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(54) Title: GENERATION OF AMPHIPHILIC NETWORK WITH AN ABILITY TO DISTINGUISH THE TRANSPORT OF IGG AND INSULIN

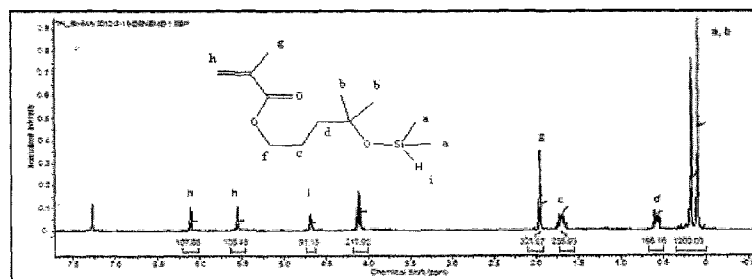


Fig. 1

(57) Abstract: A method of preparing an amphiphilic co-network comprising preparing a molecularly-bimodal crosslinkable amphiphilic graft by polymerizing a dihydrocarbylacrylamide monomer in the presence of a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture and a second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture where the molar mass ratio between average molar mass of the first asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane and average molar mass of the second asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane is between 1:2 and 1:20; and cross-linking the molecularly-bimodal crosslinkable amphiphilic graft with a siloxane compound that includes at least two Si-H bonds.

GENERATION OF AMPHIPHILIC NETWORK WITH AN ABILITY TO DISTINGUISH THE TRANSPORT OF IGG AND INSULIN

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims priority from U.S. Provisional Patent Application No. 61/831,223 filed on June 5, 2013, the contents of which are incorporated herein by reference.

FIELD OF THE INVENTION

[0002] One or more embodiments relates to amphiphilic co-networks preparable by crosslinking a molecularly-bimodal crosslinkable amphiphilic graft.

BACKGROUND OF THE INVENTION

[0003] Amphiphilic networks have been found useful as membranes for providing immunoisulatory features in bioartificial organs. Amphiphilic polymer networks can serve as a means to encapsulate and thereby immunoisolate implantable biologically active moieties. Films made from amphiphilic polymer networks have also been found to be desirable in the production of contact lenses. It has been found that current amphiphilic networks crack when dried due to development of stresses during drying.

[0004] Presently a need in the art exists for an amphiphilic co-network with improved mechanical properties that is resistant to cracking. There is also a need in the art for an amphiphilic co-network that can selectively exclude or allow the diffusion of certain molecular species.

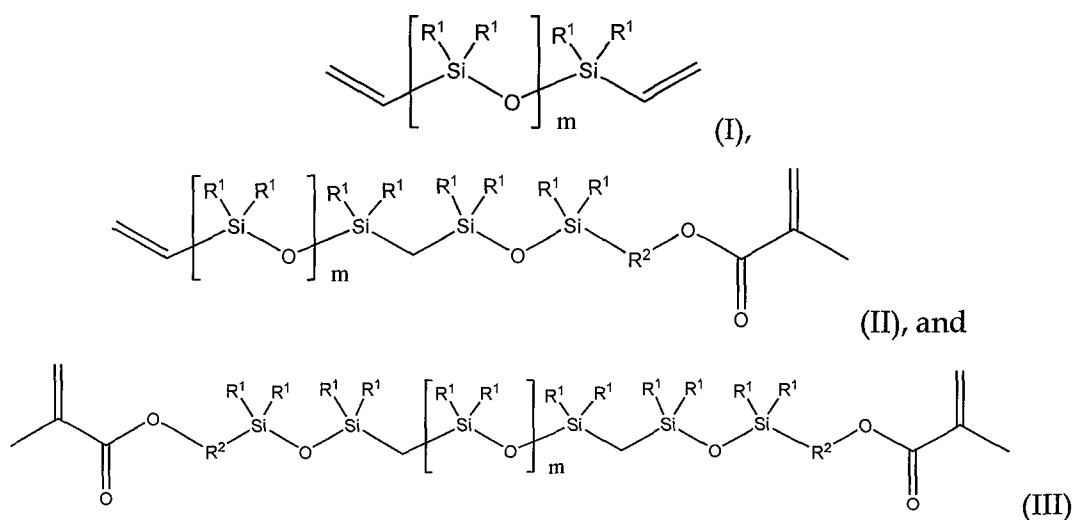
SUMMARY OF THE INVENTION

[0005] A first embodiment provides a method of preparing an amphiphilic co-network comprising preparing a molecularly-bimodal crosslinkable amphiphilic graft by polymerizing a dihydrocarbylacrylamide monomer in the presence of a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture and a second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture where the molar mass ratio between average molar mass of the first

asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane and average molar mass of the second asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane is between 1:2 and 1:20; and crosslinking the molecularly-bimodal crosslinkable amphiphilic graft with a siloxane compound that includes at least two Si-H bonds.

[0006] A second embodiment provides a method as in the first embodiment, where the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is 0.1% to 10% of the total asymmetric-telechelic polydihydrocarbylsiloxane monomer.

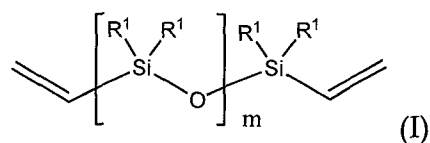
[0007] A third embodiment provides a method as in the either the first or second embodiment, where the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture includes:



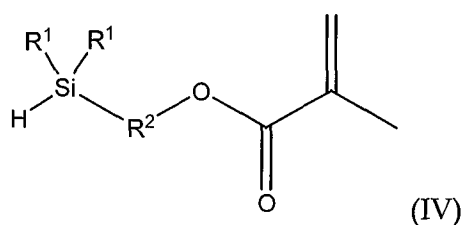
where each R^1 is individually a monovalent organic group, each R^2 is individually a divalent organic group, and each m is individually an integer from about 190 to about 320 units.

[0008] A forth embodiment provides a method as in any of the first through third embodiments, where the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is prepared by reacting a vinyl telechelic polydihydrocarbylsiloxane with a disiloxane acrylate with a telechelic

polydihydrocarbylsiloxane to disiloxane acrylate molar ratio of less than 1:2; where the vinyl telechelic polydihydrocarbylsiloxane is defined by the formula



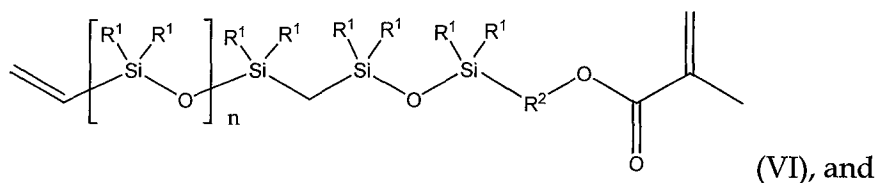
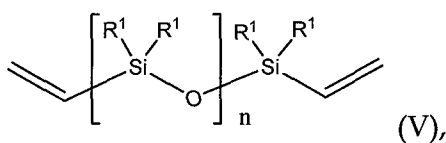
where each R¹ is individually a monovalent organic group, and wherein the disiloxane acrylate defined by the formula

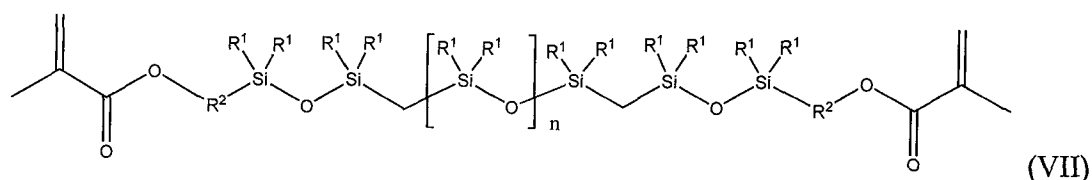


where each R¹ is individually a monovalent organic group, and R² is a divalent organic group.

[0009] A fifth embodiment provides a method as in any of the first through fourth embodiments, where each R¹ is an alkyl group of 1 to 6 carbon atoms.

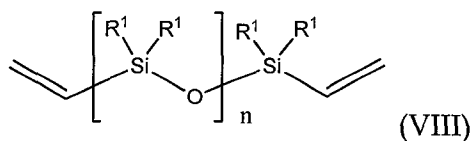
[0010] A sixth embodiment provides a method as in any of the first through fifth embodiments, where the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture includes the following:



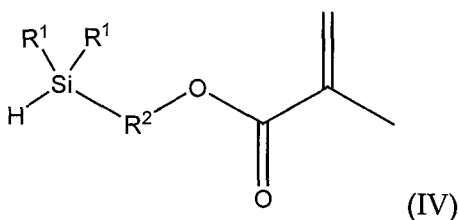


where each R^1 is individually a monovalent organic group, each R^2 is individually a divalent organic group, and each n is individually an integer from about 1100 to about 1900.

[0011] A seventh embodiment provides a method as in any of the first through sixth embodiments, where the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is prepared by reacting a vinyl telechelic polydihydrocarbylsiloxane with a disiloxane acrylate with a telechelic polydihydrocarbylsiloxane to disiloxane acrylate molar ratio of less than 1:2; where the vinyl telechelic polydihydrocarbylsiloxane is defined by the formula



where each R^1 is individually a monovalent organic group, and each n is individually an integer from about 1100 to about 1900; and wherein the disiloxane acrylate defined by the formula

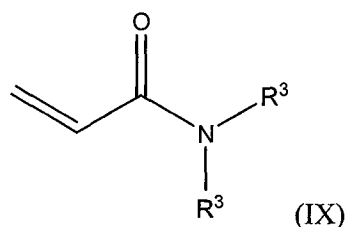


where each R^1 is individually a monovalent organic group, and R^2 is a divalent organic group.

[0012]

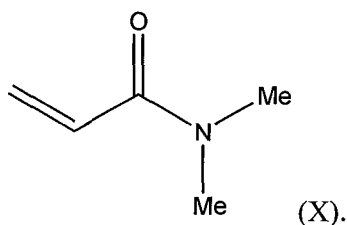
[0013] An eighth embodiment provides a method as in any of the first through seventh embodiments, where each R^1 is an alkyl group of 1 to 6 carbon atoms.

[0014] A ninth embodiment provides a method as in any of the first through eighth embodiments, where the dihydrocarbylacrylamide monomer is defined by the formula



where each R^3 is individually a monovalent organic group.

[0015] A tenth embodiment provides a method as in any of the first through ninth embodiments, where the dihydrocarbylacrylamide monomer is defined by the formula

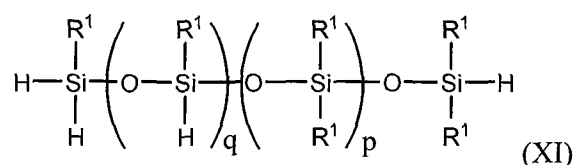


[0016] An eleventh embodiment provides a method as in any of the first through tenth embodiments, where the dihydrocarbylacrylamide monomer is between 40 and 60 wt% of the total weight of the dihydrocarbylacrylamide monomer, first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture, and second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture.

[0017]

[0018] A twelfth embodiment provides a method as in any of the first through eleventh embodiments, where the step of crosslinking the molecularly-bimodal crosslinkable amphiphilic graft with a siloxane compound that includes at least two Si-H bonds includes the use of a Karstedt catalyst to facilitate crosslinking.

[0019] A thirteenth embodiment provides a method as in any of the first through twelfth embodiments, where the siloxane compound that includes at least two Si-H bonds is defined by the formula



where each R¹ is individually a monovalent organic group, q is an integer from about 1 to about 2000 and p is an integer from about 1 to about 2000.

[0020] A fourteenth embodiment provides a method as in any of the first through thirteenth embodiments, where each R¹ is an alkyl group of 1 to 6 carbon atoms.

[0021] A fifteenth embodiment provides an amphiphilic co-network prepared by any of the first through fourteenth embodiments.

[0022] A sixteenth embodiment provides a bio-artificial organ comprising a housing with a plurality of holes on the housing, over the plurality of holes, an amphiphilic co-network prepared by any of the first through fourteenth embodiments.

[0023] A seventeenth embodiment provides a bio-artificial organ as in the sixteenth embodiment, where the housing comprises a first disc with a first raised ring around the perimeter of the disc and a concentric smaller second raised ring within the first raised ring, and a second disc with a raised ring, the raised ring of the second disc situated between the first and second raised rings of the first disc, wherein a void is present between the first disc, the second raised ring of the first disc, and the second disc, and the first disc, the second disc or both discs include a plurality of holes that connect to said void.

[0024] An eighteenth embodiment provides a bio-artificial organ as in any of the sixteenth through seventeenth embodiments, where the first raised ring and second raised ring of the first disc includes a cut out portion, and the raised ring of the second disc includes a cutout portion aligned with the cut out portion of the first disc.

BRIEF DESCRIPTION OF THE DRAWINGS

[0025] Figure 1 provides a chart of the ^1H NMR spectrum of 2-propionic acid 3-(1,1,3,3-tetramethyldisiloxaniyl)propylester (SiH-MA)

[0026] Figure 2 provides a chart of the ^1H NMR Spectrum of MA-PDMS-V.

[0027] Figure 3 provides a chart of the GPC traces of a) MA-PDMS-V -0, b) MA-PDMS-V -1, c) MA-PDMS-V -2 and d) MA-PDMS-V -5.

[0028] Figure 4 provides a chart of GPC traces of a) V-PDMS-MA, b) [PDMAAm(PDMS)]-g-PDMS-V-0, c) [PDMAAm(PDMS)]-g-PDMS-V-1, d) [PDMAAm(PDMS)]-g-PDMS-V -2, e) [PDMAAm(PDMS)]-g-PDMS-V -5.

[0029] Figure 5 provides a schematic of an instrumented system that tracks weight, thickness and birefringence and surface temperature of cast coatings during their solidification (JOEY).

[0030] Figure 6 is a graph showing curing properties of 1% PDMS APCN membrane with 1:25 crosslinking ratio.

[0031] Figure 7 is a graph showing mechanical property comparisons between 2% PDMS APCN membranes with different crosslinking ratios.

[0032] Figure 8 is a graph showing mechanical property comparisons between 5% PDMS APCN membranes with different crosslinking ratios.

[0033] Figure 9A is a graph showing mechanico-optical property comparisons between 2% PDMS APCN membranes with different crosslinking ratios.

[0034] Figure 9B is a graph showing mechanico-optical property comparisons between 2% PDMS APCN membranes with different crosslinking ratios.

[0035] Figure 10A is a graph showing mechano-optical property comparisons between 5% PDMS APCN membranes with different crosslinking ratios.

[0036] Figure 10B is a graph showing mechano-optical property comparisons between 5% PDMS APCN membranes with different crosslinking ratios.

[0037] Figure 11 is a graph showing short time tests on insulin permeation of membranes with a variety of APCN composition and crosslinkinkage.

[0038] Figure 12 is a graph showing long time tests on IgG permeation of membranes with a variety of APCN composition and crosslinkinkage.

[0039] Figure 13 is a graph showing short time tests on IgG permeation of membranes with a variety of PDMS APCN composition and crosslinkink levels.

[0040] Figure 14 is a graph showing long time tests on IgG permeation of membranes with a variety of PDMS APCN composition and crosslinkink levels.

[0041] Figure 15A is a graphic providing AFM phase and height images for 5% PDMS APCN with 1:25 crosslinking with 2 μ m scale.

[0042] Figure 15B is a graphic providing AFM phase and height images for 5% PDMS APCN with 1:25 crosslinking with 500nm scale.

[0043] Figure 16 provides a scheme for device preparation.

[0044] Figure 17A is a microscopy images of BAP device membrane after 3 weeks in buffer saline solution.

[0045] Figure 17B is a microscopy images of BAP device membrane after 3 weeks in buffer saline solution.

