Mathematics of eye

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  - Dry eye syndrome (disease of affluence: prolonged reading, driving a car, contact lenses...).
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  - How to calculate the moment of tear drying (*Break-Up-Time*, BUT) ?

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  - Keeping IOP in proper bounds is very important: too large $\rightarrow$ glaucoma, too small $\rightarrow$ hypotony.
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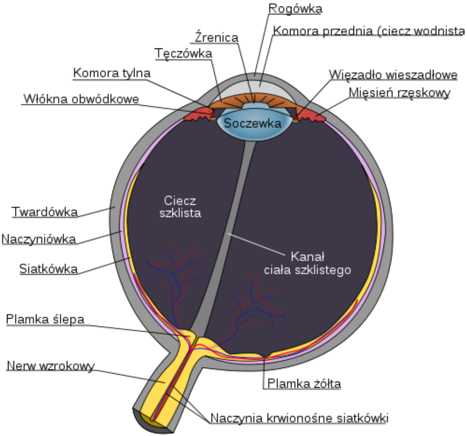
- What is the shape of the cornea?

Eye anatomy



Typical sizes:

- eye size 24mm,
- corneal diameter 11.5mm,
- corneal thickness 0.5 – 0.7mm,
- height circa 2mm.

Five layers of the cornea:

- epithelium,
- Bowman's layer,
- stroma,
- Descement's membrane,
- endothelium.

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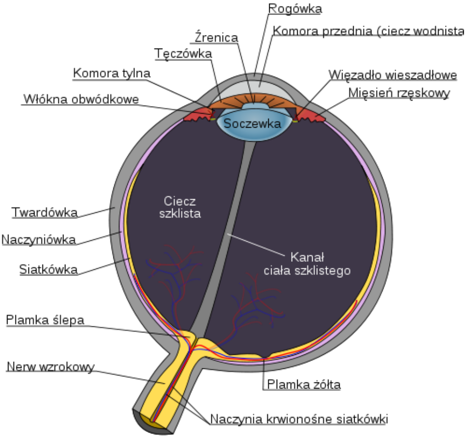

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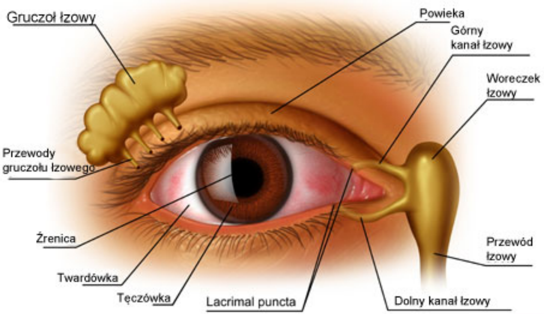
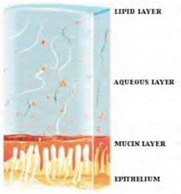
Cornea is very important - it accounts for about $\frac{2}{3}$ eye power!

Tears and their meaning





- They moisten the eye and protect from bacteria.
- Contents: water, salt (NaCl) and enzymes.
- Three layers: lipid $0.1 - 0.2\mu$m, aqueous $4 - 10\mu$m and mucus $0.5 - 1\mu$m.

Blinking and the physics

- Blinking brings the tear film over the surface of the cornea.
- Typical time between successive blinks in a healthy patient - about $5 - 8$s (in rabbit's eye - 10min!).
- Problems: too small tear production, too fast evaporation $\rightarrow$ "dry eye".

