Anup Dev Pant, PhD and Ali Vahdati, PhD Department of Engineering

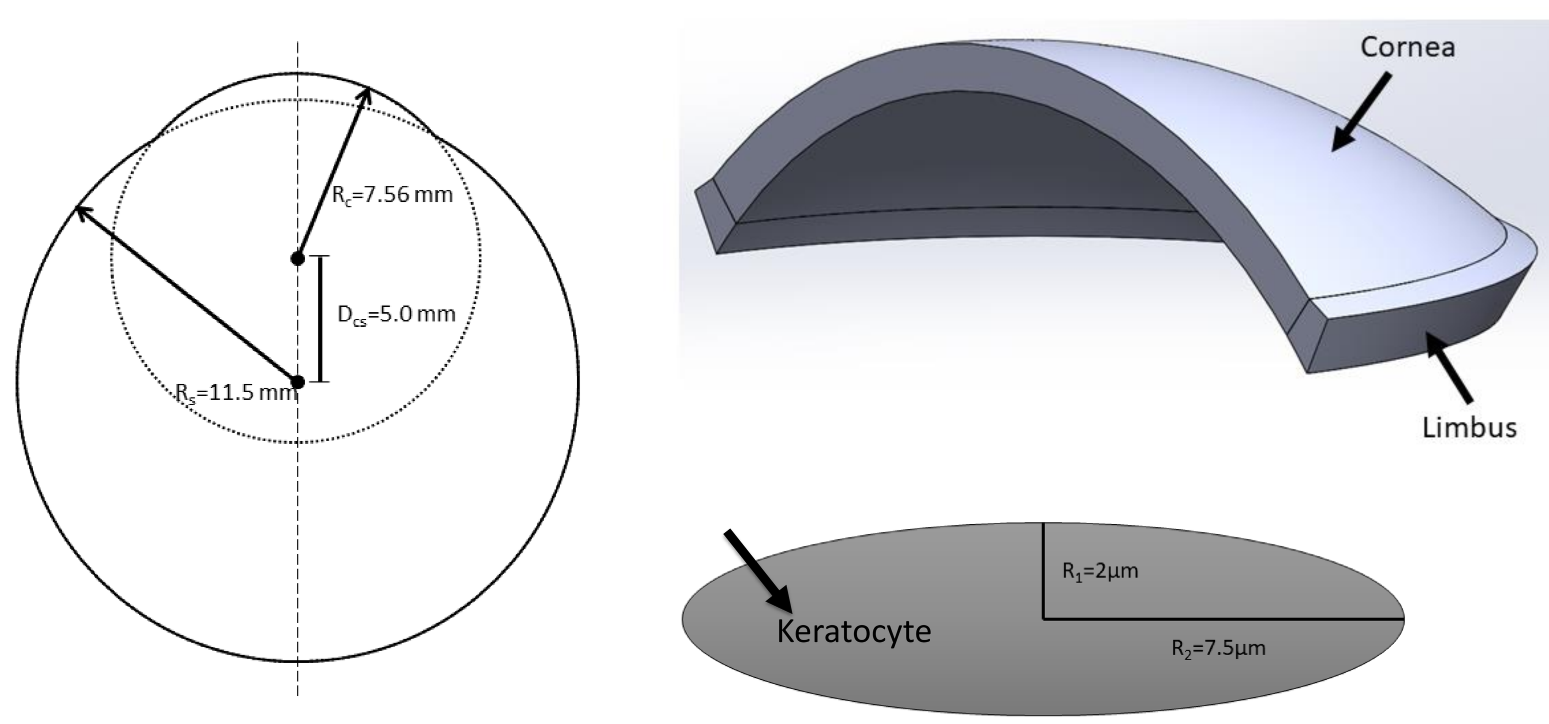
A Computational Approach to Study the Effect of Different Loading Conditions on the Corneal Cells

INTRODUCTION

- Keratocytes, the predominant cells in the cornea are critical in maintaining the normal homeostasis of the cornea as they are affected in many pathologies such as keratoconus, corneal wounds, and diabetic neuropathy.
- Multi-scale computer models of the cell-tissue-organ units are an emerging area of research with the potential to improve our understanding of various disease pathogenesis [1].
- Currently, there exist no multiscale models of the cornea that take into consideration the cellular components of the cornea, the keratocytes.
- Therefore, we developed a multiscale model of the cornea to study the effect of different mechanical loadings on the cells.

