Tool for Studying Drug Delivery to the Eye in Case of Glaucoma

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Introduction: To improve the efficiency of drug delivery to the eye clinicians are prescribing therapeutic lens containing drug. The aim of this study is to give mathematical arguments to answer the question:

TOPICAL EYE DROPS or THERAPEUTIC LENS?

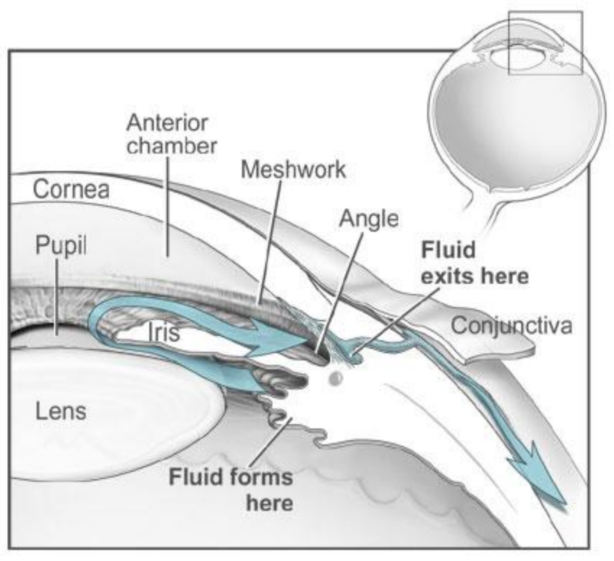

Figure 1. Fluid dynamics in the eye
(Credit: National Eye Institute, National Institutes of Health)

Mathematical model: The mathematical model takes into account (i) diffusion processes in the therapeutic lens (TL), cornea (C) and anterior chamber (AC); (ii) metabolic consuming processes of the drug in the cornea and anterior chamber; (iii) convection processes induced by the circulation of aqueous humour (AH) in the anterior chamber.

Therapeutic Lens

$$\frac{\partial C}{\partial t} = D\nabla^2 C - \lambda(C - C^b)$$

$$\frac{\partial C^b}{\partial t} = D_b\nabla^2 C^b + \lambda(C - C^b)$$

Cornea

$$\frac{\partial C_c}{\partial t} = D_c\nabla^2 C_c - K_c C_c$$

Anterior Chamber

$$\frac{\partial C_a}{\partial t} = D_a\nabla^2 C_a - \mathbf{u}.\nabla C_a - \frac{C_{la}}{V_a} C_a$$

$$\rho\frac{\partial \mathbf{u}}{\partial t} - \nabla\cdot\eta\left(\nabla\mathbf{u} + (\nabla\mathbf{u})^T\right) + \rho(\mathbf{u}\cdot\nabla)\mathbf{u} + \nabla p = 0$$

