A Hybrid Discrete–Continuum Modelling Approach to Explore the Impact of Immune Infiltration on Anti-tumour Immune Response

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Understanding the cellular processes that underlie the early stages of tumour development and tumour–immune interaction is important to guide the design of effective treatments, especially immunotherapy. For example, the infiltration of immune cells into the tumour may be associated with the prognosis in various types of tumours. This observation has led to the development of the *immunoscore* [1] as a prognostic marker in cancer patients. The immunoscore provides a score that increases with the density of immune cells present at the center and on the edges of the tumour.

In this talk, I will introduce a discrete-continuum spatial hybrid modelling approach [2] to describe the interaction dynamics between tumour cells and immune cells. In this model, the dynamics of single cells (tumour and immune cells) are described by an agent-based model, coupled with a partial differential equation (PDE) to describe the concentration of a chemoattractant. Such chemoattractant is secreted by tumour cells and dictates the movement of immune cells towards the tumour. I will then present the continuum model that can be formally obtained from such hybrid model, which is given by a coupled system that includes an integro-differential equation for the density of tumour cells, a PDE for the density of immune cells, and a PDE for the concentration of the chemoattractant. The results of computational simulations of the hybrid model will show that there is an excellent quantitative agreement between them and numerical solutions of the corresponding continuum model. These results shed light on the mechanisms that underlie the emergence of different levels of infiltration of immune cells into the tumour and elucidate how immune infiltration shapes anti-tumour immune response. Finally, I will show the impact of immune infiltration on the response of tumour cells to different types of anti-cancer immunotherapy.

References

[1] Galon, J., Bruni, D., *Nat. Rev. Drug. Discov.*, **18(3)**, 197-218 (2019)

[2] Almeida, L. et al., *Bull. Math. Biol.*, **84**, 141 (2022)