CONTROL ID: 2913137
SUBMISSION ROLE: Abstract Submission

## AUTHORS

AUTHORS (LAST NAME, FIRST NAME): Sacco, Riccardo[1]; Sala, Lorenzo[2]; Mauri, Aurelio G.[1]; Messenio, Dario[3]; Guidoboni, Giovanna[4]; Siesky, Brent[5]; Harris, Alon[5]

INSTITUTIONS (ALL):

1. Mathematics, Politecnico di Milano, Italy, Milan, Italy.
2. Université de Strasbourg, CNRS, IRMA, Strasbourg, France.
3. Eye Clinic, Department of Clinical Science, Luigi Sacco Hospital, University of Milan, Milan, Italy.
4. Department of Electrical Engineering and Computer Science, College of Engineering, University of Missouri, Columbia, MO, United States.
5. Ophthalmology, Indiana University School of Medicine, Indianapolis, IN, United States.

Commercial Relationships Disclosure (Abstract): Riccardo Sacco: Commercial Relationship: Code N (No Commercial Relationship) | Lorenzo Sala: Commercial Relationship: Code N (No Commercial Relationship) | Aurelio Mauri: Commercial Relationship: Code N (No Commercial Relationship) | Dario Messenio: Commercial Relationship: Code N (No Commercial Relationship) | Giovanna Guidoboni: Commercial Relationship: Code N (No Commercial Relationship) | Brent Siesky: Commercial Relationship: Code N (No Commercial Relationship) | Alon Harris: Commercial Relationship(s);CIPLA:Code C (Consultant) ;AdOM:Code C (Consultant) ;Oxymap:Code I (Personal Financial Interest) ;AdOM:Code I (Personal Financial Interest) ;Nano Retina:Code I (Personal Financial Interest)
Study Group: (none)

## ABSTRACT

TITLE:
A theoretical study of the role of conformational properties of transepithelial ion pumps on aqueous humor production

ABSTRACT BODY:

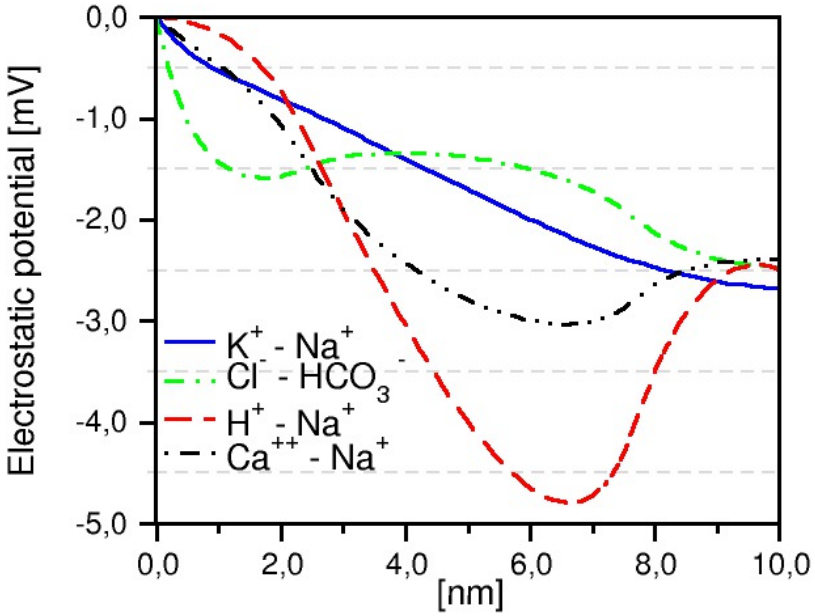
Purpose:
Intraocular pressure, resulting from the balance of aqueous humor (AH) production and drainage, is the only approved treatable risk factor in glaucoma. AH production is determined by the concurrent function of ion pumps and aquaporins in the ciliary processes but their individual contribution is difficult to characterize experimentally. In this work, we propose a mathematical model to investigate the role of conformational properties of $Na^+$-$K^+$, $Ca^{2+}$-$Na^+$, $Cl^-$-$HCO_3^-$ and $Na^+$-$H^+$ ion pumps on AH production.

Methods:
Ion pump function is modeled by coupling a velocity-extended electrochemical module for ion motion and an electrochemically driven fluid module for AH flow. Time-dependent simulations are conducted to study ion pump features as a function of (1) permanent electric charge density over the channel pump surface; (2) osmotic gradient coefficient; (3) stoichiometric ratio between ion pump currents at channel inlet and outlet.

Results:
Fig. 1 shows the steady-state electric potential V along the channel axis Z. Potential drop is due only to the electric field generated by permanent surface charge density. Despite remarkably different profiles of V inside the channel, the predicted transmembrane potential $V_m$=V(Z=10nm)-V(Z=0nm) is for all pumps in good agreement with the range [-2.7, -2.3] mV experimentally measured on monkeys. Fig. 2 shows the steady-state AH velocity along Z. Fluid motion is due only to electric pressure exerted by the ions. Model predicts a positive AH flow in all channel length for $Na^+$-$K^+$ and $Ca^{2+}$-$Na^+$ pumps, a positive AH flow in the central region for $Cl^-$-$HCO_3^-$ pump and AH flow inversion at Z=6.5nm for $Na^+$-$H^+$ pump.

