## CLAIMS

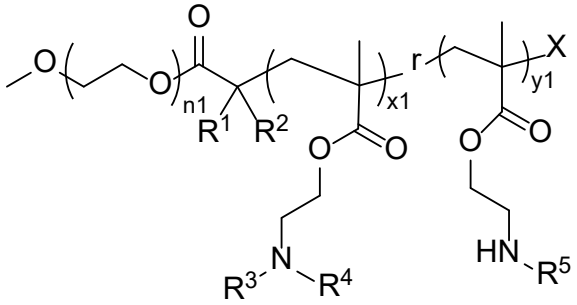
**WHAT IS CLAIMED IS:**

1. A method of making an encapsulated biomolecule comprising:

providing an encapsulation composition comprising an organic solvent, a plurality of protonated block copolymer units, and a biomolecule,

encapsulating the biomolecule within a micelle formed from the plurality of protonated block copolymer units,

wherein the block copolymer comprises poly(ethylene oxide) (PEO), and a hydrophobic polymer segment with the following structure:




wherein:

$n_1$ is an integer from about 40 to about 500;

$x_1$ is an integer from about 4 to about 250;

$y_1$ is an integer from 0 to about 10;

X is a halogen, -OH, or -C(O)OH;

$R^1$ and $R^2$ are each independently hydrogen or optionally substituted $C_1$-$C_6$ alkyl;

$R^3$ and $R^4$ are each independently an optionally substituted $C_1$-$C_6$ alkyl, $C_3$-$C_{10}$ cycloalkyl or aryl;

or $R^3$ and $R^4$ are taken together with the corresponding nitrogen to which they are attached form an optionally substituted 5 to 7-membered ring; and

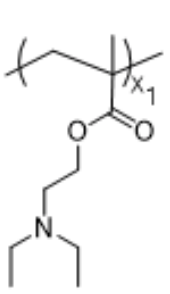
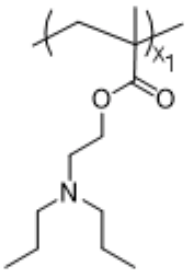
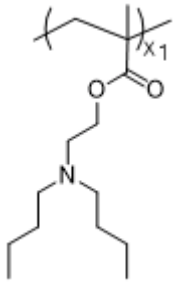
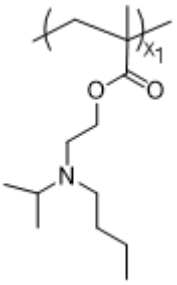
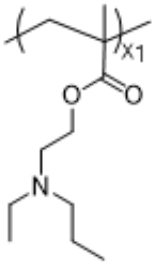
$R^5$ is hydrogen or -C(O)$CH_3$.

2. The method of claim 1, wherein the encapsulation composition is prepared by dissolving the block copolymer in an organic solvent and adding at least a molar equivalent of acid relative to the block copolymer.

3. The method of any of claims 1–2, wherein the step of encapsulating the biomolecule within the micelle comprises removing the organic solvent and acid, and adding the therapeutic agent to the polymer.

4. The method of any of claims 1–3, wherein the step of encapsulating the biomolecule within the micelle comprises dialyzing a mixture of therapeutic agent and block copolymer against a neutral buffer.

5. The method of any of claims 1–4, wherein the hydrophobic polymer segment is selected from:


, 
, 
, 
, and 
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6. The method of any claims 1-5, wherein $n_1$ is an integer from 100–250, $x_1$ is an integer from 40–200, and/or $y_1$ is 0, preferably wherein $n_1$ is an integer from 100–250, $x_1$ is an integer from 100–200, and/or $y_1$ is 0, more preferably wherein $n_1$ is an integer of about 114, $x_1$ is about 170, and/or $y_1$ is 0, and most preferably wherein $n_1$ is 114, $x_1$ is 170, and $y_1$ is 0.

7. The method of any one of claims 1-6, wherein the step of encapsulating the biomolecule is further comprising of neutralization with a neutral buffer through dialysis or mixing, wherein the neutral buffer has a pH of 7.4, and wherein the neutral buffer is sodium phosphate.

8. The method of any one of claims 1-7, the acidified plurality of block copolymer units are positively charged block copolymer units.

9. The method of any one of claims 1-8, wherein the step of encapsulating the biomolecule is further comprising of non-covalent bonding between the biomolecule and the positively charged block copolymer.

10. The method of any one of claims 1-9, wherein acidified plurality of block copolymer units are acidified by acetic acid.

11. The method of any one of claims 1-10, wherein the biomolecule is a bispecific antibody selected from the group consisting of solitomab, runimotamab, blinatumomab, odronextamab, and glofitamab, or a cytokine selected from the group consisting of interleukin-12 (IL-12), a single chain interleukin-12 (IL-12), a monovalent interleukin-12 (IL-12) fused with Fc from IgG a bivalent interleukin-12 (IL-12) fused with Fc from IgG, an interleukin-2 (IL-2)an interleukin-2 (IL-2) fused with Fc from IgG, and an interleukin-18 (IL-18).

