Additional Table 1. Commonly-used biomaterials with various elasticities and their effects on cells.

Material	Fabrication method	Elasticity	Effects on cell behaviours	Cell source	Reference
Alginate	Alginate microspheres prepared by microfluidic technology with different elasticities and microarchitectures,controlled by calcium ion concentrations.	18, 32 kPa	Elasticity and porosity regulated the fate of encapsulated MSCs through modulation of the nuclear factor-κB pathway	MSCs	34
Chitosan-hyaluronic acid	Porous chitosan–hyaluronic acid scaffolds of varied stiffness were fabricated using a phase separation method	1.41–27.7 kPa	Increased matrix stiffness resulted in increased drug resistance of glioblastoma multiforme cells, and elevated expression of drug resistance-,hypoxia-, and invasion-related genes	Glioblastoma multiforme cells	21
Dynamic protein hydrogels	A Ru^{2+}-mediated photochemical strategy was used to crosslink an aqueous solution of $FGR(G\text{-}MEP\text{-}R)_2$ into a chemically-crosslinked protein hydrogel	6–20 kPa	Human lung fibroblasts dynamically responded to changes of hydrogel mechanics in a reversible fashion, regulated by redox state	Human lung fibroblasts	39
Fibrin-alginate	Mechanical properties were tuneable via calcium chloride crosslinking	0.6–3.8 kPa	Spreading of MSCs and endothelial cells was a function of alginate crosslinking density	MSCs, endothelial cells	22
Hyaluronic acid	Methacrylated hyaluronic acid was synthesized to allow for crosslinking via Michael addition using the crosslinker dithiothreitol	0.2–4.5 kPa	Human breast cancer cell (MDA-MB-231Br) adhesion, spreading, proliferation and migration were tightly regulated by the hydrogel stiffness	MDA-MB-231Br	23
Polyacrylamide	Stiffness of polyacrylamide gels was adjusted using different monomer-to-crosslinker formulations	2–32 kPa	Cytoskeleton assembly and cell morphology were efficiently regulated by substrate stiffness	HeLa cells	24
Poly (dimethylsiloxane)	Poly(dimethylsiloxane) was used as the base material in which iron particles were embedded to create a magnetorheological elastomer, whose elasticity was controlled by the spacer distances between the magnet and the samples	10–55 kPa	The softer substrates yielded more organised sarcomeres,and sarcomere formation was positively correlated with the degree of myocyte enrichment when using human-derived induced pluripotent stem cell cardiomyocytes	Human-derived induced pluripotent stem cell cardiomyocytes, cardiac fibroblasts	25
Polyurethane	Controlling the crosslinking of tri-block copolymer and polycaprolactone triol yielded polyurethanes of varying elasticity	45.0–244.8 kPa	Scaffolds with different stiffnesses stimulated the proliferation of different types of cells	3T3 fibroblasts, MG63 cells	26
Silk fibroin	Developed by introducing inert silk fibroin nanofibres within an enzyme crosslinked system of silk fibroin	9–60 kPa	MSCs differentiated into endothelial, myoblast and osteoblast cells on the different elastic substrates	MSCs	35
Silk fibroin-collagen	The concentrations of both proteins was changed gradually while maintaining the ratio at 1:7, which resulted in a gradual change in stiffness at a fixed composition	0.1–20 kPa	High rigidity allowed human MSCs to preserve all-directional spreading with polygonal shape. Soft substrates might not maintain the polygonal shape	Human MSCs	27
Poly(ether carbonate urethane)urea	Young's modulus of scaffolds was tuned by adjusting the molecular weight of polydiol (soft segment) as well as the feed ratios of hard molecular segment to soft molecular segment	2.5–13.4 MPa	Annulus fibrosus-derived stem cells showed strong tendencies to differentiate into various types of annulus fibrosus-like cells depending on the substrate elasticity	Annulus fibrosus-derived stem cells	36, 102

