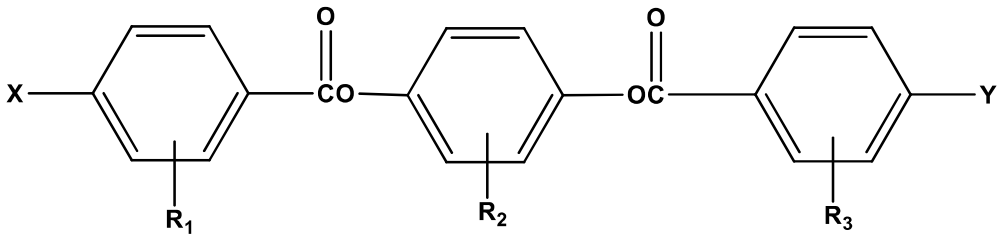
In one aspect, the present disclosure provides an additive manufactured 3D bioreactor from the polymerization of monomer, the bioreactor for growth of cells comprising a plurality of voids having a surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d** and wherein: (a) 90% or more of said voids have a selected void volume (**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%; wherein said bioreactor has a coating of a substituted or unsubstituted poly(p-xylylene), wherein said coating reduces or eliminates leaching of said monomer from said bioreactor that is toxic to living cells. In one ~~aspect~~example, the present disclosure provides a 3D bioreactor for growth of cells comprising a plurality of voids having a surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d** and wherein: (a) 90% or more of said voids have a selected void volume (**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%; and coating said bioreactor with substituted or unsubstituted poly(p-xylylene).

In yet another aspect, the present disclosure provides a method of forming a 3D bioreactor comprising: forming said 3D bioreactor by additive manufacturing by polymerization of monomer, wherein said 3D bioreactor includes a plurality of voids having a surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d** and wherein: (a) 90% or more of said voids have a selected void volume (**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0% and wherein said 3D bioreactor contains residual monomer; and coating said bioreactor with substituted or unsubstituted poly(p-xylylene)~~poly(p-xylene)~~, wherein said coating reduces or eliminates leaching of said monomer from said bioreactor that is toxic to living cells.

In ~~a further aspect~~another example, the present disclosure provides a 3D bioreactor for growth of cells comprising a plurality of voids having a surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d** and wherein: (a) 90% or more of said voids have a selected void volume

(**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%;

wherein said bioreactor comprises the polymerization product of the following monomer:



wherein X and Y comprise polymerizable groups that are polymerized by free-radical polymerization, R_2 is a bulky organic group having a bulk greater than R_1 and R_3, wherein R_2 is adapted to provide sufficient steric hindrance to achieve a nematic state at room temperature.

Brief Description Of The Drawings

FIG. 1 illustrates a section view of the 3D bioreactor fixed-bed.

FIG. 1a illustrates a unit negative model of the bioreactor that shows the overlapping of the neighborhood spheres.

FIG. 1b illustrates a unit negative model with each sphere surrounded by 12 identical neighborhood spheres.

Claims:

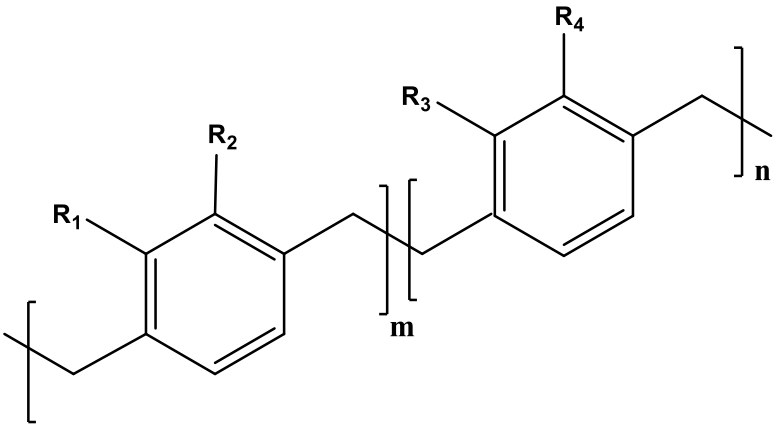
1. An additive manufactured 3D bioreactor from the polymerization of monomer, the bioreactor for growth of cells comprising

a plurality of voids having a surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d** and wherein: (a) 90% or more of said voids have a selected void volume (**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%;

wherein said bioreactor has a coating of a substituted or unsubstituted poly(p-xylylene), wherein said coating reduces or eliminates leaching of said monomer from said bioreactor that is toxic to living cells.

2. The 3D bioreactor of claim 1 wherein said bioreactor contains 0.01% by weight to 0.25% by weight of material having a MW of less than or equal to 500.

3. The 3D bioreactor of claim 1 wherein said poly(p-xylylene) has the following structure,



wherein R_1, R_2, R_3, and R_4 are selected from hydrogen, a halogen, amine ($-NH_2$), aliphatic aldehyde (-CHO), carboxylic acid functionality (-COOH), hydroxyl (-OH) or carboxylate functionality comprising $-C(O)CF_3$.

