Oxygen Diffusion in Wound Healing

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Abstract

Chronic wounds plague a large number of patients worldwide, and hyperbaric oxygen therapy has been demonstrated to allow some of these problematic wounds to follow a more typical healing profile. Unfortunately, most of the evidence regarding the pathophysiological basis of hyperbaric oxygen therapy as a treatment remains empirical. In this paper, we develop a mathematical model that allows us to quantify the diffusion of oxygen in wound bed tissue in response to treatment with hyperbaric oxygen therapy over time. We then validate our results and discuss some potential applications.

Background

Wound healing is a highly regulated and complex process. Typically, wound healing progresses through stages of hemostasis, inflammation, proliferation, and remodeling. This stage-based progression applies only to acute wounds (wounds that heal within three months) however. Chronic wounds fail to follow a stage-based progression, and heal erratically, if at all. This kind of compromised wound healing typically occurs in patients with diabetes or other conditions that impede proper circulation, such as pressure ulcers or venous leg ulcers. It is assumed that the hypoxic environment associated with the poor circulation in these conditions is to blame.

An estimated 6.5 million people in the United States suffer from chronic non-healing wounds. Approximately 15% of diabetic patients will suffer from some sort of lower limb ulcer in their lifetime, and 24% of these injuries will result in a form of limb amputation.

Hyperbaric oxygen therapy is the clinical use of oxygen at higher pressures than atmospheric pressure, and has been demonstrated to aid in the healing of difficult wounds. Typical therapy consists of placing the patient in a chamber (see **Figure 1**) maintained at 100% oxygen for a brief period of time, and multiple sessions are the norm. Patients breathe 100% oxygen most of the time, but are given periodic "air breaks" to avoid the risks associated with oxygen toxicity.

Figure 1: A hyperbaric chamber used to provide oxygen therapy to patients.

The underlying causes and pathophysiological mechanisms underlying the success of hyperbaric oxygen therapy have not been thoroughly investigated, and most of the evidence in support of its use is empirical.

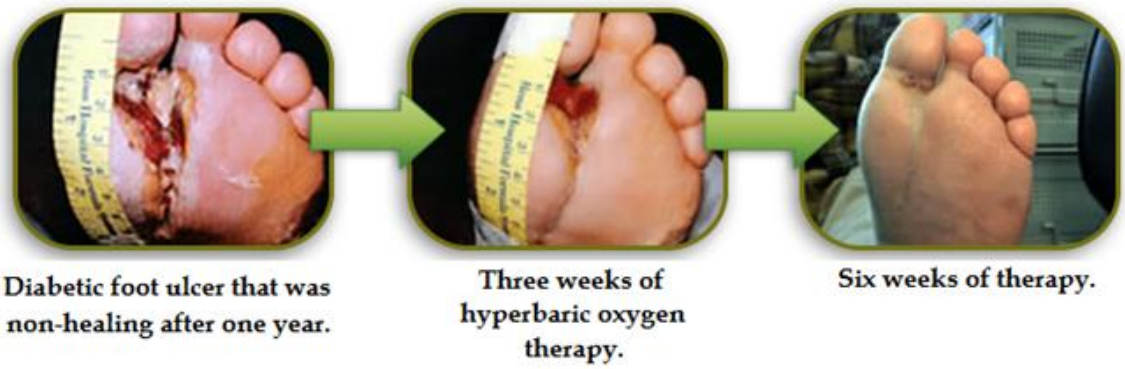

Figure 2: Progression of healing in a chronic wound in response to hyperbaric oxygen therapy.

Dr. Jennifer Flegg and Dr. Ian Turner of Queensland, Australia, have done some investigation into the diffusion of oxygen throughout tissue in response to hyperbaric oxygen therapy. The three major quantifiable phenomena they considered were the diffusion of oxygen through healthy tissues surround the wound bed, the migration of capillary tips as a result of hyperbaric oxygen therapy over time, and the resultant increase in blood vessel density that follows capillary tip migration. Drawing inspiration from their work, we sought to quantify oxygen diffusion through tissue in response to hyperbaric oxygen therapy and utilize that information to determine what rates of exposure to a highly oxygenated environment will result in significantly increased oxygen levels in the wound bed.

Mathematical Model

The mathematical model used for wound healing comprises three partial differential equations: oxygen concentration (w), capillary tip density (n), and blood vessel density (b). In this model, for simplification, we considered a one-dimensional wound in the direction of x. The edge of the wound is located at x = 0 and its center lies at x = L. The wound has symmetry around the centerline at x = L.

The equations for this model are:

1. Diffused oxygen concentration ($w(x,t)$):

$$\frac{\partial W}{\partial t} = D_w \frac{\partial^2 W}{\partial x^2} + K_2 b - K_4 W$$

Where D_w is the diffusivity constant of oxygen, $k_2 b$ is the rate of oxygen production by the blood vessels, and $k_4 w$ is rate of oxygen consumption by the tissues. D_w, k_2, and k_4 are all nonnegative constants.

2. Capillary tip density ($n(x,t)$):

$$\frac{\partial n}{\partial t} = \chi \frac{\partial}{\partial x}\left(n \frac{\partial w}{\partial x}\right) + k_5\, bH(w - w_L)H(w_H - w) - k_6 n$$

Where $H(x)$ is the Heaviside function, χ is the chemotactic coefficient, $K_5 b$ is the rate of production of capillaries from the existing blood vessels, and $k_6 n$ is rate of capillary tip death. Additionally, w_L and w_H are values for low and high oxygen concentration, respectively.

3. Blood vessel density ($b(x,t)$):

$$\frac{\partial b}{\partial t} = -\chi n \frac{\partial w}{\partial x} + b(1 - b)$$

Where $-\frac{\chi \partial w}{\partial x}$ is the speed of capillary tip migration, $b0$ is the carrying capacity rate, and k_3 is the growth rate of capillaries.

