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

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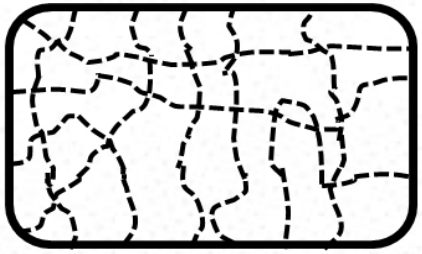
Outline

- Introduction
- Computational Methods
- Results
- Conclusions
- Suggestions?

GOAL: To investigate sutures as a drug delivery device to guide the stages of the wound healing process to promote healing and minimize scarring

Stage 1:
Hemostasis

(0 minutes – 1 hour)



A clot of fibrin and other components forms, establishing a preliminary matrix for healing

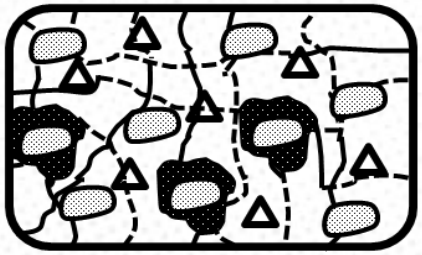
Stage 2:
Inflammation

(1 hour – 1 week)

White blood cells infiltrate the wound to disinfect the site, and chemical species[a] provide a gradient for other cells to travel to the wound space to promote healing

Stage 3:
Proliferation

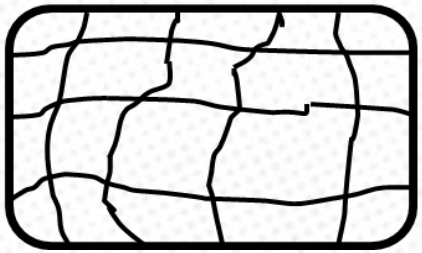
(5-7 days – 1-2 weeks)



Fibroblast cells migrate into the wound area and produce collagen to replace fibrin in the ECM and are converted into myofibroblasts for contraction

Stage 4:
Remodeling

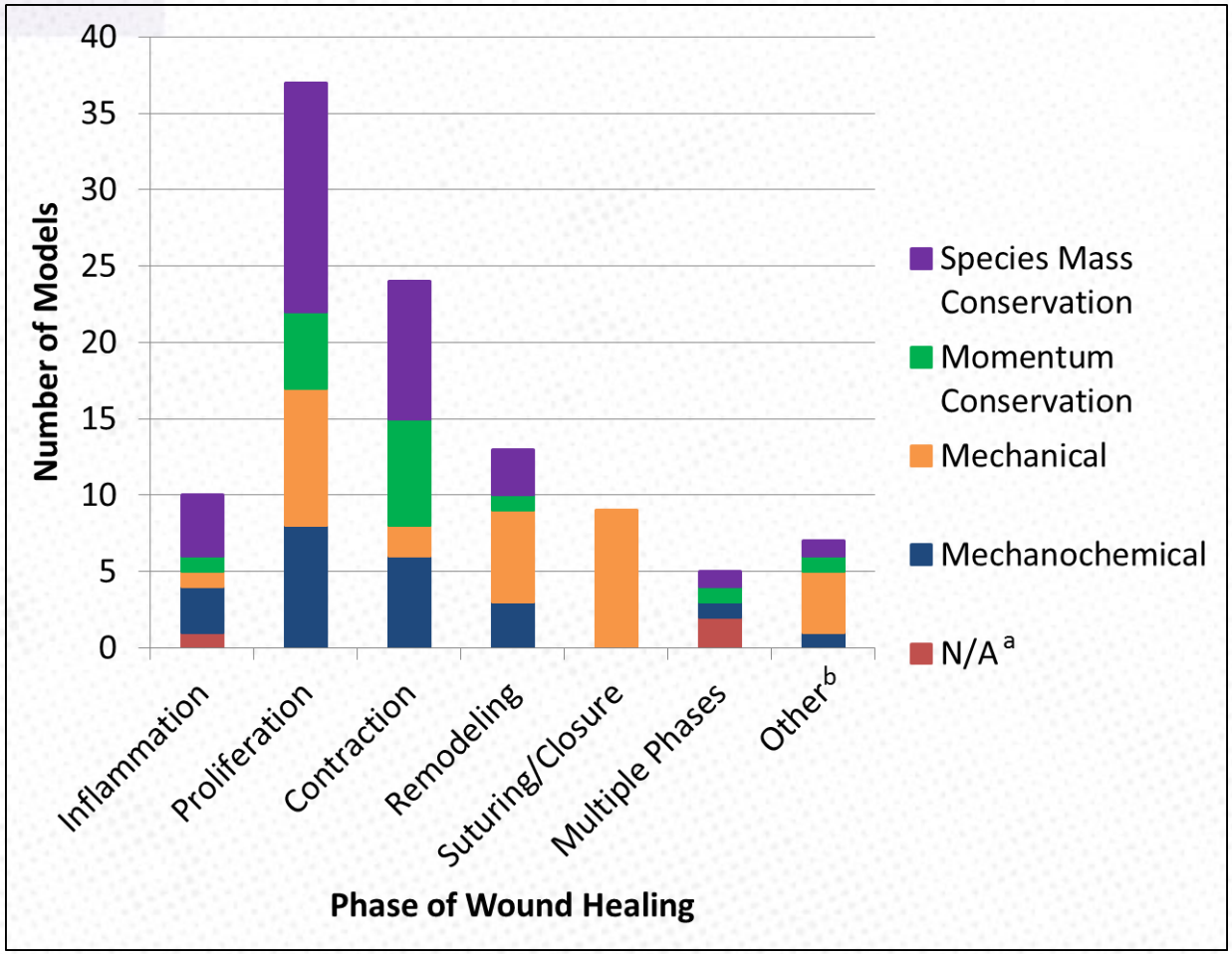
(1-2 weeks – indefinite)



Collagen fully replaces fibrin in the ECM and is oriented in the resulting scar tissue as the wound heals

Jorgensen, S. and Sanders, J. (2016) Mathematical models of wound healing and closure: A comprehensive review. Med Biol Eng Comput 54(9):1297-1316

Results of Literature Review



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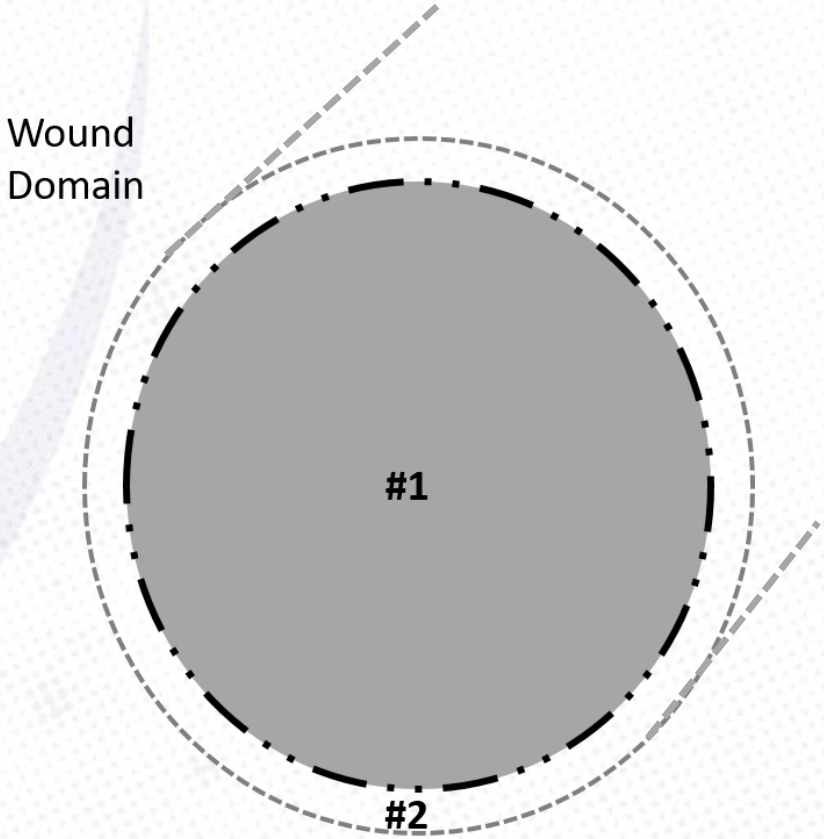
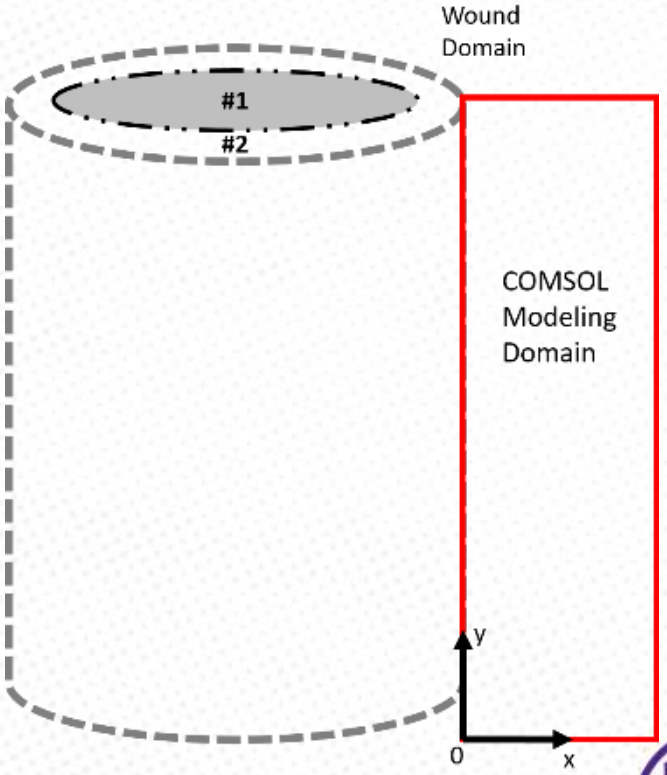
COMSOL Multiphysics, 5.0

