AI-Assisted Modeling of Vascularization in Bioprinted Skin Grafts Toward PDE-Constrained Optimization

Anil Ambrosi, Matthew Liao, Nathan Taylor, Vladislav Bukshtynov (mentor)
University of Colorado Boulder

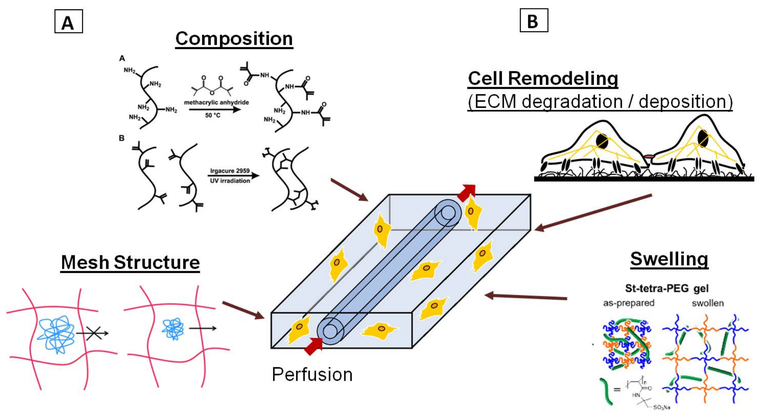
Boulder

Abstract

Bioprinted skin grafts offer a promising treatment for severe wounds, but their long-term viability depends on successful vascularization. We develop a coupled multiphysics model of fluid flow, nutrient transport, and cell population dynamics using the finite element method in `FreeFEM`. The framework provides the foundation for future PDE-constrained optimization, parameter calibration from sparse biological observations, and optimization of vascularization strategies. Current work combines mathematical modeling, scientific computing, and AI-assisted software development.

Problem Motivation

Severe skin injuries may not heal without a vascular network that delivers oxygen and nutrients to newly formed tissue. Channelized bioprinted grafts provide a promising strategy, but their performance depends on interacting biological, material, and flow processes.



Perfusion → Nutrient transport → Cell viability → Vascularization

Accurate models must capture hydrogel composition, mesh structure, swelling, and cell remodeling to support parameter calibration and optimal graft design.

Schematic adapted from Nichol et al. (2010), Wallace et al. (2013), and Nakajima et al. (2021).

AI-Assisted Research

`ChatGPT`, `GitHub Copilot`, and `Visual Studio IntelliCode` accelerated software development, numerical experiments, visualization, and documentation throughout the project.

- **Software development:** Implemented and debugged the `FreeFEM` forward solver, translated independently derived adjoint equations into code, and improved software structure.
- **Modeling and visualization:** Supported discussions of finite element discretization, coupled PDE models, optimization, κ-tests, and adapted `MATLAB` visualization routines.
- **Documentation:** Assisted with project documentation, poster preparation, and presentation materials.

AI accelerated implementation and exploration; all derivations, verification, and scientific conclusions remained under researcher supervision.

Computational Domain and Coupled Forward Model

Fluid flow: Navier–Stokes–Forchheimer

$$\rho\left(\frac{\partial \mathbf{u}}{\partial t} + \mathbf{u}\cdot\nabla\mathbf{u}\right) + \nabla p - \nabla\cdot(\mu\nabla\mathbf{u}) + \chi_p\left(\frac{\mu}{k} + \frac{\rho C_{\mathrm{ir}}}{\sqrt{k}}|\mathbf{u}|\right)\mathbf{u} = \mathbf{0},$$
$$\nabla\cdot\mathbf{u} = 0.$$

Nutrient transport

$$\frac{\partial C}{\partial t} + \mathbf{u}\cdot\nabla C - \nabla\cdot(\gamma\nabla C) + \beta N C = 0.$$

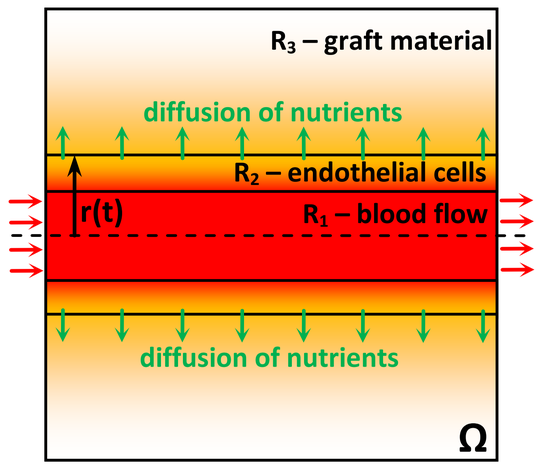
Cell population dynamics

$$\frac{\partial N}{\partial t} = \chi_s \lambda_p N(N_{\max} - N) - (1-\chi_s)\lambda_d N.$$

Swelling-driven geometry

$$r(t) = r_{\min} + (r_0 - r_{\min})e^{-St}.$$

$$\chi_p = \begin{cases} 0, & \mathbf{x}\in\Omega_f, \\ 1, & \mathbf{x}\in\Omega_p, \end{cases} \qquad \chi_s(C) = \begin{cases} 1, & C \geq C_{\mathrm{th}}, \\ 0, & C < C_{\mathrm{th}}. \end{cases}$$

