From Digital to Computational Pathology for Biomarker Discovery

Mots clés :
● Directeur de thèse : Jean-Christophe Olivo-Marin
● Co-encadrant(s) :
● Unité de recherche : Unité d’Analyse d’Images Quantitative
● Ecole doctorale : École Doctorale Informatique, Télécommunications, Électronique de Paris
● Domaine scientifique principal: Divers

Résumé du projet de recherche (Langue 1)

Aided by advanced image analysis technologies, digital pathology is revolutionizing histopathology by providing objective assessment of cellular components within tissue samples and assisting pathology grading. To date, remarkable progress has been made to obtain clinically relevant quantitative data from pathological samples, including grade-differentiating features in many pathologies. Digital pathology has a unique advantage towards studying the microenvironment in tissue because of its capacity to map the spatial context of interaction of entities of interest (i.e. cell-vessel, cell-tumor, etc.). It makes it possible to explore unexamined relationship between morphology, sub-cellular spatial distribution of proteins and protein-protein interactions. Technological developments to facilitate automated identification of tissue components and rigorous analysis of their spatial heterogeneity are still in the early stages. Objective and reproducible methods for automated identification and statistical analysis of the spatial distribution of microenvironmental components such as immune cells, fibroblasts and vessels remain an unmet need. Development in this direction will accelerate the rate at which histology data is processed as well as the translation of our knowledge of the microenvironment into biomarkers. Within this project, generic methodologies will be developed to extract the interesting features from the tissue images (cell, vessel, etc.). These methods should be able to deal with different stainings (chemical or immunohistochemical or fluorescence, etc.) and multiple factors such as tissue handling, section thickness and staining protocols that can contribute to the high variability in pathological samples. Several approaches such as graph algorithms, active contours, convolutional network would be explored by taking into account the spatial context with the quantitative spatial relations, such as force histograms to segment and extract the objects of interest. Spatial analysis will also be developed. Indeed, the pathology microenvironment consists of many different cell types, with different biological roles and therefore unique relationships with the objects of interest (cells, capillaries, etc.). Spatial analysis can help to elucidate these relationships in several ways: spatial locations, spatial relations (topology, distance), spatial interactions, spatial statistics, spatial distributions etc. with a focus on spatial statistic applied to ecology. Finally, validations will be proposed including i) accuracy and performance measures of the segmentation results, ii) reproducibility against the high variability of the images by testing as much as possible different machines (staining, image acquisition, etc.), iii) control the false positive and negative cases. To enable fair comparison across different samples, methods will be tested to ensure robustness in accounting for such variability, preferably using samples from independent, large-scale patient cohorts.

Résumé du projet de recherche (Langue 2)

Computer enhanced approaches aiming to bring quantitation and objectivity to function such as the recognition of tumor areas within the slide, the automated counting of hybridization signals or quantitation of staining intensity will soon be part of our everyday diagnostic reporting and are already receiving the necessary level of validation and regulatory approval to make this reality.