As it is shown in this model, all of the equations are dependent on each other. For instance, the PDE for diffused oxygen concentration depends on the blood vessel density, which makes the model complicated and difficult to solve. For simplification, our model only considers the diffused oxygen concentration, treating blood vessel density and capillary tip density as constants.

$$\frac{\partial W}{\partial t} = D_w \frac{\partial^2 W}{\partial x^2} + K_2 b - K_4 w$$

Boundary and initial conditions:

For boundary conditions, we assume that at the edge of the wound (x = 0), there are no capillary tips and therefore the oxygen level equilibrate so rapidly with uninjured level, meaning there is no flux of oxygen. Also, at x = L, due to spatial symmetry, the oxygen concentration flux assumed to be zero. For the initial condition, it is assumed that there are no capillary tips within the wound bed, and that blood vessel density is like that of normal tissue within a certain distance from the wound edge (0 < x < ε). Therefore, the wound is oxygenated throughout the vascularized region, and due to the high demand for oxygen at rate $k_4 w$, balances supply at rate $k_2 b$. Additionally, ε, the width of the wound margin which separates the healthy and wounded tissue, is assumed to be very small compared to L, (ε << L).

$$I.C: \qquad W(x,0) = \begin{cases} \dfrac{K_2 b_0}{K_4} & 0 < x < \varepsilon \\ 0 & \varepsilon < x < L \end{cases}$$

$$B.C: \ \left.\frac{\partial w}{\partial x}\right|_{x=0} = \left.\frac{\partial w}{\partial x}\right|_{x=L} = 0$$

Analytical Solution

Because our model for oxygen diffusion concentration returns a non-homogenous partial differential equation, separation of variables cannot be used directly. Therefore, we first have to solve for a steady-state solution in order to homogenize the equation.

The **steady-state solution** is derived as follows:

$$t \to \infty \quad \to \frac{\partial W}{\partial t} = 0$$

$$D_w \frac{\partial^2 W}{\partial x^2} + K_2 b - K_4 W = 0 \;\; \to D_w \frac{\partial^2 W}{\partial x^2} + K_4 W = -K_2 b$$

$$W(x) = \frac{K_2 b}{K_4}$$

satisfies the above equation and the given boundry condtions

$$\to \qquad W_{ss}(x) = K_2 b / K_4$$

Now we write our equation in terms of the **steady-state solution and time-varying solution.**

$$W(x,t) = W_{ss}(x) + V(x,t) \to$$

$$\frac{\partial (W_{ss}(x) + V(x,t))}{\partial t} = D_w \frac{\partial^2 (W_{ss}(x) + V(x,t))}{\partial x^2} + K_2 b - K_4 \big(W_{ss}(x) + V(x,t)\big)$$

$$\frac{\partial W_{ss}(x)}{\partial x} + \frac{\partial V}{\partial t} = D_w \frac{\partial^2 W_{ss}(x)}{\partial x^2} + D_w \frac{\partial^2 V}{\partial x^2} + K_2 b - K_4 W_{ss}(x) + K_4 V$$

$$\frac{\partial V}{\partial t} = D_w \frac{\partial^2 V}{\partial x^2} + K_2 b - K_4 W_{ss}(x) + K_4 V \quad \textit{Substitute for } W_{ss}(x) = K_2 b / K_4$$

$$\frac{\partial V}{\partial t} - D_w \frac{\partial^2 V}{\partial x^2} + K_4 V = 0$$

Now we have a **homogenous second-order partial differential equation**. Therefore, separation of variables can be applied to solve the equation as follows:

$$V(x,t) = G(t)\varphi(x)$$

$$\frac{\partial V}{\partial t} + K_4 V = D_w \frac{\partial^2 V}{\partial x^2}$$

$$\frac{\partial (G(t)\varphi(x))}{\partial t} + K_4 G(t)\varphi(x) = D_w \frac{\partial^2 (G(t)\varphi(x))}{\partial x^2}$$

$$\varphi(x)\frac{\partial G(t)}{\partial t} + K_4 G(t)\varphi(x) = D_w G(t)\frac{\partial^2 \varphi(x)}{\partial x^2}$$

Both side can be divided by: $G(t)\varphi(x).D_w$

$$1/(D_w G(t)) * \frac{\partial G(t)}{\partial t} + K_4/D_w = 1/\varphi(x) * \frac{\partial^2 \varphi(x)}{\partial x^2} = -\lambda$$

1) **Spatial Equation:** $\frac{1}{\varphi(x)} * \frac{\partial^2 \varphi(x)}{\partial x^2} = -\lambda$

2) **Transient Equation**: $1/(D_w G(t)) * \frac{\partial G(t)}{\partial t} + K_4/D_w = -\lambda$

$$\frac{\partial^2 \varphi(x)}{\partial x^2} = -\lambda\ \varphi(x)$$

$$\varphi(x) = Asin(\sqrt{\lambda}x) + Bcos(\sqrt{\lambda}x)$$

$$\frac{\partial \varphi(x)}{\partial x} = A\sqrt{\lambda}cos(\sqrt{\lambda}x) - Bsin(\sqrt{\lambda}x)$$

In order to find **λ,** we apply the boundary conditions:

$$\frac{\partial \varphi(0)}{\partial x} = A\sqrt{\lambda}cos(\sqrt{\lambda} * 0) - B\sqrt{\lambda}sin(\sqrt{\lambda} * 0) = 0$$

$$\rightarrow\ A\sqrt{\lambda} = 0 \qquad \rightarrow A = 0$$

$$\frac{\partial \varphi(L)}{\partial x} = A\sqrt{\lambda}cos\left(\sqrt{\lambda} * L\right) - B\sqrt{\lambda}sin\left(\sqrt{\lambda} * L\right) = 0$$

$$\rightarrow \ B\sqrt{\lambda}sin\left(\sqrt{\lambda} * L\right) = 0$$

$$\rightarrow \ \ sin\left(\sqrt{\lambda} * L\right) = 0 \rightarrow \quad \sqrt{\lambda L} = n\pi \ \rightarrow \ \lambda = (\frac{n\pi}{L})^2$$

The spatial equation**, $\boldsymbol{\varphi_n(x)}$**, is as follows:

$$\varphi_n(x) = B_n cos\ \left(\frac{n\pi}{L}x\right)$$

Now we need to solve for transient equation**, G(t) :**

$$\left(\frac{1}{D_w}\right)\left(\frac{1}{G(t)} * \frac{\partial G(t)}{\partial t} + K_4\right) = \ -\lambda \rightarrow \ \frac{\partial G(t)}{\partial t} = -(\lambda * D_w + K_4)G(t)$$

$$G(t) = e^{-(D_w\lambda_n + K_4)t}$$

$$\rightarrow V(x,t) = \sum_{n=1}^{\infty} B_n \cos\left(\frac{n\pi}{L}x\right) \mathrm{e}^{-(D_w\left(\frac{n\pi}{L}\right)^2 + K_4)t}$$

$\boldsymbol{V(x,t)}$ is our time varying solution to our PDE. However we first need to find our new initial condition and then use the Fourier transform in order to solve for the constant B_n.

