	Question	Value
1,1	Proposal	
1,2	Name	Computational Modelling of Cancerous Tumor-Microenvironment Interactions Informed by Spatial Transcriptomics and Perturb-seq Data
1,3	Description	The tumor microenvironment (TME) plays a critical role in cancer progression, metastasis, and response to therapy. Understanding the complex spatiotemporal interactions between tumor cells and their surrounding microenvironment—including immune cells, stromal cells, extracellular matrix, and diffusible chemical signals—is essential for developing effective therapeutic strategies. This project aims to develop a multi-scale, data-driven computational model that integrates individual cell dynamics with molecular signaling in the TME. Objectives: - Build a hybrid computational model that combines a Cellular Potts Model (CPM) to simulate cellular dynamics (e.g., migration, adhesion, proliferation) with partial differential equations (PDEs) to capture the diffusion and consumption of signaling molecules such as cytokines, chemokines, and metabolites in the microenvironment [1]. - Utilize spatial transcriptomics data [3] to parameterize spatial gene expression patterns of both tumor and stromal/immune cells, providing spatial templates for initial model conditions, cell state heterogeneity, and spatial distribution of key signaling molecules. - Leverage high-throughput Perturb-seq data [2] to identify gene regulatory pathways and infer causal mechanisms influencing cell state transitions, especially in response to specific genetic or pharmacological perturbations. Use this information to define intracellular rules governing cell fate decisions within the CPM framework. - Sheraton, Muniraj Vivek, et al. "Emergence of spatio-temporal variations in chemotherapeutic drug efficacy: in-vitro and in-Silico 3D tumour spheroid studies." BMC cancer 20 (2020): 1-16. - Dhainaut, Maxime, et al. "Spatial CRISPR genomics identifies regulators of the tumor microenvironment." Cell 185.7 (2022): 1223-1239. - Du, Yanhua, et al. "Integration of pan-cancer single-cell and spatial transcriptomics reveals stromal cell features and therapeutic targets in tumor microenvironment." Cancer Research 84.2 (2024): 192-210.
1,4	Work environment	The student will join a diverse team of researchers from the Informatics Institute (IvI) and AmsterdamUMC. This group includes experts in AI development, modeling, experimental design, and validation. Students will have the opportunity to work closely with the researchers and contribute to the development of the computational model aimed at unravelling the roles tumor and its microenvironment on cancer progression..
1,5	Expectations	The student should have good programming skills (Python)
1,8	Research Tags	Medical data, computational modelling & Health
1,9	Programmes	
1,10	Contact	Dr. Vivek Sheraton M, v.s.muniraj@uva.nl