Multiphysics Modeling of Gas Plasma-Based Wound Healing Process

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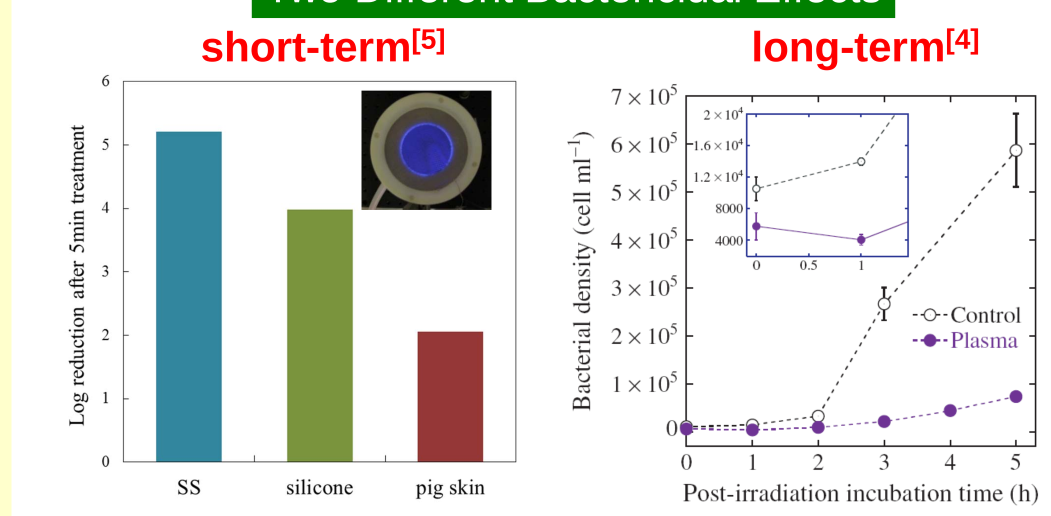
BACKGROUND

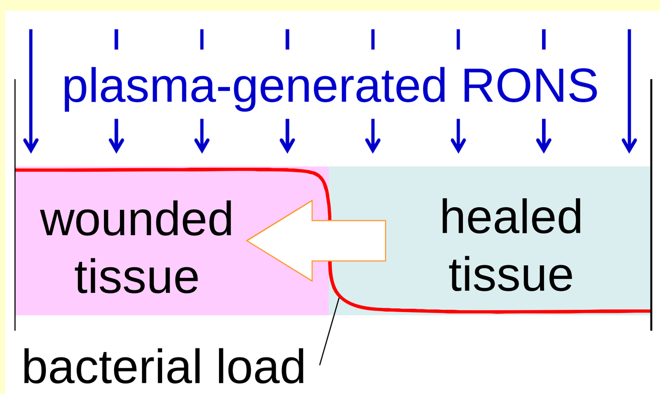
Wound healing is one of the promising applications of atmospheric pressure gas plasmas in medicine. Recent clinical studies show a significant reduction of bacterial load in treated wounds without any side-effects. [1]. Plasma-generated reactive oxygen/nitrogen species (RONS) are thought to be directly or indirectly responsible for the bacterial elimination. Previous experimental results suggest that those reactive species have both instantaneous and long-term bactericidal effect. [2-5] In order to investigate the short- and long-term antimicrobial effect on wound healing, we adapted a five species mechano-chemical model of epithelial wound healing. [6] Our preliminary simulation result [7] shows that the prolonged effect of plasmas is important and that the initial reduction in the bacterial population may not be sufficient for improved healing.

