Feature Article

High internal phase emulsion templating as a route to well-defined porous polymers

Neil R. Cameron*

Department of Chemistry and Interdisciplinary Research Centre in Polymer Science and Technology, University of Durham, South Road, Durham DH1 3LE, UK

Abstract

The use of high internal phase emulsions (HIPEs) as templates to create highly porous materials (PolyHIPEs) is described. Polymerisation occurs around emulsion droplets, which create voids in the final material. The void fraction is very high and can reach levels of 0.99. Varying the emulsion composition can control features of the morphology of the resulting porous materials, such as the void diameter and degree of interconnection. Other parameters can also be varied, for example surface area can be increased from 3 to around 700 $m^2\,g^{-1}$. Rubbery materials can be produced from hydrophobic elsatomers and PolyHIPEs with high thermo-oxidative stability are prepared from high performance materials such as poly(ether sulfone). The highly porous materials so produced are finding applications in areas such as solid supported organic chemistry, sensors, cell culturing and tissue engineering.
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1. Introduction

High internal phase emulsions (HIPEs) have been known for many years [1] and find applications in areas such as food preparation, fuels, oil recovery and cosmetics. Their defining feature is an internal, or droplet, phase volume ratio (ϕ) of 0.74 or greater (i.e. at least 74% of the volume of the emulsion is comprised of droplets). This value of ϕ represents the maximum volume ratio of uniform non-deformable spheres when packed in the most efficient manner. Since HIPEs can be formed with much higher values of ϕ, in fact up to 0.99, it is obvious that either the droplets are non-uniform in size or are deformed into polyhedra.

One application of HIPEs that has found considerable use in materials science is as templates to create highly porous structures [2]. Such materials, formed by curing the continuous, or non-droplet, phase of the emulsion, are known as PolyHIPEs. Following solidification of the continuous phase, the emulsion droplets are embedded in the resulting material. Under the correct conditions (vide infra), small interconnecting windows are formed between adjacent emulsion droplets allowing the droplet phase to be removed by drying. This produces a highly porous and permeable material, an example of which is shown in Fig. 1(a). At this point, it is instructive to define some terms that will be used subsequently. First of all, the spherical cavities in the material are referred to as 'voids' (there has been a tendency to use the term 'cell' to describe these, and indeed these materials belong to the class of open-cell (solid) foams, however, we prefer the term 'voids' since part of our work involves the culture of (biological) cells inside these materials and confusion could easily arise). Secondly, the interconnecting pores between each void and its neighbours are referred to as 'windows'. Finally, the much smaller pores present within the walls of certain PolyHIPE materials (Fig. 1(b)) are known as 'pores'.

This article reviews the work conducted by the author and his research group during the period 1991–2004, and also highlights key publications by other workers in the field that are of particular relevance.

* Tel.: +44 191 3342008; fax: +44 191 3844737.
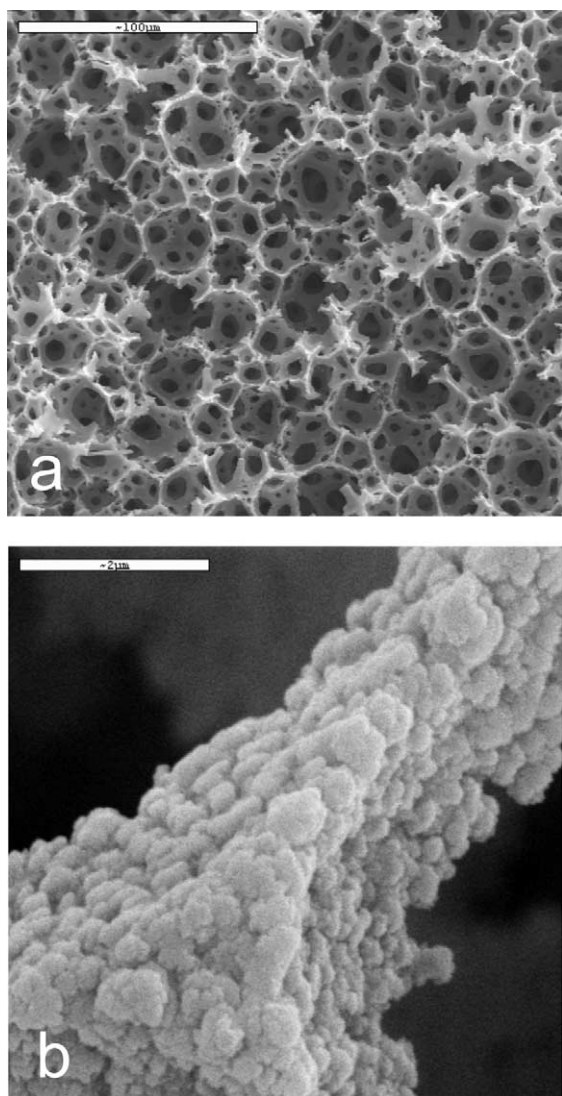 *E-mail address:* n.r.cameron@durham.ac.uk.

Fig. 1. SEMs showing the morphology of PolyHIPE materials prepared (a) without and (b) with organic phase soluble porogens. Scale bars: (a) 100 μm; (b) 2 μm ((b)is reproduced by permission of the Royal Society of Chemistry).

2. PolyHIPE preparation and chemistry

The process of preparing PolyHIPEs is extremely simple. Monomer(s) plus, usually, a crosslinker and suitable surfactant are mixed together while the droplet phase liquid is added slowly. Mixing is continued during addition to break up large droplets. Once all of the internal phase liquid has been added, the emulsion is cured in some manner and the resulting porous material is washed in a soxhlet then dried. Since we are dealing with emulsions, one of the liquid phases is usually aqueous. This can be either the droplet or the non-droplet phase. However, under certain conditions it is possible to prepare non-aqueous HIPEs [3]. To achieve this, two immiscible organic liquids are required. Hydrocarbon solvents are immiscible with polar aprotic solvents such as formamide (FA), dimethylformamide (DMF) and

dimethylsulfoxide (DMSO). The use of PEO–PPO–PEO triblock copolymer non-ionic surfactants permitted the preparation of HIPEs of petroleum ether in polar aprotic solvents. The stabilities of these nonaqueous HIPEs were generally much lower than their aqueous counterparts. Nonetheless, HIPEs that were stable for 24 h at both 30 and 60 °C could be obtained with formamide or DMSO as the continuous phase. The polymeric nature of the surfactant was found to be crucial to the ability to prepare stable HIPEs; low molar mass non-ionic surfactants such as blends of Span 80 and Tween 80 resulted usually in HIPEs that phase separated immediately. Indeed, only one HIPE composition formed successfully using lower molar mass surfactants.