MATERIALS AND METHODS

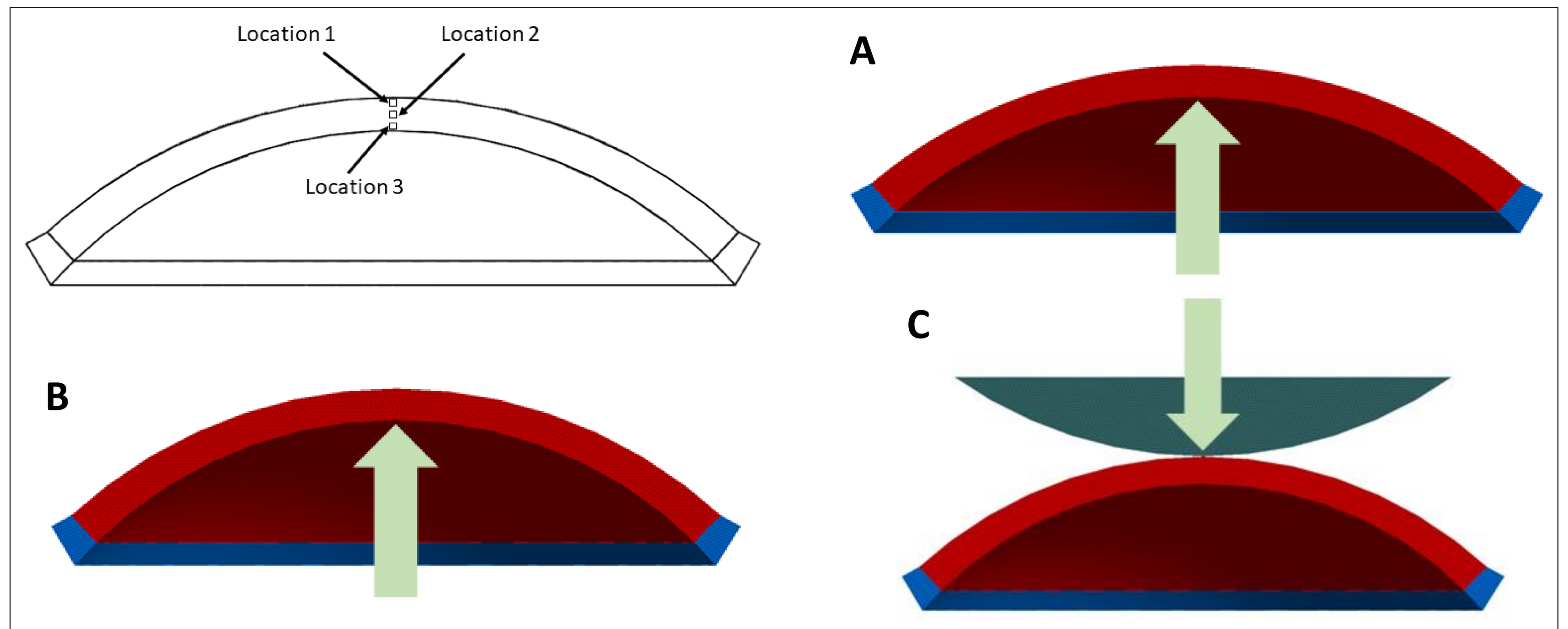
- A finite element model of the cornea including the limbus was constructed based on the geometry described by Grytz et. al. [2].



Geometry of the model, 3D model of the cornea constructed from the geometry, and geometry of the keratocyte

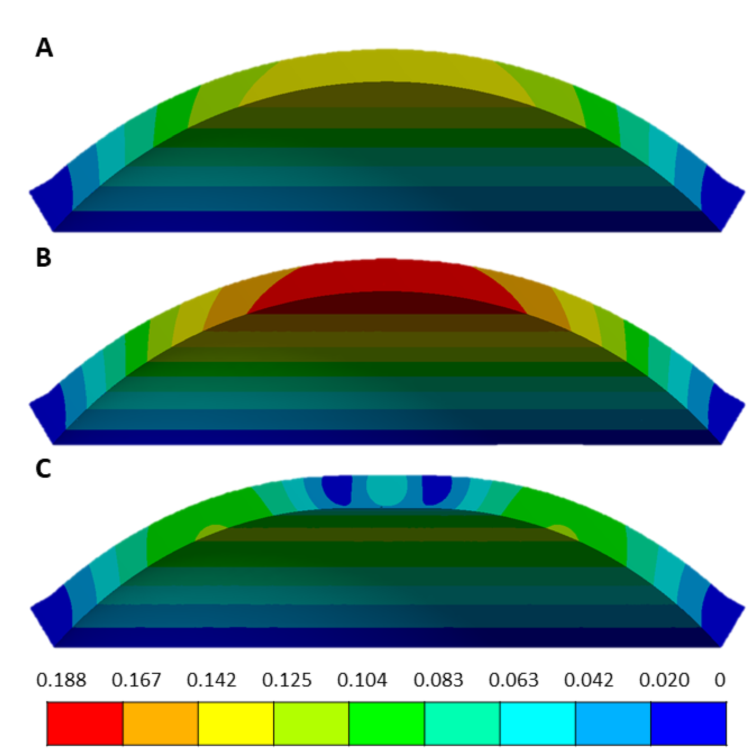
- Cornea was modeled as a Yeoh material.
- Limbus was modeled as a linear elastic material.
- Keratocyte was modeled as flat ellipsoid and an incompressible neo Hookean material.
- A sub modeling approach was used in Ansys (Ansys 19.2, Canonsburg, PA, USA) to develop the multiscale model of the keratocyte.
- Macroscopic deformation from the cornea were mapped to the keratocytes.
- Multiscale simulations were run for three different cases with the location of keratocyte changed along the thickness of the cornea.
- For each of the cell location, three different loading conditions were applied.

