Models of Wound Healing

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ABSTRACT — **Dynamic models of wound healing are mostly based on qualitative descriptions of biological systems. However, mathematical modeling methods have been used less extensively. We have developed two different models and proved good correspondence between simulation and experimental results.**

1 Preface

Wound healing is a dynamic process. Most of the methods, that have been already used in practice, evaluate the process of wound healing by observing the volume and the area of wounded tissue. Therefore some empirical models which use exponential function to describe the reduction of the wound volume have been developed[3,5].

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

2 Material

Physiological data, essential for the model construction, have been obtained mostly from the qualitative description of wound healing in publications [6,2]. In order to simplify the rather complex system we introduced new terms, which combine functionally alike wound elements.

Bricks represent the basic elements of tissue. They are used as skeleton into which other structures are inserted. *Waste* combines mostly the elements, that enable inflammation and are not present in normal tissue. It represents chemotactical and grow factors for *builders*, *cleaners* and *transport*. The function of *cleaners* is the removal of *waste* and therefore to establish the environment suitable for the building of new tissue. *Cleaners* represent chemotactical factors for *transport* and *builders*. *Builders* produce *bricks*.

Table 1: Definition of terms

item	elements of wound presented by item
bricks	collagen
waste	proteolytic enzymes, injured cells, other biologically active polypeptides, active substances of blood, derivates of phospholipides
cleaners	neutrophilic granulocytes, monocytes
builders	fibroblasts
transport	veins
protection	epidermis

Cleaners and the material that is used by *builders* are supplied by *transport*. Protection protects tissue from external influences.

Experimental data have been found at Cleveland Clinic Foundation, Ohio and at Faculty for Electrical and Computer Engineering in Ljubljana[3,4,5].

3 Method

The system of nonlinear differential equations is used. Analysis of the system and simulation of the model is carried out by the program written in "Mathematica"[8].

The model represented by the system of ordinary differential equations does not offer the possibility of dimensional presentation of wound. Therefore the original modeling method based on discretization of simulation space has been introduced[7].

A system, which provides the use of the mentioned method, has been developed. It combines the editor for model description, the simulation program and graphical interface.

CH2964-5/91/0000-0737$01.00

Let us presume that the wound is formed of one compartment only. The number of elements belonging to certain item is determined by normalized measures (measure B for ***bricks***, W for ***waste*** and T for ***transport***). The dynamical model is therefore

$$\begin{aligned} \frac{dB}{dt} &= -rWB + (sT - ds)W \\ \frac{dW}{dt} &= rWB - (sT - ds)W \qquad (1) \\ \frac{dT}{dt} &= (1-T)(1-B)W \end{aligned}$$

where d defines the rate for decomposition of ***bricks***, s defines the influence of ***transport*** and ***waste*** on the rate of synthesis and ds defines the influence of ***waste*** increase on account of the decrease of the number of ***bricks*** due to inflammation process.

The stability of the system was determined by studying linearized equations [6,7]. Figure 1 shows the example of the result of model simulation. The example of different s and d values to preliminary enlargement of wound immediately after its appearance is also shown (Figure 2).

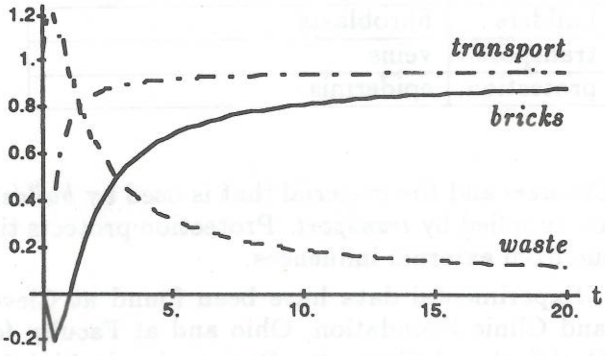

Figure 1: B, W and T values as a function of time

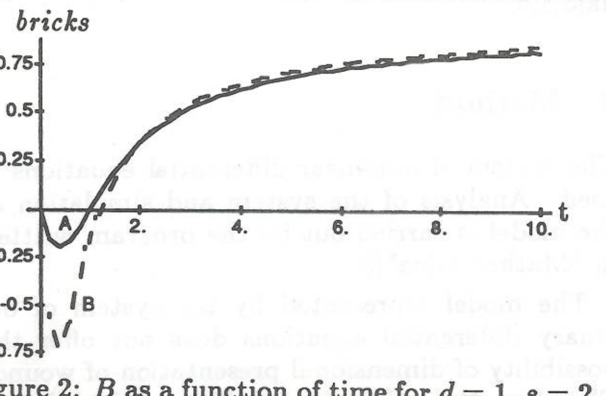

Figure 2: B as a function of time for $d = 1$, $s = 2$, $ds = 1$ (curve A) and $d = 1$, $s = 4$, $ds = 3$ (curve B)

