BRANCHING MORPHOGENESIS IN MAMMARY GLAND:

COMPUTATIONAL RECONSTRUCTION AND MATHEMATICAL MODELING OF DUCTAL TREE

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Localization. TIMC-IMAG, University Joseph Fourier, Grenoble

Period. Starting date can be as soon as January 2015 for a 5-6 month duration

Requirements. Programming skills; Strong interest for interdisciplinary research.

BACKGROUND. In mammary gland, ducts are formed through a process called **branching morphogenesis** in which ductal elongation during puberty is driven by terminal end buds (TEB). TEBs are bulbous, multi-layered structures that direct the growth of each duct throughout the fatty stroma and are thus responsible for the formation of the mammary ductal tree. TEBs generate the primary architecture as a set of tortuous trajectories invading the fat pad from the nipple (see Fig.1.[I]), exhibiting extensive dichotomous (bifurcation) and lateral branching that is essential to achieve the full arborization of the domain.

KEYWORDS. Image processing; Statistical analysis; Mathematical modeling; Persistent random walk.

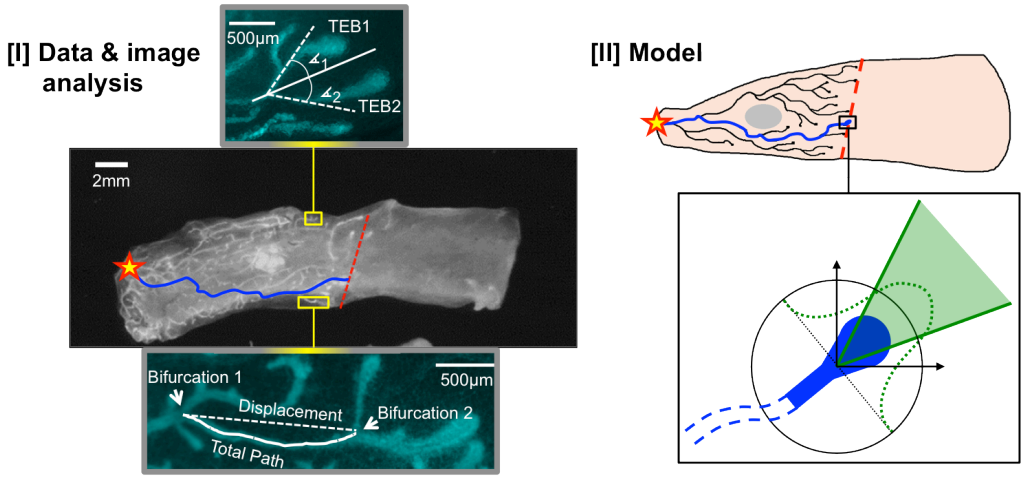

Fig.1: (**Left**) Representative ductal tree of the inguinal gland from a 7 week old mouse : Top – TEB bifurcation event and associated deflection angle ; Center – Single TEB trajectory (blue line) starts from the nipple (star) to reach the demarcating ductal front (dashed red line) ; Bottom – Tortuosity between two bifurcation events. (**Right**) Top – Schematical representation of the mammary gland ductal tree as a set of tortuous TEB trajectory ; Bottom – Single TEB (blue) in the fatty stroma with local direction of movement given by an angular distribution probability (dashed green line) corresponding to confined persistent movement (green cone).

PROJECT. Task [1] The candidate will implement, adapt and use tools of image analysis based on well-known algorithms (e.g. optimal path, ant colony optimization) to extract and reconstruct the tree skeleton of TEB trajectories from images of in-vivo mammary glands provided by our experimental partner Lewis' lab (Baylor College of Medicine, Houston, USA). This task will be performed with specific support from A. Fertin (CNRS) whose expertise lies in the development of image analysis within the Technical Platform (ICTiss) Cellular and Tissue Imaging. **Task [2]** The candidate will perform statistical analysis of the trajectories obtained by image analysis to characterize the geometrical (e.g. curvature) and topological (e.g. branching frequency) properties of the mammary gland ductal tree to derive TEB movement features. **Task [3]** The candidate will develop a mathematical model of TEB movement using the framework of transport equation for persistent biased random walk, to be informed by reorientation and bifurcation probabilities extracted from the analyzed data (see Fig.1.[II]). The candidate is expected to generate numerical simulations of the ductal tree growth by adapting an existing cellular automaton model – that is the discrete counterpart of the mathematical model – developed in our team for comparison to the original in-vivo images. This simulation platform will finally serve to test biological hypotheses on the mechanisms that mediate TEB growth and invasion, an investigation to be performed during a *possible extension of the internship as a PhD thesis follow-up*.