CLAIMS

1. A hollow bead encapsulating a single cell comprising:

a polymer shell; and

a single cell disposed within the polymer shell,

wherein the polymer shell comprises pores that allow diffusion of a reagent through the polymer shell while retaining the single cell.

2. The hollow bead of Claim 1, wherein an interior of the polymer shell comprises an aqueous environment.

3. The hollow bead of Claim 1, wherein the single cell disposed within the polymer shell is free from interaction with the polymer shell and/or is not in contact with the polymer shell.

4. The hollow bead of Claim 1, wherein the hollow bead has a diameter of 20 µm to 200 µm.

5. The hollow bead of Claim 1, wherein the polymer shell comprises a four-arm polyethylene glycol (PEG).

6. The hollow bead of Claim 1, wherein the polymer comprises, PEG, PEG-acrylate, PEG-amine, PEG-carboxylate, PEG-dithiol, PEG-epoxide, PEG-isocyanate, PEG-maleimide, polyacrylic acid (PAA), poly(methyl methacrylate) (PMMA), alginate, polystyrene (PS), polystyrene sulfonate (PSS), polyvinylpyrrolidone (PVPON), acrylamide, N,N'-bis(acryloyl)cystamine, polypropylene oxide (PPO), poly(hydroxyethyl methacrylate) (PHEMA), poly(N-isopropylacrylamide) (PNIPAAm), poly(lactic acid) (PLA), poly(lactic-co-glycolic acid) (PLGA), polycaprolactone (PCL), poly(vinylsulfonic acid) (PVSA), poly(L-aspartic acid), poly(L-glutamic acid), polylysine, agar, agarose, heparin, alginate sulfate, dextran sulfate, hyaluronan, pectin, carrageenan, gelatin, chitosan, cellulose, collagen, bisacrylamide, diacrylate, diallylamine, triallylamine, divinyl sulfone, diethyleneglycol diallyl ether, ethyleneglycol diacrylate, polymethyleneglycol diacrylate, polyethyleneglycol diacrylate, trimethylopropoane trimethacrylate, ethoxylated trimethylol triacrylate, or ethoxylated pentaerythritol tetracrylate, or combinations or mixtures thereof.

7. The hollow bead of Claim 1, wherein the polymer shell comprises a polymer formed by crosslinking PEG-maleimide and a dithiol; or PEG-epoxide and an amine; or PEG-epoxide and PEG-amine; or PEG-dithiol and PEG-acrylate.

8. The hollow bead of Claim 1, wherein the single cell is a mammalian cell.

9. The hollow bead of Claim 1, wherein the reagent comprises enzymes, chemicals, and primers having a size of less than 50 base pairs.

10. The hollow bead of Claim 1, wherein the reagent comprises lysozyme, proteinase K, random hexamers, polymerase, Φ29 DNA polymerase, Taq polymerase, Bsu polymerase, transposase, Tn5 transposase, primers, P5 adaptor sequence primers, P7 adaptor sequence primers, ligase, catalyzing enzyme, deoxynucleotide triphosphates, buffers, or divalent cations.

11. A method of encapsulating a single cell within a hollow bead, comprising:

mixing a single cell with a polymer in a spacer oil to form a mixture (a);

mixing mixture (a) with a crosslinking oil to form a polymer shell encapsulating the single cell, wherein the polymer shell comprises pores that allow diffusion of a reagent through the polymer shell while retaining the single cell.

12. The method of Claim 11, wherein the hollow bead has a diameter of 20 μm to 200 μm.

13. The method of Claim 11, wherein the polymer comprises a four-arm polyethylene glycol (PEG).

14. The method of Claim 13, wherein the four-arm polyethylene glycol (PEG) is selected from the group consisting of PEG-acrylate, PEG-amine, PEG-carboxylate, PEG-dithiol, PEG-epoxide, PEG-isocyanate, and PEG-maleimide.

15. The method of Claim 11, wherein the spacer oil comprises mineral oil or fluorocarbon oil.

16. The method of Claim 11, wherein the crosslinking oil comprises dithiol or amine dissolved in oil.

17. The method of Claim 11, wherein the single cell is a mammalian cell.

18. The method of Claim 11, wherein the reagent comprises enzymes, chemicals, and primers having a size of less than 50 base pairs.

19. The method of Claim 11, wherein the reagent comprises lysozyme, proteinase K, random hexamers, polymerase, Φ29 DNA polymerase, Taq polymerase, Bsu polymerase, transposase, Tn5 transposase, primers, P5 adaptor sequence primers, P7 adaptor sequence primers, ligase, catalyzing enzyme, deoxynucleotide triphosphates, buffers, detergents, or divalent cations.

20. The method of Claim 11, wherein the mixing comprises inputting the single cell, the polymer, the spacer oil, and the crosslinking oil into a droplet generator.

21. The method of Claim 20, wherein the droplet generator is a microfluidic chip.

22. The method of Claim 11, wherein the single cell is fixed prior to mixing by contact with a fixative.

23. The method of Claim 22, wherein the fixative comprises an alcohol, such as methanol or ethanol, or an aldehyde, such as para-formaldehyde.

24. A method of performing multiple sequential co-assays on a single cell encapsulated within a hollow bead, comprising:

obtaining a hollow bead encapsulating a single cell of any one of Claims 1-10; and

sequentially contacting the single cell with reagents to perform multiple sequential co-assays.

25. The method of Claim 24, wherein the multiple sequential co-assays comprise lysis, DNA analysis, RNA analysis, protein analysis, tagmentation, nucleic acid amplification, nucleic acid sequencing, DNA library preparation, assay for transposase accessible chromatic using sequencing (ATAC-seq), contiguity-preserving transposition (CPT-seq), single cell combinatorial indexed sequencing (SCI-seq), or single cell genome amplification, or any combination thereof performed sequentially.

26. The method of Claim 24, wherein the hollow bead encapsulating a single cell is seeded on a solid support.

27. The method of Claim 26, wherein the solid support is an etched surface, a well, a flow-cell device, a microfluidic channel, a bead, or a column.