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

[0046] One or more embodiments provides a method of preparing an amphiphilic co-network comprising preparing a molecularly-bimodal crosslinkable amphiphilic graft by polymerizing a dihydrocarbylacrylamide monomer in the presence of a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture and a second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture where the molar mass ratio between average molar mass of the first asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane and average molar mass of the second asymmetric-

telechelic monomer mixture polydihydrocarbylsiloxane is between 1:2 and 1:20; and crosslinking the molecularly-bimodal crosslinkable amphiphilic graft with a siloxane compound that includes at least two Si-H bonds. Advantageously it has been found that when a second, higher molecular weight asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is used in conjunction with a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture, the resultant amphiphilic co-network exhibits better mechanic properties and resists to cracking when dried.

[0047] The amphiphilic co-network is a polymer network that includes a hydrophobic constituent and a hydrophilic constituent. The hydrophobic constituent and a hydrophilic constituent are interconnected to create a cocontinuous morphology of hydrophobic phases and a hydrophilic phases, which allows amphiphilic co-network to have both hydrophobic pores and hydrophilic pores. The cocontinuous morphology allows the amphiphilic co-network to bipercoluate, or, in other words, allow solvents of different polarity, such as water and a hydrocarbon, to permeate separately from edge to edge of the entire amphiphilic co-network. In one or more embodiments, substantially all of the hydrophobic constituents and a hydrophilic constituents are crosslinked. In one or more embodiments, substantially all of the hydrophobic constituents and a hydrophilic constituents are crosslinked. Substantially all of the hydrophobic constituents and a hydrophilic constituents are crosslinked when there is no appreciable loss of permeability in the amphiphilic co-network. The amphiphilic co-network may be a hydrogel that swells in both water and hydrocarbons.

[0048] The molecularly-bimodal crosslinkable amphiphilic graft includes a hydrophobic constituent and a hydrophilic constituent. The hydrophilic constituent forms a backbone carrying hydrophobic branches. Each branch may include a crosslinkable end group. The molecularly-bimodal crosslinkable amphiphilic graft may include first set of hydrophobic branches and a second set of hydrophobic branches, where the second set of hydrophobic branches has a longer chain length. In one or more embodiments, the molecularly-bimodal crosslinkable amphiphilic graft may be soluble (e.g. in THF). The molecularly-

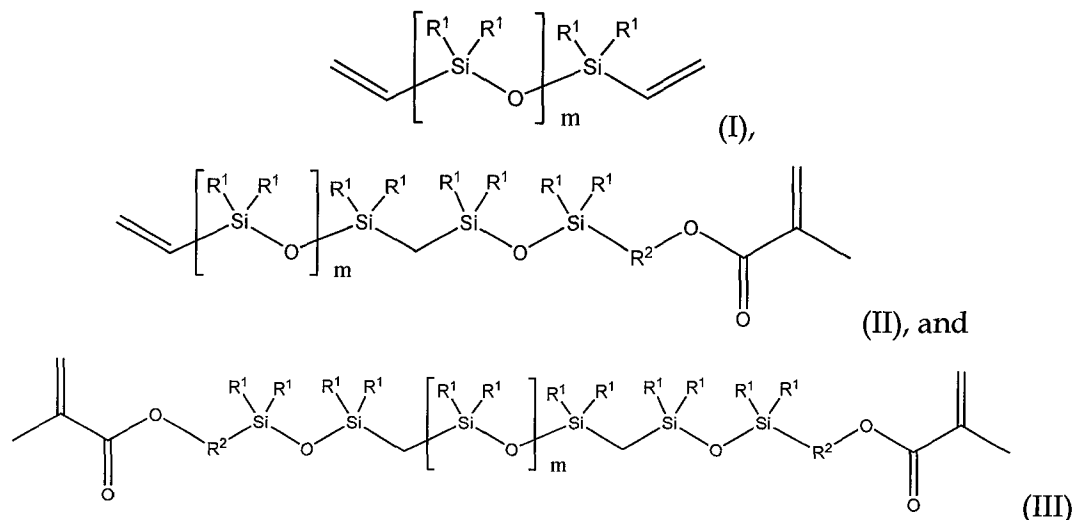
bimodal crosslinkable amphiphilic graft may be crosslinked to form an amphiphilic co-network.

[0049] As noted above, the molecularly-bimodal crosslinkable amphiphilic graft is prepared by polymerizing a dihydrocarbylacrylamide monomer in the presence of a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture and a second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture. An asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture refers to a mixture of polydihydrocarbylsiloxane monomers that include two different terminal functional groups that allow for further reaction or polymerization. The asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture may include a polydihydrocarbylsiloxane monomer (PDHS), with two first terminal functional groups (A) in a telechelic monomer (A-PDHS-A), a polydihydrocarbylsiloxane monomer, with two second terminal functional groups (B) in a telechelic monomer (B-PDHS-B), and a polydihydrocarbylsiloxane monomer, with first terminal functional groups and a second terminal functional groups in a di-end-functional monomer (A-PDHS-B).

[0050] In one or more embodiments, the molar mass ratio between average molar mass of the monomers in the first asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane and average molar mass of the monomers in the second asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane is between about 1:2 and about 1:20, in other embodiments between about 1:8 and about 1:15, in other embodiments between about 1:4 and about 1:10, and in other embodiments between about 1:5 and about 1:8.

[0051] In one or more embodiments, the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is 0.1% to 10%, in other embodiments 0.5% to 7%, and in other embodiments 1% to 5% of the total asymmetric-telechelic polydihydrocarbylsiloxane monomer. The total polydihydrocarbylsiloxane monomer is the sum of all of the polydihydrocarbylsiloxane monomer mixtures.

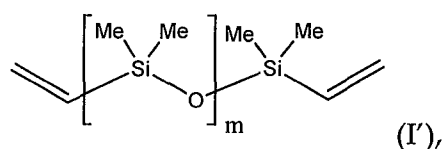
[0052] In one or more embodiments, the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture includes:

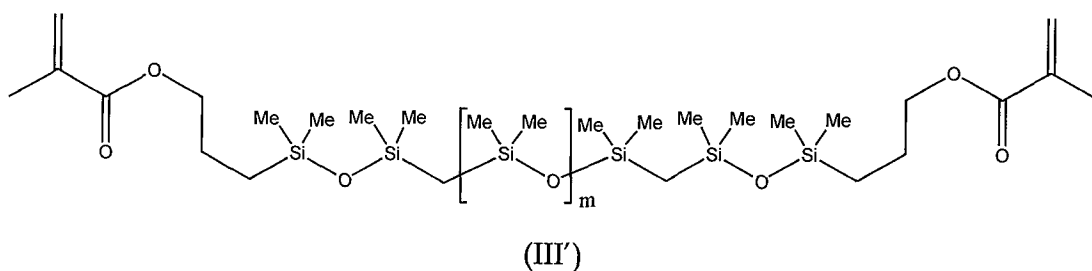
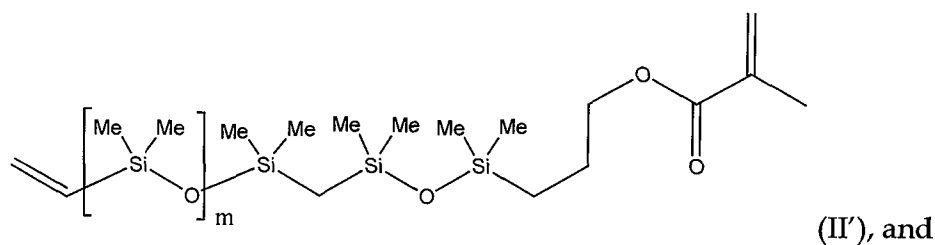


where each R^1 is individually a monovalent organic group, each R^2 is individually a divalent organic group. In one or more embodiments, the each m group of the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is individually an integer from about 100 to about 500, in other embodiments from about 180 to about 350, in other embodiments from about 190 to about 320, in other embodiments from about 195 to about 315.

[0053] In one or more embodiments, the monovalent organic R^1 groups of the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture are each individually alkyl groups of 1 to 6 carbon atoms. In one or more embodiments, the monovalent organic R^1 groups of the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture are methyl groups. In one or more embodiments, the divalent organic R^2 groups of the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture are each individually divalent alkane groups of 1 to 6 carbon atoms.

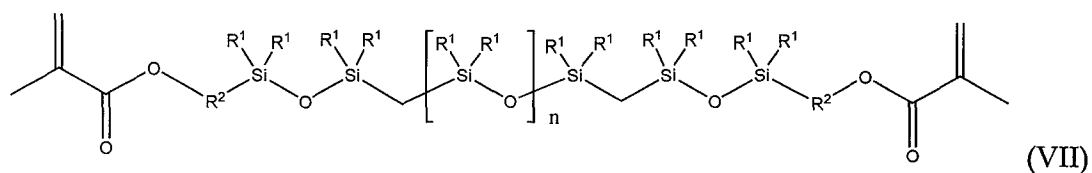
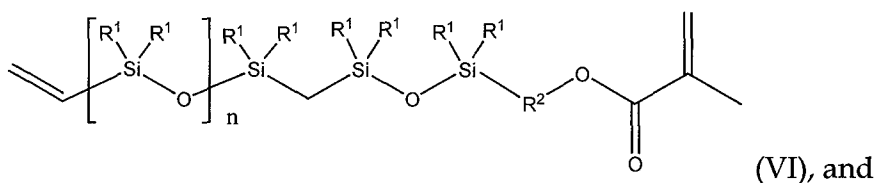
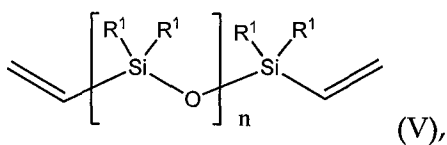
[0054] In one or more embodiments, the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture includes:





where m is defined as above.

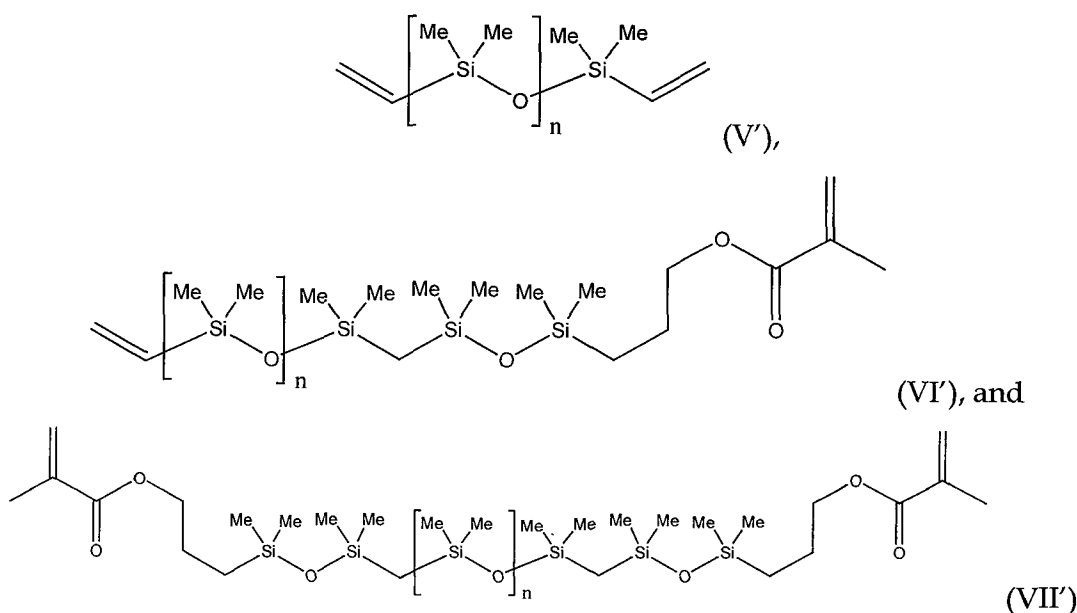
[0055] In one or more embodiments, the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture includes the following:



where each R^1 is individually a monovalent organic group, each R^2 is individually a divalent organic group. In one or more embodiments, the each n group of the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is individually an integer from about 1000 to about 2000, in other embodiments from about 1050 to about 1950, in other embodiments from about 1100 to about 1900, in other embodiments from about 1150 to about 1850.

[0056] In one or more embodiments, the monovalent organic R^1 groups of the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture are each individually alkyl groups of 1 to 6 carbon atoms. In one or more embodiments, the monovalent organic R^1 groups of the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture are methyl groups. In one or more embodiments, the divalent organic R^2 groups of the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture are each individually divalent alkane groups of 1 to 6 carbon atoms.

[0057] In one or more embodiments, the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture includes the following:



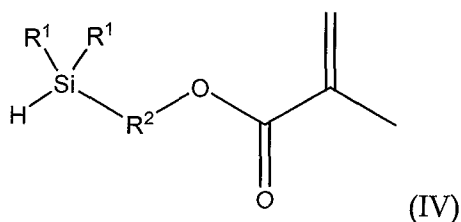
where n is defined as above.

[0058] The first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture and the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture may be prepared together or separately. In one or more embodiments, the asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is prepared by reacting a vinyl telechelic polydihydrocarbylsiloxane with a disiloxane acrylate. A telechelic polydihydrocarbylsiloxane to disiloxane acrylate molar ratio of less than 1:2 is used to produce an asymmetric-telechelic

polydihydrocarbylsiloxane monomer mixture that includes asymmetric-telechelic polydihydrocarbylsiloxane monomer vinyl and acrylate end groups. In one or more embodiments, the telechelic polydihydrocarbylsiloxane to disiloxane acrylate molar ratio less than 1:2, in other embodiments less than 1:1.5, in other embodiments less than 1:1. In one or more embodiments, where the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture and the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture are prepared together, a first vinyl telechelic polydihydrocarbylsiloxanes and a second vinyl telechelic polydihydrocarbylsiloxane with a longer chain length are reacted with a disiloxane acrylate in the same reaction mixture.

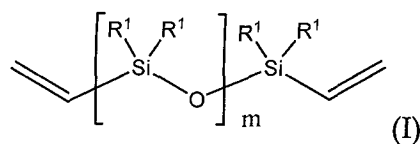
[0059] The reaction between a telechelic polydihydrocarbylsiloxane and the disiloxane acrylate is a hydrosylation reaction. In one or more embodiments a platinum catalyst may be used to facilitate the hydrosylation telechelic polydihydrocarbylsiloxane and the disiloxane acrylate. Suitable platinum catalysts include Karstedt's catalysts.

[0060] In one or more embodiments, the disiloxane acrylate suitable for use in preparing the first or the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture defined by the formula



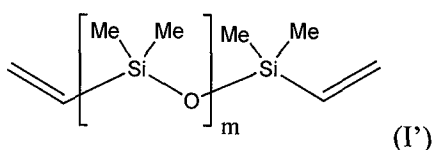
where each R¹ is individually a monovalent organic group, and R² is a divalent organic group.

[0061] In one or more embodiments, the vinyl telechelic polydihydrocarbylsiloxane suitable for use in preparing a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is defined by the formula



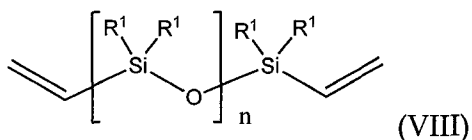
where each R^1 is individually a monovalent organic group. In one or more embodiments, the m group of the vinyl telechelic polydihydrocarbylsiloxane is an integer from about 100 to about 500, in other embodiments from about 180 to about 350, in other embodiments from about 190 to about 320, in other embodiments from about 195 to about 315.

[0062] In one or more embodiments, the vinyl telechelic polydihydrocarbylsiloxane suitable for use in preparing a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is defined by the formula



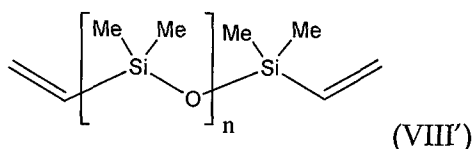
where m is defined as above.

[0063] In one or more embodiments, the vinyl telechelic polydihydrocarbylsiloxane suitable for use in preparing a second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is defined by the formula



where each R^1 is individually a monovalent organic group. In one or more embodiments, the n group of the vinyl telechelic polydihydrocarbylsiloxane is an integer from about 1050 to about 1950, in other embodiments from about 1100 to about 1900, in other embodiments from about 1150 to about 1850.

