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(G) Differential-Geometric Model of Red Blood Cell Equilibrium Shapes to Investigate Skeletal Muscle Microcirculatory Regulation

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The microcirculation serves to deliver oxygen (O2) to tissue as red blood cells (RBCs) pass through the body's smallest blood vessels, capillaries. Imaging techniques quantify O2 present in capillaries but lack effective modalities quantifying O2 entering tissue from capillaries. Thus, mathematical simulation has been used to investigate how O2 is distributed locally over a variation of metabolic demands, and to investigate mechanisms regulating capillary blood flow to meet such metabolic tissue O2 demands. Being present throughout the microcirculation, RBCs have been hypothesized as potential candidates initiating signals at the capillary level that are transmitted upstream to arterioles thereby altering capillary blood flow. It has been found that RBC deformation, as well as oxyhemoglobin desaturation, can cause release of adenosine triphosphate (ATP). It has been theorized that as RBCs deform with local blood flow, released ATP modulates upstream vessel diameter, but requires a model to systematically investigate. At baseline, RBCs possess unique shapes formed from a balance between the phospholipid bilayer membrane's surface tension, surrounding fluid osmolarity, and the curvature-dependent Canham-Helfrich-Evans (CHE) energy. To investigate how RBCs deform with blood flow stresses, a novel algorithm for red blood cell (RBC) equilibrium geometry was developed as the first step of a quantitative model for RBC-ATP release. This condensed matter theory model relied on the developing coordinate-invariant computational framework of discrete exterior calculus (DEC). Using this algorithm, several RBC geometries were observed at different surface tension (area) and osmolarity (volume) constraints. First seen throughout literature, the algorithm was able to be expressed as an implicit system, and utilized a Lie-derivative based vertex drift method to ensure the RBC meshes were well-behaved throughout deformation. The algorithm was shown to be highly stable, quantified through tracking the RBC membrane energy. Equilibrium geometries were shown to agree with literature in vivo observations, and qualitatively reproduced phenomena seen with in vivo experiments where RBCs are subjected to solutions of varying osmolarity. Future work will allow investigation of how RBCs behave under flow stresses to simulate combined shear-O2-dependent ATP release.

Keyword-1

Red blood cell

Keyword-2

microcirculation

Keyword-3

mathematical modelling

Author: AFAS, Keith

Co-author: GOLDMAN, Daniel (University of Western Ontario)

Presenter: AFAS, Keith

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