Modeling the Flow and Diffusion of Lidocaine Through Tooth and Gum

BEE 4530: Computer-Aided Engineering: Biomedical Processes

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1. Executive Summary

The movement of anesthesia around and through the tooth and gum was modeled in order to design a novel procedure to effectively anesthetize a single tooth with minimal side effects. This model includes the injection of lidocaine into the gum near the tooth, and the ensuing diffusion of anesthesia through the tooth and gum. The geometry of the tooth and gum has been drawn in two dimensions in COMSOL. The Brinkman's equations were used to model the fluid flow resulting from the initial injection through the porous media, and the mass transfer equation was used to model how the anesthesia flows through the tooth and gum after the completion of the injection through the coupling of the velocities calculated by the Brinkman's equations. The concentration of anesthesia in this region was calculated, in order to determine the amount of time the tooth is numb and the distance the anesthesia has travelled. The model showed that the optimum procedure for numbing the tooth has a long injection time of five minutes dispensing lidocaine at a slower velocity, specifically 0.018 mol/m^3. This is an important process to model because with the longer injection time the patient's discomfort can be decreased, numbness can be quickly achieved and anesthesia can last for the entirety of an average dental procedure protecting the patient from unnecessary pain.

2. Introduction

In any oral surgical procedure, one of the first steps is to anesthetize the tooth. For the lower teeth and the jaw, this method usually includes inferior alveolar nerve block. This technique stops sensation in the inferior alveolar nerve, which is located along the mandible and connects the lower teeth, lower lip, chin and tongue. To anesthetize this nerve, the dentist will need to insert the syringe posterior to the patient's last molar. This method can also anesthetize neighboring nerves, including the mental nerve and other nerves near to where the inferior alveolar nerve enters the mandible. When using this method the patient experiences discomfort during the injection itself, and then after the procedure the lip, jaw, and chin all remain numb for about 3 hours making it difficult for the patient to quickly return to normal activities. There is also a risk in this procedure that the anesthesia can diffuse to the facial nerve causing temporary facial paralysis, and in very rare cases the facial nerve can be cut by an improperly inserted syringe. This can result in permanent facial paralysis [1].

Lidocaine is a local anesthetic that is often used in dental procedures. This drug acts by blocking the voltage gated ion sodium channels of neurons, and therefore disrupting signal propagation. When enough signals are blocked, the neuron will not depolarize, and then fail to submit an action potential, which causes its anesthetic effects. If epinephrine, a vasoconstrictor, is included in the anesthesia, the absorption of lidocaine is often slowed, depending on the injection site [2].

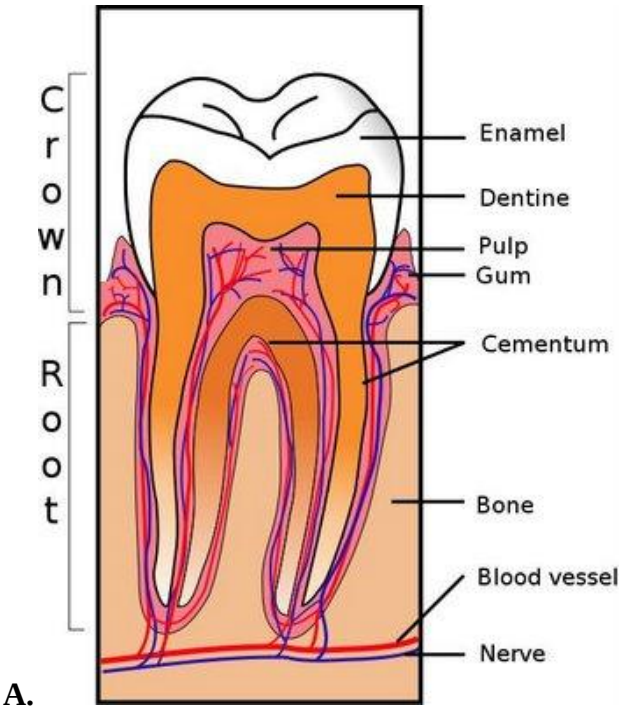
Recently, the Single Tooth Anesthesia System has been produced by Milestone Scientific (Livingston, NJ). This system is described by the company as the first computer controlled system which requires only one injection at one site to numb the tooth. As there is only a single injection site, the patient's discomfort is reduced. These advantages extend after the procedure is over because the numbness does not spread as far as it would in the traditional method. Through this method the patient regains sensation in his or her mouth more quickly and can therefore easily return to his or her normal activities [3]. The novel procedure presented in this report is based on the single injection design of the Single Tooth Anesthesia System. The model used a simplified 2D geometry of the tooth in COMSOL. The Brinkman equation was used to model the fluid flow of the initial injection, and the mass transfer equation was used to model the fluid in the tooth and gum after the injection is complete.

3. Design Objectives

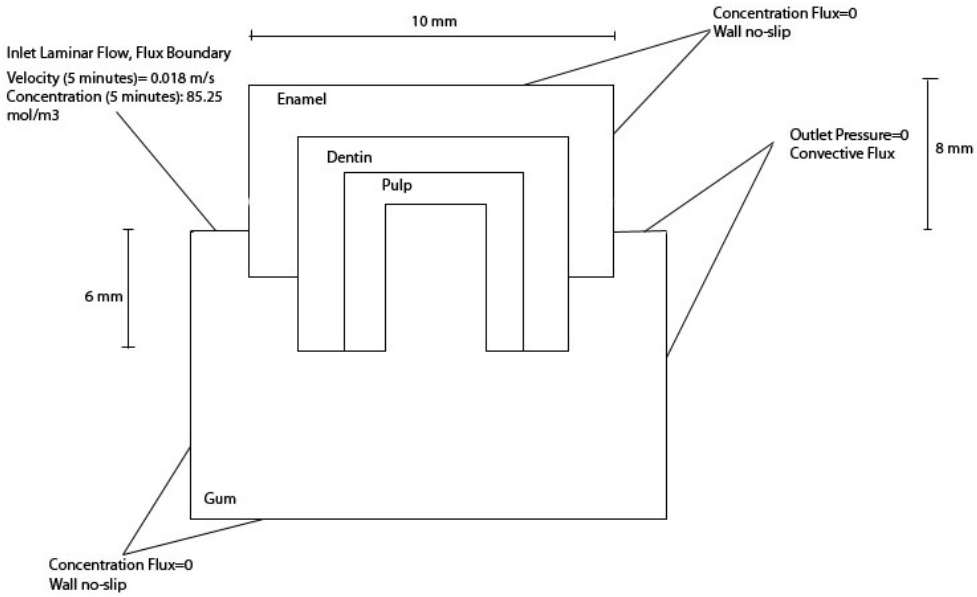
The design objective of this model is to determine how long the tooth stays numb, and how the lidocaine flows through the tooth and gum. This information can be used to design the most effective procedure for anesthetizing patients for their specific oral surgeries. Using the information that was obtained through the many different types of models, a novel procedure can be designed to effectively numb the tooth during surgery. It is important to understand the different procedures used for anesthetizing a tooth, because varying situations may warrant different procedures when there are diverse factors to consider, including length of the surgical procedure, patient variability in response to anesthesia, and type of procedure.