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- Some of the physical properties.
  - Lipid layer protects from excessive evaporation. Average evaporation rate is 15×10^{-6} kg m^2 s^{-1} for normal eyes and 60×10^{-6} kg m^2 s^{-1} for dry eyes.
  - This layer also weakens the surface tension: tear-air - 43.3mN m^{-1}, water-air - 72.3mN m^{-1}.
  - Tear film is slightly shear thinning - viscosity diminishes with the increase of shear stress.
  - In modeling it is usually assumed that tear is a Newtonian fluid and takes into account several factors: surface tension, gradients in lipid layer, evaporation, blinking, heat source and corneal geometry [1]

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Interlude: thin layer approximation

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- We scale the unknowns:

$$\epsilon = \frac{H_0}{L},\ u^* = \frac{u}{U},\ v^* = \frac{v}{\epsilon U},\ t^* = \frac{t}{L/U},\ p^* = \frac{p}{\mu UL/H_0^2},\ Re' = \epsilon^2 \frac{UL}{\nu}.$$

  xth component of the nondimensional Navier-Stokes equation then becomes (dropping asterisks):

$$\frac{\partial u}{\partial t} + u\frac{\partial u}{\partial x} + v\frac{\partial u}{\partial y} = \frac{1}{Re'}\left(-\frac{\partial p}{\partial x} + \epsilon^2 \frac{\partial^2 u}{\partial x^2} + \frac{\partial^2 u}{\partial y^2}\right).$$

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- Using the continuity equation we obtain **Reynolds equation**:

$$\frac{d}{dx}\left(h^3 \frac{\partial p}{\partial x}\right) = 6\frac{\partial h}{\partial x}.$$

Break-up time (BUT)

- It is usually defined as a first moment of dry region to appear just after blinking.
- It is a very important parameter measured by ophthalmologists. Very sensitive to ambient conditions, but usually $20 - 30$s.

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- Model: thin-layer theory ($\epsilon = d/l = x$-dimension / y-dimension) for Navier-Stokes + evaporation and gravity.

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- Typical scales:

$$d = 10\mu\text{m},\ l = 0.36\text{mm},\ \epsilon = 0.028,\ G = 0.75,\ U = 0.75\text{mms}^{-1},\ \text{Re} = 0.2.$$

- Main equation for the tear thickness:

$$h_t + \frac{E}{J_0^{-1} + h} + \left[\frac{h^3}{12}\left(h_{xxx} + G\right)\right]_x = 0,$$

where E, J_0 - constants associated with evaporation and temperature.

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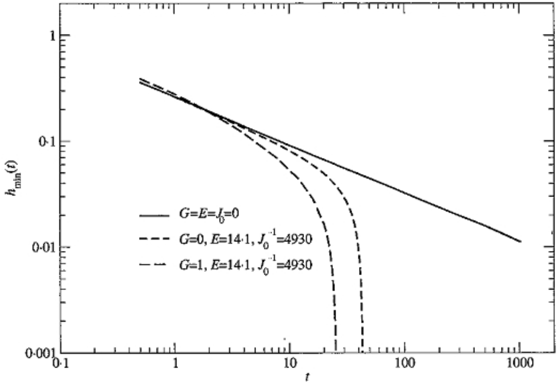
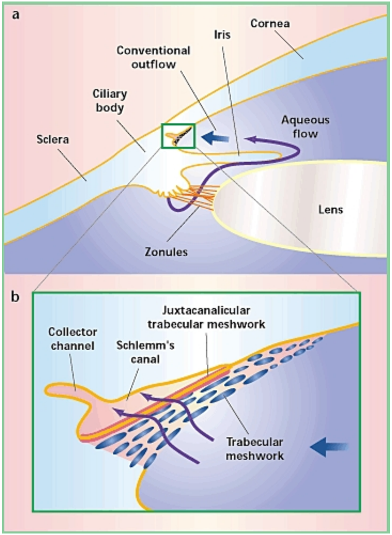
Break-up time (BUT) c.d.

- Braun and Fitt obtained a numerical solution on a 4000 point-grid. For the BUT they took the time when h became smaller that grid-size.



