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SY03.04 | **Data Integration and Modelling**

Cross-Fertilization between Computational Morphogenesis and Digital Pathology

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Introduction/ Background

We believe that Computational Morphogenesis (CM) and Digital Pathology (DP) can be combined to provide valuable tools to study cancer, and improve patient diagnosis and prognosis. CM could play a research-oriented role in the quest to understand the biological and biophysical processes that underlie the different paths of cancer development. DP can play a key role for this task. In return, domain-specific validated CM Model (CMM) such as a stage I colon cancer model could assist routine DP. Our aim is to give an outline of what DP can bring to CM and how DP can be enhanced by incorporating CMMs. In order to have a CM platform that can be tailored to produce a specific CMM, the platform must allow specifying (i) cells lineages and their properties, (ii) their interactions via autocrine, paracrine and endocrine signals and (iii) their interactions with the extracellular matrix. We now describe how data from biology and DP can provide the necessary inputs to switch from a generic CM to specific CMM.

What DP can bring to CM

In cancer studies, cell lineages and their spatial organization can be obtained via tumor-associated (TA) biomarkers such as PD-L1 - PD1 [1] and CD86 - CTLA-4 [2]. Other biomarkers of particular interest include those that characterize TA and non-TA mesenchymal stem cells [3, 4], fibroblasts [5], macrophages [6, 7], and T cells [8]. Using 3D z-staked representations, the instantaneous snapshot of the spatial organization of specific cell lineages can instruct the modeling task, and different dynamic models can be built since TA and non-TA cells of a same general class (e.g. macrophages) can have distinct phenotypes such as promoting or inhibiting tumor progression [6, 7]. Once the 3D spatial organization of the different cell-types is encoded into a CMM, reverse engineering and simulation can help determine putative initial tissue organization that may have led to the current tumor. Similarly, possible future states of the tumor can be predicted and then validated by comparing the simulated 2D/3D features by those obtained from real data. Hence, DP data could constitute one of the cornerstones of the iterative process of CMM specification, calibration, selection and validation. Enhancing DP systems by integrating CMMs Validated CMM could enhance current DP systems for patient diagnosis and prognosis. Machine learning (ML) technics have been applied to analyze 2D WSI [8, 9] and it is very likely that extending such methods to 3D tumor representations will improve the classification task. A large number of CMM-derived 3D reference models (3DRM) of, say, stage 1 colon cancer, could be produced as a complement to 3D models obtained by z-staking. The output of ML technics applied to real and simulated data could then be benchmarked by pathologists in order to assess if, when and how 3DRM can be integrated into decision-support systems dedicated to DP. We have designed a prototype generic CM tool that has been tested to generate multi-scale models of vascularized kidney structures from virtual stem cells. It can be linked to a DP platform for further developments.

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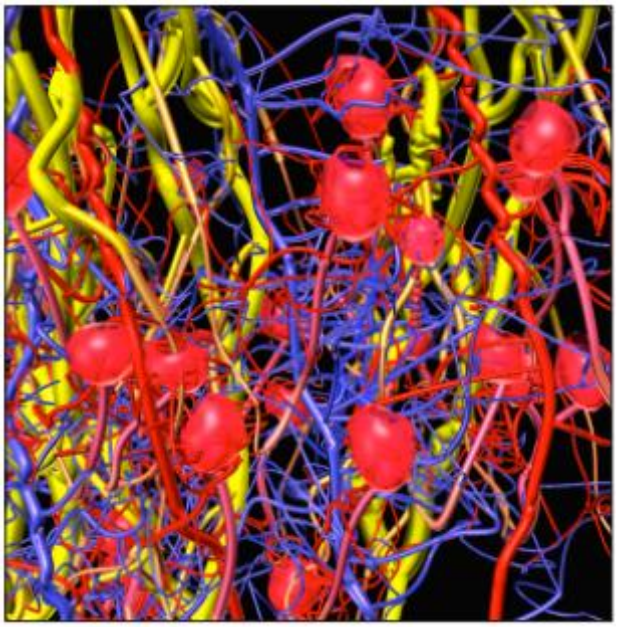

Figure 1: Multi-nephrons, collecting ducts.

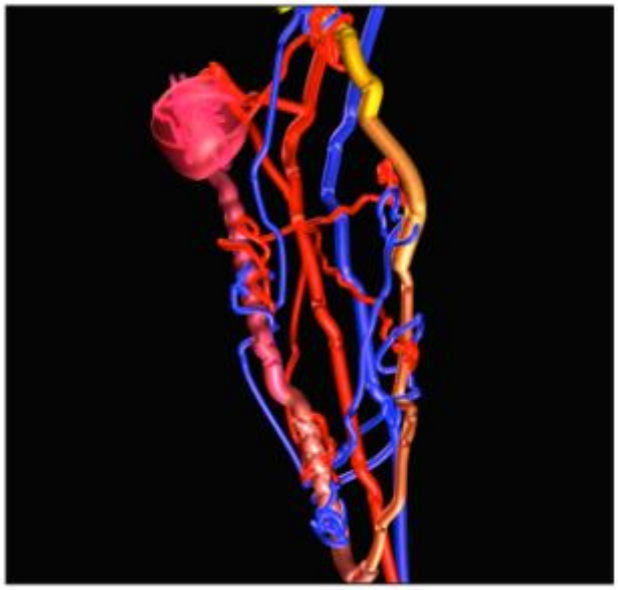

Figure 2: Single nephron generated from virtual stem cells.

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