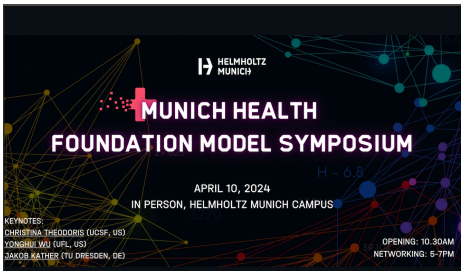

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Probabilistic modeling of tumor infiltration processes

Introduction: Spatial molecular data play a crucial role in understanding the tumor immune microenvironment (TIME). Yet, there is a notable absence of efficient computational techniques for tracking infiltration patterns within cancer tissue. Our work aims to address this gap. Through a graph-based and probabilistic modeling-based approach to spatial data representation, we describe short- and long-distance relationships within tumor tissue. Our approach facilitates the exploration of spatial homogeneity and enables an extended characterization of hot and cold tumor tissues through the infiltration patterns, potentially enabling better stratification of immunotherapy responses.

Materials & Methods: We employ a graph-based approach to represent spatial molecular data as disjoined components with unconstrained shapes, spanned on densely connected tumor tissues. In the setting of probabilistic graph models, we utilize Poisson point processes to detect infiltration patterns within the determined components. Simultaneously, Chinese restaurant processes (CRP) perform non-parametric clustering of the components, ensuring a systematic computation of the optimal number of clusters rather than imposing an arbitrary ad-hoc one. To assess the efficacy of our approach, we conducted analyses on both in-silico and non-small cell lung cancer (NSCLC) multiplex immunofluorescence (mIF) data from the Immucan consortium.

Results: Our in-silico experiments demonstrate the model's capability to accurately infer infiltration patterns from synthetic data reaching average ARI score of around 0.9. The method has proven to be robust, successfully distinguishing patterns shared among many samples, which form large clusters, as well as very small, unique ones. Thanks to the model's explicit formulation, the detected clusters provide precise insight into the composition of cellular infiltration. Moreover, the preliminary results indicate distinct immune infiltration patterns of CD8+ cells between histological subtypes of NSCLC.

Conclusions: We have demonstrated the efficacy of our approach in inferring spatial characteristics and molecular compositions of infiltration patterns in tumor tissues. With further applications of our method, we aim to unveil new biological phenomena and deepen our understanding of immune system dynamics in tumor tissues, providing insights for potential directions of improvements for immunotherapy treatment strategies.

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