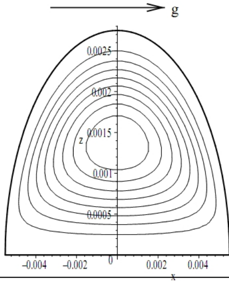
Flows in eye chambers

- Anterior chamber - a region between iris and the cornea. Posterior chamber - region between iris and lens.
- Aqueous humor - a fluid that fills the chambers (about 0.3 cm^3). It removes the products of metabolism, nourishes and provides IOP.
- It is transparent and jelly-like. It consists of water and amino acids.
- It is produces by ciliary body, from where it flows through posterior chamber, pupil and is removed in the Schlemm's canal.
- It must be conserved (!) - same amount removed as produced.
- How to describe it **mathematically?**



Flows in eye chambers cont'd.

- What causes the flow of aqueous humor? [3,4] .
  - Buoyancy is a result of temperature gradient between iris and the anterior chamber.
  - The flow is produced by ciliary body.
  - Influence of buoyancy-gravity in horizontal position (ex. during sleeping).
  - REM phase.



[3] A.D.Fitt, G.Gonzalez, *Fluid Mechanics of the Human Eye: Aqueous Humour Flow in the Anterior Chamber*
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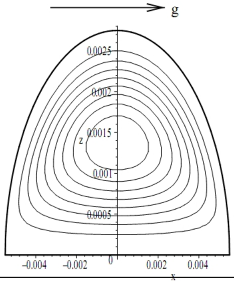

- The simplest model: Navier-Stokes equations, heat equation + Bussinesq approximation and "lubrication theory".
- It is possible to obtain an exact solution, for example

$$\psi = -\frac{(T_1 - T_0)g\alpha z^2(z-h)^2}{24\nu h}$$

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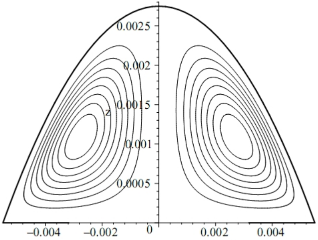
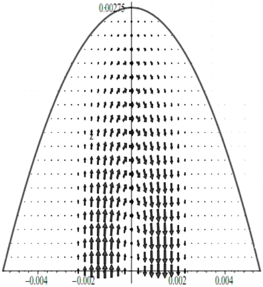
Flows in eye chambers cont'd.

- When patient is asleep, the blood flow does not necessarily balance the temperature gradient.
- A very small flow occurs that is a result of gravity and a minute temperature gradient.
- Facodenesis - lens wibrations caused by head movements.
- These vibrations have to have sufficiently small amplitude in order to provide flawless seeing.
- Fitt and Gonzalez assumed a certain periodical "‘pumping"’ speed of fluid through the pupil.
- The flow is essentially $3D$.





Flows in eye chambers cont'd. (Schlemm's Canal)

[5] Z.Ismail, A.D.Fitt, *Mathematical modelling of flow in Schlemm's Canal and its influence on primary open angle glaucoma*

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- When the anterior chamber holds too much aqueous humor (ex. when the Schlemm's Canal becomes stucked), the pressure rises.
- POAG (*Primary Open Angle Glaucoma*) $\rightarrow$ advancing and permanent eye nerve damage $\rightarrow$ blindness.

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- In [5] Authors use the Friedenwald's Law (relation between IOP and eye's volume) and thin-layer theory:

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$$(FL) \quad p_1 = p_2 \exp\left(K \ln 10(V_1 - V_2)\right).$$

- They obtained an equation that describes increase of IOP that is caused by Schlemm's Canal occlusion:

$$\frac{dp}{dt} \approx Kp\frac{dV_{in}}{dt}.$$

- This occlusion can cause the IOP to become arbitrarily large $\rightarrow$ glaucoma and blindness.

[5] Z.Ismail, A.D.Fitt, *Mathematical modelling of flow in Schlemm's Canal and its influence on primary open angle glaucoma*

IOP

[6] Markiewitz HH, *The so-called Imbert-Fick Law*

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- It provides a proper eye shape.
- Typical IOP: $10 - 20$mmHg. When $IOP > 25$mmHg glaucoma can develop (or worse...). When $IOP < 10$mmHg detunning of lens and cornea can occur (or worse...).