4. The 3D bioreactor of claim 1 wherein said coating has a thickness of 200 Angstroms to 100.0 µm.

5. The 3D bioreactor of claim 1 wherein said poly(p-xylylene) coating comprises a plurality of coating layers having different chemical composition.

6. The 3D bioreactor of claim 1 wherein polydopamine is applied to said poly(p-xylene coating) wherein said polydopamine is capable of binding additional layer or layers for cell culturing.

7. The 3D bioreactor of claim 3 wherein said substituted poly(p-xylylene)~~poly(p-xylene)~~ coating is bonded to a poly(ethylene oxide) which includes a terminally substituted antibody protein.

8. The 3D bioreactor of claim 3 wherein at least one of R_1, R_2, R_3, and R_4 are selected from an aldehyde (-CHO) and said 3D bioreactor is bonded to a poly(ethylene oxide) having a terminally substituted antibody protein, via a linkage having the following structure: -CH=N-.

9. The 3D bioreactor of claim 6 further including an extracellular matrix protein attached to said polydopamine coating.

10. The 3D bioreactor of claim 6 further including a tetrameric protein attached to said polydopamine coating.

11. The 3D bioreactor of claim 10 further including a biotinylated antibody immobilized on said tetrameric protein.

12. The 3D bioreactor of claim 10 wherein said tetrameric protein comprises avidin or streptavidin.

13. The 3D bioreactor of claim 11 wherein said biotinylated antibody comprises anti-CD-3 antibody.

14. The 3D bioreactor of claim 11 wherein said biotinylated antibody comprises anti-CD3 antibody and anti-CD28 antibody.

15. The 3D bioreactor of claim 11 wherein said biotinylated antibody comprises anti-CD3 antibody, anti-CD28 antibody and anti-CD2 antibody.

16. A method of forming a 3D bioreactor comprising:

forming said 3D bioreactor by additive manufacturing by polymerization of monomer, wherein said 3D bioreactor includes a plurality of voids having a surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d** and wherein: (a) 90% or more of said voids have a selected void volume (**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0% and wherein said 3D bioreactor contains residual monomer; and

coating said bioreactor with substituted or unsubstituted poly(p-xylylene)~~poly(p-xylene),~~ wherein said coating reduces or eliminates leaching of said monomer from said bioreactor that is toxic to living cells.

17. The method of claim 16 wherein said additive manufacturing comprises stereolithography (SLA) or digital light processing (DLP).

18. The method of claim 17 wherein said bioreactor, prior to coating with substituted or unsubstituted poly(p-xylylene)~~poly(p-xylene)~~, is exposed to UV light.

19. The method of claim 17 wherein said bioreactor, prior to coating with substituted or unsubstituted poly(p-xylylene)~~poly(p-xylene)~~, is exposed to vacuum.

20. The method of claim 17 wherein said bioreactor, prior to coating with substituted or unsubstituted poly(p-xylylene)~~poly(p-xylene)~~, is exposed to heating.

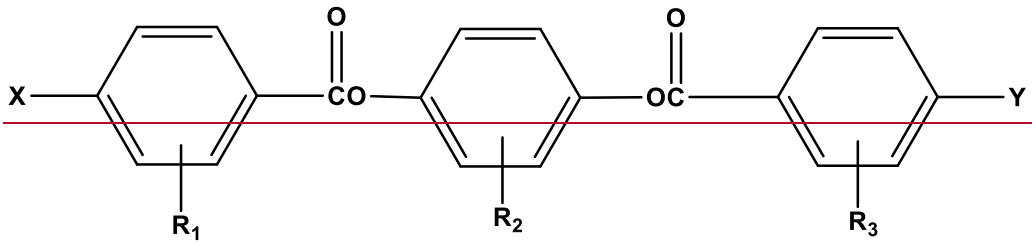
21. The method of claim 16 wherein said substituted or unsubstituted poly(p-xylylene)~~poly(p-xylene)~~ coating is exposed to UV light and ozone.

~~22. A 3D bioreactor for growth of cells comprising~~

~~a plurality of voids having a surface area for cell expansion, said plurality of voids having a diameter **D**, a plurality of pore openings between said voids having a diameter **d**, such that **D>d**~~

and wherein: (a) 90% or more of said voids have a selected void volume (**V**) that does not vary by more than +/- 10.0%; and (b) 90% or more of said pore openings between said voids have a value of **d** that does not vary by more than +/- 10.0%;

wherein said bioreactor comprises the polymerization product of the following monomer:



wherein X and Y comprise polymerizable groups that are polymerized by free-radical polymerization, R_2 is a bulky organic group having a bulk greater than R_1 and R_3, wherein R_2 is adapted to provide sufficient steric hindrance to achieve a nematic state at room temperature.