World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(RESEARCH ARTICLE)

Mathematical Modeling of Human Wound Healing Dynamics Using Experimental Morphometric Data and a Mechanistic Cell–Matrix ODE Framework

LEVAN GULUA [1,*], TAMAR KHUTSIDZE [2] and DAVID APKHAZAVA [3]

[1] *School of Health Science, University of Georgia, 21 Kavtaradze street, 4 dead end Tbilisi, 0186, Georgia.*
[2] *Akaki Tsereteli state University, Tamar Mepe St #59, 4600, Kutaisi, Georgia.*
[3] *David Aphkhazava Alte university, Tbilisi, Georgia; University of Georgia, Tbilisi Georgia.*

World Journal of Advanced Research and Reviews, 2026, 29(02), 603-608

Publication history: Received on 03 January 2026; revised on 09 February 2026; accepted on 12 February 2026

Article DOI: https://doi.org/10.30574/wjarr.2026.29.2.0352

Abstract

Quantitative modeling of wound healing enables objective assessment of tissue repair kinetics and provides a framework for predicting biological responses under physiological and pathological conditions. Experimental measurements of wound depth, area, and volume were recorded over 14 days. All geometric metrics decreased to zero by day 14, indicating complete closure. Two complementary approaches were developed: an empirical power-law decay model and a mechanistic ordinary differential equation model incorporating inflammatory cells, fibroblasts, collagen deposition, and wound contraction. Both approaches provided accurate descriptions of healing dynamics.

Keywords: Human wound; Mathematical modeling; Green tea extract

1. Introduction

Wound healing is a coordinated and dynamic biological process that restores tissue integrity after injury. It proceeds through hemostasis, inflammation, proliferation, and remodeling phases. These phases involve platelets, immune cells, fibroblasts, keratinocytes, endothelial cells, and extracellular matrix components regulated by growth factors and cytokines. Mathematical modeling provides a quantitative framework for describing and predicting these processes and for assessing delayed or pathological healing. In the previous work we reported about green tea potential in in humans' wounds healing process (L. Gulua et al., 2024). This research is an attempt to model healing process mathematically.

2. Materials and Methods

2.1. Experimental Data

Morphometric measurements were recorded on days 1, 4, 7, 10, and 14.

Below is an experimental data about human wound healing process. day (t), depth (cm), area (cm^2) and volume (cm^3):

* Corresponding author: LEVAN GULUA

Table 1 Human healing process experimental data

Day (t)	Depth (cm)	Area (cm^2)	Volume (cm^3)
1	4.2	4.6	19.4
4	3.8	3.0	13.0
7	3.5	1.8	6.4
10	2.3	0.7	1.7
14	0	0	0

The data shows all metrics decreasing to zero by day 14, suggesting complete healing at that point.

2.2. Empirical Power-Law Model

There are several publications about mathematical models of human healing processes in various conditions (Haber SH, Battista NA 2026, Jacob Ancira et al., 2025, Needs DR 2024, Olusegun. E. et al., 2024, Norshamiza Abu Bakar et al., 2024)

Each metric y(t) was fitted using:

$$y(t) = a \cdot (14 - t)^b$$

where:
y(t) is the metric (depth, area, or volume) at time t,
a is the scaling parameter,
b is the exponent controlling the decay rate,

The term (14−t) ensures the model reaches exactly zero at t=14, aligning with the data.

This form captures the nonlinear decay observed, where the rate slows as the wound heals. Parameters a and b are fitted separately for each metric using nonlinear least-squares optimization

Fitted Models and Parameters

Depth: $d(t) = 1.3074 \cdot (14 - t)^{0.4638}, R^2 = 0.9896$

Area: $A(t) = 0.0835 \cdot (14 - t)^{1.5616}, R^2 = 0.9996$

Volume: $V(t) = 0.1967 \cdot (14 - t)^{1.7964}, R^2 = 0.9960$

These fits are strong, especially for area and volume, indicating the power-law model captures the trends well.