3a. *Problem Schematic*

The model presented utilized a two dimensional geometry. The two dimensional slice was taken in the sagittal plane along the jaw line and the model is considered infinite in the direction perpendicular to the sagittal plane. An anatomically correct picture of the tooth and gum can be seen in Figure 1A. The layers of the tooth that have the largest effect on the flow of the lidocaine through the system are included as a series of rectangles in the simplified model (Figure 1B).



A.



B.

Figure 1. Schematic of tooth and gum including dimensions and boundary conditions.

The nerves that we are targeting for blockage run along the gum and into the pulp layer. These two layers, which are modeled as soft tissue, are therefore the most important to consider for the concentration of lidocaine. Alternatively, the enamel layer is modeled as basically impermeable to lidocaine. The governing equation, boundary conditions, and initial conditions for this model are described in Appendix A.

4. Results and Discussion

A novel procedure for numbing a single tooth in preparation for oral surgery has been designed using COMSOL as a simulation tool. The injection of the lidocaine into the gum lasted 5 minutes, at a velocity of 0.018 m/s. The Brinkman's equations were used to model the fluid flow through porous media. Brinkman's equations incorporate Darcy's Law and manipulate it to resemble the Navier-Stokes equation. This physics was used to find the velocity of the lidocaine solution flowing through the tooth and gum at each point. A surface plot of the velocity profile during the injection at a time of one second can be seen in Figure 2. The velocity profile indicates laminar flow moving from the inlet towards the outlet.

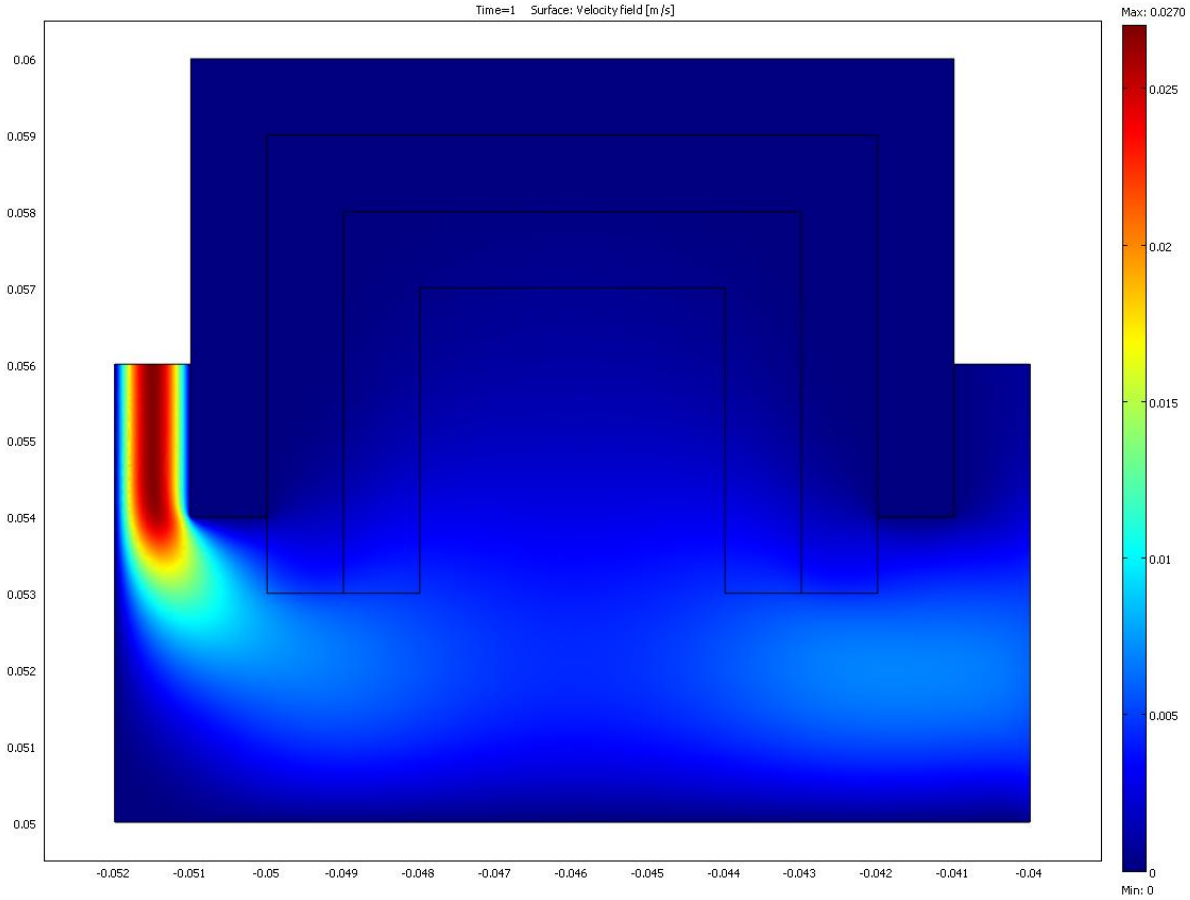


Figure 2: Velocity profile at time=1s during the injection of lidocaine into the gum

The graph of the velocity over time can be seen in Figure 3. During the injection, the average velocity in the pulp and gum remains at a constant velocity of 0.00355 m/s. This lower velocity value is due to the gum region having no velocity, allowing the average velocity in the entire region is much less than the average velocity at the inlet. After the injection duration, the velocity quickly drops to zero. The pressure in the gum remains constant during the injection,

correlating with the velocity during that time, but after the completion of the injection it quickly returns to zero (Appendix C).

