Besides pH, thermal swelling in hydrogels has been the most exploited effect for responsive gel sensors. Poly(N-isopropylacrylamide) (PNIPAAm) is among the most studied temperature responsive polymers. Temperature induced swelling is relevant in drug delivery systems and specialized temperature sensing applications at the micro- and nanoscale. Fluorescent readout of stimuli responsive micro- and nanogels is a promising method in a wide range of sensing and imaging applications (Li and Liu 2012). Covalent binding of environment sensitive fluorophores to the polymer fibers results in modulation of the fluorescent signal by changes of the hydrophobic microenvironment upon temperature induce fiber collapse. In addition, the Förster resonance energy transfer (FRET) effect can be employed for sensor readout. Swelling or shrinking of the gel changes the fluorescent donor/acceptor distance, and therefore, the FRET signal (Fig. 2d) (Hu and Liu 2010). With fluorescent nanogel particles intracellular temperature monitoring was presented (Gota et al. 2009).

Ion selective swelling in responsive gels has been achieved by introducing chemical groups to the polymer that selectively bind to an ion. For example, crown ethers bind to metallic ions, increasing the charge in the gel network and swelling occurs due to an increase of osmotic pressure (Holtz and Asher 1997). However, depending on the binding chemistry these systems may lack ion selectivity. A potassium sensor with a potassium selective membrane and a colloidal photonic crystal hydrogel (CPCH) arrangement has been proposed for whole blood potassium measurements (Fenzl et al. 2014). CPCHs include arrays of nanoparticles, which exhibit Bragg diffraction in the visible range. The induced gel shrinking in a CPCH reduces the distance of the nanoparticles and results in a shift of the diffraction peak (Fig. 2e). An ammonia responsive CPCH was suggested for point-of-care diagnostics of blood ammonia levels (Kimble et al. 2006). Similar concepts enable the measurement of toxic heavy metal ions mercury and lead in water samples (Arunbabu et al. 2011; Ye et al. 2012). Alternative methods for the implementation of periodic nanostructures as diffraction gratings in photonic hydrogels include laser interference-based photocuring, and multilayer co-polymerization (Yetisen et al. 2015). Recently, photonic hydrogels have gained interest in the development of diagnostic devices because of their simple colorimetric readout possibilities. A sensitive sensor system, based on a silver nanoparticle Bragg grating in phenylboronic modified acrylamide gel was successfully tested for glucose monitoring in urine samples under fixed pH conditions (Yetisen et al. 2014).

Functionalized (bio)chemical reactors

Despite the slower diffusion dynamics in comparison to free solution, hydrogels have found many applications as reactors in biomedical diagnostics. These gels are functionalized by incorporated biological or chemical probes, including oligonucleotides, enzymes and enzyme substrates, proteins and antibodies, or specific dyes. In contrast to conventional surface-bound assay technologies, the recognition molecules are distributed in three dimensional gel structures. A major advantage of the three dimensional loading is the enhanced signal to noise ratio. Besides reporter molecule, and hence, signal stacking, the low non-specific protein adsorption within the gel matrices increases the signal quality. As an example, Lee et al. 2013 reported