The model based on discretization of simulation space deals with ***waste***, ***bricks***, ***cleaners***, ***builders***

```
ITEMS
 WASTE,BRICK,CLEANER,BUILDER,TRANSPORT;

INIT
 ITYPE=BLOCKW,
 EXTREMES WASTE IN (0,NQ) & CLEANER IN (0,NQ),
 EXTREMES BUILDER IN (0,NQ) & BRICK IN (0,NQ),
 EXTREMES TRANSPORT IN (0,NQ),
 INVERSE WASTE;

BORDER
 BTYPE=WEXTREMES;

MODEL
 WASTE:
   IF WASTE > 0 THEN
    BEGIN
     IF BRICK > 0 THEN
      IF WASTE > OZARAZZ THEN
       BEGIN
        SUB BRICK;
        ADD WASTE
       END;
     IF WASTE > 0 THEN
      IF FIND MIN WASTE THEN
       BEGIN
         TRANS WASTE;
         ADD WASTE
       END
    END,
 CLEANER:
   IF CLEANER > 0 THEN
    BEGIN
     IF WASTE > 0 THEN
      BEGIN
       SUB WASTE;
       IF WASTE > 0 THEN
        SUB WASTE
       END;
     IF CLEANER > 0 THEN
      IF FIND MINMAX CLEANER TRANSPORT THEN
       BEGIN
        IF FOUND CLEANER 2 NQ THEN
         TRANS CLEANER
       END
      ELSE
       IF FIND MAX WASTE THEN
        TRANS CLEANER
    END,
 BUILDER:
   IF BUILDER > 0 THEN
    BEGIN
     IF &(TRANSPORT 3 TZAGRAD, BRICK 2 NQ) THEN
      ADD BRICK
     ELSE
      IF !(TRANSPORT 2 MALOT, BRICK > NQ) THEN
       IF BRICK > 0 THEN
        BEGIN
         SUB BRICK;
         ADD WASTE
        END;
     IF FIND MINMAX BUILDER CLEANER THEN
      TRANS BUILDER
     ELSE
      IF FIND MAX WASTE THEN
       TRANS BUILDER
     END,
 TRANSPORT:
   IF TRANSPORT > 0 THEN
    BEGIN
     IF BRICK > NQ THEN
      SUB TRANSPORT;
     IF TRANSPORT > 0 THEN
      IF FIND MIN TRANSPORT THEN
       TRANS TRANSPORT
     ELSE
```

```
TRANS TRANSPORT;
IF &(TRANSPORT<NQ,TRANSPORT>MTR) THEN
ADD TRANSPORT
END.
```

Figure 3 presents the results of simulation of the model. Each picture shows the distribution of certain item in the simulation space at certain time of the simulation process. Simulation time is proportional to the number of iterations of the model.

The number of the elements belonging to certain item in the simulation space division is presented by pattern intensity. The more intensive is the pattern the higher is the number of elements in division.

