Logical Breakdown: Programming Boolean-based Responsiveness into Hydrogel Biomaterials

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Abstract

The successful transport of drug- and cell-based therapeutics to diseased sites represents a major barrier in the development of clinical therapies. Targeted delivery can be mediated through degradable biomaterial vehicles that utilize disease biomarkers to trigger payload release. Here, we report a modular chemical framework for imparting hydrogels with precise degradative responsiveness by using multiple environmental cues to trigger reactions that operate user-programmable Boolean logic. By specifying the molecular architecture and connectivity of orthogonal stimuli-labile moieties within material crosslinkers, we show selective control over gel dissolution and therapeutic delivery. To illustrate the versatility of this methodology, we synthesized seventeen distinct stimuli-responsive materials that collectively yielded all possible YES/OR/AND logical outputs from input combinations involving enzyme, reductant, and light. Using these hydrogels, we demonstrate the first sequential and environmentally stimulated release of small molecules, site-specifically modified proteins, and multiple cell lines in well-defined combinations from a material. We expect these platforms will find utility in several diverse fields including drug delivery, diagnostics, and regenerative medicine.

Biography

Dr. Cole A. DeForest is the Dan Evans Career Development Assistant Professor in the Departments of Chemical Engineering and Bioengineering, and a core faculty member of the Institute for Stem Cell & Regenerative Medicine at the University of Washington (UW) where he began in 2014. He received his B.S.E. degree from Princeton University in 2006, majoring in Chemical Engineering and minoring in Material Science Engineering and Bioengineering. He earned his Ph.D. degree under the guidance of Dr. Kristi Anseth from the University of Colorado in Chemical and Biological Engineering with an additional certificate in Molecular Biophysics. His postdoctoral research was performed with Dr. David Tirrell in the Divisions of Chemistry and Chemical Engineering at Caltech. He has authored ~45 peer-reviewed articles, including as the corresponding author for those appearing in *Nature Materials*, *Nature Chemistry*, *Advanced Materials*, *JACS*, and *Nature Reviews Materials*. Dr. DeForest has received numerous research awards including the Safeway Early Career Award (2018), NSF CAREER Award (2017), AIChE 35-Under-35 Award (2017), and the Presidential Distinguished Teaching Award (2016, UW's highest teaching award).