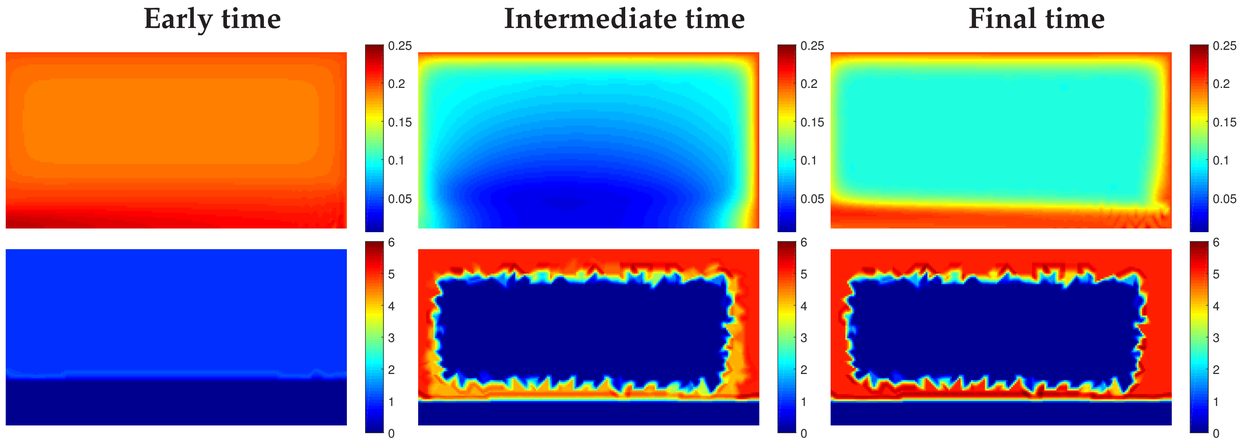


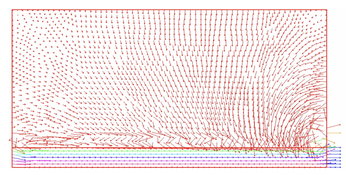
Channelized graft geometry: blood flow in Ω_f (region R_1) supplies nutrients to the porous graft Ω_p (R_2&R_3). *The solver uses upper-half symmetry; the endothelial layer is omitted.*

Flow → Nutrient transport → Cell growth/death → Evolving graft geometry

Forward Solver: Simulations, Efficiency & Optimization

Representative forward simulations: nutrient concentration C (top) and cell density N (bottom)





Velocity during active perfusion, $u_{\mathrm{perf}}(t) \neq 0$
Upper-half symmetry reduces the computational domain and approximately halves the simulation cost.

Nutrient availability evolves through convection, diffusion, and cellular consumption. The threshold-dependent population model produces spatially heterogeneous cell growth and death.

Computational efficiency of the forward solver

Core model features

- Reuse the mesh while swelling-induced changes remain negligible.
- Skip flow solves during no-infusion periods, $u_{\mathrm{perf}}(t) = 0$.
- Evaluate population dynamics analytically.

New accelerations

- Reduce the domain using upper-half symmetry.
- Deactivate flow after velocity stationarity.
- Remesh only after a prescribed change in channel diameter.

Future improvements

- Reuse assembled matrices and factorizations.
- Adapt timesteps near perfusion ON/OFF events.
- Predict and schedule necessary mesh updates.

The forward workflow avoids unnecessary PDE solves, mesh reconstruction, and history storage.

Toward PDE-constrained optimization: *current focus is careful validation of the forward and adjoint solvers before calibration.*

OPT-1: Parameter calibration

$$\min_{\mathbf{p}} \mathcal{J}_{\mathrm{cal}}(\mathbf{p}) = \frac{1}{2}\sum_{j,m}\left[N(\mathbf{x}_j, t_m; \mathbf{p}) - N^{\mathrm{obs}}_{j,m}\right]^2$$

$$\mathbf{p} = [\mu, k, C_{\mathrm{ir}}, \gamma, \beta, \lambda_p, \lambda_d, C_{\mathrm{th}}, N_{\max}, r_{\min}, S, \ldots]$$

Identify uncertain physical and biological parameters from sparse cell-density measurements.

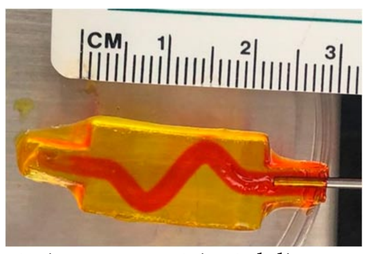
Sparse observations → Forward solve → Mismatch → Adjoint gradient → Parameter update

OPT-2: Optimal graft design

$$\min_{\Gamma,\, u_{\mathrm{perf}}} \mathcal{J}_{\mathrm{design}}$$

Possible design variables:

- channel geometry Γ;
- channel radius, spacing, and path;
- perfusion schedule $u_{\mathrm{perf}}(t)$;
- graft material properties.



Optimize channel geometry and perfusion to improve nutrient delivery, cell viability, and eventual vascularization.

Initial design → Forward prediction → Vascularization metric → Design update

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References

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