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- Measuring the actual value of IOP is crucial (but it is very sensitive on ambient conditions). This is the field of **Tonometry**.
- There are some measuring techniques:
  - from very invasive (during a surgical operation),
  - through invasive, ex. Goldman's Tonometer,
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- Imbert-Fick's "Law" (in reality: Newton's Third Law applied "by force"): IOP = value of force (in grams) needed to flatten a circle with radius of 3.06mm on the cornea [6].
- Cons: wrong physical basis, not-the-best accuracy especially for high IOP, unpleasant for the patient, ...

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- A measurement only on the basis of corneal **topography**?

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What is the shape of the cornea?

Contemporary models of corneal topography:

- The simplest: based on the conical curves - mostly parabolas and ellipses (Helmholtz, 1924) ("statistically" correct).
- Very complicated: based on shell thery and FEM.
- Models based on Zernike Polynomials (1934) - describe aberration. Lately, also Bessel functions are being used [7].
- Real models of eye.

Survey literature

1. Fowler CW, Dave TN., *Review of past and present techniques of measuring corneal topography*, Ophthalmic Physiol Opt. 14(1) (1994), 49–58,
2. Lindsay R, Smith G, Atchison D., *Descriptors of corneal shape*, Optom Vis Sci. 75(2) (1998), 156–8.
3. Y. Mejía-Barbosa, D. Malacara-Hernández, *A review of methods for measuring corneal topography*, Optometry and Vision Science 78 (2001), 240–253,

[7] J.P. Trevino et al., *Zernike vs. Bessel circular functions in visual optics*

A new model

Main assumptions [8]

- Cornea is a thin membrane (constant surface tension and lack of bending moments).
- Three forces shape the cornea: surface tension, elasticity and a pressure-force.
- In the model we describe the height of the cornea h over some reference plane Ω (here: a circle).

Equation of the corneal topography (in a nondimensional form)

$$-\nabla^2 h + ah = \frac{b}{\sqrt{1+\|\nabla h\|^2}} \quad \text{on } \Omega, \quad h = 0 \text{ na } \partial\Omega,$$

where h-rescaled, $a := \frac{kR^2}{T}$ i $b := \frac{PR}{T}$ and k-elasticity constant, T-tension, P-intraocular pressure, R-typical size of the cornea.

[8] W.Okrasiński, Ł.Płociniczak, *A Nonlinear Mathematical Model of the Corneal Shape*

A direct problem

How, from the knowledge of a and b, find the shape of the cornea h?

- We assume an axial symmetry $h = h(r)$ then a and b have to be constant.
- We solve the problem

$$-\frac{1}{r}\frac{d}{dr}\left(r\frac{dh}{dr}\right) + ah = \frac{b}{\sqrt{1+h'^2}}, \quad 0 \le r \le 1,\ h'(0) = 0,\ h(1) = 0. \quad (1)$$

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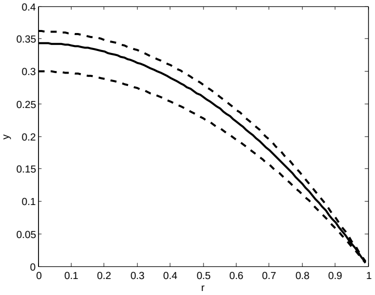
- For sufficiently small b we have existence, uniqueness, monotonicity and fundamental estimates of (1) by

$$h_0(r) := \frac{b}{a}\left(1 - \frac{I_0(\sqrt{a}r)}{I_0(\sqrt{a})}\right),$$

where I_0 is a modified Bessel function of the first kind.