New initial conditions and the solving of $\boldsymbol{B_n}$ for our time varying solution are as follows:

$$W(x,0) = \ W_{ss}(x) + \ V(x,0) \ \rightarrow \ \ V(x,0) = W(x,0) - W_{ss}(x)$$

$$W(x,0) = \begin{cases} \frac{K_2 b_0}{K_4} & 0 < x < \varepsilon \\ 0 & \varepsilon < x < L \end{cases}$$

$$\rightarrow V(x,0) = W(x,0) - W_{ss}(x) = \begin{cases} \frac{K_2 b_0}{K_4} - \frac{K_2 b}{K_4} & 0 < x < \varepsilon \\ -\frac{K_2 b_0}{K_4} & \varepsilon < x < L \end{cases}$$

$$V(x,0) = f(x)$$

$$B_n = \frac{2}{L} * \int_0^L f(x) cos\left(\frac{n\pi}{L} x\right) dx \rightarrow$$

$$B_n = \frac{2}{L} * \int_0^{\varepsilon} \frac{K_2(b_0 - b)}{K_4} \, cos\left(\frac{n\pi}{L} x\right) dx - \frac{2}{L} * \int_{\varepsilon}^{L} \frac{K_2 b}{K_4} \, cos\left(\frac{n\pi}{L} x\right) dx$$

$$B_n = \frac{2}{L} * \left(\frac{L}{n\pi}\right) * \frac{K_2(b_0 - b)}{K_4} \, sin\left(\frac{n\pi}{L} x\right)\Big|_0^{\varepsilon} - \frac{2}{L} * \left(\frac{L}{n\pi}\right) * \frac{K_2 b}{K_4} \, sin\left(\frac{n\pi}{L} x\right)\Big|_{\varepsilon}^{L}$$

$$B_n = \left(\frac{2}{n\pi}\right) * \frac{K_2 b_0}{K_4} sin\left(\frac{n\pi}{L} \varepsilon\right)$$

The time varying solution is solved by multiplying the spatial equation ($\boldsymbol{\varphi_n(x)}$) and transient equation (G(t)):

$$\rightarrow V(x,t) = \sum_{n=1}^{\infty} \left(\frac{2}{n\pi}\right) * \frac{K_2 b_0}{K_4} sin\left(\frac{n\pi}{L} \varepsilon\right) \, cos\left(\frac{n\pi}{L} x\right) e^{-(D_w\left(\frac{n\pi}{L}\right)^2 + K_4)t}$$

The final solution for oxygen concentration during wound healing, obtained by adding the steady state solution and time varying solution, is as follows:

$$\rightarrow W(x,t) = \frac{K_2 b}{K_4} + \sum_{n=1}^{\infty} \left(\frac{2}{n\pi}\right) * \frac{K_2 b_0}{K_4} sin\left(\frac{n\pi}{L} \varepsilon\right) \, cos\left(\frac{n\pi}{L} x\right) e^{-(D_w\left(\frac{n\pi}{L}\right)^2 + K_4)t}$$

In order to visualize our results, we have used parameter values from the work of Flegg et al. (2012) for the purposes of modeling. These values are listed below.

D_w = 0.18 cm^2/day
k_2 = 1.04 mmHg/vessel/day
k_4 = 1.3 ml O_2 /ml tissue/day
$\varepsilon = 0.1$ cm
L = 1 cm
$b_0 = 250$ vessels/cm

By implementing these values into our analytical solution, MATLAB was utilized to obtain the surface plots for b = 250 vessels/cm, which is a typical value for blood vessel density in tissue. The results are shown from different angles in **Figure 3**.

