Simulating ECM Mechanical Response to Wound Healing with a Spring-Turnover Model

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Contents

1 Abstract

The extracellular matrix (ECM) is a non-cellular network. In wound healing, the ECM is critical for guiding cell migration and tissue repair, yet its mechanical role remains less understood. To investigate this, we adapted a spring–turnover model in which collagen fibres are represented as elastic springs undergoing continuous addition and removal during wound closure. Two regimes were compared: an infinite bath with unlimited collagen supply and a finite bath with limited availability. Simulations revealed two outcomes: (i) efficient turnover in the infinite bath relieved stress and restored elasticity (healthy repair), (ii) collagen depletion in the finite bath caused persistent stress and incomplete stiffness recovery (chronic wounds). These results show that successful healing requires a balance between collagen supply, turnover, and growth demand.

2 Introduction

The extracellular matrix (ECM) is a non-cellular network in animals primarily composed of fibrous proteins (such as collagen, elastin, and fibronectin) and proteoglycans. It acts as a structural scaffold to tissues and regulates cell behaviour. Cells continuously deposit, remodel, and degrade ECM components, while the ECM provides biochemical and mechanical cues that influence cell migration, differentiation, and disease progression [1].

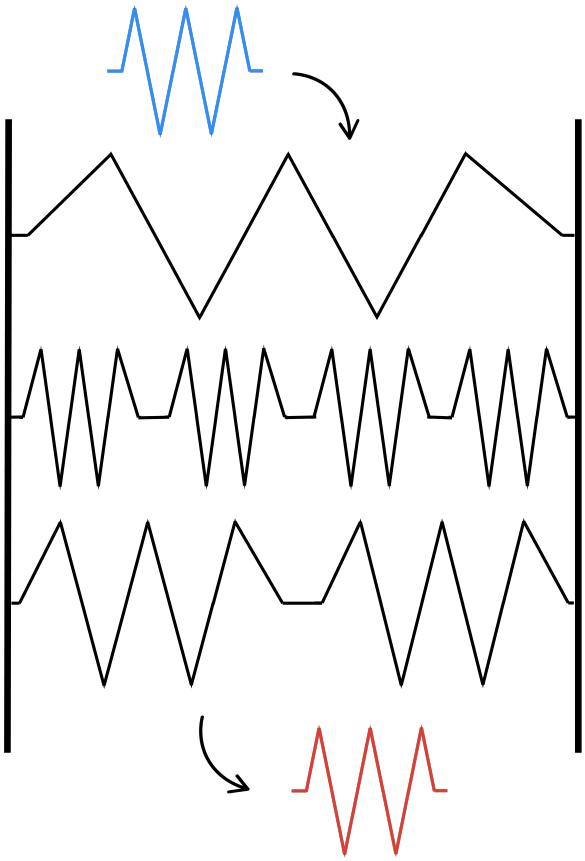
Although the biochemical regulation of the ECM has been extensively studied, its mechanical influence remains difficult to isolate experimentally. Due to its dynamic nature and interdependent relationship with cells, conducting mechanical tests on an isolated ECM is not appropriate. To address this challenge, mathematical models have been developed to simulate ECM behaviour. In particular, a spring network model representing elastic ECM components, such as collagen, was used to perform mechanical tests. Through MATLAB, the effects of turnover (continuous remodeling of the network) were incorporated into the model.

This model has been adapted here to investigate wound healing, a process that is critically dependent on ECM turnover to restore tissue integrity after injury. Wound healing has traditionally been studied from a biochemical perspective. However, during healing, the ECM is dynamic. Continuous turnover changes the mechanical environment cells experience, and ECM mechanics is highlighted as a major influence to wound healing [2].