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

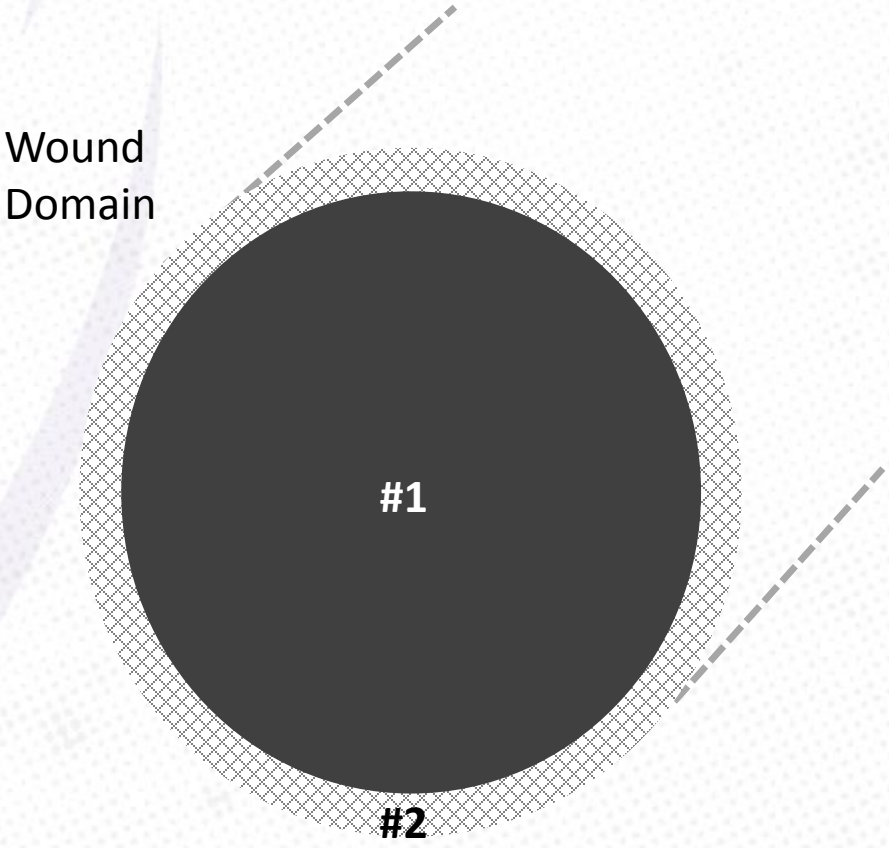
	Case 1	Case 2	Case 3
Study used in Interior Suture Domain	N/A	N/A	Time-dependent transport of diluted species
Study used in Porous Drug Coating or Porous Wall of Suture Domain	N/A	Time-dependent species transport in porous media (porosity = 0.3, 0.6, or 0.9)	Time-dependent species transport in porous media (porosity = 0.3, 0.6, or 0.9)
Study used in Wounded Dermal Tissue Domain	Time-dependent transport of diluted species	Time-dependent species transport in porous media (porosity = 1)	Time-dependent species transport in porous media (porosity = 1)

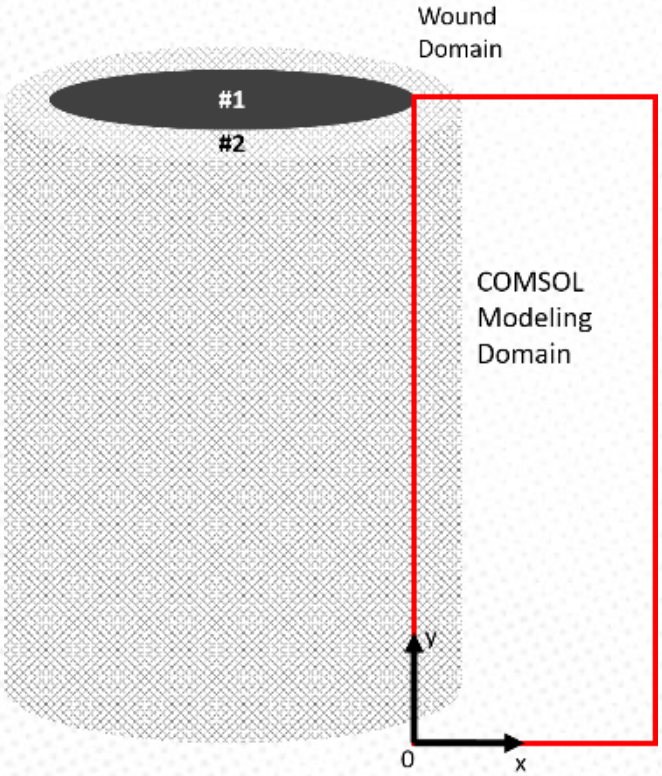
Case 1: Suture Design that Releases Drug through a Fixed Concentration Boundary