$$\nabla\cdot\mathbf{u} = 0$$

Geometry

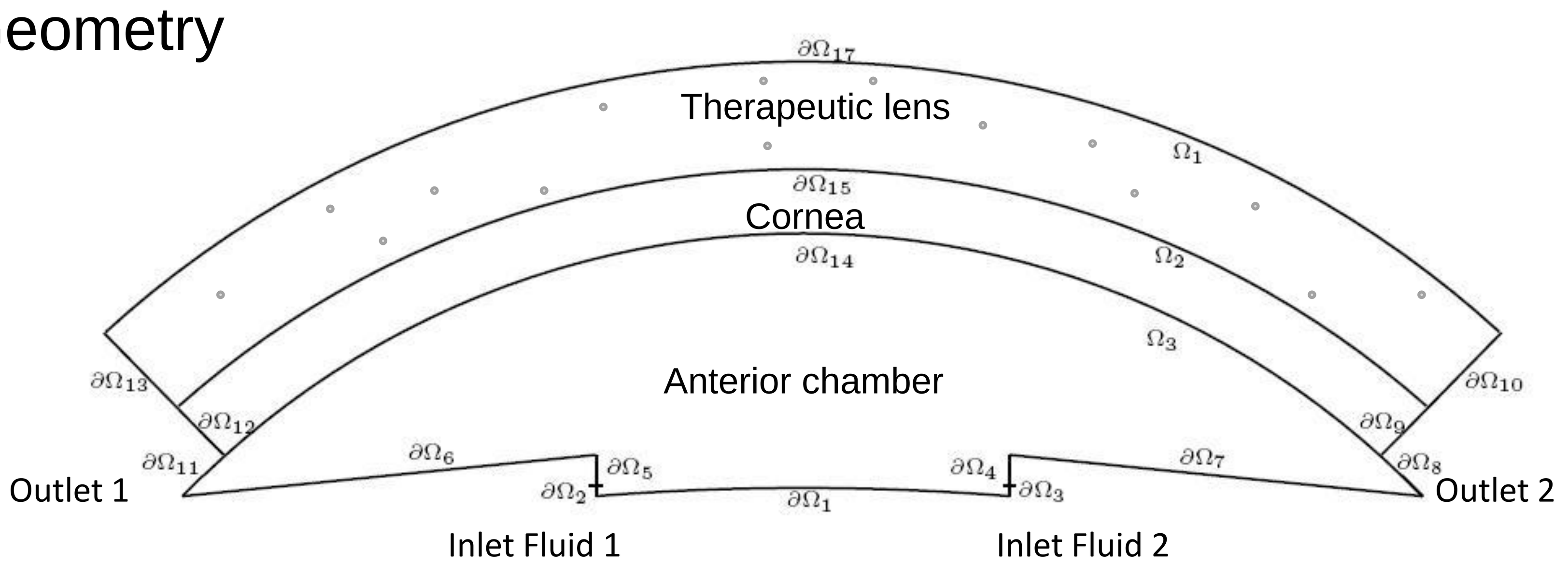

Figure 2. Geometry of the lens, cornea and anterior chamber

Initial, interface and boundary conditions

$C = C_0, \Omega_1, t = 0$

$C^b = C_0^b, \Omega_1, t = 0$

$C_c = 0, \Omega_2, t = 0$

$C_a = 0, \Omega_3, t = 0$

$\mathbf{u} = \mathbf{u}_0, \Omega_3, t = 0$

$p = p_0, \Omega_3, t = 0$

$D\nabla C.\eta = 0, \partial\Omega_{i,i=17,10,13}, t > 0$

$D_b\nabla C^b.\eta = 0, \partial\Omega_{i,i=17,15,10,13}, t > 0$

$D\nabla C.\eta = D_c\nabla C_c.\eta, \partial\Omega_{15}, t > 0$

$D_c\nabla C_c.\eta = 0, \partial\Omega_{i,i=12,9}, t > 0$

$D_c\nabla C_c.\eta = A_c(C_c - C_a), \partial\Omega_{14}, t > 0$

$D_a\nabla C_a.\eta = 0, \partial\Omega_{i,i=1,4,5,6,7}, t > 0$

$\mathbf{u} = \mathbf{u}_0^F, \partial\Omega_{i,i=2,3}, t > 0$

$\mathbf{u} = 0, \partial\Omega_{i,i=1,4,5,6,7,14}, t > 0$

$p = p_0^F, \partial\Omega_{i,i=8,11}, t > 0$

Results: In all simulations an obstruction of the trabecular mesh (TM) is considered, leading to an intraocular pressure - IOP- of 3600 Pa (in a normal eye the IOP is 1950Pa).

