Computational Modeling of Diffusion-Based Transport from Differing Designs of Drug-Containing Sutures

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INTRODUCTION:

- Millions of people are injured in a way requiring wound closure (via home remedies and/or suturing), and many have wounds that result in excessive scarring and complications.
- Wounds requiring surgical closure result in up to 11 million keloid scars.
- No combination therapy that includes simultaneous closure and medication is currently employed.

GOAL: To investigate sutures as a drug-delivery device to guide the stages of the wound healing process (Figure 1) to promote healing and minimize scarring.

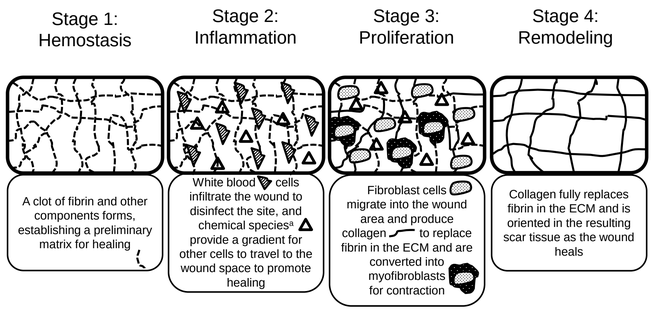


Figure 1. Phases of wound healing.[1]

COMPUTATIONAL METHODS: Concentration profiles of a hypothetical medication within a dermal wound following diffusion from various drug-loaded suture designs were predicted.

$$\frac{\partial C_A}{\partial t} = D_A\left[\frac{\partial^2 C_A}{\partial x^2} + \frac{\partial^2 C_A}{\partial y^2}\right]$$

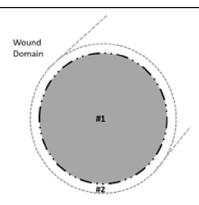
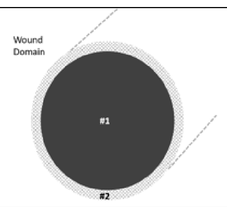
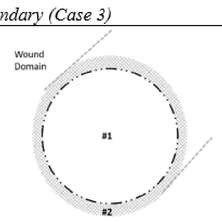
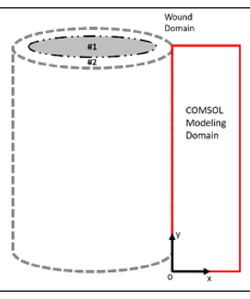
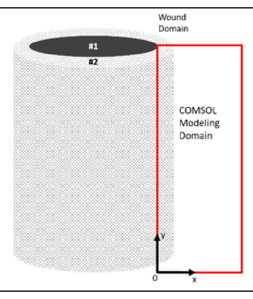
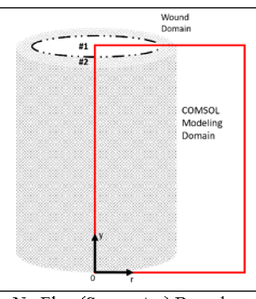
	Model #1: *Suture Utilizing a Fixed Concentration Boundary (Case 1)*	Model #2: *Drug-coated Solid Suture with Flux Boundary (Case 2)*	Model #3: *Drug-loaded Hollow Suture with Porous Wall and Flux Boundary (Case 3)*
3-D Conceptual Suture Design			
Identifying COMSOL Simulation Domain			
Left Boundary Condition, Domain 1	N/A	N/A	No Flux (Symmetry) Boundary $\frac{\partial C_{A,1}}{\partial r} = 0$ (at r = 0 mm)
Right Boundary Condition, Domain 1	N/A	N/A	Flux Boundary $\frac{\partial C_{A,1}}{\partial r} = P * (c_{A,2} - \Phi * c_{A,1})$ (at r = 0.2 mm)
Left Boundary Condition, Domain 2	N/A	No Flux Boundary $\frac{\partial C_{A,2}}{\partial x} = 0$ (at x = 0 mm)	Flux Boundary $\frac{\partial C_{A,2}}{\partial r} = P * (\Phi * c_{A,1} - c_{A,2})$ (at r = 0.2 mm)
Right Boundary Condition, Domain 2	N/A	Flux Boundary $\frac{\partial C_{A,2}}{\partial x} = P * (c_{A,2} - \Phi * c_{A,w})$ (at x = 0.08 mm)	Flux Boundary $\frac{\partial C_{A,2}}{\partial r} = P * (c_{A,w} - \Phi * c_{A,2})$ (at r = 0.28 mm)
Left Boundary Condition, Wound Domain	Fixed Concentration Boundary $C_{A,w}$ = 1,000 mol/m³ (at x = 0 mm)	Flux Boundary $\frac{\partial C_{A,w}}{\partial x}$ = P* $(\Phi * c_{A,2} - c_{A,w})$ (at x = 0.08 mm)	Flux Boundary $\frac{\partial C_{A,w}}{\partial r} = P * (\Phi * c_{A,2} - c_{A,w})$ (at r = 0.28 mm)
Right Boundary Condition, Wound Domain	No Flux Boundary $\frac{\partial C_{A,w}}{\partial x} = 0$ (at x = 0.42 mm)	No Flux Boundary $\frac{\partial C_{A,w}}{\partial x} = 0$ (at x = 0.5 mm)	No Flux Boundary $\frac{\partial C_{A,w}}{\partial r} = 0$ (at r = 0.7 mm)
Top Boundaries (All Domains)	No Flux Boundary $\frac{\partial C_{A,w}}{\partial y} = 0$ (at y = 3 mm)	No Flux Boundary $\frac{\partial C_A}{\partial y} = 0$ (at y =3 mm)	No Flux Boundary $\frac{\partial C_A}{\partial y} = 0$ (at y =3 mm)
Bottom Boundaries (All Domains)	No Flux Boundary $\frac{\partial C_{A,w}}{\partial y} = 0$ (at y = 0 mm)	No Flux Boundary $\frac{\partial C_A}{\partial y} = 0$ (at y = 0 mm)	No Flux Boundary $\frac{\partial C_A}{\partial y} = 0$ (at y = 0 mm)
Initial Condition in Domain 1	N/A	N/A	$C_{A,1}$ = 1,000 mol/m³
Initial Condition in Domain 2	N/A	$C_{A,2}$ = 1,000 mol/m³	$C_{A,2}$ = 0 mol/m³
Initial Condition in Wound Domain	$C_{A,w}$ = 0 mol/m³	$C_{A,w}$ = 0 mol/m³	$C_{A,w}$ = 0 mol/m³