By far the most widely investigated PolyHIPE base material is polystyrene. Styrene is a water-immiscible liquid, therefore water-in-oil (w/o) HIPEs are used to create polystyrene PolyHIPEs. Usually, varying quantities of a hydrophobic crosslinker, such as divinylbenzene, are also added to enhance structural stability. Other hydrophobic monomers have been used to create PolyHIPEs from w/o emulsions; the list includes 2-ethylhexyl acrylate (EHA) and methacrylate (EHMA) [4,5], butyl acrylate (BA) [4] and isobornyl acrylate (IBA) [6]. However, the use of monomers of intermediate hydrophobicity, such as methyl methacrylate (MMA) has proved more difficult. This is because a stable (at least until the onset of gelation) HIPE is required to form a homogeneous PolyHIPE. W/o emulsions formed from organic liquids of relative hydrophilicity, such as MMA, are unstable and phase separate quickly, due to partitioning of the organic in question between the two phases. Thus, it can be seen that homogeneous PolyHIPEs can only be produced from w/o HIPEs when the organic continuous phase is sufficiently hydrophobic. In the same vein, hydrophilic PolyHIPE materials can be prepared from o/w HIPEs. Hydrophobic organic liquids such as paraffin can be emulsified in an aqueous solution of acrylamide plus crosslinker, in the presence of a surfactant such as sodium dodecyl sulfate. In addition, recent work by Cooper et al. has described the preparation of a number of PolyHIPE materials using supercritical CO_2-in-water (c/w) HIPEs. Materials prepared included polyacrylamide and poly(2-hydroxyethyl acrylate) [7]. Other PolyHIPE materials that have been investigated include those prepared from urea and formaldehyde [8].

The chemistry of PolyHIPE materials can be varied in another manner. The production of PolyHIPEs with reactive handles allows further synthetic eloboration which results in alteration of the chemistry of the porous material. 4-Vinylbenzyl chloride (VBC) is a hydrophobic monomer possessing a reactive benzyl chloride group, and has been used to prepare PolyHIPE polymers [9]. HIPE preparation conditions were identical to those used to prepare polystyrene PolyHIPEs. The resulting porous materials have been functionalised with a range of nucleophilic amines, including hexamethylenetetramine (as a means of

introducing primary amine residues), morpholine and tris(2-aminoethyl)amine (trisamine) (Scheme 1) [10]. High levels of functionalisation were achieved in all cases, following optimisation of conditions. Furthermore, reactions on powdered PolyHIPE were compared with analogous reactions on monoliths (cubes of 0.5 cm per side). It was found that modifications of monoliths could occur to the same extent as powdered samples.

The phenyl rings of polystyrene can also be used as reactive 'handles' to enable chemical modification of PolyHIPE [11]. Divinylbenzene-crosslinked (5% nominal crosslink density) large cylindrical PolyHIPE monoliths were modified by electrophilic aromatic substitution to yield nitro-, bromo- and sulfonic acid substituted materials (Scheme 1). A batch process, in which the monolith and reagent solution were evacuated, then the monolith was immersed in the solution and the vessel subsequently pressurised, was used. Initial investigations revealed that sulfonation with concentrated sulfuric acid resulted in a high level of modification at the periphery of the monolith but very low levels in the interior. This was ascribed to the incompatibility between the hydrophobic polystyrene matrix and the hydrophilic reagent solution. Employing a much more hydrophobic reagent, namely lauroyl sulfate in cyclohexane, resulted in a significantly more uniform degree of substitution. The use of similarly hydrophobic

reagent solutions (nBu$_4$NNO$_3$/trifluoroacetic anhydride; Br$_2$/SnCl$_4$/CH$_2$Cl$_2$) produced nitrated and brominated polystyrene PolyHIPEs with similar extents of modification throughout the monolith interior.

3. Varying PolyHIPE morphology

PolyHIPE materials have complex morphologies. They possess spherical cavities, known as voids, and windows that interconnect these voids. Furthermore, a much finer porous texture within the walls of the base material can be created. Finally, the dimensions of the material can be varied from thin membranes to very large monolithic articles. Much is now known about the methods by which each of these parameters can be varied; this is important as any advanced materials application in which PolyHIPEs may be used will require careful control of morphology and properties.

The cellular nature of PolyHIPEs can be varied between open- and closed-cell. The first clue as to the factor(s) that influence(s) the cellular nature of the material came from the work of Williams and Wrobleski [12]. It was found that, while internal phase volume ratio played a role, surfactant concentration was in fact more important. Thus, a closed-cell poly(styrene-DVB) PolyHIPE material could be
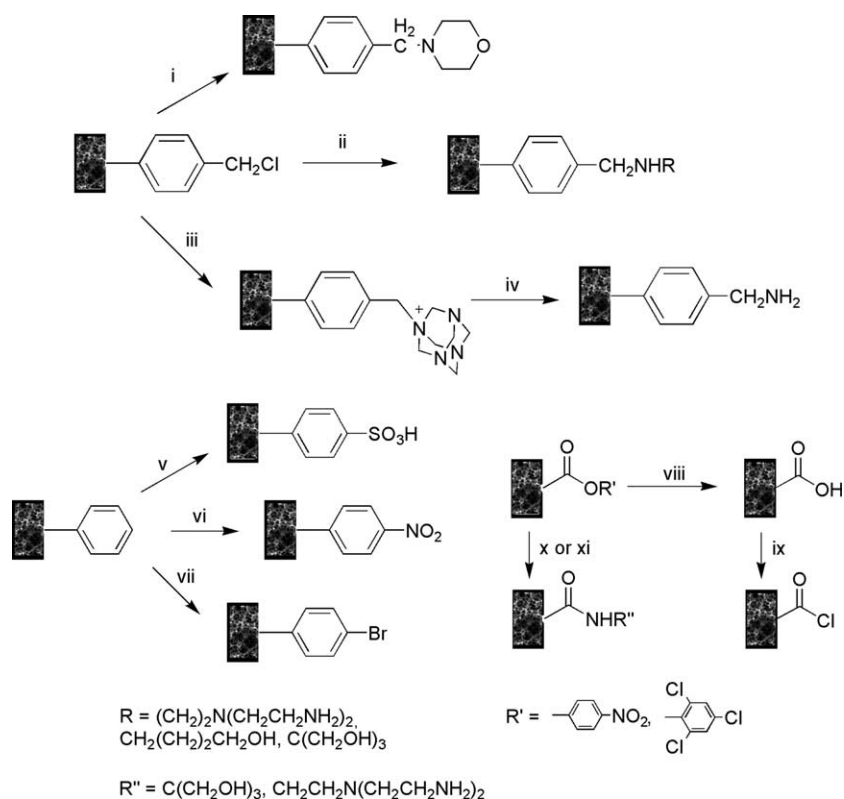
Scheme 1. Functionalisation of PolyHIPE materials. Reagents and conditions: (i) morpholine (3 eq), DMF, 60 °C, 12 h.; (ii) amine (3 eq), DMF, 60 °C (45 °C when R=(CH$_2$)$_2$N(CH$_2$CH$_2$NH$_2$)$_2$, 12 h; (iii) hexamethylenetetramine (5 eq), NaI (5 eq), EtOH, 60 °C, 12 h; (iv) c. HCl/EtOH (1:15), 75 °C, 12 h; (v) CH$_3$(CH$_2$)$_{10}$CO$_2$SO$_3$H, 55 °C, 48 h; (vi) Bu$_4$NNO$_3$/(CF$_3$CO)$_2$O, DCM, 30 °C, 24 h; (vii) Br$_2$/SnCl$_4$, DCM, 35 °C, 24 h; (viii) 1.5 M NaOH (aq), reflux, 24 h; (ix) SOCl$_2$, CH$_3$CN, 40 °C, 2 h; (x) 5 eq H$_2$NC(CH$_2$OH)$_3$, DMF, 60 °C, 6 h; (xi) 5 eq N(CH$_2$CH$_2$NH$_2$)$_3$, DMF, 60 °C, 6 h.