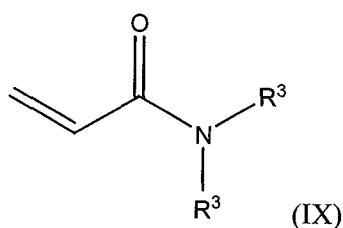
[0064] In one or more embodiments, the vinyl telechelic polydihydrocarbylsiloxane suitable for use in preparing a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is defined by the formula



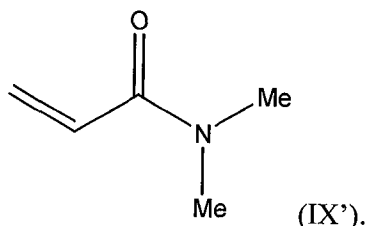
where n is defined as above.

[0065] The first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture and the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture may be combined with a dihydrocarbylacrylamide monomer. The dihydrocarbylacrylamide monomer may be polymerized to prepare the molecularly-bimodal crosslinkable amphiphilic graft. The polymerization may take place under free radical conditions. In one or more embodiments the dihydrocarbylacrylamide monomer may be between about 40 and about 70 wt%, in other embodiments about 45 and about 65 wt%, and in other embodiments about 50 and about 60 wt% of the total weight of the dihydrocarbylacrylamide monomer, first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture, and second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture.

[0066] In one or more embodiments, the dihydrocarbylacrylamide monomer may be defined by the formula



where each R^3 is individually a monovalent organic group. In one or more embodiments, where the monovalent groups are each methyl groups, the dihydrocarbylacrylamide monomer may be defined by the formula



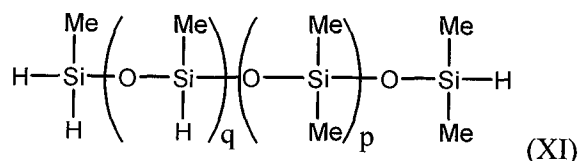
[0067] As noted above, molecularly-bimodal crosslinkable amphiphilic graft is crosslinked with a siloxane compound that includes at least two Si-H bonds. The crosslinking reaction between the crosslinkable amphiphilic graft and the siloxane compound that includes at least two Si-H bonds is a hydrosylation reaction. In one or more embodiments a platinum catalyst may be used to facilitate the hydrosylation telechelic polydihydrocarbylsiloxane and the disiloxane acrylate. Suitable platinum catalysts include Karstedt's catalysts.

[0068] In one or more embodiments, the amount of siloxane compound that includes at least two Si-H bonds may be characterized in reference to the amount of vinyl end groups present in the molecularly-bimodal crosslinkable amphiphilic graft. In one or more embodiments, the vinyl group to Si-H bond ratio is about 1:1 to about 1:30, in other embodiments about 1:3 to about 1:25, and in other embodiments about 1:5 to about 1:10.

[0069] In one or more embodiments, the amount of siloxane compound that includes at least two Si-H bonds may be characterized by the percent weight of the siloxane compound that includes at least two Si-H bonds of the total of the molecularly-bimodal crosslinkable amphiphilic graft and the siloxane compound that includes at least two Si-H bonds. In one or more embodiments, the percent weight of the siloxane compound that includes at least two Si-H bonds is from about 1% to about 30%, in other embodiments from about 3 to about 25%, and in other embodiments about 5% to about 10%.

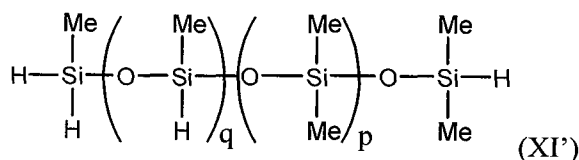
Suitable siloxane compounds that includes at least two Si-H bonds for crosslinking the crosslinkable amphiphilic graft may be found in U.S. Pat. Nos.

8,247,515 and 8,067,521, both of which are incorporated by reference. In one or more embodiments, the siloxane compound that includes at least two Si-H bonds may be defined by the formula



where each R^1 is individually a monovalent organic group. In one or more embodiments, q is an integer from about 1 to about 2000, in other embodiments, from 3 to 100, in other embodiments, 5 to 50, and in other embodiments, 10 to 30. p is an integer from about 1 to about 2000. In one or more embodiments, p is an integer from about 1 to about 2000, in other embodiments, from 3 to 100, in other embodiments, 5 to 50, and in other embodiments, 10 to 30.

[0070] In one or more embodiments, the siloxane compound that includes at least two Si-H bonds may be defined by the formula



where p and q are defined as above.

[0071] Monovalent organic groups suitable for use in amphiphilic co-network include linear branched or cyclic substituted or unsubstituted alkyl and aryl groups that include from 1 to 6 carbon atoms, in other embodiments from 2 to 4 carbon atom and in other embodiments, 3 carbon atoms. Suitable substitutions include replacing a hydrogen or a carbon atom with an oxygen atom, nitrogen atom, sulfur atom, or a halogen atom. In one or more embodiments, the monovalent organic group is an alkyl of 1 to 6 carbon atoms. Suitable alkyl group of 1 to 6 carbon atoms include, but are not limited to, methyl, ethyl, propyl,

isopropyl, isobutyl, tertbutyl, n-butyl, sec-butyl, isopentyl, tertpentyl, n-pentyl, sec-pentyl, terthexyl, n-hexyl, isohexyl, sec-hexyl, and cyclohexyl groups.

[0072] Divalent organic groups suitable for use in amphiphilic co-network include linear branched or cyclic substituted or unsubstituted alkane and aromatic group that include from 1 to 6 carbon atoms, in other embodiments from 2 to 4 carbon atom and in other embodiments, 3 carbon atoms with two hydrogen atoms removed to create two valences. Suitable substitutions include replacing a hydrogen or a carbon atom with an oxygen atom, nitrogen atom, sulfur atom, or a halogen atom. In one or more embodiments, the divalent organic group may be an alkane of 1 to 6 carbon atoms two hydrogen atoms removed. Suitable alkane of 1 to 6 carbon atoms include groups for use as divalent groups include, but are not limited to, methane, ethane, propane, isopropane, isobutane, tertbutane, n-butane, sec-butane, isopentane, tertpentane, n-pentane, sec-pentane, terthexane, n-hexane, isohexane, sec-hexane, and cyclohexane groups.

[0073] Advantageously, the amphiphilic co-network may be prepared with controlled pore diameters. The pore diameter of the amphiphilic co-network is the width of the opening of pore. In one or more embodiments, the amphiphilic co-network may be used as a membrane in a bio-artificial organ. In order to avoid hyperacute rejection, the antibodies of the bio-artificial organ recipients of should be prevented from "seeing" the foreign proteins and activating complement. The amphiphilic co-network should also reliably safeguard the patient from infectious processes (e.g., bacteria) unwittingly transferred with the bio-artificial organ. The pore diameters of the amphiphilic co-network used for immunoisolation may be of a sufficient size to allow insulin, glucose, oxygen, and carbon dioxide to pass freely. These molecules have diameters less than 35 Angstroms (3.5 nm). The pore diameters of the amphiphilic co-network used for immunoisolation may also be of a sufficient size exclude the immigration of immunoglobulins, complement, and cytokines (e.g., tumor necrosis factor) providing immunoisolation. In one or more embodiments, the amphiphilic co-network has hydrophilic pore dimensions in the range of about 3.0 nm to about 4.0 nm.

[0074] In one or more embodiments, the bio-artificial organ may be a bio-artificial pancreas. Advantageously, it has been found that the amphiphilic co-network allows the rapid diffusion of insulin, but is impermeable to immunoglobulin G (IgG). Suitable bio-artificial pancreas are disclosed in U.S. Pat. Nos. 8,247,515; 8,067,521; 8,702,810 and all of which are incorporated by reference.

[0075] In one or more embodiments, the bio-artificial organ comprises a housing with a plurality of holes on the housing, over the plurality of holes, an amphiphilic co-network. In these or other embodiments, the housing of the bioartificial organ, which may be referred to as a scaffold, comprises a first disc with a with a first raised ring around the perimeter of the disc and a concentric smaller second raised ring within the first raised ring, and a second disc with a raised ring, the raised ring of the second disc situated between the first and second raised rings of the first disc, wherein a void is present between the first disc, the second raised ring of the first disc, and the second disc, and the first disc, the second disc or both discs include a plurality of holes that connect to said void. The first raised ring and second raised ring of the first disc may include a cut out portion, and the raised ring of the second disc may include a cutout portion aligned with the cut out portion of the first disc. The cut out portion may be adapted to fill the void. In one or more embodiments the void is filled with islets of langerhorn.

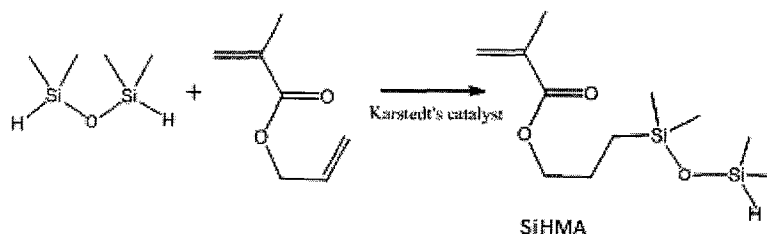
[0076] While particular embodiments of the invention have been disclosed in detail herein, it should be appreciated that the invention is not limited thereto or thereby inasmuch as variations on the invention herein will be readily appreciated by those of ordinary skill in the art. The scope of the invention shall be appreciated from the claims that follow.

EXAMPLES

Synthesis of Poly(N,N-dimethylacrylamide)/Polydimethylsiloxane Conetworks

a) Synthesis of 2-propionic acid 3-(1,1,3,3-tetramethyldisiloxanyl)propyl ester (SiHMA)

[0077] The synthesis strategy for SiHMA is given by the following scheme:



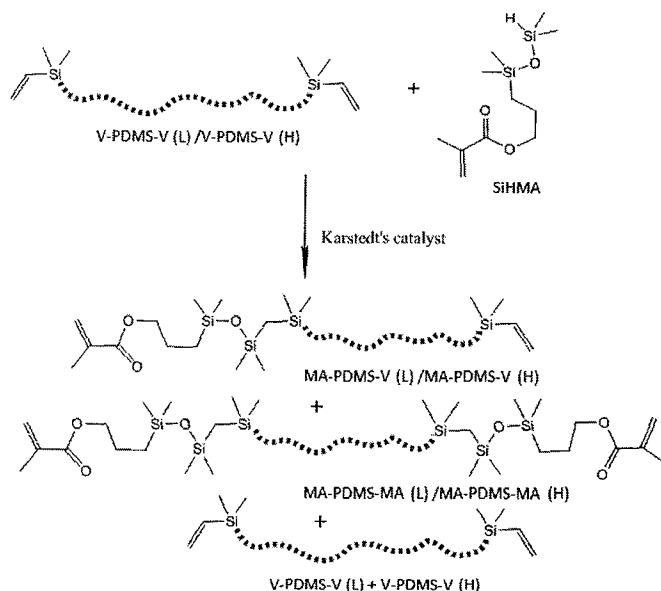
[0078] Thus, tetramethyldisiloxane (134 g, 1 mol) and allyl methacrylate (126 g, 1 mol) were placed in a round bottom flask. The reaction was started by the addition of Karstedt's catalyst (0.5 mL) and the mixture was stirred for 3 h. Then triphenylphosphine (10 mL) was added and the charge was vacuum distilled at 50 °C. The product (SiHMA) is a colorless liquid with a boiling point of 62 °C. Proton NMR spectroscopy confirmed the expected structure (Figure 1).

[0079] The spectrum shows a multiplet at 4.67 ppm, which indicates the presence of the SiH group, and the characteristic resonances at 6.2 and 5.6 ppm (for the olefinic protons) and at 1.9 ppm (for the methyl protons) are associated with the methacrylate (MA) group.

b) Synthesis of the Asymmetric-Telechelic Macromonomer (MA-PDMS-V)

[0080] Molecularly-bimodal crosslinkable branches (MA-PDMS-V) of bAPG were prepared by combining SiHMA with two different molecular weight (17,200 and 117,500 g/mol) vinyl ditelechelic PDMSs (V-PDMS-V)s by hydrosilation.

[0081] The following scheme shows the transformations and the structure of the products:



In this scheme the dotted line stands for the low or high molecular weight PDMSs.

[0082] Thus, V-PDMS-V and SiHMA were placed in a 500 mL round bottom flask and dissolved in freshly distilled toluene at room temperature. Then various compositions (1 - 5%) high molecular weight V-PDMS-V(H) and low molecular weight V-PDMS-V(L) were added to the system. Reagent quantities and stoichiometry are shown in Table 1. Hydrosilylation was started by the addition of Karstedt's catalysts, and the charge was stirred while heating at 50 °C for 2 h.

Table 1. Reaction Conditions for the Preparation of Assymmetric Telechelic MA-PDMS-V Macromer*

	MA-PDMS-V-0	MA-PDMS-V-1	MA-PDMS-V-2	MA-PDMS-V-5
V-PDMS-V(L) (17200 g/mol)	0.250 mmol (100 %)	0.248 mmol (99 %)	0.245 mmol (98 %)	0.238 mmol (95 %)
V-PDMS-V(H) (117500 g/mol)	—	2.5x10 ⁻³ mmol (1%)	5.0x10 ⁻³ mmol (2 %)	12.5x10 ⁻³ mmol (5 %)

*Each compositions contained SiHMA= 0.25 mmol, Karstedt catalyst (3% xylene solution) = 0.02 mL, and toluene = 23 mL.

[0083] The product was characterized by ^1H NMR spectroscopy and GPC. (Figures 2 and 3)

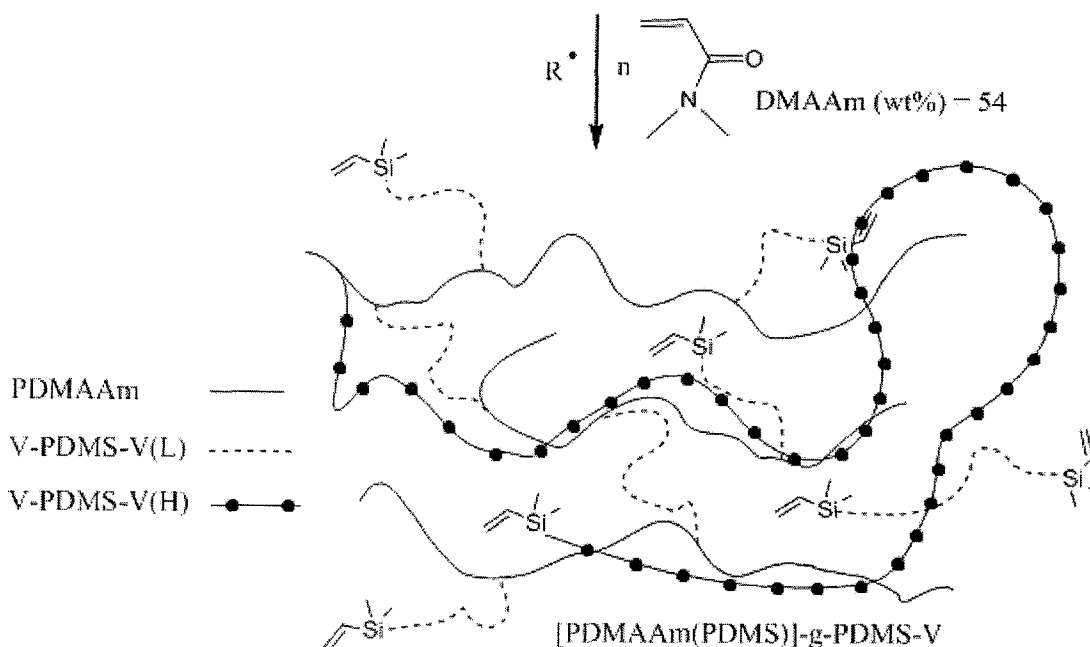
[0084] The resonances associated with the SiH proton (4.67 ppm) disappeared . The resonance for the CH_2 protons, which arose by hydrosilation of $-\text{Si}-\text{CH}=\text{CH}_2$ by SiHMA, appears at 0.4 ppm.

