SHELL SEMINAR SERIES
CHEMICAL & BIOLOGICAL ENGINEERING

Interfacial Rheology and How We Breathe

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ABSTRACT A less appreciated role of lung surfactant is to insure uniform lung inflation. The dependence of the Laplace pressure, $\Delta P = 2\gamma/R$, on alveolar radius, R, means that interconnected bubbles or alveoli are at best metastable if γ is constant. However, while not generally appreciated in the medical literature, but well known in the foam and emulsion stability literature, the dynamic resistance of an interfacial film to compression can reverse the Laplace instability. The dilatational modulus, $\varepsilon = A\,\partial\gamma/\partial A$, relates the change in surface tension, γ, to the change in molecular area, A, as the interface is compressed at frequency, ω (ranging from 1-20 radians/second for normal breathing). If the dilatational modulus is large enough, the resistance to interfacial compression can overcome the Laplace pressure so that the gas pressure in the alveolus no longer increases with decreasing radius. For $(2\varepsilon-\gamma) > 0$, the Laplace pressure decreases with decreasing radius and increases with increasing radius, which reverses the Laplace instability, thereby stabilizing the alveoli against collapse. Under normal conditions, lung surfactant generates conditions such that $(2\varepsilon-\gamma) > 0$, and the lung remains stable. However, during Acute Respiratory Distress Syndrome, trauma or disease leads to a dramatic increase in the concentration of albumin and lysophosphatidylcholine, soluble surface-active molecules that compete for the interface with lung surfactant. Using a newly designed capillary microtensiometer, we have found that the lysophosphatidylcholines, a product of the inflammation induced degradation of phospholipids, causes the dilatational modulus to decrease as $\omega^{1/2}$, resulting in $(2\varepsilon-\gamma) < 0$ creating conditions that induce the Laplace instability, and perhaps ARDS, which kills 50,000 people each year with no known cure. Our results suggest that increasing the breathing frequency or decreasing the lysophosphatidylcholine concentration can increase the dilatational modulus and may restore proper lung function to ARDS patients.

BIO **Dr. Joseph Zasadzinski**'s research centers on the interfacial and self-assembling properties of biologically relevant surfactants such as lipids and proteins. His group tries to understand how the fundamental chemistry and physics of lung surfactant monolayers and bilayers influence their physiological role of lowering surface tension in the human lung. Dysfunction of this system leads to neonatal and adult respiratory distress syndrome, which affects 100,000 people each year, with a 40% mortality rate. His group believes that the problem is due to competition between serum proteins and lung surfactants for the interface during the inflammation that accompanies disease. He has built novel two-dimensional shear and dilatational rheometers that they couple to fluorescence imaging techniques to relate interfacial mechanics to composition and morphology. They are showing that the Laplace instability, caused by a lack of dynamic changes in surface tension during breathing, may be responsible for causing lung dysfunction during respiratory distress.

His second area of interest is creating novel plasmon resonant gold nanostructures that strongly interact with near infrared (NIR) light. NIR is physiologically benign and can transmit through centimeters of tissue which makes it ideal for triggering local biological processes such as disrupting endosomes to release genetic materials to the cell cytoplasm with incredible spatial and temporal control. The laser pulses create cavitation-like nanobubbles around gold nanoparticles that can disrupt endosomes and nearly instantaneously release the desired protein or genetic material directly to the cytoplasm with high viability and efficiency. His group is currently developing high throughput methods to create cell-based "drugs" by delivering mRNA to natural killer and T-cells to enhance the immune system response to cancer. The mRNA can code for chimeric antigen receptor proteins that help the immune cells target the cancer, but disappear after the cancer is gone. He creates lipid-based liposomes to encapsulate and protect the mRNA during endocytosis and delivery, then use the NIR light to generate nanobubbles to rupture the liposomes and endosomes to deliver the mRNA directly to the cytosol at high throughput and with high cell viability.

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