Two Different Bactericidal Effects

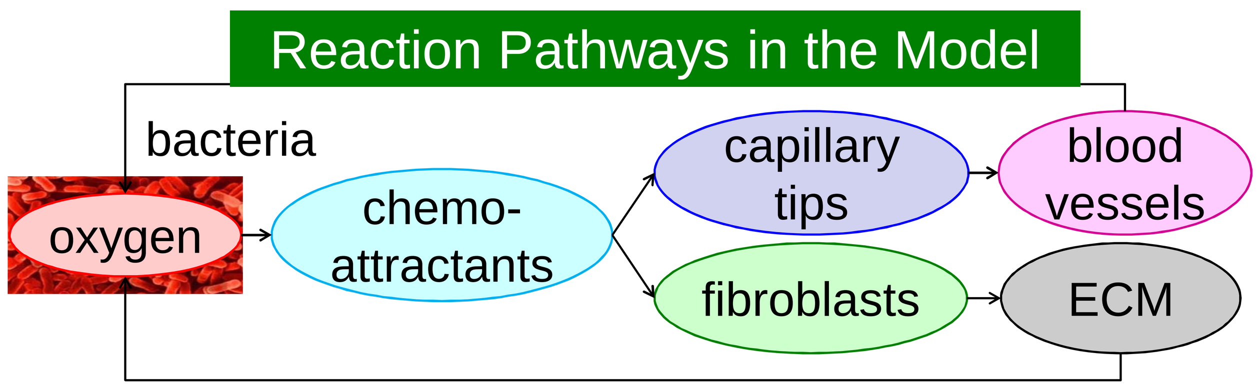


MODEL DESCRIPTION

- 6-species PDEs
- 1-D Cartesian coordinates
- modified parameters
- additional terms for plasma treatment



Reaction Pathways in the Model



Governing Equations

- **Oxygen: c**

$$\frac{\partial c}{\partial t}+\nabla\cdot(-D_c\nabla c)=-\left(\frac{k_1}{1+k_b e}P_n+k_2 e\right)\frac{c}{k_3+c}-k_4 bc+k_5 b$$

plasma treatment; consumption by bacteria

- **Chemoattractants : a**

$$\frac{\partial a}{\partial t}+\nabla\cdot(-D_a\nabla a)=-k_6 ab-k_7 a+\frac{k_8 H(c-c_L)H(c_H-c)}{1+e}$$

production

- **Capillary tips: n**

$$\frac{\partial n}{\partial t}+\nabla\cdot(-D_n\nabla n)=\nabla\cdot\left(\frac{-\kappa_n en}{(1+e^2)(1+a)^2}\nabla a\right)+a(k_9 b+k_{10}n)-n(k_{11}n+k_{12}b)$$

chemotaxis

- **Blood vessels: b**

$$\frac{\partial b}{\partial t}=-\frac{\kappa_n en}{(1+e^2)(1+a)^2}\nabla a+k_{13}b(k_{14}e+k_{15}f-b)$$

production by capillary tips

- **Fibroblasts: f**

$$\frac{\partial f}{\partial t}+\nabla\cdot(-D_f\nabla f)=\nabla\cdot\left(\frac{-\kappa_f f}{(1+a)^2}\nabla a\right)+\frac{k_{16}fc}{1+c}-\frac{k_{17}f^2}{(1+c)(1+e)}$$