[0085] According to the symmetrical monomodal GPC traces, the high molecular weight MA-PDMS-V was homogeneously integrated into the the graft. The shift of the elution peaks toward increased molecular weights with increasing amount of MA-PDMS-V further indicates the incorporation of the high molecular weight MA-PDMS-V.

c) Synthesis of [PDMAAm(PDMS)]-g-PDMS-V (bAPG)

[0086] The free radical terpolymerization of DMAAm plus MA-PDMS- V and MA-PDMS-MA yields a bAPG consisting a PDMAAm backbone carrying - PDMS-V branches. The vinylsilyl termini do not copolymerize with the MA groups under free radical conditions; therefore the bAPG remains soluble. The following scheme helps to visualize the synthetic strategy:

[0087] Mixture of MA-PDMS-V(L)/MA-PDMS-V (H), MA-PDMS-MA(L)/MA-PDMS-MA (H) and V-PDMS-V(L)/V-PDMS-V (H) (see scheme in b) above)



[0088] Thus, freshly distilled DMAAm (3.57 g), various mixtures of 0, 1, 2 and 5 % low and high molecular weight MA-PDMS-V (total = 0.25 mmol), and 65 mL toluene were placed in a 500 mL round bottom flask and stirred under a nitrogen atmosphere. Then AIBN (5.36 mg) was added and the solution was stirred at 65 °C for 24 h. The solvent was evaporated under vacuum and the solid bAPG was recovered. Conversion was found to be quantitative.

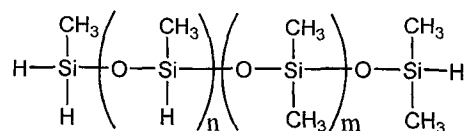
[0089] Depending on the overall composition, i.e., on the amount of low and high molecular weight MA-PDMS-V, the products were optically clear rigid (MA-PDMS-V-0 and MA-PDMS-V-1) or flexible (MA-PDMS-V-2 and MA-PDMS-V-5) materials.

[0090] Figure 4 shows GPC traces of the four representative grafts containing 0, 1, 2, and 5 % V-PDMS-MA(H), and the V-PDMS-MA for comparison.

[0091] The position of the main elution peak of V-PDMS-MA shifts to lower retention times (higher molecular weights) with increasing V-PDMS-MA concentration, which indicates successful grafting. Moreover, the noticeable broadening of the peaks with increasing V-PDMS-MA(H) content suggests that the presence of V-PDMS-MA(H) did not affect grafting efficiency or architectural homogeneity.

d) Crosslinking the bAPG to bAPCN and the Preparation of Membranes

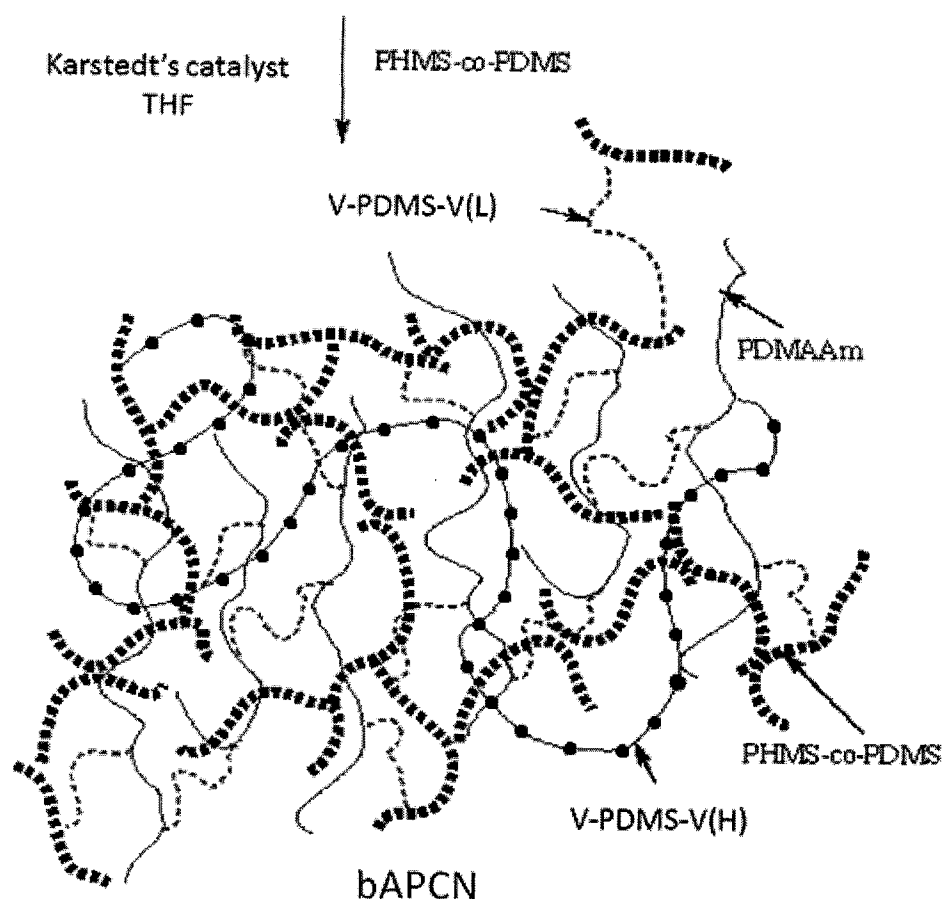
[0092] The molecularly-bimodal amphiphilic graft was crosslinked by hydrosilation of the pendant -PDMS-V branches by the use of a polyhydrosiloxane-PDMS copolymer (PHMS-co-PDMS). The structure of the crosslinker was:



Crosslinker : PHMS-co-PDMS : 30 mol % PHMS

[0093] The following equation shows the network formation effected by the use of this crosslinker, and the structure of the target bAPCN membrane:

[PDMAAm(PDMS)]-g-PDMS-V



[0094] A series of four membranes were prepared as follows:

[0095] Four bAPGs ([PDMAAm(PDMS)]-g-PDMS-V of 0, 1, 2, and 5%) (0.9 g) were mixed with the above crosslinker in three ratios (allyl chain end/hydrosiloxane molar ratio = 1:5, 1:10 and 1:25), and crosslinked with a Karstedt's catalyst (25 μ L) in THF (8 mL) solvent. The bAPGs were homogenized with the crosslinker in THF common solvent by strong stirring for 10 min under a nitrogen atmosphere. Then the homogeneous solution was poured on a Teflon sheet and thin films of controlled thicknesses were prepared using a doctor's blade. The film then was kept at room temperature overnight and subsequently cured at 70°C for 24 h. All the bAPCN films were homogeneous and optically clear.

Curing Properties

[0096] Instrumented device (internally called JOEY) developed to track the thickness, weight, birefringence of coating during drying (patent pending) was

used to track temporal changes in these physical parameters during the curing of the membrane. This real-time instrument (Figure 5) follows in-plane and out-of-plane birefringence, weight, thickness, and surface temperature during the course of solvent evaporation and crosslinking of membrane. The membrane is cast on a glass substrate with thickness controlled Dr. Blade with an initial casting gap of 400 μ m then placed into JOEY for testing.

[0097] As shown in Figure 6. Weight rapidly decreased in first 5000 seconds as solvent evaporates at early stages. Following this initial stage, the rate of weight reduction decreased substantially and continue to decrease until the end of curing.. No changes in birefringence is observed during drying and crosslinking. The thickness increase during curing may be related to undulations created during the process.

Mechanical Properties

[0098] The mechanical and mechano-optical properties of the APCN membrane were measured using a unique computer controlled machine that was developed at The University of Akron, in the Polymer Engineering Department. This machine is equipped with two opposing crossheads that move in synch with each other and the strain on the sample is measured by laser micrometer that measures the width at the symmetry midplane as well as high speed video that records the locations of four painted dots on the dumbbell shaped sample. Birefringence is continuously monitored by spectral birefringence system developed in Cakmak's research group.. The details of the stretching-birefringence apparatus were reported earlier. Dumbbell samples of 40.5 (gauge length =19.5mm) by 25mm were stretched at room temperature at a stretching rate of 100mm/min.

Mechanical properties

[0099] Figure 7 and 8 shows the mechanical properties of 2% PDMS APCN and 5% films with three different crosslink levels 5,10, 25% . Over 5% crosslink

the elongation to break and tensile strength increases in these films indicating superior mechanical properties are obtained in these membranes that is suited for production of membranes and with these mechanical properties their survival after implantation is greatly enhanced.

[00100] The polymers with a higher concentration of both the HMW PDMS and crosslinker exhibited the best mechanical properties.

Mechanical-optical test results:

[00101] Figure 9 shows strain optical and stress optical behavior of 10-25% crosslink at 2% PDMS APCN. The data indicate that these polymers exhibit negative intrinsic birefringence and chain orientation (molecular level strain) almost linearly correlated with the macroscopic strain that is applied. Stress optical behavior is found to be quite non-linear.

[00102] At 5% APCN both crosslinking levels indicate the strain optical and stress optical behaviors are nonlinear though the polymer is still exhibit negative intrinsic birefringence ($\Delta N_{12} = n_1 - n_2$) 1=stretching direction, 2= transverse direction) birefringence become increasingly negative as the films are stretched

Permeabilities

[00103] The permeability tests were conducted using a pre-described diffusion chamber. ~ 60– 160 μm thick membranes having a diffusion area of 2cm^2 were placed between the receiver and donor chambers and mixed at 37°C . The systems were mixed at 150 rpm to eliminate the boundary layer effect in a G24 Environmental incubator shaker from New Brunswick Scientific.

[00104] Permeability P can be obtained from the slope of $-\ln(\Delta C_t / \Delta C_0)$ versus time plots, and using

$$\frac{(C_{d,t} - C_{r,t})}{(C_{d,0} - C_{r,t})} = \frac{\Delta C_t}{\Delta C_0} = \exp(-P\beta t)$$

Where $C_{d,0}$ and $C_{d,t}$ are concentrations of a solute in the donor chamber at time $t = 0$ and t , and $C_{r,0}$ and $C_{r,t}$ are those in the receiving chamber at $t = 0$ and time t , respectively. The diffusion cell constant (β) can be calculated by:

$$\beta = \frac{A}{L} (V_d^{-1} + V_r^{-1})$$

Insulin permeability

[00105] Insulin permeability tests were carried out using 400 μ g/ml insulin (bovine, containing ~ 0.5% zinc,) concentration in PBS in the donor chamber. To prevent the formation of insulin aggregates, solutions were stabilized with 0.15% n-octyl β -D-glucopyranoside and 0.05% sodium azide was added as anti-bacterial. The sets of experiments were separated into two groups of short and long time experiments to be able to get sufficient amount of material out of the 2ml receiver chamber for enzyme-linked immunoabsorbent assays. For the short time experiments, a 100 μ l of sample was taken every 5min for the first 20min and for the long time experiment same amount is taken every 20min for 100min. Insulin concentrations were determined using an insulin enzyme-linked immunoabsorbent assay (ELISA) kit from microplate colors using a spectrophotometer at the North East Ohio Medical School (NEOMED) Spectramax Plus operated at 505nm.

[00106] The diffusion of Insulin is faster than in the previous generation with a 100% permeation in less than 20 min.

IgG permeability

[00107] IgG permeability tests were carried out using 800 μ g/ml human IgG concentration in the donor chamber. The sets of experiments were separated in the same way with insulin permeability experiments. For the short time experiments, 100 μ l of sample was taken every 20min for the first 60min and for the long time experiment same amount is taken every 12hours for 1.5days. Insulin

concentrations were determined using a human IgG enzyme-linked immunoabsorbent assay (ELISA) kit from microplate colors using a spectrophotometer in NEOMED Spectramax Plus operated at 450nm.

[00108] The ability of the membranes to stop/delay the diffusion of IgG has a strong relationship with the amount of HMW PDMS. The samples with the highest concentration of HMW PDMS (5%) had the best IgG blockage.

Morphology

AFM

[00109] Solution cast and cured samples were used in AFM experiments. The height and phase images were obtained by using a Nanoscope III Multimode microscope from Digital Instruments operating in the tapping mode with aluminum-coated AFM probe (Nanosensors_ PPP-NCHR, length 125 mm, width 30 mm, thickness 4 mm, 330 kHz frequency).

[00110] The polymer with a higher concentration of both the HMW PDMS and crosslinker exhibited the highly ordered, homogeneous channel like morphology acting as perfect chromatographic column for insulin and IgG separation.

Device Preparation

[00111] Our BAP consists of the APCN membrane deposited on a flexible but stiff scaffold. The preparation of the device until Islets of Langerhans addition and complete seal with a biocompatible silicone elastomer can be seen from figure 16.

Optical Microscopy

[00112] The BAP device was immersed in a petri dish filled with buffer saline solution for 3 weeks to evaluate the interface connectivity of scaffold and membrane as well as the overall device integrity.

[00113] There is no tear or holes on the membrane even after 3 weeks in buffer solution. Some wrinkles can be observed due to the swelling property of the membrane which did not changed the device integrity.

Enhancement of membrane strength in swollen state:

[00114] In order to enhance the strength of the membrane, nanofiber reinforcement process may be implemented. This is typically accomplished as follows.

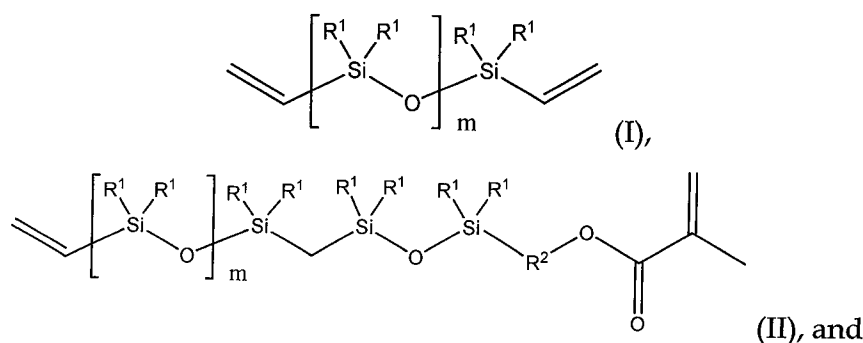
[00115] Following the scaffold manufacturing and punching out the hole in the center of both walls, electrospinning of a suitable dope (fiber precursor) is affected. For this a variety of materials could be used. These include biocompatible polyurethanes, rubbers, etc that have physical and/or chemical affinity to membrane material for interfacial strength. One preferred method is to develop electrospinnable formulation that in turn including the same family of material developed in this patent disclosure. By increasing the high molecular weight PDMS concentration and increasing the solution viscosity (through reduction of solvent content) one could obtain electrospinnable solution (dope). This in-turn, is used to create a thin nanomat (web) of nanofibers crisscrossing the opening of the device. When needed curing step is added facilitating increased strength within the nanofibers and at the junctions where they touch each other facilitating stronger interfiber bonding. Following this process the membrane precursor is delivered to this nanomat taking care that the nanofibers are uniformly coated. Subsequent curing and closure of the two halves of the device and opening of the islet delivery hole completes the process of making the devices.

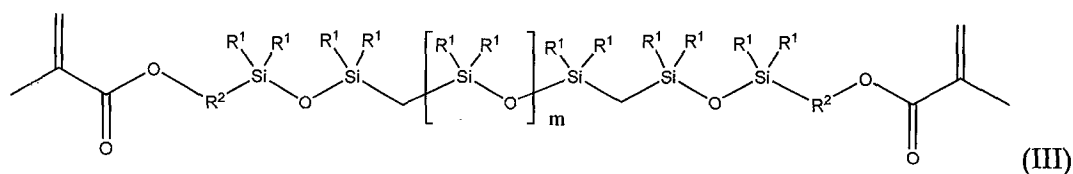
[00116] Various modifications and alterations that do not depart from the scope and spirit of this invention will become apparent to those skilled in the art. This invention is not to be duly limited to the illustrative embodiments set forth herein.

