Commentary

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Envisions Living Cells as Complex Dynamical Colloidal Systems

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Description

Coacervation, phase transitions, emergent properties, and ionic association are important concepts from colloidal physical chemistry that are currently entering the lexicon of cellular biology. This is mostly due to recent experimental observations of liquid phase coexistence in the cell cytosol. However, the application of these ideas to cell biology is not new from a historical perspective. They were important concepts in the so-called protoplasmic doctrine, a different approach to cell physiology that has been mostly forgotten. The Association-Induction Hypothesis (AIH), developed by Gilbert N. Ling in 1962, is the most comprehensive theory to emerge from this school of thought. The AIH's view of living cells as fluid-filled vesicles is called into question by the abundance of theory and experimental evidence supporting the AIH's view of living cells as complex dynamical colloidal systems. The purpose of this review is to present and discuss how the AIH can be used to comprehend a number of experimental observations made in our lab using living suspensions of the yeast Saccharomyces cerevisiae that exhibit glycolytic oscillations. In particular, the AIH helped us mechanistically integrate the basis of the strong temporal coupling between ATP and a number of cellular properties, including intracellular water dipolar relaxation and intracellular K+ concentration, both of which are fundamentally influenced by the colloidal physical chemistry of the cell interior.

Natural Variability in the Partial Pressure of CO2

Ocean acidification is the process by which anthropogenic CO2 gas dissolves into oceanic waters, lowering pH and the saturation state of calcium carbonate as atmospheric CO2 levels rise as a result of human activity. According to recent research, coastal waters in the US Northeast, such as the Mid-Atlantic Bight and the Gulf of Maine, may be more susceptible to acidification than previously thought. In comparison to other shelf systems, this region has a lower buffering capacity and averages lower pH and aragonite saturation states (Ar). This indicates that they are closer to being under saturated and that the pH will change more quickly as anthropogenic CO2 is added. The health of the ecosystem in the Northeastern United States, as well as the profitability of wild fisheries, aquaculture, and tourist economies, all depend on how the region's chemistry and biology respond to ocean acidification. Riverine inputs, seasonal cycles in primary production, and changes in sea-surface temperature are the primary drivers of natural variability in the partial pressure of CO2 (pCO2) on the Northeast US coastal shelf. Consequently, there is already a significant natural seasonal variation in pCO2 levels in the region. The lowest levels of surface pCO2 occur in the Gulf of Maine during the springtime. Similar to pre-industrial atmospheric levels), whereas surface waters reach 550 atm in late fall and early winter, well above the current global atmospheric average. The system experiences a very different type and timing of natural variability compared to what has been documented on the West Coast, which experiences episodic high CO2 during the periodic upwelling of CO2 enriched subsurface water, with greatest intensity in the spring and summer. However, the implications of this seasonal variation in pCO2 on the local biota have not yet been examined. It is important to know how this annual variability affects organismal responses because it could cause predictable periods of high CO2 stress that can be reduced by local acclimatization to high CO2.

Local Chemistry of Complex Biological Tissues

Osteoblasts on embedded biomaterials sense both substrate science and mechanical improvement. Numerous studies have examined the osteoblasts' responses to mechanical stimulus and substrate chemistry alone. The effects of substrate chemistry and 12 dyn/cm2 physiological flow shear stress (FSS) on primary rat osteoblasts (ROBs), including the releases of ATP, nitric oxide (NO), and prostaglandin E2, are the focus of this investigation. The various substrate chemistries were provided by self-assembled monolayers (SAMs) on glass slides containing –OH, –CH3, and –NH2, and the physiological FSS were produced by a parallel-plate fluid flow system. The releases of ATP, NO, and PGE2 were unaffected by substrate chemistry alone. However, when ROBs were exposed to both FSS and substrate chemistry, the ATP releases of NH2 were upregulated approximately 12-fold in comparison to the ATP releases of CH3 and OH, which were also upregulated 7-fold at the peak. The releases of NO and PGE2 showed similar patterns. ATP, NO, and PGE2 were all expressed in the order NH2-FSS>Glass-FSS>CH3-FSS>OH-FSS. The optimal combination of the chemistry of the substrate and the physiological FSS was produced by ROBs on NH2. On a

variety of SAMs lacking FSS, ROBs' focal adhesion (FA) formation and F-actin organization were investigated.CH3 and OH produced the worst results, while NH2 produced the best. Releases of PGE2, NO, and/or ATP induced by FSS were significantly reduced when FAs were inhibited or F-actin was disrupted. As a result, a mechanism was proposed that the optimal substrate chemistry and 12 dyn/cm2 physiological FSS are achieved through ROBs' best F-actin organization and FA formation on NH2.The design of bioreactors for bone tissue engineering and implanted biomaterials is guided by this mechanism. All biological tissues exhibit spatial heterogeneity at the molecular scale, which is fundamentally linked to their native functions and pathology. Imaging tools that can identify the intrinsic molecular features in a sample without sacrificing high spatial resolution are necessary for probing the local chemistry of complex biological tissues. In this talk, I will talk about how we dealt with this problem of measuring the chemistry and morphology of lipid inclusions in situ. For the purpose of determining the biochemistry of lipid droplets and oil bodies with high spatial resolution in a variety of samples; we have developed nonlinear label-free microscopy and the associated analytical tools. Importantly, rather than physical chemical ratios, our method produces quantities that are physiologically relevant (chain length and saturation).I will demonstrate how we have utilized this capability to map the adaptation of lipid droplet chemical composition in white and brown adipose tissue to a diet high in fat. I will present preliminary findings from our research on the role of lipid droplets in neurological disorders. In the future, we plan to investigate a wider range of disease pathologies.