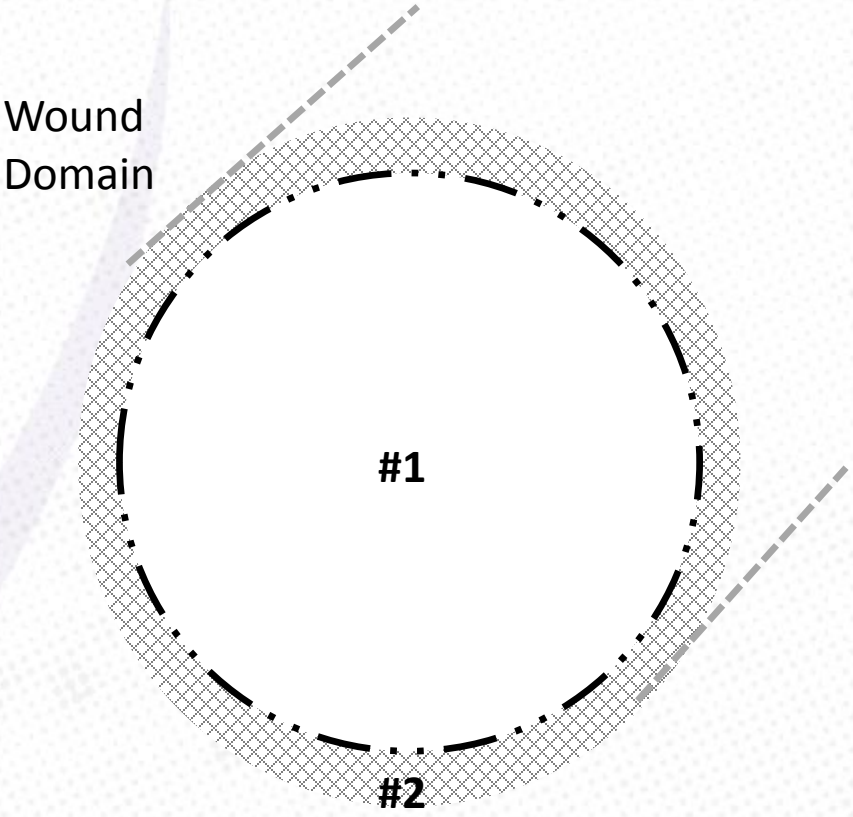


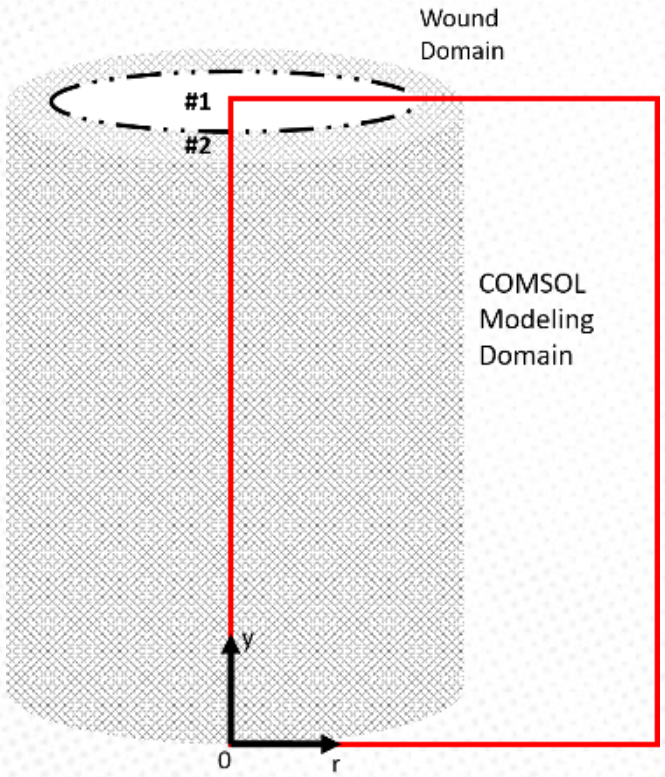
Case 2: Drug-Coated Solid Suture





Case 3: Drug-Loaded, Hollow Suture with Porous Wall





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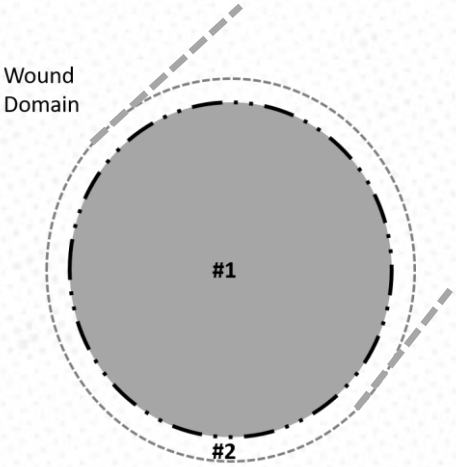
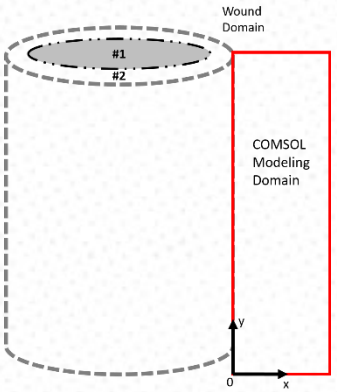
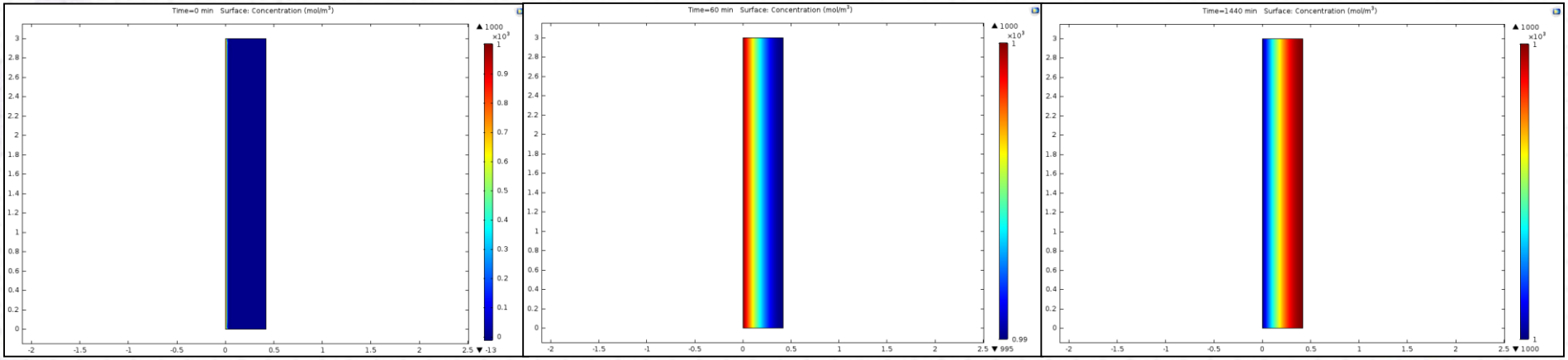
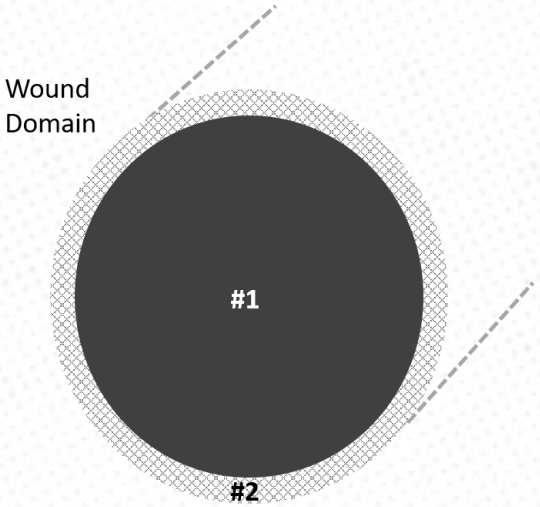
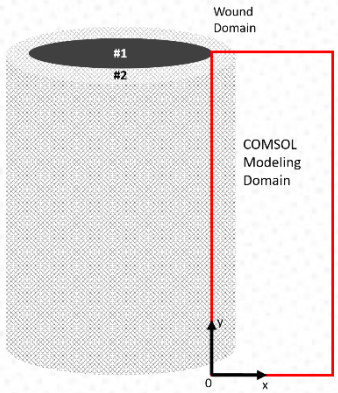


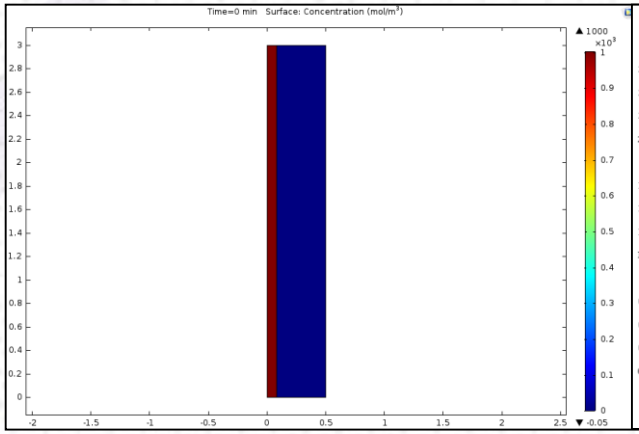


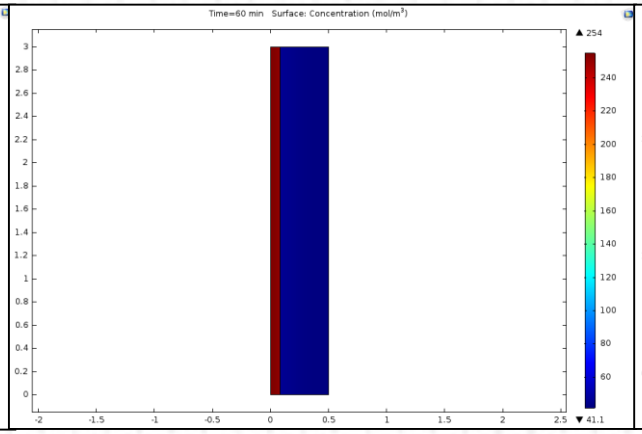


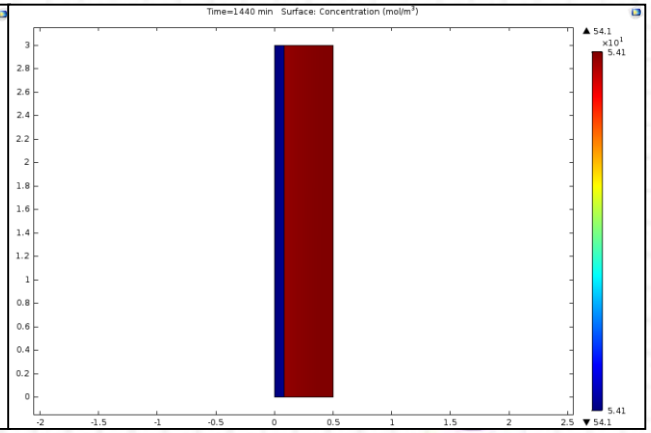
Case 2: Drug-Coated Solid Suture











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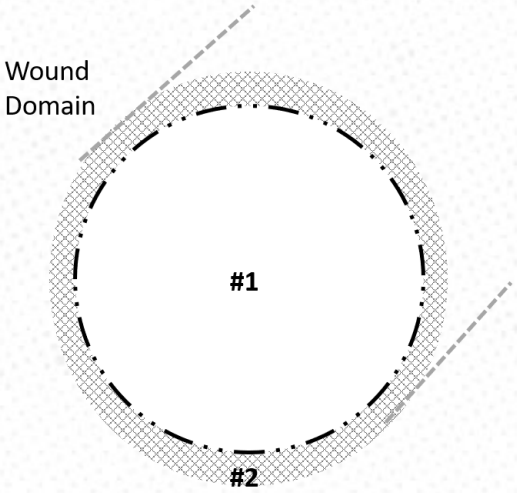
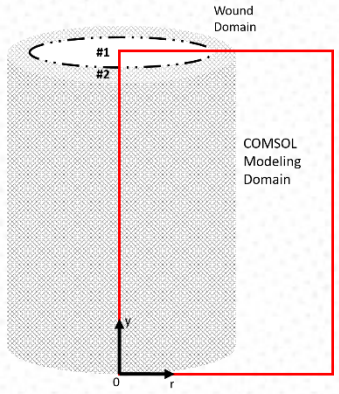
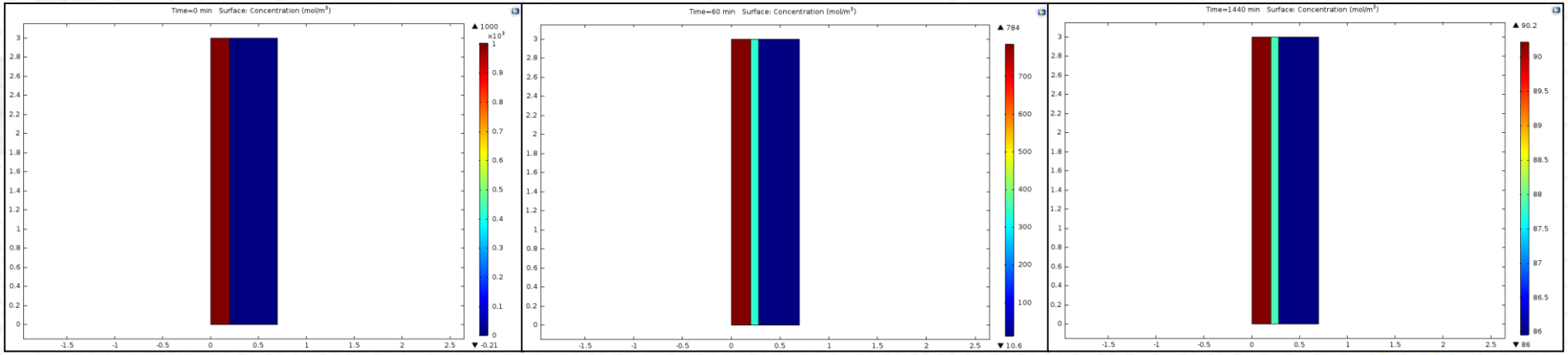
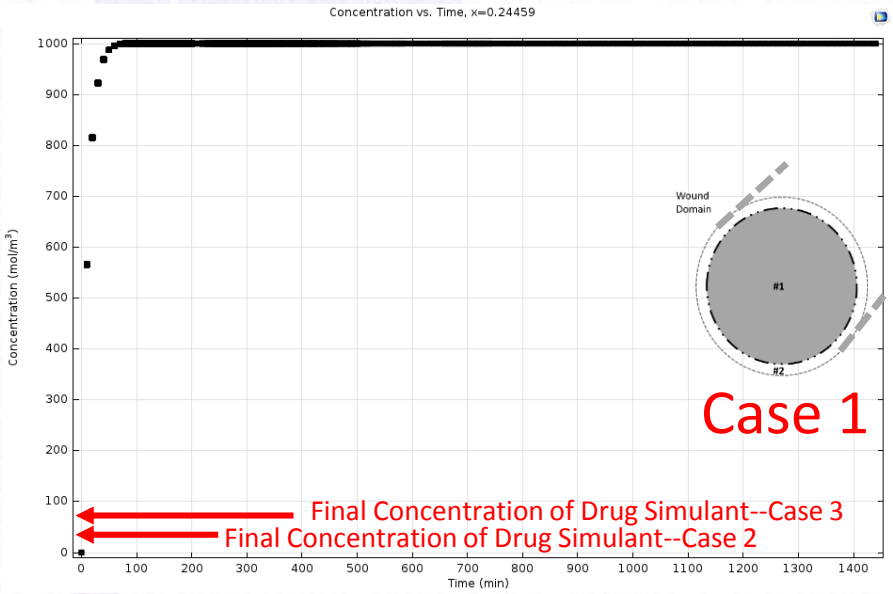
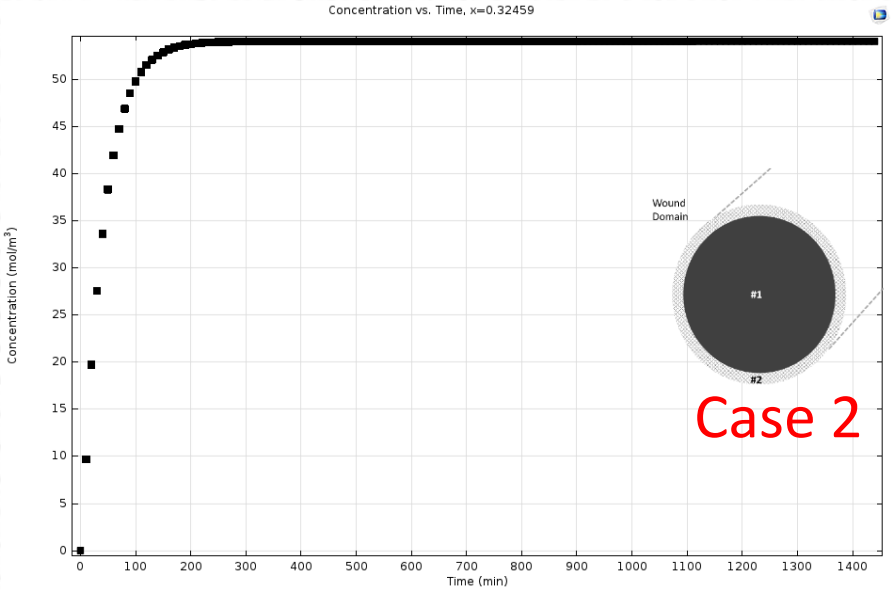


