Quantifying physical changes in red blood cells as they mature in the bloodstream

October 9 2014

During their approximately 100-day lifespan in the bloodstream, red blood cells lose membrane surface area, volume, and hemoglobin content. A study publishing this week in *PLOS Computational Biology* finds that of these three changes, only the observed surface-area loss can be explained by RBCs shedding small hemoglobin-containing vesicles budding off their cells' membrane.

Red blood cell concentration, mean volume, and hemoglobin content are routinely measured in the complete blood count, a fundamental clinical test essential to the screening, diagnosis, and management of most diseases. Variation in mean volume and hemoglobin content is associated with many important clinical conditions, but we do not understand the mechanisms controlling these physical characteristics of red blood cells. Vesicle shedding had been thought to be the most important, but researchers Roy Malka and John Higgins from Massachusetts General Hospital/Harvard Medical School, with colleagues from Massachusetts Institute of Technology, show that a dominant role for vesicle shedding would violate empirical geometric and biophysical constraints. An additional unknown process must be primarily responsible. The study shows that this important process must be coupled to changes in red blood cell surface area and quantifies the magnitude of its effects.

The study required a multidisciplinary team with expertise in applied mathematics, engineering and medicine. The work combines mathematical modeling of the mechanism that changes the physical properties of the cells, clinical measurements of both cellular volume

and hemoglobin content, and data from a new system for characterizing the non-water cellular mass of individual cells.

Maturation of red blood cells in the circulation, the subject of this study, is one of the three major components controlling the population of red blood cells, the other two being their production by the bone marrow and clearance from the circulation.

The researchers conclude that the quantitative characterization of red blood cell loss processes will help "focus future investigation of the molecular mechanisms of red blood cell maturation", the characterization of which "may help in the early detection of clinical conditions where the maturation pattern is altered".

More information: Malka R, Delgado FF, Manalis SR, Higgins JM (2014) In Vivo Volume and Hemoglobin Dynamics of Human Red Blood Cells. *PLoS Comput Biol* 10(10):e1003839. DOI: 10.1371/journal.pcbi.1003839