University of Leicester

EPSRC DLA Studentship

First Supervisor	Dr Yang Hu
School/Department	School of Computing and Mathematical Sciences
Email	hy208@leicester.ac.uk

Second Supervisor	Dr Esther Moss
School/Department	Department of Genetics and Genome Biology
Email	em321@leicester.ac.uk

Additional Supervisor	Professor Shigang Yue (sy237@le.ac.uk)

Section 2 – *Project Information*

Project Title	Biophysically Constrained Dynamic Graph AI for Modelling Tumour Microenvironment Evolution in Uterine Cancer

Project Summary

Uterine cancer is a major women's health challenge in the UK, with around 9,800 new cases annually and approximately 2,600 deaths per year [1]. Beyond overall burden, there is increasing evidence of clinically meaningful heterogeneity in presentation, outcomes and treatment response across patient groups, including disparities associated with ethnic background [2]. This reinforces the need for earlier, more accurate risk stratification and more personalised pathways of care, and aligns with EPSRC priorities in healthcare technologies that emphasise advanced modelling, predictive analytics and decision-support systems.

Digital pathology offers a scalable substrate for such innovation, yet current computational pathology approaches commonly fall into two improvable paradigms. First, high-representation-capacity computer-vision models often require large cohorts and intensive computing, and may learn brittle correlates that do not generalise across centres or staining and artefact variation. Second, classical pipelines that rely on counts and basic morphometrics (e.g., cell size and density) provide weak representations of tissue organisation and overlook interaction structure within the tumour microenvironment (TME).

This project proposes an engineering-led alternative: dynamic, multi-scale graph AI in which tissue is represented as a hierarchical, evolving network of cells and tissue components, explicitly modelling neighbourhood structure and interaction motifs. Crucially, the learning problem will be constrained by biophysical priors derived from established multicellular modelling formalisms (e.g., Cellular Potts and vertex models), which capture how adhesion, packing, mechanical forces and rearrangements shape tissue architecture. Rather than attempting full mechanistic simulation, these principles will be translated into learnable constraints (regularisers, invariances and feasible transition rules) that guide representation learning under limited labels and sparse temporal sampling.

The resulting representations will enable: (1) interpretable modelling of TME state and microenvironment evolution across disease stages or longitudinal specimens; (2) spatially referenced evidence suitable for expert review (regions, cell-type neighbourhoods, interaction changes); and (3) tighter, lower-noise association discovery with multi-omics biomarkers for molecular subtyping and prognosis. Where well-curated multi-ethnic cohorts are available, the same evidence-centric pipeline will support AI-driven hypothesis generation and testing of whether microenvironmental pathways and tissue-omics links are consistent across groups or indicate actionable differences. Methodological generality will be prioritised for reuse across cancer types and institutions.

The project will proceed in three technical routes.

1. Representation extraction and distillation: pathology foundation models [3] will provide expertise-rich multi-scale tissue embeddings; knowledge distillation will compress this capability into efficient graph encoders operating on cell- and region-level tissue graphs. [4]
2. Biophysically constrained dynamics: dynamic graph models (state-space, neural ODE and temporal-attention variants) will be developed to infer microenvironment trajectories from sparse time points or stage-ordered cohorts, while explicitly tracing disease-linked microenvironment evolution pathways on tissue maps (i.e., where and how interaction structure changes as progression unfolds). Constraints inspired by multicellular biophysics (e.g., packing/adhesion consistency, mechanically plausible neighbourhood transitions, and ECM-mediated influence fields) will regularise feasible change.
3. Cross-modal alignment and tasks: multimodal contrastive learning will align graph-derived microenvironment states with omics profiles to support molecular subtyping, prognostic stratification and biomarker discovery, returning uncertainty-aware, tissue-grounded explanations suitable for expert review.

In summary, this PhD project will develop a new generation of dynamic graph AI for computational pathology, treating histology as an evolving interaction network of cells and tissue components. The central vision is to reconstruct microenvironment evolution pathways on tissue maps, showing where, how and why neighbourhood structure changes as disease progresses, and to align these patterns with multi-omics signals to enable molecular subtyping, prognostic stratification and biomarker hypothesis generation [5]. The project is intentionally engineering and AI technical-led: it advances biophysically constrained learning, customisable model distillation from pathology foundation models, spatial/temporal tissue graph modelling under weak supervision, and uncertainty-aware, tissue-grounded explanations designed for expert review. The student will receive rigorous but supportive training in interpretable machine learning, foundation model developing/application, trustworthy AI, reproducible research software engineering, and interdisciplinary translation with precision health partners, preparing them for academic or industrial R&D careers in "AI for science".

References

1. Cancer Research UK. Uterine cancer statistics [Internet]. London: Cancer Research UK; [cited 2026 Jan 12]. Available from: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/uterine-cancer.
2. Azarianpour S, Khalighi S, Aggarwal A, et al. Computational image and molecular analysis reveal unique prognostic features of immune architecture in African Versus European American women with endometrial cancer[J]. NPJ Precision Oncology, 2025, 9(1): 203.
3. Vanea C, Džigurski J, Rukins V, et al. Mapping cell-to-tissue graphs across human placenta histology whole slide images using deep learning with HAPPY[J]. Nature Communications, 2024, 15(1): 2710.
4. Ding T, Wagner S J, Song A H, et al. A multimodal whole-slide foundation model for pathology[J]. Nature medicine, 2025: 1-13.
5. Volinsky-Fremond S, Horeweg N, Andani S, et al. Prediction of recurrence risk in endometrial cancer with multimodal deep learning[J]. Nature medicine, 2024, 30(7): 1962-1973.