MATERIALS AND METHODS

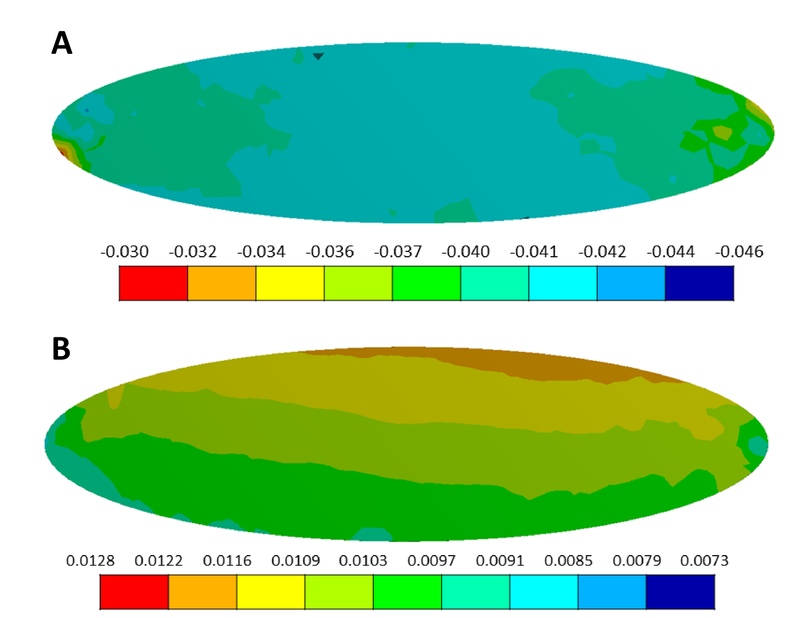


Application of different loading conditions at different cell location. (A) Application of 15mm Hg pressure to the deflated corneal geometry to simulate normal IOP, (B) Application of additional pressure to the inflated corneal geometry to simulate IOP spike, and (C) Application of downward displacement to the inflated corneal geometry to simulate eye rubbing loading condition.

RESULTS



Total deformation (mm) in the cornea when the cornea is subjected to (A) normal IOP, (B) IOP spike of 5 mm Hg, and (C) eye rubbing loading condition using 0.2 mm downward displacement.



(A) Minimum principal strain distribution in the cell located near the posterior surface of the cornea under eye IOP spike of 5mm Hg loading condition, and (B) Maximum principal strain distribution in the cell located near the anterior surface of the cornea under 0.2 mm eye rubbing loading condition.

- Cells near the anterior surface of the stroma experience large principal stress under normal IOP and under IOP spike.
- Under eye rubbing, cells throughout the thickness of the cornea experience similar magnitude of principal stress, although cells near the anterior and middle of the stroma experience compressive stress whereas the posterior cells experience tensile stress.

RESULTS

Table 1: Average of maximum and minimum principal stress under different location at different loading condition

Cell Location	Principal stress under normal IOP (KPa)		Principal stress following IOP spike of 5 mm Hg (KPa)		Principal stress under -0.2mm (KPa)	
	Maximum	Minimum	Maximum	Minimum	Maximum	Minimum
Near the anterior surface of the stroma	2.25	2.10	2.72	2.53	-30.70	-30.76
In the middle of the stroma	1.94	1.79	2.53	2.33	-30.72	-30.92
Near the posterior surface of the stroma	0.40	0.25	0.42	0.23	30.78	30.38

Table 2: Average of maximum and minimum principal strain under different location at different loading condition

Location of the cell	Principal strain under normal IOP (mm/mm)		Principal strain following IOP spike of 5 mm Hg (mm/mm)		Principal strain under -0.2mm (mm/mm)	
	Maximum	Minimum	Maximum	Minimum	Maximum	Minimum
Near the anterior surface of the stroma	0.016	-0.031	0.021	-0.040	0.011	-0.009
In the middle of the stroma	0.016	-0.031	0.021	-0.040	0.022	-0.042
Near the posterior surface of the stroma	0.016	-0.031	0.021	-0.040	0.045	-0.085

- The maximum and minimum principal strain remains constant through the thickness under normal IOP loading and IOP spike loading.
- Cells located near the posterior surface of the stroma exhibit maximum and minimum principal strain under complex loading such as eye rubbing.

DISCUSSION

- Mechanical stimulus plays a major role in regulating the structure and function of many tissue through cellular activity and mechanobiology.
- Corneal fibroblasts too, respond actively to the changes in the local matrix stress to restore normal homeostasis [3] .
- Hence, understanding the mechanical environment of these cells under different loading conditions and at different locations will open avenues in understanding the pathologies of different corneal diseases and conditions.

REFERENCES

1. Alber, M. et al. Digit. Med. 2, 1–11 (2019).
2. Grytz, R. & Meschke, G. Biomech. Model. Mechanobiol. 9, 225–235 (2010).
3. Petroll, W. M., Vishwanath, M. & Ma, Investig. Opthalmology Vis. Sci. 45, 3466 (2004).