

Claims

1. A system for fabricating nanoparticles, the system comprising:
 - a mixing zone;
 - a first conduit configured to permit a flow of first solvent along a first flow
 - 5 direction to the mixing zone;
 - a second conduit configured to permit a flow of second solvent to the mixing zone, wherein:
 - the second conduit extends coaxially into the first conduit;
 - the second conduit comprises an opening substantially orthogonal to the
 - 10 first flow direction, and wherein said opening is configured to introduce a flow of said second solvent at the mixing zone in a second flow direction;
 - wherein the second flow direction is substantially orthogonal to the first flow direction ; and
 - 15 wherein one of the first solvent or second solvent contains nanoparticle precursors.
2. The system of any one of the preceding claims, wherein the second conduit is inserted into the first conduit and protrudes coaxially into the first conduit such
- 20 that the mixing zone occurs downstream of the first conduit.
3. The system of any one of the preceding claims, wherein the second conduit comprises a plurality of openings.
- 25 4. The system of any one of the preceding claims, wherein the second conduit comprises two openings, wherein the second opening is located on the opposite side of the first opening.
5. The system of any one of the preceding claims, wherein the average Reynolds
- 30 number at the mixing zone is about 400 to about 12,000.
6. The system of any one of the preceding claims, wherein the first conduit comprises a cylindrical tube, and wherein the first flow direction comprises an

axial direction of the tube and the second flow direction comprises a radial direction of the cylindrical tube.

5 7. The system of claim 6, wherein the second conduit comprises a needle having a side-opening, wherein said side-opening faces a radial direction of the cylindrical tube.

10 8. The system of any one of the preceding claims, wherein the first solvent is an antisolvent, and the second solvent is an organic solvent containing nanoparticle precursors.

15 9. The system of any one of the preceding claims, wherein at least one parameter is controlled to control a size of the nanoparticles in the nanoparticle dispersion and/or a rate of nanoparticle fabrication of the system, wherein the at least one parameter is selected from the group consisting of Reynolds number, flow rate, ratio of the antisolvent to solvent, precursor concentration, and precursor composition.

20 10. A method of fabricating nanoparticles, the method comprising:
(i) supplying a flow of first solvent in a first flow direction through a first conduit to a mixing zone;
(ii) supplying a flow of second solvent through a second conduit to a mixing zone, wherein the second conduit extends coaxially into the first conduit for introducing the flow of second solvent within the flow of the first solvent,
25 wherein at least one of the first solvent or second solvent contains nanoparticle precursors;
(iii) introducing the flow of second solvent within the flow of first solvent in a second flow direction, wherein the second flow direction is substantially orthogonal to the first flow direction; and
30 (iv) mixing the flow of first solvent and flow of second solvent to form a mixed stream comprising a nanoparticle dispersion based on the nanoparticle precursors.

11. The method of claim 10, wherein the first solvent is an antisolvent, and the second solvent is an organic solvent containing nanoparticle precursors.

12. The method of claim 10 or 11, wherein step (iv) comprises cross-current mixing.
13. The method of any one of claims 10 to 12, wherein step (iii) occurs downstream of the first conduit.
- 5 14. The method of any one of claims 10 to 13, wherein the mixed stream has a Reynolds number of about 400 to about 12,000.
- 10 15. The method of any one of claims 10 to 14, wherein the total flow rate of the mixed stream is between about 30 mL/min to about 700 mL/min.
16. The method of any one of claims 10 to 15, wherein the size of the fabricated nanoparticles are substantially uniform.
- 15 17. The method of claim 16, wherein the nanoparticles have a polydispersity index (PDI) of about ≤ 0.15 .
18. The method of any one of claims 10 to 17, wherein the nanoparticle precursors are selected from the group consisting of organic molecules, drug molecules, 20 metal oxides, dyes, polymers, conjugated polymers, proteins, biological molecules, fluorescent molecules, metal oxides, and lipid vesicles.
19. The method of any one of claims 10 to 18, wherein the nanoparticle precursors are selected from the group consisting of 4,7-bis[4-(1,2,2- 25 triphenylvinyl)phenyl]benzo-2,1,3- thiadiazole (BTPEBT), 1,2-Distearoyl-*sn*-glycero-3-phosphoethanolamine-polyethylene glycol (DSPE-PEG), 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[amino(polyethylene glycol)] (DSPE-PEG-NH₂), 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-polyethylene glycol-carboxylic acid (DSPE-PEG-COOH), 1,2-distearoyl-*sn*- 30 glycero-3-phosphoethanolamine-N-[maleimide(polyethylene glycol)] (DSPE-PEG-MAL), poly(lactide-co-glycolic acid) (PLGA), polystyrene (PS), tamoxifen (TAM), doxorubicin (DOX), camptothecin (CPT), conjugated polymer (CP), iron oxide (IO), poly(diketopyrrolopyrrole-terthiophene) (PDPP3T) and 4,6-diphenyl-2-carbazolyl-1,3,5-triazine (DPhCzT).