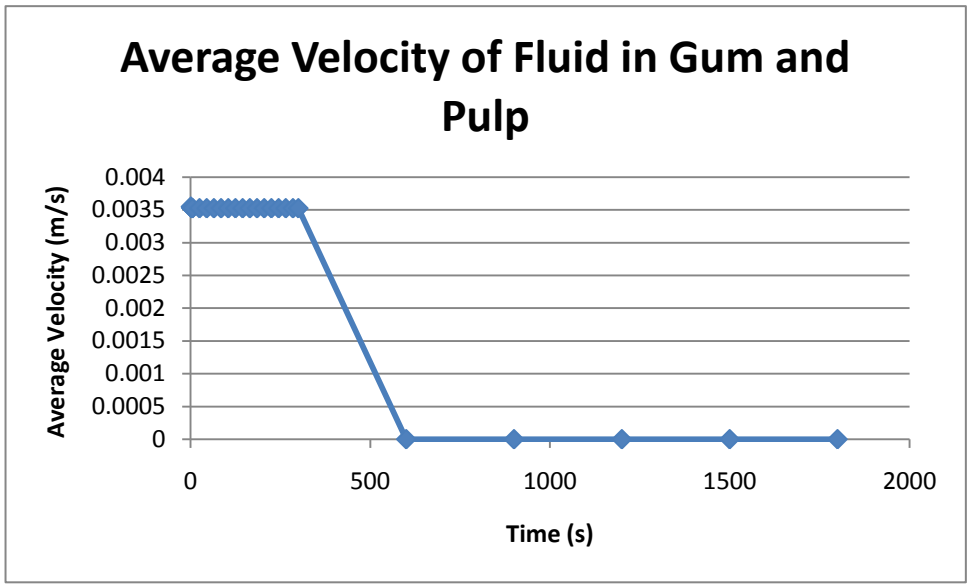


Figure 3: The average velocity of the lidocaine flowing through the gum and pulp.

The concentration of the injected lidocaine is 85.35 mol/m^3 which is constant at the inlet boundary for the first 5 minutes [4]. The mass transfer equation was used to model the diffusion of lidocaine into the pulp. The velocities calculated above by the Brinkman equation were used as the convective velocity terms in the mass transfer equation coupling the two equations. A surface plot of the concentration of the drug in the tooth and gum at 1800 seconds is seen below (Figure 4). This surface plot indicates the lidocaine has filled the gum and moved up into the pulp and dentin layers of the tooth. However, the lidocaine hardly enters the enamel layer as expected, because the enamel layer is modeled as basically impermeable to lidocaine.

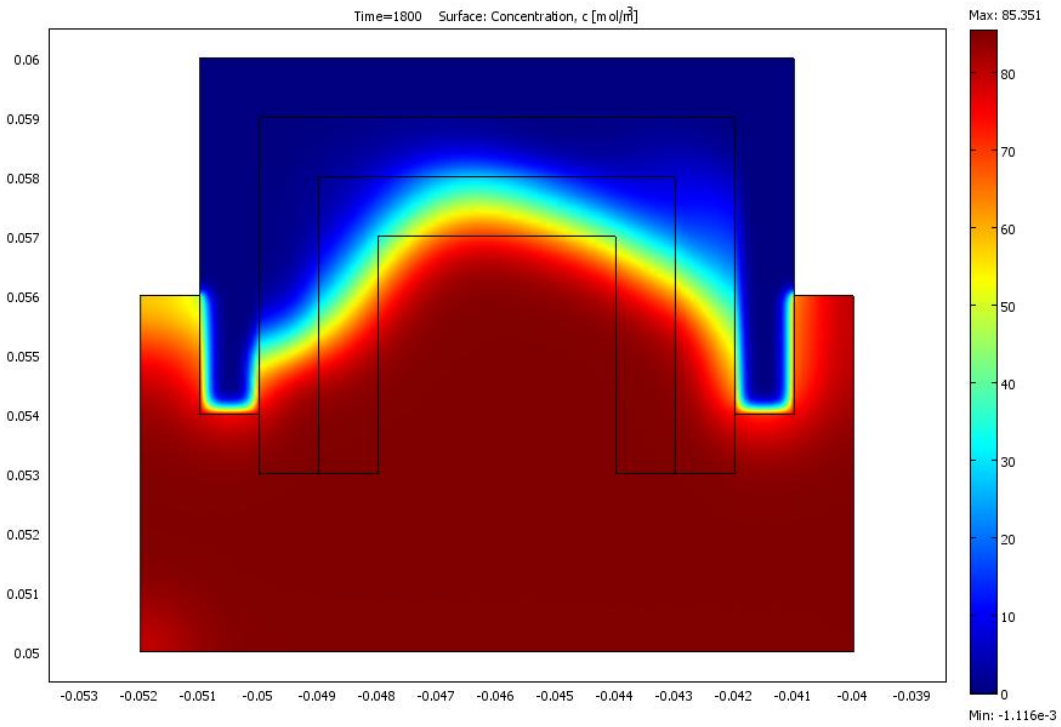


Figure 4: Concentration profile at time=1800s at convergence

During the injection, the concentration profile largely follows the trend of the velocity profile as the fluid moves from the inlet toward the outlet. This is because during the injection the convection, which is coupled to the velocity, makes the largest contribution to the movement of lidocaine. However, after the injection, when the velocities slow to zero, diffusion is the largest contributing factor to the movement of the lidocaine. This allows the lidocaine to diffuse upward into the pulp layer which contains the nerves.

After the solution is determined in COMSOL, the average concentration in the gum and pulp is determined (Figure 5). The average concentration increases very rapidly over the first few minutes and then appears to level off near a concentration of 80 mol/m^3. This concentration remains fairly constant throughout the thirty minute duration, and begins to slowly decrease as it diffuses out of the area. This indicates the physical validity of the simulation.