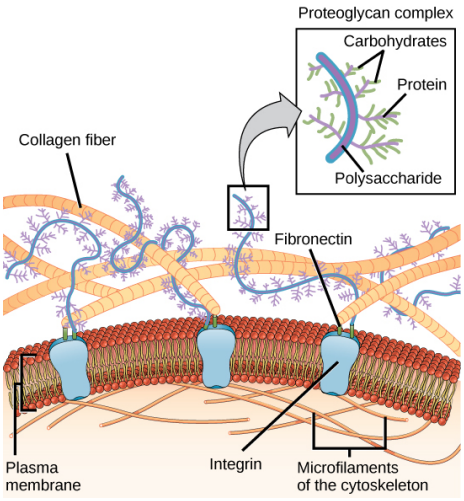
In this study, by simulating how the network remodels during wound gap filling, we aim to identify the mechanical conditions that optimize healing. This is particularly important because abnormal stiffening of the ECM after wound closure has been associated with pathological outcomes such as fibrosis and tumor progression [7]. Despite the biological significance of these processes, the mechanical role of ECM turnover in wound healing is still poorly understood. The present work addresses this gap by extending the spring-turnover model to explore how turnover influences both tissue repair and the mechanical environment of the ECM.

3 Methodology

The model adapted to study the ECM during wound healing is illustrated in Figure 1. The ECM's main load-bearing component, collagen, behaves elastically and is therefore represented by a spring. Springs arranged in series form a chain, representing a single collagen fibre, while the ECM as a whole is modelled as a network of fibres in parallel between two walls. This network undergoes turnover, meaning springs can be added or removed from the chains over time.



(a) ECM spring model

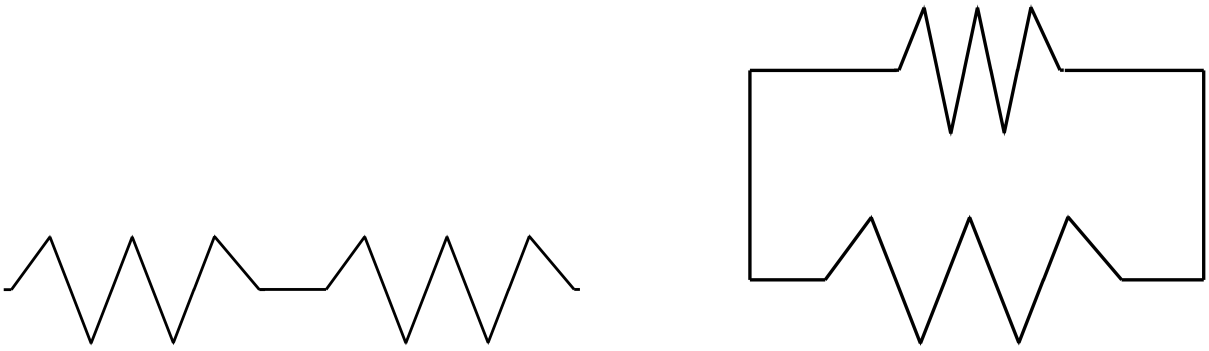


(b) ECM Illustration [6]

Figure 1: ECM spring model vs Illustration of real ECM. The model in (a) shows the minimal mechanical model used here: each collagen fiber is a series chain of springs and turnover (addition/removal events) remodels the network.

3.1 Spring Turnover Model

To capture how turnover affects the ECM's mechanical behaviour and thereby wound healing, the numerical solver relies on two simple rules:



(a) Springs in series (b) Springs in parallel

Figure 2: Illustration of springs arranged in series and in parallel.

3.1.1 Springs in series

For springs arranged in series, the force experienced by all springs are equal. This force is given by Hooke's Law as follows

$$F = k\Delta L. \tag{1}$$

So, for n springs arranged as in Fig. 2a, the force is given by

$$F = k_1\Delta L_1 \ = k_2\Delta L_2 = ... = k_n\Delta L_n, \tag{2}$$

where $\Delta L = L - l$ is the extension or the difference between the current length and rest length of the spring and k is the spring constant. Since the length of the chain is the sum of the lengths of all springs, we can consider the chain a single spring following Hooke's law with spring constant k and a force equal to that of individual springs. The following relationship is derived

$$\frac{1}{k} = \sum_{i=1}^{n} \frac{1}{i}. \tag{3}$$

From this we obtain the harmonic mean rule. This is when a chain in series has a lower effective stiffness than that of the individual springs.