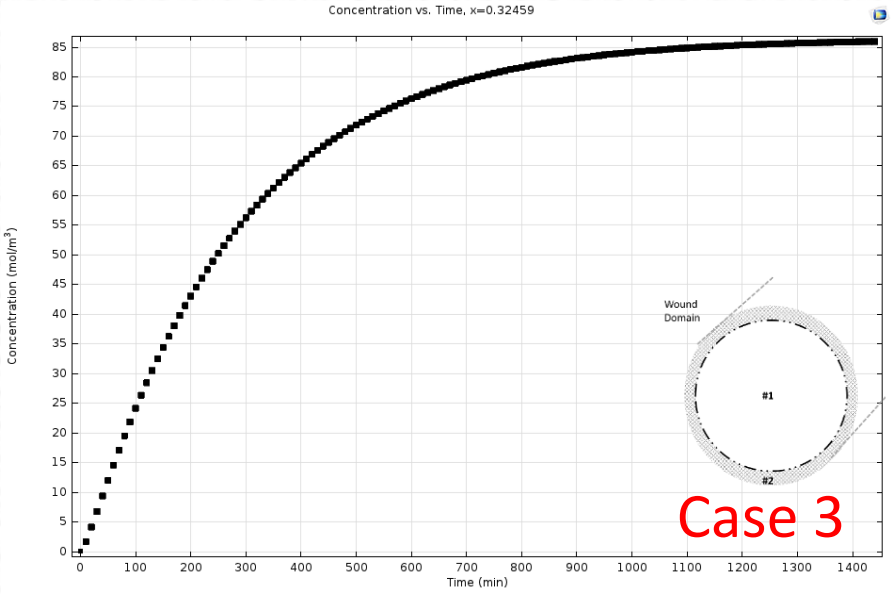




Results of Each Case







Concluding Remarks

GOAL: To investigate sutures as a drug delivery device to guide the stages of the wound healing process to promote healing and minimize scarring

- COMSOL Modeling of Drug-Containing Sutures
  - Concentration profiles of drug simulant that might result from three designs of sutures
  - Results suggest time-varying effects associated with suture design
- Next Steps
  - Better match the suture designs to physiology by combining with experimental studies/physiological parameters

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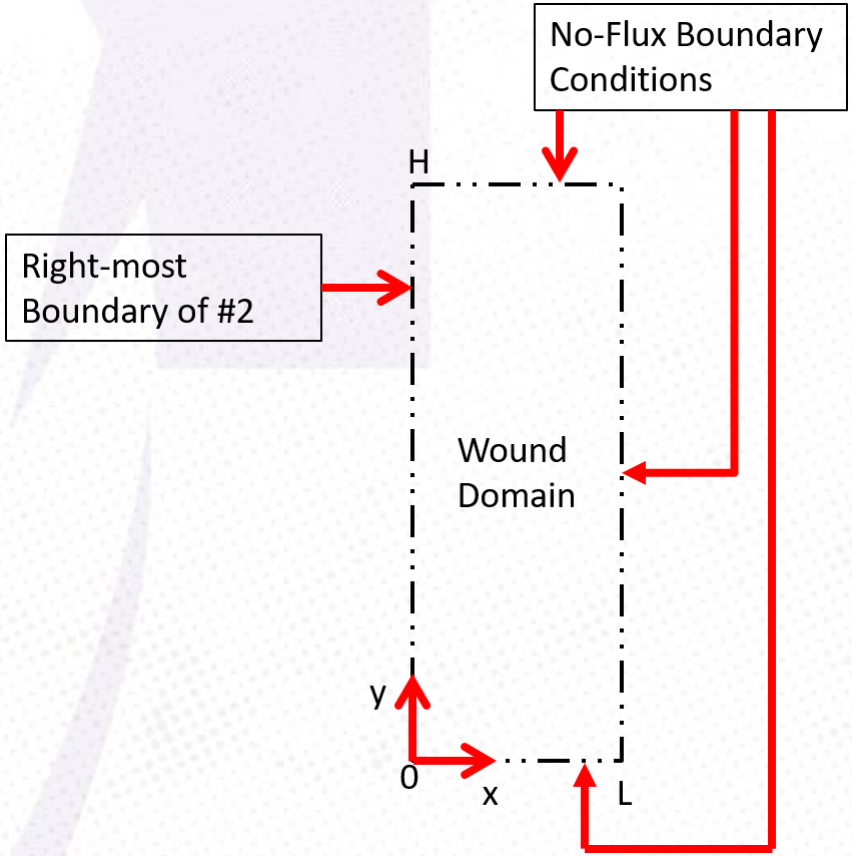
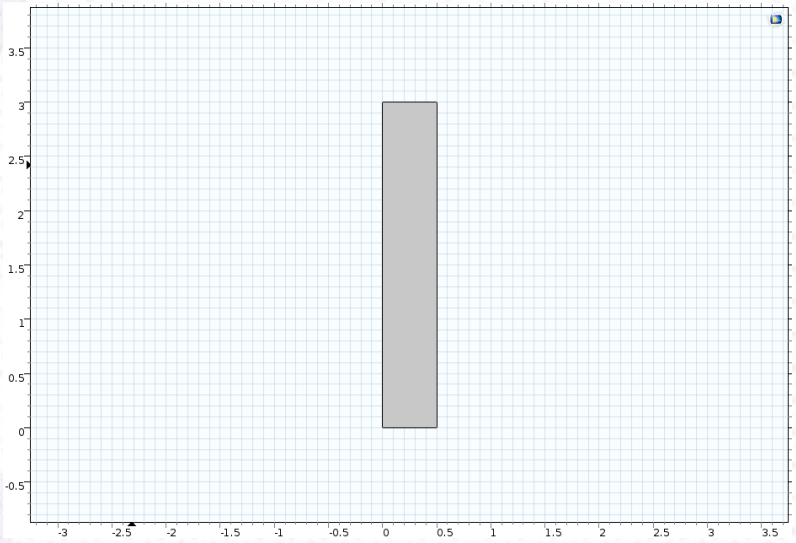
Questions?

Extra Slides





- Species mass continuity equation
- Assumptions
  - Fick's Law of Diffusion
  - Diffusion in x- and y-directions only
  - No reaction occurring in the bulk of the domain

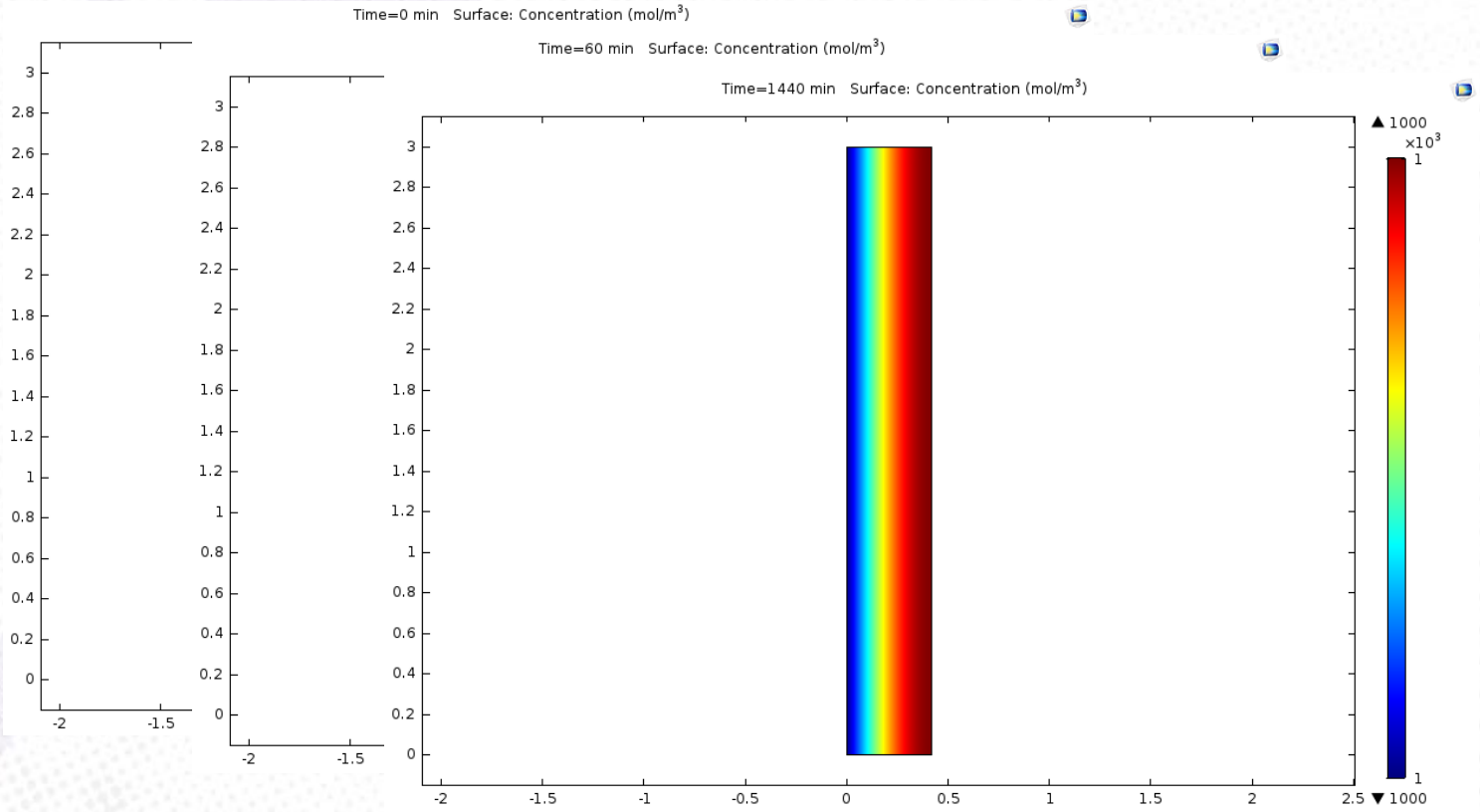
Dimensions of COMSOL Model		"Physics" for COMSOL Simulation		Parameters of COMSOL Simulation	
Width of Interior Suture Domain	N/A	Study used in Interior Suture Domain	N/A	Diffusion Coefficient of Drug Simulant	$1 * 10^{-10}$ m^2/s
Width of Porous Drug Coating or Porous Wall of Suture Domain	N/A	Study used in Porous Drug Coating or Porous Wall of Suture Domain	N/A	Permeability	N/A
Width of Wounded Dermal Tissue Domain	0.42 mm	Study used in Wounded Dermal Tissue Domain	Time-dependent transport of diluted species	Partition Coefficient	N/A
Height of Domain(s)	3 mm			Initial Concentration of Drug Simulant	1,000 mol/m^3 (Left Boundary)
				Initial Concentration of Drug Simulant Elsewhere	0 mol/m^3

