Supplemental Material

Table S1. Qualitative comparison of Q3D, FEM, and PBPK (ODE-based) modeling strategies.

Parameter	Q3D	PBPK (ODE)	FEM
Mathematical Foundation	Uses partial differential equations (PDE)	Uses ordinary differential equations (ODE)	Uses partial differential equations (PDE)
Model Development Complexity and Time	Moderate: CoBi platform simplifies setup, minimal manual coding of equations	Low to High: simple for basic models, complex when discretization needed (100s of equations/loops)	High: complex mesh setup and implementation
Computational Speed	Moderate: faster than FEM, slightly slower than ODEs	Fast: fastest among the three approaches	Slow: most computationally intensive
Computational Resources	Moderate to low resource requirements	Low resource requirements	High resource requirements
Mesh Setup	Mesh setup is simple and user friendly	Not applicable (no spatial discretization)	Manual mesh setup is difficult and time-consuming
Accuracy	Good spatial resolution with quasi-3D approximations	Limited spatial resolution, suitable for lumped parameter models	Highest accuracy with full 3D spatial resolution
Visualization Capabilities	Strong visualization capabilities	Limited visualization (typically 1D plots)	Excellent 3D visualization capabilities
Multiphysics Coupling	Easier coupling compared to manual approaches, using CoBi	Manual coupling required - more complex to implement	Easier coupling within FEM framework
Scalability	Good scalability and works well for extended domains and layered tissues	Excellent for simple models, limited for spatially discretized problems	Limited scalability due to computational demands
User Expertise Required	Moderate: Requires some platform familiarity.	Low to High: Depends on model complexity	High: Requires FEM expertise and mesh generation skills
Best Use Cases	Problems with skewed aspect ratios (similar to 1D geometry), moderate complexity requiring spatial detail with computational efficiency	Simple lumped parameter models, rapid prototyping	Complex 3D geometries, high-accuracy applications requiring full 3D spatial resolution where FEM complexity is justified

Table S2. ODEs characterizing species transport between all ocular regions.

Ocular Region	**Species Transport Equation**
Upper Bulbar Conjunctiva (UB)	$V_{UB}\frac{dC_{UB}}{dt} = J_{UB-TF} + J_{UF-UB} + J_{UM-UB} - J_{UB-Elim}$
Upper Palpebral Conjunctiva (UP)	$V_{UP}\frac{dC_{PU}}{dt} = J_{UF-UP} - J_{UP-Elim}$
Upper Fornical Sac (UF)	$V_{UF}\frac{dC_{UF}}{dt} = \frac{dC_{diss,UF}}{dt} - J_{UM-UF} - J_{UF-UP} - J_{UF-UB} - \frac{dV_{UF}}{dt}C_{UF}$
Upper Meniscus (UM)	$V_{UM}\frac{dC_{UM}}{dt} = \frac{dC_{diss,UM}}{dt} + J_{UM-UF} - J_{UM-UB} - J_{UM-Drain} - \frac{dV_{UM}}{dt}C_{UM}$
Tear Film (TF)	$V_{TF}\frac{dC_{TF}}{dt} = \frac{dC_{diss,TF}}{dt} - J_{LB-TF} - J_{UB-TF} - J_{CorEpi-TF} - \frac{dV_{TF}}{dt}C_{TF}$
Lower Meniscus (LM)	$V_{LM}\frac{dC_{LM}}{dt} = \frac{dC_{diss,LM}}{dt} + J_{LM-LF} - J_{LM-LB} - J_{LM-Drain} - \frac{dV_{LM}}{dt}C_{LM}$
Lower Fornical Sac (LF)	$V_{LF}\frac{dC_{LF}}{dt} = \frac{dC_{diss,LF}}{dt} - J_{LM-LF} - J_{LF-LP} - J_{LF-LB} - \frac{dV_{LF}}{dt}C_{LF}$
Lower Palpebral Conjunctiva (LP)	$V_{LP}\frac{dC_{LP}}{dt} = J_{LF-LP} - J_{LP-Elim}$
Lower Bulbar Conjunctiva (LB)	$V_{LB}\frac{dC_{LB}}{dt} = J_{LB-TF} + J_{LF-LB} + J_{LM-LB} - J_{LB-Elim}$
Cornea Epithelium (CorEpi)	$V_{CorEpi}\frac{dC_{CorEpi}}{dt} = J_{CorEpi-TF} - J_{CorEpi-CorStr}$
Cornea Stroma (CorStr)	$V_{CorStr}\frac{dC_{CorStr}}{dt} = J_{CorEpi-CorStr} - J_{CorStr-CorEndo}$
Cornea Endothelium (CorEndo)	$V_{CorEndo}\frac{dC_{CorEndo}}{dt} = J_{CorStr-CorEndo} - J_{CorEndo-AH}$
Aqueous Humor (AH)	$V_{AH}\frac{dC_{AH}}{dt} = J_{AH-Sec} + J_{CorEndo-AH} - J_{AH-ICB} - J_{AH-Lens} - J_{AH-VIT} - J_{AH-Drain}$
Iris-Ciliary Body (ICB)	$V_{ICB}\frac{dC_{ICB}}{dt} = J_{AH-ICB} - J_{ICB-Elim}$
Lens	$V_{Lens}\frac{dC_{Lens}}{dt} = J_{AH-Lens} - J_{Lens-VIT}$
Vitreous Body (VIT)	$V_{VIT}\frac{dC_{VIT}}{dt} = J_{Lens-VIT} + J_{AH-VIT} - J_{VIT-NFL} - J_{VIT\ (conv)}$
Retinal Nerve Fiber Layer (NFL)	$V_{NFL}\frac{dC_{NFL}}{dt} = J_{VIT-NFL} - J_{NFL-GCL} - J_{VIT-NFL(conv)}$
Retinal Ganglion Cell Layer (GCL)	$V_{GCL}\frac{dC_{GCL}}{dt} = J_{NFL-GCL} - J_{GCL-IPL} - J_{GCL-Elim} - J_{NFL-GCL(conv)}$
Retinal Inner Plexiform Layer (IPL)	$V_{IPL}\frac{dC_{IPL}}{dt} = J_{GCL-IPL} - J_{IPL-INL} - J_{IPL-Elim} - J_{GCL-IPL(conv)}$
Retinal Inner Nuclear Layer (INL)	$V_{INL}\frac{dC_{INL}}{dt} = J_{IPL-INL} - J_{INL-OPL} - J_{IPL-INL(conv)}$
Retinal Outer Plexiform Layer (OPL)	$V_{OPL}\frac{dC_{OPL}}{dt} = J_{INL-OPL} - J_{OPL-ONL} - J_{OPL-Elim} - J_{INL-OPL(conv)}$
Retinal Outer Nuclear Layer (ONL)	$V_{OPL}\frac{dC_{ONL}}{dt} = J_{OPL-ONL} - J_{ONL-PL} - J_{OPL-ONL(conv)}$
Retinal Photoreceptor Layer (PL)	$V_{PL}\frac{dC_{PL}}{dt} = J_{ONL-PL} - J_{PL-RPE} - J_{ONL-PL(conv)}$
Retinal Pigmented Epithelium (RPE)	$V_{RPE}\frac{dC_{RPE}}{dt} = J_{PL-RPE} - J_{RPE-CH} - J_{PL-RPE(conv)}$
Choroid (CH)	$V_{CH}\frac{dC_{CH}}{dt} = J_{RPE-CH} - J_{CH-SCL} - J_{CH-Elim} - J_{RPE-CH(conv)}$
Sclera (SCL)	$V_{SCL}\frac{dC_{SCL}}{dt} = J_{CH-SCL} - J_{SCL} - J_{CH-SCL(conv)}$