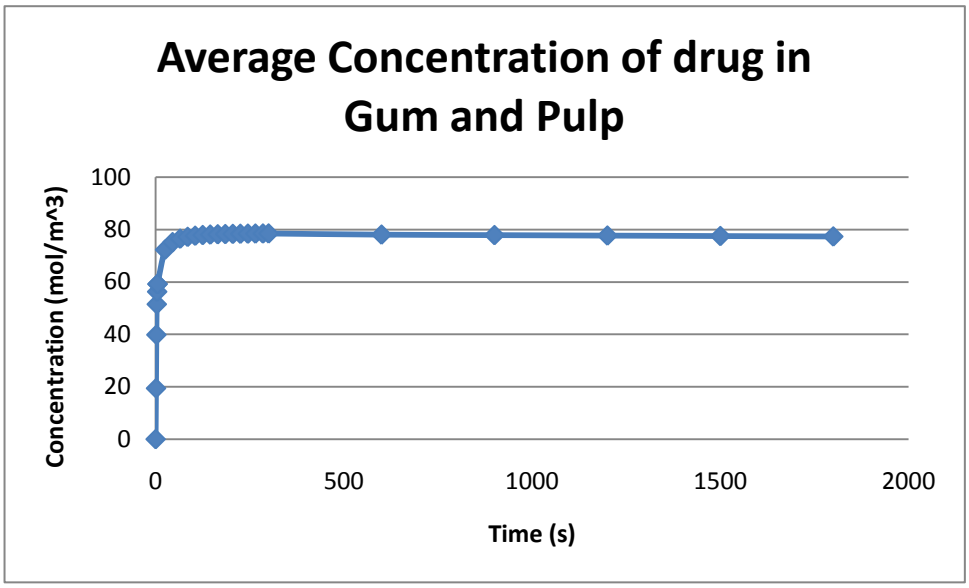


Figure 5: The average concentration of lidocaine in the gum and pulp as a function of time

In this novel procedure, the tooth was determined to be numb within three minutes. The threshold for numbness was assumed to be half of the initial concentration or 43 mol/m^3. The average concentration in the gum and pulp was about 80 mol/m^3, therefore, it can be concluded definitively that numbness was achieved.

Simplifications in this model lead to some design limitations. One of which was the inclusion of an outlet for the incompressible fluid instead of modeling the swelling of the tissue. The modeling of tissue swelling would have been a difficult task, which would require an understanding of how and where the swelling would occur, as well as make a moving boundary in the COMSOL simulations a necessity. The outlet causes the fluid flow to have directed motion from the inlet to the outlet. This results in the drug not flowing very far into the tooth layers. In reality, the injected fluid is free to flow in any direction because there is no directed fluid movement. The input velocities that could be chosen were also affected by the use of an outlet. High initial velocities result in anesthesia flowing out of the system too quickly, leading to unphysical results. This simulation also did not include the degradation of drug in the tissue, because for the short periods of time we were modeling, this constant was negligible. The use of a vasoconstrictor also reduces the affect of the degradation. If the model is run for a longer period of time, the degradation of the drug in the tissue would have an impact on how long the tooth and gum remain numb.

4a. *Accuracy Check*

To check the accuracy of the model a professional dentist was consulted regarding the specific anesthetic that is normally used, the amount of drug that is typically used to numb one

tooth and the duration of the numbness in the region of interest. Dr. Kanthasamy Ragunanthan stated that for a three to four hour procedure on the lower jaw, three injections are needed with the amount of anesthesia determined by the person's weight. However, no more than 10 carpules for a male and no more than 9 carpules for a female are injected into the tooth, with each carpule containing 1.8 ml of anesthesic solution with 2% lidocaine [5].

Different values relevant to this model have been previously documented in literature including the duration of time that the numbing agent lasts in the pulp and soft tissue. For 2% Lidocaine with epinephrine 1:100 000, anesthesia lasts about 1 hour in the pulp and in soft tissue, anesthesia remains for approximately 2.5 hours. When using 2% Lidocaine with epinephrine 1:50 000, on average the pulp anesthesia lasts in excess of 1 hour, so this is recommended for oral surgery requiring prolonged duration of anesthesia and pronounced hemostasis. It was also discovered that the average onset time of anesthesia in the pulp in a molar is 10.8 +/- 2 minutes [6].

Milestone Scientific, the company that manufactures the Single Tooth Anesthesia System provides some instructions for their product, such as volume of different numbing agents that should be used. Lisa Urban, a representative of Milestone Scientific, stated that about .9 ml to 1.8 ml or a half to a full carpule of anesthesia is injected in their model for a procedure lasting for thirty to forty-five minutes [7]. However, the concentration inside the pulp that is needed such that the nerves located there are numb was not provided. A threshold of fifty percent of the initial concentration injected was assumed as the required amount for numbing the tooth. In the model generated by COMSOL, the average concentration in the pulp at the end of a 45 minute procedure is approximately 80 mol/m^3, which is above the set threshold of 50 percent required, indicating that the region is numb as previously documented.

4b. *Sensitivity Analysis*

A sensitivity analysis was performed on the permeability and diffusion coefficient of the gum, pulp, enamel, and dentin. Because a 20 percent variability of properties of biological tissues is generally present, and the properties mentioned were rather difficult to find in the literature, the sensitivity analysis was performed by varying parameters by 25% [8]. The model was run by varying one of these parameters at a time, and the average concentration of drug in the tooth was determined. A bar graph can then be made showing how the average concentration varies with these parameters. Table 1 shows the parameters and ranges used. It should be noted that the pulp is being modeled with the same parameters as the gum.

Table 1: The parameters used in the sensitivity analysis of the model

	Permeability (m^2/s)			Diffusion Coefficient (m^2/s)		
	Low	Normal	High	Low	Normal	High
Enamel	7.25E-21	1E-20	1.25E-20	5.85E-12	7.8E-12	9.75E-12
Dentin	3.75E-8	5E-8	6.25E-8	5.85E-11	7.8E-11	9.75E-11
Gum/pulp	3.75E-6	5E-6	6.25E-6	1.5625E-10	1.25E-10	9.375E-11

The sensitivity analysis bar graphs indicate that the model is most sensitive to the permeability of dentin. Dentin provides a boundary between the impermeable enamel and the pulp. If the dentin is more permeable, the drug can easily flow to the pulp. Conversely, when the dentin is less permeable, the drug has to flow around the dentin to reach the pulp. Because the enamel is being modeled as nearly impermeable, it serves only as a barrier, and therefore, the model is not very sensitive to the enamel parameters. It is surprising, however that the model is not very sensitive to the permeability of the gum and pulp, because these subdomains are where the drug is acting. In general, the model is less sensitive to diffusivity than it is to permeability. The variable used to determine the sensitivities of these parameters was the average concentration of lidocaine in two distinct subdomains, the gum and the pulp. This is important because the inferior alveolar nerve is located in the gum and the concentration in that area needs to be at a level that numbs the tooth. The nerves inside the tooth, though, are located in the pulp, so that has a more localized effect on numbness of that particular tooth.