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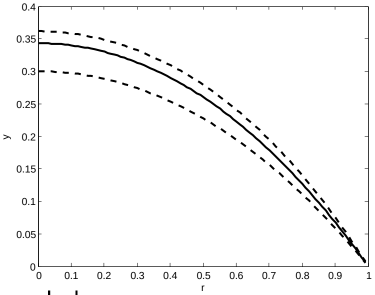

- For small values of a the solution (1) is a parabola.

Direct problem cont.

Theorem 1

Let $b \leq \frac{\sqrt{a}}{I_1(\sqrt{a})} \frac{\sqrt{2I_0(\sqrt{a})-1}}{I_0(\sqrt{a})-1}$. The solution of (1) is a positive, nonincreasing function f for which we have

$$Ah_1 \leq h \leq h_0,$$

where h_0 is defined by the formula

$$h_0(r) := \frac{b}{a}\left(1 - \frac{I_0(\sqrt{a}r)}{I_0(\sqrt{a})}\right),$$

and h_1 is the next approximation in the successive approximation scheme. Moreover,

$$A = \sqrt{\frac{1 + h_0'(1)^2}{1 + \left(2 - \frac{1}{I_0(\sqrt{a})}\right) h_0'(1)^2}}.$$

Inverse problem

How to find *a* and *b* when we know *h*?

- Problems of this kind are usually **ill-posed**, that is they do not fulfill one of the following conditions
  - they have a solution,
  - they have an unique solution,
  - small error in the initial data causes small error in the output (stability).

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  1. a i b are constant and unknown $\rightarrow$ nonlinear problem,
  2. a is known and constant but b (not necessarily constant) has to be found $\rightarrow$ linear problem.

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  2. a is known and constant but b (not necessarily constant) has to be found $\rightarrow$ linear problem.
- **Remark:** We cannot hope for an unique solution - we look for a solution in the L^2 norm sense (least-squares).

The nonliear inverse problem (a, b constant and unknown)

In subsequent considerations we will assume that the curvature of the cornea is small. It simplifies the equation

$$-\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial h}{\partial r}\right)+ah=b, \quad h'(0)=1, \quad h(1)=0.$$

[10] W.Okrasiński, Ł.Płociniczak, *Nonliear Parameter Identification in Corneal Geometry Model*

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- The nonlinear problem can be solved in a two-step method [10] :
  1. First, using the general theory we find

$$b^{\dagger} = b^{\dagger}(a) = \frac{\langle f(a,\cdot), h\rangle}{\|f(a,\cdot)\|^2},$$

where $f(a,r) := \frac{b}{a}\left(1 - \frac{I_0(\sqrt{a}r)}{I_0(\sqrt{a})}\right)$.

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The nonliear inverse problem (a, b constant and unknown)

In subsequent considerations we will assume that the curvature of the cornea is small. It simplifies the equation

$$-\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial h}{\partial r}\right) + ah = b, \quad h'(0) = 1, \quad h(1) = 0.$$

- The nonlinear problem can be solved in a two-step method [10] :
  1. First, using the general theory we find
  $$b^{\dagger} = b^{\dagger}(a) = \frac{\langle f(a,\cdot), h\rangle}{\|f(a,\cdot)\|^2},$$
  where $f(a,r) := \frac{b}{a}\left(1 - \frac{I_0(\sqrt{a}r)}{I_0(\sqrt{a})}\right)$.
  2. Then, we solve a nonlinear problem of fining a. We use an iterative method similar to the Newton's tangent scheme (a new proof of convergence)
  $$a_{n+1} = a_n + \Delta a_n, \quad \Delta a_n = \frac{\left\langle h - f(a_n,\cdot), \frac{\partial}{\partial a} b^{\dagger}(a) f(a;\cdot)\right\rangle}{\left\|\frac{\partial}{\partial a} b^{\dagger}(a) f(a;\cdot)\right\|^2}.$$

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The linear inverse problem (a constant and known, b unknown)

$$-\frac{1}{r}\frac{\partial}{\partial r}\left(r\frac{\partial h}{\partial r}\right)+\frac{1}{r^2}\frac{\partial^2 h}{\partial \theta^2}+ah=b, \quad h|_{\partial\Omega}=0,$$

where $\partial\Omega$ is an unit circle.

