A Mathematical Model for Lymphangiogenesis in Wound Healing

Arianna Bianchi (Dep. of Mathematics)
Supervisors: J.A. Sherratt, K. Painter

The Model
In last decade, several studies have been published suggesting that lymphangiogenesis may play an important role in wound healing process. In particular, enhanced lymphangiogenesis could contribute to resolve inflammation in chronic wounds.

In contrast to angiogenesis' case, few mathematical models exist which describe the formation of lymphatic capillaries. Here we present one that addresses the regeneration of the lymphatic structure after injury.

We considered five factors (variables) to describe the basic dynamics of the process.

VARIABLES:
* Active TGF-β concentration (pg/mm³)
* Inflammatory Macrophages density (cells/mm³)
* VEGF concentration (pg/mm³)
* Lymphatic Endothelial Cells density (cells/mm³)
* Lymphatic Capillaries density (cells/mm³)

The Equations
The interactions among the variables are described through a system of ODEs.

To each variable corresponds an equation that tells how the concentration/density of that quantity varies in time.

A solution of the system is a set of five functions that describe how the amount of the different cells and proteins changes as time passes.

In order to solve the system, we require an initial condition for each variable and about 30 parameters in total: these have been calculated from real datasets when possible, or estimated otherwise.

Rate of change of TGF-β =

- activation by enzymes & MØs
- decay

Rate of change of Macrophages =

- constant chemotaxis by TGF-β
- logistic growth - removal and metamorphosis

Rate of change of VEGF =

- constant source + production by MØs - decay - use by LECs

Rate of change of LECs =

- growth upregulated by VEGF and downregulated by TGF-β
- inflow and chemotaxis - crowding effect - self-organization in capillaries

Rate of change of Capillaries =

- self-organization of LECs

Simulation Output
A simulation of the model was performed using MatLab: the solutions' plots are then compared with real datasets found in the literature.

From: Al-Mulla et al. 2011
From: Mirza & Koh 2011
From: Al-Mulla et al. 2011
From: Rutkowski et al. 2006
From: Boardman & Swartz 2003