CLAIMS

What is claimed is:

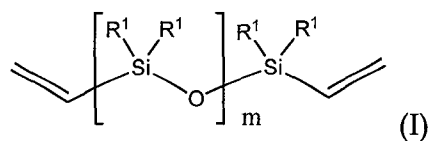
1. A method of preparing an amphiphilic co-network comprising
 preparing a molecularly-bimodal crosslinkable amphiphilic graft by polymerizing a dihydrocarbylacrylamide monomer in the presence of a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture and a second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture where the molar mass ratio between average molar mass of the first asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane and average molar mass of the second asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane is between 1:2 and 1:20; and
 crosslinking the molecularly-bimodal crosslinkable amphiphilic graft with a siloxane compound that includes at least two Si-H bonds.
2. The method of claim 1, where the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is 0.1% to 10% of the total asymmetric-telechelic polydihydrocarbylsiloxane monomer.
3. The method of claim 1, where the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture includes:



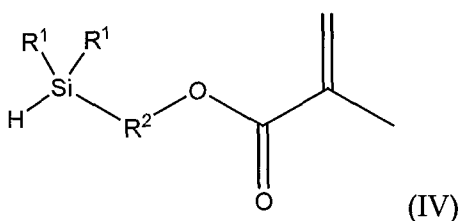


where each R^1 is individually a monovalent organic group, each R^2 is individually a divalent organic group, and each m is individually an integer from about 190 to about 320 units.

4. The method of claim 3, where the first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is prepared by reacting a vinyl telechelic polydihydrocarbylsiloxane with a disiloxane acrylate with a telechelic polydihydrocarbylsiloxane to disiloxane acrylate molar ratio of less than 1:2; where the vinyl telechelic polydihydrocarbylsiloxane is defined by the formula

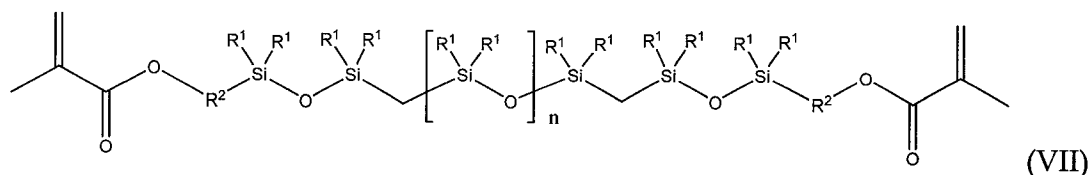
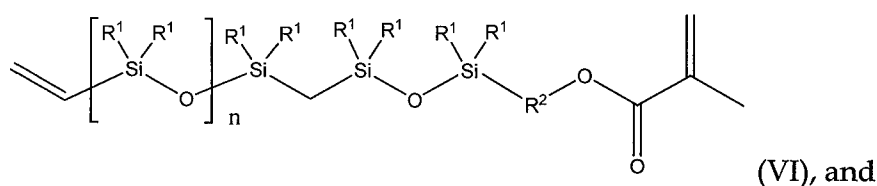
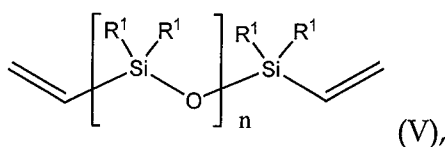


where each R^1 is individually a monovalent organic group, and wherein the disiloxane acrylate defined by the formula



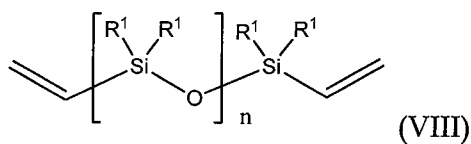
where each R^1 is individually a monovalent organic group, and R^2 is a divalent organic group.

5. The method of claim 3, where each R^1 is an alkyl group of 1 to 6 carbon atoms.
6. The method of claim 1, where the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture includes the following:

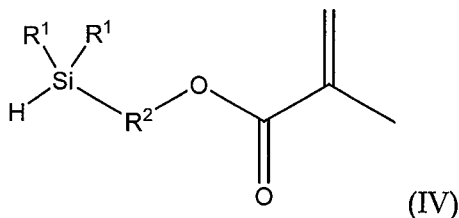


where each R^1 is individually a monovalent organic group, each R^2 is individually a divalent organic group, and each n is individually an integer from about 1100 to about 1900.

7. The method of claim 6, where the second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture is prepared by reacting a vinyl telechelic polydihydrocarbylsiloxane with a disiloxane acrylate with a telechelic polydihydrocarbylsiloxane to disiloxane acrylate molar ratio of less than 1:2;
where the vinyl telechelic polydihydrocarbylsiloxane is defined by the formula



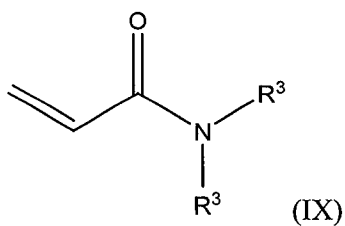
where each R^1 is individually a monovalent organic group, and each n is individually an integer from about 1100 to about 1900; and wherein the disiloxane acrylate defined by the formula



where each R^1 is individually a monovalent organic group, and R^2 is a divalent organic group.

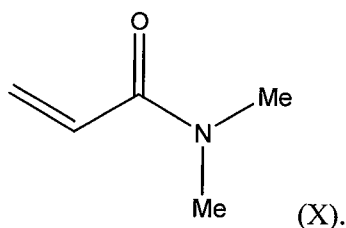
8. The method of claim 6, where each R^1 is an alkyl group of 1 to 6 carbon atoms.

9. The method of claim 1, where the dihydrocarbylacrylamide monomer is defined by the formula



where each R^3 is individually a monovalent organic group.

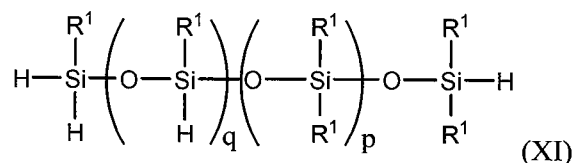
10. The method of claim 9, where the the dihydrocarbylacrylamide monomer is defined by the formula



11. The method of claim 1, where the dihydrocarbylacrylamide monomer is between 40 and 60 wt% of the total weight of the dihydrocarbylacrylamide monomer, first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture, and second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture.

12. The method of claim 1, where the step of crosslinking the molecularly-bimodal crosslinkable amphiphilic graft with a siloxane compound that includes at least two Si-H bonds includes the use of a Karstedt catalyst to facilitate crosslinking.

13. The method of claim 1, where the siloxane compound that includes at least two Si-H bonds is defined by the formula



where each R¹ is individually a monovalent organic group, q is an integer from about 1 to about 2000 and p is an integer from about 1 to about 2000.

14. The method of claim 13, where each R¹ is an alkyl group of 1 to 6 carbon atoms.

15. An amphiphilic co-network prepared by the method of claim 1.

16. A bio-artificial organ comprising
- a housing with a plurality of holes on the housing, over the plurality of holes, an amphiphilic co-network prepared by
- preparing molecularly-bimodal crosslinkable amphiphilic graft by polymerizing a dihydrocarbylacrylamide monomer in the presence of a first asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture and a second asymmetric-telechelic polydihydrocarbylsiloxane monomer mixture where the molar mass ratio between average molar mass of the first asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane and average molar mass of the second asymmetric-telechelic monomer mixture polydihydrocarbylsiloxane is between 1:2 and 1:20; and
- crosslinking the molecularly-bimodal crosslinkable amphiphilic graft with a siloxane compound that includes at least two Si-H bonds.
17. The bioartificial organ of claim 17, where the housing comprises
- a first disc with a first raised ring around the perimeter of the disc and a concentric smaller second raised ring within the first raised ring, and
- a second disc with a raised ring, the raised ring of the second disc situated between the first and second raised rings of the first disc,
- wherein a void is present between the first disc, the second raised ring of the first disc, and the second disc, and the first disc, the second disc or both discs include a plurality of holes that connect to said void.
18. The bioartificial organ of claim 17, where the first raised ring and second raised ring of the first disc includes a cut out portion, and
- the raised ring of the second disc includes a cutout portion aligned with the cut out portion of the first disc.

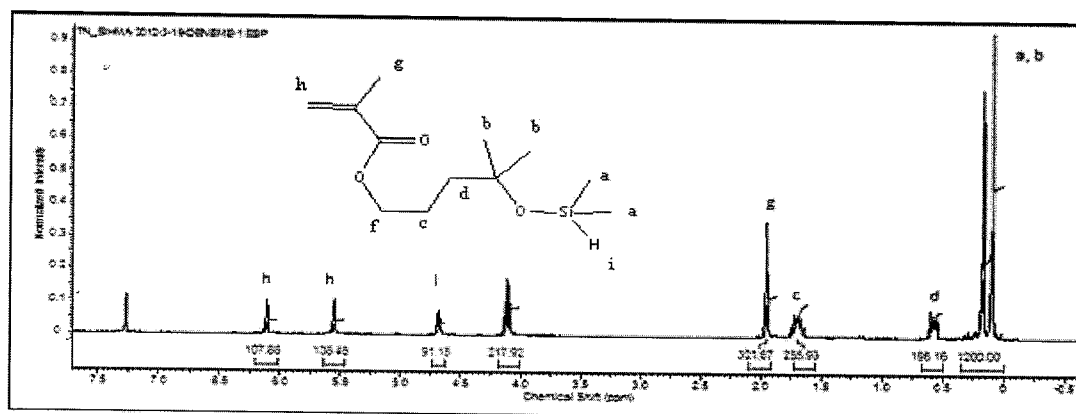


Fig. 1

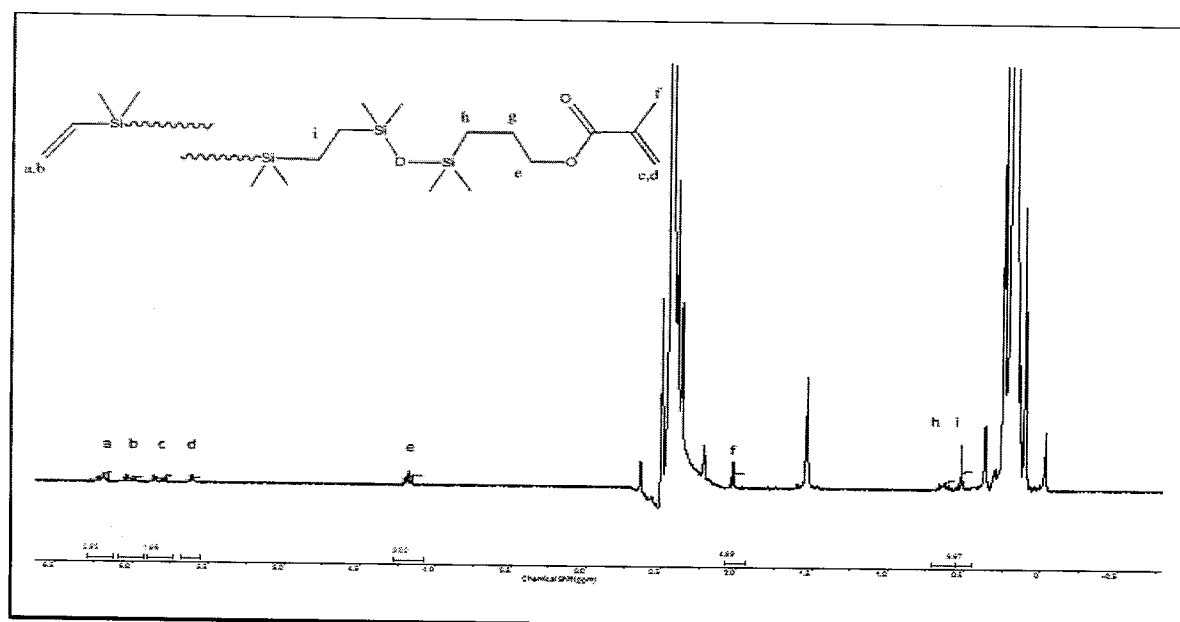


Fig. 2

DRAWING SHEET 3/21

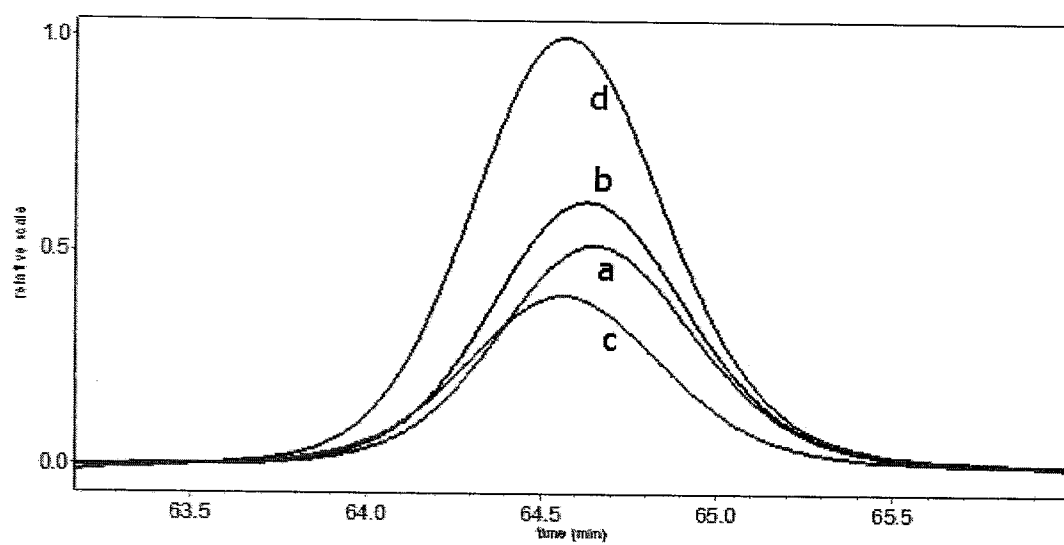
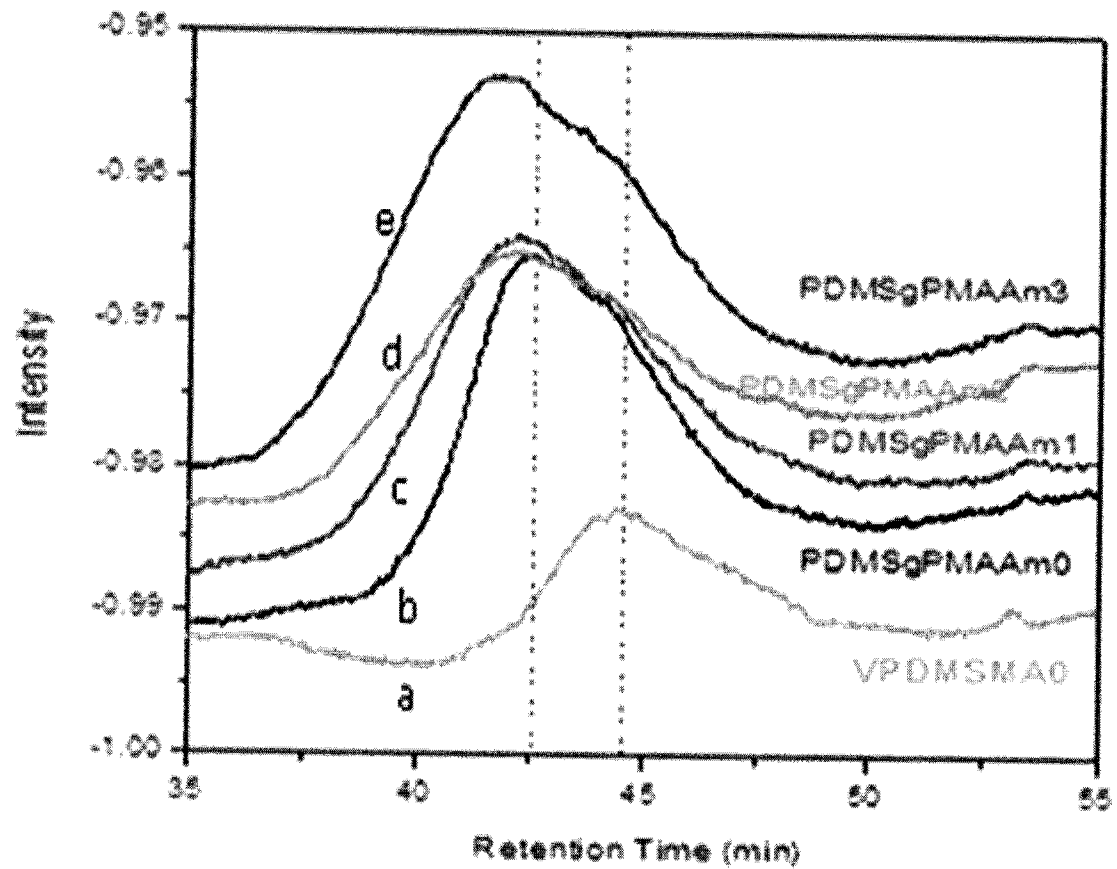


