Claims

1. A composite material comprising:

a substrate; and

a patterned hydrogel disposed on the substrate, wherein:

the patterned hydrogel comprises stimulus-responsive constitutional units and constitutional units comprising one or more target molecule recognition moieties;

the stimulus-responsive constitutional units are responsive to a stimulus and are configured to produce a stress value S_1 to the patterned hydrogel when the stimulus is applied;

the target molecule recognition moieties are responsive to a target molecule and are configured to impart a stress value S_2 to the patterned hydrogel upon interaction with the target molecule;

the patterned hydrogel is configured to reversibly buckle and/or reversibly swell when a threshold stress level T of the patterned hydrogel is crossed,

wherein the patterned hydrogel comprises constitutional units comprising a moiety targeted to a biomolecule that recruits an enzyme that is capable of catalysing a crosslinking reaction and/or a cleavage reaction.

2. The composite material according to Claim 1, wherein the one or more target molecule recognition moieties comprise a moiety selected from the group consisting of a crosslinkable moiety, a cleavable crosslinking moiety, and a moiety capable of covalently bonding to a polar molecule, optionally wherein the crosslinkable moiety and/or a cleavable crosslinking moiety comprises a redox-responsive moiety.

3. The composite material according to Claim 2, wherein the crosslinkable moiety is a moiety capable of being crosslinked by a biomolecule (e.g. an enzyme) and/or wherein the cleavable crosslinking moiety is a moiety capable of being cleaved by a biomolecule (e.g. an enzyme).

4. The composite material according to Claim 3, wherein the biomolecule is an enzyme selected from the group consisting of an oxidase enzyme, a peroxidase enzyme, a protease and an enzyme that cleaves DNA,

optionally wherein:

the enzyme is selected from the group consisting of thioredoxin, glutaredoxin, horseradish peroxidase (HRP), glucose oxidase, glutathione peroxidase, laccase, tyrosinase and glutathione reductase.

5. The composite material according to any one of Claims 2 to 4, wherein the crosslinkable moiety is capable of being crosslinked by horseradish peroxidase,
optionally wherein the crosslinkable moiety comprises phenol moiety (e.g. a tyrosine moiety), a thiol moiety, a catechol moiety (e.g. a dopamine moiety or a 3,4-dihydroxybenzylamine moiety).

6. The composite material according to any one of the preceding claims, wherein the one or more target molecule recognition moieties comprise a moiety capable of reacting with a mixture of formaldehyde and tris(hydroxymethyl)aminomethane to form a functional group having the formula $–CH_2\text{-}NHC(CH_2OH)_3$,

optionally wherein the one or more target molecule recognition moieties comprise a a phenol ring (e.g. a tyrosine moiety) or a catechol ring (e.g. a dopamine moiety or a 3,4-dihydroxybenzylamine moiety).

7. The composite material according to any one of the preceding claims, wherein the biomolecule is selected from the group consisting of a protein biomarker, a DNA sequence, and an RNA sequence.

8. The composite material according to any one of the preceding claims, wherein the enzyme is selected from the group consisting of an oxidase enzyme, a peroxidase enzyme, a protease and an enzyme that cleaves DNA,
more optionally wherein the enzyme is selected from the group consisting of horseradish peroxidase (HRP), glucose oxidase, glutathione peroxidase, laccase, tyrosinase and glutathione reductase.

9. The composite material according to Claim 7, wherein the biomolecule is selected from the group consisting of CD63, CD24, EpCAM, EGFR, MUC1, CD125, HER2 and CEA.

10. The composite material according to any one of the preceding claims, wherein:

the one or more target molecule recognition moieties comprise a crosslinkable moiety and/or a cleavable crosslinking moiety; and
the patterned hydrogel comprises constitutional units comprising a bio-moiety that recruits an enzyme that is capable of catalysing a crosslinking reaction between the crosslinkable moieties, or a cleavage reaction of a cleavable crosslinking moiety, which crosslinking reaction or cleavage reaction imparts a stress value S_2 to the patterned hydrogel,
optionally wherein the constitutional units comprising a crosslinkable moiety and/or a cleavable crosslinking moiety comprise a redox-responsive moiety.

11. The composite material according to any one of the preceding claims, wherein:
(a) the constitutional units comprising one or more target molecule recognition moieties comprise constitutional units comprising a crosslinkable moiety selected from the group consisting of a phenol moiety (e.g. a tyrosine moiety) and a thiol moiety,
optionally wherein the constitutional units comprising or more target molecule recognition moieties comprise constitutional units derived from one or more of the group consisting of N-acryloyltyramine (NATA), 2-mercaptoethyl acrylate and N-(2-mercaptoethyl)acrylamide (MEAM); or
(b) the constitutional units comprising one or more target molecule recognition moieties comprise constitutional units comprising a cleavable crosslinking moiety selected from the group consisting of a disulfide moiety and a thioketal moiety,
optionally wherein the cleavable crosslinking moiety is derived from N,N′-Bis(acryloyl)cystamine, N,N'-((propane-2,2-diylbis(sulfanediyl))bis(ethane-2,1-diyl))diacrylamide, or disulfanediylbis(ethane-2,1-diyl) diacrylate.

