Optimization under uncertainty
of tear substitute rheological properties

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Overview of the talk

• what is a « tear substitute » and why should the properties of this fluid be optimized?

• how is this flow numerically modelled for an efficient prediction of its behaviour?

• what are the parameters and objectives of the (deterministic and stochastic) optimization problems we wish to solve?

• what kind of results do we obtain and what can we conclude from these results?
The eye seen as a fluidic device

Role of the tear film:
- remove foreign bodies
- lubricate the contact with the eyelids
- form a high-quality optical interface

Film formed by a coating process when the eyelid blinks
Context of the work

Dry eye syndrome

- the tear fluid lacks certain components or is produced in insufficient quantities

⇒ dry spots appear between blinks (irritation of the eye)

⇒ tear substitute must be prescribed to hydrate and lubricate the surface
Context of the work

Tear substitute

Must also meet some performance criteria:

• remain on the eye surface as long as possible to delay the formation of dry spots without being too frequently used

• disturb the user’s vision as little as possible by forming a protective film of constant thickness
Context of the work

Tear substitute

Three different types of substitutes are available on the market, classified according to their rheological properties:

- Newtonian products
- Shear-thinning products
- Products with a yield point (viscoplastic fluids)
  \[\{\text{non-Newtonian behaviour}\}\]

*De Loubens et al, Investigative Ophtalmology and Visual Science, 2009*
Objective of the work

Previous studies have shown Newtonian substitutes cannot form a stable, homogeneous film

(Jones et al, Bulletin of Mathematical Biology, 2006 & 2008)

⇒ study of non-Newtonian (shear-thinning) tear substitutes and optimization of their performance
Numerical modelling

Geometry simplification

moving

thin tear film of height $h(x,t)$

fixed
Numerical modelling

Rheological description

Several laws available for modelling shear thinning behaviour

⇒ Ellis model is retained:

\[ \mu = \frac{\mu_0}{1 + (|\tau_{xy}'/\tau_{1/2}'|)^{\alpha-1}} \]

- Viscosity at the Newtonian plateau
- Shear stress
- Shear stress such that \( \mu = \mu_0/2 \)
- Shear thinning coefficient
  \((\alpha > 1)\)
Numerical modelling

Rheological description

![Graph showing viscosity vs shear rate for Substitute 1 and Substitute 2, with a fit curve for the Ellis model.](image)
Numerical modelling

Film dynamics

• lubrication approximation
• gravity and evaporation effects neglected
• mass and momentum conservation
+ boundary conditions at the film surface

⇒ single partial differential equation
describing the evolution of the film height $h(x,t)$
Numerical modelling

Film dynamics

Evolution of the (non-dimensional) film height $h(x,t)$ governed by:

$$\frac{\partial h}{\partial t} + \frac{\partial}{\partial x} \left[ \frac{1}{Ca} \left\{ \varepsilon^3 \frac{h^3}{3} \frac{\partial^3 h}{\partial x^3} \right\} + \varepsilon^{3\alpha} L_2^{\alpha-1} \frac{h^{\alpha+2}}{(\alpha + 2)} \frac{\partial^3 h}{\partial x^3} \right] = 0$$

I : effects of the Newtonian behaviour, $Ca(\mu_0,\sigma) =$ capillary number where $\sigma =$ film surface tension

II : effects of shear-thinning behaviour, $L_2 (\sigma, \tau_{1/2}) =$ ratio between capillarity and shear-thinning, $\alpha =$ shear-thinning coefficient
Numerical modelling

Film dynamics

PDE on $h(x,t)$ completed by prescribed boundary conditions:
- no flux at the lower eyelid
- flux at the upper eyelid proportional to its velocity
Numerical modelling

Numerical solution of the PDE:

• implicit scheme
  (first-order in time, second-order in space)

• time interval: \([t=0,t=T=40]\)

• time-step: 0.002 (hence 20 000 iterations)

• space discretization: 1000 points

• grid convergence checked
Numerical modelling

Computed evolution of $h(x,t)$ during blinking
Case of the natural tears (Newtonian case)
Optimization problem: set-up

Minimize height difference over the eye pupil
(Maximize flatness at t=T)

Maximize the minimal film height reached during blinking

EYE PUPIL
Optimization problem: set-up

- Objective 1: \( \max( h_{\text{minglob}} ) \)
  \( h_{\text{minglob}} \): normalized by the natural tear value

- Objective 2: \( \min( \delta h_{\text{pupil}} ) \)
  \( \delta h_{\text{pupil}} \): normalized by the natural tear value

- Parameters:
  \( Ca \in [0.005, 0.5] \)
  \( \alpha \in [1, 5] \)
  \( L_2 \in [1, 10000] \)
Optimization problem: set-up

- Single and bi-objective optimization performed using the GA available in *modeFRONTIER*®

Population size: 50 individuals
Number of generations: 50

Cost of a single individual evaluation ≈ 5 s
(on a local cluster)
Optimization problem: deterministic results
Optimization problem: deterministic results

Pareto front in the objective plane

- Objective 1 (maximal height)
- Objective 2 (flatness)

- max(obj1)
- min(obj2)
- max(obj1) & min(obj2)
- Pareto G1
- Pareto G2
- Pareto G3
Optimization problem: deterministic results

Pareto front in the parameter plane ($\alpha$, $Ca$)

- $\alpha = 5$, $Ca = 0.5$ (G1)
- $\alpha = 5$, $Ca \in [1E-2, 0.5]$ (G3)
- $\alpha = 5$, $Ca \in [5E-3, 1E-2]$ (G2)
Optimization problem: deterministic results

Pareto front in the parameter plane \((\alpha, L_2)\)

\[ \alpha = 5, \ L_2 \approx 10000 \]

\[ \alpha = 5, \ L_2 \in [9600,10000] \]

\[ \alpha = 5, \ L_2 \in [6,30] \]

G1

G2

G3
Optimization problem: deterministic results

Objective 1 (maximal height)

Objective 2 (flatness)

min(obj2)
\( \alpha=5 \)
\( Ca=0.5 \)
\( L_2=6 \)

max(obj1)
\( \alpha=5 \)
\( Ca=0.5 \)
\( L_2=10000 \)

\( \alpha=5 \)
\( Ca \in [1E-2,0.5] \)
\( L_2 \in [9600,10000] \)

\( \alpha=5 \)
\( Ca \in [5E-3,1E-2] \)
\( L_2 \approx 10000 \)
Optimization problem: deterministic results

Film height distribution at final time
Optimization problem: stochastic analysis

Optimization of tear substitute performances performed with uncertainty on the rheological parameters:

- $\alpha$, $\text{Ca}$ known with a $\pm 5\%$ uncertainty  
  + an irreducible error  
  (fraction of the total interval of variation)

- $L_2$ known with a $\pm 10\%$ uncertainty  
  + an irreducible error  
  (fraction of the total interval of variation)

Use of the MORDO function available in *modeFRONTIER*®
Optimization problem: stochastic analysis

Bi-objective problem with $\alpha$ uncertain (Ca and $L_2$ deterministic)

Low sensitivity of performance to the uncertainty on $\alpha$
Systematic similar studies
with the other parameters taken as uncertain,
for both objective 1 (height) and objective 2 (flatness)

⇒ systematic conclusion on the low sensitivity of the performance to these (decoupled) uncertainties
Conclusion and perspectives

• Optimal rheological properties have been found for shear-thinning tear substitutes

with confidence on the low sensitivity of the performance to the practical uncertainty on the fluid properties

⇒ a coupled stochastic optimization is under way

• The same methodology will be applied to the study of visco-plastic tear substitutes which could further improve product performance.