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Stimulus-responsive hydrogels: Theory, modern advances, and applications

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ABSTRACT

Over the past century, hydrogels have emerged as effective materials for an immense variety of applications. The unique network structure of hydrogels enables very high levels of hydrophilicity and biocompatibility, while at the same time exhibiting the soft physical properties associated with living tissue, making them ideal biomaterials. Stimulus-responsive hydrogels have been especially impactful, allowing for unprecedented levels of control over material properties in response to external cues. This enhanced control has enabled groundbreaking advances in healthcare, allowing for more effective treatment of a vast array of diseases and improved approaches for tissue engineering and wound healing. In this extensive review, we identify and discuss the multitude of response modalities that have been developed, including temperature, pH, chemical, light, electro, and shear-sensitive hydrogels. We discuss the theoretical analysis of hydrogel properties and the mechanisms used to create these responses, highlighting both the pioneering and most recent work in all of these fields. Finally, we review the many current and proposed applications of these hydrogels in medicine and industry.

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Hydrogels are three dimensional network structures consisting of polymeric chains joined by tie points or joints and swollen in water up to thermodynamic equilibrium. This is a simple and quite accurate definition of these materials, which have become so popular in numerous applications over the past 50 years. While this general definition has been used to present and analyze swollen crosslinked hydrogels, especially as defined in our 1986–1987 books on "Hydrogels in Medicine and Pharmacy," there have been variations of this basic definition and deviations from the basic thermodynamic and structural equations that define their performance.

While Paul Flory set the basic theories for hydrogel analysis, it is interesting to note that hydrogels had been prepared long before his original theoretical treatments were established. Indeed, early work on crosslinked polymers and networks first appeared in German literature in the mid-1930s. Meanwhile significant work on the behavior of "natural hydrocolloids" appeared in the late 1930s, but without structural insight. In addition, work in that period and in the 1940s concentrated mostly on reaction kinetics and mechanical properties of the ensuing networks.

PJ Flory (1944–1952; Nobel prize 1974) set the main framework of analysis of gels with his thermodynamic theories, statistical