Dimensions and Parameters of Conceptual Domain		Parameters Used in COMSOL Simulation	
Assumed Width (Radius) of Interior Suture Domain	$6.0 * 10^{-4}$ m	Physics used in Wound Domain for COMSOL Simulation	Time-dependent transport of diluted species in porous media
Calculated Width of Outer Transport Domain of Suture	$3.25 * 10^{-5}$ m	Porosity Assumed for Wound Domain	0.1
Width of Wounded Dermal Tissue Domain	$4.2 * 10^{-4}$ m	Diffusion Coefficient of Drug Simulant	$1 * 10^{-11}$ m^2/s
Height of All Domains	$3 * 10^{-3}$ m	Initial Concentration of Drug Simulant	900 mol/m^3 (Left Boundary)
Assumed Initial Concentration of Drug Simulant in Interior Suture Domain	1,000 mol/m^3	Initial Concentration of Drug Simulant Elsewhere	0 mol/m^3
Assumed Initial Concentration of Drug Simulant in Outer Transport Domain of Suture	0 mol/m^3 (Allowed to quickly accumulate and not drop below 900 mol/m^3 during the duration of the validation simulation)		

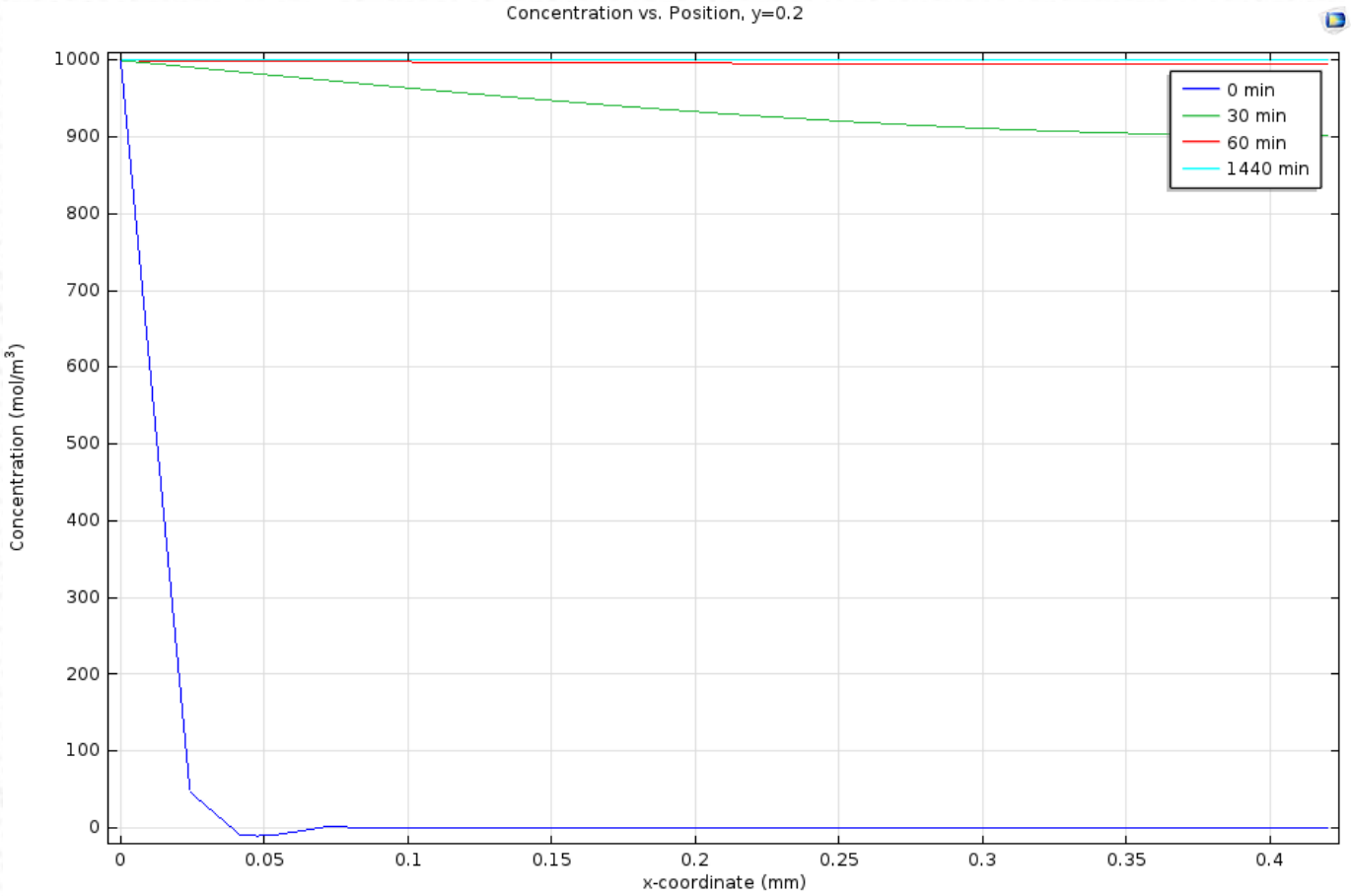
Dimensions of COMSOL Model		"Physics" for COMSOL Simulation		Parameters of COMSOL Simulation	
Width of Interior Suture Domain	N/A	Study used in Interior Suture Domain	N/A	Diffusion Coefficient of Drug Simulant	$1 * 10^{-10}$ m^2/s
Width of Porous Drug Coating or Porous Wall of Suture Domain	0.08 mm	Study used in Porous Drug Coating or Porous Wall of Suture Domain	Time-dependent species transport in porous media (porosity = 0.3, 0.6, or 0.9)	Permeability	$1*10^{-6}$ m^2/s
Width of Wounded Dermal Tissue Domain	0.42 mm	Study used in Wounded Dermal Tissue Domain	Time-dependent species transport in porous media (porosity = 1)	Partition Coefficient	1
Height of Domain(s)	3 mm			Initial Concentration of Drug Simulant	1,000 mol/m^3 (Drug-Coated Portion of Suture Domain)
				Initial Concentration of Drug Simulant Elsewhere	0 mol/m^3

Dimensions of COMSOL Model		"Physics" for COMSOL Simulation		Parameters of COMSOL Simulation	
Width of Interior Suture Domain	0.2 mm	Study used in Interior Suture Domain	Time-dependent transport of diluted species	Diffusion Coefficient of Drug Simulant	$1 * 10^{-10}$ m^2/s
Width of Porous Drug Coating or Porous Wall of Suture Domain	0.08 mm	Study used in Porous Drug Coating or Porous Wall of Suture Domain	Time-dependent species transport in porous media (porosity = 0.3, 0.6, or 0.9)	Permeability	$1*10^{-6}$ m^2/s
Width of Wounded Dermal Tissue Domain	0.42 mm	Study used in Wounded Dermal Tissue Domain	Time-dependent species transport in porous media (porosity = 1)	Partition Coefficient	1
Height of Domain(s)	3 mm			Initial Concentration of Drug Simulant	1,000 mol/m^3 (Interior Suture Domain)
				Initial Concentration of Drug Simulant Elsewhere	0 mol/m^3