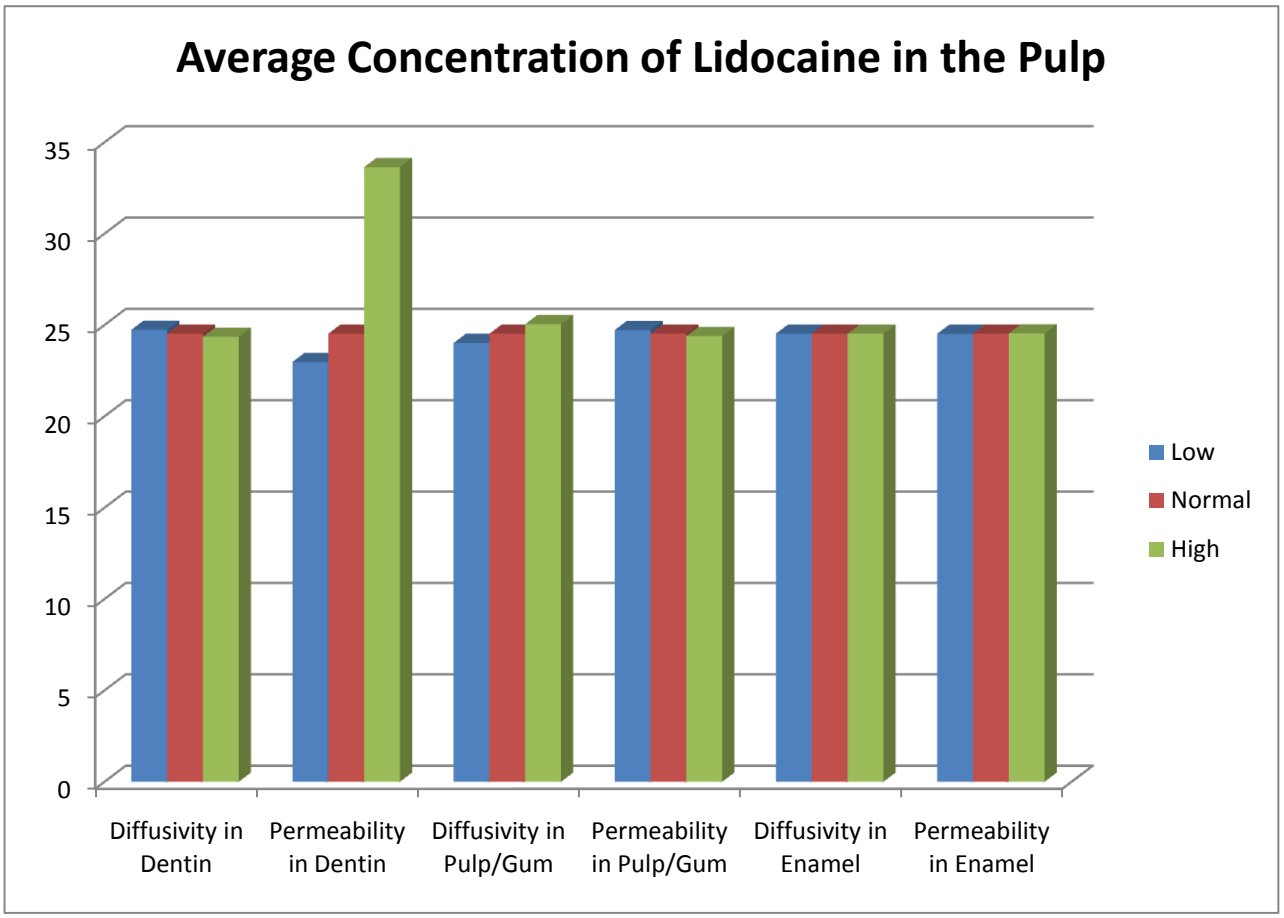


Figure 4: This sensitivity analysis was performed by determining the average concentration of lidocaine in the pulp when the different parameters are used in each of the subdomains