20. The method of any one of claims 10 to 19, wherein the nanoparticles are core-shell nanoparticles,

5 wherein the core is selected from the group consisting of 4,7-bis[4-(1,2,2-triphenylvinyl)phenyl]benzo-2,1,3- thiadiazole (BTPEBT); tamoxifen (TAM); doxorubicin (DOX), camptothecin (CPT); conjugated polymer (CP); iron oxide (IO) and poly(diketopyrrolopyrrole-terthiophene) (PDPP3T); and 4,6-diphenyl-2-carbazolyl-1,3,5-triazine (DPhCzT), and

10 the shell is selected from the group consisting of 1,2-Distearoyl-*sn*-glycero-3-phosphoethanolamine-polyethylene glycol (DSPE-PEG); 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[amino(polyethylene glycol)] (DSPE-PEG-NH₂); 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-polyethylene glycol-carboxylic acid (DSPE-PEG-COOH); 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[maleimide(polyethylene glycol)] (DSPE-PEG-MAL); poly(lactide-co-glycolic acid) (PLGA); and polystyrene (PS).

21. The method of any one of claims 10 to 20, wherein the nanoparticles are selected from the group consisting of:

- 20 (i) 4,7-bis[4-(1,2,2-triphenylvinyl)phenyl]benzo-2,1,3- thiadiazole (BTPEBT) encapsulated by 1,2-Distearoyl-*sn*-glycero-3-phosphoethanolamine-polyethylene glycol (DSPE-PEG);
- (ii) BTPEBT encapsulated by 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[amino(polyethylene glycol)] (DSPE-PEG-NH₂);
- 25 (iii) BTPEBT encapsulated by 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-polyethylene glycol-carboxylic acid (DSPE-PEG-COOH);
- (iv) BTPEBT encapsulated by 1,2-distearoyl-*sn*-glycero-3-phosphoethanolamine-N-[maleimide(polyethylene glycol)] (DSPE-PEG-MAL);
- 30 (v) BTPEBT encapsulated by poly(lactide-co-glycolic acid) (PLGA);
- (vi) BTPEBT encapsulated by polystyrene (PS);
- (vii) tamoxifen (TAM) encapsulated by DSPE-PEG;
- (viii) TAM encapsulated by PLGA;
- (ix) TAM encapsulated by PS;

- (x) doxorubicin (DOX) encapsulated by DSPE-PEG
(xi) DOX encapsulated by PLGA;
(xii) DOX encapsulated by PS;
(xiii) camptothecin (CPT) encapsulated by DSPE-PEG;
5 (xiv) CPT encapsulated by PLGA;
(xv) poly(diketopyrrolopyrrole-terthiophene (PDPP3T) encapsulated by DSPE-PEG;
(xvi) CP encapsulated by PLGA;
(xvii) iron oxide (IO) and PDPP3T encapsulated by DSPE-PEG;
10 (xviii) IO and PDPP3T encapsulated by PLGA; and
(xix) DPhCzT encapsulated by DSPE-PEG.
22. The method of any one of the claims 10 to 21, wherein at least one parameter is controlled to control a size of the nanoparticles in the nanoparticle dispersion
15 and/or a rate of nanoparticle fabrication of the system, wherein the at least one parameter is selected from the group consisting of Reynolds number, flow rate, ratio of the antisolvent to solvent, precursor concentration, and precursor composition.
- 20 23. The method of claim 22, wherein the ratio of antisolvent to solvent solvent is in the range of about 5:1 to 15:1, wherein said solvent contains nanoparticle precursors.
24. The method of any one of claims 10 to 23, wherein the nanoparticles are core-shell nanoparticles, and wherein the ratio of shell nanoparticle precursor to core
25 nanoparticle precursor is in the range of about 1:1 to 4:1.
25. Use of the system of any one of claims 1 to 9 in the method of any one of claims
30 10 to 24.
26. Nanoparticles produced by the method of any one of claims 10 to 24.