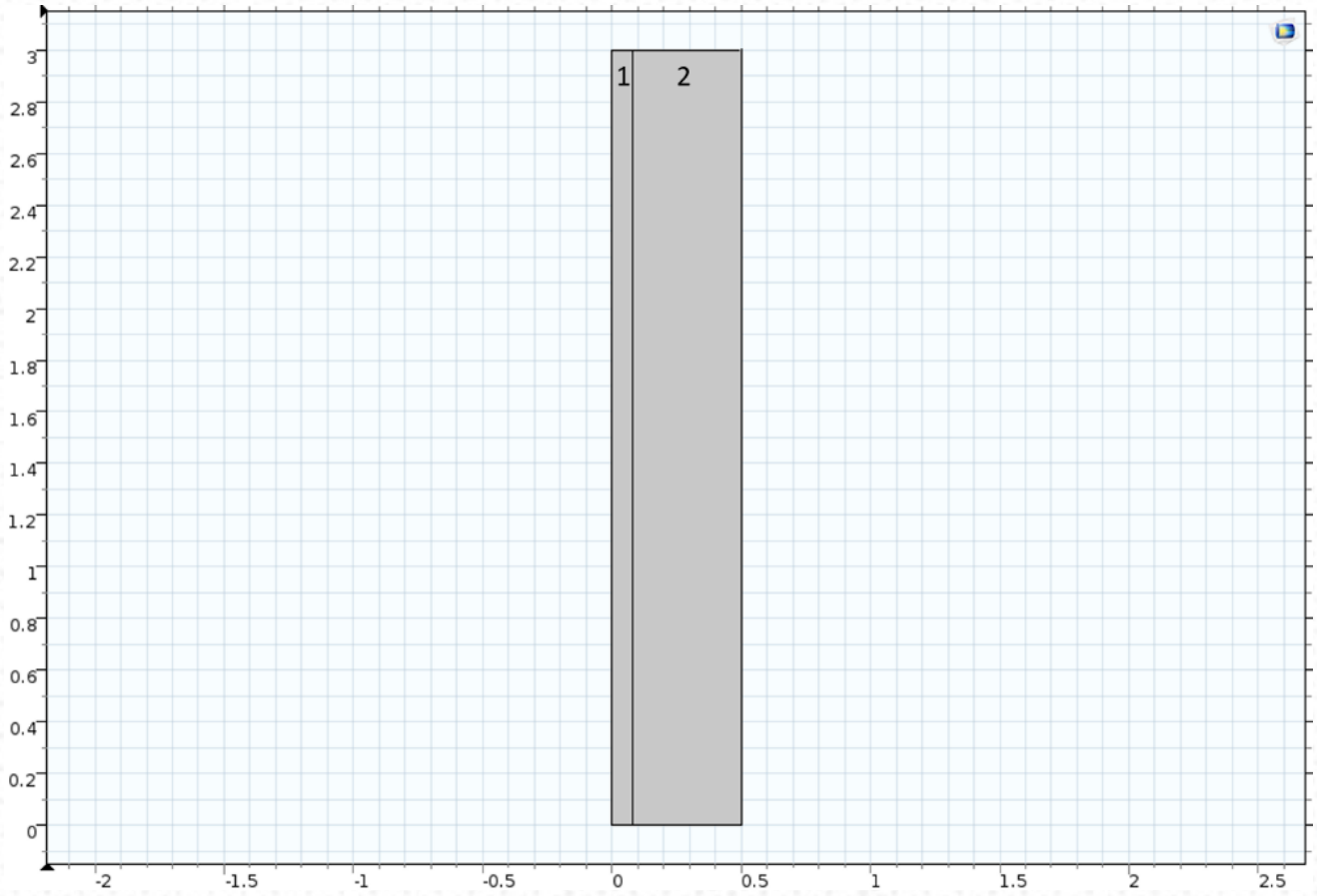
Results of Case 1



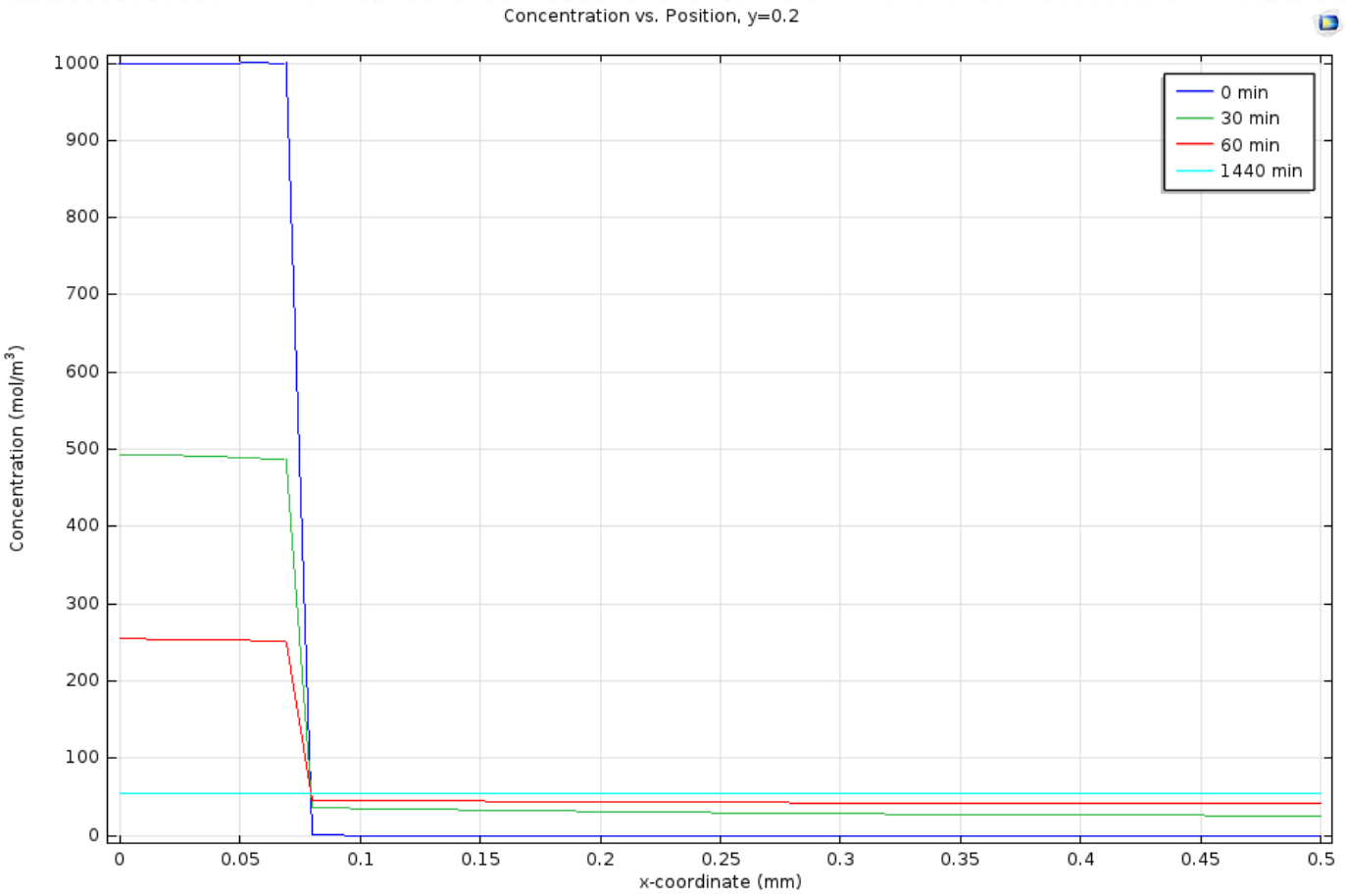
Results of Case 1, Continued



Case 2: Drug-Coated Solid Suture Design



Results of Case 2, Continued



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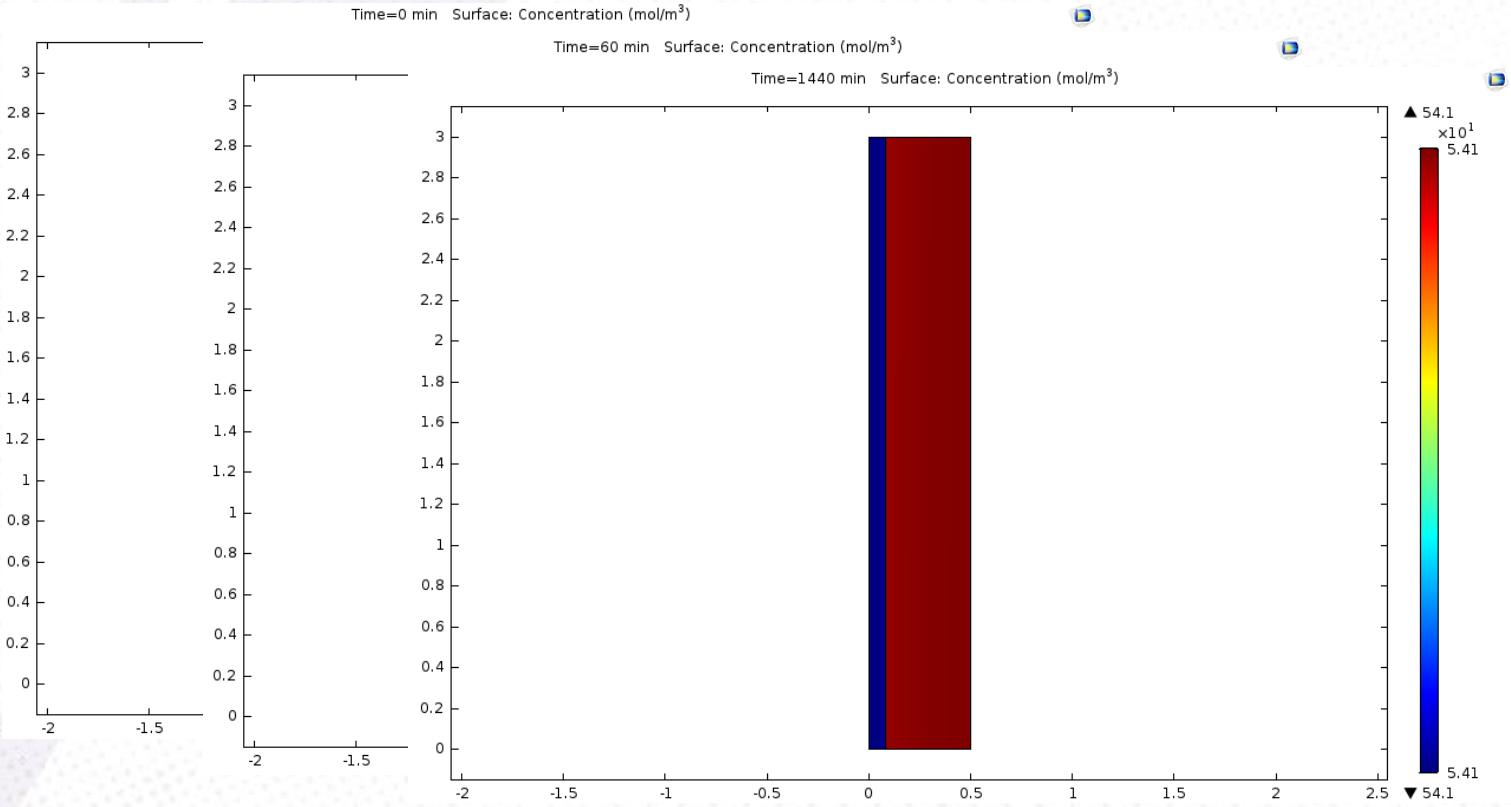
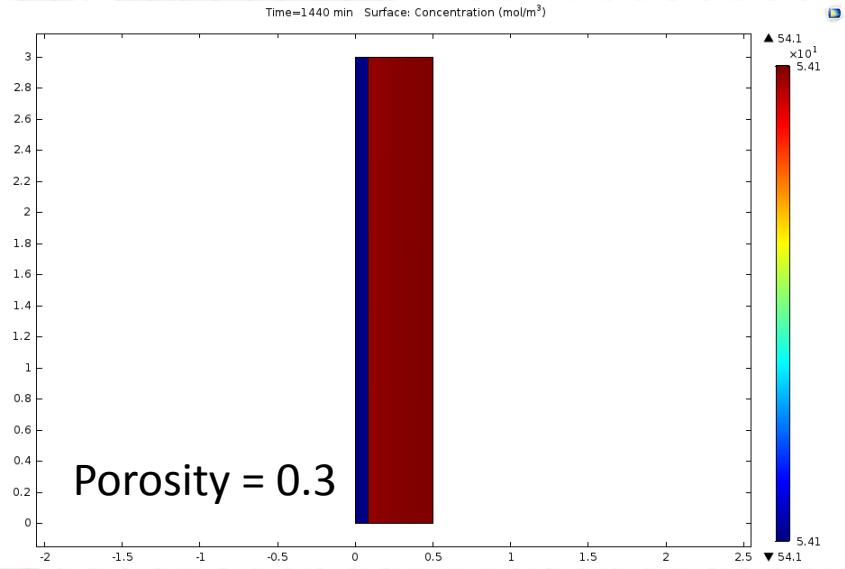
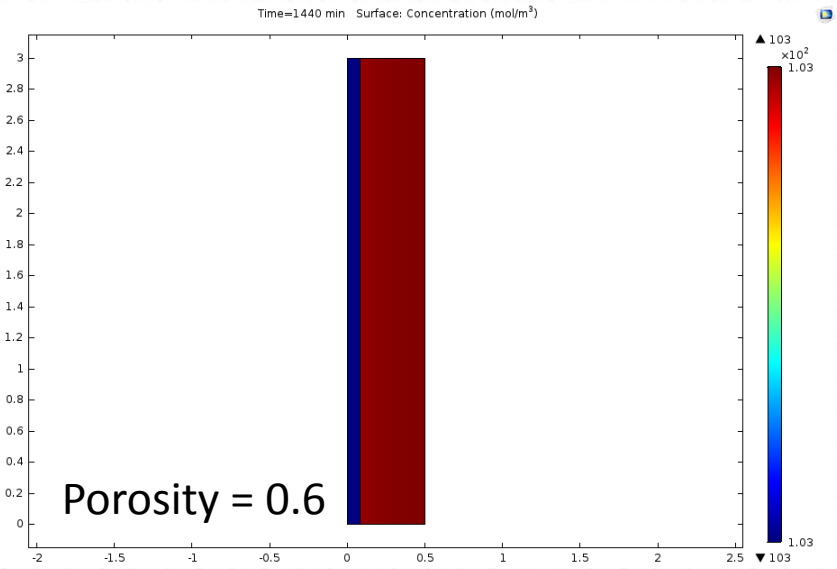
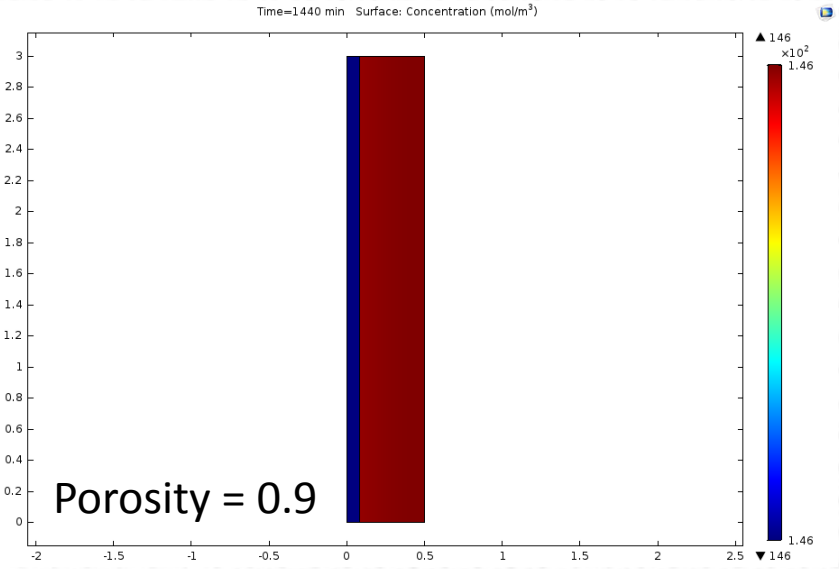