[9] Ł.Płociniczak, W.Okrasiński, *Regularization of an Ill-posed Model in Corneal Topography*

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where $\partial\Omega$ is an unit circle.

- We use eigenfunctions [9] $\Phi_{nm}(r,\theta):=\frac{1}{\sqrt{4\pi}}\frac{I_n(\mu_{nm}r)}{I_{n+1}(\mu_{nm})}e^{in\theta}$, where μ_{nm} is m-th zero of I_n (nth order modified Bessel function of the first kind).

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- **Remark:** $a-\mu_{nm}^2 \to \infty$, which destroys stability: small error in h will cause the series to become divergent.

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- **Remark:** $a-\mu_{nm}^2 \to \infty$, which destroys stability: small error in h will cause the series to become divergent.
- A regularization is neccessary

$$b_{\alpha,T(N,M)} := \sum_{\substack{n=-N,\\ m=1}}^{N,M}\frac{\langle h,\Phi_{nm}\rangle}{\alpha+\frac{1}{a-\mu_{nm}^2}}\Phi_{nm}.$$

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The linear inverse problem (a constant and known, b unknown) cont'd.

How much $b^{\delta}_{\alpha,T}$ is different from the true value b? (If $\left\| h^{\delta} - h \right\| \leq \delta$).

Theorem 2

We have

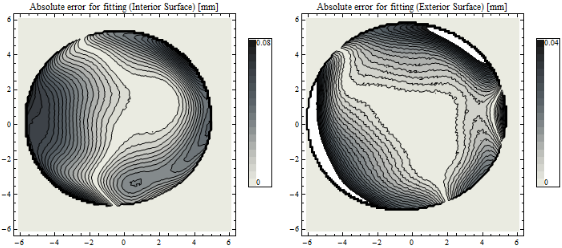
$$\left\| b^{\delta}_{\alpha,T(N,M)} - b \right\| \leq 2\sqrt{D\delta},$$

if only $\alpha = \alpha(\delta)$, $N = N(\delta)$, $M = M(\delta)$ are chosen, as to

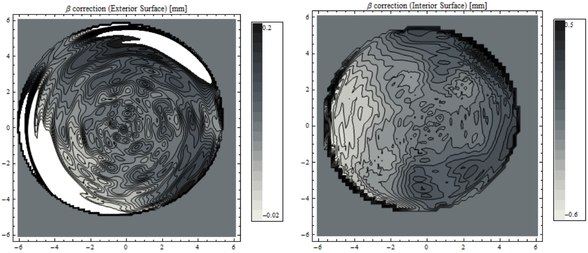
$$\alpha + C(N, M) = \sqrt{\frac{\delta}{D}},$$

where $\|y\| \leq D$ and $C(N, M) := \inf\{\frac{1}{a-\mu^2_{nm}} : |n| \leq N, m \leq M\}$.

Numerics



Fitting errors, with a_0 i b_0 constant.



β, where $b = b_0 + \beta$.

Summary

- Mathematical modeling in problems associated with eye is very desired.
- It is a source of very interesting and nontrivial problems from different fields on mathematics.
- Further progress in medicine will be very dependent on mathematics.
- We obtained a new, easy to apply, model of corneal topography based on physical principles.
- We have presented a new and fast iterative method of determining unknown parameters in the inverse problem.
  - Methods of finding a and b guarantee good model fitting (with small error).
  - Coefficients a and b are associated with measurable parameters of the cornea, and thus can be important in diagnosis and treating eye diseases.
  - The function β contains information about lack of axial symmetry of the cornea.

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