New Model of the Human Cornea according to the Hall-Petch Relationship

by

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THE HUMAN CORNEA AS A MICRO MULTILAYERS CRYSTAL LATTICE. BIO-MECHANICAL AND TENSILE PROPERTIES ACCORDING TO THE "HALL-PETCH" RELATIONSHIP.

Abstract

This paper is proposing to the scientific community a new, original approach to the problem of the bio-mechanical and tensile study of the human cornea. By overturning the traditional "classic" approach, focusing mainly on the analysis of the collagen fibril composition and distribution, and on the yield stress of the Stroma only (in the wrong assumption of its alleged "major importance", as a layer making 90% of corneal thickness), we introduce herewith a new approach, considering the human cornea as a micro multilayers crystal lattice, in which the whole bio-mechanical yield stress of the 5 layers (membranes) can be simultaneously and precisely calculated according to the "Hall-Petch" relationship for micro and nano multilayers materials.

Introduction

One of the main problem, in the analysis of the human cornea for medical and surgical purposes, and in the recent evolution of bio-mechanical studies, for manufacturing of bio-synthetic corneas, was mainly the "optical" and "biological" approach to the analysis of the human cornea.

In other words, for too many years and decades, the human cornea was analyzed mainly from an optical and medical approach (refractive defects and organic diseases), and from a purely "biological" standpoint, i.e, analysis of the cells and fibrils making the composition of the 5 corneal layers (Epithelium, Bowman's membrane, Stroma, Descemet's membrane, Endothelium).

However, strange as it may seem, for too long a physics and engineering full analysis of the human cornea was lacking, an analysis trying to better clarify the mechanical and tensile behavior of the corneal structure, and with a yield stress analysis, in order to better and precisely understand the mechanical strength of the corneal structure, and to plan more precisely new biosyntetic tissues and/or medical/surgical interventions.

1) The importance of studies on corneal yield stress.

A meaningful progress in this direction was made with the more recent studies on yield stress, by J. Hjortdal in 1996,regarding the central area of the cornea then followed by A. Pandolfi, G. Holzapfel in 2008, on the whole corneal structure.

The only flaws, in pioneering works handling the study of the yield stress of the human cornea, were in the misuse of the von Mises yield stress tensor (Pandolfi, Holzapfel), that is correct to calculate the yield stress of steel and concrete beams and structures, but is not suitable to analyze a colloidal structure as the human cornea, undergoing huge hydrostatic/volumetric changes, leading thereby to theoretical conclusions that were often mismatching with experimental results.

Moreover, all the papers handling the human cornea, so far, are always focusing mainly on the central stroma, as the most thick corneal layer, almost totally disregarding the other "smaller" layers, for a yield stress analysis.

In a study of 2010: "Biomechanics: principles, trends and applications", one of the authors, Ahmed Elsheikh, wrote at p. 60: "*The mechanical behavior of the human cornea is dominated by the stroma, that forms 90% of its thickness.*".

2) New model. The human cornea as a micro multilayers crystal lattice. Bio mechanical and tensile properties according to the Hall-Petch relationship.

Therefore, after realizing that the "path" (full analysis of corneal yield stress) showed by the first studies on yield stress was correct, but maybe it was necessary to choose a better corneal model, I tried to devise it.

I realized that the main drawback of the current bio-mechanical models is in their failure to grasp the peculiar, and somehow unique structural and morphological features of human cornea.