3.1.2 Springs in parallel

In contrast, when springs are arranged in parallel the situation is reversed. Instead of sharing the same force, each spring experiences the same extension, and the total force carried by the chain is the sum of the forces in each spring.

$$F = \sum_{i=1}^{n} k_i\Delta L_i \tag{4}$$

The effective stiffness of the springs in parallel is given by

$$k = \sum_{i=1}^{n} k_i. \tag{5}$$

This leads to the second rule: the effective stiffness of springs in parallel is greater than that of an individual spring.

3.1.3 ODE Solver

While these two rules describe the instantaneous mechanics of the system, the ECM is not static. In living tissue, collagen is constantly deposited and degraded, so the lengths of fibres evolve over time. To capture this, the model includes turnover, where springs can be added to or removed from chains. This dynamic behaviour is expressed through a simple gain–loss equation (ODE), which updates the number of fibres of each length as time progresses. At every timestep, the ODE determines how the distribution of chain lengths changes, and the series/parallel rules are then applied to recalculate the overall network stress.

The dynamics are written as a gain–loss equation for the number of chains of length n, denoted $N_n(t)$

$$\frac{\mathrm{d}N_n}{\mathrm{d}t} = p_{n-1}N_{n-1} - (p_n + q_n)N_n + q_{n+1}N_{n+1}, \tag{6}$$

where N_n is the number of fibres/chains containing n spring units and p_n and q_n are respectively the rates of addition and removal of springs to chains.

The turnover rates are arbitrary functions that depend on the energetic cost of adding or removing a spring. Adding a spring reduces the elastic energy if the chain is overstretched while removing a spring from a chain that is already taut increases energy so removal is disfavoured. To illustrate, consider a stretched chain of 5 springs. Adding a sixth spring shares the load over more elements, lowering the elastic energy. The model therefore assigns a high p_5 function. By contrast, removing a spring from a chain of 2 units would make it very overstretched and costly, so q_2 would be small. This reflects the biological idea that turnover is more likely if it lowers the mechanical energy of the ECM, consistent with cells preferentially depositing collagen where strain is high.

In addition to elastic energy, there is a baseline cost for binding or unbinding a unit, representing biochemical constraints. In the code, this is treated as a constant offset. The total energetic cost of an event is given by the baseline cost and elastic work. If the change reduces elastic energy, the event is energetically favourable. If it increases energy, the rate is suppressed exponentially. This rule biases turnover toward relieving stress, while still allowing random addition/removal events at a lower rate.

To evolve the model, we must specify how the ECM is loaded or grown. The code allows three boundary condition types:

- Imposed strain: the gap is stretched according to a prescribed function (e.g. constant, ramped, or oscillating).
- Imposed stress: a constant external force is applied.
- Growth boundary condition: the domain itself grows at a constant rate,

$$\lambda(t) = \lambda_0 + gt, \tag{7}$$

  where $\lambda = L/l$ is the stretch and g the growth rate.

For wound healing, we select the growth condition, since it best mimics the biological process where cells remodel the ECM to close the wound rather than being externally stretched.

3.2 Healing Model

We adapted this model to the case study of wound healing. To mimic this process, we used the growth boundary condition. We let the system grow to fill a gap. The system also underwent turnover, representing the natural process of collagen being deposited and degraded in the ECM.

Two ways of modelling collagen supply were compared. First, we let the system evolve under an abundant supply of springs. Addition is only limited by the turnover rate. Second, we looked into a finite bath, where addition depends on a reservoir of available collagen that can be depleted. This represents chronic wounds, where supply is impaired, either because collagen synthesis is insufficient or degradation by MMPs (Matrix metalloproteinases) is excessive [3,4]. This distinction allows us to compare mechanical outcomes of normal vs impaired wound healing.

