Fig. 6(a) and (b)). Whilst this would have had some impact on reducing the porosity of the filter, the benefits of the wettable coating far outweighed this, producing a surface that would wet far more rapidly and with much higher surface tension liquids compared to the uncoated filter. All of the filters used in this study were coated at a polymer concentration of  $10 \text{ mg ml}^{-1}$ . We have shown previously that this concentration could be optimized in order to reduce webbing, whilst maintaining the wetting ability and haemocompatibility of the filter [12].

The haemocompatibility of the polymer coating was initially assessed using the fibrinogen ELISA assay. Thrombus formation occurs through a cascade of reactions by which normally inactive factors become active either by proteolytic action or foreign surface contact. Fibrinogen is a protein found in high concentration in the blood ( $2000\text{-}4500 \text{ } \mu\text{g/ml}$ ) that when activated, is polymerized into a gel of fibrin strands that give structure to the forming clot. This protein is therefore an obvious marker for assessing these potential non-thrombogenic materials. Table III summarizes the results

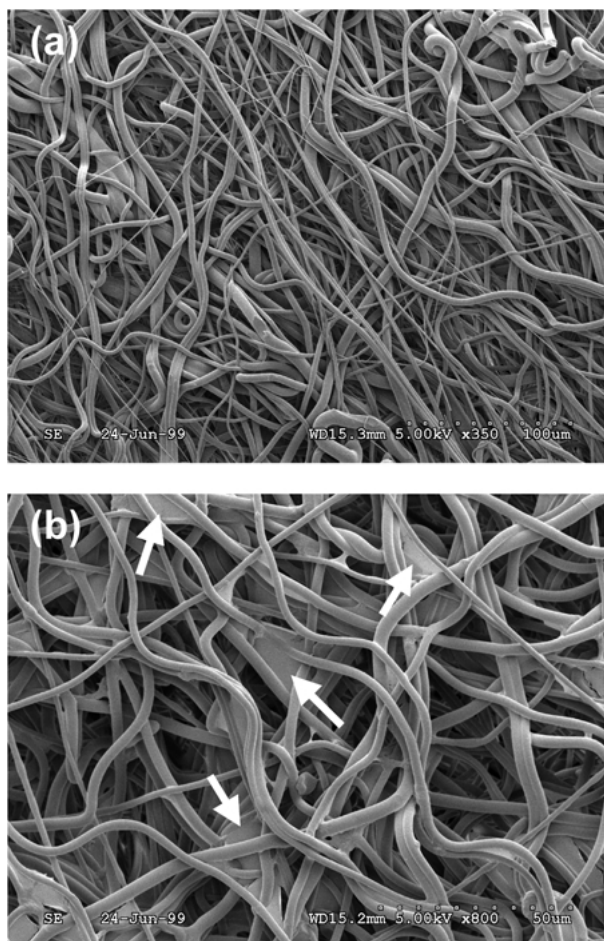


Figure 6 Scanning electron micrographs of (a) uncoated PET fiber mat; (b) PC coated PET fiber mat (note some webbing produced by the coating as indicated by the arrows). Both filters are pictured before use.

obtained with a selection of polymers and shows that all of the coatings were capable of significantly reducing the amount of fibrinogen adsorption compared to the uncoated PET substrate ( $p > 0.001$  for all samples by Student's  $t$ -test). There was no statistical difference between the different polymer coatings.

Scanning electron microscopy (SEM) of the filter surface after whole blood contact revealed that a typical filter coated with any of the PC polymer formulations

TABLE II Dynamic contact angle and critical wetting surface tension data for a series of modified PC polymer coatings

Polymer formulae	$\theta_A(^{\circ})$	$\theta_R(^{\circ})$	CWST ( $\text{mNm}^{-1}$ )
MPC <sub>37</sub> LMA <sub>63</sub>	$105 \pm 3$	$25 \pm 8$	45
MPC <sub>25</sub> BMA <sub>55</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	$103 \pm 6$	$11 \pm 10$	45
MPC <sub>25</sub> NNDMA <sub>55</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	$56 \pm 3$	$52 \pm 4$	> 78
MPC <sub>25</sub> PEGMA <sub>55</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	$43 \pm 2$	$38 \pm 6$	> 78

TABLE III Fibrinogen adsorption ELISA assay data for a series of modified PC polymer coatings

