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# A FINITE ELEMENT MODEL FOR WOUND HEALING

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## ABSTRACT

Wound healing proceeds by a number of (partially) overlapping steps: bleeding, blood clotting, removal of contaminants and bacteria, wound closure by cell mitosis and migration towards the wound center, repair of the vascular network, and wound contraction along lines of equal tension.

We consider a model due to Adam [1] for the closure of a wound. The model is based on an epidermal growth factor that stimulates cell division and growth. Cell division, and hence also wound closure, takes place if the epidermal growth factor exceeds a threshold value. In the model, a wound heals as a result of a generic growth factor. Consider a computational domain, $\Omega$, then the wound is located within $\Omega$. The wound is surrounded by an active layer, denoted by $\Omega_a$, in which the growth factor is produced. The growth factor is also subject to decay and diffusion, which is formulated mathematically by

$$\begin{aligned} &\frac{\partial c}{\partial t} = D\Delta c + Pf(x,y) - \lambda c, \\ &f = f(x,y) = \begin{cases} 1, & (x,y) \in \Omega_a, \\ 0, & (x,y) \in \Omega \setminus \Omega_a, \end{cases} \end{aligned} \tag{1}$$

where the function $f(x,y)$ expresses that the growth factor is produced in the active layer only. Here $c$ represents the concentration of this growth factor, which enhances the proliferation of cells. We assume that healing at a certain location of the wound edge takes place if and only if the growth factor concentration exceeds a threshold concentration $\hat{c}$. Furthermore, the rate of closure is assumed to depend on the local curvature of the wound edge, hence

$$v_n = (\alpha + \beta\kappa)H(c - \hat{c}), \quad (x,y) \in \Gamma(t), \tag{2}$$

where $\kappa$ represents the local curvature, further $\alpha$ and $\beta$ are nonnegative constants and $v_n$ represents the normal component of the velocity of the wound edge where the unit normal vector points into the wound.

In order to have cell division, a sufficient supply of nutrients and oxygen to the wound site is indispensible. This is accomplished by the regeneration of the damaged vascular network underneath the wound

site. This regeneration is commonly referred to as angiogenesis. For the regeneration of capillaries, the model due to Maggelakis [2] is used. The model is based on the assumption that the shortage on oxygen triggers the macrophages on the wound site to produce their macrophage derived growth factors. These growth factors enhance the regeneration of capillaries that supply the oxygen to the wound site such that wound closure sets in.

The equations are solved using finite element techniques, in which the moving boundary in the closure part is tracked using a level set method with a fast marching method for the reinitialization of the level set function.

In our present and past work, the models due to Adam [1] and Maggelakis [2] have been coupled. An present innovation is the coupling with mechanical effects since the local strain of the extracellular matrix (ECM) has a significant influence on the cellular movement and on the formation of capillaries. We follow the models due to Murray [3] and Maini *et al.* [4]. The deformations imply that a 'convective' term to the conservation equations has to be added of $\nabla \cdot (c_p \mathbf{u}_t)$, where $c_p$ represents one of the concentrations and $\mathbf{u}$ denotes the displacement vector of the ECM. Further, we need to track the ECM density and to deal with a mechanical balance. This is expressed mathematically by

$$\begin{aligned} \frac{\partial \rho}{\partial t} + \nabla \cdot (\rho \mathbf{u}) &= 0, \\ \nabla \cdot \sigma &= s\rho \mathbf{u}, \end{aligned} \tag{3}$$

in which $\rho$ and $\sigma$ respectively denote the ECM density and the stress tensor. According to Murray [3], the stress tensor consists of a viscous and of an elastic term. For the relation between the elastic stress and strain, Hooke's Law is used. The right hand side of the above equation is the body force acting on the ECM, which is assumed to be proportional to the ECM density and its displacement. The viscous part contains a time derivative of the strain and dilation. The cell motility depends on the local strain. Since the cell motility around the wound edge is modeled by equation (2), the constants $\alpha$ and $\beta$ depend on the local stress and hence equation (2) has to be adjusted accordingly. This is necessary, since maintaining $\alpha$ and $\beta$ constant during the simulation, will give predictions in which a wound tends to become more circular. However, according to Murray [3], a wound tends to become more elongated in reality since faster healing seems to occur in directions normal to the lines of equal tension.

It is one of our aims to investigate the influence of the local stresses on the wound healing process. As far as we know, the presented approach consists of a combination of accepted theories, but it is novel as such.

## REFERENCES


[1] F.J. Vermolen, E. van Baaren and J.A. Adam. "A simplified model for growth factor induced healing of wounds", *Math. and Comput. Model.*, Vol. **44**, 887–898, 2006.

[2] S.A. Maggelakis. "A mathematical model of tissue replacement during epidermal wound healing", Appl. Math. Model., Vol. **27**, 189–196, 2003.

[3] J.D. Murray. *Mathematical biology II: Spatial models and biomedical applications*, 3rd. Edition, Springer, 2003.

[4] L. Olsen, J.A. Sherratt and P. Maini. "A mechanochemical model for adult dermal wound contraction and the permanence of the contracted tissue displacement profile". *J. theor. Biol.*, Vol. **177**, 113–128, 1995.