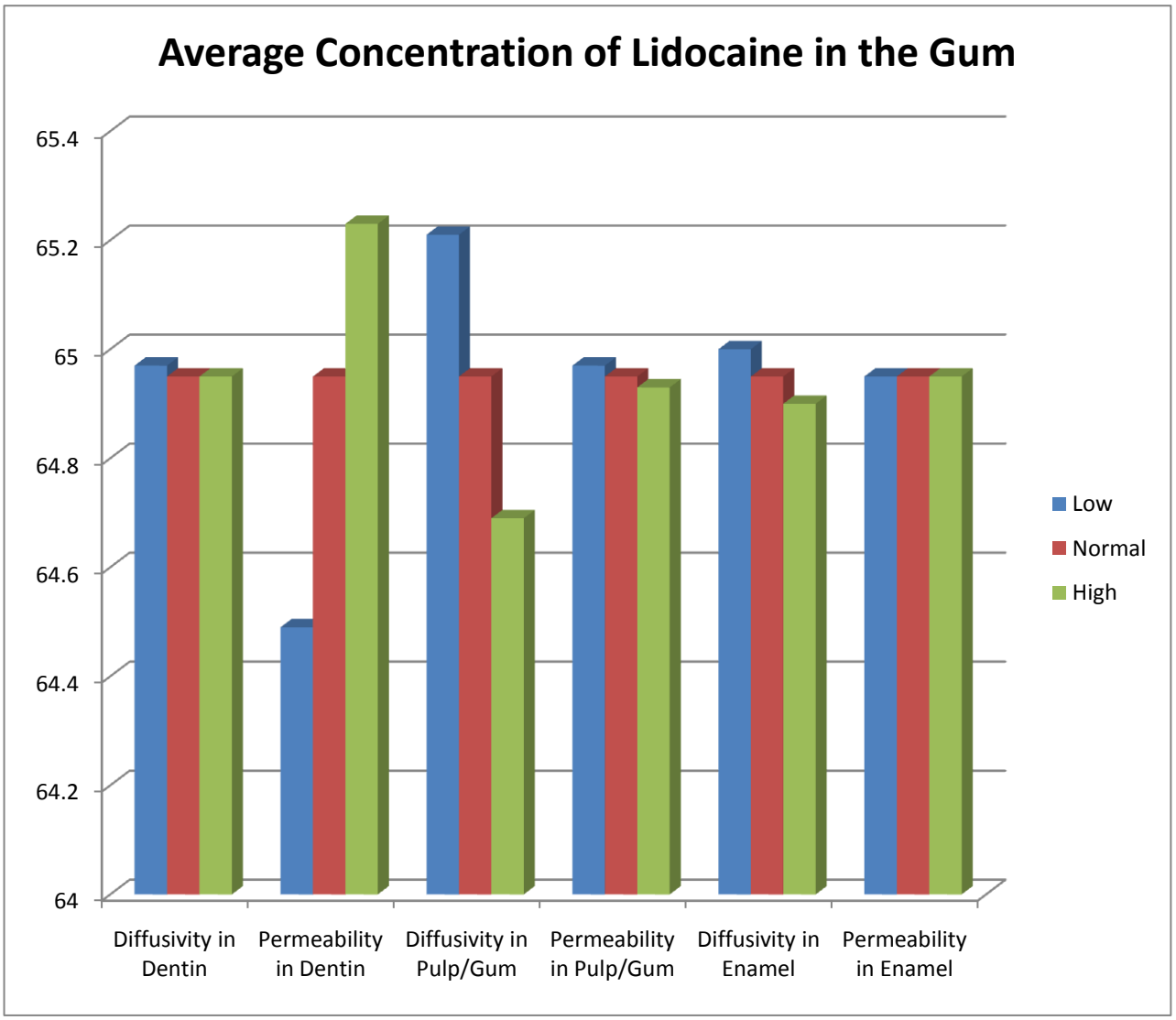


Figure 5: This sensitivity analysis was performed by determining the average concentration of lidocaine in the gum when the different parameters are used in each of the subdomains

5. Conclusion and Design Recommendations

This model was used to design a novel procedure for numbing the tooth, which used a longer injection time than traditional procedures with a slower initial velocity into the gum. This design effectively numbed the tooth within three minutes and remained numb for 45 minutes, providing a safer and more comfortable procedure with minimal side effects. The injection lasted for five minutes, which is reasonable since in many traditional anesthetic procedures the onset of numbness is at least ten minutes. An injection velocity of 0.018 m/s was used and an initial concentration of drug injected into the gum of 85.35 mol/m^3 was used. The combined effect of the slower injection velocity and longer injection time minimized discomfort due to

lowered pressure of injection. This model had an onset of numbness of about three minutes, which is shorter than the conventional 10 minutes for other procedures. As a degradation rate was not included in the model, a quantitative time limit of numbness could not be concluded. However, our model, combined with what is known about other procedures, allowed for the estimation that anesthesia will remain in the tooth for at least 45 minutes. This is supported by the fact that the degradation rate is low, as epinephrine, a vasoconstrictor in the injection solution, prevents plasma clearance of lidocaine.

There are many constraints that could affect the use of this procedure in a clinical setting. An economic constraint of this design is that it requires the purchase and manufacturing of an automated system with a computer controlled injection. This system will involve a higher start up cost than traditional procedures and therefore its use could be limited to more intensive dental surgeries. There are also social constraints to this type of procedure; many patients may be uncomfortable with the thought of a needle in their gum for an extended period of time. This might be especially applicable to children who may be fidgeting during the procedure. On the other hand, there are patients who may appreciate the limited initial pressure and discomfort that this method offers.

The computer aided modeling allows an engineer or dentist to track the movement of fluid through the gum and tooth, to get a more accurate time of when the tooth is completely numb to begin a surgical procedure. The concentration of the drug can be determined through time, to ensure that the patient's tooth stays numb for the entire procedure. The novel method that is proposed includes processes that could be made more efficient by further research and design in this area. This includes modeling the swelling of the tissue when the incompressible fluid is injected, rather than providing an outlet for that fluid to make the system more physiologically relevant. From the sensitivity analysis, it was determined that the parameters of dentin were the most sensitive to change, and therefore obtaining more accurate parameters will improve the model. Including a more accurate geometry, possibly through the use of CT scan or other imaging modalities, would improve the model further. Because quantitative values for a level of numbness were not found, a threshold was set. The threshold, while being a good estimate, may not be the most accurate. One of the factors contributing to this is the different reactions a patient may have to anesthesia based on size and other biological factors. Improving these design recommendations would move this model closer to physiological conditions.

Appendix A: Mathematical Statement of the Problem

The governing equations used in this simulation, along with the boundary conditions and initial conditions can be found below.

Governing Equations:

$$\textbf{Brinkman Equation}: \quad \frac{\rho}{\emptyset}\frac{\partial u_x}{\partial t} = -\frac{\partial P}{\partial x} - \frac{\mu}{\kappa}u_x + \frac{\mu_e}{\emptyset}\frac{\partial^2 u}{\partial x^2}$$

$$\frac{\rho}{\emptyset}\frac{\partial u_y}{\partial t} = -\frac{\partial P}{\partial y} - \frac{\mu}{\kappa}u_y + \frac{\mu_e}{\emptyset}\frac{\partial^2 u}{\partial y^2}$$

In these equations ρ is the density of the fluid, ∅ is the porosity of the domain, u is the velocity of the fluid in the indicated direction, P is the pressure, κ is the permeability of the domain, μ is the viscosity of the liquid, and μ_e is the dilatational viscosity of the liquid.

$$\textbf{Mass Transfer}: \frac{\partial C}{\partial t} + (v_x\frac{\partial C}{\partial x} + v_y\frac{\partial C}{\partial y}) = D_{AB}(v_x\frac{\partial^2 C}{\partial x^2} + v_y\frac{\partial^2 C}{\partial y^2})$$

In this equation C is the concentration of liquid in the domain, v is the velocity of the fluid in the indicated direction, and D_{AB} is the diffusion coefficient of the domain.