$$b = 250\ vessels/cm$$

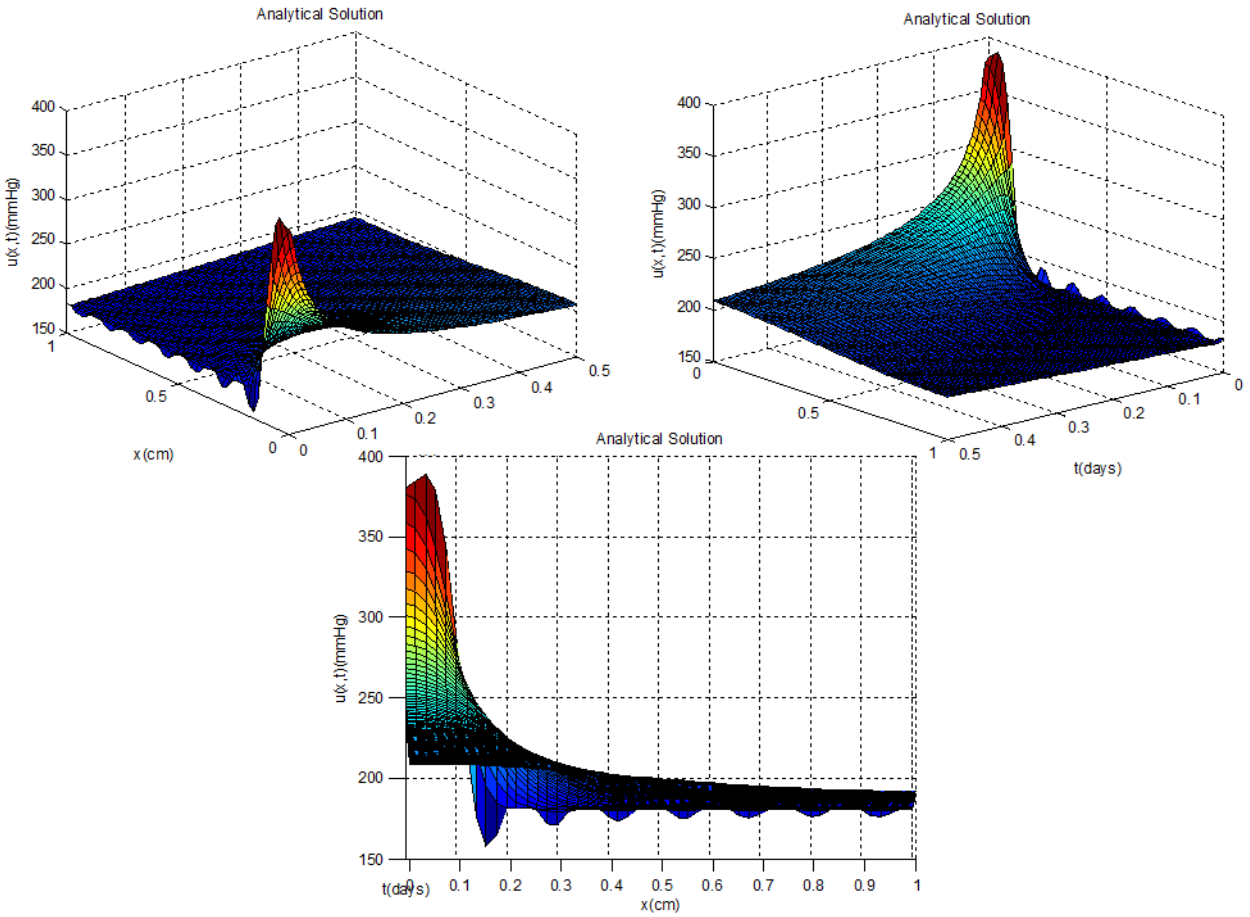

Figure 3: Oxygen concentration as a function of time and distance from the wound edge at a blood vessel density of 250 vessels/cm.

As can be seen from our surface plots, oxygen levels during hyperbaric oxygen therapy are highest at the edge of the wound bed, quickly depleting to values consistent with surrounding healthy tissue. Because those results are dependent on a typical value for blood vessel density (b = 250 vessels/cm), we also considered smaller values of b (b = 200, 100, and 10) in order to assess changes that would occur in our model for patients with decreasing amounts of circulation and functional capillary density. The results are shown in **Figure 4, Figure 5, and Figure 6**.

$$b = 200\ vessels/cm$$

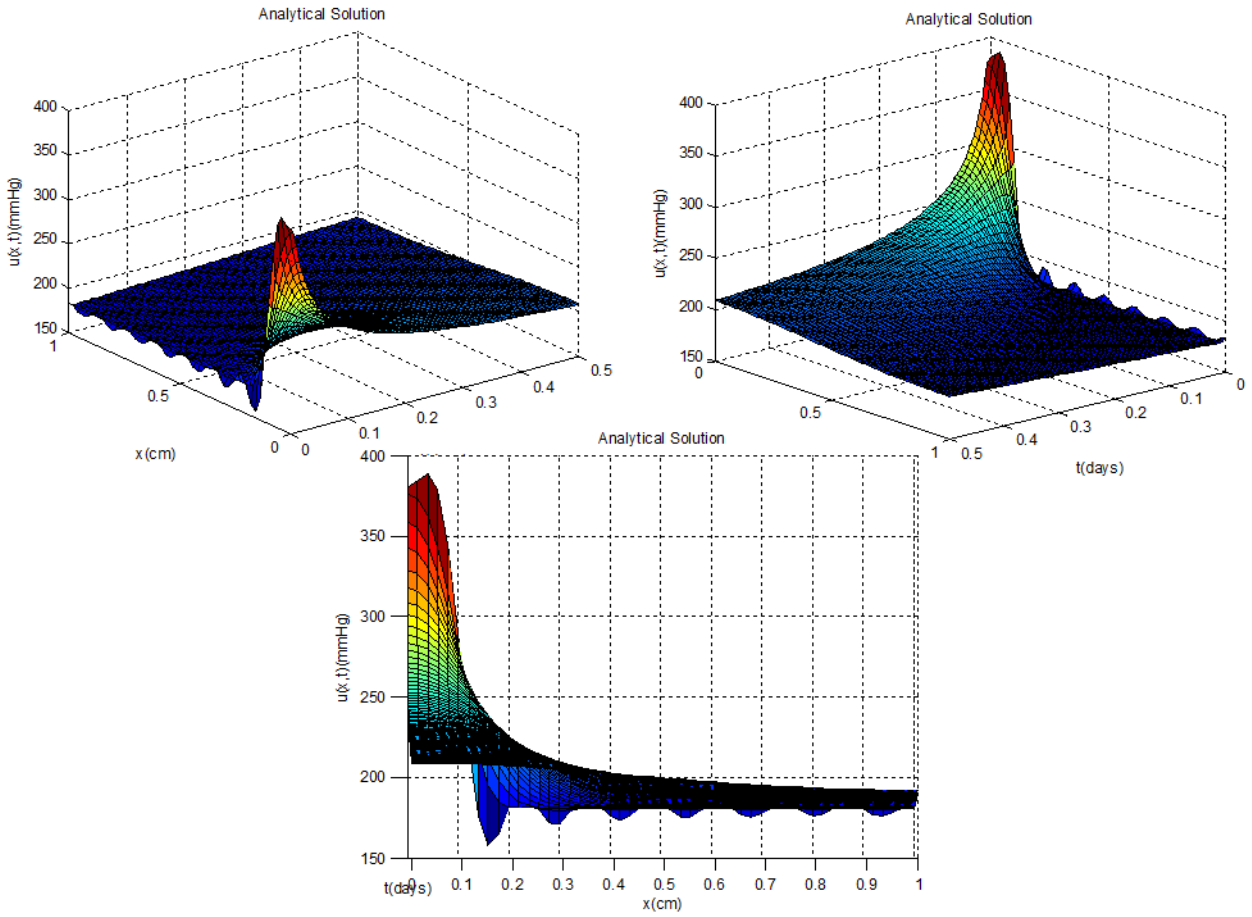

Figure 4: Oxygen concentration as a function of time and distance from the wound edge at a blood vessel density of 200 vessels/cm

