# Numerical Methods for Wound Healing PDE: A Comprehensive Analysis

## Problem Statement

We consider the wound healing partial differential equation (PDE) with nonlinear diffusion and logistic growth:

$$\frac{\partial u}{\partial t} = D\frac{\partial}{\partial r}\left(\left(1-\frac{u}{u_0}\right)^p \frac{\partial u}{\partial r}\right) + s_c u\left(1-\frac{u}{u_0}\right)$$

where:

- $u(r,t)$: Cell density (cells/cm$^3$)
- $r$: Spatial coordinate (cm), $0 \le r \le r_0$
- $t$: Time (s)
- $u_0$: Carrying capacity (normalized to 1)
- $r_0$: Wound half-width (0.5 cm)
- $D$: Cell diffusivity ($2.0 \times 10^{-9}$ cm$^2$/s)
- $p$: Nonlinear diffusion exponent (0, 1, or 5)
- $s_c$: Proliferation rate (0 or $8.0 \times 10^{-6}$ s$^{-1}$)

**Initial condition:**

$$u(r,0) = 0 \quad \text{for} \quad r > 0$$

**Boundary conditions:**

$$u(0,t) = u_0 = 1 \qquad \text{(Dirichlet)}$$
$$\frac{\partial u}{\partial r}(r_0,t) = 0 \qquad \text{(Neumann)}$$

## Analytical Solution (Special Case: $p = 0$, $s_c = 0$)

When $p = 0$ and $s_c = 0$, the PDE simplifies to the heat equation:

$$\frac{\partial u}{\partial t} = D\frac{\partial^2 u}{\partial r^2}$$

### Solution Derivation

Decompose $u(r,t) = u_s(r) + v(r,t)$, where $u_s(r)$ is the steady-state solution satisfying:

$$D\frac{d^2u_s}{dr^2} = 0, \quad u_s(0) = 1, \quad \frac{du_s}{dr}(r_0) = 0$$

Solving gives $u_s(r) = 1$. Then $v(r,t) = u(r,t) - 1$ satisfies:

$$\frac{\partial v}{\partial t} = D\frac{\partial^2 v}{\partial r^2}, \quad v(0,t) = 0, \quad \frac{\partial v}{\partial r}(r_0,t) = 0, \quad v(r,0) = -1$$

Using separation of variables $v(r,t) = R(r)T(t)$:

$$\frac{T'}{DT} = \frac{R''}{R} = -\lambda^2$$

The spatial ODE $R'' + \lambda^2 R = 0$ with $R(0) = 0$ and $R'(r_0) = 0$ has solutions:

$$R_m(r) = \sin\left(\frac{(2m-1)\pi r}{2r_0}\right), \quad \lambda_m = \frac{(2m-1)\pi}{2r_0}, \quad m = 1, 2, \ldots$$

The temporal solution is $T_m(t) = e^{-D\lambda_m^2 t}$. The general solution is:

$$v(r,t) = \sum_{m=1}^{\infty} c_m e^{-D\lambda_m^2 t} \sin\left(\frac{(2m-1)\pi r}{2r_0}\right)$$

Applying the initial condition $v(r,0) = -1$:

$$-1 = \sum_{m=1}^{\infty} c_m \sin\left(\frac{(2m-1)\pi r}{2r_0}\right)$$

The coefficients are:

$$c_m = -\frac{4}{(2m-1)\pi}$$

Thus the complete solution is:

$$\boxed{u(r,t) = 1 - \sum_{m=1}^{\infty} \frac{4}{(2m-1)\pi} \exp\left(-D\left(\frac{(2m-1)\pi}{2r_0}\right)^2 t\right) \sin\left(\frac{(2m-1)\pi r}{2r_0}\right)}$$

# Numerical Methods

## Explicit Finite Difference (Forward Euler)

The expanded PDE is discretized as:

$$\frac{\partial u}{\partial t} \approx \frac{u_i^{n+1} - u_i^n}{\Delta t}$$

$$\frac{\partial^2 u}{\partial r^2} \approx \frac{u_{i+1}^n - 2u_i^n + u_{i-1}^n}{(\Delta r)^2}, \quad \left(\frac{\partial u}{\partial r}\right)^2 \approx \left(\frac{u_{i+1}^n - u_{i-1}^n}{2\Delta r}\right)^2$$

The update equation for interior points ($i = 2, \ldots, N-1$) is:

$$u_i^{n+1} = u_i^n + \Delta t \Bigg[ D \Bigg( \underbrace{\left(1 - \frac{u_i^n}{u_0}\right)^p \frac{u_{i+1}^n - 2u_i^n + u_{i-1}^n}{(\Delta r)^2}}_{\text{Diffusion}} \\ \underbrace{- \frac{p}{u_0} \left(1 - \frac{u_i^n}{u_0}\right)^{p-1} \left(\frac{u_{i+1}^n - u_{i-1}^n}{2\Delta r}\right)^2}_{\text{Nonlinear flux}} \Bigg) \\ \underbrace{+ s_c u_i^n \left(1 - \frac{u_i^n}{u_0}\right)}_{\text{Source}} \Bigg] \quad (1)$$