Initial Conditions:

At time = 0 s, concentration of drug in all subdomains is 0 mol/m^3
At time = 0 s, velocity of fluid in all subdomains is 0 m/s.

Boundary Conditions:

Along most the outside of the tooth and gum the boundary for the Brinkman's equation is a wall with no slip, and for the convection equation the boundary condition along most of the outside of the tooth and gum is insulation/symmetry.

In this simulation fluid enters, so there must be an inlet and an outlet. At the inlet, which is on the left side of the gum, the boundary condition is laminar inflow, with the velocity values set as a function of time, exactly 0.018 m/s during the first five minutes of the simulation, and is zero for the rest of the simulation. The inlet also has a flux boundary condition, which is a function of time. The concentration has been set at 85.35 mol/m^3 for the first five minutes of the model when the injection is taking place, and zero for the rest of the simulation. This concentration function has been multiplied by the velocity to obtain the flux boundary condition at the inlet.

The incompressible fluid must also have an outlet, and this is the boundary on the right side of the gum. The outlet boundary condition for the Brinkman's equations was pressure with no viscous stress, and we set the pressure to be zero. The outlet boundary condition for the convection and diffusion equations was convective flux.

Parameters:

Table 2. Physical Properties of Lidocaine

Property	**Value**	**Source**
Density	1000 kg/m^3	Approximated to that of water
Viscosity	$0.653*10^{-3}$ kg/ms	Approximated to that of water
Dilatational Viscosity	0.0024 Pa s	Approximated to that of water
Concentration	85.35 mol/m^3	Daily Med [9]

Table 3. Physical properties for gum/bone and pulp layers

Property	**Value**	**Source**
Porosity*	0.3	Billington et al. [10]
Permeability*	$5.00*10^{-6}$ m^2/s	Yao and Gu [11]
Diffusivity*	$1.25*10^{-10}$ m^2/s	Derby et al. [12]

*Properties were approximated to that of soft tissue

Table 4. Physical properties for dentin layer

Property	**Value**	**Source**
Porosity	0.3	Vennat et al. 2008 [13]
Permeability	$5.00*10^{-8}$ m^2/s	***see below

Diffusivity**	$7.8*10^{-11}$ m^2/s	Datta et al. [8]

******Diffusivity was approximated using the diffusivity of hydrogen peroxide through dentin

Table 5. Physical properties for enamel layer

Property	**Value**	**Source**
Porosity	.001	***see below
Permeability	$1*10^{-20}$ m^2/s	***see below
Diffusivity	$7.8*10^{-12}$ m^2/s	***see below

***For some of the parameter values we were unable to find exact values in literature. In order to determine what values to use for these parameters we did a number of things. First, for the diffusivity of dentin and enamel we knew the diffusivity of hydrogen peroxide through each layer. We used these values as a starting point. We also wanted to model the enamel as essentially impermeable to the lidocaine. This led us to choose extremely small values for porosity, permeability and diffusivity. Because COMSOL could not solve with a zero value for porosity or permeability, we decided to simply make them significantly smaller than the values for dentin, gum, and pulp. For diffusivity, however, we found that an order of magnitude smaller than the dentin was sufficient and gave us desired results. For the dentin permeability, we wanted the value to be in between that of pulp and enamel. We settled on a value in between these two that was closer to the pulp permeability. In order to verify these values we performed sensitivity analysis on each one and found that altering the values did not change the concentration of lidocaine in the gum or pulp. This sensitivity analysis led us to be satisfied that these parameters are as accurate as possible.

Appendix B: Solution Strategy

Solver

To solve our model, we used the direct finite element method, specifically the UMFPACK solver. Our model was simplified to a two-dimensional geometry and this solver gave us an appropriate convergence of concentration values.

Time Step

The problem was solved transiently for 1800 seconds by using a variable time stepping method. The injection period for the anesthesia was set to five minutes. Large changes in

concentration occurred during this injection period and so smaller time steps were taken during this period. A larger time step was used for later times in order to determine the persistence of the anesthesia in the gum and pulp layers of the tooth. A time step of one second was used for the first five seconds, a time step of 20 seconds was used for a period from five seconds to 300 seconds and a time step of 300 seconds was used for a period from 300 seconds to 1800 seconds.

Tolerance

A relative tolerance of 0.01 was used, while an absolute tolerance of 0.10 was used. We increased the absolute tolerance from the default value of 0.0010 to help the convergence of the concentration values. For our problem, we are only analyzing the average concentration values in the gum and pulp regions. Therefore, extremely precise values of concentration are not necessary and increasing the absolute tolerance is justified.

Mesh

To solve our problem, a free mesh with 2D, 3-noded triangular elements was used (Figure B1). Mesh was refined by increasing the number elements at the edges near the injection site and by the outlet site since this is where the biggest changes in concentration were observed.