$$b = 100\ vessels/cm$$

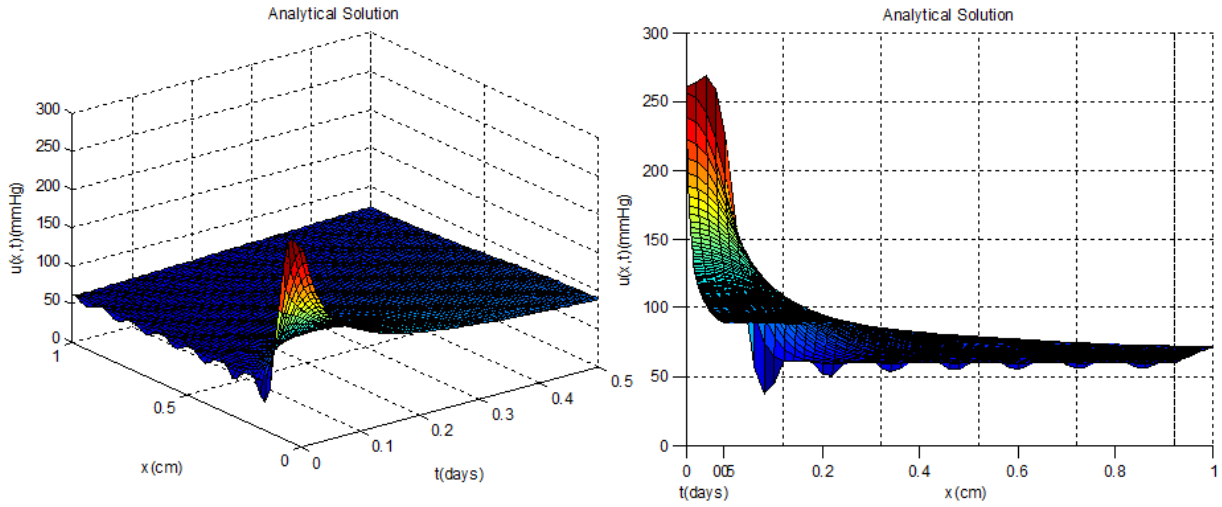

Figure 5: Oxygen concentration as a function of time and distance from the wound edge at a blood vessel density of 100 vessels/cm.

$$b = 10\ vessels/cm$$

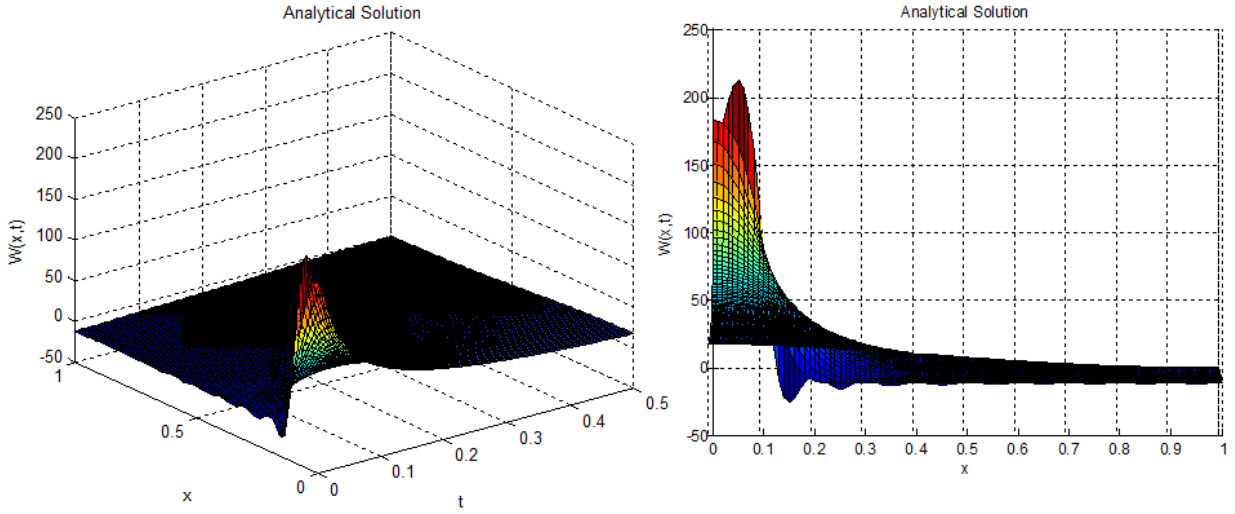

Figure 6: Oxygen concentration as a function of time and distance from the wound edge at a blood vessel density of 10 vessels/cm.

See **Figure 7** below for a comparison of the four surface plots side-by-side.

