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Modelling Across Scales in Development and Disease

Abstract

Most biological systems span multiple spatial and temporal scales. It is often the case that the experimental data is available at a coarse-grained level, while the process of interest operates at much finer scales. Mathematical modelling can help the understanding of how dynamical interactions at different scales filter through at the level of the observable data.

I will talk about two model systems, the developing brain and cancer, to show how data-driven modelling can describe the processes of interest and make testable predictions.

Neurogenesis is the process by which neurons are produced by neural progenitor cells. Many factors influence how neurogenesis differs between species, leading to brains of different shapes and sizes. In order to understand the divergence of evolutionary trajectories resulting in such diversity, we must study and compare the developmental programmes in different species. Critically, to fully understand neurogenesis in development, we are faced with the challenge of understanding the temporal changes in cell division strategy.

Resistance to targeted therapies in a class of cancers (e.g. melanoma and non small cell lung cancer) is poorly understood and seems to be the result of complex interactions between the cancer cells, the host tissue, and the drug. Using a mathematical and computational framework to bridge between experimental models and scales, we can separate intrinsic and extrinsic components of resistance. The ultimate goal is to design an intermittent treatment protocol able to control the emergence of resistance during drug administration, while limiting tumour regrowth during treatment holidays.

The power of these interdisciplinary efforts is to drive an understanding of what is known, and what is left to discover, planning onwards to systematically fill in the gaps. For both systems I will present some preliminary findings and highlight the current limitations in the interpretation of model predictions, identifying a specific need for experimental quantifications.