Therapeutic lens

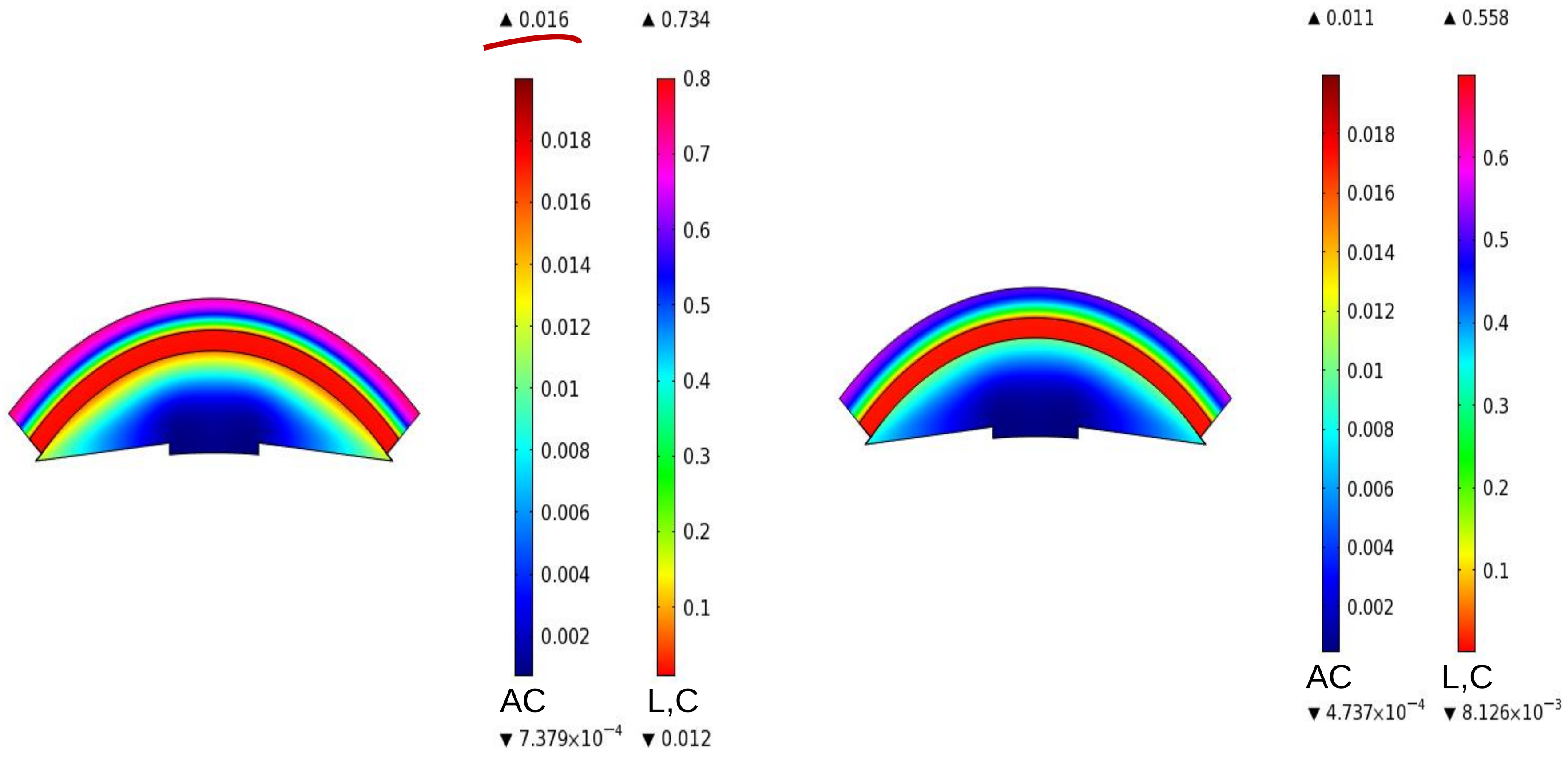

Figure 3. Drug concentration at 1h (left) and 2 h (right)

Topical administration

Tear Film $$\frac{\partial C_T}{\partial t} = D_a\nabla^2 C_T - \frac{S}{V_L + V_i e^{-k_d t}} C_T, \Omega_1$$

