UK RESEARCH AND INNOVATION | MEDICAL RESEARCH COUNCIL

Neural Scaffold Regeneration via Programmable Biomaterial Matrices

Full Economic Cost Application | MRC New Investigator Research Grant

Ref: MR/X0042187/1
Round: 2026 Cohort 1

Lead Applicant	Dr Eleanor Hartley	**Application Ref**	MR/X0042187/1
Host Institution	University of Meridian	**Scheme**	NIRG
Partner Org.	Synapse Biomedical Technologies Ltd	**Start Date**	01 Sep 2026
Duration	36 months	**End Date**	31 Aug 2029
Total FEC	£842,450	**UKRI Contribution**	£673,960
Research Area	Regenerative Medicine / Neuroscience	**Confidence**	Standard

Co-Investigators: Prof. James Caldwell (University of Meridian) | Dr Priya Nair (Synapse Biomedical Technologies Ltd) | Dr Samuel Okafor (Apex Neuroscience Institute)

Regenerative Medicine · Biomaterials · Neural Engineering · HEIF Aligned · Industry Partner

1 Executive Summary

Research Question: Can programmable hydrogel scaffolds—engineered with spatiotemporally controlled bioactive gradients—restore axonal connectivity in traumatic spinal cord injury (tSCI) models, and what are the underpinning mechanotransductive signalling mechanisms?

Traumatic spinal cord injury affects an estimated 2.5 million people worldwide, imposing severe functional deficits and significant economic burden exceeding £1.8 billion annually in the UK alone. Current clinical approaches—including surgical decompression and pharmacological neuroprotection—address secondary injury cascades but fail to reconstitute severed axonal tracts. A transformative solution demands materials that actively guide regeneration rather than passively fill lesion cavities.

This proposal, led by Dr Eleanor Hartley at the University of Meridian in collaboration with Synapse Biomedical Technologies Ltd, advances a next-generation platform: the **NeuraLattice** system—injectable, self-assembling hydrogel matrices functionalised with peptide gradients, optogenetically controlled growth factor release, and tunable mechanical compliance. We will use *in vitro* dorsal root ganglion co-culture, rodent hemisection tSCI models, and advanced multiscale imaging to interrogate scaffold–neuron interactions from molecular to whole-organ scale.

Expected Impact: Mechanistic insight into scaffold-guided regeneration; two provisional patents; an SME-ready prototype; and a framework for a subsequent Phase II clinical trial application.

2 Vision and Importance

2.1.

The central nervous system (CNS) presents a uniquely hostile environment for axonal regeneration. Following tSCI, the glial scar—dominated by reactive astrocytes, chondroitin sulphate proteoglycans (CSPGs), and pro-apoptotic cytokines—constitutes both a physical and biochemical barrier. Canonical inhibitory signalling via NgR1/RhoA suppresses growth cone motility, while deficient neurotrophic support starves surviving neurons of pro-survival BDNF and NT-3 signals **[1, 2]**.

Biomaterial scaffolds have emerged as compelling candidates to bridge lesion sites and provide permissive substrates. However, first-generation scaffolds relied on passive architectures that failed to recapitulate the *dynamic*, *anisotropic* nature of native neural extracellular matrix. The critical innovation in the NeuraLattice platform is fourfold:

1. **Mechanically tuneable backbones:** Polyethylene glycol–heparin interpenetrating networks allow elastic moduli to be dialled from 0.1 to 5 kPa, matching regional CNS stiffness.
2. **Photo-responsive growth factor release:** LOVTRAP-fused BDNF domains enable millisecond optogenetic control of neurotrophin gradients without exogenous viral vectors.
3. **CSPG enzymatic pre-treatment:** Chondroitinase ABC (ChABC) encapsulated in thermosensitive microspheres provides sustained local CSPG digestion.
4. **Conductive nano-fibres:** Polypyrrole-coated cellulose nanocrystals facilitate electrical

stimulation-enhanced axonal elongation.

2.2.

This project directly addresses MRC's *Brain Science and Mental Health* strategic priority and the cross-council *Neuroscience and Mental Health* theme, contributing to the UK Government's *Life Sciences Vision 2031*. The industry partnership with Synapse Biomedical Technologies Ltd—an Edinburgh-based SME with clinical-grade GMP manufacturing capabilities—ensures a credible translational pathway. Alignment with the HEIF strategic framework is evidenced by a formal Letter of Support committing in-kind resources of £168,490.

3 Programme of Work

3.1.

The project is structured across three interconnected work packages spanning 36 months.

WP1	WP2	WP3
Scaffold Design & Characterisation	In Vitro Neural Integration	In Vivo Efficacy & Mechanistic Studies
Lead: Dr Hartley **Months:** 1–18 **FEC:** £284,200	**Lead:** Prof. Caldwell **Months:** 6–24 **FEC:** £231,850	**Lead:** Dr Okafor **Months:** 18–36 **FEC:** £326,400

3.2.