Fig. 3

FIG. 4



Fig, 4

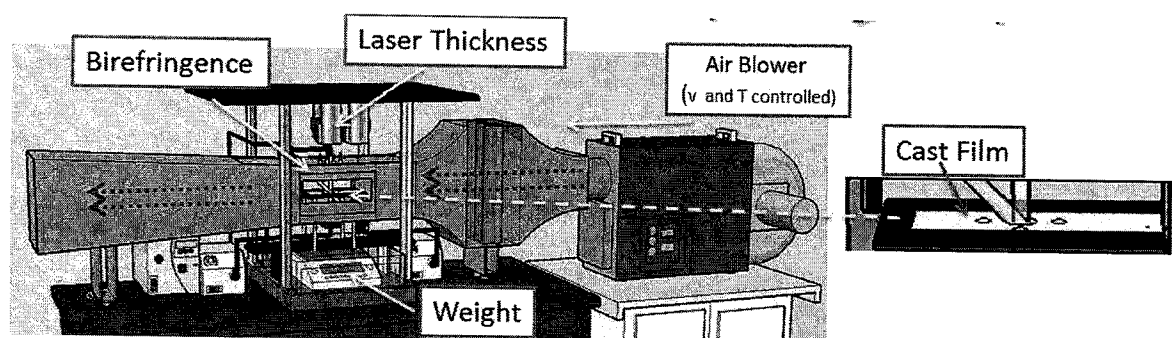


Fig. 5

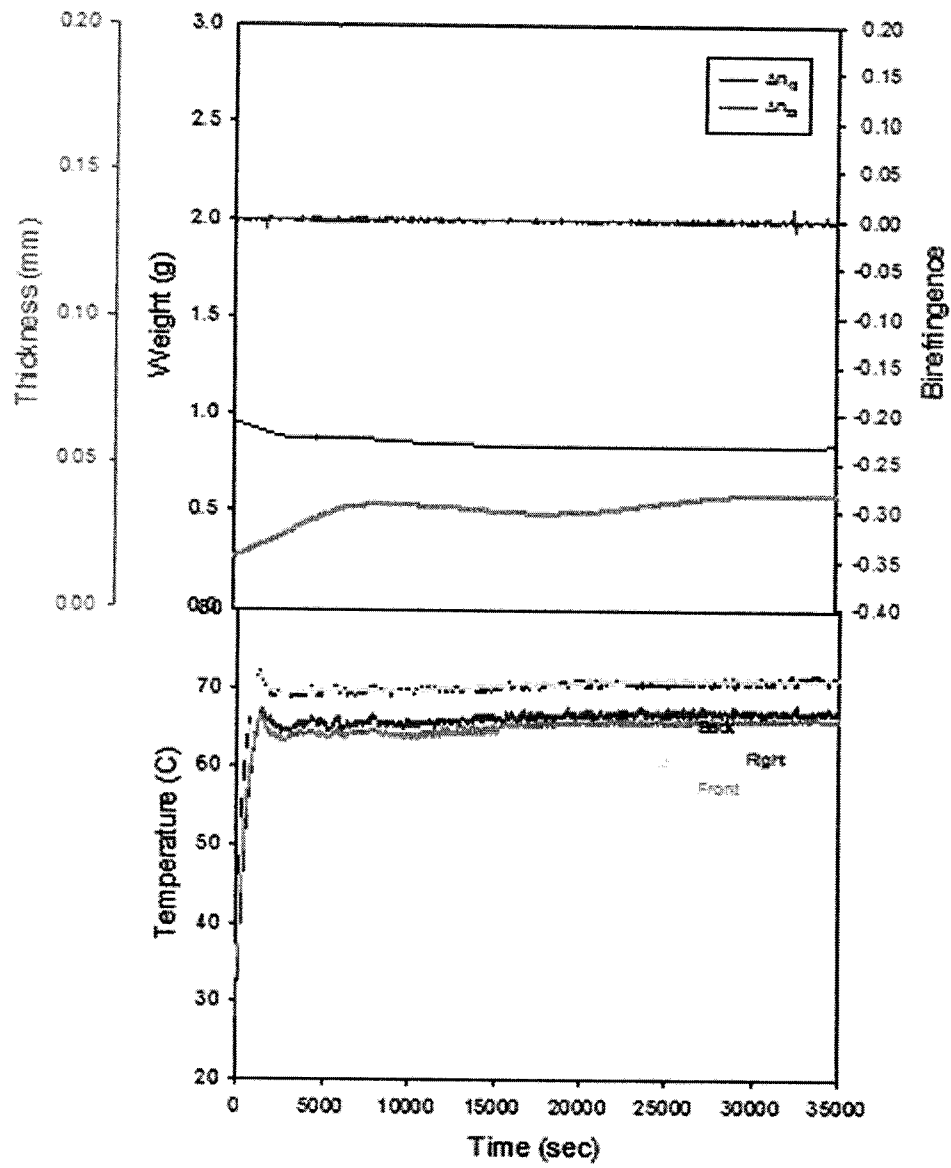


Fig. 6

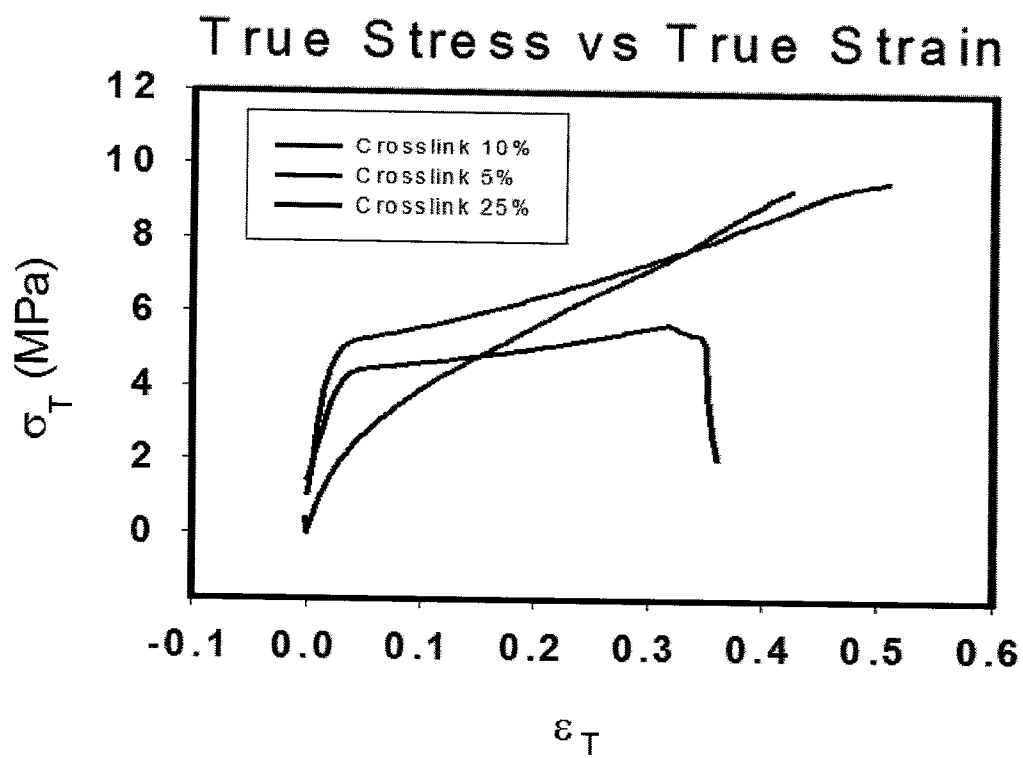


Fig. 7

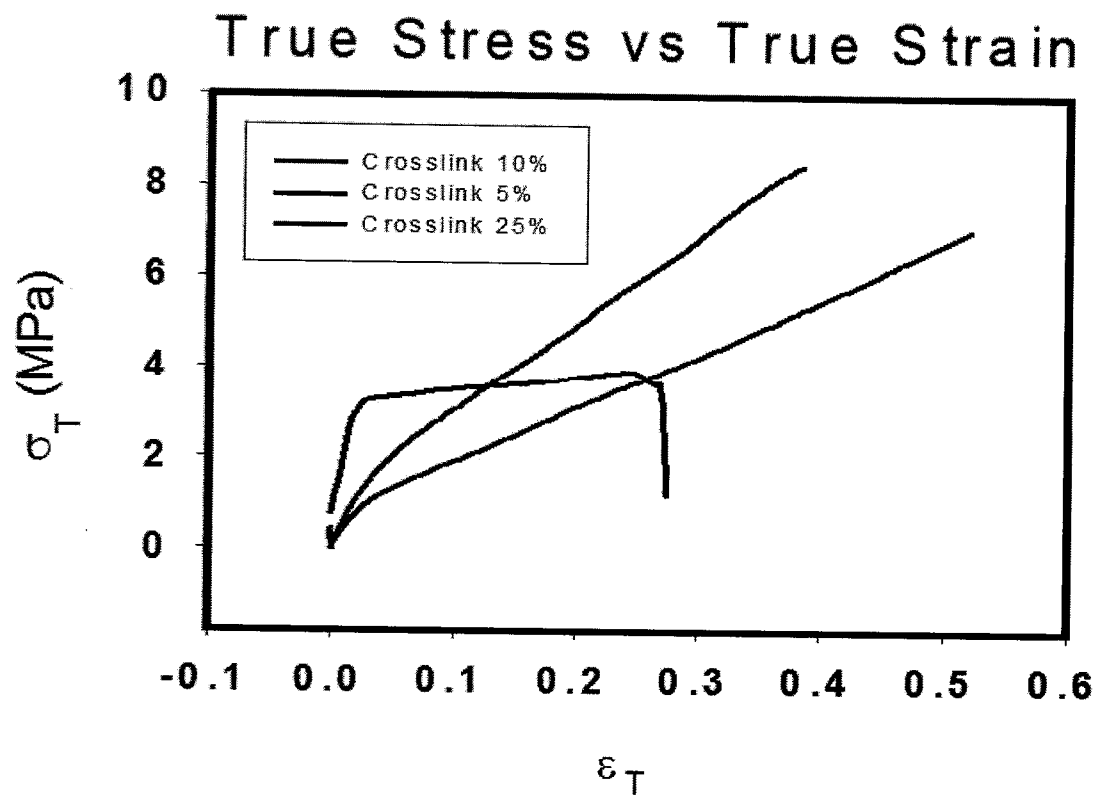


Fig. 8

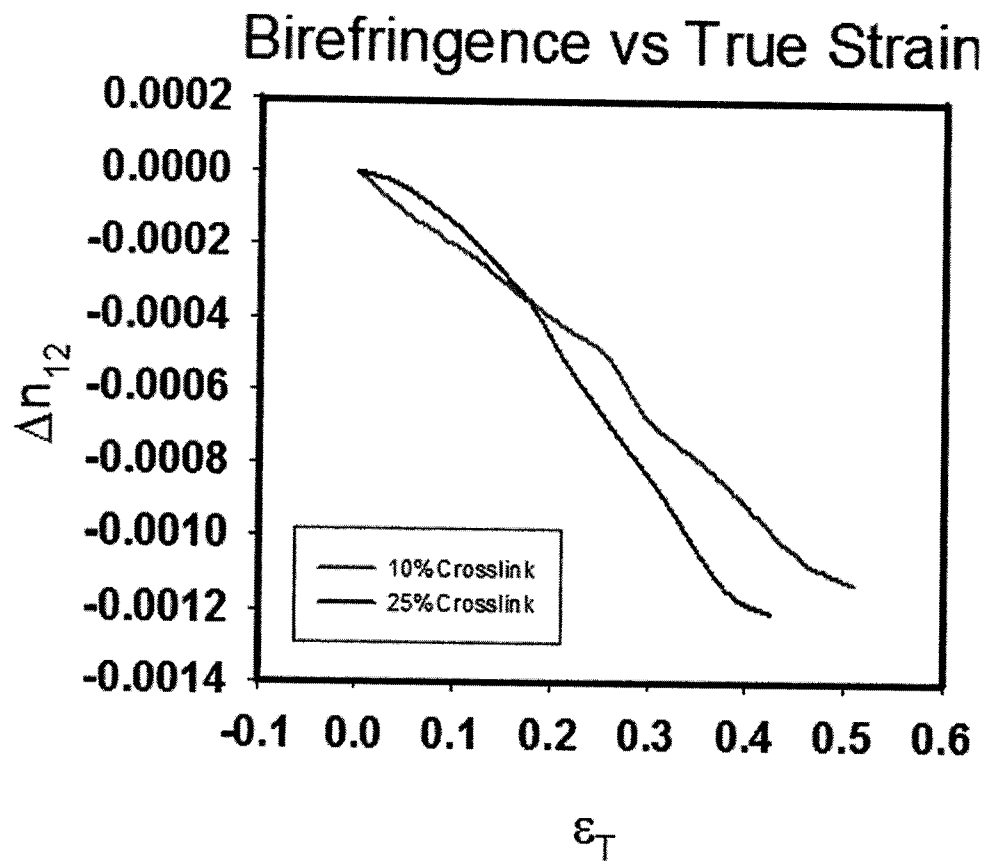


Fig 9A

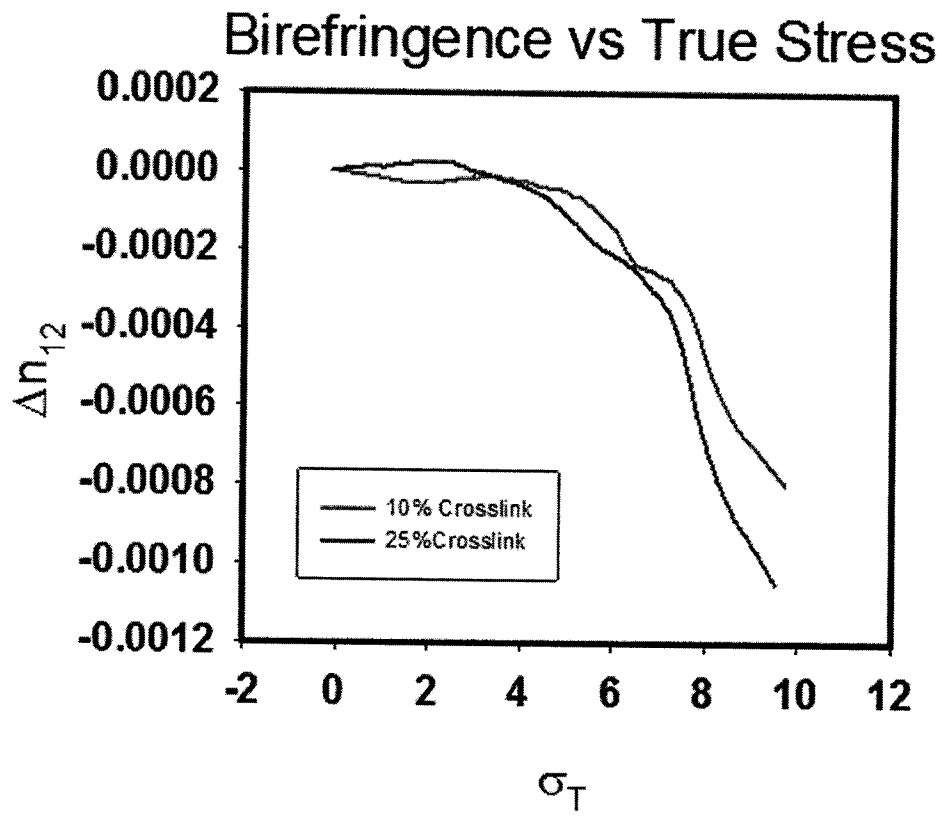


Fig 9B

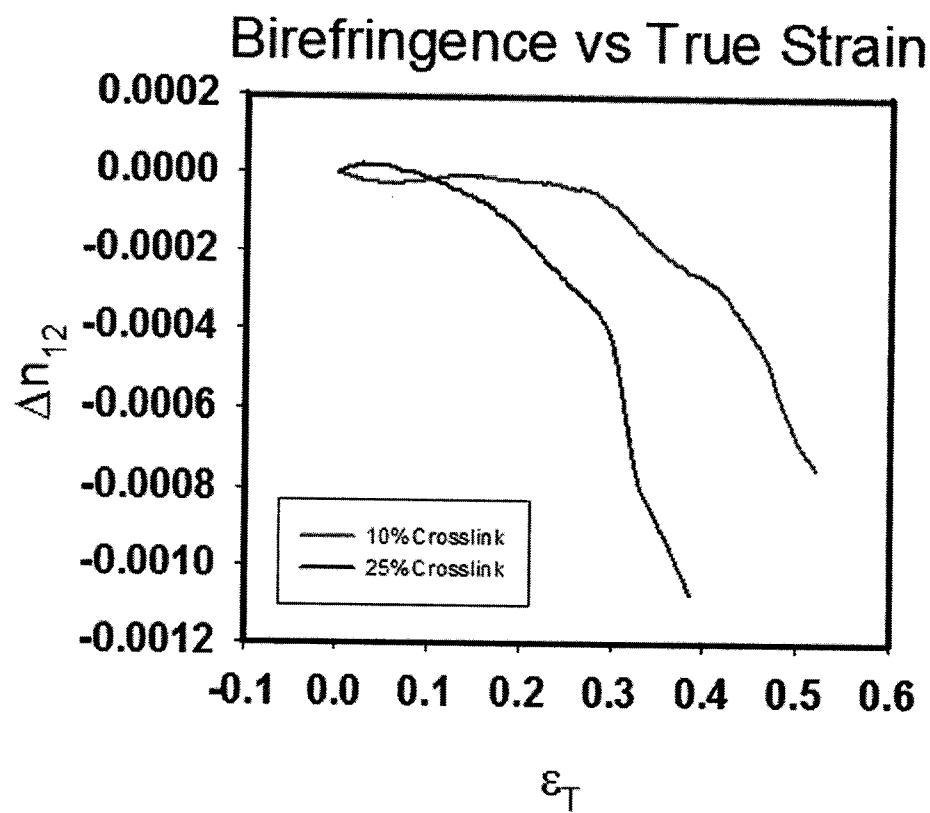


Fig. 10A

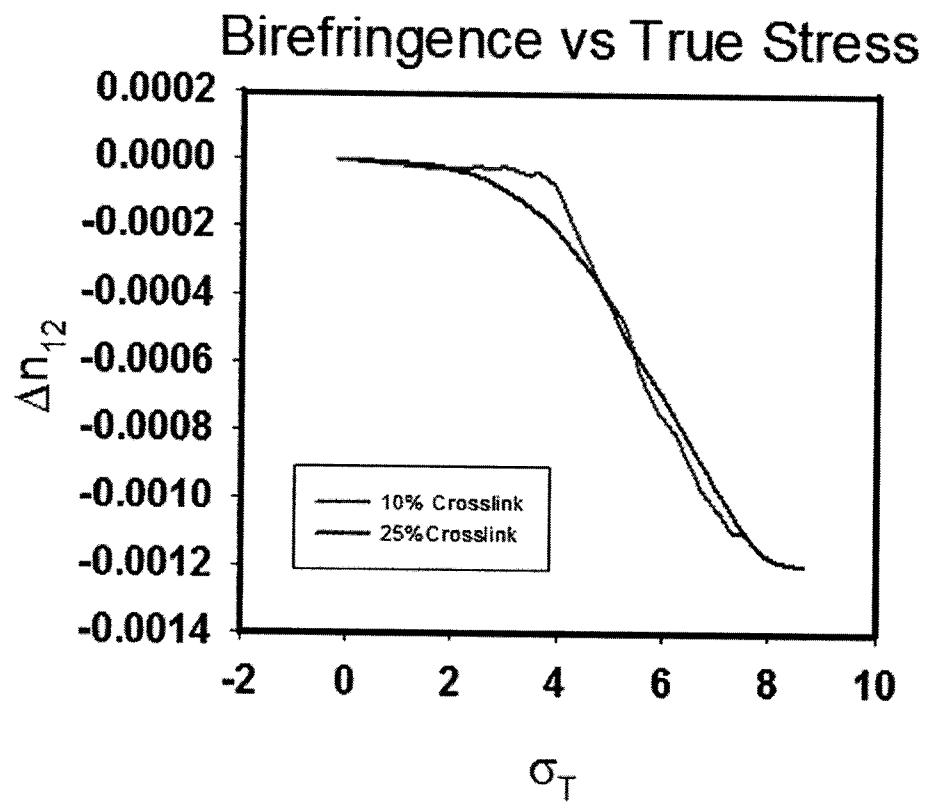


Fig. 10B

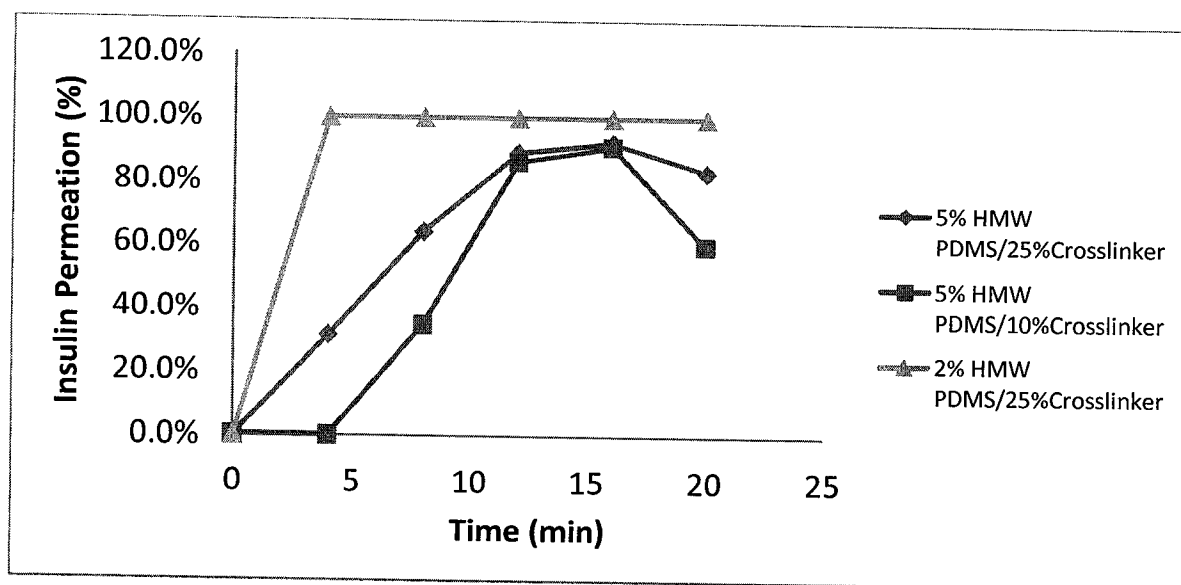


Fig. 11

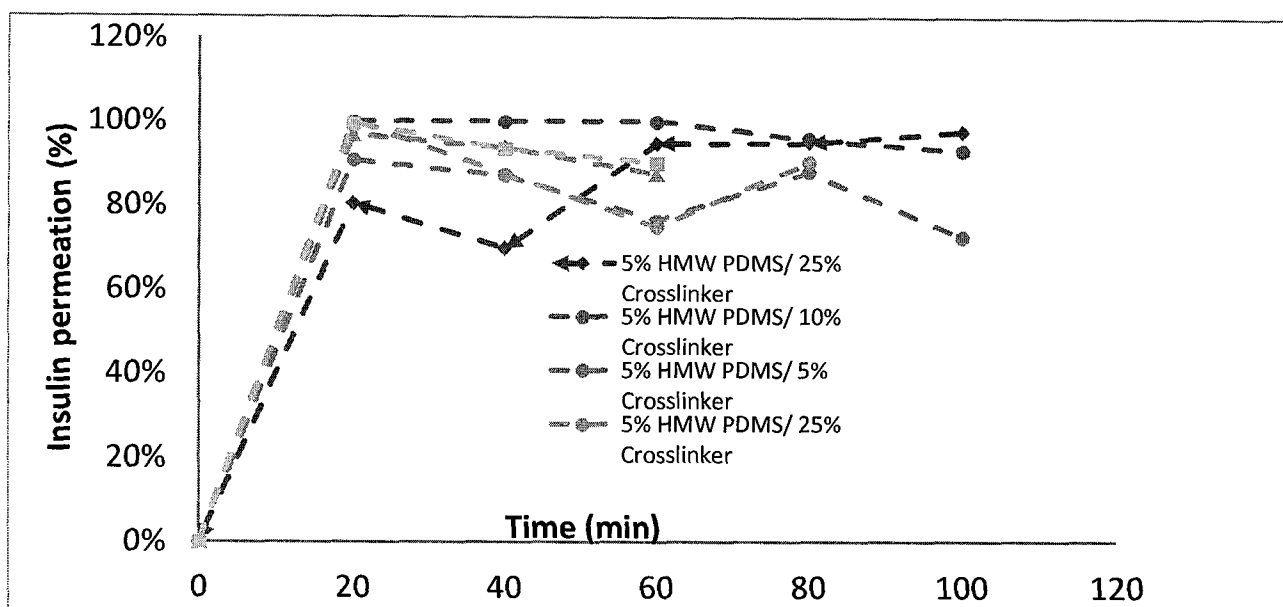


Fig. 12

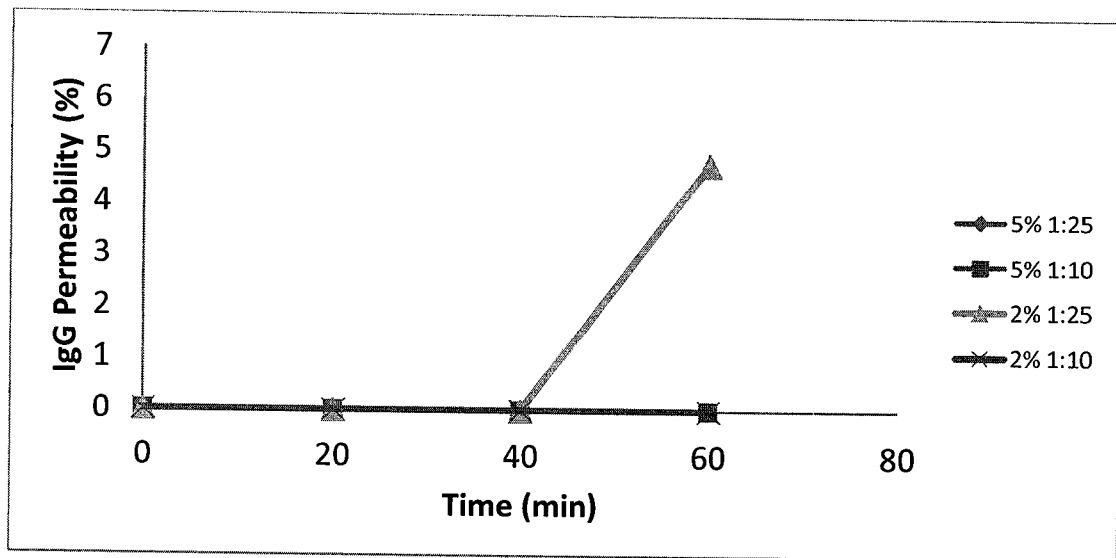


Fig. 13

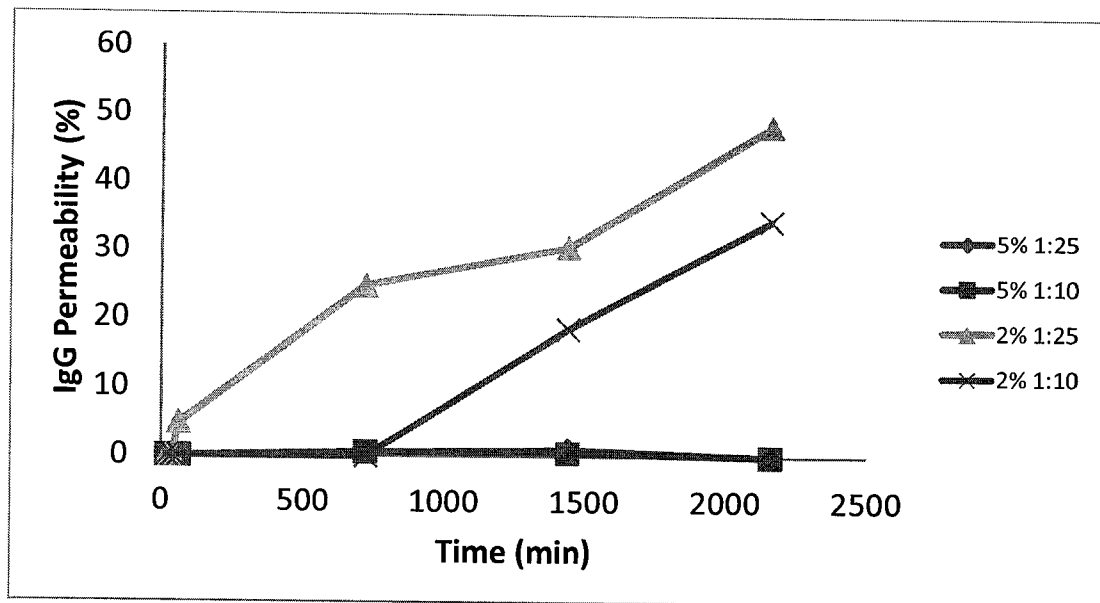


Fig. 14

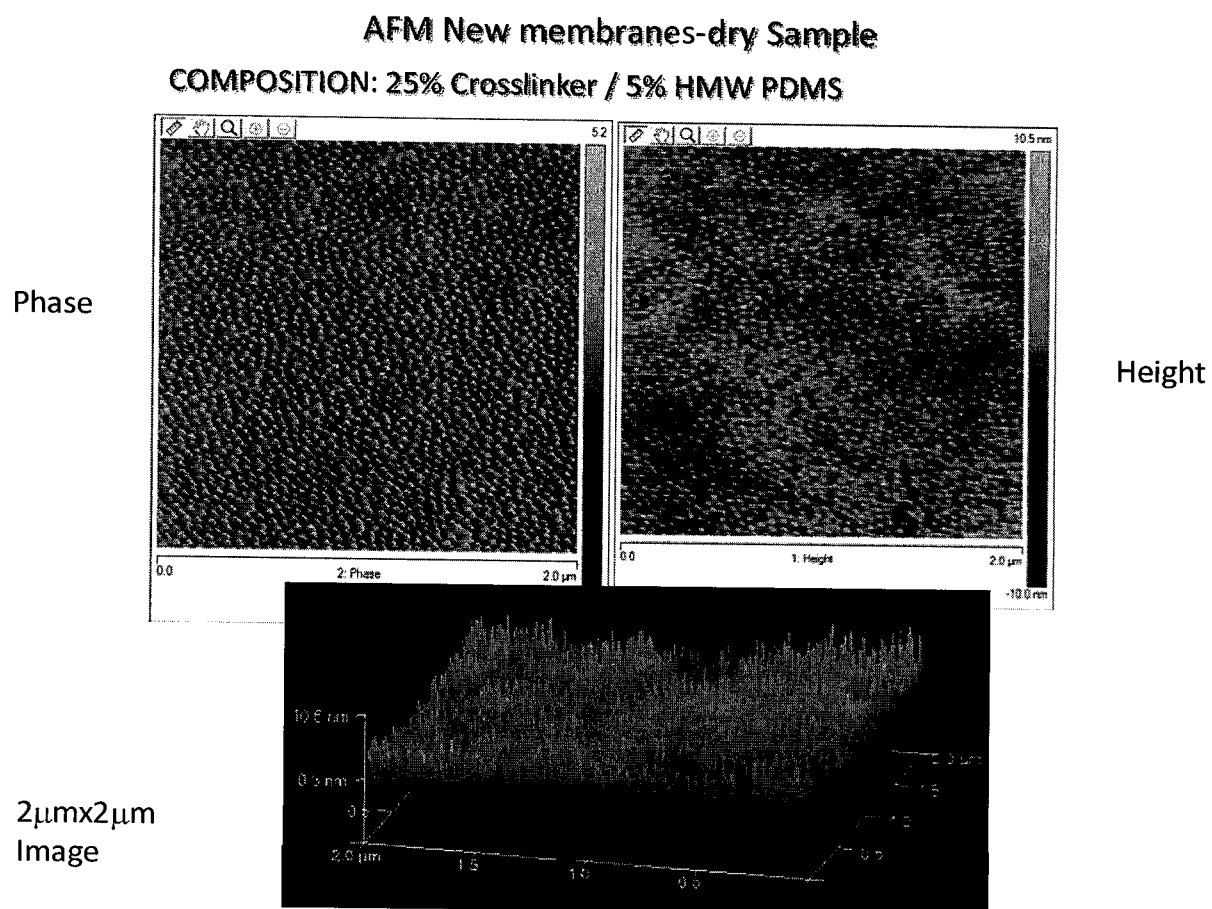


Fig. 15A

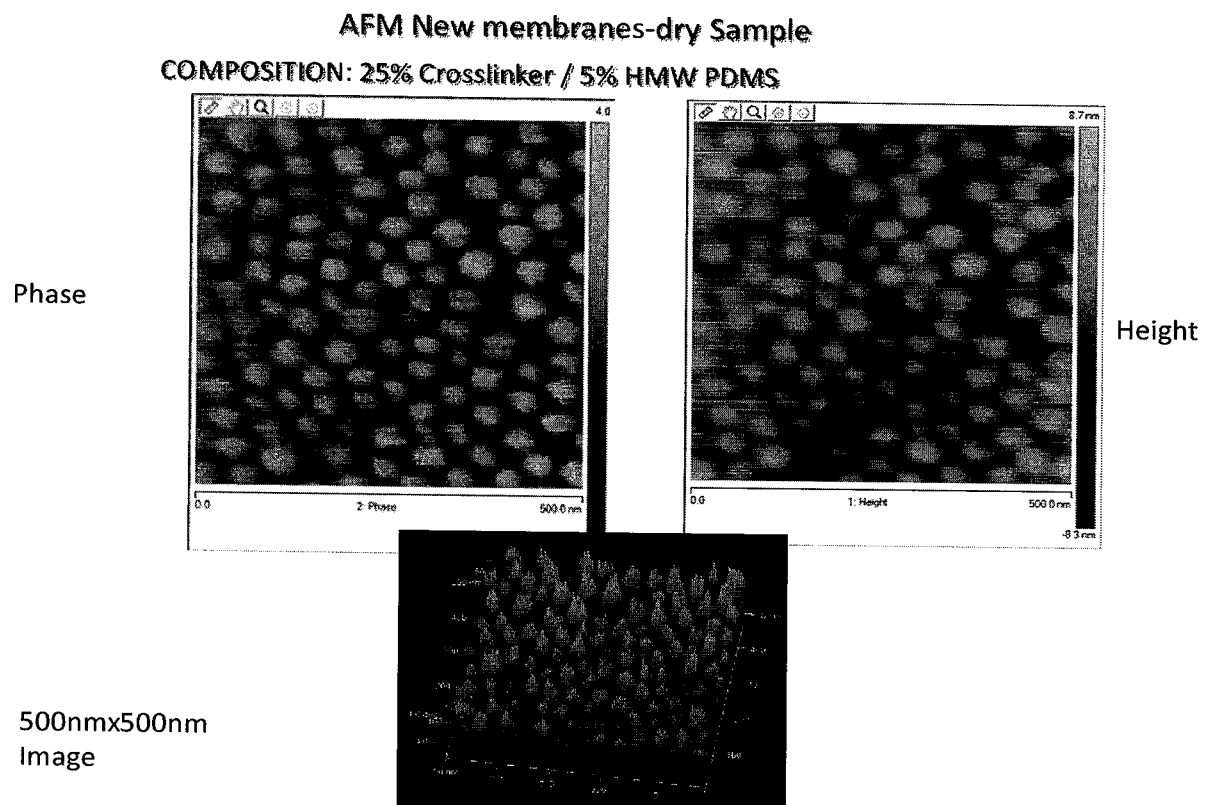
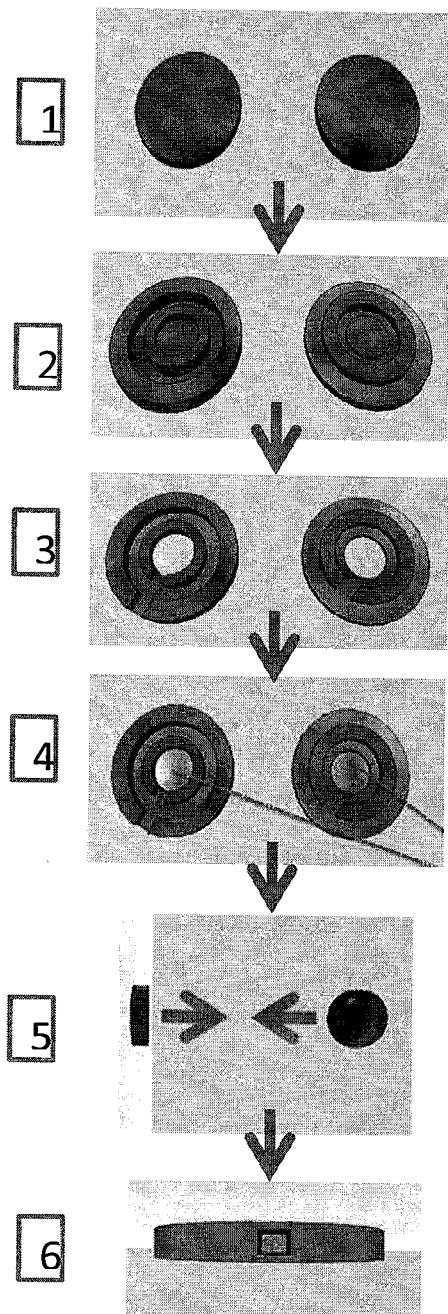


Fig. 15B



- Compression mold medical grade TPU pallets to get two circular, flat films
- Compression mold the circular parts in scaffold mold