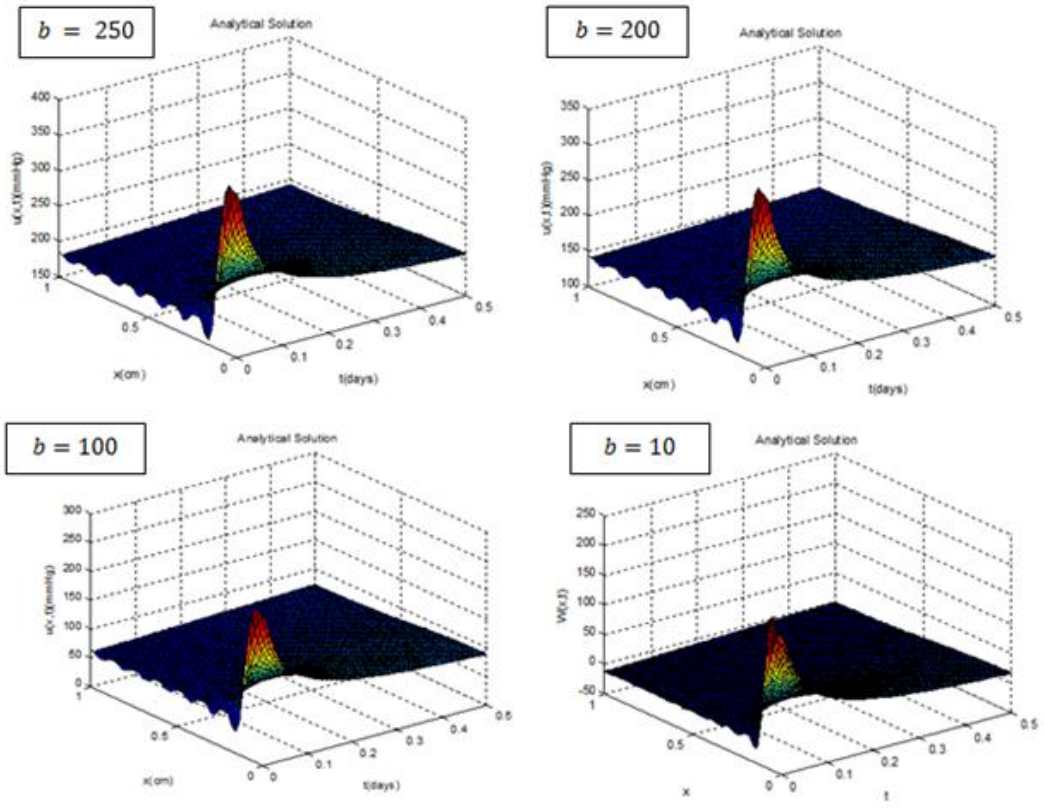

Figure 7: Oxygen concentration as a function of time and distance from the wound edge at varying values of blood vessel density.

As can be seen most clearly in **Figure 7**, noting the change in z-axis values, as blood vessel density decreases, so too do the peak levels of oxygen concentration decrease at the edge of the wound bed. At t = 0, corresponding to the time point directly after a hyperbaric oxygen therapy session has ended, oxygen concentration at the very edge of the wound bed (x = 0) has peaked at approximately 385 mmHg for a surrounding blood vessel density of 250 vessels/cm, while has peaked at only 210 mmHg for a surrounding blood vessel density of 10 vessels/cm. Baseline oxygen levels for surrounding tissue follow a similar trend, resting at approximately 205 mmHg for b = 250 vessels/cm and approximately 0 mmHg for b = 10 vessels/cm. The latter condition is associated with extreme cases of diseases that severely impair regional functional capillary density, and it is expected that response to hyperbaric oxygen therapy in these patients will be poor, as threshold oxygen levels (even near the edge of the wound bed) will not be reached or maintained after therapy at a level that facilitates wound healing.

In order to compare trends in our results to a similar model proposed by Flegg et al (2012), we also plotted the oxygen concentration versus distance from the wound center at different time

intervals corresponding to successive treatment sessions, between which blood vessel density is expected to increase, as shown in **Figure 8**.

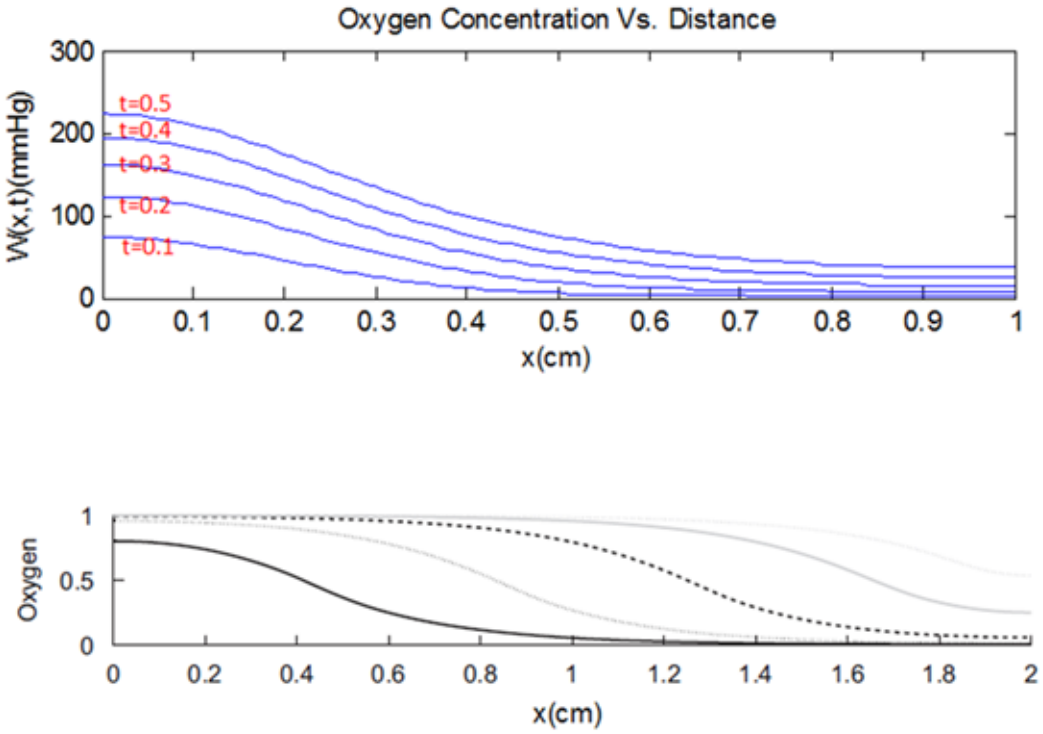

Figure 8: 2D plots comparing our analytical solution (top) with solutions obtained by Flegg et al. (2012) (bottom), demonstrating comparable results in trends. For our analytical plot, *t* is in units of days and an initial blood vessel density of 10 vessels/cm was used.

Although a direct comparison is impossible to make here due to Dr. Flegg's non-dimensionalization of their equation and differences in simplifications, we were mainly interested in the trends seen as we approached the center of the wound bed. We were pleased to see that both our and their results followed a similar profile, having an initial plateau phase before dropping off to negligible concentrations near the center of the wound.

Numerical Solution

We also used the finite difference method within MATLAB in order to compare our analytical results with a more accurate numerical approximation. Utilizing a value of b = 100, we were able to achieve validation of the method we utilized in deriving our analytical solution. As seen in **Figure 9**, results were largely comparable. Similar comparisons were attained for all values of b. As noted in our discussion of our 2D plots, differences can be accounted for in our simplification of the problem, as we treated b as a constant in contrast with the time-dependent nature of b seen in the full scenario. Additionally, some minor discrepancies in our finite difference analysis result from the fact that the surface plots in our finite difference analysis could only be discretized up to the point depicted in **Figure 9**, as further discretization rendered plots black due to the way MATLAB produces surface plots with large numbers of points.

