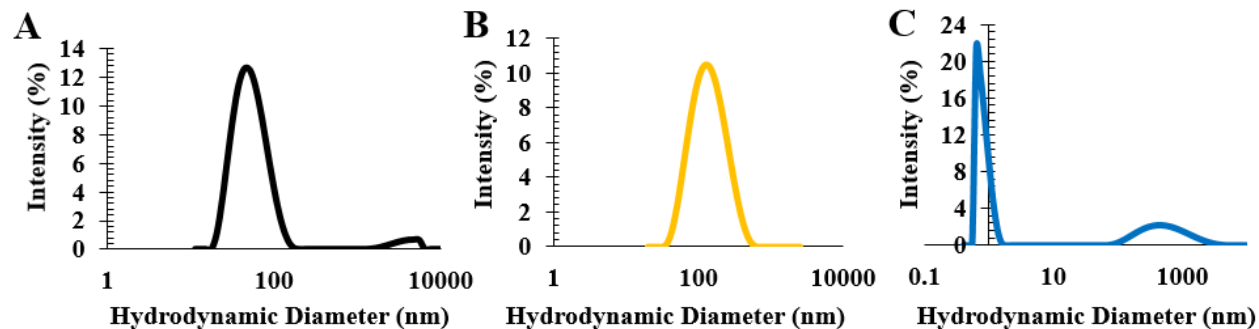
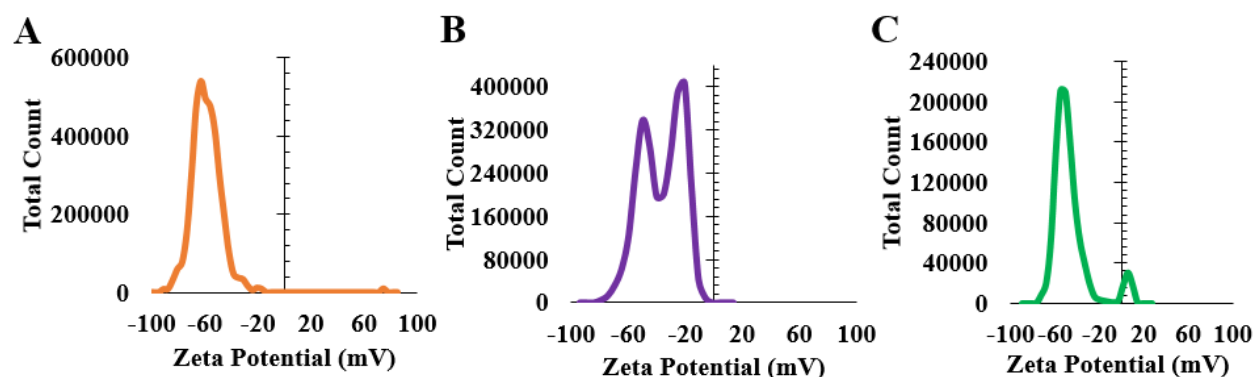


Development of ionic liquid-coated PLGA nanoparticles for applications in intravenous drug delivery

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Supplementary Figure 1. Troubleshooting size spectra of synthesized nanoparticles using DLS. A.) Some ILs can have thick or solid gel-like consistency (such as long saturated alkyl chains) and may not cap and form a separate aggregate in solution. This can be remedied by either heating the IL up before dropping, experimentally dissolving the IL in various % (wt/vol) of acetonitrile, or massing the IL on a spatula and allowing the stir bar to whip it into solution at 800 RPM once placed in the center of the flask. This result can also occur when IL is not added at 800 RPM as the stir rate at 1200 RPM will be too fast and prevent the anion and cation from self-assembling. B) Bare PLGA encapsulating 3% (wt/wt) DiD creates a large, unstable, and undesirable NP for coating with IL. Encapsulate 1-2% DiD (wt/wt of polymer). C) Multiple simultaneous droplets, or uncontrolled squirting motions of the organic phase into the aqueous phase will not efficiently form a nanovesicle and stably encapsulate the DiD dye, resulting in its release into solution (peak at 1 nm) with empty large unstable PLGA vesicles (1000 nm). Ensure each organic droplet is delivered every 3 seconds to the center of the vortex at one thumb's distance from the mouth of the flask.



Supplementary Figure 2. Troubleshooting zeta potential spectra of synthesized nanoparticles by DLS. A.) Adding IL in excess of 20 mg/mg PLGA (in the previously prescribed density range), such as 30 mg, will coat the PLGA nanoparticle, but will cause bulkiness in the outer anion coating with excess falling out of solution, indicated by the presence of several small positive cation peaks. B.) Failing to add IL in the center/correct height of the flask, adding IL at higher than 800 RPM, stirring for longer than the recommended time for IL addition, attempting to add an unstable IL with many oxygen moieties or very long alkyl chains, or attempting to add an IL with multiple anions will yield improperly coated PLGA NPs, indicated by the bare PLGA NP peak at -20 mV, and the coated peak at -50 mV. C) Using an improper stir bar, such as one that has a spherical or barrel shape, in contrast to the recommended pill shape for 100 mL round bottom flasks (RBFs) or 20 mL scintillation vials, will interfere with the electrostatic assembly of the IL on the surface of the PLGA NPs, resulting in an unstably coated nanoparticle.