A SYNTHETIC EMBRYONATED AVIAN EGGSHELL COMPUTATIONAL MODELED TO PREDICT THE OXYGEN TRANSPORT

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INTRODUCTION

The striking pandemic infection of Sars-Cov-2 highlighted the compelling need of experimental models aimed at speeding up the discovery and preclinical testing of new biological drugs[1], especially for drugs targeting the micro circulation (e.g. in diabetes, retinal disease, kidney disease, virology, etc.). Similarly, the vascular network is the key point in antiangiogenic, antibody-based and small molecule-based drug development for cancer research. The chicken embryo seems to be the perfect candidate to allow fast and versatile studies on a functional vascular network in response to injected targets. To this end, we computationally modeled an embryo at different developing time points (Figure 1, a) to identify a synthetic eggshell substitutive material providing physiological oxygenation.

METHODS

We performed computational simulations (COMSOL) to model a living chicken embryo at the 8th day of development and characterize its own protective shell. Thus, we modeled the egg as a prolate ellipsoid having radius of 1.4 and 1.7cm and a mesh having 195k tetrahedral elements. We assumed the eggshell as a porous material having a thickness of 300µm, porosity ~2% and tortuosity parameter equal to 1, juxtaposed to a thin film constituted by inner and outer shell layers having a total thickness of 65µm. We assumed the embryo localization in the central part of the egg having above an air sac of volume equal to 3 cm^3 and an albumen layer of 18cm^3 into the lower portion. For the chorioallantoic membrane, i.e. the embryo respiratory organ, we assumed a consuming surface of ~ 41cm^2 with a peak oxygen consumption, V_{max}, equal to 5.14x10^{-6} mol/m^2s and a kinetic governed by the Michaelis-Menten law (Figure1, b-c). Then, we assumed varying thickness of a membrane substitute material made of PDMS, with thicknesses of 100, 365, 800 µm.

RESULTS

Oxygen concentration decreased alongside the eggshell thickness with a concentration drop lower than 1% from the egg outer to inner boundaries. The air sac mean oxygen concentration resulted equal to 8.152mol/m^3. Simulations performed on PDMS showed a decrease in air sac concentration ranging from 20% to 98% (Figure1, e) with respect to physiological values, considering the thinner and the thicker PDMS layer, respectively.

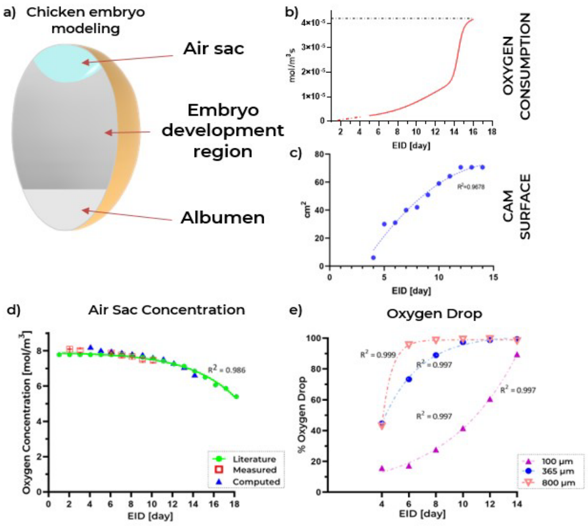

Figure 1: a) Geometric modeling of an embryonated chicken eggshell. b) Michaelis-Menten curve of the oxygen consumption during embryo development. c) Mathematical fitting of the CAM development during the embryo development. d) Computational prediction of the oxygen drop inside the egg air sac. b) Computational prediction of the oxygen drop through PDMS membranes having thicknesses of 100, 365, 800 mm.

DISCUSSION

We developed a computational model able to predict oxygen concentration values in a chicken embryo at embryonic developing day 8. Our model agrees with experimental values found in literature[2] with a mean error lower than 3% (Figure1, d). We are now performing measurements to validate boundary condition assumed in model, to calibrate the model and to extend its validity up to the 12th day of embryonic development. We are also experimentally testing our first synthetic eggshell substitute made of PDMS.

References

1. Raimondi et al., 2020;
2. Ackerman and Rahn., 1980

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