produced at a value of $\phi = 0.97$ by employing a relatively low concentration of surfactant ([Span80]=5% (w/w) relative to monomer phase). It was suggested that an increasing surfactant concentration caused thinning of the monomer films separating adjacent emulsion droplets. At a certain critical film thickness, windows between adjacent droplets would be produced on curing. This implied that the cause of window formation is volume contraction on conversion of monomer to polymer, a well-known feature in vinyl polymerisation chemistry. Subsequent studies of partially cured styrene/DVB HIPEs by cryo-SEM confirmed this hypothesis [13]. HIPEs were cured for various time intervals over 4 h, then were frozen in liquid nitrogen, cryo-sectioned and the frozen HIPE cross-section was imaged. Ablation of the ice inside frozen emulsion droplets was performed to investigate the structure of the films surrounding emulsion droplets. It was found that the point at which the first windows appeared coincided with the gelation point of the polymerising emulsion, strongly suggesting that windows are created by volume contraction on polymerisation. This manifestation of shrinkage as windows formation is due to the fact that the monomer films separating emulsion droplets are at their thinnest at the points of nearest contact between adjacent droplets. It is worth pointing out that there is no bulk shrinkage on curing of HIPEs as the shrinkage occurs internally, i.e. between adjacent emulsion droplets.

The average void diameter in a PolyHIPE material can be varied over a range from around 1 μm to greater than 100 μm. Seminal work from Unilever [14] and by Williams et al. [15] provided the first suggestions as to the parameters that control the void diameter. It was noticed [15] that increasing the DVB:styrene ratio in a styrene/DVB HIPE, from 0 to 100% DVB, caused a small but significant decrease in average void diameter from 15 to 5 μm. DVB is more hydrophobic than styrene, thus it was hypothesised that the decrease in void diameter was caused by a decrease in HIPE droplet diameter, itself a result of increased emulsion stability due to the presence of increasing levels of DVB (increased emulsion stability results in a smaller average droplet size, due to the (presumed) lower interfacial tension which permits a larger interfacial area). An increase in surfactant concentration also resulted in a decrease in average void diameter, again due to increased emulsion stability. However, above 50% (w/w) surfactant concentration relative to monomer content, weak unconnected porous materials were obtained. Finally, a dramatic influence of electrolyte content in the aqueous phase on average void diameter was demonstrated. Increasing the concentration of aqueous solution of K_2SO_4 from 10^{-6} to 10 g/100 ml, with AIBN as initiator, resulting in a 10-fold decrease of void diameter (from around 50–5 μm). Again, this is related to emulsion stability; increasing electrolyte concentration reduces the propensity for Ostwald ripening, a process whereby large droplets grow at the expense of smaller ones due to migration of droplet phase molecules

through the continuous phase. The outcome of Ostwald ripening is progressive coarsening of the emulsion, which leads to coalescence and, eventually, emulsion break-down. Therefore, preventing or limiting Ostwald ripening leads to a more stable emulsion with a smaller average droplet diameter.

There is further evidence that the composition of the HIPE non-droplet phase can influence void size. For example, it was noticed that PolyHIPEs prepared from VBC and DVB had smaller average void diameters than those prepared from styrene and DVB [16]. Additionally, the void diameter decreased with increasing VBC content, to less than 5 μm (Fig. 2). It was suggested that perhaps VBC was co-adsorbing at the emulsion interface with the surfactant, thus lowering the interfacial tension. However,
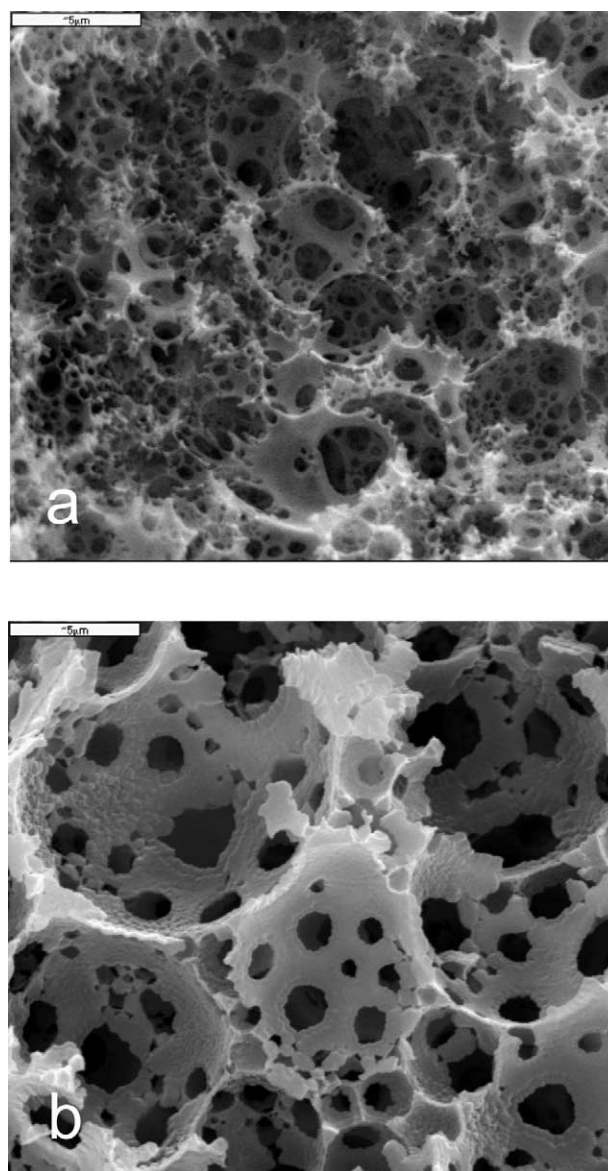