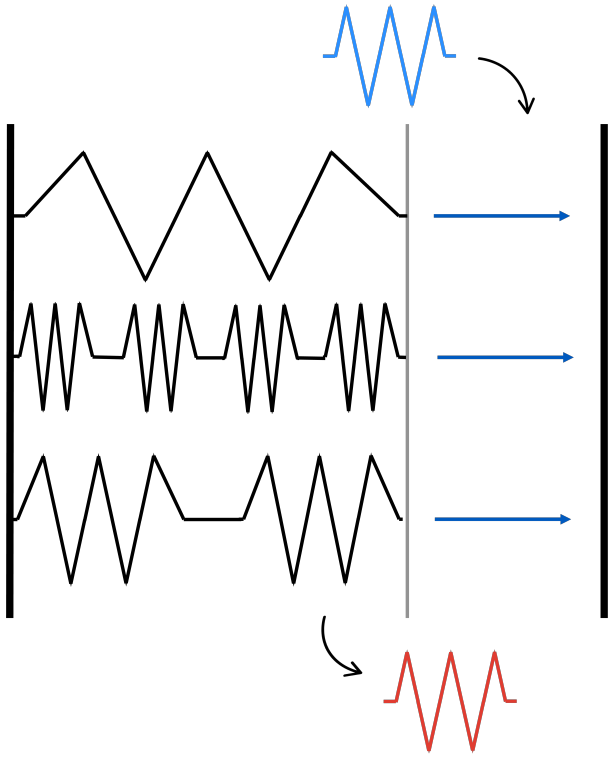


Figure 3: Illustration of ECM during wound healing. The ECM is let to grow to fill a gap/wound.

Our hypothesis is that when the reservoir is small, chains cannot grow quickly (which is important in healing) enough to match growth producing higher stress. We believe the ECM is subjected to a time/stress trade off, which would be especially highlighted in a limited supply context.

3.2.1 Outcome Metrics

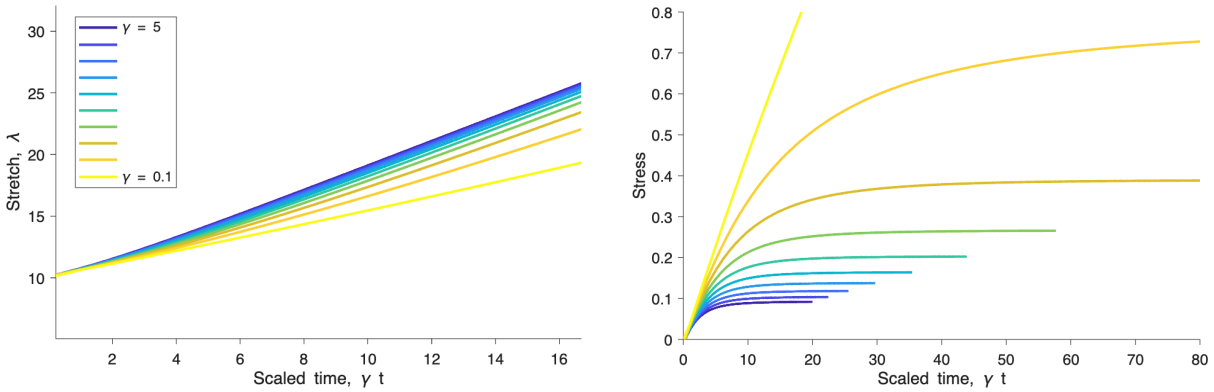
We implemented the model in MATLAB. An initial ECM size was established, determining the maximum chain lengths and the simulation time. A range of turnover rates ($\gamma = 0.1 - 5$) were set. For each turnover rate, a corresponding growth rate was also set (where $g = 1/\gamma$). This allowed us to explore how the balance between growth speed and turnover capacity affects healing. For each run, we recorded the time evolution of stretch (size) and stress in the ECM. From these outputs, we extracted biologically relevant measures:

- Healing time: how quickly the wound gap closes / reaches the desired size.
- Peak stress: maximum mechanical load during healing.

By quantifying these outcomes under both infinite and finite bath regimes, the model allows us to test how collagen turnover and supply availability control the mechanical environment of wound healing. Together, these metrics quantify the trade-off between healing speed and mechanical safety (avoiding excessive stress or stiffening).

