are particularly well positioned to provide structural anisotropy. Electrospinning techniques have been used to create hydrogel materials with aligned fibres of various sizes and composition. For example, taking advantage of the process of electrospinning, hydrogels formed by aligned fibres have been used to align cells such as myoblasts (Wang et al. 2015) and endothelial cells (Eslami et al. 2014).

Another approach to create fibrous-hydrogels takes advantage of molecular self-assembly. Peptide-based hydrogels are particularly attractive given the possibility to control epitope presentation while creating well-defined nanostructures such as nanoscale fibres, tapes, and ribbons (Zhang 2003). However, controlling self-assembly hierarchically beyond the low nanoscale formation of one-dimensional structures and into the required 3D organization of hydrogels has been a difficult challenge (Smith et al. 2011). Stupp and colleagues have developed strategies based on the application of shear stresses (Mata et al. 2009) or evolving bilayer-to-nanofibre assemblies (Zhang et al. 2010), resulting in 3D hydrogels with domains of aligned nanofibres capable of guiding cell migration and growth. Molecular self-assembly has also been used to assemble nanostructures at higher scales including membranes made from nanofibres organized in precise microscale structures including layers (Inostroza-Brito et al. 2015; Ladet et al. 2008) or orthogonally assembled fibres (Capito et al. 2008; Zha et al. 2016). Other approaches to provide physical anisotropy have included the use of additional materials, for example in the form of particles, to the hydrogel to reinforce their mechanical properties (Liu et al. 2015a) and better control the final hydrogel structure (Studart 2015) and more sophisticated methods involving for example acoustic waves to create 3D patterns (Bouyer et al. 2016). Hydrogels exhibiting environments with distinct mechanical properties can also be created employing top-down techniques such as microfluidics (Orsi et al. 2014) or by creating composites including for example blends of chitosan, gelatine, hyaluronic acid, and ß-tricalcium phosphate capable of recreating articular cartilage (Walker and Madihally 2015) or silk and cardiac-derived ECM composites to be used for cardiac tissue engineering (Stoppel et al. 2015).

Strategies to create chemical anisotropy

In addition to creating structural anisotropy, the development of hydrogels with precise chemical anisotropy is a major goal. The groups of Molly Shoichet, Jennifer West, and Kristy Anseth have pioneered leading photo-patterning strategies capable of immobilizing signalling molecules within 3D hydrogels. For example, using a laser beam, cylindrical patterns of the peptide GRGDS have been generated within modified agarose hydrogels, creating one-dimensional cell-adhesive patterns capable of guiding neuronal growth (Fig. 3b) (Luo and Shoichet 2004). Similar patterns have been created using either a two-photon laser scanning to create RGDS patterns within polyethylene-glycol (PEG) hydrogels (Hoffmann and West 2013) or a multiphoton laser scanning lithography technique to immobilise vitronectin within PEG hydrogels (Fig. 3c) (DeForest and Tirrell 2015).

These approaches take advantage of the opportunities of using light as a patterning tool in order to maximize precision and develop 3D hydrogel environments with distinct and precise chemical patterns. However, in order to provide a more robust approach capable of enabling chemical anisotropy within a broader spectrum of