1) From a structural point of view our human cornea is a crystal lattice (collagen fibrils + endothelial/epithelial cells)
2) From a morphological standpoint, our human cornea is a micro-film (whose average thickness is around 560/600 µm) made of 5 micro-layers (Epithelium, Bowman's membrane, Stroma, Descemet's membrane, Basement/Endothelium).
After coupling the fundamental features above, the question is:
Is there a model, in Physics, whose ability to mathematically describe the behavior of micro multilayers crystal lattices has succesfully and experimentally been tested in recent times?
Of course there is!
According to the " Hall-Petch relationship" (that was discovered almost 60 years ago, but curiously it was never applied so far to make a model of human cornea) , we know that in a crystal lattice there is an inverse relationship between a grain size and its yield stress , as follows:
(1)

$$\sigma y \propto \lambda -1/2$$

In the formulation above:
σy = the yield stress
λ = grain size

Therefore,the Hall-Petch relationships foresees that in a crystal lattice, on a micro/nano scale, as the grain size decreases, its yield strenght increases.
http://en.wikipedia.org/wiki/Grain_boundary_strengthening
The Hall-Petch relationship is experimentally valid also for the layer's (containing grains) thickness (L), in a range from 1 mm. up to 1 µm as follows:
(2)

$$\sigma y = \sigma i + k/\sqrt{L}$$

Where L is the thickness of each layer, and σi is the resistance stress due to lactice friction (usually very negligible), in a slip plane where in a boundary location a pile-up of dislocations is taking place.
Now, in this model, the key-concept is played by the dislocation of crystal grains.
A dislocation is simply a defect in the atomic or molecular crystal structure of lattice, whose size and extension is measured by the Burger's vector.
Since a dislocation in a crystal sequence generates a repulsive stress field, that requires further energy to remove, the more we have dislocations piling-up (clusters of dislocations), the more the yielding stress of the crystal layer increases.
Since it is statistically much easier to find more dislocations whenever you have thinner layers of materials piling up in a constant volume (the more layers you have, the more dislocations you get), this is the reason why more thinner layers piling-up mean more yield stress, and hence a hardening of the material.
This is the reason why in many industries, as well as in nano-technologies, reduction of layers' size is normally used for hardening of materials (for an interesting "hardening law" in slip planes, see Cuitino, Ortiz, 1992)
Furthermore, it is experimentally proved that dislocations increase more in boundary layers and slip planes of layers, because in boundary layers repulsive forces are stronger than elsewhere. (see: "A

Continuum Plasticity Model that Accounts for Size Effect and Hardening in Thin Films, Hunter A., Kavuri H., Koslovski M., 2008)

Hall Petch equations and concepts have successfully proved to be experimentally precise and effective, in more than 50 years, in the calculation of tensile, mechanical, thermodynamic, etc., properties of micro and nano materials, and of the relevant energies involved therein.

Therefore, the new model of cornea's bio-mechanic and tensile properties that I'm proposing herewith, is entirely established on compelling experimental evidences – according to the Hall-Petch relationship – and is much more precise and sophisticated than the "classic" models currently in use.

This model can precisely 100% describe tensile and bio-mechanical properties of any corneas, both healthy and sick, because this model is devised according to the precise size of any layers of any corneas, and it is shaped according to a faithful description of mechanical behavior of micro/nano multilayers materials

Let's see how we have to change our old beliefs, after analyzing a yield stress behavior of a normal (healthy) cornea, according to the Hall-Petch relationship.

It is important to notice that – in this Hall-Petch model – fibril/grain analysis (stiffening, orientation, etc.) becomes much less important than boundary layers' analysis, because in human cornea fibrils (=crystal grains) are normally much more symmetrically and regularly ordered in each different layer (even in sick corneas!), to allow transparency, and therefore dislocation forces are not so strong as in boundary layers and within slip planes of each layer.

Now, let's take a normal cornea, whose total thickness is ~ 560 µm.

Layers' thickness is as follows:

1) Epithelium = 50 µm
2) Bowman's membrane = 10 µm
3) Stroma = 485 µm
4) Descemet's membrane = 9 µm
5) Basement/Endothelium = 5 µm

According to the Hall-Petch relationship, any layers above provide a "contribution" to the total yield stress, in inverse relationship to their thickness L ($\sigma y = \sigma i + k/\sqrt{L}$).