chemotaxis

- **Extracellular matrix (ECM): e**

$$\frac{\partial e}{\partial t}=k_{18}f\,c(k_{19}c-e)$$

deposition

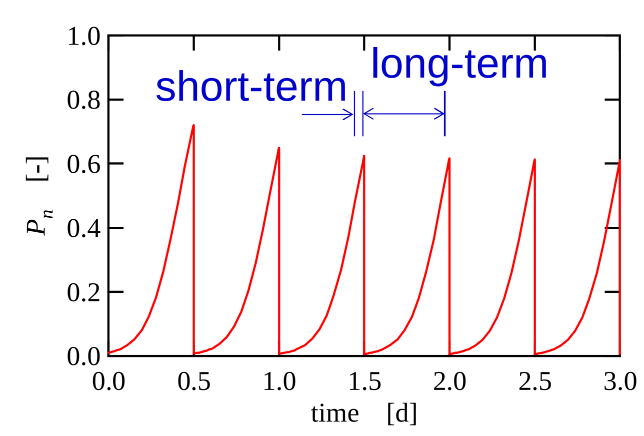
SIMULATION RESULTS

Bactericidal Effects of Plasmas

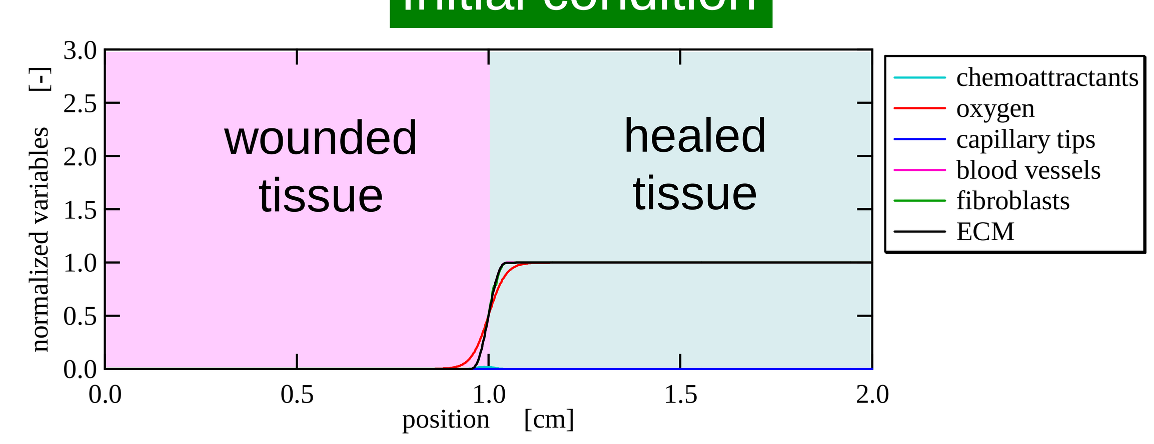
Twice/day plasma treatment

- Short-term effect: 99% direct reduction (R)
- Long-term effect: 90 min doubling time (k_p)

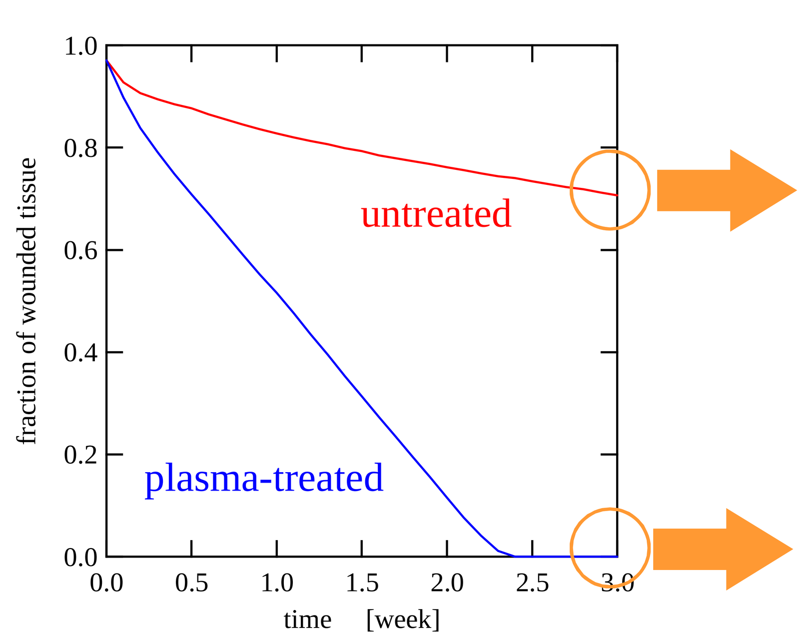
Fraction of bacterial load: $P_n=\frac{RP_{n-1}\exp(k_p t)}{1+RP_{n-1}\{\exp(k_p t)-1\}}$