Fig. 2. SEMs of VBC–DVB PolyHIPEs: (a) 87.5 mol% VBC; (b) 12.5 mol% VBC (reproduced by permission of the Royal Society of Chemistry).

attempts to measure the interfacial tension in such systems failed (the densities of the two phases were too similar to permit the use of the spinning drop method). Nonetheless, pressure–area curves for monolayers of solutions representing the organic (non-droplet) phase of these emulsions spread on a sub-phase of a composition equal to that of the aqueous phase indicated that indeed VBC was co-adsorbed at the interface (Fig. 3). The molecular area at which a condensed film was formed increased with increasing VBC:DVB ratio. Although these data were obtained from an air–water rather than an oil–water interface, we believe that they are still relevant, qualitatively at least, to real emulsions. A similar effect on PolyHIPE void size on addition of chlorinated (non-polymerisable) solvents to the organic phase was also observed in our laboratory [17]. Experiments with a Langmuir trough also confirmed that co-adsorption of the chlorinated organic at the interface was decreasing void diameter.

For certain applications, it is advantageous to prepare materials with much larger average void diameters, i.e. up to 200 μm. Tissue engineering, in which cells are cultured in a biocompatible and biodegradable porous support material, requires average void and window diameters that permit cells to migrate through the material. Biological cells have diameters in the range of microns to tens of microns. Fortunately, PolyHIPE materials with such large void diameters can be prepared by a 'controlled coalescence' technique. Adding small quantities of water-miscible organic species to the HIPE aqueous phase promotes Ostwald ripening, leading to a significant increase in average void diameter [18]. For example, the addition of just 1% (v/v) of THF to the aqueous phase of a styrene/DVB
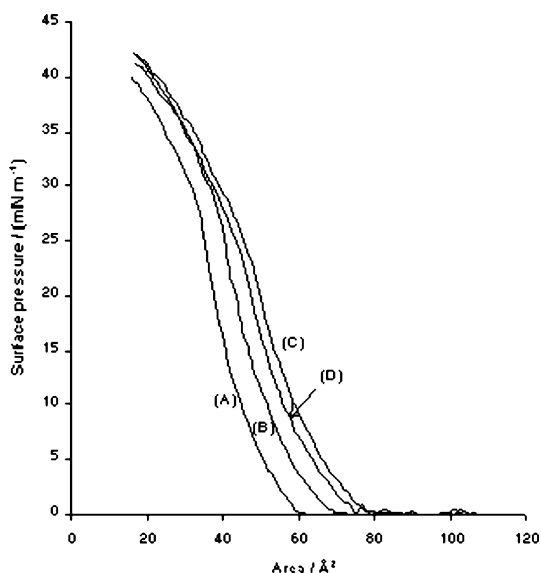
HIPE resulted in a homogeneous material with void sizes in the range 50–150 μm (Fig. 4). It is postulated that the water-miscible solvent facilitates transport of water molecules from small to large droplets through the hydrophobic continuous phase, leading to an increase in average droplet (and therefore PolyHIPE void) diameter.

Since PolyHIPEs are produced by a simple moulding process, in which the liquid precursor emulsion is placed in some polymerisation vessel or mould, a wide range of sample shapes and sizes is available. Typically, emulsions are produced on a 50 ml scale and are conveniently polymerised inside plastic bottles in an oven. However, in our group HIPEs have been made on a scale up to 3 L and polymerised in plastic trays. The resulting macro-samples were cut into test bars for mechanical testing. It has been found that the nature of the mould substrate against which a PolyHIPE material is prepared has a profound influence on its surface morphology and degree of adhesion to the mould. Glass causes significant bonding of poly(styrene/DVB) materials to its surface and the PolyHIPE surface in contact with the glass has a different morphology from the fractured surface (Fig. 5(a)). Problems with HIPE stability were encountered when using PVC as a mould substrate, which could be due to leaching of plasticizer. In addition, samples that did form tended to adhere to the substrate. Polypropylene did not result in adhesion, however, the surfaces polymerised against the substrate were largely of a closed-cell structure. This is presumably due to the presence of a surface film of monomer, caused by localised HIPE collapse at the HIPE-substrate interface. Preferential wetting of the mould surface by either phase of the emulsion could cause phase separation; the resulting monomer film becomes a surface skin on polymerisation. PTFE, on the other hand, does not produce adhesion and gives an open-cell morphology at the PolyHIPE-mould interface (Fig. 5(b)). Homogeneous PolyHIPE membranes of thickness down to 100 μm were produced using a mould made from PTFE plates and a spacer ring of defined thickness. The results described above are only partially in accord with those of

Fig. 3. π-A curves for films containing: (a) Span 80 alone; (b) Span 80 (17 mol% relative to total oil phase) plus DVB; (c) Span 80 (17 mol% relative to total oil phase) plus VBC; (d) Span 80 (17 mol% relative to total oil phase) plus DVB-VBC (50:50 mol. mixture) (reproduced by permission of the Royal Society of Chemistry).
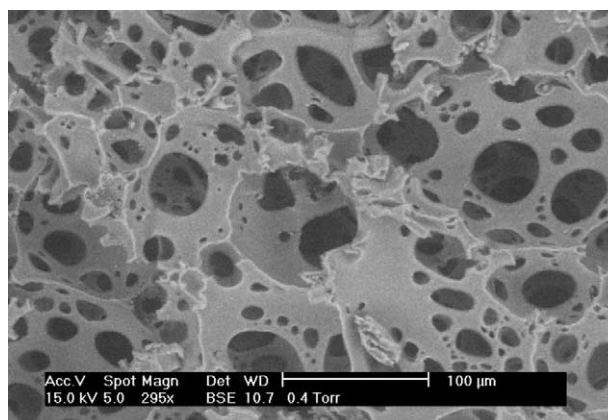