Additional Table 1. Continued

Material	Fabrication method	Elasticity	Effects on cell behaviours	Cell source	Reference
PEG	Stiffness was adjusted by adding various PEG monomers and the photoinitiator lithium phenyl-2,4,6-trimethylbenzoylphosphinate	1.5–12.6 kPa	The functional and molecular outputs of adult mouse ventricular myocytes were dependent on the PEG hydrogel stiffness	Adult mouse ventricular myocytes	28
Poly(L-lactide-co-caprolactone)/ poly(L-lactic acid)	Fibre stiffness was controlled by altering the flow rates of the poly(L-lactic acid)-core and poly(L-lactide-co-caprolactone)-shell solutions.	14.7–2141.7 MPa	Higher stiffness of the aligned fibrous substrates was found to significantly encourage the proliferation and migration of human umbilical artery smooth muscle cells	Human umbilical arterial smooth muscle cells	29
GelMA hydrogels	Prepared by photocrosslinking methacrylate gelatine and adjusting the stiffness by varying the concentration	3–180 kPa	PC12 cell viability, adhesion, spreading and average neurite length were influenced by stiffness	PC12 cells	30
GelMA/PEGDA hydrogels	Prepared by photocrosslinking methacrylate gelatine and adjusting the stiffness with the crosslinker PEGDA	4, 40 kPa	Increased matrix stiffness promoted osteogenic differentiation of MSCs	MSCs	31
GelMA/Collagen hydrogels	Prepared by mixing collagen and GelMA to form an interpenetrating network	2–12 kPa	With the increase of matrix stiffness, the invasion and sprouting of the two cells decreased regardless of fibre content	MDA-MB-231Br and endothelial cells	32
Alginate/GelMA hydrogels	Prepared by mixing alginate and GelMA	6–13 kPa	The expression level of MSC osteogenesis markers was enhanced with the increase in the matrix elastic modulus	MSCs	33

FGR(G-MEP-R)$_2$: TNfn3-GB1–resilin-(GB1-MEP-resilin)$_2$; GelMA: gelatin methacryloyl; MSC: mesenchymal stem cell; PEG: polyethylene glycol; PEGDA: polyethylene glycol diacrylate.

Additional Table 2. Scaffolds with tuneable viscoelasticity through various crosslinkers and their effects on cells.

Biomaterials	Fabrication method	Viscoelasticity	Effects on cell behaviours	Cell source	Reference
Alginate hydrogels	Prepared by ionic crosslinking of alginate	Obtained by covalently or ionically crosslinking alginate gels with the same initial Young's modulus by adjusting the concentration of crosslinker	Both computational modelling and experimental studies revealed that spreading of cells cultured on soft substrates that exhibit stress relaxation is greater than cell spreading on elastic substrates of the same modulus, but similar to that of cells spreading on stiffer elastic substrates	U2OS & 3T3 fibroblasts	72
	Prepared by ionic crosslinking of alginate	The time for the initial stress of the material to be relaxed to half its value during a stress relaxation test ($\tau_{1/2}$) was modulated from ~1 minute to ~1 hour by controlling the molecular weight of alginate	Cell spreading, proliferation, and osteogenic differentiation of MSCs were all enhanced in cells cultured in gels with faster relaxation	MSCs	73
Alginate-PEG hydrogels	Prepared by ionic crosslinking of PEG-functionalised alginate	PEG acts as a spacer to provide a steric spacing of crosslinking zones in alginate. Increased concentration and molecular weight of the PEG resulted in faster stress relaxation, a high loss modulus, and increased creep	The hydrogels can be used for 3D culture. Faster relaxation led to increased spreading and proliferation of fibroblasts, and enhanced osteogenic differentiation of MSCs	3T3 fibroblasts; MSCs	74
Alginate interpenetrating network as an artificial ECM	Prepared by a combination of ionic and covalent cross-linking of click-functionalised alginate, interpenetrating with fibrillar collagen type I	Varying the mode and magnitude of crosslinking enables tuneable stiffness and viscoelasticity	MSC expression of immunomodulatory markers was differentially impacted by the viscoelasticity and stiffness of the matrix	MSCs	75
Boronate ester hydrogel	Prepared by reversible boronate esterification of boronic acid with vic-diols	Viscoelasticity increased as a function of the boronic acid and vicinal diol concentration, and also increased with decreasing cross-linker concentration, where the maximal loss tangent achieved was 0.55 at 0.1 rad/s	The cell area and nuclear area, focal adhesion tension, and subcellular location of YAP/TAZ were found to be lower for cells cultured on viscoelastic hydrogels compared to elastic hydrogels with a similar storage modulus	NIH-3T3 cells	78
Boronate-based hydrogels	Based on reversible boronate bonds	Relaxation time constants on the order of seconds or less	Fast relaxation matrix mechanics are found to promote cell–matrix interactions, leading to spreading and an increase in nuclear volume, and induce YAP/TAZ binding domain nuclear localization at longer times	MSCs	79
Collagen gels	Fabricated by adjusting pH	Strain-enhanced stress relaxation of collagen gels arises from force-dependent unbinding of weak bonds between collagen fibres	-	-	76
Hyaluronic acid hydrogels	Crosslinked via photo-responsive guest–host pairing of azobenzene to β-cyclodextrin	Relaxation time from 6 seconds to minutes	The hydrogels maintained a high level of viability after 3 days of culture	NIH 3T3 cells	77