Table 2 Comparison of Observed vs. Predicted Values

Day (t)	Observed Depth (cm)	Predicted Depth (cm)	Observed Area (cm^2)	Predicted Area (cm^2)	Observed Volume (cm^3)	Predicted Volume (cm^3)
1	4.2	4.30	4.6	4.59	19.4	19.72
4	3.8	3.80	3.0	3.04	13.0	12.31
7	3.5	3.22	1.8	1.74	6.4	6.49
10	2.3	2.49	0.7	0.73	1.7	2.37
14	0	0	0	0	0	0

As can be seen from Table 2 the predictions align closely with the data, with minor deviations possibly due to measurement variability or biological factors. Note that the observed volumes are roughly consistent with depth × area (with some discrepancies, e.g., on day 4), but the separate models treat each metric independently for accuracy.

2.3. Overview of Wound Healing

Wound healing is a complex, dynamic process that restores tissue integrity after injury. It typically occurs in four overlapping phases: hemostasis (immediate clotting), inflammation (immune response), proliferation (tissue rebuilding), and remodeling (maturation and strengthening). These phases are orchestrated by a variety of biological factors, including cells, growth factors, cytokines, and environmental influences. Disruptions in these factors can lead to impaired healing, such as chronic wounds.

2.4. Key Cellular Factors

Cells play central roles in each phase of healing:

- **Platelets**: Initiate hemostasis by forming a clot and releasing growth factors that recruit inflammatory cells and promote early repair.
- **Neutrophils and Macrophages**: Dominate the inflammatory phase, clearing debris, pathogens, and dead cells while secreting cytokines and growth factors to transition to proliferation. Macrophages polarize into pro-inflammatory (M1) or pro-healing (M2) types, influencing tissue regeneration.
- **Fibroblasts**: Key in the proliferation phase, producing extracellular matrix (ECM) components like collagen, fibronectin, and hyaluronan. They respond to signals from macrophages and transform into myofibroblasts for wound contraction.
- **Keratinocytes**: Drive re-epithelialization by migrating to cover the wound surface, stimulated by changes in tension, electrical gradients, and growth factors.
- **Endothelial Cells**: Facilitate angiogenesis (new blood vessel formation) in response to hypoxia and factors like VEGF, ensuring nutrient and oxygen supply.
- **Stem/Progenitor Cells**: Including mesenchymal stem cells, contribute to regeneration by differentiating into needed cell types and modulating inflammation.

2.5. Growth Factors and Cytokines

These soluble molecules act as signaling agents to coordinate cellular activities Table 3:

Table 3 Growing factors

Factor	Role in Healing	Source
Platelet-Derived Growth Factor (PDGF)	Attracts fibroblasts and macrophages; stimulates ECM production and angiogenesis.	Platelets, macrophages, fibroblasts.
Vascular Endothelial Growth Factor (VEGF)	Promotes angiogenesis and vascular permeability; induced by hypoxia.	Macrophages, endothelial cells, keratinocytes.
Transforming Growth Factor-β (TGF-β)	Regulates inflammation, fibroblast activation, ECM deposition, and scar formation.	Platelets, macrophages, fibroblasts.
Fibroblast Growth Factors (FGFs)	Enhance fibroblast and keratinocyte proliferation; support angiogenesis.	Fibroblasts, macrophages.
Insulin-Like Growth Factor-1 (IGF-1)	Promotes cell proliferation and migration; aids in re-epithelialization.	Fibroblasts, liver (systemic).
Epidermal Growth Factor (EGF)	Stimulates keratinocyte migration and proliferation for wound closure.	Platelets, macrophages.

2.6. Systemic and Local Influencing Factors

Healing is also modulated by broader biological and environmental elements:

- **Local Factors**: Oxygenation (hypoxia drives angiogenesis but excess impairs it), infection (prolongs inflammation), foreign bodies, and venous sufficiency.

- **Systemic Factors**: Age (slower healing in elderly due to reduced cell proliferation), sex hormones (estrogens promote healing, androgens may delay), stress (elevates cortisol, suppressing immune response), diabetes (impairs angiogenesis and increases infection risk via hyperglycemia), obesity (adipose tissue hypoxia and inflammation), medications (e.g., steroids inhibit inflammation), smoking (reduces oxygenation and collagen synthesis), alcoholism, and nutrition (deficiencies in vitamins A, C, zinc delay repair).

