

CLAIMS

1. A core-shell micro-particle comprising a biodegradable polymer with at least two
5 or more surface cavities.
2. The core-shell micro-particle according to claim 1, wherein the biodegradable polymer is an aliphatic polyester (including but not limited to poly(lactic-co-glycolic acid) (PLGA), polylactic acid (PLA), polyglycolic acid (PGA),
10 polycaprolactone (PCL), poly(butylene succinate) and its copolymers, poly(p-dioxanone) (PPDO), poly(hydroxybutyrate) (PHB), and polycarbonates), aromatic copolyester (including but not limited to poly(butylene adipate-co-terephthalate) (PBAT)), polyamide and poly(ester-amide), polyurethanes, polyanhydrides, polysaccharides, (including but not limited to chitosan, cellulose,
15 and hyaluronic acid), and blends or copolymers of the aforementioned examples.
3. The core-shell micro-particle according to claim 1 or 2, wherein the surface cavities are indentations on the shell, and/or form hierarchical porous shell with the hollow core.
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4. The core-shell micro-particle according to any one of claims 1 to 3, wherein the shell may comprise of hydrophobic chemicals such as drugs like sirolimus, steroids, dexamethasone, etc.
- 25 5. The core-shell micro-particle according to any one of claims 1 to 4, wherein the core comprises a hydrophilic drugs like peptides, proteins, and vaccines provided that the surface cavities do not form tunnels to the core.
6. The core-shell microparticle according to any one of claims 1 to 5, wherein the
30 microparticle has an average diameter of 5 to 10 μm .

7. The core-shell microparticle according to claim 6, wherein the microparticle has an average diameter of 5 to 6 μm .
8. An ultrasound contrast agent comprising a microparticle according to any one of claims 1 to 7.
9. Use of the core-shell micro-particle according to any one of the claims 1 to 7, or the ultrasound contrast agent of claim 8, in drug delivery, contrast enhancement, subharmonic imaging enhancement, theranostics, and/or any combination of the aforementioned applications.
10. The use according to claims 9, wherein the core-shell micro-particle is
- (a) introduced into a blood vessel (e.g., through intravenous injection, local deliver, intramuscular injection, catheter injection, etc.) or topically (e.g., through a cream, gel, etc.); and
- (b) subjected to a pressure wave (e.g., ultrasound, focused ultrasound, shockwaves, etc.) such that the core-shell micro-particle is embedded into biological tissue (e.g., the wall of the blood vessel, skin, tumor, etc.).
11. The use of claim 9 or claim 10, wherein the core-shell microparticle or the ultrasound contrast agent is used as an ultrasound contrast agent.
12. The use of claim 9 or claim 10, wherein the core-shell microparticle or the ultrasound contrast agent is used as a subharmonic imaging contrast agent.
13. A method of drug delivery comprising
- (c) administering an effective amount of the core-shell micro-particle according to any one of the claims 1 to 7, which core shell microparticle contains one or more drugs; and

(d) subjecting the core-shell microparticle or ultrasound contrast agent to a pressure wave at the site for drug delivery, such that the core-shell microparticle or ultrasound contrast agent is embedded into biological tissue at the site.

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14. A method according to claim 13, wherein the administration is to a blood vessel or to the skin.

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15. A method according to claim 13 or 14, wherein the method further comprises subjecting the site to ultrasound imaging.

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16. A method of ultrasound contrast enhancement comprising
(a) delivering the core-shell micro-particle according to any one of claims 1 to 7, or the ultrasound contrast agent of claim 8, to a site which is to be imaged; and
(b) subjecting the site to ultrasound imaging.

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17. The method of claim 16, wherein the delivery step comprises introducing the core-shell microparticle or ultrasound contrast agent into a blood vessel or onto the skin, and subjecting the core-shell microparticle or ultrasound contrast agent to a pressure wave such that the core-shell microparticle or ultrasound contrast agent is embedded into biological tissue.

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18. The method of any one of claims 15 to 17, wherein the imaging technique is subharmonic imaging.

19. The method of any one of claims 15 to 18, wherein the subharmonic imaging is carried out with an MI of 1.4 or less.

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20. The method of any one of claims 15 to 19 wherein the subharmonic imaging is carried out with an MI of 0.8 or less.

21. The method of any one of claims 16 to 20, wherein the core-shell microparticle or ultrasound contrast agent comprises one or more drugs, and wherein the one or

more drugs are delivered to the biological tissue in which the core-shell microparticle or ultrasound contrast agent is embedded.

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