- Precise holes added into parts using 23G needle holding parts attached together on a clamp
- BAP membrane material is drop cast on the

Fig. 16

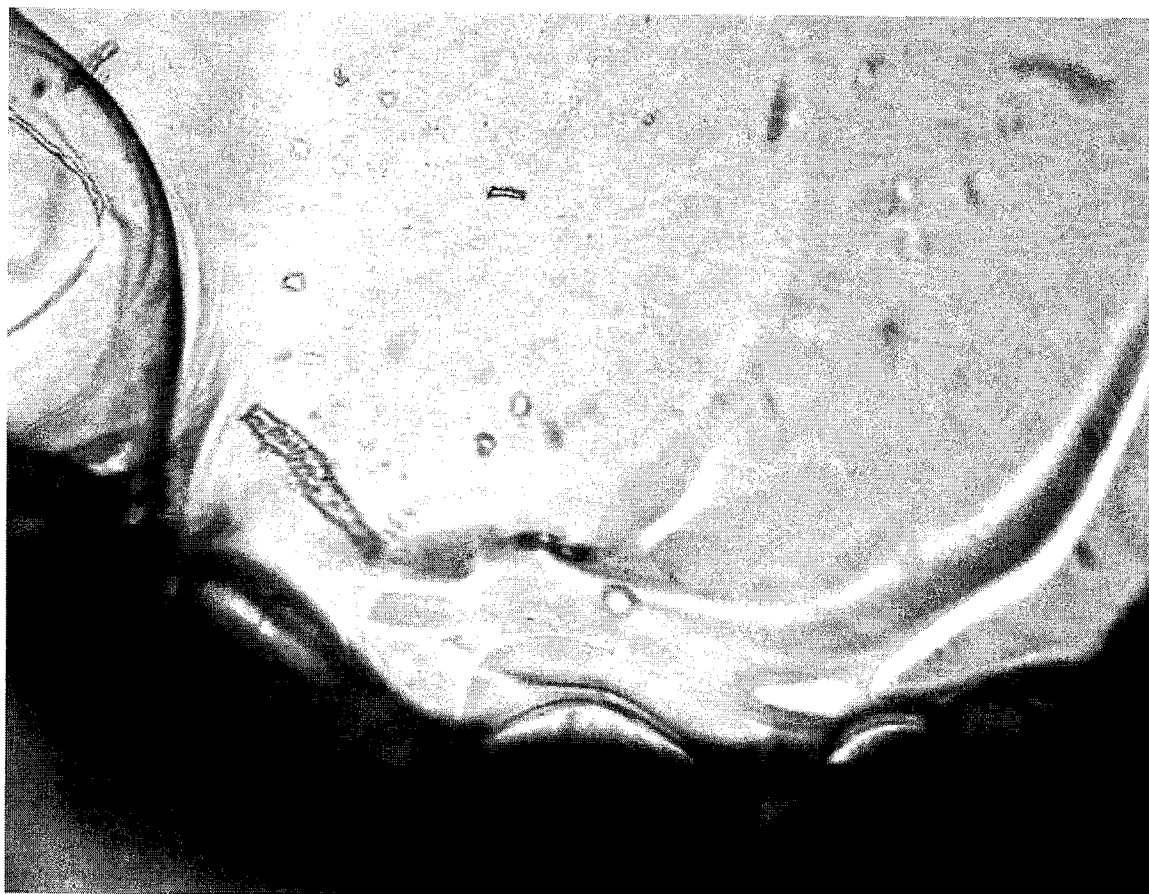


Fig. 17A

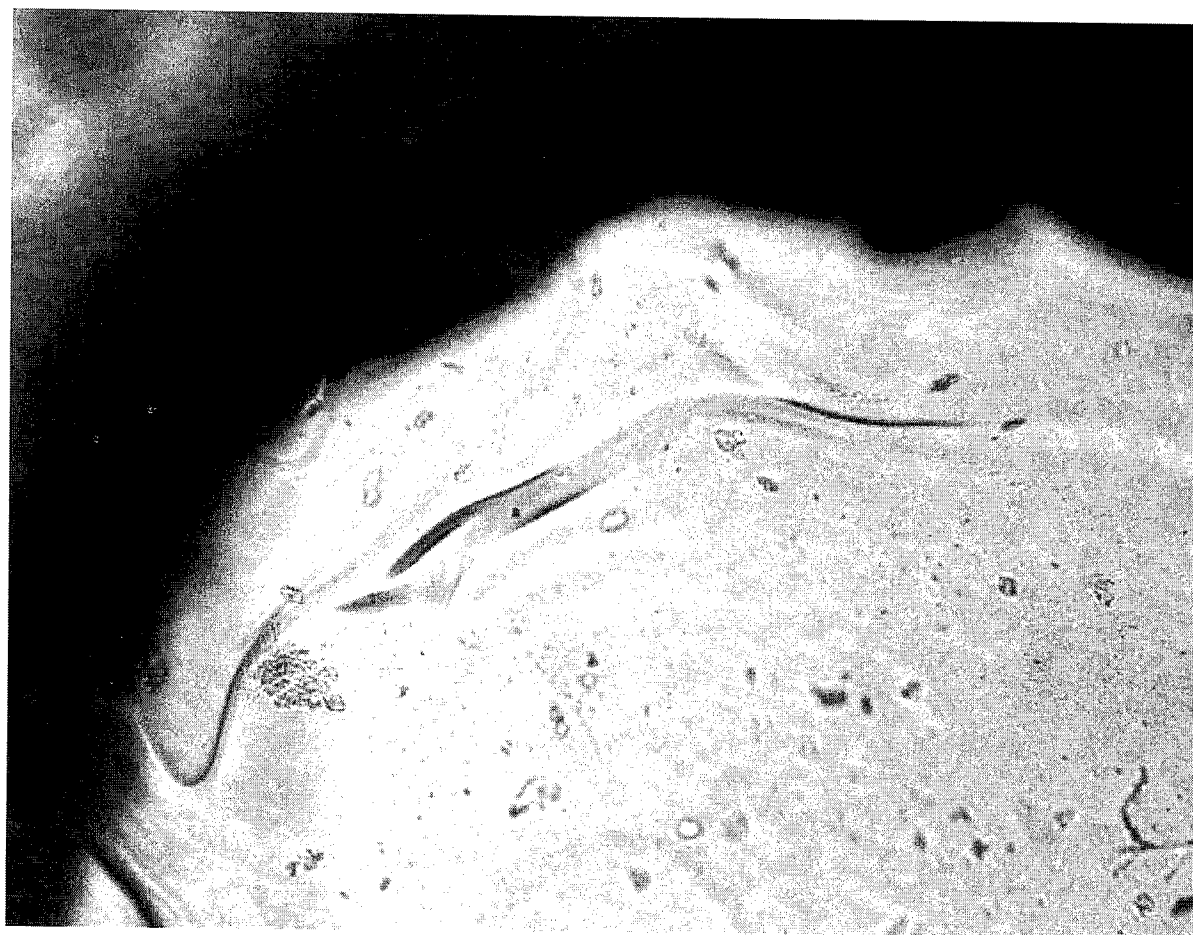


Fig. 17B

INTERNATIONAL SEARCH REPORT

International application No.

PCT/US 14/41100

A. CLASSIFICATION OF SUBJECT MATTER.

IPC(8) - C08G 77/12 (2014.01)

CPC - C08G 77/12; C08G 77/20

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC(8) - C08G 77/12 (2014.01)

CPC - C08G 77/12; C08G 77/20

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched
USPC - 528/31,528/32;435/395,370Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)
Minesoft Patbase, Google Scholar: dihydrocarbylacrylamide, asymmetric-telechelic, (bioartificial organs) and polydihydrocarbylsiloxane, INV = ((CAKMAK w2 Mukerrem) or (NUGAY w2 Turgut) or (NUGAY w2 Nihan) or (KENNEDY w2 Joseph)), TA = (siloxane and (Si-H) w2 bonds), (bioartificial w2 organ*) and concentric

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US 2010/0048818 A1 (Kennedy et al.) 25 February 2010 (25.02.2010) para [0002], [0013], [0024], [0026], [0027], [0035], [0074], [0079], Figure 1, Table 1,	1-18
Y	US 2003/0022991 A1 (Kennedy et al.) 30 January 2003 (30.01.2003) para [0060], [0067], Table 1	1-15
Y	US 3450736 A (Monterey) 17 June 1969 (17.06.1969) col 1, lines 65-70; col 2, lines 5-10	13, 14
Y	US 2010/0209468 A1 (Kennedy et al.) 19 August 2010 (19.08.2010) para [0011], [0046], [0057], [0085] [0102], [0108], [0112], Table 1, Fig 2	16-18
Y	US 2007/0238176 A1 (MacDonald et al) 11 October 2007 (11.10.2007) Figures 6F, 6J, 6K, 7, 10B, para [0126], [0127], [0129]	17, 18

☐ Further documents are listed in the continuation of Box C.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

03 September 2014 (03.09.2014)

Date of mailing of the international search report

09 SEP 2014

Name and mailing address of the ISA/US

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