Mulholland Dr. Multiscale molecular modeling of the self-assembly of di/triblock copolymers for drug delivery

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Polymeric drug carriers have traditionally been considered important for enhancing drug stability and solubility, and improving transport properties of pharmaceutical molecules. Drug carriers in the form of microspheres, nanoparticles, solution-dispersed polymeric micelles, hydrogels, or polymer– drug conjugates have been used to encapsulate hydrophobic drugs and other bioactive molecules, which are released in a controlled manner over a long period of time. An important requirement for these drug delivery systems is that they be biocompatible. Two polymers extensively studied in this regard are poly (lactide) (PLA) and poly (ethylene oxide) (PEO). Both polymers are biodegradable, adapt well to biological environments, and do not have adverse effects on blood and tissues. Due to such unique properties, copolymers of PEO/PLA with AB and ABA architectures have generated broad interest in nanomedicine applications. Nonetheless, a systematic investigation of the main structural and physical factors influencing the ultimate morphology and structure of the block polymer nanoscopic aggregates is still lacking, as it understandably requires a mammoth experimental effort. Molecular simulation techniques, as time and cost efficient tools, can not only complement experimental works, but also eventually give a preview of phenomena prior to experiments. In this work we report the results of a complete study on the self-assembly of PLA/PEO di/triblock copolymers in aqueous environment based on a multiscale molecular modeling recipe. In details, atomistic molecular dynamics simulations were used to obtain dissipative particle dynamics (DPD) input parameters, and this mesoscale technique was employed to derive the entire phase diagrams for these systems.