12. The composite material according to any one of the preceding claims, wherein the composite material comprises a stimulus-transmitting layer disposed between the substrate and the patterned hydrogel, which stimulus-transmitting layer comprises a stimulus-transmitting material capable of transmitting a stimulus to the stimulus-responsive constitutional units,
where said stimulus-responsive constitutional units are responsive to said stimulus,
optionally wherein said stimulus-transmitting layer has a thickness of from 5 to 50 nm.

13. The composite material according to Claim 12, wherein the stimulus-transmitting material is selected from one or more of the group consisting of a thermally conductive material and an electrically conductive material,
optionally wherein the stimulus-transmitting material is a thermally conductive material,
more optionally wherein the thermally conductive material is a photothermally conductive material, such as a photothermally conductive material configured to apply a thermal stimulus to the stimulus-responsive constitutional units upon plasmonic heating of the photothermally conductive material.

14. The composite material according to Claim 13, wherein the thermally conductive material is selected from one or more of the group consisting of gold, silver, copper, aluminium, Cu_xS, platinum and zinc (e.g. gold),
optionally wherein the thermally conductive material is gold.

15. The composite material according to any one of the preceding claims, wherein the stimulus-responsive constitutional units are selected from one or more of the group consisting of thermally-responsive constitutional units, electrically-responsive constitutional units, optically-responsive constitutional units, magnetic-responsive constitutional units and pH-responsive constitutional units,
optionally wherein the wherein the stimulus-responsive constitutional units are selected from one or more of the group consisting of thermally-responsive constitutional units and pH-responsive constitutional units.

16. The composite material according to Claim 15, wherein:
(a) the thermally-responsive constitutional units are formed from one or more of the group consisting of of N-isopropylacrylamide (NIPAM), di(ethylene glycol)methylether methacrylate (DEGMA), triethylene glycol acrylate (TEGA), N-vinylcaprolactam (NVCL) and N-ethyl-N-methylacrylamide (EMA); or
(b) the pH-responsive constitutional units are formed from acrylic acid (AA), methacrylic acid (MAA) , 4-vinylbenzoic acid (VBA), 2-(demethylamino)ethyl methacrylate (DMAEMA), 2-(diethylamino)ethyl methacrylate (DEAEMA), 2-vinylpyridine (2VP), 11-acrylamidoundecanoic acid (AaU) and sodium 2-acrylamido-2-methylpropanesulfonate (AMPS).

17. The composite material according to any one of the preceding claims, wherein the patterned hydrogel is patterned to have a lattice structure,
optionally wherein the lattice structure comprises substantially square-shaped holes.

18. The composite material according to any one of the preceding claims, wherein the reversible buckling and/or reversible swelling of the patterned hydrogel is detectable by scanning electron microscopy and/or laser diffraction,
optionally wherein the patterned hydrogel comprises left-handed and right-handed structures.

19. A method of detecting a biomolecule target in a sample, comprising the steps:
(i) providing a composite material according to any one of Claims 1 to 18, and a source of a stimulus to which the stimulus-responsive material is responsive;
(ii) applying the stimulus at a first magnitude to the composite material in the presence of said sample;
(iii) repeating step (ii) at a different stimulus magnitude to determine the threshold stress level T;

(iv) contacting the composite material with a sample and simultaneously applying the stimulus at a magnitude for which:

$S_1 < T$ and $S_1 + S_2 > T$, or

$S_1 > T$ and $S_1 + S_2 < T$;

(v) determining the presence of said biomolecule target upon detecting a conformational change (e.g. change in buckling state) of the patterned hydrogel, wherein

a change in buckling state indicates the presence of said biomolecule target.

20. The method according to Claim 19, wherein the source of a stimulus to which the stimulus-responsive material is responsive is a source of thermal energy or a pH change,

optionally wherein the source of thermal energy is a source of electromagnetic radiation,

more optionally wherein irradiation of the stimulus-transmitting material, when present, by the source of thermal energy (e.g. a source of electromagnetic radiation) provides plasmonic heating of the stimulus-responsive material.

21. The method according to Claim 19 or 20, wherein the buckling and/or swelling of the patterned hydrogel is determined using scanning electron microscopy (SEM).

22. The method according to Claim 19 or 20, wherein the conformational change of the patterned hydrogel is determined using laser diffraction,

optionally wherein the patterned hydrogel comprises left-handed and/or right-handed structures.

23. The method according to any one of Claims 19 to 22, wherein:

(a) the one or more target molecule recognition moieties comprise crosslinkable moieties; and

(b) the patterned hydrogel comprises constitutional units comprising a moiety (e.g. an antibody) targeted to a biomolecule that recruits an enzyme that is capable of catalysing a crosslinking reaction of the crosslinkable moieties,

optionally wherein the enzyme is selected from the group consisting of an oxidase enzyme, a peroxidase enzyme, a protease and an enzyme that cleaves DNA,

more optionally wherein the enzyme is selected from the group consisting of horseradish peroxidase (HRP), glucose oxidase, and glutathione peroxidase.

24. The method according to Claim 23, wherein the patterned hydrogel comprises constitutional units comprising a moiety (e.g. an antibody) targeted to a biomolecule selected from the group consisting of CD63, CD24, EpCAM, EGFR, MUC1, CD125.

25. The method according to Claim 23 or 24, wherein the crosslinkable moieties comprise tyrosine moieties, and where the enzyme is horseradish peroxidase (HRP).