Quantifying the Behavior of pH-Responsive Hydrogels

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Hydrogels are an important class of responsive materials with significant utility in the biomedical sector. Our efforts in this area have yielded a large family of (primarily epoxy-based) hydrogel networks – stable, robust, biocompatible materials capable of pH-responsive swelling, absorption and release. The impetus for the creation of these materials was the hypothesis that it should be possible to create a hydrogel capable of absorbing acidic waste, releasing nutrients and supporting cells in culture. Subsequent studies have borne out this hypothesis, with these materials enabling long-term mammalian cell culture without human intervention. As an example, this is demonstrated in the context of the culture of SA-13 human-human hybridomas. The biocompatibility of these materials is excellent so long as the extractable fraction is kept low, and we have further demonstrated that their presence does not induce differentiation in stem cells. At the same time, these efforts have made clear that different cell lines differ greatly in terms of activity and optimal growth conditions, and that there remains a need not just to create such materials, but to design them to possess very specific properties. With this in mind, we report on our efforts to quantify and predict the behavior of these hydrogels. Flory-Rehner network theory has been used to predict the maximum extent of swelling, with additional mathematical modeling enabling us to describe swelling kinetics in further detail. Release characteristics are shown to be directly related to the aforementioned swelling metrics, and acid absorption capacity is predicted based on compositional arguments and confirmed to be consistent with observed behavior as well. While there is still work to be done to describe the behavior of pH-responsive hydrogels especially in the partially to fully charged state, these efforts enable us to predict the behavior of any number of new additions to our family of pH-responsive hydrogels in advance of their synthesis. The ability to use simple analytical predictions to guide the design of new and useful responsive materials represents an important step in their continued development.