4 Results

4.1 Infinite Bath

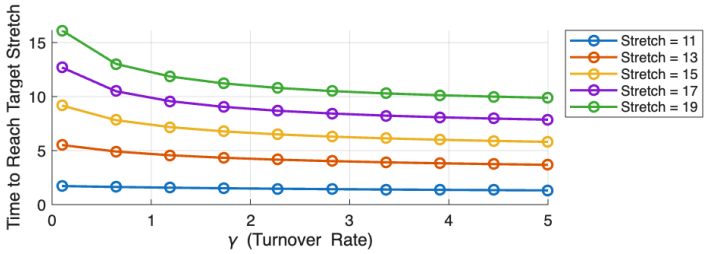


(a) Stretch vs Time

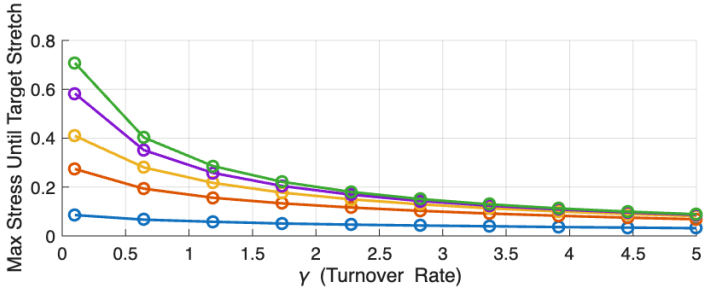
(b) Stress vs Time

Figure 4: Comparison of stretch and stress in the infinite bath case. We used 10 turnover rates ranging from 0.1 to 5 with highest rate being blue and lowest yellow.

In infinite bath simulations (Figure 4), the stretch increased steadily over time under all turnover rates, consistent with the imposed growth condition and the unlimited availability of collagen. Stress initially rose sharply, but then plateaued as turnover redistributed load among fibres. The plateau level depended strongly on turnover: high turnover reduced stress, whereas low turnover left residual stress. Together, these results suggest that even with unlimited collagen, effective stress relief during healing requires sufficiently rapid turnover.



(a) Time to Heal against Turnover Rate



(b) Maximum Stress until wound closed against Turnover Rate

Figure 5: Plots of time to heal and maximum stress reached during healing against turnover rate. The system was let to grow to different target stretches (closing wounds of different sizes) recording the maximum stress and time to heal.

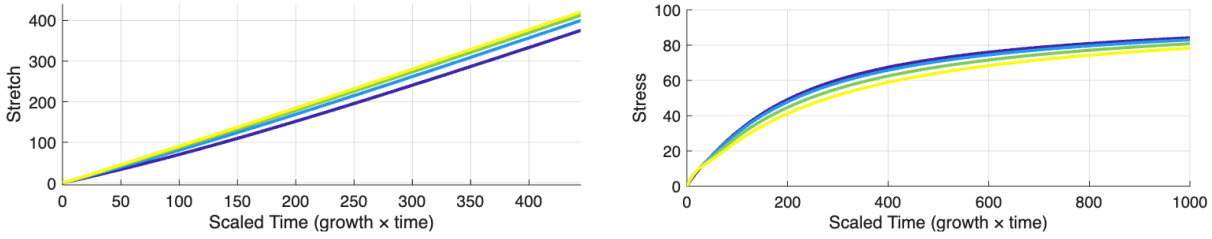
Across all closure targets (stretch = 11, 13, 15, 17, 19), the scaled healing time decreases monotonically as the turnover rate γ increases. The curves have a clear diminishing-returns shape: the largest drop in healing time occurs when γ increases from very low values (left side of the plot), whereas further increases beyond $\gamma \approx 1;2$ produce only modest gains. Higher stretch targets (e.g., 17–19) are shifted upward because more matrix must be produced to reach the target, but they preserve the same trend.

This indicates that when collagen supply is abundant (infinite bath), faster turnover mainly accelerates mechanical catch-up early, shortening the time needed to reach a given degree of closure; once turnover is "fast enough," additional increases yield little extra speed.

Plotting peak stress against γ reveals that faster growth (larger γ) leads to lower peak stresses. Curves for larger closure targets sit higher, showing that pushing the tissue further in the same time window amplifies the maximum load experienced by the ECM. Together with the top panel, this establishes a clear trade-off in the idealised unlimited-supply setting: increasing turnover helps you heal faster and reduces stress, while increasing growth demand raises the stress the ECM must bear.