Table 1. Domains, boundary conditions, and initial conditions used in COMSOL simulations for each suture design. Note: $C_{A,1}$, $C_{A,2}$, and $C_{A,w}$ are the drug concentrations in domain 1, domain 2, and the wound domain, respectively.

RESULTS:

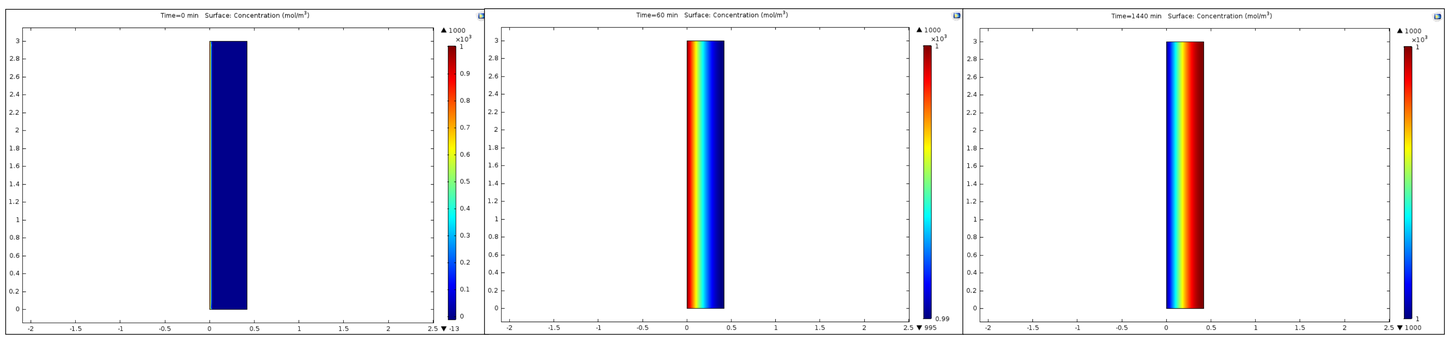


Figure 2. Case 1: Suture Utilizing a Fixed Concentration Boundary.

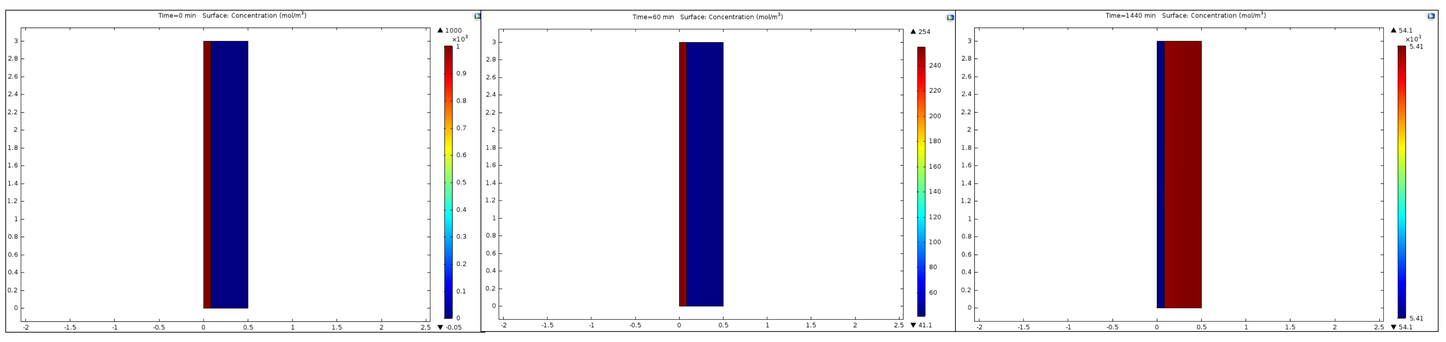


Figure 3. Case 2: Drug-coated Solid Suture with Flux Boundary.