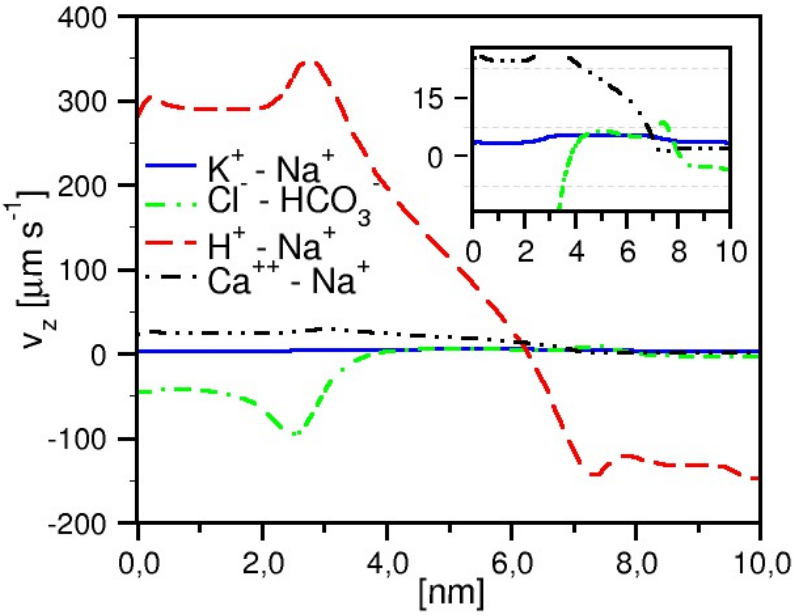
Conclusions:
The proposed mathematical model allowed us to simulate the four main ion pumps involved in AH production. Predicted transepithelial potential and AH flow are in good agreement with measured data and biophysical intuition. Results support adopting the theoretical tool as a virtual laboratory to verify conjectures, compare different scenarios

and complement the indispensable animal model in patient-specific therapy design.




<br />

Fig. 1. Spatial distribution of electric potential along channel axis. Blue: $K^{+}$-$Na^{+}$ pump. Black: $Ca^{2+}$-$Na^{+}$ pump. Green: $Cl^{-}$-$HCO_3^{-}$ pump. Red: $H^{+}$-$Na^{+}$ pump.




<br />
Fig. 2. Spatial distribution of AH velocity along channel axis. Blue: $K^+$-$Na^+$ pump. Black: $Ca^{2+}$-$Na^+$ pump. Green: $Cl^-$-$HCO_3^-$ pump. Red: $H^+$-$Na^+$ pump.

**Layman Abstract (optional): Provide a 50-200 word description of your work that non-scientists can understand. Describe the big picture and the implications of your findings, not the study itself and the associated details.:**
Intraocular pressure, resulting from the balance of aqueous humor (AH) production and drainage, is the only approved treatable risk factor in glaucoma. In this work, we propose a mathematical model to investigate the role of conformational properties of $Na^+$-$K^+$, $Ca^{2+}$-$Na^+$, $Cl^-$-$HCO_3^-$ and $Na^+$-$H^+$ pumps on AH production.

## DETAILS

**PRESENTATION TYPE:** #1 Paper, #2 Poster
**CURRENT REVIEWING CODE:** 2650 ion channels, aquaporins, membrane properties and epithelial transport - PH
**CURRENT SECTION:** Physiology/Pharmacology
**Clinical Trial Registration (Abstract):** No
**Other Registry Site (Abstract):** (none)
**Registration Number (Abstract):** (none)
**Date Trial was Registered (MM/DD/YYYY) (Abstract):** (none)
**Date Trial Began (MM/DD/YYYY) (Abstract):** (none)
**Grant Support (Abstract):** No
**Support Detail (Abstract):** None

## TRAVEL GRANTS and AWARDS APPLICATIONS

**AWARDS:**

## AFFIRMATIONS

**Affirmations:** Affirmation that submission of this abstract has been approved by the Principal Investigator.
**Affirmations:** Affirmation that abstract data/conclusions have not been published; not redundant with other submissions from same investigators.
**Affirmations:** Affirmation to reveal essential structure, novel compound elements, or identify new gene compounds.
**Affirmations:** Affirmation to present same work as abstract submission.
**Affirmations:** Affirmation of copyright transfer from each author to ARVO, or certification of public domain abstract.
**Affirmations:** Affirmation of compliance with ARVO's Statement for Use of Animals.
**Affirmations:** Affirmation to pay Annual Meeting's full registration fee.
**Affirmations:** Affirmation of compliance with ARVO's Statement for Use of Human Subjects and/or Declaration of Helsinki.
**Affirmations:** Affirmation of compliance with ARVO policy on registering clinical trials.