So, we have, for each layers, a yield stress contribution as follows:

1) Epithelium = $K^* 1/\sqrt{50} = K^*0.14$
2) Bowman's membrane = $K^*1/\sqrt{10} = K^*0.31$
3) Stroma = $K^*1/\sqrt{485} = K^*0.045$
4) Descemet's membrane = $K^* 1/\sqrt{9} = K^*0.33$
5) Basement/Endothelium = $K^* 1/\sqrt{5} = K^*0.45$

Supposing (to simplify) K = 1, we have a total corneal yield stress : 0.14 + 0.31 + 0.045 + 0.33 + 0.45 = 1.275

% yield stress contribution of each layer is:

Epit. = 0.14/1.275 = 11%

Bowman = 0.31/1.275 = 24.3%

Stroma = 0.045/1.275 = 3.5%

Descemet = 0.33/1.275 = 25.9%

Endot. = 0.45/1.275 = 35.3%

As you can see, Stroma's contribution to the total yield stress (according to the Hall-Petch relationship) is just a mean 3.5%, whereas the thinner layers, surrounding the Stroma, provide much more important contributions, keeping the mechanical stability and tensile strength of the whole corneal structure!

But let's now analyze the mechanical situation and yield stress of a sick cornea, a keratoconic cornea (medium/advanced keratoconus).

In order to make things even more similar to some real situation, let's suppose that keratoconus (as many times happens in advanced keratoconus) made Bowman's membrane literally disappear (it is

not very dangerous, because normally this complication does not affect corneal transparency, as with Descemet's membrane breaking), and other layers shrink for an average 10%.
So we have, for our keratoconic cornea:
Epit. = 45 μm
Stroma = 430 μm
Descemet = 8 μm
End. = 4 μm
According to the Hall-Petch, we shall have:
Epit. = K* 1/√45 = K*0.15
Stroma = K* 1/√430 = K*0.048
Descemet = K*1/√8 = K*0.35
Endot. = K* 1/√4 = K.0.5
After simplifying (K = 1) , we have a contribution of each layer to the total yield stress which is:
0.15 + 0.048 + 0.35 + 0. 5 = 1.048
% yield stress contribution of each layer to total yield stress is:
Epit. = 0.15/1.048 = 14.3 %
Stroma = 0.048/1.048 = 4.5%
Descemet = 0.35/1.048 = 33.4%
Endot. = 0.5/1.048 = 47.7%
In a keratoconic cornea, most (more than 80%!) of total yield stress is sustained by the inner and thinner layers, whereas stroma's contribution to the yield stress is just 4.5%!
But this explains also why only a small percentage of patients, between 2-4%, during their life, undergo a Descemet's membrane breaking (mostly due to poor contact lenses care, eye rubbing, traumas and accidents).
It is interesting to note that – according to this new Hall-Petch corneal model, it makes no sense, and it is totally incorrect to analyze - as it was done till now - the yield stress of any corneal layer <u>alone.</u>
If we have – for instance – a single corneal layer (as the stroma) whose breaking stress point is – say - 100 (dyne, kPa, etc., no matter) alone, then if we guess a 4 layers' cornea, as the keratoconic cornea above, it will take a more than double yield stress (100/47.7) namely more than 200, to cause a breaking in the strongest layer (Endothelium).
This new model accounts precisely for a simultaneous and integrated analysis of all corneal layers together, after taking the exact size of any of them.
It is possible to make a further "refinement" of the model, by introducing a numerical discretized analysis, according to a Mohr method (by calculating the yield stress of the outside layer, i.e. Epithelium, with a variation of the shear stress according to the tangential stress), but basically the Hall-Petch relationship alone can fully and precisely describe <u>any</u> mechanical yield stress on any layers.