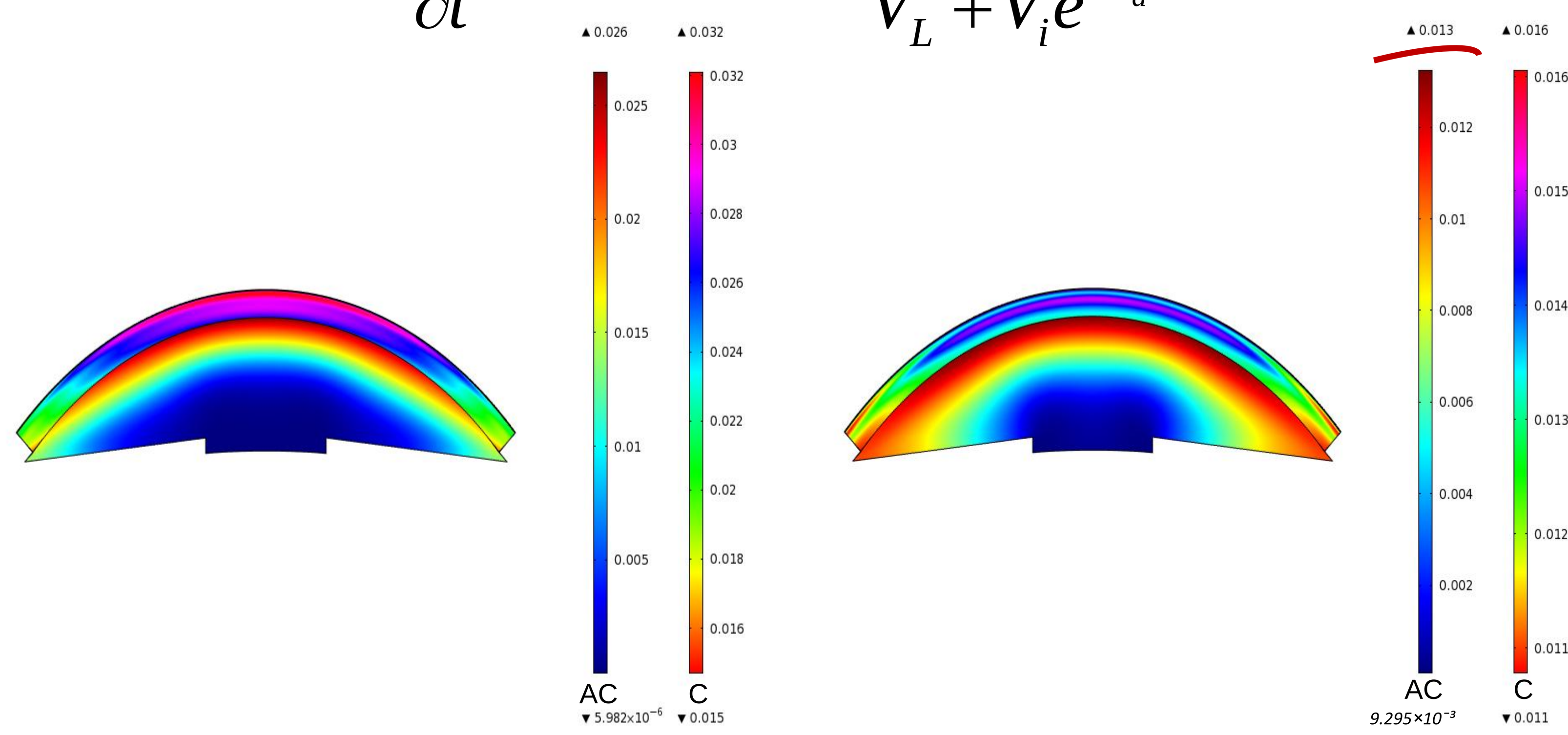

Figure 4. Drug concentration at t=100s (left) and t=300s (right)

Variables and Parameters

initial concentration - $C_0 = 1.147, C_0^b = 0.209\,(mol/m^3)$

diffusion coefficient - $D = 3.333\times10^{-11}, D_c = 5.74\times10^{-9}, D_a = 5\times10^{-9}\ (m^2/s)$

transfer, metabolic and drainage rate - $\lambda = 2\times10^{-4}, K_c = 1.0713\times10^{-5}(s^{-1}), k_d = 1.45\,(\min^{-1})$

clearance, lacrimal secretion - $C_{la} = 30\,(\mu l/\min), S = 1.2\,(\mu l/\min)$

volume - AC, TF, TF+Drop, surface area of the cornea - $V_a = 1000, V_L = 7, V_i = 10\,(\mu l), A_c = 0.1$

average velocity and IOP - $u_0 = 1.2\times10^{-3}(m/s),\ p_0^F = p_0 = 1950(Pa)$

initial concentration - drop - $C_{T0} = 5\times10^{-3}(g/cm^3)$

Conclusions: Therapeutic lenses are more efficient than topical administration in the glaucoma treatment: higher drug concentration is obtained and for a longer period of time (see red marks in Fig. 3 and 4). At present a more realistic model where TM is represented as a porous media is being implemented. Simulations of therapeutic effects of different drugs in the IOP are also being developed.

References:

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