Boundary conditions:

$$u_1^{n+1} = 1 \quad \text{(Dirichlet)}$$
$$u_N^{n+1} = u_{N-1}^{n+1} \quad \text{(Neumann)}$$

Stability requires:

$$\Delta t \leq \frac{(\Delta r)^2}{2D}$$

## Implicit Finite Difference (Backward Euler)

Discretize at $t_{n+1}$:

$$\frac{u_i^{n+1} - u_i^n}{\Delta t} = D \Bigg[ \left(1 - \frac{u_i^{n+1}}{u_0}\right)^p \frac{u_{i+1}^{n+1} - 2u_i^{n+1} + u_{i-1}^{n+1}}{(\Delta r)^2} \\ - \frac{p}{u_0} \left(1 - \frac{u_i^{n+1}}{u_0}\right)^{p-1} \left(\frac{u_{i+1}^{n+1} - u_{i-1}^{n+1}}{2\Delta r}\right)^2 \Bigg] \\ + s_c u_i^{n+1} \left(1 - \frac{u_i^{n+1}}{u_0}\right) \quad (2)$$

This forms a nonlinear system:

$$F_i(\mathbf{u}^{n+1}) = u_i^{n+1} - u_i^n - \Delta t \cdot \mathrm{RHS}(\mathbf{u}^{n+1}) = 0$$

Solved with Newton-Raphson:

$$J(\mathbf{u}_k)\delta\mathbf{u} = -\mathbf{F}(\mathbf{u}_k), \quad \mathbf{u}_{k+1} = \mathbf{u}_k + \delta\mathbf{u}$$

where $J_{ij} = \partial F_i / \partial u_j^{n+1}$ is the Jacobian.

## Crank-Nicolson Method

Average explicit and implicit terms:

$$\frac{u_i^{n+1}-u_i^n}{\Delta t} = \frac{1}{2}\Bigg[D\left(\left(1-\frac{u_i^n}{u_0}\right)^p \frac{u_{i+1}^n-2u_i^n+u_{i-1}^n}{(\Delta r)^2} - \frac{p}{u_0}\left(1-\frac{u_i^n}{u_0}\right)^{p-1}\left(\frac{u_{i+1}^n-u_{i-1}^n}{2\Delta r}\right)^2\right)$$
$$+s_c u_i^n\left(1-\frac{u_i^n}{u_0}\right)\Bigg]$$
$$+\frac{1}{2}\Bigg[D\left(\left(1-\frac{u_i^{n+1}}{u_0}\right)^p \frac{u_{i+1}^{n+1}-2u_i^{n+1}+u_{i-1}^{n+1}}{(\Delta r)^2} - \frac{p}{u_0}\left(1-\frac{u_i^{n+1}}{u_0}\right)^{p-1}\left(\frac{u_{i+1}^{n+1}-u_{i-1}^{n+1}}{2\Delta r}\right)^2\right)$$
$$+s_c u_i^{n+1}\left(1-\frac{u_i^{n+1}}{u_0}\right)\Bigg]$$

Solved as a nonlinear system using Newton-Raphson. Second-order accurate and unconditionally stable.

## Method of Lines (MOL)

The Method of Lines discretizes spatial derivatives to convert the PDE into a system of ODEs.

### Spatial Discretization

Define grid points $r_i = (i-1)\Delta r$ with $\Delta r = r_0/(N-1)$. Let $u_i(t) = u(r_i, t)$.

For interior points ($i = 2, \ldots, N-1$):

$$\frac{du_i}{dt} = D\left[\left(1-\frac{u_i}{u_0}\right)^p \frac{u_{i+1}-2u_i+u_{i-1}}{(\Delta r)^2} - \frac{p}{u_0}\left(1-\frac{u_i}{u_0}\right)^{p-1}\left(\frac{u_{i+1}-u_{i-1}}{2\Delta r}\right)^2\right] + s_c u_i\left(1-\frac{u_i}{u_0}\right)$$

### Boundary Conditions

- Dirichlet at $r = 0$ ($i = 1$):

$$u_1(t) = 1 \implies \frac{du_1}{dt} = 0$$

- Neumann at $r = r_0$ ($i = N$): Using ghost point $u_{N+1}$:

$$\frac{u_{N+1}-u_{N-1}}{2\Delta r} = 0 \implies u_{N+1} = u_{N-1}$$

Then:

$$\frac{du_N}{dt} = D\left(1-\frac{u_N}{u_0}\right)^p \frac{2(u_{N-1}-u_N)}{(\Delta r)^2} + s_c u_N\left(1-\frac{u_N}{u_0}\right)$$

### Initial Conditions

$$u_i(0) = \begin{cases} 1 & i = 1 \\ 0 & i = 2, \ldots, N \end{cases}$$

### Time Integration

Solve the ODE system:

$$\frac{d\mathbf{u}}{dt} = \mathbf{F}(t, \mathbf{u}), \quad \mathbf{u}(0) = \mathbf{u}_0$$

using a stiff ODE solver (e.g., BDF method).