Additional Table 2. Continued

Biomaterials	Fabrication method	Viscoelasticity	Effects on cell behaviours	Cell source	Reference
Hyaluronic acid	Combined light-mediated covalent and supramolecular crosslinking was used to afford spatiotemporal control of the viscoelastic network	Significantly higher loss moduli compared to elastic group. Photopatterning enabled presentation of dynamic, heterogeneous viscoelastic properties	LX-2 cells respond to the viscoelastic hydrogel by displaying reductions in spread area, MRTF-A nuclear translation, and organisation of actin stress fibres	LX-2 stellate cells	80
Hyaluronic acid–collagen hydrogels	Interpenetrating network based on HA crosslinked with dynamic hydrazone bonds with collagen type I	The time for the initial stress of the material to be relaxed to half its value during a stress relaxation test ($\tau_{1/2}$) was modulated from ~233 seconds to > 18000 seconds	Faster relaxation promotes cell spreading, fibre remodelling, and focal adhesion formation in 3D culture	Human MSCs	81
Oxime cross-linked alginate hydrogels	Formed by mixing alkoxyamine-containing alginate with aldehyde-containing alginate	Stress-relaxation was tuneable by varying the composition or environmental factors	The gels showed very nice short-term cytocompatibility with the encapsulated cells. Growth and migration benefited from the stress relaxation capability	2PK3 cells	82
PEG hydrogels	Crosslinked by reversible hydrazone bonds	$\tau_{1/2}$ could be varied from 5–6000 seconds by changing the number of PEG or by changing the ratio of benzaldehyde to aliphatic aldehyde crosslinkers	Covalently-adaptable hydrogels allowed for the development of physiologically-relevant morphologies, whereas non-adaptable gels prevented cytoskeletal rearrangement and extension	C2C12 myoblasts	83
Thioester hydrogel	Photopolymerisation between PEG-SH and thioester-containing divinyl crosslinker	Through control of pH, gel stoichiometry, and crosslinker structure, viscoelastic properties were modulated across several orders of magnitude	MSCs encapsulated in the thioester hydrogels were able to elongate in 3D and display increased proliferation relative to those in static hydrogels	MSCs	84
Hyaluronic acid and PEG	A DN was formed based on the combination of supramolecular GH hyaluronic acid networks with covalent networks from the photocrosslinking of PEG-fibrinogen and PEG-diacrylate	Dependent on the polymer concentration the GH network	The increase of GH concentration led to the enhancement of the viscosity of the DN hydrogel and the enhancement of cell spreading and proliferation	MSCs	85

3D: three dimentional; ECM: extracellular matrix; DN: double network; GH: guest-host; HA: hyaluronic acid; MSC: mesenchymal stem cell; PEG: polyethylene glycol; PEG-SH: eight-arm PEG thiol macromers; TAZ: transcriptional coactivator with PDZ-binding motif; YAP: yes-associated protein; $\tau_{1/2}$: stress relaxation rate.