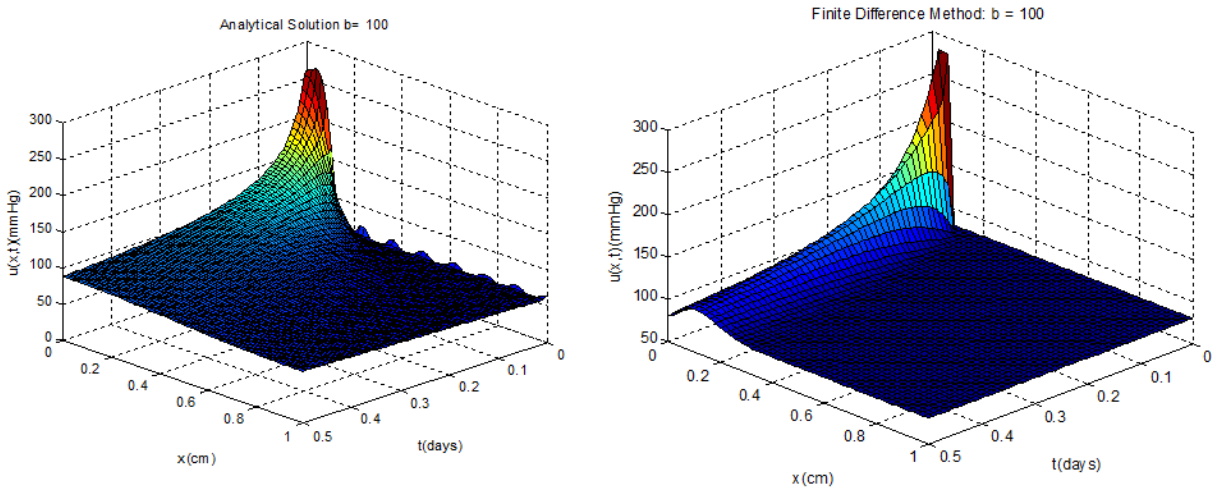

Figure 9: Surface plots comparing our analytical solution with a solution obtained via the finite difference method, demonstrating comparable results for a value of b = 100.

Applications and Conclusion

We have analyzed mathematically how oxygen diffuses into the wound space from the surrounding healthy tissue and establishes a local oxygen gradient, down which capillary tips migrate. Our 3-D surface plots show the change of oxygen concentration as a function of both time and space. As was seen upon varying the parameter that corresponds to blood vessel density, the values of oxygen concentration shift downward as blood vessel density decreases, while distribution with respect to distance and time remains the same. We can utilize this facet of our model to compare the efficacy of treatments that are routinely used to treat non-healing wounds.

To establish the necessary conditions for successful wound healing, we use the k_2, k_4 parameter analysis utilized by Flegg et al. (2009), which we will briefly discuss. In the steady state scenario, the oxygen concentration *w(x)* is too low for capillary tip production to occur, and blood vessel density does not change from its initial profile. Therefore $b = b(x,0) = H(\varepsilon - x)$. From this, we note the full analytical solution for oxygen diffusion alongside the two conditions under which our model predicts a failure of healing for the steady-state scenario where x = [0,1].

$$w(x) = \begin{cases} \dfrac{k2}{k4}\left(1 - \dfrac{sinh\left(\sqrt{k_4}(1-\varepsilon)\right)}{sinh\left(\sqrt{k_4}\right)} cosh\left(\sqrt{k_4}x\right)\right) & 0 \le x \le \varepsilon \\ \dfrac{k_2}{k_4}\dfrac{sinh(\sqrt{k_4}\varepsilon)}{sinh(\sqrt{k_4})} cosh(\sqrt{k_4}(1-x)) & 0 < x \le 1 \end{cases}$$

Additionally, we have the inequalities:

$$\frac{k_2}{k_4}\left(1 - \frac{\sinh(\sqrt{k_4}(1-\varepsilon))}{\sinh(\sqrt{k_4})}\right) < w_L$$

$$\frac{k_2}{k_4}\frac{\sinh(k_4\varepsilon)}{\sinh(\sqrt{k_4})} > w_H$$

From which we can determine:

$$w_L\left(1 - \frac{\sinh(\sqrt{k_4}(1-\varepsilon))}{\sinh(\sqrt{k_4})}\right)^{-1} < \frac{k_2}{k_4} < w_H \frac{\sinh(k_4)}{\sinh(\varepsilon\sqrt{k_4})}$$

which gives us the inequalities that k_2 and k_4 must fall within in order for healing to occur. Knowing this, we can utilize the 2-D plot below (**Figure 10**), which compares parametric regions of successful vs. unsuccessful wound healing.