## Finite Element Method (FEM)

### Weak Form Derivation

Multiply by test function $v(r)$ with $v(0) = 0$:

$$\int_0^{r_0} \frac{\partial u}{\partial t} v dr = \int_0^{r_0} \left[ D \frac{\partial}{\partial r} \left( \left(1 - \frac{u}{u_0}\right)^p \frac{\partial u}{\partial r} \right) + s_c u \left(1 - \frac{u}{u_0}\right) \right] v dr$$

Integrate diffusion term by parts:

$$\int_0^{r_0} D \frac{\partial}{\partial r} \left( \left(1 - \frac{u}{u_0}\right)^p \frac{\partial u}{\partial r} \right) v dr = \left[ D \left(1 - \frac{u}{u_0}\right)^p \frac{\partial u}{\partial r} v \right]_0^{r_0} - \int_0^{r_0} D \left(1 - \frac{u}{u_0}\right)^p \frac{\partial u}{\partial r} \frac{\partial v}{\partial r} dr$$

Boundary term vanishes due to $v(0) = 0$ and $\partial u/\partial r(r_0) = 0$, yielding:

$$\boxed{\int_0^{r_0} \frac{\partial u}{\partial t} v dr + \int_0^{r_0} D \left(1 - \frac{u}{u_0}\right)^p \frac{\partial u}{\partial r} \frac{\partial v}{\partial r} dr = \int_0^{r_0} s_c u \left(1 - \frac{u}{u_0}\right) v dr}$$

### Spatial Discretization

Discretize domain $[0, r_0]$ into $N$ nodes with piecewise linear basis functions $\phi_j(r)$. Approximate solution:

$$u_h(r, t) = \phi_1(r) + \sum_{j=2}^{N} u_j(t) \phi_j(r)$$

where $u_1(t) = 1$ (Dirichlet condition).

### Semidiscrete System

For test functions $v = \phi_i$ $(i = 2, \ldots, N)$:

$$\sum_{j=2}^{N} \frac{du_j}{dt} \underbrace{\int_0^{r_0} \phi_i \phi_j dr}_{M_{ij}} + \sum_{j=2}^{N} u_j(t) \underbrace{\int_0^{r_0} D \left(1 - \frac{u_h}{u_0}\right)^p \frac{d\phi_i}{dr} \frac{d\phi_j}{dr} dr}_{K_{ij}(u)} = \underbrace{\int_0^{r_0} s_c u_h \left(1 - \frac{u_h}{u_0}\right) \phi_i dr}_{f_i(u)}$$

Resulting in:

$$M \frac{d\mathbf{u}}{dt} + K(\mathbf{u})\mathbf{u} = \mathbf{f}(\mathbf{u})$$

where $\mathbf{u} = [u_2, \ldots, u_N]^T$.

**Time Discretization (Backward Euler)**

$$M\frac{\mathbf{u}^{n+1}-\mathbf{u}^{n}}{\Delta t}+K(\mathbf{u}^{n+1})\mathbf{u}^{n+1}=\mathbf{f}(\mathbf{u}^{n+1})$$

Rearrange to nonlinear system:

$$\mathbf{G}(\mathbf{u}^{n+1})=M\mathbf{u}^{n+1}+\Delta tK(\mathbf{u}^{n+1})\mathbf{u}^{n+1}-\Delta t\mathbf{f}(\mathbf{u}^{n+1})-M\mathbf{u}^{n}=\mathbf{0}$$

Solved with Newton-Raphson method.

# Summary of Methods

Table 1: Comparison of Numerical Methods

| **Method** | **Accuracy** | **Stability** | **Nonlinear Handling** | **Complexity** | **Best Use Case** |
|---|---|---|---|---|---|
| Explicit Euler | $O(\Delta t, \Delta r^2)$ | Conditional | Explicit | Low | Prototyping |
| Implicit Euler | $O(\Delta t, \Delta r^2)$ | Unconditional | Newton | Medium | Long simulations |
| Crank-Nicolson | $O(\Delta t^2, \Delta r^2)$ | Unconditional | Newton | Medium | High accuracy |
| MOL | $O(\Delta r^2)$ | Solver-dependent | ODE solver | Medium | Adaptive stepping |
| FEM | $O(\Delta r^m)$ | Unconditional | Newton | High | Complex geometries |

**Key Observations:**

- Explicit Euler is simplest but requires small $\Delta t$ for stability
- Implicit methods handle stiffness but require nonlinear solves
- Crank-Nicolson provides best accuracy/stability balance for uniform grids
- MOL offers adaptive time stepping with spatial discretization flexibility
- FEM is most flexible for complex domains and boundary conditions