Fig. 4. SEM of a styrene-DVB PolyHIPE material prepared with 1% (v/v) THF in the aqueous phase.
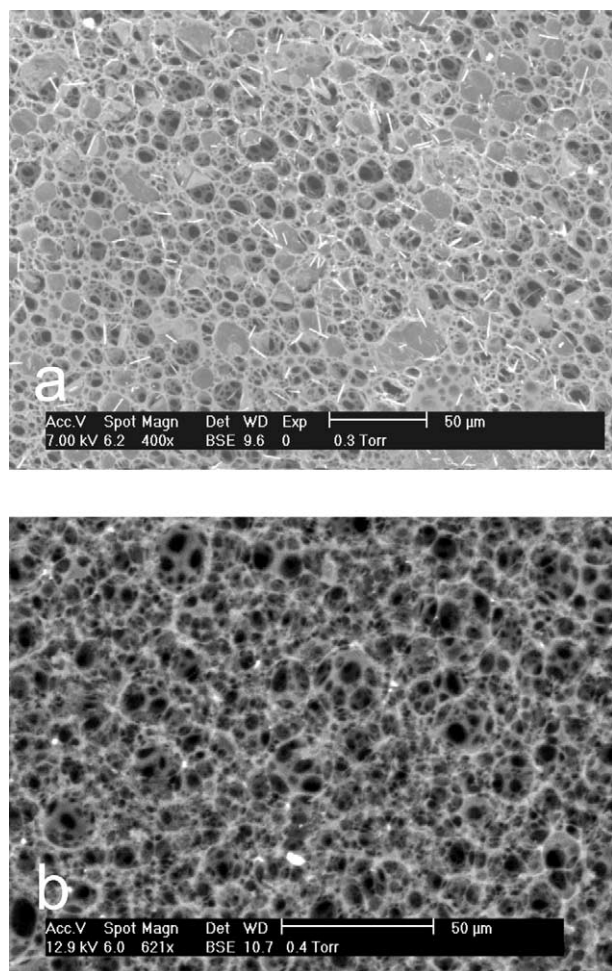
Fig. 5. SEMs showing the morphology of the PolyHIPE surface in contact with different mould substrates: (a) glass; (b) PTFE.

Akay et al. [19], who related the structure of emulsion derived polymer foams to the solubility parameter difference ($\Delta\delta$) between monomer and substrate. In that work, it was found that polyethylene (which is presumed to be similar to polypropylene) resulted in a closed cell surface and PVC lead to adhesion. On the other hand, glass ($\Delta\delta >$ 180) gave rise to an open-cell structure, whereas PTFE ($\Delta\delta = -6.5$) resulted in a closed cell surface, whereas in our hands the opposite was found. Reasons for this discrepancy could include differences in composition or preparation method of the emulsions in our work compared to that of Akay et al.

4. PolyHIPE properties

The surface area of PolyHIPE materials prepared as described so far is modest: 3–20 $m^2 g^{-1}$ is the likely range of values [20]. Although the morphology of the material is highly porous and interconnected, the relatively large void size (microns to 10s of microns) results in a low surface area. Certain potential applications of PolyHIPE materials,

for example their use as supports for catalysts or as stationary phases for chromatography, require much higher surface areas. For example, typical silica packing materials for liquid chromatography have surface areas around 200–300 $m^2 g^{-1}$ and heterogeneous catalysts often have values in excess of 500 $m^2 g^{-1}$. The reason for this is that, in these applications, all of the action takes place at the solid surface. Therefore, high capacities or rapid exchange processes require as high a surface area as possible. Fortunately, there are methods to increase the surface area of PolyHIPEs. Seminal work by Sherrington and co-workers [20], which makes use of the considerable volume of literature on morphology control of permanently porous polymer resin beads [21], describes how values of up to 350 $m^2 g^{-1}$ can be achieved by replacing some of the monomer (up to 50% by vol.) with a non-polymerisable (water-immiscible) organic solvent, in conjunction with a high crosslinker content. During polymerisation, phase separation within the monomeric continuous phase occurs, resulting in a morphology that resembles closely that of a permanently porous, or 'macroporous', polymer bead (Fig. 1(b)). The resulting material has a hierarchical pore structure: large voids, which are imprints of the HIPE droplets; interconnecting windows between each void and its neighbours; and pores, within the polymer walls and struts that comprise the solid phase of the material.

Although the surface area of such materials is high, their mechanical properties are seriously compromised. This results in collapse of the monolithic structure when subjected to the flow-through of liquids. Consequently, a study of the influence of different organic porogenic solvents on the surface area of poly(divinylbenzene) PolyHIPEs was embarked upon, in order to produce high surface area materials with better mechanical performance. It was found that changing the solvent from toluene (T) to chlorobenzene (CB) to 2-chloroethylbenzene (CEB) produced an increase in BET surface area from 350 to 550 $m^2 g^{-1}$ [17]. This was attributed to a change in solubility parameter of the solvent from 18.2 to 20.1 $MPa^{1/2}$. The closer the value of the solvent to that of the polymer, the later in the course of the polymerisation phase separation occurs. This produces smaller microgel particles with smaller pores between them, and hence a larger surface area. However, this was accompanied by an apparent change in morphology of the material to one that less resembled that of a standard PolyHIPE material. TEM images however, confirmed the cellular nature of the material; it appeared that the windows had become enlarged to such an extent that the cellular morphology was not immediately obvious by SEM (Fig. 6). An increase in window diameter is indicative of an increase in emulsion stability (vide supra); this was confirmed by experiments involving compression of monolayers of the different HIPE organic phases, in which it was observed that CEB gave rise to the most densely packed interface. Although variation of the organic porogen resulted in an increase in surface area,
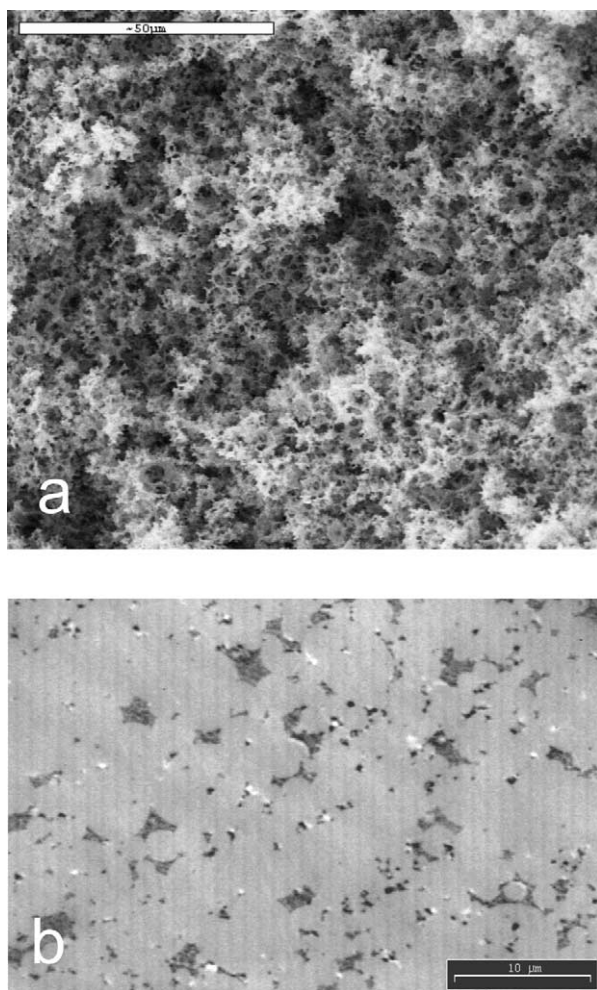
Fig. 6. (a) SEM and (b) TEM of DVB PolyHIPE prepared with CEB in the organic phase (1:1 vol. ratio to DVB) (reproduced by permission of the Royal Society of Chemistry).