Polymer formulae	Absorbance @ 450 nm	Standard deviation	% Reduction in Fg adsorption
PET	0.993	0.091	-NA-
MPC <sub>37</sub> LMA <sub>63</sub>	0.192	0.009	80.7
MPC <sub>25</sub> BMA <sub>55</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	0.245	0.021	75.3
MPC <sub>25</sub> NNDMA <sub>55</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	0.235	0.014	76.3
MPC <sub>25</sub> PEGMA <sub>55</sub> HPMA <sub>15</sub> TSMA <sub>5</sub>	0.228	0.018	77.0

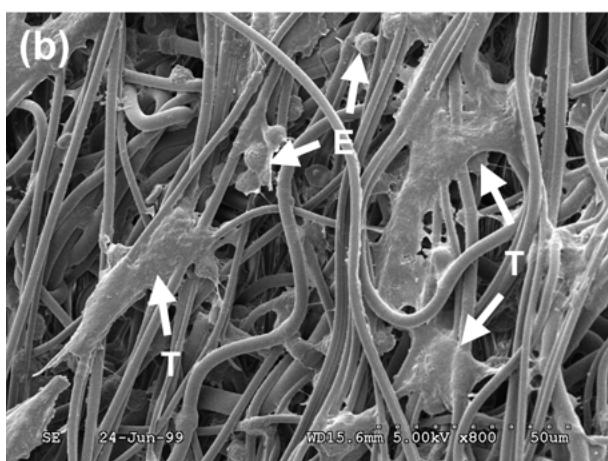
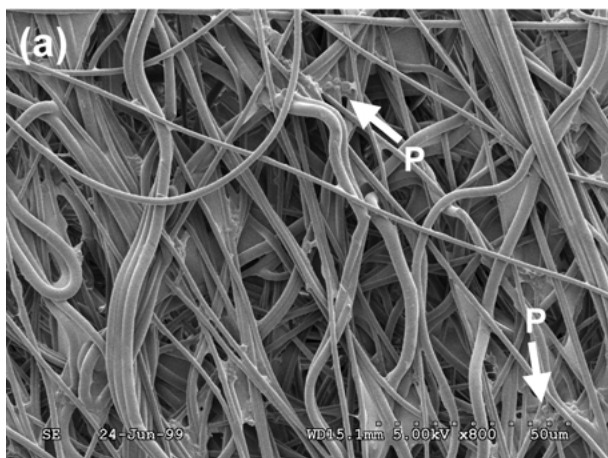


Figure 7 Scanning electron micrographs of blood contacted filters (a) PC coated fiber mat (note occasional webbing and non-activated platelets on the fiber surfaces); (b) uncoated fiber mat showing areas of thrombotic matrix (T), and trapped erythrocytes (E).

was largely free of proteinaceous or cellular material. Fig. 7(a) shows such an SEM image, again several areas of webbing between the fibers are evident. Interestingly, platelets were observed on occasion (P), but they are clearly non-aggregated and maintain their discoid shape, indicating they were passively sitting on the PC coated surface and were not activated. The uncoated filter on the other hand (Fig. 7(b)) clearly shows areas of thrombotic matrix (T), occasionally with erythrocytes entrapped within the network (E). The uncoated PET filter mat is clearly not haemocompatible and activates components within the blood resulting in thrombus formation and ultimately a reduction in valuable platelet recovery.

#### 4. Conclusions

This study has demonstrated that when attempting to modify a particular property of a device's performance, in this instance to improve the compatibility of a leukocyte filter with blood platelets in order to increase their recovery, attention must also be paid to the impact of this modification on other aspects of the device's function. Whilst the use of a simple PC-based copolymer that has proved useful in rendering many other surfaces

haemocompatible in the past, certainly improved the haemocompatibility characteristics of the filter, the wetting properties were adversely affected. With the development and surface characterization of alternative crosslinkable coating polymer systems, it was apparent that even small amounts of hydrophobe had a major influence on the surface properties. Only by completely replacing the hydrophobic content of the polymer with hydrophilic moieties such as NNDMA and PEGMA, were spontaneously wettable surfaces with low initial  $\theta_A$  and minimal hysteresis obtained. When coated onto the leukocyte filtration material, the desired CWST's  $> 78 \text{ mNm}^{-1}$  were obtained and blood-contact SEM showed the coatings to have excellent haemocompatibility.

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