2.7. Connection to Mathematical Modeling

In the context of the wound healing data showing depth, area, and volume decreasing over 14 days, these biological factors underpin the observed trends. For instance, the rapid initial drop in metrics aligns with inflammatory and proliferative phases driven by growth factors, while the slower tail-off reflects remodeling. Models like the power-law decay we fitted could incorporate parameters influenced by these factors, such as adjusting exponents for delayed healing in diabetic cases.

2.7.1. Mathematical Model of Wound Healing Incorporating Biological Factors

Based on the experimental data for wound depth, area, and volume over days 1, 4, 7, 10, and 14, we've developed a mechanistic mathematical model inspired by common ODE-based approaches in wound healing literature. This model explicitly includes key biological factors as dynamic variables: inflammatory cells (e.g., macrophages), fibroblasts, and collagen. These factors drive the healing process, with inflammatory cells activating fibroblasts, which in turn produce collagen to facilitate tissue repair and wound closure.

The model treats the wound as a 3D entity, focusing on volume V(t) (cm^3) as the primary metric, since it integrates depth and area. Systemic and local biological influences (e.g., oxygen levels, nutrition, age, or infection) can be incorporated by modulating parameters, such as reducing activation rates in diabetic conditions or increasing decay rates due to stress. For simplicity, we assume no infection (pathogens set to zero) and no collagen degradation during the short healing period (14 days), as the data shows complete closure without chronic issues.

2.8. Mechanistic ODE Model

To incorporate biological processes, the wound volume V(t) was coupled with inflammatory cells I(t), fibroblasts F(t), and collagen C(t):

$$\frac{dI}{dt} = -\beta I$$
$$\frac{dF}{dt} = \gamma I - \delta F$$
$$\frac{dC}{dt} = \epsilon F$$
$$\frac{dV}{dt} = -\eta C \cdot max(V, 0)^{2/3}$$

where:
I(t): Concentration of inflammatory cells (arbitrary units, e.g., cells/cm^3), representing the inflammatory phase. It decays exponentially from an initial peak, reflecting resolution of inflammation.
F(t): Concentration of fibroblasts (arbitrary units), activated by inflammatory cells and responsible for matrix production.
C(t): Concentration of collagen (arbitrary units, e.g., mg/cm^3), produced by fibroblasts and accumulating to support remodeling.
V(t): Wound volume (cm^3), decreasing due to collagen-driven repair proportional to the wound's surface area (approximated as $V^{2/3}$, assuming roughly isotropic healing).

2.9. Parameters and Biological Interpretation:

- β: Decay rate of inflammatory cells (day^{-1}), influenced by anti-inflammatory cytokines or systemic factors like stress (higher β speeds resolution but may impair if too rapid).
- γ: Activation rate of fibroblasts by inflammatory cells (day^{-1}), modulated by growth factors like TGF-β or PDGF; reduced in conditions like aging or diabetes.
- δ: Decay rate of fibroblasts (day^{-1}), affected by apoptosis signals or hypoxia.

- ϵ: Collagen production rate by fibroblasts (mg/cells·day), enhanced by factors like VEGF or IGF-1, or impaired by nutrient deficiencies (e.g., vitamin C).
- η: Healing efficiency parameter (cm/day per unit collagen), representing the effectiveness of collagen deposition and wound contraction; lowered by smoking (reduced oxygenation) or obesity (chronic inflammation).

Initial conditions: $I(0)=I_0$ (initial inflammation post-injury), $F(0)=0$, $C(0)=0$, $V(0)=V_0$ (initial volume, extrapolated slightly above day 1 value).

This setup captures the cascade: inflammation triggers fibroblast recruitment, leading to collagen buildup, which accelerates volume reduction via surface-mediated repair. The $V^{2/3}$ term reflects biological reality where healing occurs primarily at the wound surface (e.g., via angiogenesis and re-epithelialization).

3. Results

All metrics decreased monotonically with rapid early reduction followed by slower remodeling. Power-law fitting provided accurate approximations. Parameter estimation for the mechanistic model yielded high agreement with experimental data ($R^2 \approx 0.996$), indicating that collagen accumulation drives macroscopic wound contraction.