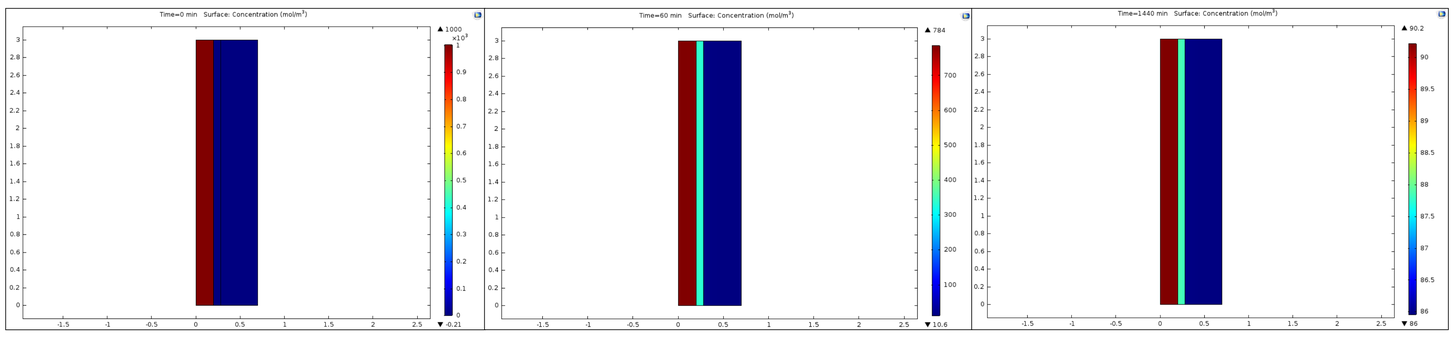


Figure 4. Case 3: Drug-loaded Hollow Suture with Porous Wall and Flux Boundary.

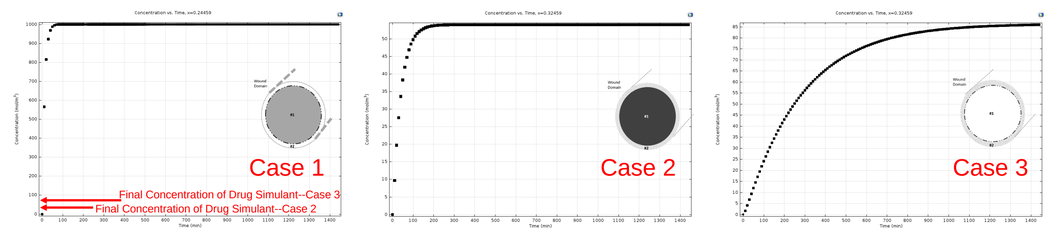


Figure 5. The concentration profile that develops along a specified vertical cut-line within the domains of Case 1, Case 2, and Case 3, respectively.

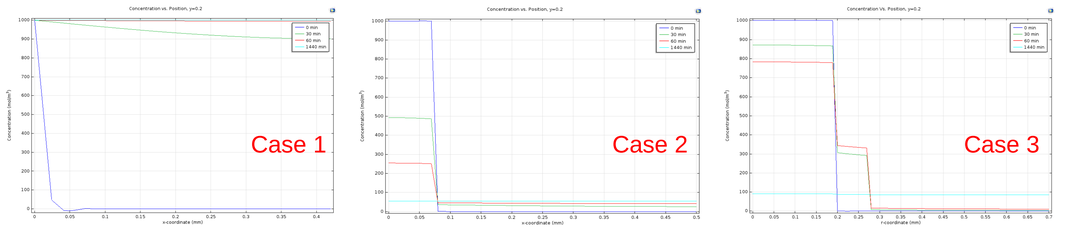


Figure 6. The concentration profile that develops along a specified horizontal cut-line within the domains of Case 1, Case 2, and Case 3, respectively.

CONCLUSIONS: Mathematical modeling and computer simulations often present a more viable option than experimentation for testing trial-and-error designs for new products such as biomedical devices or sutures. This work presents three designs and associated simulation results for drug-delivering sutures. While presented only for diffusion of a drug simulant from a suture to the wound area, the nature of simulation lends itself to the adaptation towards more complicated methods of drug delivery from sutures and other transdermal applications. Future work might include modifying the produced COMSOL model to apply parameters that are more fitting to the physiology of wound healing.

REFERENCES:

1. Jorgensen, S. and R. Sanders, Mathematical Models of Wound Healing and Closure: A Comprehensive Review, Medical & Biological Engineering and Computing, Volume 54, 1297-1316, (2016)

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