

on the 1000-fold sensitivity increase of a three dimensional hydrogel assay for Sjögren's syndrome specific marker in comparison to a surface bound version of the same marker. In addition, immobilized proteins exhibit increased stability over time in contrast to surface binding methods (Rubina et al. 2008). An overview of functionalized gel structures in different diagnostic assay formats is given in Table 2. These assays utilize all kinds of gel structuring techniques as previously discussed. Main analytes are nucleic acids from pathogens, protein markers, toxins, enzymes, and glucose. While nucleic acid and protein detection mainly is adopted from classical methods, different enzymes (e.g., secreted by pathogens) can be detected by their digestion of labeled substrates as parts of the gel matrix with a corresponding dye release or FRET signal. These substrates are sometimes also referred to as bioresponsive polymers. A distinct approach for a bioresponsive gel sensor was presented by Wei et al. 2015. Two

Table 2. Biochemical gel sensor overview.

Gel type	Readout	Analyte	Reference
Microfluidic barcoded PEG-DA microparticle sandwich assay	Fluorescent labeling	Interleukin-2 10 pg/ml	Appleyard et al. 2011
Pin dispensed methacrylamide microarrays for hybridization and sandwich assays	Fluorescent labeling	M. tuberculosis, HIV, HBV, HCV virus, protein tumor markers	Gryadunov et al. 2011
Alginate-stained peptidoglycan gel double layer	Dye release upon digestion	Wound infection, lysozyme	Hasmann et al. 2011
Photomask patterned PEG-DA micropatches, immobilized enzyme and quantum dots	QD fluorescence quenching	Phenol 1 μ M, glucose 50 μ M, alcohol 70 μ M	Jang et al. 2010b, 2012
Conjugated enzyme-carboxy seminaphthofluorescein in emulsion polymerized microspheres	Self-referenced dual emission fluorescence	Organophosphate, paraoxon 5 μ M	Lee et al. 2009
Macroporous nanofiber-PAM matrix in 96 well plate	Absorbance immunoassay	Sjögren's syndrome, anti-SSB/La antibody 10 pM	Lee et al. 2013
UV beam polymerized PEG-DA enzyme micropatches in microfluidic channels	Colorimetric	Glucose and protein in human urine samples	Lin et al. 2011
Casted PAM micropillars with primers and polymerase	Real-time PCR, fluorescence	Herpes simplex virus from swab samples	Manage et al. 2012
Photopatterned pHEMA enzyme membranes	Electrochemical	Glucose 0.1 mM, lactate 50 μ M in whole blood	Moser et al. 2002
<i>In situ</i> polymerized PEG-DA microstructures with labeled substrate/protein specific dye	Fluorescent, colorimetric	Matrix metallo proteinase 470 ng/ml, total protein 20–140 μ g/ml, WBC counts	Puchberger-Engel et al. 2014
Casted PAM gel strips with primers and polymerase	Real-time PCR, fluorescence	Malaria, Plasmodium falciparum from whole blood	Taylor et al. 2014
PNIPAAm waveguide in surface plasmon resonance setup	Label free optical	Imunoglobulin G 10 pM, 17beta-estradiol 50 pg/ml	Zhang et al. 2013