# POLYMER-NANOPARTICLE INTERACTIONS IN SUPRAMOLECULAR HYDROGELS: ENABLING LONG-TERM ANTIBODY DELIVERY

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Antibody drugs are a rapidly growing set of therapeutics that increasingly prove effective for clinical applications spanning from macular degeneration treatments, to targeted cancer therapies, and to passive immunization. These antibody treatments can be engineered to target almost any cell surface moiety and their production has since been scaled to an industrial level. Despite these advances, parenteral administration of antibodies is severely constrained by high viscosities at desirable doses, poor long-term antibody stability, high required frequency of administration, and therapeutically suboptimal pharmacokinetics. Herein, we demonstrate the development of supramolecular polymer-nanoparticle (PNP) interactions between poly(ethylene glycol)-poly(lactic acid) block copolymer nanoparticles (PEG-PLA) and modified hydroxypropylmethylcellulose (HPMC-x) polymers to engineer shear-thinning, self-healing hydrogels capable of stabilizing and delivering high concentrations of antibodies over prolonged timeframes (Figure 1). The PNP interactions underpinning the behavior of these materials afford injectability and tunable mechanical properties, while also controlling antibody release kinetics. In this work, we investigate how the thermodynamics of the PNP interaction affect *in vitro* and *in vivo* antibody release kinetics, pharmacokinetics, and bioavailability. Analysis of PEG-PLA surface density, HPMC-x hydrophobicity and modification extent, and hydrogel formulation reveal explicit design handles relating PNP thermodynamics to *in vivo* antibody release kinetics via subcutaneous injection. Differences in antibody release kinetics between *in vitro* and *in vivo* experiments were examined through mathematical modelling, revealing possible mechanisms of antibody uptake from subcutaneous space to the bloodstream when compared to literature. Overall, this work presents a robust set of design parameters to tune PNP interactions to develop a new nanotechnology-based platform for long-term, controlled antibody delivery.

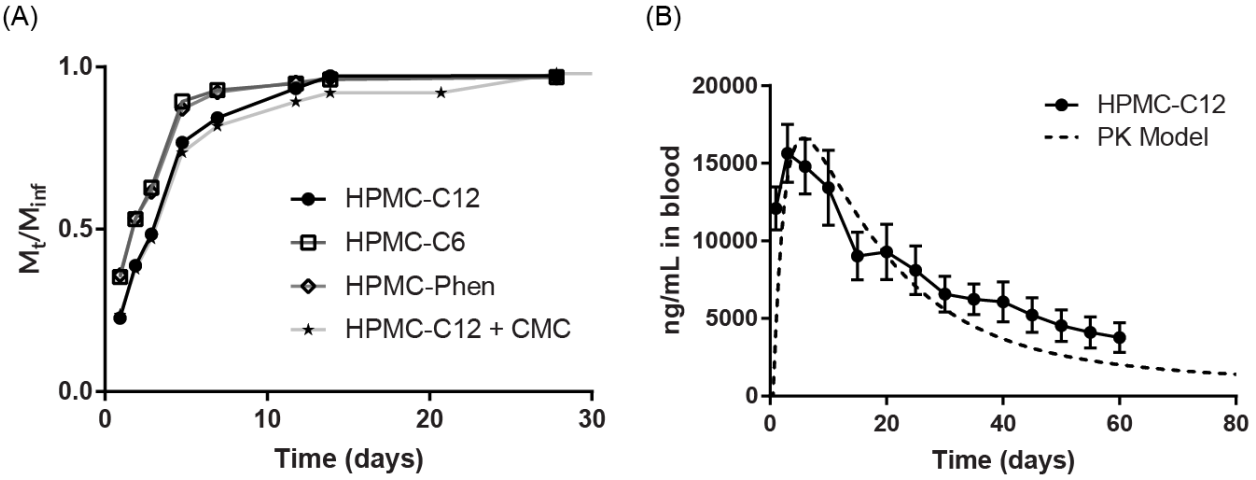


*Figure 1 – (A) In vitro experiments characterizing the delivery of a model drug, which exhibits distinct release profiles depending on functional group attached to HPMC. These functional groups exhibited varying interaction strengths with PEG-PLA nanoparticles and formed gels with different mechanical and antibody release properties. (B) Serum concentration of anti-OVA antibodies delivered from a hydrogel formulation after subcutaneous injection into C57BL6 mice. The dotted line represents a pharmacokinetic (PK) model that accounts for kinetics of antibody release from the hydrogel, uptake into the bloodstream via subcutaneous space, and decay from the bloodstream.*