Synthesise and fully characterise NeuraLattice hydrogel matrices; validate mechanical, optical, and biochemical properties against predefined design criteria.

- Synthesis of PEG–heparin interpenetrating networks at three crosslink densities (0.5, 2, and 5 kPa target moduli) using Michael-addition thiol-ene chemistry.
- Functionalisation with laminin-derived IKVAV and YIGSR peptide sequences via maleimide coupling; quantification by BCA and XPS.
- LOVTRAP-BDNF domain expression in HEK293T cells; LOV2 photocycle characterisation by circular dichroism and SPR.
- Electrospinning of polypyrrole-cellulose composite fibres; conductivity measured by four-probe resistivity at 37°C.
- Rheological profiling (oscillatory shear, 0.1–100 rad/s) to confirm injectability and gelation kinetics ($<$90 s at 37°C).

D1.1 Optimised hydrogel synthesis protocol (M6); D1.2 Characterisation data package for Synapse Biomedical regulatory dossier (M12); D1.3 Provisional patent application (M18).

3.3.

Establish that NeuraLattice scaffolds promote directed neurite outgrowth, reduce CSPG inhibition, and enhance synaptogenesis in primary neuronal and co-culture models.

- Rat embryonic DRG isolation and seeding onto scaffolds at three moduli; neurite length quantified by automated ImageJ macro at 24, 72, and 168 h.
- Optogenetic BDNF release (5 mW/cm^2, 488 nm, 10 ms pulses) tested against slow-release PLGA microsphere controls and vehicle.
- Live calcium imaging (GCaMP6f lentiviral transduction) to assess network activity under electrical stimulation (50 mV/cm, 20 Hz biphasic pulses).
- Transcriptomic profiling (bulk RNA-seq, $n = 4$ per condition) to identify mechanotransductive gene signatures (YAP/TAZ, Piezo1).

D2.1 Dose–response neurite outgrowth dataset (M15); D2.2 RNA-seq data deposited in ArrayExpress (M20); D2.3 Co-authored manuscript submitted to *Nature Biomedical Engineering* (M24).

3.4.

Validate NeuraLattice efficacy in a rat thoracic hemisection model (T9 level); delineate mechanotransductive signalling cascades mediating functional recovery.

- Home Office PPL held by Dr Okafor (Apex Neuroscience Institute); 60 Sprague Dawley rats allocated across sham, acellular hydrogel, NeuraLattice, and positive control (Matrigel) cohorts ($n = 15$ per group; power calculated at 80% for BBB locomotion score difference of 3 points, $\alpha = 0.05$).
- Functional assessment: Basso, Beattie, Bresnahan (BBB) scale at weekly intervals; ladder rung walk; von Frey sensory thresholds.
- Light sheet fluorescence microscopy (LaVision BioTec UltraMicroscope II) of cleared tissue; 3D axonal tract reconstruction.
- Phosphoproteomics (TMT-10plex, Orbitrap Eclipse) at M24 and M30 to map RhoA/ROCK and mTOR pathway activation dynamics.

D3.1 BBB functional dataset with statistical analysis (M30); D3.2 3D atlas of scaffold integration deposited as open dataset (M33); D3.3 Second provisional patent for ChABC-microsphere system (M34); D3.4 Final project report and data management plan update (M36).

4 Project Timeline

Work Package / Milestone	Year 1				Year 2				Year 3			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
WP1 Scaffold synthesis												
WP1 Characterisation												
WP2 DRG culture												
WP2 Transcriptomics												
WP3 Animal experiments												
WP3 Phosphoproteomics												
Patent filings												
Dissemination												

5 Team and Resources

5.1.

Lead Applicant

Dr Eleanor Hartley, PhD
Senior Lecturer, Biomaterials Engineering
University of Meridian, School of Life Sciences

- 12 years post-doctoral experience in scaffold design
- 45 peer-reviewed publications; h-index 22
- Holds EPSRC Fellowship (EP/T00421X/1)
- Responsible for WP1 & overall project management

Co-Investigator

Prof. James Caldwell, DPhil
Professor of Translational Neuroscience
University of Meridian, Department of Neuroscience

- Expert in spinal cord injury models (20+ years)
- 97 publications; h-index 41
- Co-director, Meridian Neuroscience Institute
- Responsible for WP2 design & delivery

Industry Co-Investigator

Dr Priya Nair, PhD
Head of Translational Research
Synapse Biomedical Technologies Ltd, Edinburgh

- GMP biologics formulation expertise
- Leads IP and regulatory strategy for Synapse
- Provides £168,490 in-kind contribution
- Responsible for IP, scale-up, and TRL advancement

External Collaborator

Dr Samuel Okafor, PhD
Principal Research Scientist
Apex Neuroscience Institute, London

- PPL holder for rodent spinal cord models
- Specialist in light-sheet imaging & 3D reconstruction
- Access to LaVision UltraMicroscope II facility
- Responsible for WP3 *in vivo* studies

Postdoctoral Researchers: 2.0 FTE postdoctoral research associates (PDRA) are budgeted—one specialist in hydrogel synthesis (Grade 7, University of Meridian), and one in animal behaviour assessment (Grade 7, Apex Neuroscience Institute). Both will be recruited via open competition in Month 1.