Results of Case 2, Continued

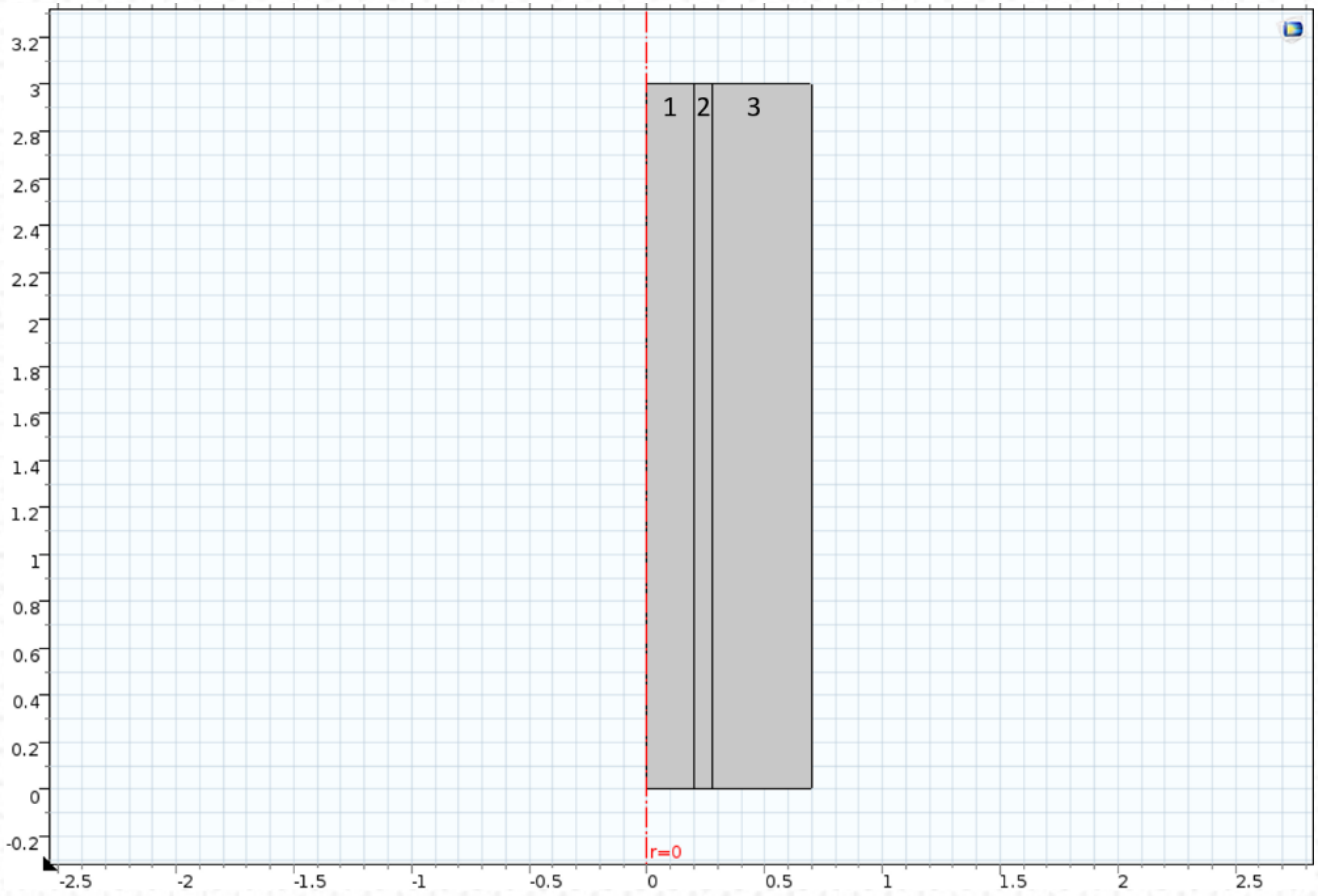




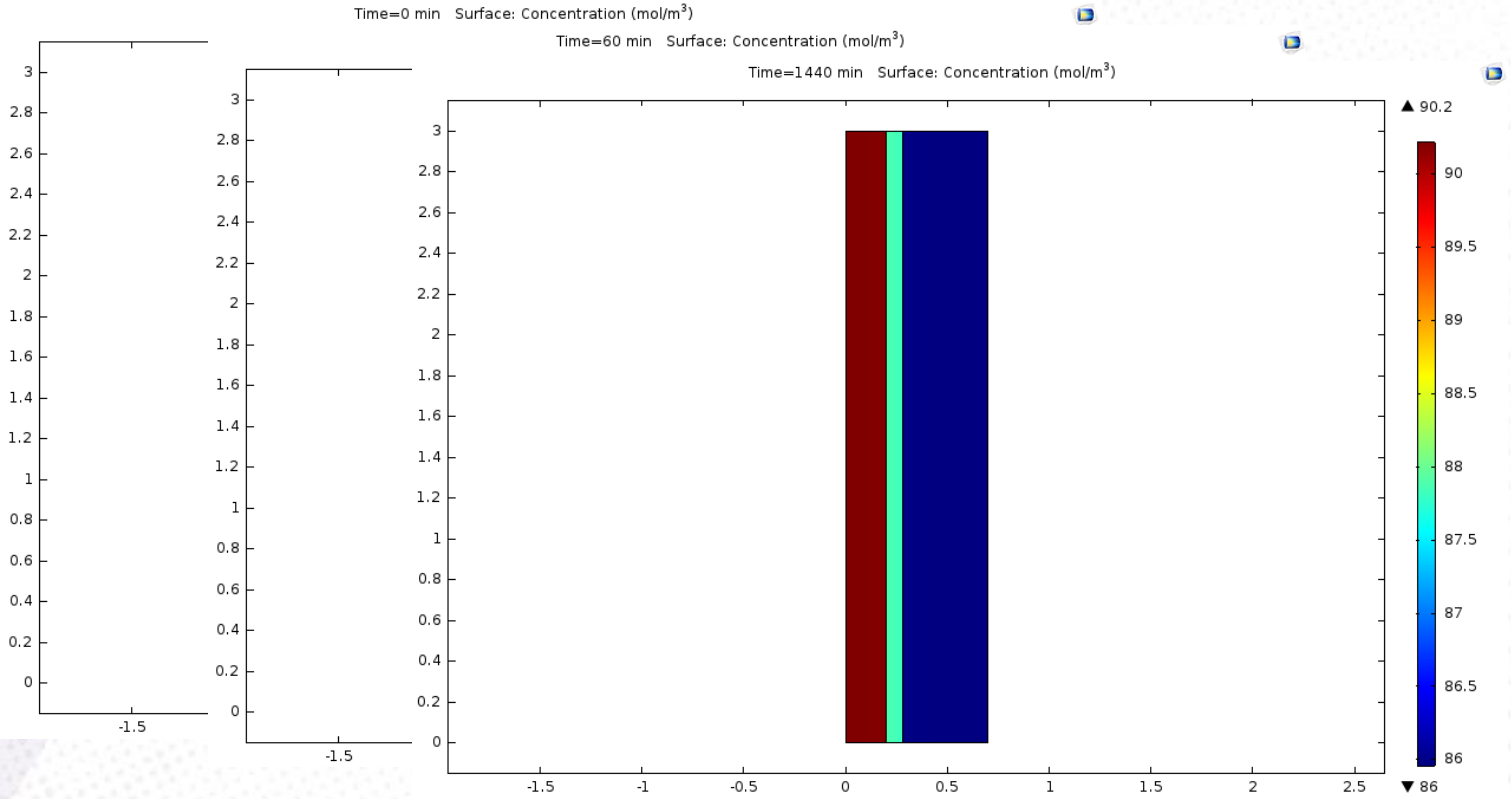


Porosity of the drug-coated portion of the solid suture increases, resulting increase in final concentration of drug simulant