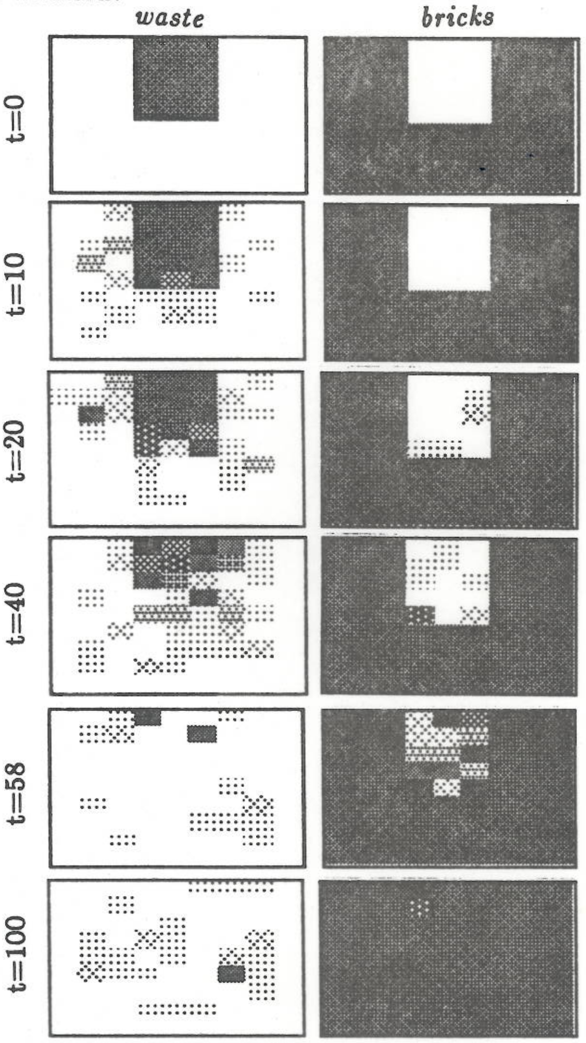

Figure 3: The results of model simulation for *bricks* and *waste*

5 Conclusion

The results of simulation of dynamic models have been compared with experimental data. Figure 4

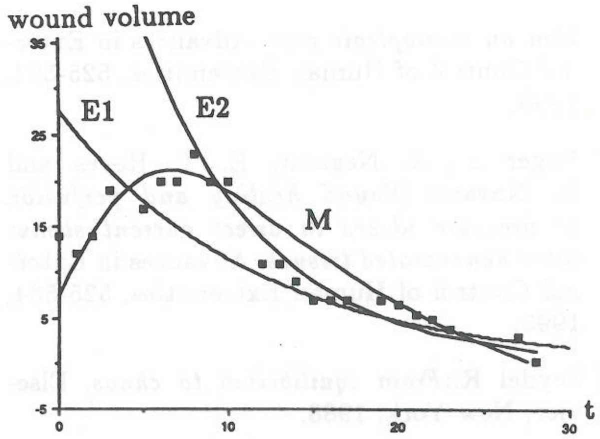

Figure 4: Comparison of wound volumes

presents the comparison of wound volumes as a function of time for different models. Experimental data is shown by the points in the diagram. The behavior of dynamic model (1) is presented by the curve M. The number of *bricks* has been used as a measure for wound volume (the higher the number of *bricks* the smaller the volume). Exponential functions E1 and E2 are empirical models gained according to all data and according to data from the maximum wound volume on.

It is evident that dynamic model (1) provides much better prediction of wound volume changes than both empirical models.

The analysis of both developed models shows important influence of preliminary enlargement of wound immediately after its appearance to the process of wound healing. This corresponds with the actual healing process.

We expect these suggested models to be applicable to bed sores or other chronic wounds.

References

[1] Ferluga D. in A. Vizjak: *Vnetnice in kemični vnetni faktorji*. Ljubljana, Katedra za patologijo Medicinske fakultete v Ljubljani, 1986.

[2] Hunt K.T.: *The physiology of wound healing.* Annals Emerg. Med. ,12:23-31, 1988.

[3] Krošelj P., V. Valenčič, A. Stefanovska., L. Vodovnik, R. Karba, A. Jerčinovič.: *Baza za zbiranje in obdelavo podatkov o električnem celjenju preležanin.* Proceedings of $XXXIV^{th}$ conference of electronics, telecommunications, automation and nuclear engineering, Zagreb, 1990.

[4] Negami S., T. F. McGovern, E. T. Reyes, E. Z. Browne and S. I. Reger: *An experimen-*

tion on monoplegic pigs. Advances in External Control of Human Extremities, 525-534, 1990.

[5] Reger S., S. Negami, E. T. Reyes and R. Navarro: *Wound healing and perfusion of pressure ulcers in direct current stimulated deneverated tissues.* Advances in External Control of Human Extremities, 525-534, 1990.

[6] Seydel R.: *From equilibrium to chaos.* Elsevier, New York, 1988.

[7] Zupan B., T. Šketa: *Modeliranje celjenja ran.* Delo po razpisu za Prešernovo nagrado študentom, Ljubljana, Fakulteta za elektrotehniko in računalništvo, 1990.

[8] Wolfram S.: *Mathematica.* Addison-Wesley Publishing Company, Inc., Redwood City, 1988.

6th Mediterranean Electrotehnical Conference

22-24 May 1991

"Cankarjev dom" – Cultural and Congress Center

Ljubljana, Slovenia, Yugoslavia

Proceedings
Volume I

Edited by

Baldomir Zajc

Franc Solina

IEEE Catalog Number: 91CH2964-5
ISBN 0-87942-655-1 Softbound Edition
ISBN 0-87942-656-x Casebound Edition
ISBN 0-87942-657-8 Microfiche Edition
Library of Congress Number 90-86045