<u>3. The human cornea, the inelastic collisions and the Hall-Petch relationship</u>

It is very interesting to see that this new Hall-Petch model (in which the thinner layers are stronger and providing a better contribution to the mechanical stability of the whole structure) is fully in agreement with an important feature of the human cornea: a S-W-S (i.e. stronger – weaker – stronger) or S-B-S (small-big-small) model of our corneal bio-mechanical structure can fully explain why our cornea and eye can better distribute and withstand many strong collisions (as the eye traumas in boxing, and other sport activities, for instance).
Actually, any collision by an external source against our cornea, can easily be described, in Physics, according to the equations of inelastic collisions.
An inelastic collision, is a collision in which kinetic energy is dispersed (into heat mainly) and not conserved.
A typical inelastic collision is the collision of a car bumping into another still in front of it, and dragging the latter with it for some meters.

In our cornea, since we have 5 layers closely connected together, any time a collision of an external force against our eye is taking place, and the outermost thinner (and strongest) layers (Epithelium + Bowman's membrane) are colliding against Stroma, then we can mathematically describe such collision as follows:
(3)

ma* ua + Mb*ub =(ma + Mb) * V

where:
ma = mass of the smaller body (Endothelium + Bowman's layer)
Mb = mass of the bigger body (Stroma layer)
ua = velocity of the smaller body before impact
ub = velocity of the bigger body before impact
V = final velocity after impact
http://en.wikipedia.org/wiki/Inelastic_collision

Now, in our cornea, the mass of the smaller outside layers is just around 5 (%) whereas mass of stroma is nearly 90 (%).
If we suppose an initial velocity of the smaller body around 2 (m/sec^2), after the impact with the external force, and an initial velocity = 0 for the bigger body (the bigger body is still, and gets the collision from the smaller body), then we can introduce magnitudes as follows:
5 * 2 + 90*0 = (5 + 90) * V
10 = 95* V
V = 0.1
As we can see, smaller (and stronger) corneal layers closely connected with a bigger corneal layer as stroma, can reduce a lot the final velocity (= kinetic energy) of the impact, that is dispersed into heat energy.
On the contrary, a reverse situation, in which the bigger layer was colliding against a smaller layer: (90* 2) + 5*0 = (5+90) * V, would make:
V = 180/95
V = 1.9
Namely a big (and destructive) kinetic energy, 19 times bigger than with a S-B-S (small-big-small) distribution!

4. Human cornea as a fractal-like structure

This new model of human cornea according to the Hall-Petch relationship, and the new discovery of the real and precise contributions of any layers to the total yield stress, can highlight another important and fascinating feature of the human cornea, according to its bio-mechanic and tensile properties.
(see for this topic :Li, Y., Ortiz, C., Boyce, M.C., " A Bio-inspired Mechanical, Deterministic Fractal Model for Hierarchical Suture Joints", Physical Review E, in press, 2012.)
Human cornea is a fractal-like bio- mechanical structure, in which – as in many other structures - we find an integumentary protective system , where 2 thinner (but stronger, i.e. having a bigger yield stress) outside layers surround and protect an inner "softer" (i.e. having less yield stress) biological structure.
Most of these structures have a similar % distribution in thickness of stronger and weaker layers, namely, a 10-15% of thinner and stronger outside layers (like Descemet, Bowman, Epithelium and Endothelium), and a 80-90% of weaker and softer internal layer (like Stroma).
We can find similar fractal-like structures in our bones (outside compact [cortical] layer, and inside soft trabecular [cancellous] layer), tooth (enamel + dentin + cementum covering the pulp), blood vessels (thick outermost layer = connective stronger tissue: tunica externa, surrounding inner layer of soft tissue: tunica media + endothelian cells making the so called tunica intima), skin (epidermis + derma lying on undercutaneus adipose tissue), etc.

In conclusion, I believe this new model of human cornea can successfully be used to describe and simultaneously calculate any yield stress of ALL the layers of our human cornea, by simply considering their sizes, taking as a basic parameter an average yield stress of human corneas, and it is a meaningful improvement of the previous models, allowing a better planning of medical/surgical intervention and/or a better planning and manufacturing of bio-synthetic corneas.

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