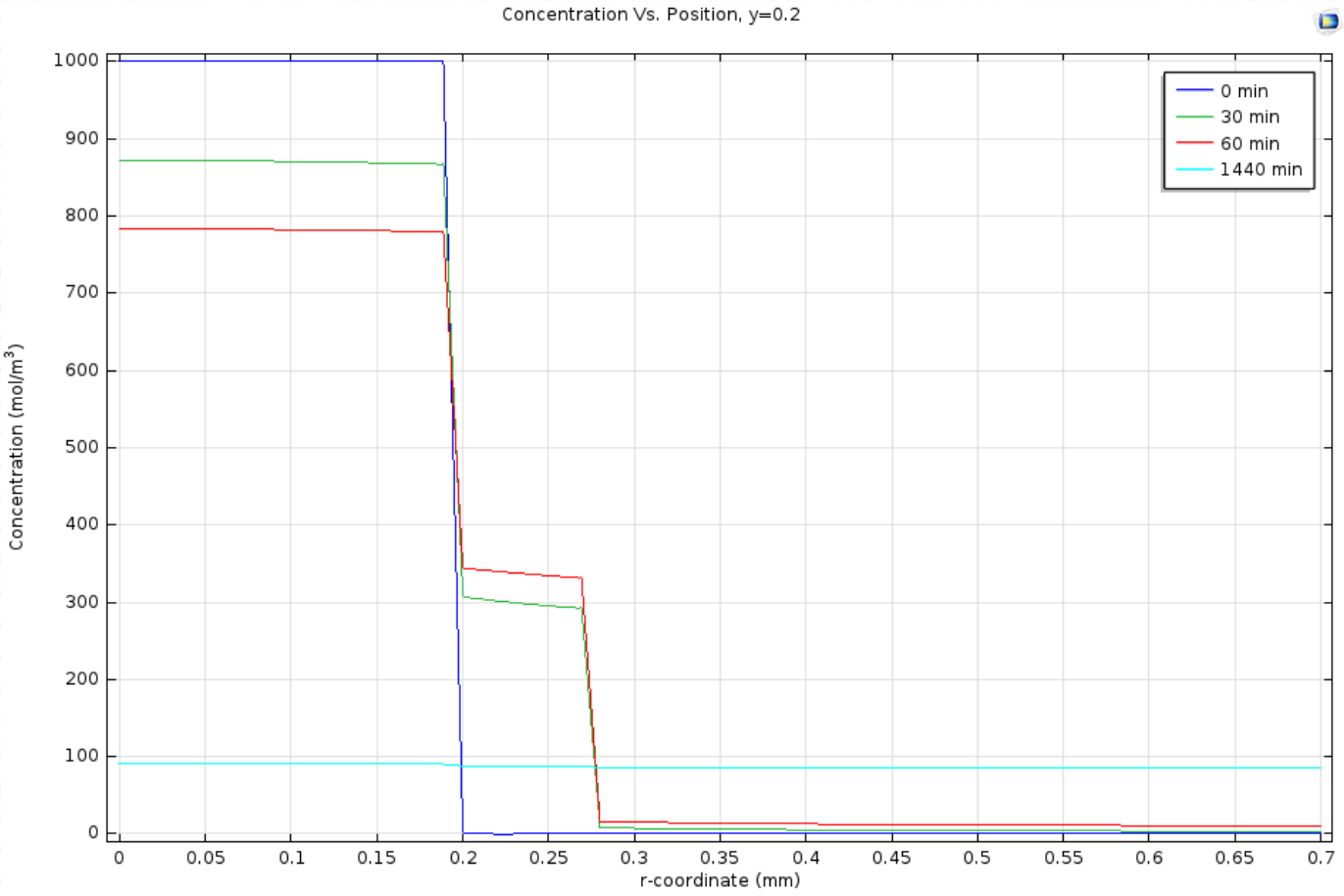
Case 3: Drug-Loaded, Hollow Suture with Porous Wall



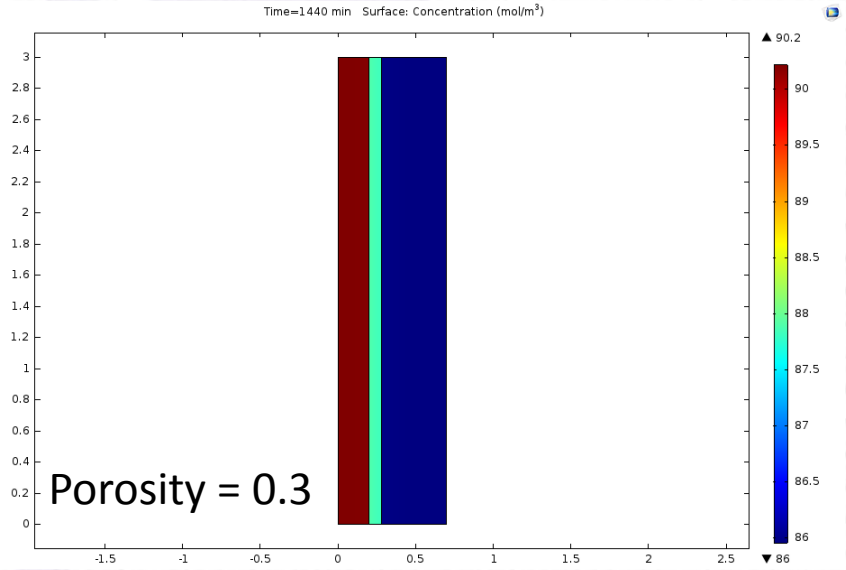
Results of Case 3

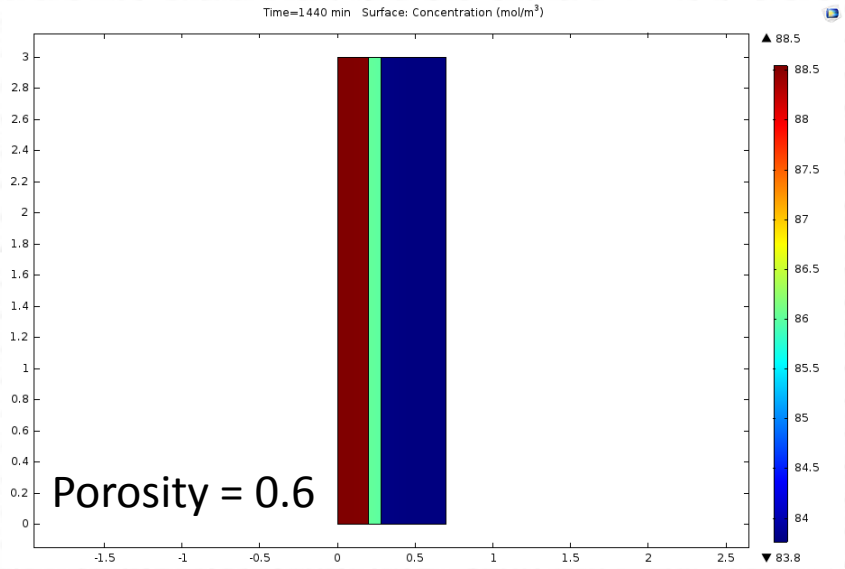


Results of Case 3, Continued

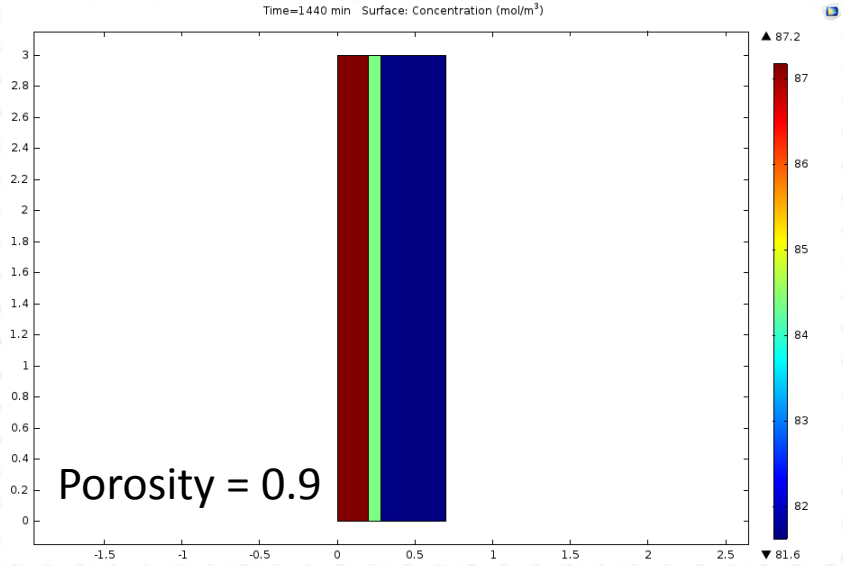


Results of Case 3, Continued





Porosity of the porous wall of the suture increases, resulting in a more uniform distribution throughout the simulation domains



Results of Case 3, Continued