A Dynamic Model of Wound Healing

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Abstract - Mathematical modelling methods have been used to describe complex processes of wound healing dynamics. A reasonable simplification of the physiological data has been considered and functional elements of the wound were defined.

I. Introduction

Wound healing is a complex dynamic process. Most of the methods that have already being used in practice evaluate the process of wound healing by observing the volume and the area of wounded tissue. In order to describe the reduction of the wound volume some empirical models have been developed. Mainly a simple exponential function is used [2].

These models do not consider complex wound healing dynamics which include onset, wound propagation and healing. In most cases they dealing solely with one of the mentioned processes and are useful in its evaluation.

Our purpose is to propose a model of wound healing dynamics based on the known physiology of healing and its simplifications. The possibility of determinig parameters, which significantly affect the healing process and make possible better correspondence between simulation and experimental results is expected.

II. Material

A few new terms have been introduced in order to simplify the complex wound healing functional elements. These simplifications are based on physiological data and have been obtained from the qualitative description of healing mechanisms for acute and chronic wounds in related publications [1]. Six functional wound elements were introduced, the terms and definitions of which are shown in table I.

Item	*Elements of wound*
bricks	collagen, elastic fibres epidermal cells basic connective substances
waste	proteolytic enzymes, injured cells, biologically active polypeptides, active substances of blood, monokines, derivate of phospholipides
cleaners	neutrophilic granulocytes, monocyes
builders	fibroblasts
transport	vessels
protector	epidermis

TABLE I
DEFINITIONS OF WOUND ELEMENTS

Bricks represents the essential elements of tissue. They are used as a skeleton onto which other structures are built. *Waste* combines the elements that enable inflammation and are not present in healthy tissue. It represents chemotactical and growth factors for *builders, cleaners* and *transport*. The function of *cleaners* is to remove waste and thereby to estasblish the necessary enviromental conditions of the *waste* and therefore to establish the environmental conditions for the build up of a new tissue growth. The *cleaners* represent chemotactical factors for the *transport* and *builders*. The *builders* produce *bricks*. *Cleaners* and the material that is used by *builders* are supplied by *transport*. And finally, the *protectors* protect tissue from external influences.

III. Method

A system of nonlinear ordinal differential equation was developed. Analysis of the system and simulation of the mathematical model was carried out by

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a programme written in "Mathematica" [3]. It was presumed that the wound was comprissed of one compartment only. The number of elements belonging to a certain item according to a normalised measure of concentrations B for *bricks* and W for *waste*. The role of builders, transport and protection was to join a common factor F. A theory of competition between B and W was applied and the influence of the additional, related factor F took place in the model proposed. A descriptive model of wound healing was postulated: The concentration of bricks B and wastes W inside the wound are determined by the process of their competition and limited growth. The growth of the bricks is influenced by factor F which also controls the speed of waste destruction. The concentration of factor F is increased by the content of waste W and is decreased in the presence of bricks B. The growth of the factor F is also limited.

The dynamic mathematical model of the basic wound healing mechanisms described above is defined by a system of nonlinear, differential equations:

$$\begin{aligned}\frac{dB}{dt} &= r_b\, F\, B\Big(1-\frac{B}{k_b}-\alpha\frac{W}{k_b}\Big)\\ \frac{dW}{dt} &= r_w\, W\Big(1-\frac{W}{k_w}-\beta\, F\frac{W}{k_w}\Big)\\ \frac{dF}{dt} &= F(1-F)\, B\,(1-B)\end{aligned}$$

where B is density of *bricks*, W is density of *waste*, F is density of other factors, r_b and r_w are growth velocity constants, and k_b and k_w are capacities of *bricks* and *waste* respectively. α and β define mutual influence constants. All coefficients are nonnegative.

The stationary points of the system were analysed analytically by means of a Jacobi matrix and their eigenvalues values. But the most illustrative way to present the system characteristics is by simulation of the model.

IV. Results and Discussion

The Runge-Kutta integration method is used and results are plotted in a phase plane of B and W. If the constants $r_b = 1$, $r_w = 1$,$\alpha = 2$ and $\beta = 2$ are chosen, for the initial condition:

$P_1: \; B_0 = 0.6 \; W_0 = 0.1 \; F_0 = 0.5;$

$P_2: \; B_0 = 0.5 \; W_0 = 0.1 \; F_0 = 0.5;$

and if the F is considered as a constant value in the time interval during observation of the system, the results of the simulation are shown in Fig. 1. From the initial condition P_1 the system converged at stabile point E_1 which means the wound is filled with the *waste* and therefore the chronic wound was not healing. From the initial point P_2 the dynamic system converged at stabile point E_2. This reforce to the conditions where the wound was healing because it was filled with *bricks*.

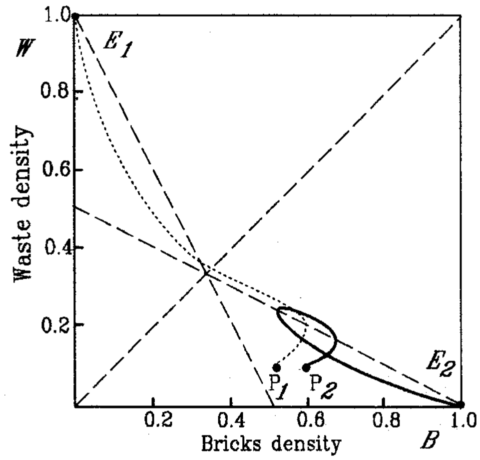

Figure 1: Trajectories of simulation in phase plane B – *brics*, W – *waste*) for chosen initial conditions P_1 with dashed line and for P_2 with solid line.

In this way a complete analysis of the mathematical model might be performed, and convergence regions of three-dimensional space of the variables B, W and F can be determinated in dependence of the constants of the model.

Even this simplified model shows how the process of wound healing is difficult to analyse. However, the possibility of the parameters having an influence on healing is evident, especially in a preliminary enlargement of the wound immediately after its appearance.

References

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