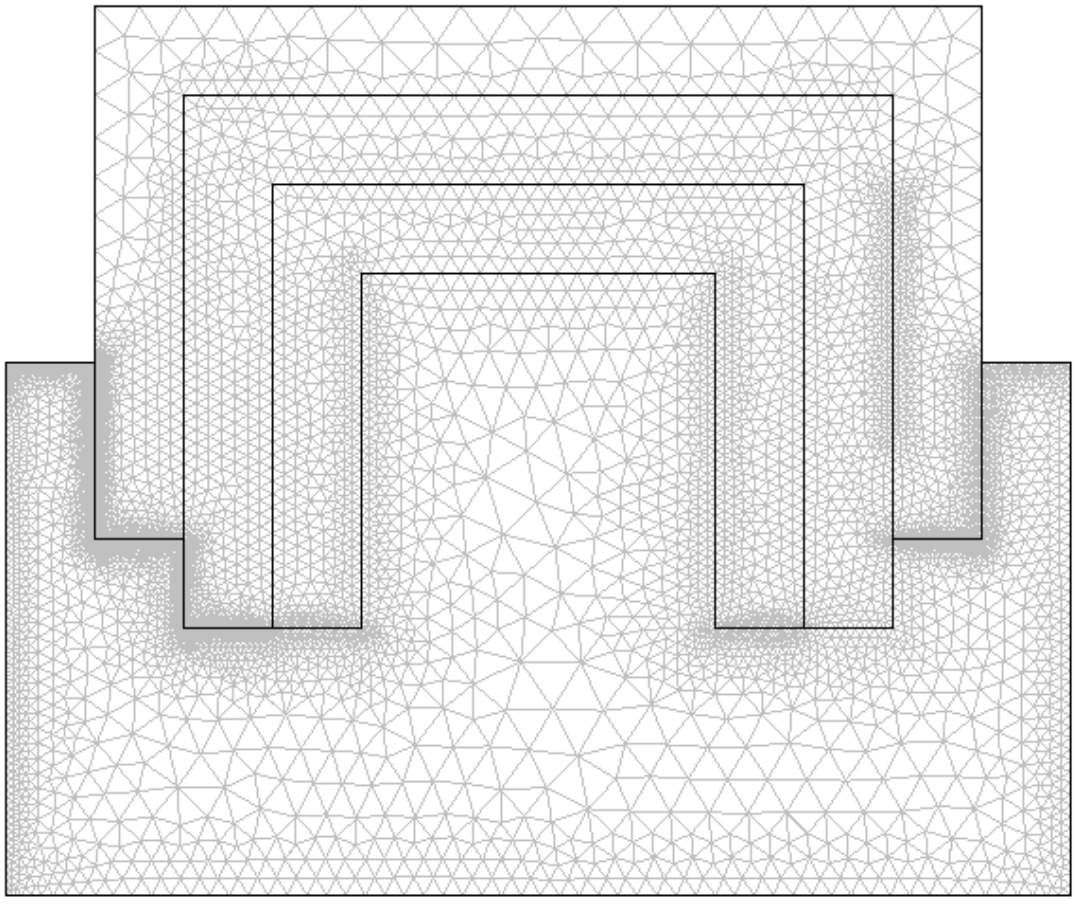


Figure B1. Finalized element mesh containing 14229 elements determined from mesh convergence (Figure B2)

The mesh was left very coarse in the enamel layer because the layer has low diffusivity and permeability values and therefore is virtually a barrier for the drug. In the solution, very little of the lidocaine was observed in the enamel layer, justifying our use of a coarse mesh for this layer. Our mesh seemed to converge at about 14229 elements (Figure B2). At or above 14229 elements, our solution for average concentration in the gum and pulp layers no longer depends on the size of the mesh.

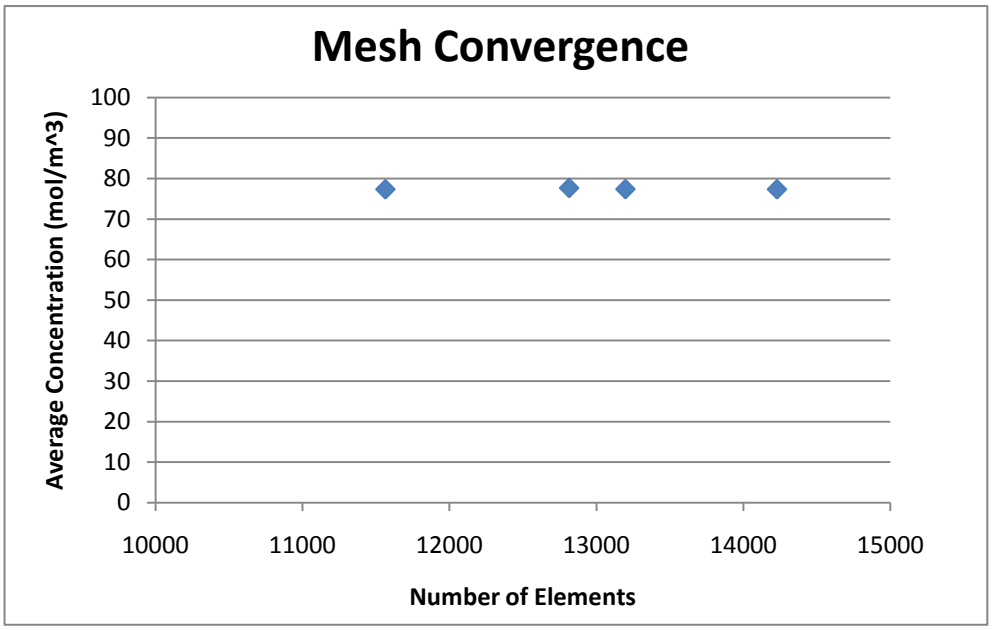


Figure B2. Mesh convergence for the average concentration in the gum and pulp layers at t=1800s

Appendix C: Additional Visuals

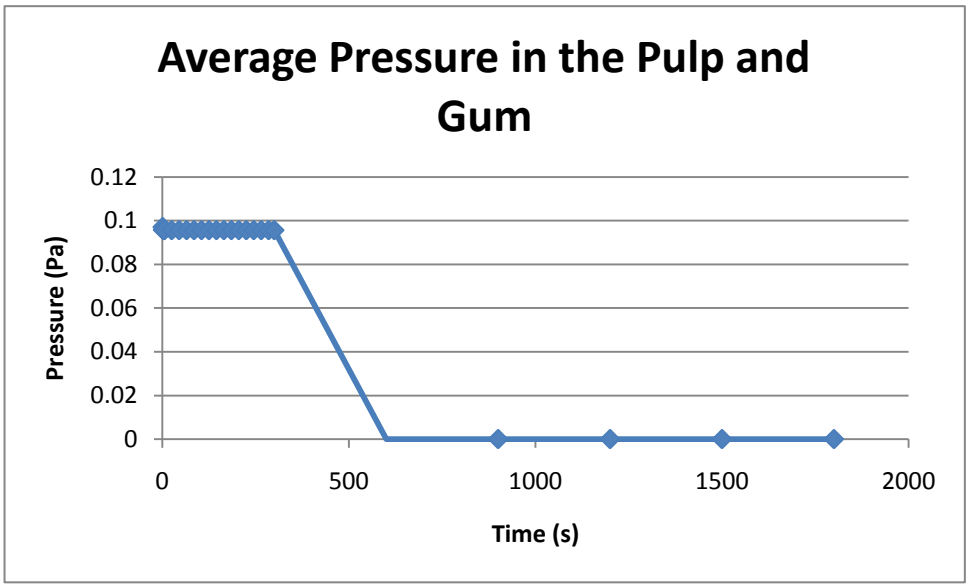


Figure C1. Average Pressure in the pulp and gum over time.

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