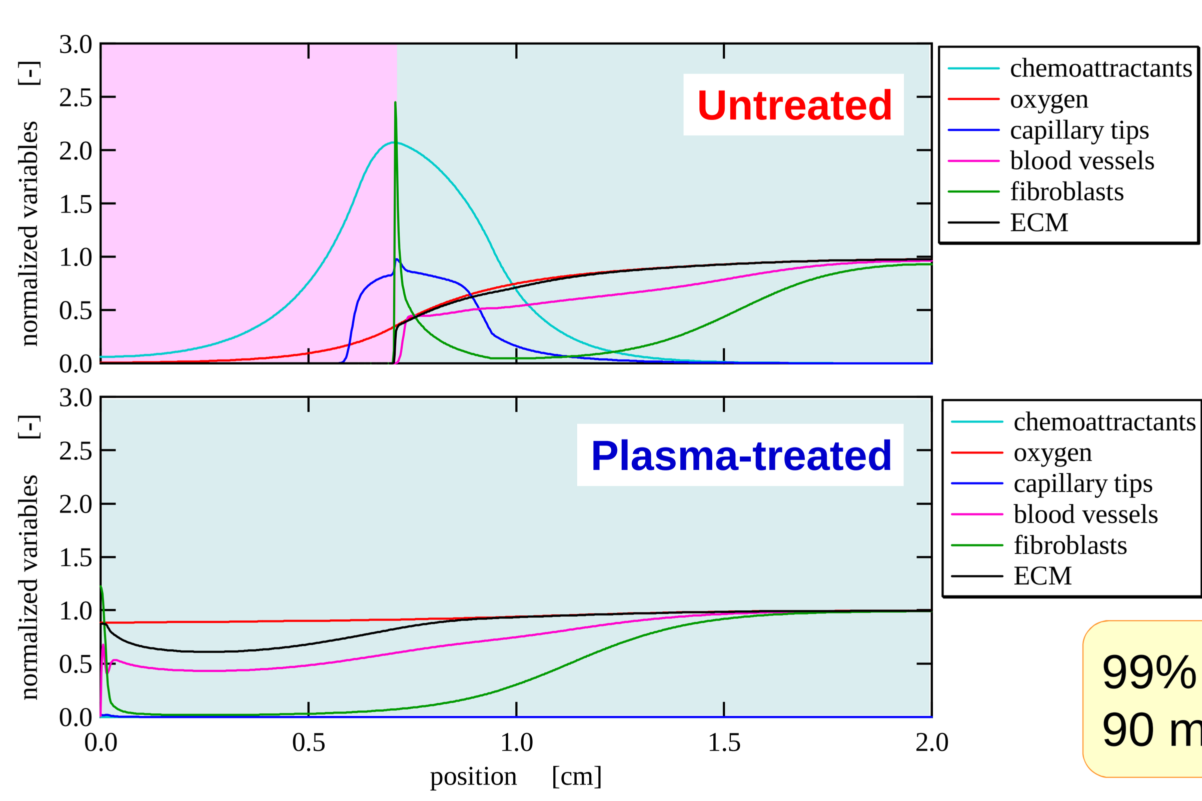
Initial condition



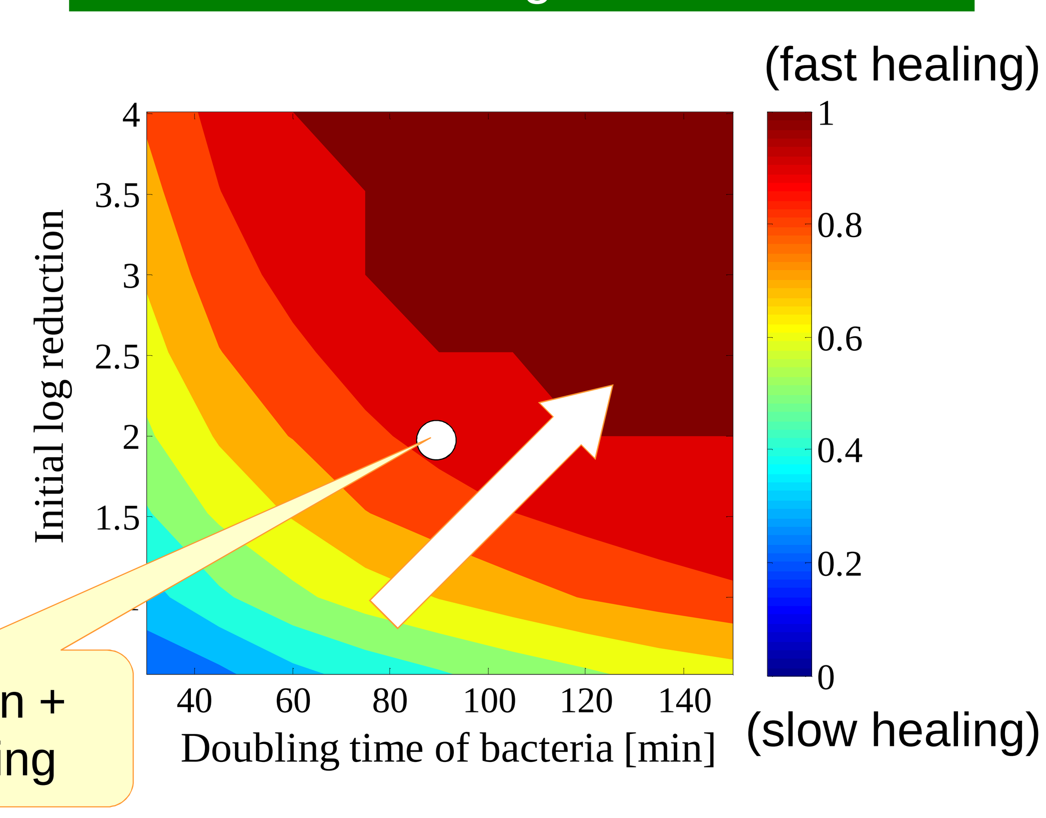
Fraction of wounded tissue



Chronic Wound Healing After 3 weeks



Contribution of long/short-term effect



CONCLUDING REMARKS

- ✓ We developed a 6-species mechano-chemical wound healing model with plasma sterilization effects. In our model, the reduction of bacterial load increases oxygen concentration in wound and promote the healing process.
- ✓ We proposed that gas plasma treatment of wound has two effects: the initial reduction of bacterial load (short-term effect) and the delay of bacterial growth rate (long-term effect).
- ✓ The present results suggest several important directions for coupling plasma models with models of tissue biochemical responses.

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