12. The method of any one of claims 1-11, wherein the micelle comprises of about 0.1%wt. to about 20%wt. biomolecule.

13. The method of any one of claims 1-12, wherein the micelle has a diameter of about 25 to about 50 nm.

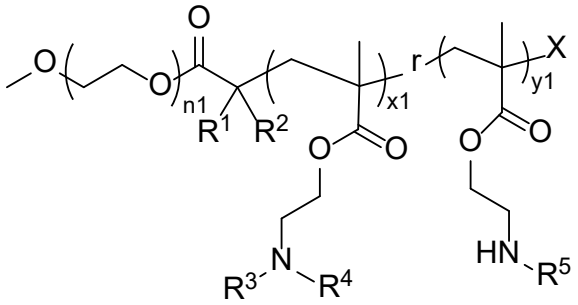
14. The method of any one of claims 1-13, wherein the micelle has a pH transition point that is between 4-8, 6-7.5, or 4.5-6.5.

15. The method of any one of claims 1-14, wherein the composition has a pH response of less than 0.25 or 0.15 pH units.

16. An intermediate composition for making an encapsulated biomolecule comprising:

a biomolecule; and

a plurality of protonated block copolymer units, the block copolymer comprising poly(ethylene oxide) (PEO), and a hydrophobic polymer segment with the following structure:



wherein:

$n_1$ is an integer from about 40 to about 500;

$x_1$ is an integer from about 4 to about 250;

$y_1$ is an integer from 0 to about 10;

X is a halogen, -OH, or -C(O)OH;

$R^1$ and $R^2$ are each independently hydrogen or optionally substituted $C_1$-$C_6$ alkyl;

$R^3$ and $R^4$ are each independently an optionally substituted $C_1$-$C_6$ alkyl, $C_3$-$C_{10}$ cycloalkyl or aryl;

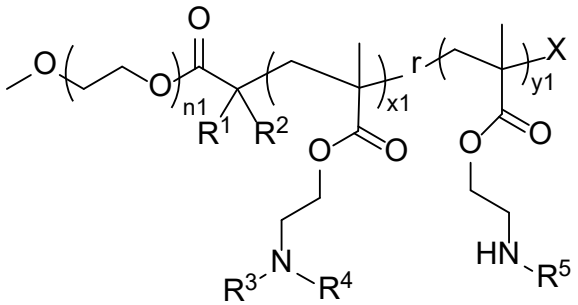
or $R^3$ and $R^4$ are taken together with the corresponding nitrogen to which they are attached form an optionally substituted 5 to 7-membered ring; and

$R^5$ is hydrogen or -C(O)$CH_3$.

17. A micelle encapsulated biomolecule comprising:

a biomolecule; and

a plurality of protonated block copolymer units, the block copolymer comprising poly(ethylene oxide) (PEO), and a hydrophobic polymer segment with the following structure:



wherein:

$n_1$ is an integer from about 40 to about 500;

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X is a halogen, -OH, or -C(O)OH;

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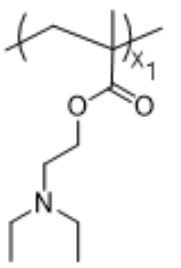
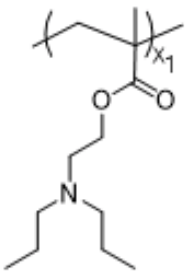
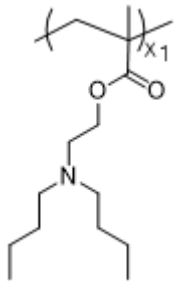
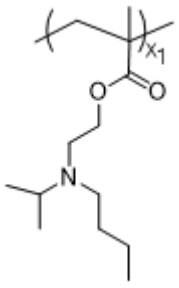
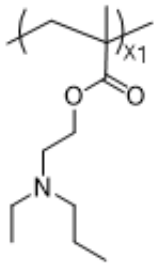
or $R^3$ and $R^4$ are taken together with the corresponding nitrogen to which they are attached form an optionally substituted 5 to 7-membered ring; and

$R^5$ is hydrogen or -C(O)$CH_3$.

18. The micelle encapsulated biomolecule of claim 17, wherein the biomolecule is a protein having a molecular weight of at least 6kDa.

19. The micelle encapsulated biomolecule of any one of claims 17–18, wherein the biomolecule is a cytokine or bispecific antibody.

20. The micelle encapsulated biomolecule of any one of claims 17–19, wherein the hydrophobic polymer segment is selected from:


, 
, 
, 
, and 
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