PhD Student: 1.0 FTE fully funded PhD studentship for transcriptomic and bioinformatic analysis, supervised jointly by Dr Hartley and Prof. Caldwell.

6 Budget Summary

Budget Heading	FEC (£)	UKRI (£)	Partner (£)
Directly Incurred – Staff (PDRAs × 2, PhD)	421,200	421,200	0
Directly Incurred – Travel & Subsistence	18,400	18,400	0
Directly Incurred – Equipment (rheometer, electrospinning)	62,500	62,500	0
Directly Incurred – Consumables	78,360	78,360	0
Directly Incurred – Animal Costs (PPL, husbandry)	54,200	54,200	0
Directly Incurred – Publication & Dissemination	12,000	12,000	0
Directly Allocated – Principal Investigator (20% FTE)	48,300	0	48,300
Directly Allocated – Co-I Caldwell (10% FTE)	22,000	0	22,000
Directly Allocated – Estates & Indirects	57,000	27,300	29,700
Synapse Biomedical In-Kind (GMP formulation support)	68,490	0	68,490
Total	**842,450**	**673,960**	**168,490**

UKRI contribution is 80% FEC; partner contribution covers 20% FEC for directly allocated staff costs and in-kind GMP resources.

7 Pathways to Impact

Impact Summary

This research targets three pathways to impact spanning academic, clinical, and commercial dimensions.

Academic	Publication of $\geq$4 high-impact papers (target journals: *Nature Biomedical Engineering*, *Advanced Materials*, *Biomaterials*); open data deposition; international conference keynotes (SFN, TERMIS).
Clinical	Mechanistic insights will directly inform a £3.2M NIHR Invention for Innovation (i4i) application targeting first-in-human feasibility (planned 2030); Dr Hartley has a confirmed Letter of Support from Meridian University Hospitals NHS Trust.
Commercial	Two provisional patents will be filed (M18, M34). Synapse Biomedical Technologies Ltd will lead commercial development; Technology Transfer Office agreement in place. A technology readiness level (TRL) advance from 3 to 5 is projected within the grant period.

7.1.

Dr Hartley will deliver two public lectures per annum through the University of Meridian *Science in Society* programme and contribute to the MRC-funded *Brain Awareness Week* outreach campaign. A dedicated project website will be maintained with lay summaries, data visualisations, and video explainers accessible to people living with spinal cord injury and patient advocacy groups including the Spinal Injuries Association (SIA). Social media engagement (`#NeuraLattice`) will amplify reach across X and LinkedIn.

8 Ethical Considerations

All animal work is governed by the Animals (Scientific Procedures) Act 1986 (ASPA) under a Home Office Project Licence held by Dr Samuel Okafor. The 3Rs (Replacement, Reduction, Refinement) principles are strictly observed: sample sizes are minimised consistent with statistical power ($n = 15$ per group); validated humane endpoints are defined; animals are housed in enriched environments with ad libitum food and water. No human tissue or participants are involved. Data management complies with GDPR and the University of Meridian Research Data Policy (v3.2, 2024); all raw data will be FAIR-archived in the UK Data Service within six months of acquisition.

9 References

[1] GrandPre T, Li S, Bhathagar R. Nogo-A signalling restricts axon regeneration in the adult CNS. *Nature Neuroscience*. 2022;25(4):410–421.

[2] Bradbury EJ, Burnside ER. Moving beyond the glial scar for spinal cord repair. *Nature Communications*. 2019;10:3879.

[3] Courtine G, Sofroniew MV. Spinal cord repair: advances in biology and technology. *Nature Medicine*. 2019;25:898–908.

[4] Lutolf MP, Hubbell JA. Synthetic biomaterials as instructive extracellular microenvironments for morphogenesis in tissue engineering. *Nature Biotechnology*. 2005;23:47–55.

[5] Bhattacharya D, Rogerson PJ. Mechanotransduction in neural regeneration: from biophysics to clinical translation. *Advanced Materials*. 2024;36:2309841.

This application was prepared in accordance with UKRI guidance on Full Economic Costing (fEC) and the MRC New Investigator Research Grant guidelines (version April 2026). All budgetary figures are in GBP at 2026 prices. Indirect costs calculated at the University of Meridian's TRAC-agreed rate of 46.2%. For queries contact the Research Office: `grants@meridian.ac.uk` | Tel: +44 (0)1234 567 890.