Table 1
Variation of surface area of PolyHIPE materials with internal phase volume ratio (ϕ)

ϕ	Surface area/m^2 g^{-1}
0.75	457 ± 8
0.85	472 ± 3
0.90	346 ± 26
0.92	236 ± 11

Organic phase: divinylbenzene and chlorobenzene (1:1 volume ratio).

DVB and each porogen in question gave maximum surface area values for the corresponding PolyHIPE materials. All PolyHIPE materials were found to have much lower surface area values than the corresponding resins. However, interestingly, the difference in surface area values between PolyHIPE and the resin prepared with a given solvent depends strongly on the solvent. Relatively polar solvents, such as chlorobenzene, could potentially solubilise larger amounts of water than more hydrophobic solvents, such as chloroethylbenzene. The former solvent results in a polymerising medium that is a poorer solvent for the developing polymer, and thus a low value of surface area is obtained. Solubilisation of water molecules by the organic porogen promotes Ostwald ripening; the influence of Ostwald ripening is further suggested by the observation that polar solvents, such as CB, result in a large decrease in surface area as ϕ increases, whereas less polar solvents (CEB) in fact result in an increase in surface area with ϕ.

Changing the surfactant employed from sorbitan mono-oleate (Span 80) to a 3-component mixture [23] of cetyltrimethylammonium bromide (CTAB), dodecylbenzenesulfonic acid, sodium salt (DDBSS) and sorbitan mono-laurate (Span 20) produced some further insights [24]. With this surfactant mixture, surface area values were much higher in almost every case than with Span 80 (for CB: 689 compared to 346 m^2 g^{-1}). Mixtures of ionic and non-ionic surfactants are known to form a more robust interfacial film around each emulsion droplet, leading to enhanced emulsion stability [25]. Indeed, placing carefully a mixture of monomer and surfactant onto an aqueous solution representing the HIPE dispersed phase in a beaker resulted in the formation of a noticeable film at the interface. It is suggested that the strong interfacial film limits or prevents Ostwald ripening, therefore the organic phase contains less water and so is a better solvent for the growing polymer network. Phase separation occurs at a later stage during polymerisation leading to a surface area that approaches the 'true' value produced from DVB and the solvent in question. Further evidence for the lower extent of Ostwald ripening was provided by NMR experiments, using a bipolar pulse pair stimulated echo (BPPSTE) pulse sequence, to determine the self-diffusion coefficient of water. This was found to be around three times higher when Span 80 was used as the surfactant compared to the surfactant mixture (Fig. 7).

Different applications of PolyHIPEs in materials science will require different materials properties (physical,

the mechanical properties were not improved. This was attributed to the (apparently) non-cellular morphology of the materials, and it was hypothesised that mixtures of porogenic solvents could lead to high surface area materials with the expected cellular structure of PolyHIPEs. From extensive studies, it was found that a 1:1 (v:v) mixture of CEB and CB resulted in a material with a high surface area (550 m^2 g^{-1}) that still retained the expected PolyHIPE morphology. Such materials were found to be substantially more robust than those prepared with CEB alone.

In the course of this work, we found, rather surprisingly, that the internal phase volume ratio, ϕ, can have a profound influence on the BET surface area. For example, increasing ϕ from 0.75 to 0.85, 0.90 and 0.92 with chlorobenzene as porogen resulted in a decrease of surface area from 457 to 236 m^2 g^{-1} (Table 1) [22]. Thus, it seemed that the origin of the surface area value of a given PolyHIPE material produced with a porogenic solvent in the continuous phase is more complex than originally thought. Preparation of permanently porous resins from homogeneous solutions of
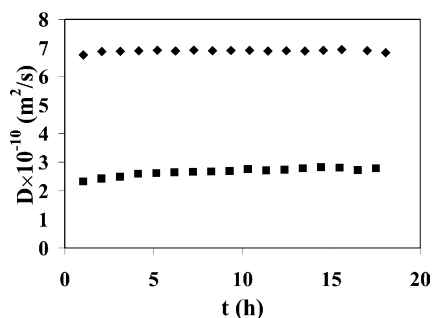
Fig. 7. Self-diffusion coefficient of water, at 25 °C, in two emulsions of the same composition of the continuous and dispersed phases (DVB 80% and CB) but incorporating two different surfactants: (♦) SPAN 80; (■) mixture of SPAN 20, DDBSS and CTAB (reprinted with permission from [24]. Copyright (2004) American Chemical Society).

mechanical, thermal etc.), therefore good control over properties would be desirable. A considerable amount of work has been done in this area. Elastomeric materials derived from hydrophobic monomers that produce low T_g polymers, such as 2-ethylhexylacrylate (EHA) and n-butyl acrylate (BA), have been described previously [4]. The hydrophobicity of the elastomer ensures that emulsion stability is not compromised. Mixtures of, for example, styrene and EHA, plus DVB as crosslinker, give rise to PolyHIPEs with T_g values intermediate between those of the two homopolymers. Materials that have a T_g below room temperature (EHA content greater than 40 mol%, at a crosslinking level of 10%) are indeed elastomeric in nature. Interestingly, a non-linear relationship between T_g and monomer mixture composition was found [5]. This relationship showed a similar trend to that predicted by Barton's model [26], although the actual values did not agree with theory. For EHA copolymers, a steady decrease in T_g was observed at low EHA levels, however T_g was then more or less constant until 30 mol% EHA, after which it again decreased steadily. The initial drop in T_g was ascribed to the introduction of highly flexible EHA units into the polymer backbone. The second decrease after the plateau region is suggested to coincide with the presence of EHA–EHA diads, which have significantly more flexibility than EHA–styrene diads. The reactivity ratios of styrene (M_1) and EHA (M_2) are $r_1 = 0.91$ and $r_2 = 0.29$, thus EHA diads are only likely to occur in significant numbers above a certain EHA concentration.