In the infinite-bath regime, supply never limits deposition, so outcomes are controlled by the balance between turnover capacity and growth demand. Turning up turnover γ both shortens healing time and keeps peak stresses low, improving the mechanical environment for cells. Conversely, a larger gap to fill elevates peak stress, which could hinder "healthy healing" even though collagen is plentiful. This behaviour suggests a practical guideline: there exists a "fast-enough" turnover range beyond which additional acceleration yields minimal benefit, whereas even a modest reduction in growth demand can markedly lower peak stresses.

4.2 Finite Bath



(a) Stretch in infinite bath

(b) Stress in infinite bath

Figure 6: Comparison of stretch and stress in the finite bath case at a fixed growth rate (g=10). The bath sizes are between range from 1 to 2 with yellow being the highest bath size and purple the lowest.

In the finite bath simulations (Figure 6), stretch again increased approximately linearly with time under all conditions. However, bath size affected the overall extension achieved: larger baths permitted greater stretch, while smaller baths lagged slightly. The stress curves revealed a stronger dependence on supply. In systems with small baths, stress rose rapidly and stabilised at a high level, while larger baths reduced both the rate of stress build-up and the final plateau value. This indicates that limited collagen supply impairs the ECM's ability to remodel under growth, leading to sustained mechanical loading. Biologically, this behaviour mirrors chronic wounds, in which insufficient collagen deposition or excessive degradation prevents the ECM from relaxing, thereby maintaining a mechanically unfavourable environment.

4.3 Comparison

The simulations highlight how the mechanical environment of the ECM during wound healing depends not only on the imposed growth rate but also on the availability of collagen supply. Comparing the infinite- and finite-bath regimes reveals two distinct healing scenarios.

In the infinite bath case, collagen supply is unlimited, so turnover can always keep pace with imposed growth. Stretch increases smoothly, and stress rises initially but then relaxes to a low plateau. This corresponds to healthy wound healing, where abundant collagen deposition allows the ECM to remodel effectively. In this regime, the tissue regains its elasticity and avoids residual stress, creating a permissive environment for cell migration, angiogenesis, and eventual scar resolution [3,5].

By contrast, in the finite bath case, collagen availability is limited. While stretch still increases, its extent is reduced for smaller bath sizes. More importantly, stress accumulates and stabilises at much

higher levels than in the infinite bath. This persistent stress reflects the inability of turnover to fully relieve mechanical load when supply is exhausted. Biologically, this behaviour mimics chronic wounds, in which excessive ECM degradation (e.g. due to overactive MMPs) or insufficient collagen deposition prevents proper scaffold formation. The tissue remains mechanically tense, impairing cell infiltration and delaying closure [5].

These two outcomes map onto clinically relevant conditions:

- Healthy repair (infinite bath): efficient turnover, low residual stress, recovery of elasticity.
- Pathological repair (finite bath): limited supply, persistent stress, stiffer wounds.

This comparison underscores a central conclusion: collagen turnover and supply are equally important for wound healing mechanics. Abundant supply alone is not sufficient if turnover is too slow, and fast turnover cannot rescue healing if supply is depleted. Only when growth demand is balanced by both adequate supply and efficient turnover does the ECM remodel in a way that promotes functional repair.

5 Conclusions

This study applied a spring–turnover model of the extracellular matrix (ECM) to investigate the mechanical dimension of wound healing. By representing collagen fibres as elastic springs that undergo continuous addition and removal, and by imposing a growth boundary condition to mimic wound gap closure, we explored how turnover dynamics and collagen availability shape the mechanical environment during repair.

The simulations reveal two distinct outcomes. Under conditions of abundant supply and efficient turnover (infinite bath), the ECM remodels effectively: stress is relieved, corresponding to healthy wound healing. When supply is limited (finite bath), stress accumulates, reflecting the mechanical dysfunction characteristic of chronic wounds.

Together, these results highlight that successful healing depends not only on collagen availability but also on the balance between growth demand and turnover capacity. Further work could be done to summarise these behaviours in regime maps, so that the model can provide a compact framework for identifying conditions that promote healthy repair or pathological outcomes. It would also be interesting to analyse the stiffness before and after healing of the ECM and compare with litterature to understand if wounds really do cause stiffening. The stiffness can be further analysed to link the mechanics of the ECM with conditions such as fibrosis. While simplified, this case study demonstrates the value of the mathematical modelling of biological systems.

6 Bibliography

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