Table S3. Dexamethasone assumptions and calibrated parameters.

Description	**Parameter**	**Value**
Cornea drug permeability [m/s]	$P_{cornea}^{\#}$	2.5×10^{-8}
Conjunctiva drug permeability [m/s]	$P_{conj}^{\#}$	1.0×10^{-7}
Iris ciliary body drug permeability [m/s]	P_{ICB}^{*}	3.5×10^{-9}
Lens drug permeability [m/s]	P_{Lens}^{*}	1.0×10^{-9}
Cornea and aqueous humor drug permeability [m/s]	$P_{cor\text{-}AH}^{*}$	5.3×10^{-8}
Aqueous humor and vitreous body drug permeability [m/s]	$P_{AH\text{-}VIT}^{*}$	6.5×10^{-9}
Diffusivity of drug in the tear film regions [m/s]	D_{tf}^{*}	9.6×10^{-12}
Diffusivity of drug in the posterior eye segments [m/s]	D_{post}^{*}	4.0×10^{-5}
Elimination through the upper palpebral conjunctiva [m^3/s]	$Elim_{UP}^{*}$	4.0×10^{-15}
Elimination through the lower palpebral conjunctiva [m^3/s]	$Elim_{LP}^{*}$	4.0×10^{-15}
Elimination through the upper bulbar conjunctiva [m^3/s]	$Elim_{UB}^{*}$	4.0×10^{-15}
Elimination through the lower bulbar conjunctiva [m^3/s]	$Elim_{LB}^{*}$	4.0×10^{-15}
Elimination through the ICB [m^3/s]	$Elim_{ICB}^{*}$	6.0×10^{-15}
Elimination through the GCL [m^3/s]	$Elim_{GCL}^{*}$	5.0×10^{-15}
Elimination through the IPL [m^3/s]	$Elim_{IPL}^{*}$	5.0×10^{-15}
Elimination through the OPL [m^3/s]	$Elim_{OPL}^{*}$	5.0×10^{-15}
Elimination through the choroid [m^3/s]	$Elim_{CH}^{*}$	5.0×10^{-15}
Mixing parameter for lower meniscus	$beta_L$	1
Mixing parameter for upper meniscus	$beta_U$	1
# = calculated; * = estimated		

Table S4. Calculated and estimated ocular areas.

Description	**Parameter**	**Area [m^2]**
Exposed area of the cornea	$A_{cornea}^{\#}$	1.3×10^{-4}
Area of upper palpebral conjunctiva	$A_{UP}^{\#}$	5.1×10^{-4}
Area of lower palpebral conjunctiva	$A_{LP}^{\#}$	3.7×10^{-4}
Area of upper bulbar conjunctiva	$A_{UB}^{\#}$	5.3×10^{-4}
Area of lower bulbar conjunctiva	$A_{LB}^{\#}$	4.3×10^{-4}
Interfacial area between upper fornix and conjunctiva	$A_{UF}^{\#}$	1.0×10^{-3}
Interfacial area between lower fornix and conjunctiva	$A_{LF}^{\#}$	7.4×10^{-4}
Interfacial area between upper meniscus and conjunctiva	$A_{UM}^{\#}$	2.1×10^{-5}
Interfacial area between lower meniscus and conjunctiva	$A_{LM}^{\#}$	6.8×10^{-5}
Interfacial area between AH and ICB	A_{ICB*}	7.0×10^{-4}
Interfacial area between AH and lens	A_{Lens*}	6.2×10^{-7}
Retinal surface area	$A_{Retina*}$	1.2×10^{-3}
# = calculated; * = estimated		