A different elastomer, namely 2-ethylhexyl methacrylate (EHMA), shows different behaviour. In this case there is again a sudden decrease in T_g at low EHMA content, however afterwards T_g decreases slowly and steadily until almost 100% EHMA content. The reactivity ratios for styrene (M_1) and n-hexylmethacrylate (M_2) are $r_1 = 0.45$ and $r_2 = 0.65$, thus there is a greater chance of EHMA–EHMA diads occurring at lower concentration (assuming the reactivity ratios for styrene and EHMA are the same as for styrene and HMA). Therefore, it is suggested that the initial drop in T_g is due to the increased free volume from the bulky side group of EHMA and the high chain flexibility resulting from EHMA–EHMA diads at the lowest content of EHMA studied.

The thermo-oxidative stability of PolyHIPE materials is another useful parameter to vary. In particular, it would be advantageous to prepare materials from high performance polymers, such as polyamides or poly(ether ketone)s, since these would be expected to have higher thermo-oxidative stabilities than materials derived from vinyl monomers. Oligomers of poly(ether sulfone) were end-functionalised with maleimide groups, and these were copolymerised with either styrene, DVB or a bis(vinyl ether) monomer derived from Bisphenol A, in the continuous phase of a HIPE [27]. This yielded a range of novel, PES-based open-cell PolyHIPE materials with nominal porosities up to 88%. Since the surfactant and PES oligomers could only be cosolubilised in dipolar aprotic solvents such as DMF, it was necessary to employ a non-aqueous HIPE strategy to prepare the materials. The resulting PolyHIPEs were found to have much higher thermo-oxidative stabilities than styrene/DVB PolyHIPEs; greater than 60% of the sample mass was still present at 500 °C under an atmosphere of air, whereas the latter materials had lost 50% of their mass at 350 °C.

5. Applications of PolyHIPEs

PolyHIPE materials have found use in a wide variety of applications. One area in which they have been exploited extensively is as supports for solid phase synthesis. Work by Sherrington and Small describes the use of crosslinked polystyrene PolyHIPE in granular form as a support for a polyacrylamide gel used in solid phase peptide synthesis [28]. Functionalisation of the PolyHIPE surface to yield carbon–carbon double bonds led to covalent anchoring of the gel support to the rigid polystyrene matrix. Subsequently, monolithic polystyrene PolyHIPEs were functionalised by electrophilic aromatic substitution, employing hydrophobic reagents, to introduce $-SO_3H$, $-Br$ and $-NO_2$ groups [11]. The sulfonic acid modified materials were used in monolithic form as solid phase acid catalysts for the hydration of cyclohexene in a two-phase liquid–liquid process [29]. The highly interconnected nature of the PolyHIPE support produced an effect similar to that of a static mixer, resulting in a high interfacial area between the aqueous and organic phases.

More recent work in this area describes the production of amine-functionalised PolyHIPEs, in both granular and monolithic forms [10]. VBC was used as a comonomer with styrene and DVB to yield PolyHIPE materials with reactive benzyl chloride handles for further elaboration. Subsequent reaction under optimised conditions led to materials with high loadings of various amine functionalities. The trisamine-modified materials were used as scavengers for 4-chlorobenzoylchloride, to probe their

utility as electrophile scavenger resins. Scavenging was found to be extremely rapid. In addition, monolithic scavenging rods were prepared in columns (5 cm length, 4.2 mm i.d.) and used in a flow-through manner. It was found that complete scavenging was achieved after two passes of the electrophile solution through the column. Furthermore, PolyHIPE-based supports were found to have greater capacities and faster scavenging kinetics than a commercial trisamine resin.

In addition to reactive benzyl chloride groups, active aryl esters have been employed as a means of functionalisation of PolyHIPE supports for solid phase chemistry [30]. PolyHIPE materials were prepared from active ester acrylates such as p-nitrophenyl acrylate and 2,4,6-trichlorophenyl acrylate (Fig. 8). These were then elaborated into supports possessing acid chloride, amino or hydroxy functionality, using simple chemistry (Scheme 1). Loadings of up to 10.9 mmol g^{-1} (–OH groups) were achieved. Other workers have employed the unreacted carbon–carbon double bonds from DVB as a means to functionalise PolyHIPE materials [31]. Various radical reactions were employed to introduce a wide range of functionality (–Br, –NH$_2$, –OH, etc.).

Another application in which PolyHIPE materials have been found to be beneficial is as matrices from which to prepare electrochemical sensors. It was proposed that the porous nature of the PolyHIPE material would enable the integration of separation with sensing, allowing the sensors to be used in the presence of contaminants found in 'real' liquid media (soil particles, blood cells, proteins, etc.). Optimisation of PolyHIPE preparation conditions, including the level of surfactant and the type of mould substrate employed, allowed the production of membranes of thickness down to 100 μm and possessing large (>6 cm^2) areas free of pin-holes and other defects. Such membranes were impregnated with solutions of ionophore (for K$^+$: valinomycin), plasticiser and lipophilic anion. Weight gains of up to 200% while still retaining open porosity were obtained. The resulting porous sensor substrates were
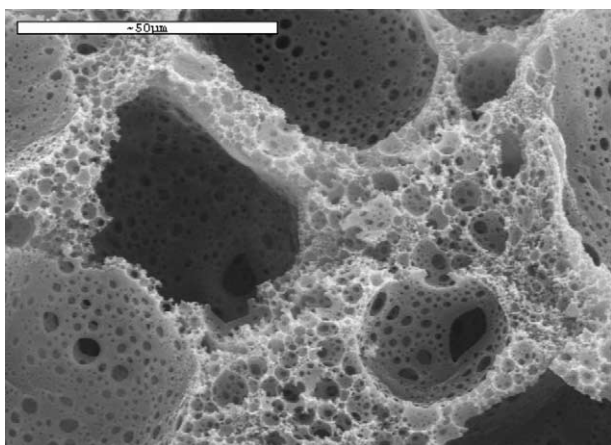
mounted into a standard electrode body between inner filling and sample solutions. A Nernstian response to K$^+$ down to low analyte concentration (10^{-5}) was observed (Fig. 9). In addition, response times were fast (always $<$ 60 s) and selectivity coefficients for K$^+$ over Na$^+$ or Li$^+$ were around 10^3.