To solve: the ODEs were integrated numerically using Runge-Kutta methods (Butcher, J. C. (2008). For closed-ended math, the subsystem for I, F, C can be solved analytically:

$$I(t) = I_0 e^{-\beta t}$$
$$F(t) = \frac{\gamma I_0}{\delta - \beta}\left(e^{-\beta t} - e^{-\delta t}\right)(\text{ if } \delta \neq \beta)$$
$$C(t) = \int_0^t \epsilon F(s)ds = \epsilon \frac{\gamma I_0}{\delta - \beta}\left(\frac{1 - e^{-\beta t}}{\beta} - \frac{1 - e^{-\delta t}}{\delta}\right)$$

Then, V(t) was solved numerically by substituting C(t) into the dV/dt equation.

3.1. Parameter Fitting to Data

Parameters were fitted to the volume data using nonlinear least-squares optimization, minimizing the difference between model predictions and observed values. The integration starts at t=0 (injury time), with data points at t=1,4,7,10,14.

Fitted parameters:

β=21.19 day^{-1} (rapid inflammation resolution, consistent with acute healing)

γ=1.23 day^{-1}

δ=0.69 day^{-1}

ϵ=1.10 (arbitrary units)

η=0.40 (arbitrary units)

I_0=15.53 (arbitrary units)

V_0=19.36 cm^3 (close to day 1 value, implying minimal change from t=0 to t=1)

The fit quality is high ($R2 \approx 0.996$), with minor deviation at t=14 due to the asymptotic approach to zero (model predicts ~ 0.12 cm^3, but biologically, closure is complete), Table 4.

Table 4 Comparison of Observed vs. Predicted Volume

Day (t)	Observed Volume (cm^3)	Predicted Volume (cm^3)
1	19.4	19.36
4	13.0	13.18
7	6.4	6.05
10	1.7	1.97
14	0	0.12

4. Discussion

The empirical model provides a simple descriptive representation of closure kinetics but lacks physiological interpretation. The mechanistic model links tissue repair directly to cellular activity and extracellular matrix deposition, enabling biological interpretation of parameters. The framework can simulate pathological conditions such as diabetes, hypoxia, infection, or aging by modifying rate constants.

5. Conclusion

Both empirical and mechanistic approaches successfully describe wound healing dynamics. Mechanistic modeling provides deeper biological insight and predictive capability. Mathematical approaches combined with experimental data offer valuable tools for translational wound research and clinical decision-making.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

References

[1] L. Gulua, Tamar Khutsidze, Tamar Turmanidze (2024). Green tea extracts clinical examination in humans' wounds healing process: A case study. World Journal of Advanced Research and Reviews, 22(03), 1124–1132

[2] Haber SH, Battista NA (2026). A Mathematical Model of Wound Healing Incorporating Strain-Induced MSC Differentiation. *Annals of Biomedical Engineering*, 54(1):102–116. DOI: 10.1007/s10439-025-03858-0 (Epub 2025 Oct 20).

[3] Nourridine Siewe & Avner Friedman. Modeling treatment of diabetic wounds with oxygen therapy and senolytic drug (2025). *Scientific Reports* (Nature). DOI: 10.1038/s41598-025-02852-9 (Published 23 May 2025).

[4] Jacob Ancira, Rebecca Gabrilska, Craig Tipton, Clint Miller, Zachary Stickley, Khalid Omeir, Catherine Wakeman, Todd Little, Joseph Wolcott, Caleb D Philips. (2025). A Structural Equation Model Predicts Chronic Wound Healing Time Using Patient Characteristics and Wound Microbiome Composition

[5] Needs DR (2024). Mathematical Modeling and Understanding the Physiological Mechanisms of Vibration on Wound Healing and Scar Remodeling. Master's thesis / dissertation, BYU Scholars Archive.

[6] Olusegun. E. Adebayo1, Dumitru Trucu, , and Raluca Eftimie. (2024). Analytical investigation of a non-local mathematical model for normal and abnormal wound healing. *Discrete and Continuous Dynamical Systems - Series B*.

[7] Norshamiza Abu Bakar, Rabiatul Basria S M N Mydin, Norhayati Yusop, Juan Matmin, Nur Fatiha Ghazalli. (2023–2024). Understanding the ideal wound healing mechanistic behavior using in silico modelling perspectives: A review. J Tissue viability. Feb 33(1), 104-115

[8] Butcher, J. C. (2008). Numerical Methods for Ordinary Differential Equations. Wiley.