On a mathematical model of epidermal wound healing in Drosophila embryos

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Wound closure is critical for correct functioning of multicellular organisms, since gaps in tissue can occur at all stages of life either due to natural events, such as development or organ remodelling, or as a result of injurious events [1, 2]. In all cases prompt closure of a gap is important for the restoration of physiological functions. Consequently, improving our knowledge of the driving mechanical forces during wound closure is crucial for a better understanding of biophysics of this phenomenon.

In this talk we consider epidermal wound healing in Drosophila embryos. Current mathematical models in this area focus either on the mechanical role of wound's boundary or on the mechanical role of the tissue surrounding the wound [3–5]. Furthermore, typically, existing models aim to describe in vitro experiments with tissue layers [5, 6]. Here we propose a nonlinear mathematical model of wound closure in Drosophila embryos that quantitatively captures the kinetics of wound healing observed in vivo. The model takes into account coupling between forces generated by actomyosin cable and shape-dependent linear and nonlinear epidermal elasticity. We assume that the elastic response generated by surrounding cells is a nonlinear function of the deformation of a wound's initial shape.

From a mathematical point of view, the proposed model is a system of two nonlinear parabolic partial differential equations with three main parameters that correspond to actomyosin cable and linear and nonlinear elasticity. We also consider an invariant reduction of the proposed model that corresponds to circular wounds. We demonstrate that there is a saddle-node bifurcation in this reduction, that describes switching between healing and non-healing. This switching is determined by interaction between contracting and elastic forces and wound's initial size.

We fit the model with in vivo experimental data obtained in Jerome Solon's group. The experiments are made on living drosophila embryos and consist of making small laser cuts in them. As a result, time evolution of a wound's boundary and wound's area are available for comparison with the model.

In order to obtain estimations of the model parameters we use a Bayesian statistical approach, where probability distributions for the values of the parameters are calculated. We demonstrate that there is qualitative and quantitative agreement between the model and the experimental data both in the area kinetics and wounds shape. We also show that there is a correlation between the concentration of myosin and fitted value of the parameter responsible for the line tension at the wound boundary.

Finally, we introduce non-dimensional variables and reduce the number of parameters to two. This allows us to find an analytic parametric representation of the bifurcation curve in the circular approximation. We demonstrate that all wounds from the control group lie within the healing region in the phase diagram, which corresponds to the experimental data. Finally, we believe that it is possible to introduce genetic perturbations that will produce switching from healing to non-healing, that is points on the phase diagram will cross the bifurcation line.

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