PolyHIPE-based amperometric biosensors have also been described. The base material was rendered conducting by the incorporation of high levels (up to 100 wt%) of graphite particles. Subsequently, the electron mediator ferrocene (Fc) was incorporated by chemical grafting, either to benzyl chloride residues in the base material from VBC as comonomer, or by physical deposition of Fc-modified VBC copolymer. Finally, horseradish peroxidase (HRP) was immobilised by deposition or by reaction with epoxy groups (introduced via the use of glycidyl methacrylate as comonomer). The resulting biosensors were able to detect hydrogen peroxide down to concentrations of 10^{-7} M. This can be used as part of a sensor for cholesterol, as the oxidation of this by molecular oxygen generates hydrogen peroxide.

PolyHIPE materials have been used in biological and biomedical applications. For example, potential substrates for tissue engineering have been described. PolyHIPE materials containing biodegradable polyesters such as poly(ε-caprolactone) [32] or polylactide [33] were prepared. Polyester telechelic oligomers were acrylated then copolymerised (with a vinyl monomer such as styrene or MMA) in the continuous phase of a HIPE. The maximum amount of polyester that could be incorporated in this manner was 60% (w/w). The resulting porous materials were investigated regarding their abilities to support the growth of different cell or tissue types. Human skin fibroblasts were seen to grow over periods of up to 7 days (maximum length of time studied). SEM indicated that the cells had a flattened morphology, were presenting many projections and were making contact with each other. Micrographs of stained
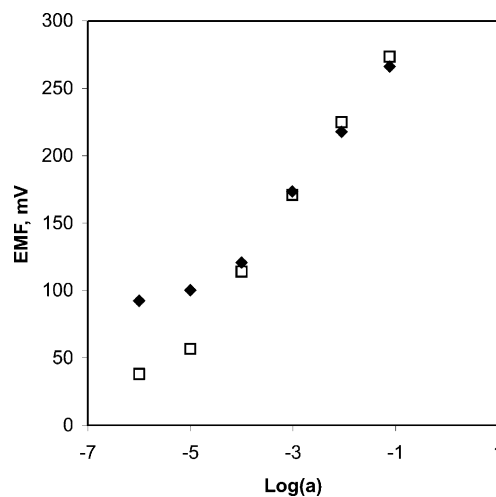

Fig. 8. SEM of p-nitrophenyl acrylate PolyHIPE material.

Fig. 9. Typical potentiometric response of K$^+$ ion selective electrodes: (♦) PVC; (□) PolyHIPE membrane.

samples indicated that the cells had the spindle morphology indicative of cell proliferation and tissue growth. Subsequent work with rat skin and whole chick embryo explants indicated that all cell types grew well and that the porous matrices displayed excellent biocompatibility.

Cells have been grown in PolyHIPE materials for applications other than tissue engineering. Non-biodegradable polystyrene PolyHIPEs with large voids (diameter 50–100 μm) were produced by a controlled coalescence technique (vide supra). The resulting materials were coated in laminin and poly(D-lysine), then seeded with neurons derived from human embryonal carcinoma (EC) stem cells [18]. The neurons were seen to grow well over periods of up to 7 days. Furthermore, neurite outgrowth was seen to be greater in the PolyHIPE supports (growth in 3D) compared to experiments conducted with tissue culture plastic (growth in 2D) (Fig. 10). Protein analysis indicated that cells grown in 3D were expressing higher levels of markers of later stages of neuronal development than those grown in 2D. The potential use of these results lies in the area of cell culturing, where the porous 3D matrices could lead to the production of populations of cells at a more advanced stage of development than those grown in 2D.

6. Conclusions

Polymerisation of the continuous phase of HIPEs leads to the production of a diverse range of PolyHIPE materials that are finding applications in several areas of materials science. Methodologies exist to prepare well-defined materials, where features of the morphology such as void size, degree of interconnection and physical form of the material are controlled to a high extent. Furthermore, the physical, mechanical and thermo-oxidative properties can be varied to tailor materials to different applications. It is expected that further developments in this area will extend the range of applications of emulsion-templated porous materials.
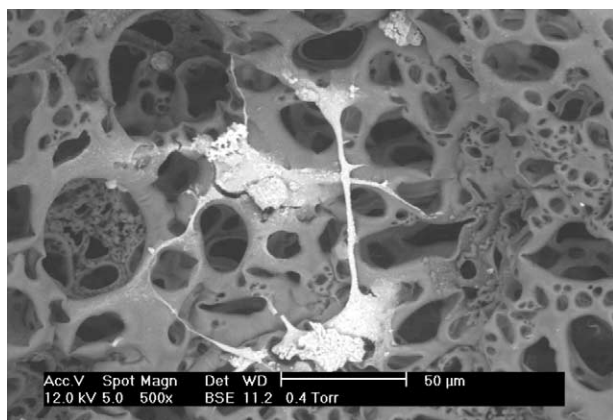

Fig. 10. SEM of neurons derived from embryonal carcinoma stem cells growing on PolyHIPE pre-coated in laminin and poly(D-lysine).

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Dr **Neil R. Cameron** was born in Ayr, Scotland, in 1969 and studied chemistry at the University of Strathclyde in Glasgow, graduating with 1st class honours in July 1991. He then remained at Strathclyde to undertake a PhD with Professor David Sherrington, working on highly porous polymer materials (PolyHIPEs), from October 1991 and graduating in 1995. His first post-doctoral position, on nitr-oxide-mediated polymerisations, was at the Eindhoven University of Technology in the Netherlands with Professor Anton German, from April 1995 until March 1996, after which he returned to the UK as a post-doctoral associate in the laboratory of Professor Iain Cowie at Heriot Watt University in Edinburgh, investigating ageing of polymer blends. In October 1997 he joined the academic staff in the Chemistry Department at the University of Durham. His research interests are in synthetic macromolecular chemistry. One of his main research programmes involves the preparation of highly porous materials for use in a variety of applications. His work to date has led to over 40 publications and he has significant current funding from a variety of sources (UK research councils, E.U., industry and charities). In 2003 he became the Associate Director (for Durham) of the Interdisciplinary Research Centre in Polymer Science and Technology (Polymer IRC) and he was awarded the 2003 Young Researchers' Award by the Macro Group UK, a joint subject group of the Royal Society of Chemistry and the Society for Chemical Industry.