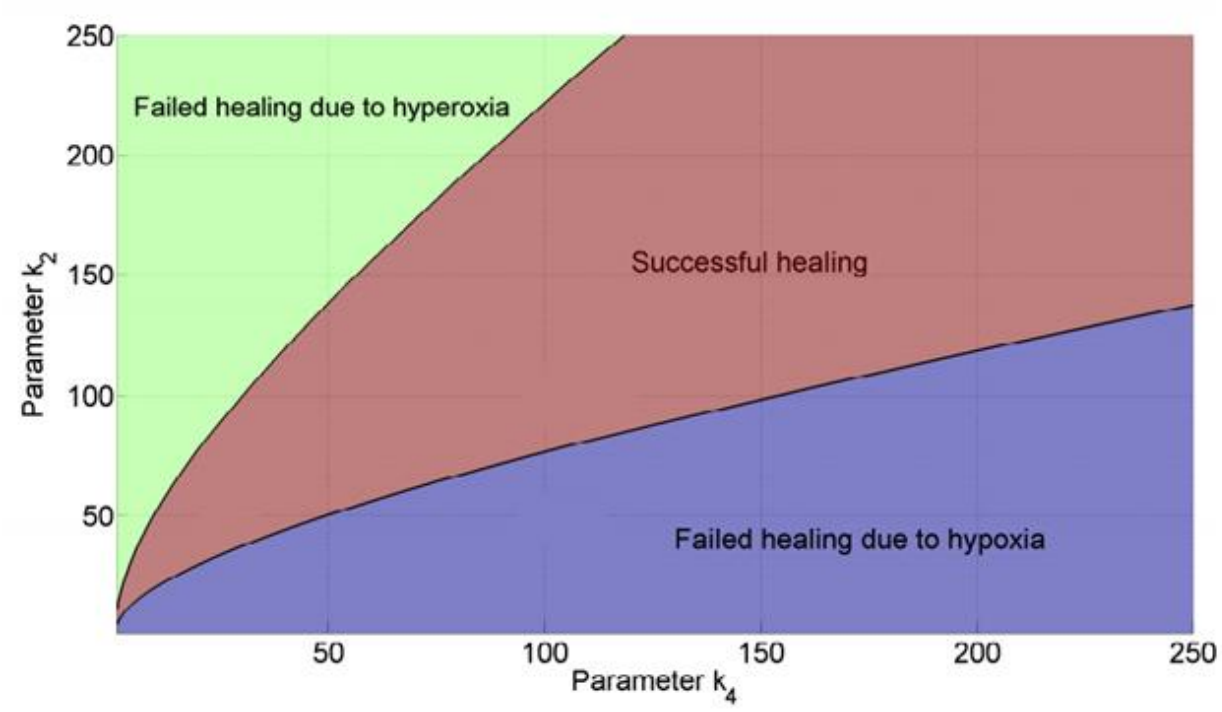

Figure 10: Overview of (k_2, k_4) parameter space, showing regionalization of successful and unsuccessful healing. Parameter values used are $w_L = 0.3$, $w_H = 0.7$, and $\varepsilon = 0.05$.

Diabetic wounds are often low in oxygen due to an over-abundance of oxygen consuming inflammatory cells and bacteria. A common treatment for these types of wounds is debridement, where the infected tissue is removed, which would correspond to a decrease in k_4. Arterial leg wounds are also associated with low oxygen levels. However, this is typically due to poor arterial flow, and a common treatment is revascularization surgery that restores this arterial flow. In this scenario, revascularization will effectively increase the oxygen supply rate parameter k_2. We can incorporate hyperbaric oxygen therapy (HBOT) into our model by assuming that during its application, the oxygen supply increases so that $k_2^{HBOT} = k_2 + \Delta k_2$ ($\Delta k_2 > 0$).

In conclusion, we are able to utilize a model of oxygen diffusion to evaluate the effect of treating chronic wounds with HBOT. While the exact reasons for the improved healing rates remain unclear, we are able to quantifiably predict whether or not healing will occur, allowing better protocols to be made for appropriate patients with chronic non-healing wounds.

References

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[2] J. Flegg, H. Byrne, M. Flegg, S McElwain. Wound healing angiogenesis: The clinical implications of a simple mathematical model. *Journal of Theoretical Biology*. 300 (2012); 309 – 316.

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[5] O. Lerman, R. Galiano, M. Armour, J. Levine, G. Gurtner. Cellular dysfunction in the diabetic fibroblast. *American Journal of Pathology*. 162 (2003); 303-312.

MATLAB Code:

```
%%%%%%%%%%%%%%%%%%%%%%%% ANALYTICAL SOLUTION %%%%%%%%%%%%%%%%%%%%%%%%

clear all;
close all;
clc;

dw = 0.18;
k2 = 1.04;
k4 = 1.3;
ep = 0.1;
L = 1;
tmesh = 0.0:0.005:0.5;
xmesh= 0:0.01:L;
b_0 = 250

% b = 250;
% b = 200;
% b = 100;
b = 10;

[t,x] = meshgrid(tmesh,xmesh); % Analytical Solution
sol_ana=0
 for n= 1:20
An=(2/(n*pi))*(k2*b_0/k4)*sin(n*pi*ep./L)
sol_ana=sol_ana + An.*cos((n.*pi./L).*x).*exp((dw.*(n*pi/L)^2+k4).*(-t))
 end
 sol_ana=sol_ana+(k2*b./k4)


figure(1)  % Surface Plots
surf(t,x,sol_ana);
title('Analytical Solution');
xlabel('t(days)');
ylabel('x(cm)');
zlabel('w(x,t)(mmHg)');

sol_ana1=0 % Analytical Solution for 2D Plotting
for t1=0.1:0.1:0.5
 for n= 1:20
An=(2/(n*pi))*(k2*b_0/k4)*sin(n*pi*ep/L)
sol_ana1=sol_ana1 + An.*cos((n.*pi/L).*x).*exp((dw.*(n*pi/L)^2+k4).*(-t1))
 end
 sol_ana1=sol_ana1+(k2*b/k4)

figure(2) % 2D Plots
plot(x,sol_ana1,'b');
hold on
title('Oxygen Concentration vs. Distance');
xlabel('x(cm)');
ylabel('W(x,t)(mmHg)');
```

```
%%%%%%%%%%%%%%%%%%%%%%%% NUMERICAL SOLUTION %%%%%%%%%%%%%%%%%%%%%%%%

clear all;
close all;

dw = .18;
k2 = 1.04;
k4 = 1.3;
e = 0.1;
L = 1;
b0 = 250;

% b = 250;
% b = 200;
% b = 100;
b = 10;

t = 0:.005:0.5;
s = 0:0.01:L;

[t,s] = meshgrid(t,s);

uss = (k2*b)/k4;
V = 0;

% Finite Difference Method

for n = 1:15
    Bn =(2./(n.*pi)).*((k2.*b0)./k4).*sin((n.*pi.*e)./L);
    V = V + Bn.*(cos((n.*pi.*s)./L).*exp(((dw.*(((n.*pi)./L).^2))+k4).*(-
t)));
end
anal_sol = V + uss;


figure(1) % Surface Plot
surf(t,s,anal_sol);
title('Analytical Solution');
xlabel('t(days)');
ylabel('x(cm)');
zlabel('W(x,t)(mmHg)');
```